Safety and Performance of Q-Fix™ All-Suture Anchor System

Protocol Number:	17-5010-11
Protocol Version and Date:	Version 2.0 05SEP2019
Study Product Name:	Q-Fix™ All-Suture Anchor System
Sponsor:	Smith & Nephew, Inc.

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 "Safety and Performance of Q-Fix™ All-Suture Anchor System", version 2.0, dated 05SEP2019, and agree to abide by all provisions set forth herein.

I agree to comply with the Investigator's Obligations stipulated in Section 15.0 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			

1.2 SPONSOR APPROVAL

	Job title	DocuSign Stamp
Shirley Mak-Parisi, Regional Operations Manager	ROM	DocuSigned by: Signer Name: Shirley Mak-Parisi Signing Reason: I have reviewed this document Signing Time: 06-Sep-2019 | 14:57:46 BST 72696DE2BF3F44E4853E034C1C6E1C5D
Stephan Mangin, Clinical Strategy Lead	Director, Clinical	DocuSigned by: Stephan Mangin Signer Name: Stephan Mangin Signing Reason: I approve this document Signing Time: 09-Sep-2019 | 16:55:19 BST 77573411150E4841B3F03589FBBD3EAD
Alan Rossington, Head of Global Biostatistics	Director of Biostatistics	DocuSigned by: Alan Rossington Signer Name: Alan Rossington Signing Reason: I approve this document Signing Time: 09-Sep-2019 | 20:12:03 BST 556E7DBFCA8A4287A7EE3EE9B5B3ABFD
Luca Orlandini, Medical Affairs Representative	Vice Presiden Global Medical Affairs	DocuSigned by: Signer Name: Luca Orlandini Signing Reason: I approve this document Signing Time: 06-Sep-2019 | 10:14:20 BST FC872951AC1C4261B85EC7A7CD09ACDC

2. SYNOPSIS

Title of Study:	Safety and Performance of Q-Fix™ All-Suture Anchor System
Study Design:	A retrospective, multi-center, case series
Study Type:	Observational, post-market, clinical follow-up study
Study Product:	Q-Fix™ All-Suture Anchor System Model Specification 72290123 1.8MM MINI 25-1800 1.8MM 25-2800 2.8MM
Study Purpose:	Post-market clinical follow-up needed to address existing clinical data and gaps on the existing Q-Fix™ device and meet existing MDD/MEDDEV requirements
Primary Objective:	To assess the safety and performance data of the Q-Fix™ All-Suture Anchor System.
Statistical Rationale:	The study sample was decided based on the feasibility of recruitment, enrollment and follow-up considerations. Based on the results of a 1.8% failure rate for the Q-Fix™ Suture Anchor in the study conducted by Byrd et al[25], it is reasonable to estimate a success rate of 95% for the Q-Fix™ Suture Anchors in this study. The proportions of clinical success as defined in this study will be displayed with a confidence interval.
Sample Size:	A total minimum sample size of 90 subjects is proposed with a maximum of 450 subjects (depending on market share) for approved joint indications. Please see table below for enrollment distribution

	<table><tr><th>Joint indication</th><th>Number of Subjects</th></tr><tr><td>Hip</td><td>Minimum 30 Maximum 150</td></tr><tr><td>Shoulder</td><td>Minimum 30 Maximum 150</td></tr><tr><td>Knee</td><td>Minimum 30 Maximum 150</td></tr></table>
Number of Study Sites:	Approximately 3 sites for each joint indication: up to 9 sites total
Targeted Global Regions:	United States (US)
Inclusion Criteria:	1. Subject has undergone arthroscopic or open soft tissue repair with Q-Fix™ All-Suture Anchor System 2. Subject was ≥ 13 of age at time of surgery
Exclusion Criteria:	1. Subject is ≤ 6 months post-operative 2. Subject is entered in another investigational drug, biologic, or device study or has been treated with an investigational product within 12 months post-operative.
Study Duration:	The expected timeline for the study is a total of approximately 2.5 years: • 6 months for site initiation • 16 months for subject enrollment • 2 months for follow-up • 6 months to analyze the data and prepare the final study report.

