PMCF Study on PEEK Suture Anchors for Hip Indications

Protocol Number:	2018.14.SMD.PEEK.RET.HIP
Protocol Version:	Version 2.0
Date:	03 April 19
Study Product Names:	PEEK Hip Suture Anchors Bioraptor Knotless Suture Anchor SpeedLock Hip Suture Anchor
Sponsor:	Smith & Nephew Orthopaedics 7135 Goodlett Farms Parkway Cordova, TN 38016

1. SIGNATURES

1.1 PROTOCOL SIGNATURE PAGE

This page will be returned to Smith & Nephew Inc. and a copy retained at the investigational site.

I have read the attached protocol entitled "PMCF Study on PEEK Suture Anchors for Hip Indications", version 2.0, dated 03April2019, and agree to abide by all provisions set forth herein.
I agree to comply with the Investigator's Obligations stipulated in Section 26.1 of the protocol,
I agree to ensure that the confidential information contained in this document will not be used for any purpose other than the conduct of the described clinical investigation without the prior written consent of Smith & Nephew, Inc.

Role	Name	Signature*	Date Signed* (DD-MMM-YYYY)
Principal Investigator			

2. REVISION HISTORY, OWNERSHIP, AND APPROVALS:

2.1 REVISION HISTORY

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Version	Page	Item	Original	New	Reason
1.0	N/A	N/A	Initial Protocol	Revision 2.0	N/A
2.0	2	Protocol Signature Page	1.0 12Sep18	2.0 03April19	Administrative
2.0	3	Revision History	Initial	Protocol Amendment 2	Administrative
2.0	19	Signatures	Sponsor Signatures	Removed duplicate sponsor signature lines	Administrative
2.0	20, 32	Part Numbers	N/A	Added: Part numbers as of September 2018	Administrative
2.0	20	Min/Max	Minimum, n=40 Maximum, n=80	Minimum number of subjects, n=40 Maximum number of subjects, n=240	Administrative/Clarification
2.0	20	Enrollment Distribution	N/A	Enrollment distribution: Up to three sites will enroll a maximum of 40 subjects per anchor configuration; therefore, no more than 120 subjects will be enrolled for any anchor type.	Rationale for enrollment distribution among sites and between anchors.
2.0	21	Sample Size	**PEEK Anchor** / **Minimum** / **Maximum** Bioraptor Knotless Suture Anchor / 20 / 40	**PEEK Anchor** / **Minimum Number of Subjects/Site** / **Maximum Number of Subjects/Site** / **Maximum Number of Subjects**	Administrative/Clarification

Version	Page	Item	Original	New	Reason
			SpeedLock Hip: 20 / 40	Bioraptor Knotless Suture Anchor: 20 subjects per site / 40 subjects per site / 120 subjects SpeedLock Hip: 20 subjects per site / 40 subjects per site / 120 subjects Total: 40 subjects / 80 subjects / 240 subjects **for the Study**	
2.0	21	Inclusion Criteria	1. Subjects who have undergone shoulder joint repair using the study devices. 2. Subjects aged 18 years and older at the time of surgery.	1. Subjects who have undergone shoulder joint repair using the study devices. 2. Subjects aged 18 years and older at the time of surgery. 3. Subjects must have had a visit to their provider between 3 and 15 months post-operative.	Clarification
2.0	21	Exclusion Criteria	1. Subjects who are < 12 months post-operative. 2. Subject is entered in another investigational drug, biologic, or device study or has been treated with an investigational	1. Subjects who are < 12 months post-operative. 2. Subject is entered in another investigational drug, biologic, or device study or has been treated with an investigational product within 30 days prior to surgery.	Clarification

Version	Page	Item	Original	New	Reason
			product within 30 days prior to surgery.	3. Subject had off-label use of the PEEK suture anchor during surgery.	
2.0	21, 37	Primary Endpoint	Clinical success rate (%) at 6 months post-operative.	Clinical success rate (%) at 6 months post-operative based on standard of care.	Clarification
2.0	21, 37	Secondary Endpoint	Clinical success rate (%) at 12 months post-operative.	Clinical success rate (%) at 12 months post-operative based on standard of care.	Clarification
2.0	23	SOE/ICF	NA if waiver of consent approved by IRB	NA if waiver of consent granted by IRB	Clarification
2.0	23	SOE/Footnote	NA	[2] End of Study CRF can be completed at 6 months if the subject did not have a 12-month visit.	Clarification
2.0	27	List of Abbreviations	BMI PHI PROs	Removed. Not applicable.	Administrative
2.0	Throughout	Minor formatting corrections	—	—	Administrative
2.0	30	IFUs	**PEEK Suture Anchor** | **IFU**	**PEEK Suture Anchor** | **IFU**	Administrative

Version	Page	Item	Original	New	Reason
			Bioraptor Knotless Suture Anchor — 10600479 2/17, Rev E SpeedLock — P/N 62513 March 2017, Rev B	Bioraptor Knotless Suture Anchor — 10600479 2/17, Rev E SpeedLock Hip Suture Anchor — P/N 62513 March 2017, Rev B	
2.0	30	IFU	N/A	Instructions for Use document numbers have been provided as a reference but may not have been the version used at the time of surgery.	Clarification
2.0	33	Subject Population	Enrollment will be in sequential order based on the date of their surgical procedure with the investigational device, i.e. earliest to latest.	Enrollment will be in sequential order based on the date of their surgical procedure with the investigational device, i.e. time of surgery to present day.	Clarification
2.0	33	Inclusion Criteria	1. Subjects who have undergone shoulder joint repair using the study devices. 2. Subjects aged 18 years and older at the time of surgery.	1. Subjects who have undergone shoulder joint repair using the study devices. 2. Subjects aged 18 years and older at the time of surgery. 3. Subjects must have had a visit to their provider between 3 and 15 months post-operative.	Clarification
2.0	34	Exclusion Criteria	1. Subjects who are < 12 months post-operative. 2. Subject is entered in another investigational drug, biologic,	1. Subjects who are < 12 months post-operative. 2. Subject is entered in another investigational drug, biologic, or device study or has been treated with	Clarification

Version	Page	Item	Original	New	Reason
			or device study or has been treated with an investigational product within 30 days prior to surgery.	an investigational product within 30 days prior to surgery. 3. Subject had off-label use of the PEEK suture anchor during surgery.	
2.0	35	LTFU	A subject will be considered lost to follow-up if he/she did not return for follow-up per the study doctor's standard of care.	N/A	Removed, as it is not applicable to this study.
2.0	36	Study Design	This is a retrospective, open-label, multicenter study to collect clinical data that will evaluate post-market safety and performance of the PEEK suture anchors in the hip. A minimum of 40 subjects and maximum of 80 subjects in the United States who underwent surgery in the hip using the Smith & Nephew PEEK anchor sutures are planned to be enrolled into the study	This is a retrospective, open-label, multicenter study to collect clinical data that will evaluate post-market safety and performance of the PEEK suture anchors in the hip. A minimum of 40 subjects and a maximum of 240 subjects in the United States who underwent surgery in the hip using the Smith & Nephew PEEK suture anchors are planned to be enrolled into the study after the fulfilment of all inclusion and exclusion criteria. Up to three sites will enroll a minimum of 20 subjects and a maximum of 40 subjects per anchor	Clarification

