CLINICAL INVESTIGATON PLAN

WRIGHT FOOT & ANKLE POST-MARKET OBSERVATIONAL STUDY

FOOT AND ANKLE PRODUCTS

CIP Identification
Clinical Investigation Plan (CIP) Number: ***INT19-MDR-001*** *Date:* ***18-APR-2019*** *Version:* ***2***
Sponsor
Sponsor Name: ***Wright Medical*** *Address:* ***1023 Cherry Road*** *Telephone:* ***901-867-9971*** *Fax:* ***901-290-5801*** *ClinicalTrials.gov*: **NCT04118894**

Statement of Confidentiality
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PROTOCOL SIGNATURE PAGE

Wright Foot & Ankle Post-Market Observational Study

Protocol Number: INT19-MDR-001

Legal Representative of the sponsor

Name: Jennifer Seidman *Signature:* Jennifer Seidman *Date:* 18 Apr 2019
Title: Clinical Affairs Manager

Name: Jozef Murar *Signature:* *Date:* 18 APR 2019
Title: Director Clinical Affairs

Name: Leslie Fitch *Signature:* *Date:* 18-April-2019
Title: Sr. Manager, Regulatory Affairs

Investigator

I have read Protocol [Number] dated [DD-MMM-YYYY] including all appendices, and agree to conduct the Clinical Investigation in accordance with the protocol. The protocol must also be approved by the IRB and regulatory authorities as appropriate, before implementation at the site. I agree to implement the protocol only after all necessary approvals have been obtained and the sponsor has confirmed that it is acceptable to do so.

Name: *Signature:* *Date:*
Title: Principal Investigator *Site Number:*

LIST OF ACRONYM AND DEFINITIONS

AE	*Adverse event*
CI	*Clinical Investigation*
CIP	*Clinical Investigation Plan*
CV	*Curriculum Vitae*
CRF	*Case Report Form*
EC	*Ethics Committee*
EDC	*Electronic Data Capture System*
EQ-5D	*A standardized health-related quality of life instrument by the EuroQuol Group*
FAAM	*Foot and Ankle Ability Measure*
GCP	*Good Clinical Practices*
GMP	*Good Manufacturing Practice*
ICH	*International Conference on Harmonization*
ID	*Investigational Device*
IRB	*Institutional Review Board*
PI	*Principle Investigator*
PROM	*Patient Reported Outcome Measure*
REC	*Research Ethical Committee*
SAE	*Serious Adverse Event*
USAE	*Unexpected Serous Adverse Event*

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1.0 Synopsis

Sponsor	*Wright Medical*
Clinical Investigation Title	*Wright Foot & Ankle Post-Market Observational Study*
Device Name and Description	*Data will be collected only for approved or cleared Wright Medical products*
Intended Use and Indications for Use	*The Instructions for Use (IFU) for each individual product can be found at http://www.wright.com/prescribing-use-3 or can be provided at your request*
Clinical Investigation Purpose / Rational	*Collect data needed to satisfy the Medical Device Regulations (MDR)*
Clinical Investigation Design	*Global, multi-center, post-market observational study. Data will be collected at baseline, surgery, at last scheduled standard of care and/or surgeon release follow-up (FU) time point.* *Additionally, PROMs and safety may be followed yearly to sufficiently assess the safety of the product over the clinical lifetime as needed based on the current risk analysis for the product.*
Clinical Investigation Objectives	*Demonstrate the safety and performance of the Wright product by:* • *Comparing the improvements in patient-reported pain and social interaction for quality of life from pre-op through post-operatively, assessed by the EQ-5D-5L.* • *Comparing the improvement in patient-reported function scores from pre-op through post-operatively, assessed by the FAAM* • *Identifying and reporting the safety of the implant in terms of complications and adverse events.* • *Conducting a surgeon survey including radiographic assessment of fusion and consolidation time* • *Conducting patient surveys to assess current implant status (to include complications)*
Clinical Investigation Endpoints	*Patient Outcome Measures (EQ-5D and FAAM) and adverse events*
Inclusion Criteria	*Subjects to be included in the study must meet all of the following criteria:*