Primary endpoint:	• Clinical success rate, defined as subjects without re-intervention at 6 months post-operative, as assessed by the surgeon
Secondary endpoints:	• Clinical success rate, defined as subjects without re-intervention at 12 months post-operative, as assessed by the surgeon • Visual Analog Scale (VAS) - pain • Range of Motion (ROM) • Clinical success rate in adolescents and young adults, defined as subjects ages 13-21 years of age without re-intervention at 6 and 12 months post-operative
Safety Endpoints:	• Device-related re-intervention • All adverse events (AEs) occurring from the time of surgery until revision or study completion • Device related AEs and serious adverse events (SAE's)

3. STUDY SCHEMATIC

Table 1: Schedule of Events

Schedule of Events	Chart Review [1,2]		
	Screening	**182 days post-op 6M (±91 Days)**	**365 days post-op 12M (± 91 Days)**
Inclusion/Exclusion	X		
Case History Review***	X		
Implant Status[3]	X	X	X
VAS	X	X	X
ROM	X	X	X
Concomitant Medications, Procedures[4]	*	*	*
AE Assessment	*	*	*
Study Implant Disposition	*	*	*
Serious Adverse Event (SAE) / Adverse Device Effect (ADE) / Device Deficiency (DevD) Assessment	*	*	*
End of Study/Subject disposition	*	*	*

[1] Given the retrospective study design, data will be collected to the extent it is available.
[2] Informed consent/waiver of informed consent from the IRB must be obtained prior to retrospective data collection.
[3] Subjects who have undergone a revision procedure of the anchor will be considered terminated from the study from the date of the revision. Study related data will not be collected following the date of the revision.
[4] Any concomitant medications/ procedures associated with an AE, SAE or SADE will be recorded.
* If applicable
*** Review of subject demographics, medical history, operative, post-operative, discharge, and cumulative AE's occurring since date of surgery

4. TABLE OF CONTENTS

4.1 TABLE OF TABLES

4.2 TABLE OF FIGURES

4.3 LIST OF ABBREVIATIONS

Abbreviation	Definition
ADE	Adverse Device Effect(s)
AE	Adverse Event(s)
AOL	Activities of Daily Living
CRF	Case Report Form(s)
CSR	Clinical study Report
CTA	Clinical Trial Agreement
CV	Curriculum Vitae
DevD	Device Deficiency(ies)
FU	Follow-Up

Abbreviation	Definition
GCP	Good Clinical Practice
IBT	Iliotibial Band Syndrome
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
ICMJE	International Committee of Medical Journal Editors
IFU	Instructions for Use
IP	Investigational Product
IRB	Institutional Review Board
ISF	Investigator Site File
ISO	International Organization for Standardization
LCL	Lateral Collateral Ligament
MCL	Medial Collateral Ligament
MEDDEV	MasterControl European Medical Device Vigilance System
MDD	Medical Device Directive
NA or N/A	Not Applicable
NSAIDs	Nonsteroidal anti-inflammatory drugs
NSAE	Non-Serious Adverse Event(s)
PI	Principal Investigator
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

Abbreviation	Definition
SLAP	Superior Labral Tear from Anterior to Posterior
UHMWPE	Ultra-high molecular weight polyethylene
USADE	Unanticipated Serious Adverse Device Effect(s)
VAS	Visual Analog Scale
VMO	Vastus Medialis Obliquus

5. INTRODUCTION

5.1 BACKGROUND

Bone anchor fixation devices are typically indicated for a variety of repairs in the shoulder, elbow, hand/wrist, hip, knee and foot/ankle. There are numerous alternative therapy options associated with these indications including conservative therapies such as rest, nonsteroidal anti-inflammatory drugs (NSAIDs), injection of steroids with lidocaine, and physical therapy. Several clinical studies were identified that reported higher clinical outcomes, or the ability to return to previous level of activity [1,2] , or lower complication/reinjury rate [2,3] in patients that were treated surgically rather than conservatively. When conservative therapy does not offer relief of symptoms for the patient, surgical intervention is often recommended. One method of surgical intervention is to repair using an implant such as an interference screw or suture anchor. Interference screws provide a press fit between bone to bone, or bone to graft/tendon whereas suture anchors approximate soft tissue with an implant embedded in the bone. The use of suture anchors may provide advantages such as reduced operative time, ease of access to the site of implantation, improved suture material, decreased stress along the suture line, greater repair strength, and improved consistency of load-to-failure characteristics [4-7.] Patient bone density, repair location, potential allergies, the operation being performed and surgeon preference determine the size, type and composition of the anchor needed to secure the soft tissue to the bone [8].