Version	Page	Item	Original	New	Reason
			after the fulfillment of all inclusion and exclusion criteria. ~~It is also planned that each investigational site would enroll a minimum of 6 subjects.~~	configuration; therefore, not more than 120 subjects will be enrolled for any anchor type.	
2.0	37	Secondary Endpoint	The secondary endpoint will be clinical success rate (%) at 12 months post-operative based on standard of care. Clinical success has previously been defined.	The secondary endpoint will be clinical success rate (%) at 12 months post-operative based on standard of care. Clinical success has previously been defined. It is expected that per physician's standard of care, 12-month clinical data may not be available for all subjects.	Clarification
2.0	39	Concomitant Medications and Therapies	Any concomitant medications associated with an AE, SAE or SADE will be recorded.	Any concomitant medications associated with an AE, SAE or SADE will be recorded. Concomitant medications will be recorded from the time of surgery through 12 months. If the subject's final visit occurred at 6 months, concomitant medications will be collect through 6 months.	Clarification

Version	Page	Item	Original	New	Reason
2.0	39	General	Smith & Nephew's Global Biostatistics group will conduct the statistical analysis for this study. Unless otherwise stated, all significance tests will be two-sided, performed at the 5% significance level.	Smith & Nephew's Global Biostatistics group or designee will conduct the statistical analysis for this study. Unless otherwise stated, all significance tests will be two-sided, performed at the 5% significance level.	Clarification
2.0	39	General	Resulting p-values will be quoted and 95% two-sided confidence intervals will be generated where appropriate.	Resulting p-values will be provided and 95% two-sided confidence intervals will be generated where appropriate.	Clarification
2.0	41	Safety Analysis	A listing of concomitant medications will be provided by subject for AEs,	A listing of concomitant medications will be provided by subject.	Clarification
2.0	42	Other Endpoint Analysis	The derivation of surgeon reported outcomes used in summarizing this data for the study will be described in the SAP and will be summarized as	The derivation of surgeon reported outcomes used in summarizing this data for the study will be described in the SAP and will be summarized as appropriate using descriptive	Clarification

Version	Page	Item	Original	New	Reason
			appropriate using descriptive summary characteristics for continuous or categorical endpoints. ~~Differences from screening/baseline to 6 months and 12 months will be similarly summarized and/or compared.~~	summary characteristics for continuous or categorical endpoints at 6 months and 12 months.	
2.0	42	Sample Size Justification	With an assumption of a 91% clinical success rate to be obtained in each of the PEEK anchor sutures and a corresponding 95% CI between 80% and 100%, enrolling between 20 and 40 subjects for each PEEK anchor suture's precision analysis would provide between 15.2% to 71% probability. Thus, an overall minimum of 40 and maximum of 80 subjects who had previously undergone surgery	With an assumption of a 91% clinical success rate to be obtained in each of the PEEK anchor sutures and a corresponding 95% CI between 80% and 100%, enrolling between 20 and 120 subjects for each PEEK anchor suture's precision analysis will provide between 15.2% to 95% probability. Thus, an overall minimum of 40 and maximum of 240 subjects who had previously undergone surgery of the hip using PEEK anchor sutures will be enrolled into the study. Additionally, a minimum of 20 subjects will be enrolled at any investigational site.	Clarification

Version	Page	Item	Original	New	Reason
			of the hip using PEEK anchor sutures would be enrolled into the study. Additionally, a minimum of 6 subjects would be enrolled at any investigational site.		
2.0	43	AE Definitions	All adverse events will be captured.	All adverse events will be captured from the time of surgery through the 12 month follow-up visit.	Clarification
2.0	47	Reporting Procedures	AE of any kind and DevD will be recorded in the applicable CRF and source notes. The Investigator will evaluate all AE for relationship to the device and procedure, if applicable, seriousness, and severity. ADE, SAE, and DevD will be entered into the CRF and reported to the Sponsor within 24 hours of the investigator being	AE of any kind and DevD will be recorded in the applicable CRF and source notes. The Investigator will evaluate all AE for relationship to the device and procedure, if applicable, seriousness, and severity. ADE, SAE, and DevD will be entered into the CRF and reported to the Sponsor within 24 hours of the investigator being informed about the event (Figure 1). Applicable to the retrospective study design, 24 hour reporting begins at the time the Investigator was informed of the event under the auspice of the clinical study.	Clarification implemented as it is applicable for a retrospective study.

Version	Page	Item	Original	New	Reason
			informed about the event (Figure 1). For ADE and DevD, details of the product/procedure related to the event will be included and where applicable, pictures taken of the device. The deficient product should be retained for return to S&N unless it is contaminated (e.g. used dressings must not be retained). ~~Updates to submitted information will be recorded in the CRF within 24 hours of the information being available to the investigator.~~	For ADE and DevD, details of the product/procedure related to the event will be included and where applicable and available, pictures taken of the device. If available, the deficient product should be retained for return to S&N unless it is contaminated (e.g. used dressings must not be retained).	
2.0	N/A	Follow-up of Subjects with Adverse Events	For subjects who are experiencing ongoing unresolved AE at the time of their study completion or early discontinuation from the study, it is recommended that the Investigator	Removed	Clarification implemented as it is applicable for a retrospective study

Version	Page	Item	Original	New	Reason
			schedule an appropriate follow-up visit in order to determine the outcome of the event. Any additional data must be documented and available to the Sponsor who will determine whether the data need to be documented within the CRF/Clinical Study Report.		
2.0	N/A	Ongoing Adverse Events at Study Discontinuation	Adverse events which are related to a study procedure or S&N IP and are ongoing at end of subject's participation: The event should be followed until it is either resolved or until the event has become chronic and is not expected to further improve based on Investigator's review of the event.	Removed	Clarification implemented as it is applicable for a retrospective study

Version	Page	Item	Original	New	Reason
			Adverse events which are not related to a study procedure or S&N IP and are ongoing at end of subject's participation should be followed for 30 days after discontinuation or if the AE is resolved, whichever is sooner. At the time of data analysis (e.g. interim or final), an evaluation of ongoing events should take place and be listed as ongoing in the safety table.		
	49	Investigator Obligations (Financial Disclosure)	In addition, the PI will ensure that the Financial Disclosure Statements will be completed by the PI and the Sub-Investigator upon entry into the study and as any changes that affect their financial disclosure status occur during	Removed	Clarification- Financial disclosures is not applicable.

Version	Page	Item	Original	New	Reason
			the course of the study and up to one year after study completion.		
	49	Sponsor and Monitor Obligations	The Sponsor will designate a monitor to conduct regular monitoring visits. The purpose of these visits are to ~~ensure the wellbeing of the subjects are protected~~ and that data is accurate, complete and verifiable from source documents.	The Sponsor will designate a monitor to conduct regular monitoring visits. The purpose of these visits are to ensure that data is accurate, complete and verifiable from source documents.	Clarification implemented as it is applicable for a retrospective study
	50	End of Study	The end of study is defined as the date of the last subject, last visit (LSLV). No additional care for subjects will be provided under the protocol ~~will be provided once their participation in the study has ended.~~ Should circumstances arise which require the termination of the entire	The end of study is defined as the date of the last subject, last visit (LSLV). No additional care for subjects will be provided under the protocol as this is a retrospective study. Should circumstances arise which require the termination of the entire study prior to its planned completion (e.g. safety concerns) or circumstances arise which mean the end of the participation of an individual site (e.g. departure of	Clarification implemented as it is applicable for a retrospective study.

Version	Page	Item	Original	New	Reason
			study prior to its planned completion (e.g. safety concerns) or circumstances arise which mean the end of the participation of an individual site (e.g. departure of Investigator, non-compliance), then this will be undertaken according to the SOPs of the Sponsor. ~~All reasonable efforts should be made to retain the subjects for the 12-month post-operative follow-up of this study. A study termination CRF needs to be completed for any subject that does not complete the study, to document the reason for termination.~~	Investigator, non-compliance), then this will be undertaken according to the SOPs of the Sponsor.	