	• *Willing and able to consent to participate (written, informed consent);* • *Willing and able to attend/complete the requested follow-up visits;* • *Considered for treatment with one or more approved or cleared Wright Medical products included in this study*
Exclusion Criteria	*Subjects will be excluded from the study if they meet any of the following criteria:* • *Subjects determined, by the investigator, to be an inappropriate candidate for the procedure indicated;* • *Unable to consent to participate (written, informed consent);* • *Unable to attend/complete the requested follow-up visits*
Visit Schedule	*Pre-op/Op, and Last scheduled standard of care and/or surgeon release follow-up (FU) time point. Additionally, PROMS and safety may be followed yearly to sufficiently assess the safety of the product throughout the defined product clinical lifetime as needed based on the current risk analysis for the product.*
Statistical Methods	*Descriptive statistics, Kaplan Meier survival analysis and Life tables*
Duration of Clinical Investigation	*Expected enrollment is 5 years* *Based on varied definitions of product clinical lifetime, the follow-up period will be 12wks to 10 years*
Number of Sites and Subjects	*n = a minimum of 40 patients per device or until sufficient data is collected to satisfy the notified bodies* *5 to 15 sites*
Committees (e.g., safety, steering) and/or Core Labs	*none*

2.0 Background

The European Union (EU) Medical Device Regulation (MDR) 2017/83/EC is a new regulation that applies to all medical device manufactures who intend to market their products in the EU. The EU MDR has increased the requirements for clinical data needed for products to maintain certification. Under the regulation, the manufacture must proactively collect and evaluate clinical data to establish and verify:

- that under normal conditions of use, a device achieves the performance intended as specified by the manufacturer;
- the clinical benefits of a device as specified by the manufacturer;
- the clinical safety of the device;
    - Identify previously unknown side-effects;
    - Monitor the intended side-effects and contraindications;
    - Identify and analyze emerging risks on the basis of factual evidence;
- ensure the continued acceptability of the benefit / risk ratio; and
- systemic misuse or off-label use with a view to verify the intended purpose is correct.

Wright Medical is conducting this observational study to meet the new clinical data requirements for the EU MDR.

The purpose of this post-market clinical observational study is to demonstrate the safety and performance of the Wright product after implantation over standard follow-up period using patient reported outcome measures related to quality of life, pain and functional improvements, safety of the implants, as well as radiographic assessments (X-Rays).

The outcome measures collected in this study will be analyzed and reported as required for local, regional, and country requirements (i.e., regulatory authorities and notified bodies).

3.0 Identification and Description of Device

3.1 Summary description

Data will be collected only for approved or cleared Wright Medical products

3.2 Manufacturer Details

Wright Medical is the manufacturer or distributor for all devices. These products are manufactured according to International Conference on Harmonization (ICH) Good Clinical Practices (GCP) in accordance with applicable Good Manufacturing Practice (GMP) and ISO 14155:2011: through relevant manufacturing and related validation processes.

3.3 Device and Components

All products in the table below can be included in the study. Additional products may be added as they become available for this post-market study

Wright Products[1]	
VALOR	*HV Screws*
ALLOMATRIX	*Jones Fracture*
OSTEOSET	*ORTHOLOC Forefoot Fracture*
SWANSON TOES	*FUSEFORCE Staples*
PRO-TOE VO	*G-FORCE*
PRODENSE	*ORTHOLOC 3Di Ankle Fracture Plating System*
SYNCHFIX	*SALVATION Plating*
MIS BUNION	*Quick Staple*
BIOARCH	*ORTHOLOC Calc Fracture*
PHALINX	*ORTHOLOC 3Di Small Bones*
GRAVITY SUTURE ANCHORS	*ORTHOLOC 3Di Midfoot/Flatfoot*
ORTHOLOC 3Di	*CROSSCHECK 3Di*
DARTFIRE	*Biofoam Wedges*
MICA Screws	*Omnitech*
CHARLOTTE MUC Screws	*Omnievo*
SALVATION External Fixation	*CHARLOTTE SNAP OFF SCREWS*
SALVATION Beams & Bolts	*TELYA*

DARCO Headless Screws	*UNIMA*
CLAW II Plating System	*DARCO Plantar Lapidus*
DARCO Headed Screws	*ORTHOLOC 3Di Ankle Fusion Plating System*

1 Not all products are available in all geographies

3.4 Population and Indications for Use

The Instructions for Use (IFU) for each individual product can be found at http://www.wright.com/prescribing-use-3 or can be provided at your request.