Non-absorbable, soft suture anchors have recently been introduced for use in arthroscopic or open soft tissue to bone reattachment. Soft suture anchors or all-suture anchors are completely suture-based implants. The anchors usually come with single or double loaded suture options. Soft anchors are usually smaller than hard anchors; hence the volume of bone removed is less, which is especially helpful should subsequent revision be necessary[9-10]. Additionally, the small size enables placement of anchors in very close proximity to each other allowing multiple sutures/fixation points per unit area of soft tissue[9]. The few studies that have investigated all-suture anchor biomechanics, such as cyclic loading and pullout mechanics, suggest that they are comparable to traditional anchors[10-13]. Soft anchors have also been

reported to provide a comparable, or even higher, mechanical strength than that measured for the interference screw technique[14].

Typically, manufacturers of anchor systems market suture anchors preloaded with suture(s) that the anchor has been designed and tested with; furthermore, the manufacturer's Instructions for Use (IFU) will specify the type of suture and how many strands may be used with an anchor. Suture anchors are continuously evolving to improve anchor strength and to facilitate arthroscopic or open procedures. Soft suture anchors are the newer anchors on the market that have pursued fixation differently with the all-suture design. The JuggerKnot 1.4 was the first all-suture construct that was designed to avoid potential sequalae from the migration and third body wear of a rigid anchor body, to provide radiographic images unobscured by metal hardware, and to facilitate revision procedures. The small 1.4 mm diameter of the drill hole helps to minimize compromise to the bone while allowing for multiple points of soft tissue fixation[15].

Based on the injury type and the anatomical position of the injury, the single- and double-loaded Q-Fix™ Suture Anchor designs offer the surgeon more flexibility when determining the type of repair. The smaller footprint required by these devices allows the placement of multiple implants in a limited area, which promotes greater tissue-to-bone contact.

A summary of known and potential risks and benefits to humans can be found in the IFU.

5.2 STUDY PURPOSE

Post-market clinical follow-up needed to address existing clinical data and gaps on the existing Q-Fix™ device and meet existing MDD/MEDDEV requirements.

5.3 SAFETY CONSIDERATIONS

The Q-Fix™ All- Suture Anchor System is intended to be used for soft tissue to bone fixation in the Shoulder, Knee, and Hip. Representative language of the contraindications and potential adverse effects from the Q-Fix™ All-Suture Anchor can be found in the Instructions for Use (IFU). Cleaning and Sterilization Language can be found on the Reusable Surgical Instruments IFU.

6. STUDY RELATED RISKS

6.1 STUDY POSSIBLE RISKS

As a result of participating in the study, there could be a risk of loss of protected subject information confidentiality. All applicable confidentiality standards and data protection and privacy laws will be followed by the Sponsor to ensure that data collected is handled in confidence. Data will be coded and handled only by appropriately qualified and authorized personnel.

6.2 STUDY RELATED BENEFITS

Because the surgery and all the follow-up visits are the same as if the subject would not participate in this study, there are no additional medical benefits associated with participating in this study. The information gained from this study may help improve the treatment of people that need to undergo any of the procedures included in this study.

7. OBJECTIVE(S)

7.1 PRIMARY OBJECTIVE

The primary objective of this study is to assess the safety and performance of the Q-Fix™ All-Suture Anchor System.

8. STUDY PRODUCT(S)

8.1 IDENTIFICATION

8.1.1 Indications

The Q-Fix™ All-Suture Anchor System is intended to be used for soft tissue to bone fixation for:

- **Shoulder**: Bankart lesion repair; superior labral tear from anterior to posterior(SLAP) lesion repair; acromio-clavicular repair; capsular shift/capsulolabral reconstruction; deltoid repair; rotator cuff repair; biceps tenodesis.
- **Hip**: Acetabular labral repair.
- **Knee**: Extra-capsular repair: medial collateral ligament (MCL), lateral collateral ligament (LCL) and posterior oblique ligament; Iliotibial band tenodesis (IBT); patellar tendon repair; vastus medialis obliquus advancement (VMO); joint capsule closure

Note: Foot, ankle, elbow, hand and wrist indications are not included in the above list as data will not be collected. As the study is collecting real world data retrospectively, data may be collected on the shoulder, knee, or hip beyond the indications listed above.