Version	Page	Item	Original	New	Reason
	50	Revision of the Study Device	If a subject has bilateral implants and has a revision, ~~the subject will be maintained in the study and both implants will continue to be followed per the protocol visit schedule~~	If a subject has bilateral implants and has a revision, both implants will continue to be followed per the protocol visit schedule.	Clarification implemented as it is applicable for a retrospective study.

3. SPONSOR APPROVAL

	Job title	DocuSign Stamp
Sr. Vice President, Chief Medical Officer, Global R&D	Weymann, Andy	DocuSigned by: Signer Name: Andy Weymann Signing Reason: I approve this document Signing Time: 08-Apr-2019 | 16:52 BST 675C45EC25704A5FB20A08674419D6D8
Head of Global Clinical Strategy	Hanson, Beate	DocuSigned by: Beate Hanson Signer Name: Beate Hanson Signing Reason: I approve this document Signing Time: 08-Apr-2019 | 16:06 BST A491AB16277146CA9C8B8366F1B6BEA5
Head of Global Biostatistics and Data Management	Rossington, Alan	DocuSigned by: Alan Rossington Signer Name: Alan Rossington Signing Reason: I approve this document Signing Time: 04-Apr-2019 | 20:26 BST 556E7DBFCA8A4287A7EE3EE9B5B3ABFD
Medical Affairs Representative	Orlandini, Luca	DocuSigned by: Signer Name: Luca Orlandini Signing Reason: I approve this document Signing Time: 05-Apr-2019 | 17:26 BST FC872951AC1C4261B85EC7A7CD09ACDC

4. SYNOPSIS

Title of Study:	PMCF Study on PEEK Suture Anchors for Hip Indications
Study Design:	Multi-center, retrospective case series.
Study Type:	Post-market Clinical Follow-up
Study Products:	*PEEK Suture Anchors for Hip* **Part numbers as of September 2018* Bioraptor Knotless Suture Anchor — 72202397 SpeedLock Hip Suture Anchor — OM-7500
Intended Use:	The PEEK anchors are intended to be used for soft tissue to bone fixation in the hip following hip capsule repair.
Study Purpose:	Assess safety and performance post-market of the PEEK suture anchor devices to address clinical data gaps for MDR.
Primary Outcome:	Evidence of safety and performance of the PEEK suture anchor devices in the hip.
Statistical Rationale:	The sample size for this study is determined based on the feasibility of recruitment, enrolment and follow-up considerations. The study is therefore not powered for any statistical hypothesis testing but will be able to estimate a clinical success rate of 91% with a 95% confidence interval (CI) of 80% to 100%.
Sample Size:	Minimum number of subjects, n=40 Maximum number of subjects, n=240 Enrollment distribution: Up to three sites will enroll a maximum of 40 subjects per anchor configuration therefore no more than 120 subjects will be enrolled for any anchor type.

	PEEK Anchor	**Minimum Number of Subjects/Site**	**Maximum Number of Subjects/Site**	**Maximum Number of Subjects for the Study**
	Bioraptor Knotless Suture Anchor	20 subjects per site	40 subjects per site	120 subjects
	SpeedLock Hip	20 subjects per site	40subjects per site	120 subjects
	Total	40 subjects	80 subjects	240 subjects
Number of Study Sites:	Up to 6 sites			
Targeted Global Regions:	USA			
Inclusion Criteria:	1. Subjects who have undergone hip joint repair using the study devices. 2. Subjects aged 18 years and older at the time of surgery. 3. Subjects must have had a visit to their provider between 6 and 15 months post-operative.			
Exclusion Criteria:	1. Subjects who are < 12 months post-operative. 2. Subject is entered in another investigational drug, biologic, or device study or has been treated with an investigational product within 30 days prior to surgery. 3. Subject had off-label use of the PEEK suture anchor during surgery.			
Study Duration:	Twelve month follow-up			
Primary Endpoint:	Clinical success rate (%) at 6 months post-operative based on standard of care			
Secondary Endpoint:	Clinical success rate (%) at 12 months post-operative based on standard of care			
Exploratory Outcomes:	Surgeon Reported Outcomes based on data collected on the subject's medical chart as standard of care at study sites. These may include but not restricted to the following:			

	• Range of Motion (ROM)
	  • Flexion
	  • Extension
	  • Abduction
	  • Adduction
	  • External/Internal Rotation
	• Pain assessed by VAS

Safety Endpoints:	• All AEs, SAEs and complications including intra-operative adverse events and complications. • Device related intervention • Device deficiency

5. SCHEDULE OF EVENTS

Table 1: Schedule of Events

Schedule of Events	Chart Review	
	182 days post-op **6M (±91 Days)**	**365 days post-op** **12M (± 91 Days)**
Informed Consent	X NA if waiver of consent granted by IRB	
Inclusion/Exclusion	X	
Demographics/Medical History	X	
VAS, ROM	X	X
Operative Data Collection	X	
Implant Status and / or Disposition	X	X
Concomitant Medications or Therapies[1]	X	X
AE, SAE and DevD Assessment	X	X
End of Study		X[2]

[1] Any concomitant medications associated with an AE, SA(D)E will be recorded.

[2] End of Study CRF can be completed at 6 months if the subject did not have a 12-month visit.

6. TABLE OF CONTENTS

TABLES

FIGURES

7. LIST OF ABBREVIATIONS

Abbreviation	Term
ABHI	Association of British Healthcare Industries
ABS	Acrylonitrile Butadiene Styrene
ADE	Adverse Device Effect(s)
AE	Adverse Event(s)
ASADE	Anticipated Serious Adverse Device Effect
CFR	Code of Federal Regulations
CI	Confidence Interval
CRF	Case Report Form(s)
CSR	Clinical Study Report
CTA	Clinical Trial Agreement
CV	Curriculum Vitae
DevD	Device Deficiency(ies)
GCP	Good Clinical Practice
HHS	Health and Human Services
ICH	International Conference on Harmonisation
ICMJE	International Committee of Medical Journal Editors
IEC	International Ethics Committee
IFU	Instructions for Use
IP	Investigational Product
IRB	Institutional Review Board
ISF	Investigator Site File
ISO	International Organization for Standardization
LSLV	Last subject, last visit

Abbreviation	Term
MDR	Medical Device Regulation
N (or n)	Total Sample Size (or subgroup sample size)
NA or N/A	Not Applicable
PEEK / PK	Polyetheretherketone
PI	Principal Investigator
PMCF	Post-market Clinical Follow-up
PP	Per-protocol Population
ROM	Range of Motion
S&N	Smith & Nephew Inc.
SADE	Serious Adverse Device Effect(s)
SAE	Serious Adverse Event(s)
SAF	Safety Population
SAP	Statistical Analysis Plan
USADE	Unanticipated Serious Adverse Device Effect(s)
VAS	Visual Analogue Scale

8. INTRODUCTION

Suture anchors are small fixation devices used in surgical procedures for attaching or reattaching tendons and ligaments to bone. The size and type of anchor used depends on the patient's bone density and the procedure performed.

Suture anchors are made of three components: the anchor which is inserted into the bone; the eyelet – which is a hole or a loop in the anchor that the suture passes through to link the anchor to the suture; and the suture – which is attached to the anchor through the eyelet of the anchor. An anchor- receiving hole is first drilled in the bone at the desired point of tissue reattachment. A suture anchor is deployed in the hole using an appropriate installation tool. This effectively locks the suture to the bone, with the free end(s) of the suture extending out the bone. Soft tissue is then moved into position over the hole containing the deployed suture anchor. As this is done, the free end(s) of the suture is (are) passed through or around the soft tissue so that the free end(s) of the suture reside(s) on the far (i.e., non-bone) side of the soft tissue. The suture is now used to tie the soft tissue securely to the bone.