3.5 Traceability

N/A

3.6 Training required

Clinical Research Sites will be identified to participate in the study based on current experience, and training in the use of the Wright Medical Products and according to ICH GCP guidelines and ISO 14155: 2011 which states; qualified by education, training and experience to perform his or her respective task(s). It is the expectation the surgeon will adhere to and follow each Wright Medical Product Surgical Technique and have knowledge of the contraindications as provided in the IFU.

3.7 Surgical procedure

Surgical Technique for each individual product can be found at http://www.wright.com/healthcare-professionals/literature-videos or can be provided at your request.

4.0 Risk/Benefit of the investigational device and clinical investigation

4.1 Potential Benefits

This is an observational study, so participation may not result in direct benefit to the subject. The use of information contained within the database may be of future benefit to subjects undergoing certain orthopedic procedures.

4.2 Potential Risks

As this is observational study, there are no foreseeable risks of physical harm associated with participation in this study, since the study involves only data collection.

4.3 Risk Minimization

As this is an observational study, there no foreseeable risks to minimize.

5.0 Objectives and endpoints

5.1 Objective

The objective is to demonstrate the safety and performance of the Wright product after implantation over standard follow-up period using patient reported outcome measures related to quality of life, pain and functional improvements, safety of the implants, as well as radiographic assessments (X-Rays)

5.2 Hypotheses

Show that Wright Products are safe and effective

5.3 Intended Use

IFU for each individual product can be found at http://www.wright.com/prescribing-use-3 or can be provided at your request.

5.4 Endpoints

The primary endpoint is to demonstrate the safety and performance of the Wright product by:

- Comparing the improvements in patient-reported pain and social interaction for quality of life from pre-op through post-operatively, assessed by the EQ-5D-5L

Secondary endpoints:

- Comparing the improvement in patient-reported function scores from pre-op through post-operatively, assessed by the Foot and Ankle Ability Measure (FAAM)
- Identifying and reporting the safety of the implant in terms of complications and adverse events.
- Conducting a surgeon survey including radiographic assessment of fusion and consolidation time
- Conducting patient surveys to assess current implant status (to include complications)

6.0 Design of the clinical investigation

6.1 Generalities

6.1.1 Clinical Investigation Design Summary

The selected design is a global, multi-center, non-randomized, prospective observational study. The study subjects included are those treated with one or more approved or cleared Wright Medical products included in this study. Wright Medical may adjust enrollment requirements or close enrollment for a certain device due to the Sponsor's needs. Sites will be notified prior to any changes.

6.1.2 Methods and Timing for Assessing, recording and Analyzing Variables

Procedures	***Pre-op/ Op***	***Final Clinical Follow-Up Visit*** *(Op to 1yr)*	***1-10 yr*** *(-/+1 yr) (yearly as necessary)*[4]	***Study Close***
Informed Consent	X			
Inclusion/Exclusion Criteria	X			
Medical History/Demographics	X			
Operative (Surgical) procedure/device	X			
EQ-5D	X	X	X	
FAAM	X	X	X	
Surgeon Survey with radiographic assessment		X		
Adverse Event Assessment	X	X	X[3]	
Patient Survey			X	
End of Study				X
Surgical Intervention[1]				
**Sponsor-approved Unscheduled Visit* [2]				

[1]&[2] These are not scheduled time point events but will be observed throughout study participation

[3] Only required when patient survey indicates an adverse event occurred

[4] Follow-up time points only executed if needed per device clinical lifetime definition

6.2 Subjects

6.2.1 Eligibility Criteria (Inclusion/Exclusion)

6.2.1.1 Inclusion Criteria

Subjects to be included in the study must meet all of the following criteria:

- Willing and able to consent to participate (written, informed consent);
- Willing and able to attend/complete the requested follow-up visits;
- Considered for treatment with one or more approved or cleared Wright Medical products included in this study.