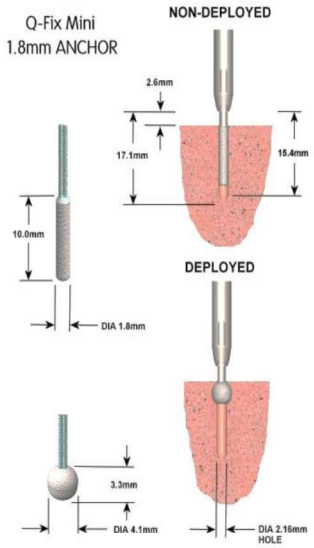
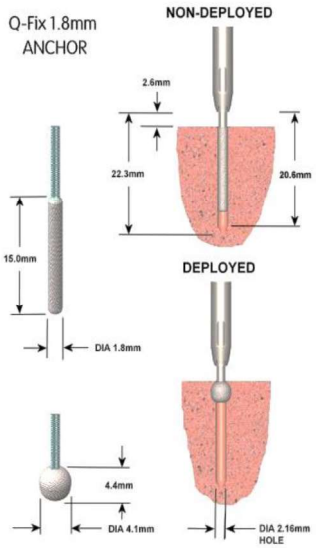
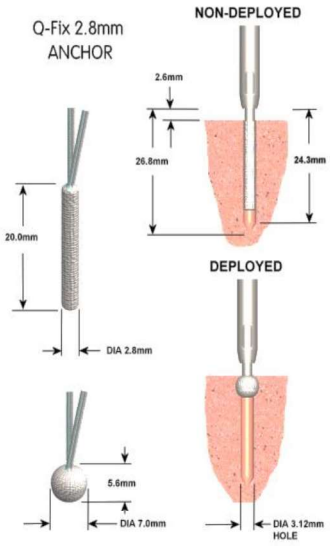
8.1.2 Device Information

The Q-Fix™ All-Suture Anchor System also known as the Q-Fix™ Soft Suture Anchor System/ Q-Fix™ Soft Suture Anchor/ Q-Fix™ Suture Anchor is available in 1.8 mm (single suture loaded) and 2.8 mm (double suture loaded) sizes; is manufactured from braided polyester with ultra-high molecular weight polyethylene (UHMWPE) suture; and is pre-loaded into a disposable tool designed to facilitate direct insertion into a pre-drilled or pre-punched bone hole. Table 8.1-1 demonstrates the model, specifications, dimensions and product description of the Q-Fix™ All- Suture Anchor System.

The Q-Fix™ MINI Suture Anchor minimizes bone removal by shortening the drill tunnel depth by 5mm. This drill depth of 17.1mm is approximately 23% shorter than the existing Q- Fix™ 1.8mm anchor.

When the soft suture anchor is deployed into the predrilled/punched hole, the suture legs are tensioned, increasing the soft anchor's diameter, locking the anchor suture against the cortical bone. The soft suture nature of the anchor allows the suture to be placed in a tunnel with a smaller diameter, preserving more bone.

Table 8.1-1: Product performance, structural composition and specification model of device

Model	**72290123**	**25-1800**	**25-2800**
Specification	**1.8 mm MINI**	**1.8 mm**	**2.8 mm**
Dimensions			
Diagram			
Product description	1.8 mm wide x 10mm long Q-Fix™ MINI All-suture Anchor, single-loaded with a #2 MAGNUMWIRE™ suture	1.8 mm wide x 15mm long Q-Fix™ All-suture Anchor, single-loaded with a #2 MAGNUMWIRE™ suture	2.8 mm wide x 20mm long Q-Fix™ All-suture Anchor, double-loaded with a #2 MAGNUMWIRE™ suture

Q-Fix™ Soft Suture Anchor Disposable Surgical Instruments and Instrument Kits

The Q-Fix™ Soft Suture Anchor Disposable Surgical Instruments and Instrument Kits contain sterile, single-use disposable devices. The kit includes a drill, a drill guide and an obturator.

Q-Fix™ Soft Suture Anchor Reusable Surgical Instruments

The Pathfinders and Bone Punch devices are manufactured of surgical stainless steel with a part of the device including plastic. The Q-Fix™ Reusable Drill Guides and Obturators are made of surgical stainless steel with Acetal Copolymer handles.

ArthroCare Corporation is a wholly-owned subsidiary of Smith & Nephew, Inc. ArthroCare Corporation is the legal manufacturer of the study devices. Smith & Nephew, Inc. globally distributes the study devices

8.2 PRODUCT USE

Each device is packaged with an IFU (62526.en) [21] to ensure that the device is used properly and for the intended procedures. For the purposes of this protocol, unless otherwise noted in the operative report, the delivery system for the device worked correctly since the device was deployed.

8.3 SURGICAL TECHNIQUE

The operative visit of this study is retrospective. The use of the Q-Fix™ All-Suture Anchor System was performed per standard of care at the participating study sites.