Smith & Nephew offers a variety of suture anchors including several polyetheretherketone (PEEK) suture anchors soft tissue to bone repair. The PEEK devices included in study are all single use, sterile devices comprised of machined component anchor bodies that are manufactured from PEEK-OPTIMA Polymer (LT1). This material meets ISO 10993 biocompatibility requirements for implant devices, bone/tissue contact and permanent contact. The anchor tips are molded components which are also manufactured from PEEK-OPTIMA Polymer (LT3). PEEK-OPTIMA polymers provide an ideal combination of strength, biocompatibility, reviseability and inherent radiolucent characteristics. Smith & Nephew also provides a variety of reusable and disposable

instrumentation used in conjunction with the suture anchors including awls, dilators, drills, guides, obturators and wires.

8.1 Study Purpose

The purpose of this study is to conduct post-market clinical follow-up regarding the safety and performance of the PEEK anchors as required per MDR.

8.2 Safety Considerations

Refer to the IFUs.

Table 2: Instructions for Use Reference Numbers

Instructions for use document numbers have been provided as a reference but may not have been the version used at the time of surgery.

PEEK Suture Anchor	IFU
Bioraptor Knotless Suture Anchor	10600479 2/17, Rev E
SpeedLock Hip Suture Anchor	P/N 62513 March 2017, Rev B

9. OBJECTIVE

9.1 Primary Objective

The primary objective of this study is to assess safety and performance post-market of the PEEK anchor devices in the hip.

10. STUDY PRODUCT(S)

10.1 BIORAPTOR® KNOTLESS SUTURE ANCHOR

The BIORAPTOR® Knotless Suture Anchor is a single use, sterile, tap-in anchor that is manufactured from PEEK-OPTIMA® from Invibio®. The anchor is pre-assembled on an inserter comprised of a stainless steel shaft and an ABS and polycarbonate handle. The anchor is sized appropriately to facilitate both hip and shoulder procedures. The design consists of an outer anchor body and an inner shaft plug. The ribbed anchor, loaded with suture tails, is tapped into a pre-drilled prepared hole. The surgeon is now able to reapproximate the tissue to the appropriate tension and then use the torque-limiting knob on the insertion device that moves the inner plug down to lock the plug and achieve a secure fixation.

10.2 SpeedLock Hip Suture Anchor

The SpeedLock Knotless Fixation Device is an implant that facilitates the attachment of tissue to bone. The SpeedLock system consists of a fixation device pre-loaded with a suture snare in an inserter handle. The SpeedLock implant is a knotless fixation device, in other words surgical knots are not necessary for fixation of suture to tissue.

10.3 Indications

The Smith & Nephew PEEK anchors are intended to be used for soft tissue to bone fixation in the hip following hip capsule repair.

Table 3: Part Numbers

Peek Suture Anchors for the Hip

**Part numbers as of September 2018*

Bioraptor Knotless Suture Anchor	72202397
SpeedLock Hip Suture Anchor	OM-7500

10.4 PRODUCT USE

All study related procedures using the PEEK suture anchors in the hip have been performed according to the recommended surgical technique described in the labelling and the instructions for use.

11. SUBJECT ENROLLMENT AND WITHDRAWAL

Investigators will screen all subjects that have undergone usage of the PEEK suture anchors in the hip using only the existing information in the medical records.

Investigators will conduct a chart review after IRB approval has been granted. All subjects whose chart undergoes the screening process will be documented on a Screening and Enrollment Log, with the reason for exclusion noted, if applicable. The Investigator or designee must notify the Sponsor upon subject enrollment.

11.1 SUBJECT POPULATION

To minimize the potential for selection bias, Investigators will screen and subsequently enroll subjects (after fulfilling all inclusion and exclusion criteria) on whom PEEK suture anchors in the hip were implanted. Enrollment will be in sequential order based on the date of their surgical procedure with the investigational device, i.e. time of surgery to present day.

11.2 INCLUSION CRITERIA

Subjects will be considered qualified for enrollment if they meet the following criteria:

1. Subjects who have undergone hip joint repair using the study devices.
2. Subjects aged 18 years and older at the time of surgery.

3. Subjects must have had a visit to their provider between 3 and 15 months post-operative.

11.3 Exclusion Criteria

Any one (1) of the following criteria will disqualify a potential subject from participation in the study:

1. Subjects who are < 12 months post-operative.
2. Subject is entered in another investigational drug, biologic, or device study or has been treated with an investigational product within 30 days prior to surgery.
3. Subject had off-label use of the PEEK suture anchor during surgery.

11.4 Screening

Participating study sites are required to document all screened subjects considered for inclusion in this study. If a subject is excluded from the study, the reasons for exclusion will be documented in the subject's source documents and noted on the Screening and Enrollment Log.

11.5 Informed Consent

For adults and children, a waiver or alteration of the requirements for obtaining informed consent can occur under any of the following three provisions set forth by HHS:
Research in general: an IRB may waive or alter the requirement of informed consent under 45 CFR 46.116(d), provided that the IRB finds and documents that all of the following four conditions are met: [3]

1. the research involves no more than minimal risk to the participants;
2. the waiver or alteration will not adversely affect the rights and welfare of the participants;

3. the research could not practicably be carried out without the waiver or alteration; and
4. whenever appropriate, the participants will be provided with additional pertinent information after participation.

11.6 Enrollment

Enrollment in this study shall occur when subjects have meet inclusion criteria and none of the exclusion criteria. When a subject is enrolled for the left hip as well as the right hip, only one subject ID will be allocated.

11.7 Lost to Follow-Up

Not applicable.

11.8 Withdrawal

11.8.1 Withdrawal from the Study

The Investigator may withdraw subjects from the study for many reasons, including but not limited to the following:

- At the discretion of the Investigator.
- If the Investigator or the Sponsor stops the study for any reason and decides to withdraw subject(s) from the study.

For each case, information will be documented in the source document and the Case Report Form (CRF), detailing circumstances leading to the withdrawal.

Subjects who are withdrawn will not be re-entered into the study at a later date. Data collected up to the point of withdrawal may be used but no additional data for that subject may be collected.

12. STUDY DESIGN

12.1 STUDY DESIGN

This is a retrospective, open-label, multi-center study to collect clinical data that will evaluate post-market safety and performance of the PEEK suture anchors in the hip. A minimum of 40 subjects and a maximum of 240 subjects in the United States who underwent surgery in the hip using the Smith & Nephew PEEK suture anchors are planned to be enrolled into the study after the fulfilment of all inclusion and exclusion criteria. Up to three sites will enroll a minimum of 20 subjects and a maximum of 40 subjects per anchor configuration; therefore, not more than 120 subjects will be enrolled for any anchor type.

Data obtained from enrolled eligible subjects will subsequently be recorded on case report forms.

Table 4: Enrollment

PEEK Anchor	Minimum Number of Subjects/Site	Maximum Number of Subjects/Site	Maximum Number of Subjects for the Study
Bioraptor Knotless Suture Anchor	20 subjects per site	40 per site	120 subjects
SpeedLock Hip	20 subjects per site	40 per site	120 subjects
Total	*40 subjects*	*80 subjects*	*240 subjects*

12.2 ALLOCATION AND BLINDING

This study is not randomized or blinded.

12.3 STUDY ENDPOINTS

12.3.1 Primary Endpoint

The primary endpoint will be clinical success rate (%) at 6 months post-operative based on standard of care. Clinical success is defined as hip repairs without signs of device failure and/or re-intervention as assessed by the surgeon.