6.2.1.2 Exclusion Criteria

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

- Subjects determined, by the investigator, to be an inappropriate candidate for the procedure indicated;
- Unable to consent to participate (written, informed consent);
- Unable to attend/complete the requested follow-up visits;

6.2.2 Criteria and Procedures for Subject Withdrawal or Discontinuation

Subjects maintain the right to discontinue their participation in the study at any point without penalty or loss of benefit to which the subject is otherwise entitled per ICH E6 4.8.10(m) guidelines. If at any time the study device is removed, the subject will be discontinued from the study unless the subject has other study devices remaining.

6.2.3 Point of enrollment

Subjects will be considered enrolled in the study when they have:
Been informed of all aspects of the study and have signed Informed Consent document

- Acknowledged the appropriate patient data release information (included in the Informed Consent document)
- Satisfied the Inclusion/Exclusion Criteria
- Implanted with an approved or cleared Wright Medical product included in this study

Investigators should document subject enrollment by completing the enrollment logs located within the site's trial master file. The Source documentation should clearly state that all inclusion and exclusion criteria have been met and the patient data release and informed consent documents have been signed and appropriately dated prior to any study related activity.

The investigative sites will be assigned three-digit a site code ***, and at enrollment the subject will be assigned a sequential subject identification number corresponding to the order the subject was enrolled (i.e. the first subject enrolled at each site will be site number *** followed by subject identifier 001). The assigned codes will be used to identify the subject on all case report forms. All investigative sites will be provided protocol training during the site initiation visits.

6.2.4 Total expected duration of the clinical investigation

The total study duration from, first patient, first visit, (FPFV) to last patient, last visit (LPLV) could potentially be up to 15 years. The sites will send the EQ5D-5L, FAAM and Patient Survey to consented and enrolled patients for completion. The site will input information into the electronic data capture (EDC) system. If survey indicates there was an adverse event associated with the Wright Medical product, the site will make every attempt to reach the subject and complete an adverse event assessment form.

6.2.5 Expected duration of each subject's participation

Based on varied definitions of product clinical lifetime, the follow-up period will be 12 weeks to 10 years

6.2.6 Number of Subjects required to be included in the CI

We will prospectively collect EQ-5D-5L for subjects enrolled in this study. Because the devices are utilized in a variety of skeletal anatomic locations within the foot and ankle, a literature search was conducted to better understand the EQ-5D outcomes for various orthopedic procedures. Hasson et al. (Hasson et al. Spine. 33(25): 2819-2830, 2008) reported on EQ-5D outcomes from various procedures, including arthrodesis of the ankle or subtalar joints. The sample size calculation is based on precision of estimate from the post-operative EQ-5D: 0.549 ± 0.313 (mean ± SD). Using the standard deviation (0.313), a sample size was calculated:

Alpha=0.05	Half width (precision) = 0.1	Standard deviation = 0.313	Side=2	n=38

Based on this calculation, a minimum sample size for each device: n = 40 or until sufficient data is collected to satisfy the notified bodies.

6.2.7 Estimated enrollment time

The enrollment period will be 5 years

6.3 Procedure

6.3.1 Clinical Investigation Summary

Overview of all the clinical investigation related procedures that subjects undergo during the clinical investigation.

6.3.2 Screening

Subjects with interest in participating in the study, after signing the informed consent document, will then be invited to participate if they meet the Inclusion Criteria.

6.3.3 Informed Consent

Prior to conducting any protocol required data collection, including evaluations and questionnaires, written informed consent must be obtained

from the subject in compliance with 21 CFR Part 50 or if required the 2005 Mental Capacity Act.

Subjects will be recruited based on interest in participating in the study. All subjects will be consented by an appropriately trained clinician or research staff using the IRB/EC/REC approved consent form in order to participate in the study and prior to any data collection, or any study procedure. The study clinician or research staff will assess whether the subject can give informed consent or not during the consent process. The potential participant must be allowed ample time to review the informed consent and should be allowed to take the time to read, review, ask questions, and receive answers as well as being fully informed of all aspects of the study before a decision is made to participate.

6.3.4 Schedule of Visits and Assessment Requirements

Subjects will be seen pre-operatively, at the operative visit and prospectively at the Final Clinical Follow-Up visit required as determined by the physician as the last standard of care visit for the procedure performed.

Additionally, PROMS and safety may be followed yearly to sufficiently assess the safety of the product over the clinical lifetime as needed based on the current risk analysis for the product.

6.3.5 Procedures and Patient Assessments

6.3.5.1 Baseline Visit

The subject will be assessed for eligibility and given time to review and sign the informed consent. Once the subject has signed the informed consent, the subject's medical history and demographic information will be collected and recorded onto the demographic case report form. The following information will be collected on these forms:

- Month and Year of birth
- Gender
- Height
- Weight
- BMI calculation
- Smoking status
- Race
- Concomitant health conditions (diabetes and other medical conditions, etc.)

The subjects will be given the patient reported outcome measures (PROM) to complete. The measures include:

- EQ-5D-5L is a generic health survey that can be used to compare improvement across different interventions and measure changes in health-related quality of life over time.
- Foot and Ankle Ability Measure (FAAM) is a PROM designed to be a comprehensive assessment of physical performance amongst individuals with a range of leg, foot and ankle disorders. Unlike many PROMs, FAAM is not a disease-specific measure but is instead region-specific

6.3.5.2 Procedure Visit

The information related to the subject's operation will be collected and recorded according to the Operative Information Case Report Forms. The following operative information related to the primary procedure will be documented on these forms:

- Indication
- Procedure
- Any previous surgery to index procedure
- Date of operation
- Site location
- Op report uploaded with patient identifiers removed
- Intraoperative complications (to be collected on the Adverse Event Case Report Form)
- Product description, product code, lot number for each Wright Product component implanted
- Any additional Wright Product (not included in the study) that was used in the procedure

6.3.5.3 Follow-up Visits

Subjects will be seen prospectively at the Final Clinical Follow-Up visit required as determined by the physician as standard of care for the procedure performed. At this visit the subject will be given the EQ-5D and the FAAM to complete. The subject will also be assessed for any adverse events. The data provided on the adverse event case report form will be queried to assess as whether they were unanticipated and for severity. These will be reported accordingly. The surgeon will be given The Surgeon Survey with Radiographic Assessment to complete at this visit. The following information will be collected from the survey:

- Imaging available
- Performance of Wright product
- Fusion/Consolidation time for applicable products

PROMs and safety may be followed yearly to sufficiently assess the safety of the product over the clinical lifetime as needed based on the current risk analysis for the product. If a subject's product meets this requirement, the subject will be followed yearly until the requirement is met. At those visits, the site will send the subject the EQ-5D and FAAM to complete as well as the Patient Survey to assess safety. The survey will collect the following data:

- Complications
- Device removal

6.3.5.4 Clinical Investigations Exit

Individual subject enrollment will be considered complete once the subject has completed all of their study visits required by the study protocol.

6.4 Clinical Investigation Monitoring

The study will be monitored by Wright Medical or its authorized representatives in accordance with the internal procedures of Wright Medical. The frequency of the visits (on-site or remote) will be determined by Wright. This may vary based on the enrollment and data collected at the sites, any compliance concerns and need for additional training and oversight.

Upon study commencement, regular on-site or remote monitoring visits will be conducted to ensure:

- ongoing compliance with the study protocol;
- ongoing compliance with any conditions of approval of the reviewing IRB/EC/REC;
- maintenance of complete study and regulatory records
- continued acceptability of the site's facilities

Source documents and Investigator site files will be reviewed during the monitoring visits, including, but is not limited to:

- reviewing electronic case report forms for accuracy and completeness;
- verifying timely and accurate data collection (in comparison with the source documentation);
- reviewing and resolving missing or inconsistent study data;
- verifying the investigational site maintains all required source documents, supporting medical records, and signed Informed Consent Documents; and
- verifying the investigational site maintains documentation and reports for any AEs

Monitors will evaluate and summarize the results of each visit in a written report that identifies any repeated data problems and providing specific recommendations for the resolution of noted deficiencies.