12.3.2 Secondary Endpoints

The secondary endpoint will be clinical success rate (%) at 12 months post-operative based on standard of care. Clinical success has previously been defined. It is expected that per physician's standard of care, 12 month clinical data will be consistently be available.

12.3.3 Safety Endpoints

Safety endpoints will include but not restricted to the following events:

- All adverse events, SAEs and complications occurring from the time of enrollment until study termination or study completion including intra-operative adverse events and complications.
- Device related intervention.
- Device deficiency.

12.3.4 Other Endpoints

Surgeon Reported Outcomes would constitute other endpoints and may include but not restricted to the following:

- Range of Motion (ROM)
  - Flexion
  - Extension

- Abduction
- Adduction
- External/Internal Rotation

- Pain assessed by VAS

13. STUDY PROCEDURES

13.1 6 MONTHS POST-OP CHART REVIEW

NOTE: Any subject, who meets the inclusion/exclusion criteria, will be assigned a subject number.

1. Subject should undergo the informed consent process and sign the informed consent *only* if a waiver of consent has not been approved by the IRB.
2. Screen the subject's chart for protocol inclusion/exclusion criteria.
3. Obtain demographic information and a medical history.
4. VAS, ROM.
5. Operative Data Collection – review operative case notes.
6. Implant Status / Disposition.
7. Document concomitant medications and/or therapies associated with an AE, SA(D)E
8. Review the subject's chart for AEs, SAEs and Device Deficiencies, including inter-operative. AEs, SAEs and DevDs should be documented from the time of surgery through the study duration.

13.2 12 MONTHS POST-OP CHART REVIEW

1. VAS, ROM
2. Implant Status/Disposition
3. Document concomitant medications and/or therapies associated with an AE, SA(D)E
4. Review the subject's chart for AEs, SAEs and Device Deficiencies including inter-operative. AEs, SAEs and DevDs should be documented from the time of surgery through the study duration.
5. Complete the End of Study CRF.

13.3 CONCOMITANT MEDICATIONS AND THERAPIES

Any concomitant medications associated with an AE, SAE or SADE will be recorded. Concomitant medications will be recorded from the time of surgery through 12 months. If the subject's final visit occurred at 6 months, concomitant medications will be collect through 6 months.

14. STATISTICAL DESIGN

A Statistical Analysis Plan (SAP) will be written and finalized prior to database lock. The analyses specified in the protocol will be a microcosm of the detailed analyses to be contained in the SAP. If there are changes to or additional analyses required to the analysis described below, it will be described in the SAP and the Clinical Study Report (CSR).

14.1 GENERAL

Smith & Nephew's Global Biostatistics group or designee will conduct the statistical analysis for this study. Unless otherwise stated, all significance tests will be two-sided, performed at the 5%

significance level. Resulting p-values will be provided and 95% two-sided confidence intervals will be generated where appropriate.

Where data summaries are specified, categorical and ordinal variables will be summarized with frequencies and percentages. Continuous variables will be summarized with the following summary statistics: number of observations, mean, median, standard deviation, minimum and maximum values. All analyses will be performed in SAS version 9.3 (or later).

14.2 Analysis Populations

The following analysis populations will be used for this study:

- **Safety Population (SAF):** This includes all subjects who enroll in the study who had previously undergone hip repair using PEEK suture anchors, i.e. subjects who would provide retrospective data.
- **Per-Protocol Population (PP):** This includes all subjects in the Safety Population, who have no significant protocol deviations and who meet all the inclusion/exclusion criteria.

14.3 Efficacy Analysis

14.3.1 Analysis of Primary Endpoint

The rate (%) of clinical success of all the PEEK suture anchor devices combined at 6 months post-operative will be summarized as a frequency and percentage. A 95% two-sided exact CI for a single proportion will be presented using Clopper-Pearson's method [1]. The same type analysis would be carried out for each of the 2 different PEEK suture anchors used in the study. These

analyses will be carried out using the per protocol population as the primary analysis population with the safety population used for sensitivity analysis.

14.3.2 Analysis of Secondary Endpoints

The analysis of the following secondary endpoint will be carried out using the safety population.

- The rate (%) of clinical success of all the PEEK suture anchors combined at 12 months post-operative will be summarized as described for the analysis of the primary endpoint. This analysis will also be repeated for each of the 2 different types of PEEK suture anchors used in the study.

14.4 Safety Analyses

- All safety endpoints will be summarized using the safety population. The incidence of events encountered on study will be summarized using frequencies and percentages. An overall AE table will be summarized using the overall incidence according to subjects with at least one AE; subjects with at least one AE by worst severity (mild, moderate, or severe); subjects with at least one AE by worst outcome; subjects with one AE that led to study discontinuation; subjects with at least one AE by relatedness to investigational device; SAEs; ADEs; ASADEs; USADEs and SADEs as applicable. A cumulative summary by the number of events encountered within each classification will also be summarized. The incidence of subjects reporting device deficiencies will additionally be summarized.
- Each of the AE classifications will further be summarized by event using the frequencies (n) and percentages (%) of subjects with each event as well as the ccumulative events/episodes per event.
- A listing of concomitant medications will be provided by subject.

Additional summaries of safety endpoints, if applicable, will be described in the SAP.

14.5 OTHER ENDPOINT ANALYSES

- The analyses of other endpoints will be carried out using the safety population. Overall, device-related failure and device-related re-intervention encountered on-study will be summarized independently as frequencies and percentages. A 95% two-sided exact CI for a single proportion will be presented for each proportion using Clopper-Pearson's method (1934).
- The derivation of surgeon reported outcomes used in summarizing this data for the study will be described in the SAP and will be summarized as appropriate using descriptive summary characteristics for continuous or categorical endpoints at 6 months and 12 months

13.6 Interim Analyses

Not applicable

15. SAMPLE SIZE JUSTIFICATION

This study is precision-based, as a result, the sample size is not based on statistical power calculations.

The sample size for this study is determined based on the feasibility of recruitment, enrollment and follow-up considerations. The study is therefore not powered for any statistical hypothesis testing but will be able to estimate a clinical success rate of 91% with a 95% confidence interval (CI) of 80% to 100%.

With an assumption of a 91% clinical success rate to be obtained in each of the PEEK anchor sutures and a corresponding 95% CI between 80% and 100%, enrolling between 20 and 120 subjects for each PEEK anchor suture's precision analysis will provide between 15.2% to 95% probability. Thus, an overall minimum of 40 and maximum of 240 subjects who had previously undergone surgery of the hip using PEEK anchor sutures will be enrolled into the study. Additionally, a minimum of 20 subjects will be enrolled at any investigational site.

16. ADVERSE EVENTS AND DEVICE DEFICIENCIES

16.1 DEFINITIONS

The categories of adverse events are shown in Table 4. The definitions for each of these categories are given in the subsequent sections (see reference within the table). All adverse events will be captured from the time of surgery through the 12-month follow-up visit.

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Table 5: Categories of Adverse Events

	NOT DEVICE-RELATED	DEVICE- OR PROCEDURE-RELATED	
NON-SERIOUS	ADVERSE EVENT (AE)	ADVERSE DEVICE EFFECT (ADE)	
SERIOUS	SERIOUS ADVERSE EVENT (SAE)	SERIOUS ADVERSE DEVICE EFFECT (SADE)	
		ANTICIPATED	**UNANTICIPATED**
		ANTICIPATED SERIOUS ADVERSE DEVICE EFFECT (ASADE)	UNANTICIPATED SERIOUS ADVERSE DEVICE EFFECT (USADE)

16.1.1 Adverse Event

An Adverse Event (AE) is any untoward medical occurrence temporally associated with the use of an IP/Ancillary Product, whether or not considered causally related to that IP/Ancillary Product. AE is used both to refer to AE which are non-serious non-IP or procedure-related and as an umbrella term referring to adverse events of all classifications.