7.0 Statistical Considerations

7.1 Study design

This study is a global, multi-center, post-market observational study to demonstrate the safety and performance of the Wright products listed in Section 3.3. Data will be collected at baseline, surgery, at the last scheduled standard of care and/or surgeon release follow-up (FU) time point. The subjects improvement in post-surgical quality of life will be assessed using EQ-5D-5L and Foot and Ankle Ability Measure (FAAM).

An adverse event resulting from the presence or performance of the device and removal due to implant failure will determine the survivorship of the Wright product. Further, safety will be assessed by subject experience of device complication and adverse events during the study period.

All effectiveness and safety analysis will be performed separately for each Wright Medical device included in the study.

7.2 Sample Size

We will prospectively collect EQ-5D-5L for subjects enrolled in this study. Because the devices are utilized in a variety of skeletal anatomic locations within the foot and ankle, a literature search was conducted to better understand the EQ-5D outcomes for various orthopedic procedures. Hasson et al. (Hasson et al. Spine. 33(25): 2819-2830, 2008) reported on EQ-5D outcomes from various procedures, including arthrodesis of the ankle or subtalar joints. The sample size calculation is based on precision of estimate from the post-operative EQ-5D: 0.549 ± 0.313 (mean ± SD). Using the standard deviation (0.313), a sample size was calculated:

Alpha = 0.05	Half width (precision) = 0.1	Standard deviation = 0.313	Side = 2	n = 38

Based on this calculation, a minimum sample size for each device: n = 40 or until sufficient data is collected to satisfy the notified bodies.

7.3 Data Analysis

Improvements in subject quality of life after surgery will be assessed by constructing 95% confidence interval for the mean change from baseline score in EQ-5D-5L and FAMM total and component scores.

Survivorship of a Wright product will be assessed based on adverse event resulting from the presence or performance of the device. The Kaplan Meier survivorship method and life table analysis will be employed. Time to adverse event due to the presence or performance of the implant will be the survivorship endpoint for each Wright device. Also, time to reoperation to exchange or remove any part of the Wright device due to failure of the implant will also determine the Wright product survivorship. Subjects who will not experience these events will be censored at the last follow-up visit. The Kaplan Meier survival curve and the 95% Confidence Interval will be constructed.

Safety endpoints will include all adverse events (AE), serious AE (SAE), unanticipated adverse device effects (UADEs).

All subjects enrolled in the study will be assessed for safety. Adverse events and other safety evaluations will be reported as frequency and rates as appropriate, cumulative over the different follow-up schedules.

8.0 Data and Quality Management, Confidentiality, Protocol Amendment

8.1 Data Management

All information will be collected according to the protocol and defined case report forms. Investigator subject records (e.g. medical records, imaging reports, or surgical notes) will be considered source documents for the study. This information will be entered by the site through a web-based portal provided by Wright Medical. Data will be received by Wright Medical through the EDC system. The Investigator must allow Wright Medical or its representative's access to the subject files. This access includes inspection of records.

In order to facilitate potential site monitoring visits, the investigator is required to keep records, including the identity of all participating subjects, all original signed Informed Consent Documents, and source documents. These records must be retained by the investigating site according to local regulations as specified in the Clinical Trial Agreement.

If the Investigator relocates, retires, or for any reason withdraws from the study, Wright Medical should be notified ahead of time. The study records must then be transferred to an acceptable designee (another investigator, institution, or Wright Medical). The investigator must obtain Wright Medical's written permission before disposing of any records.

8.2 Confidentiality

The study team will ensure that the participants' anonymity is maintained. The participants will be identified only by study number on the electronic CRF. All documents will be stored securely and only accessible by study staff and authorized

personnel. To ensure confidentiality, none of the data stored or transferred electronically will contain personal identifiers.

8.3 Amending the Protocol

Amendments cannot be made to the study protocol without the written consent of Wright Medical. Additionally, amendments to the study protocol must be approved by the IRB/EC/REC prior to their implementation.