An AE can be any unfavorable and unintended sign (for example, an abnormal laboratory finding), symptom, or disease. For reporting purposes, emphasis is placed first and foremost on whether or not the event constitutes an untoward medical occurrence.

16.1.2 Adverse Device Effect

An Adverse Device Effect (ADE) is an adverse event that, in the opinion of the investigator, is related to the IP or the procedure.

Not Related - An AE is considered to be not related to the use of an IP or the procedure when the effect is DEFINITELY UNRELATED or UNLIKELY to have any relationship to the use of the IP or the procedure.

Related – An AE is considered to be related to the use of an IP or the procedure when there is a POSSIBLE, PROBABLE, or DEFINITE relationship between the AE and the use of the IP or the procedure.

16.1.3 Serious Adverse Events and Serious Adverse Device Effects

An AE or ADE is considered a **Serious** Adverse Event (SAE) or **Serious** Adverse Device Effects (SADE) if, in the view of either the Investigator or the Sponsor, it:

- Results in death.
- Is life-threatening (*NOTE*: The term "life-threatening" in the definition of "serious" refers to an event/reaction in which the subject was at risk of death at the time of the event/reaction; it does not refer to an event/ reaction which hypothetically might have caused death if it were more severe).
- Requires in subject hospitalization or results in prolongation of existing hospitalization.
- Results in persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions.
- Is a congenital anomaly/birth defect.
- Is a medically important event or reaction.

Medical and scientific judgment should be exercised in deciding whether other situations should be considered serious such as important medical events that might not be immediately life

threatening or result in death or hospitalization but might jeopardize the subject or might require intervention to prevent one of the other outcomes listed in the definition above. Examples of such events are intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias, or convulsions that do not result in hospitalization, or development of drug dependency or drug abuse.

16.1.4 Anticipated/Unanticipated Serious Adverse Device Effect

An Unanticipated Serious Adverse Device Effect (USADE) is a serious ADE that meets any of the above definitions but is also considered, by the Investigator, to be caused by or related to the IP, not previously identified in nature, severity or degree in the IFU.

An Anticipated Serious Adverse Device Effect (ASADE) is a serious ADE that does not meet the criteria for a USADE.

16.1.5 Severity

The severity of every AE will be assessed by the PI or medically qualified site staff to whom the responsibility has been delegated and documented on the delegation of authority log. AE should be classified as mild, moderate, or severe, regardless of whether or not the AE are considered to be serious or non-serious. The classification should be based on the following definitions:

Mild - An event is mild if the subject is aware of, but can easily tolerate the sign or symptom.

Moderate - An event is moderate if the sign or symptom results in discomfort significant enough to cause interference with the subject's usual activities.

Severe - An event is severe if the sign or symptom is incapacitating and results in the subject's inability to work or engage in their usual activities.

16.1.6 Device Deficiency

A Device Deficiency (DevD) is an inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance. DevD includes malfunctions, use errors and inadequate labelling.

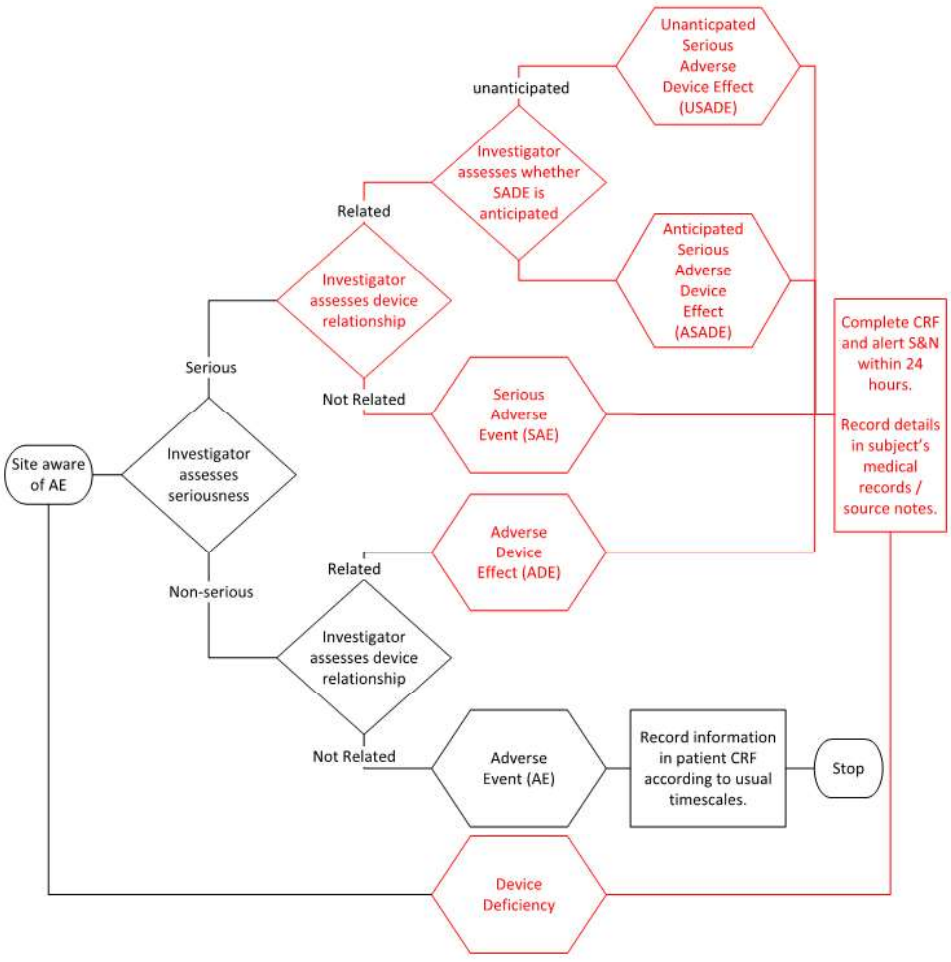
16.2 Reporting Procedures

AE of any kind and DevD will be recorded in the applicable CRF and source notes. The Investigator will evaluate all AE for relationship to the device and procedure, if applicable, seriousness, and severity. ADE, SAE, and DevD will be entered into the CRF and reported to the Sponsor within 24 hours of the investigator being informed about the event (Figure 1). Applicable to the retrospective study design, 24 hour reporting begins at the time the Investigator was informed of the event under the auspice of the clinical study. For ADE and DevD, details of the product/procedure related to the event will be included and where applicable and available, pictures taken of the device. If available the deficient product should be retained for return to S&N unless it is contaminated (e.g. used dressings must not be retained).

All SAE and ADE will be reviewed by a medically qualified person appointed by the Sponsor to determine which, if any, meet criteria for expedited reporting to the regulatory authorities. The investigator will inform the IRB/IEC of adverse events according to the IRB/IEC requirements. Depending on the nature of the adverse event, S&N may request copies of the subject's medical records, imaging, operative notes, as well as results of any relevant laboratory tests performed or

other documentation related to the AE. If the subject was hospitalized, a copy of the discharge summary may be requested by S&N and should be forwarded as soon as it becomes available. In certain cases, S&N also may request a letter from the Investigator that summarizes the events related to the case.

Figure 1: Evaluation and Reporting of AE and DevD



Reference the ISF Sponsor Contact Information Sheet to report SAE, unanticipated ADE and SADE, anticipated SADE, and DevD.

17. INVESTIGATOR OBLIGATIONS

The Principal Investigator will comply with the commitments outlined in the Statement of Investigator, provided by the Sponsor, and with Good Clinical Practice (GCP), and all applicable regulatory requirements as outlined in Section 26.1 of this protocol.

18. SPONSOR AND MONITOR RESPONSIBILITIES

The Sponsor will designate a monitor to conduct regular monitoring visits. The purpose of these visits are to ensure that data is accurate, complete and verifiable from source documents.

19. PROTOCOL AMENDMENTS

Amendments should be made only in exceptional cases once the study has started. Protocol amendments must be approved by the protocol signatories prior to submission to the IRB. Protocol amendments need to be approved by the IRB and Regulatory Authority (ies), as applicable prior to implementation at the site.

20. CONFIDENTIALITY OF THE STUDY

The confidentiality of this study and associated documents is governed by the terms of the Clinical Trial Agreement (CTA).

21. STATEMENTS OF COMPLIANCE

This clinical study will be performed in compliance with the ethical principles of the Declaration of Helsinki; ISO 14155: Clinical investigation of medical devices – Good Clinical Practice and ICH-E6.

This clinical study will not commence until the required approval/favorable opinion from the IRB or regulatory authority has been obtained. Any additional requirements imposed by the IRB or regulatory authority will be followed.

Public/Products Liability Insurance has been purchased by Smith & Nephew plc. Worldwide and incorporates coverage for personal injury in respect of clinical studies. The Sponsor agrees to operate in good faith and in accordance with ABHI (Association of British Healthcare Industries) guidelines regarding compensation for injury arising in the course of clinical studies.

22. END OF STUDY

The end of study is defined as the date of the last subject, last visit (LSLV). No additional care for subjects will be provided under the protocol, as this is a retrospective study.

Should circumstances arise which require the termination of the entire study prior to its planned completion (e.g. safety concerns) or circumstances arise which mean the end of the participation of an individual site (e.g. departure of Investigator, non-compliance), and then this will be undertaken according to the SOPs of the Sponsor.

23. REVISION OF THE STUDY DEVICE

If a subject has bilateral implants and has a revision, both implants will continue to be followed per the protocol visit schedule.

24. PUBLICATION POLICY

24.1 PUBLICATION OF STUDY DATA

The preparation and submission for publication of manuscripts containing the study results shall be in accordance with a process determined by the Clinical Trial Agreements between the study Sponsor and participating institutions. The publication or presentation of any study results shall comply with all applicable privacy laws, including, but not limited to the Health Insurance Portability and Accountability Act of 1996.

24.2 DATA SHARING

Smith & Nephew is committed to upholding the highest ethical and legal standards involved in conducting clinical trials. Smith & Nephew therefore supports the data sharing requirements of The International Committee of Medical Journal Editors (ICMJE) published on the 6th June 2017 [2]. In accordance, Smith & Nephew will consider requests to share individual (de-identified) participant data that underlie the results of any interventional clinical trial, as presented from the 1st July 2018 within an ICMJE associated journal. Requests made by researchers who provide a methodologically sound proposal will be considered. Requests may include data that underlie results presented in text, tables, figures and appendices, together with data dictionaries. Availability of these data will begin 9 months and end 36 months after article publication. Data supplied may only be used by the researcher(s) named in the approved research proposal for the purposes of achieving the aims of the analyses specified therein. All proposals should be directed to datasharing.gcs@smith-nephew.com. To gain access, data requestors will need to sign a data access agreement.

25. REFERENCES

1. Clopper, CJ & Pearson ES. (1934) The use of confidence or fiducial limits illustrated in the case of the binomial. *Biometrika*, 26, 404–413.
2. Taichman, DB, et al. Data Sharing Statements for Clinical Trials: A Requirement of the International Committee of Medical Journal Editors. Ann Intern Med. 2017. 6th June. doi:10.7326/M17-1028

26. APPENDICES

26.1 PRINCIPAL INVESTIGATOR OBLIGATIONS (ISO14155)

1. General:
    a. The role of the PI is to implement and manage the day-to-day conduct of the clinical investigation as well as ensure data integrity and the rights, safety, and well-being of the subjects involved in the clinical investigation.
2. Qualification of the PI. The PI shall:
    a. be qualified by education, training, and experience to assume responsibility for the proper conduct of the clinical investigation in accordance with this International Standard; evidence of such qualifications of the PI and key members of the investigation site team shall be provided to the Sponsor through up-to-date Curriculum Vitae (CV) or other relevant documentation,
    b. be experienced in the field of application and trained in the use of the investigational device under consideration,
    c. disclose potential conflicts of interest, including financial, that interfere with the conduct of the clinical investigation or interpretation of results, and
    d. be knowledgeable with the method of obtaining informed consent.
3. Qualification of investigation site. The PI shall be able to demonstrate that the proposed investigation site:
    a. has the required number of eligible subjects needed within the agreed recruitment period, and

b. has one or more qualified investigators, a qualified investigation site team and adequate facilities for the foreseen duration of the clinical investigation.

4. Communication with the IEC. The PI shall:

a. provide the Sponsor with copies of any clinical-investigation-related communications between the PI and the IEC,

b. comply with the requirements described in 4.5 of ISO 14155:

i. Submit to the IEC the following information, any amendments and any additional documentation required by the IEC: the Protocol; IB or equivalent; informed consent form and any other written information provided to subjects; procedures for recruiting subjects and advertising materials, if any; a copy of the CV of the PI(s) for with the IEC has oversight.

ii. Provide documentation of the IECs approval/favorable opinion, identifying the documents and amendments on which the opinion was based, to the Sponsor, prior to commencing the clinical investigation.

iii. Submit the following to the IEC if required by national regulations, the protocol or IEC, whichever is more stringent:

1. SAEs
2. Requests for deviations, and reports of deviations, if the deviation affects subject's rights, safety, and well-being, or the scientific integrity of the clinical investigation. Document and report to the Sponsor and IEC a report of deviations made to protect the rights, safety, and well-being of human subjects under emergency circumstances.
3. Progress reports, including safety summary and deviations

4. Amendments to any documents already approved by the IEC.
5. If applicable, notifications of suspension or premature termination
6. If applicable, justification and request for resuming the clinical investigation after suspension.
7. Clinical investigation report or summary.

iv. As a minimum, during the clinical investigation, the following information shall be obtained in writing from the IEC prior to implementation:

1. Approval/favorable opinion of amendments
2. Approval of the request for deviations that can affect the subject's rights, safety, and well-being or scientific integrity of the clinical investigation
3. Approval for resumption of a suspended clinical investigation if applicable.

c. obtain the written and dated approval/favorable opinion of the IEC for the clinical investigation before recruiting subjects and implementing all subsequent amendments, if required,

d. promptly report any deviations from the protocol that affect the rights, safety or well-being of the subject or the scientific integrity of the clinical investigation, including those which occur under emergency circumstances, if required by the IEC, protocol or national regulations. In particular circumstances, the communication with the IEC can be performed by the Sponsor, partly or in full, in which case the Sponsor shall keep the Principal Investigator informed.