9.0 Deviations from the CIP

Investigators should not deviate from the study protocol except to deliver emergency care or to eliminate an immediate hazard to the subject. Deviations should be reported by completing the Protocol Deviation Case Report Form. Investigators must report all deviations from the study protocol to Wright Medical or its designated representatives. Additionally, any deviations found during monitoring visits must also be reported to Wright Medical or its designated representatives. All deviations with the potential to affect subject safety, rights, or well-being will also be reported to the IRB/EC/REC as soon as possible; based on the IRB/EC/REC requirements within the jurisdiction with each site.

10.0 Statement of Compliance

10.1 Institutional Review Board/Ethical Review Committee

It is the responsibility of the principal investigator at each participating site to obtain prospective approval of the study protocol, protocol amendments, Subject information sheets, Informed Consent documents, and any other relevant documents, if applicable, from the IRB/EC/REC. All correspondence with the IRB/EC/REC should be retained in the site's Investigator Master File. Copies of IRB/EC/REC approvals must be forwarded to Wright Medical or its designated representative prior to enrolling subjects. The Investigator must immediately report to Wright Medical or its designated representative if the IRB/EC/REC withdraws its approval of the study for any reason.

10.2 Statement of Compliance

This study will be conducted in accordance with ISO 14155: 2011-Clinical investigations, 21 CFR Part 11, 50, 54, 56, and the ethical principles originating from the Declaration of Helsinki, GCPs, and in compliance with local regulatory requirements. This study will be registered with ClinicalTrials.gov.

11.0 Adverse Events

11.1 Definitions

11.1.1 Adverse Event (AE):

An AE or adverse event is:

Adverse event means any untoward medical occurrence associated with the use of an intervention in humans, whether or not considered intervention-related

11.1.2 Serious Adverse Event (SAE)
An adverse event is serious when it:

- Led to death
- Led to serious deterioration in the health the subject, that either resulted in
    - A life threatening illness or injury, or
    - A permanent impairment of a body structure or a body function, or
    - In-patient or prolonged hospitalization, or
    - Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,
- Led to fetal distress, fetal death or congenital abnormality or birth defect.

11.1.3 Unanticipated Adverse Device Effect (UADE)
An adverse reaction that is both unexpected (not consistent with the applicable product information) and also meets the definition of a Serious Adverse Event/Reaction

11.2 Adverse Event Relatedness
The relationship of the adverse event to the study device or the implant procedure should be reported on the adverse event data collection form.

- Device Related: An adverse event that results from the presence or performance of the device.
- Procedure Related: An adverse event that occurs as a result of the implant procedure.

11.3 Adverse Event Assessment
The subjects will be assessed for adverse events at the operative visit and post-operatively. The site will be given an adverse event case report form to complete. The information collected on the assessment will include the following:

- Date of event or onset
- Procedure related
- Device related
- Narrative of adverse event
- Treatment required
- SAE
- Subject withdrawal
- Hospitalization
- Adverse event outcome

- Mode of sponsor notification
- Date of resolution

The data provided on the adverse event case report form will be queried to assess as whether they were unanticipated and for severity. These will be reported accordingly

11.4 Adverse Event Reporting

[Reference: MDR Article 80 Recording and reporting of adverse events that occur during clinical investigations.]

11.4.1 Investigators Reporting

Recording and Reporting Adverse Events - Investigator Responsibilities

- Record protocol required AE's together with an assessment as recorded in the Adverse Event Case Report Forms;
- Supply Wright Medical, upon their request, with any additional information related to the safety reporting of a particular AE;
- If subject answers in patient survey in EDC system at visits (year 1-10) that a possible AE occurred, the site will contact patient to determine if an AE occurred and if yes, complete the Adverse Event Case Report Form.
- If the subject comes back to the site after the last scheduled follow-up but prior to study completion, the site should complete an Adverse Event Case Report form if the subject has experienced an AE.

Recording and Reporting Serious Adverse Events (SAE's) – (Immediately Reportable) Investigator Responsibilities

- The investigator must report the following events to the Sponsor within 24 hours after learning of the event, regardless of relationship to study, using the appropriate SAE reporting form and guidelines;
- The investigator must report new significant follow-up information for these events to the Sponsor within 24 hours after becoming aware of the information. New significant information includes the following:
    - New signs or symptoms or a change in the diagnosis.
    - Significant new diagnostic test results.
    - Change in causality based on new information.
    - Change in the event/s outcome, including recovery.
    - Additional narrative information on clinical course of the event.

11.4.2 Sponsor Reporting

Recording and Reporting Adverse Events - Wright Medical Responsibilities

Wright Medical is responsible for the classification of AEs and ongoing safety evaluation of the study and will:

- Review the Investigator's assessment of all AEs; determine and document, in writing, the seriousness of the adverse event and relationship of the adverse event to the implanted components.

In case of a disagreement between Wright Medical and the Investigator, Wright Medical shall:

- Communicate both opinions to concerned parties; and
- As required, ensure that the IRB/EC/REC and regulatory authorities are informed of significant new information involving the product during the study
- Or seek independent review as needed.

Recording and Reporting Serious Adverse Events (SAE's) – Wright Medical Sponsor Responsibilities

- SAEs must be summarized on the annual report to the IRB/EC/REC

Recording and Reporting Unanticipated Adverse Device Effect (UADE)– Wright Medical Sponsor Responsibilities

- UADEs must be reported to the IRB/EC/REC in accordance with GCP guidelines i.e. 7 or 15 day

12.0 Planned Clinical Investigation Closure, Early Termination of Clinical Investigation or Clinical Investigation Suspension

12.1 Planned Clinical Investigation Closure

The study will be considered complete once the last subject at the last active site has completed their study visits required by the study protocol. Additionally, the following activities must be completed at each site before the study is considered complete:

- All essential documents are complete and up to date;
- The Investigator has completed and submitted all required case report forms; and
- Arrangements are made for archiving and record retention.

All IRB's/EC/REC's have been notified of the conclusion of the study

12.2 Early Termination or Suspension

Wright Medical reserves the right to discontinue the study at any time and will notify each investigator immediately at the time of such a decision. Formal documentation will be provided to the investigators to notify their IRB/EC/REC, research institutions. After such a decision, the Investigator must contact all participating subjects to notify them of this decision and its impact on their follow-up.

12.3 Criteria and arrangements for suspension or premature termination of the whole CI or of the CI in one or more site(s).
Wright Medical reserves the right to terminate a non-performing site. Reasons for considering early termination or suspension of an individual site may include, but are not limited to:

- Site non-compliance with study protocol or failure to comply with government or local regulations;
- Failure to submit data in a timely manner;
- Failure to comply with or act upon findings; and
- Failure to maintain pace to complete enrollment.

13.0 Publication Policy

There isn't a plan to submit the data for publication

14.0 Bibliography

21 CFR Part 11:
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=11&showFR=1

21 CFR Part 50:
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=50&showFR=1

21 CFR Part 54:
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=54&showFR=1

21 CFR Part 56:
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=56&showFR=1

EQ-5D-5L Questionnaire; EQ-5D™ is a trade mark of the EuroQol Research Foundation.

EU Regulation 2017/745, also known as the EU Medical Device Regulation (EU MDR)
https://publications.europa.eu/en/publication-detail/-/publication/83bdc18f-315d-11e7-9412-01aa75ed71a1/language-en/format-PDF/source-58036705

GCP Guidelines:
https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R1_Guideline.pdf

Hansson T, Hansson E, Malchau H. A comparison of common elective orthopaedic surgical procedures. *SPINE* 2008; 33; 25; 2819-2830.

ICH E6 4.8.10(m): https://ichgcp.net/48-informed-consent-of-trial-subjects/

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Maher A, Kilmartin, T. An analysis of Euroqol EQ5D and Manchester Oxford Foot Questionnaire. *Journal of Foot and Ankle Research* 2012; 5; 7

Martin RL, Irrgang JJ, Burdett RG. Evidence of Validity for the Foot and Ankle Ability Measure (FAAM). Foot & Ankle International 2005; 26; 11; 968-983