5. Informed consent process. The PI shall:

a. General:

i. Informed consent shall be obtained in writing from the subject and the process shall be documented before any procedure specific to the clinical investigation is applied to the subject; except when special circumstances for emergency treatments apply (see below)

ii. The informed consent form consists of an information form and informed consent signature form. These two forms can either be combined in one document or separated into two documents

b. Process of obtaining informed consent. The general process for obtaining informed consent shall be documented in the protocol and shall comply with the following. These requirements also apply with respect to informed consent obtained from a subject's legally authorized representative:

i. Ensure that the PI or his/her authorized designee conducts the informed consent process

ii. Include all aspects of the clinical investigation that are relevant to the subject's decision to participate throughout the clinical investigation

iii. Avoid any coercion or undue improper influence on, or inducement of, the subject to participate

iv. Not waive or appear to waive the subject's legal rights

v. Use native non-technical language that is understandable to the subject

vi. Provide ample time for the subject to read and understand the informed consent form and to consider participation in the clinical investigation

vii. Include personally dated signatures and the PI or an authorized designee responsible for conducting the informed consent process

viii. Show how informed consent will be obtained in special circumstances (see below) where the subject is unable to provide him or herself, and

ix. Ensure important new information is provided to new and existing subjects throughout the clinical investigation.

c. Special circumstances for informed consent (the following provisions are subject to national regulations):

i. Subject needing legally authorized representatives: the legally authorized representative may give informed consent only if a subject is unable to make the decision to participate in a clinical investigation (e.g. infant, child, or juvenile, seriously ill or unconscious subject, mentally ill person, mentally handicapped person). In such cases, the subject shall also be informed about the clinical investigation within his/her ability to understand.

ii. Subject unable to read or write: informed consent shall be obtained through a supervised oral process if a subject or legally authorized representative is unable to read or write. An independent witness shall be present throughout the process. The written informed consent form and any other information shall be read aloud and explained to the prospective subject or his/her legally authorized representative and, whenever possible, either shall sign and personally date the informed consent form. The witness also signs and personally dates the informed consent for attesting that the information was accurately explained and that the informed consent was freely given.

iii. Emergency treatments:

1. For clinical investigations involving emergency treatments, when prior informed consent of the subject is not possible because of the subject's medical condition, the informed consent of the subject's legally authorized representative, if present, shall be requested.
2. When it is not possible to obtain prior informed consent from the subject, and the subject's legally authorized representative, is not available, the subject may still be enrolled if a specific process has been described in the protocol.
3. Arrangements shall be made to inform the subject or legally authorized representative, as soon as possible, about the subject's inclusion in the clinical investigation and about all aspects of the clinical investigation.
4. The subject shall be asked to provide informed consent for continued participation as soon as his/her medical condition allows.

d. The Principal Investigator may not enroll a subject without obtaining informed consent of the subject or his/her legally authorized representative only when the following conditions are fulfilled: the prospective subject fulfils the emergency conditions and is obviously in a life-threatening situation; no sufficient clinical benefits are anticipated from the currently available treatment; there is a fair possibility that the life-threatening risk to the prospective subject can be avoided if the investigational device is used; anticipated risks are outweighed by the potential benefits of applying the investigational device ; the legally authorized representative cannot be promptly reached and informed.

e. Information provided to the subject. All information pertinent to the clinical investigation, including at least the following, shall be provided in writing and in native, non-technical

language that is understandable to the subject (or the subject's legally authorized representative):

i. Description and purpose
ii. Potential benefits
iii. Risks and inconveniences or the subject and, when applicable, for any embryo, foetus or nursing infant
iv. Alternative procedures
v. Confidentiality
vi. Compensation
vii. Anticipated expenses, if any, to be borne by the subject for participating in the clinical investigation
viii. Information on the role of Sponsor's representative in the clinical investigation
ix. Contact persons
x. Statement declaring that new findings or the reasons for any amendment to the protocol that affect the subject's continued participation shall be made available to the subject.
xi. Statement indicating that, upon the subject's approval, the subject's personal physician will be informed of the subject's participation in the clinical investigation
xii. Termination procedures

f. Informed consent signature shall contain the following:
   i. The voluntary agreement to participate in the clinical investigation and follow the investigator's instructions
   ii. A statement declaring that refusal of participation incurs no penalty for the subject

iii. A statement declaring that discontinuation at any time incurs no penalty for the subject

iv. A statement with regard to the possible consequences of withdrawal

v. An acknowledgement of the information provided and confirmation that all the subject's questions were answered

vi. A statement confirming that the subject or his/her legally authorized representative agrees to the use of the subject's relevant personal data for the purpose of the clinical investigation

vii. A statement confirming that the subject or his/her legally authorized representative agrees that Sponsor's representatives, regulatory authorities and IEC representatives will be granted direct access to the subject's medical records.

g. New information: if new information becomes available that can significantly affect a subject's future health and medical care, that information shall be provided to the subject(s) affected in written form. If relevant, all affected subjects shall be asked to confirm their continuing consent in writing.

h. ensure compliance with the applicable regulatory requirements and ethical principles for the process of obtaining informed consent, and

i. ensure and document appropriate training if an authorized designee is appointed to conduct the informed consent process.

6. Compliance with the protocol. The Principal Investigator shall:

a. indicate his/her acceptance of the protocol in writing,

b. conduct the clinical investigation in compliance with the protocol,

c. create and maintain source documents throughout the clinical investigation and make them available as requested during monitoring visits or audits,
d. ensure that the investigational device is used solely by authorized users as specified in 6.2, and in accordance with the protocol and instructions for use,
e. propose to the Sponsor any appropriate modification(s) of the protocol or investigational device or of the use of the investigational device,
f. refrain from implementing any modifications to the protocol without agreement from the Sponsor, IEC and regulatory authorities, if required,
g. document and explain any deviation from the approved protocol that occurred during the course of the clinical investigation,
h. ensure that an adequate investigation site team and facilities exist and are maintained and documented during the clinical investigation,
i. ensure that maintenance and calibration of the equipment relevant for the assessment of the clinical investigation is appropriately performed and documented, where applicable,
j. ensure the accuracy, completeness, legibility and timeliness of the data reported to the Sponsor in the CRF and in all required reports,
k. maintain the device accountability records,
l. allow and support the Sponsor to perform monitoring and auditing activities,
m. be accessible to the monitor and respond to questions during monitoring visits,
n. allow and support regulatory authorities and the IEC when performing auditing activities,
o. ensure that all clinical-investigation-related records are retained as required taking measures to prevent accidental or premature destruction, and

p. review and sign the clinical investigation report, as applicable.

7. Medical care of subjects. The Principal Investigator shall

a. provide adequate medical care to a subject during and after a subject's participation in a clinical investigation in the case of adverse events,

b. inform the subject of the nature and possible cause of any adverse events experienced,

c. provide the subject with the necessary instructions on proper use, handling, storage, and return of the investigational device, when it is used or operated by the subject,

d. inform the subject of any new significant findings occurring during the clinical investigation, including the need for additional medical care that may be required,

e. provide the subject with well-defined procedures for possible emergency situations related to the clinical investigation, and make the necessary arrangements for emergency treatment, including decoding procedures for blinded/masked clinical investigations, as needed,

f. ensure that clinical records are clearly marked to indicate that the subject is enrolled in a particular clinical investigation,

g. if appropriate, subjects enrolled in the clinical investigation shall be provided with some means of showing their participation in the clinical investigation, together with identification and compliance information for concomitant treatment measures (contact address and telephone numbers shall be provided),

h. inform, with the subject's approval or when required by national regulations, the subject's personal physician about the subject's participation in the clinical investigation, and

i. make all reasonable efforts to ascertain the reason(s) for a subject's premature withdrawal from the clinical investigation while fully respecting the subject's rights.

8. Safety reporting. The Principal Investigator shall:

a. record every adverse event and observed device deficiency, together with an assessment,

b. report to the Sponsor, without unjustified delay, all serious adverse events and device deficiencies that could have led to a serious adverse device effect; this information shall be promptly followed by detailed written reports, as specified in the protocol,

c. c) report to the IEC serious adverse events and device deficiencies that could have led to a serious adverse device effect, if required by the national regulations or protocol or by the IEC,

d. report to regulatory authorities serious adverse events and device deficiencies that could have led to a serious adverse device effect, as required by the national regulations, and

e. supply the Sponsor, upon Sponsor's request, with any additional information related to the safety reporting of a particular event.