9. SUBJECT ENROLLMENT AND WITHDRAWAL

9.1 SUBJECT POPULATION

To eliminate the potential for bias, Investigators will consecutively screen subjects by date of surgery, starting with subjects that have undergone arthroscopic or open soft tissue repair with Q-Fix™ All-Suture

Anchor system in the past 12 months as of the IRB approval date, or using another date as agreed upon by the Investigators and site. In addition, to ensure enrollment of Q-Fix™ MINI subjects, a different enrollment start date may be selected to enroll Q-Fix™ MINI subjects only.

9.2 INCLUSION CRITERIA

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

1. Subject has undergone arthroscopic or open soft tissue repair with Q-Fix™ All-Suture Anchor System
2. Subject was ≥ 13 of age at time of surgery

9.3 EXCLUSION CRITERIA

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

1. Subject is ≤ 6 months post-operative
2. Subject is entered in another investigational drug, biologic, or device study or has been treated with an investigational product within 12 months post-operative.

9.4 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.

If during screening, a subject is found to have had re-intervention of the Q-Fix™ All-Suture Anchor system, the subject is still eligible to be enrolled in the study. Site staff will complete an End of Study Case Report Form (CRF) for all subjects who do not finish the study, documenting the reason for withdrawal.

9.5 INFORMED CONSENT

Study sites will obtain Institutional Review Board (IRB) approval for this study.

An IRB waiver of informed consent for study participation should be requested for those subjects who meet eligibility criteria and have retrospectively completed a 12 month postoperative visit, are deceased, or are lost to follow-up, per IRB policy. If allowed, a retrospective data set will be collected on these subjects. A copy of the waiver of informed consent will be placed in the subject file.

A waiver or alteration of the requirements for obtaining informed consent can occur under any of the following three provisions set forth by the Department of Health and Human Health Services:

- 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:

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.

If an IRB waiver is not granted, then the informed consent shall be obtained from all study subjects according to ISO 14155 guidelines and all applicable national regulations. Potential subjects must be informed as to the purpose of the study and the potential risks and benefits known or that can be reasonably predicted or expected as described in the written consent form. The subject, or their legally authorized representative, will then **read**, **sign**, and **personally date** the IRB approved informed consent document(s) (see below for difficulties with reading and writing). If the subject is an adolescent ages 13-17 years old, a signed adolescent informed consent form will be required of the subject as well as a

signed parental informed consent form of a parent or guardian. Additionally, the individual who obtains consent from the subject will sign and date the informed consent document. A copy of the signed informed consent documentation will be provided to the subject, a copy will be placed in the subject's medical record, and the original filed in the Investigator Site File (ISF).

If a subject refuses participation, no further information will be collected. Reason for exclusion should be noted on the Screening and Enrollment Log.

9.6 ENROLLMENT

Enrollment in this study shall occur when subjects have met inclusion criteria and none of the exclusion criteria.

For screening, only information in the medical records will be reviewed. Once a subject has completed the informed consent process, if required by the IRB, or a waiver of consent is granted, the subject will be considered enrolled and assigned a consecutive Subject Identification (ID) number.

9.7 LOST TO FOLLOW-UP

A subject will be considered lost to follow-up if he/she did not return to for follow-up per the study Investigator's standard of care.

9.8 WITHDRAWAL

9.8.1 Conditions for Study Termination

All reasonable efforts should be made to collect 12 month postoperative data on all subjects enrolled in this study. There are multiple reasons a subject may be terminated from the study. For each case, information will be obtained on the End of Study CRF, detailing circumstances leading to the withdrawal.

9.8.1.1 *Voluntary Withdrawal*

Study participation is voluntary and subjects may withdraw from the study without giving reason for doing so.

9.8.1.2 *Study Termination by Investigator/Sponsor*

The Investigator **should** withdraw subjects from the study if the Investigator or the Sponsor stops the study for any reason

9.8.1.3 *Use of Data Following Withdrawal*

In cases where the subject withdraws consent, the data collected up to the point of withdrawal may be used but no additional data for that subject may be collected.

9.8.1.4 *Study Site Discontinuation*

A specific study site in this multicenter study may also warrant termination under the following conditions:

- non-compliance to Good Clinical Practice (GCP) or protocol
- failure to enroll subjects
- major protocol deviations
- inaccurate or incomplete data
- unsafe or unethical practices
- safety or performance considerations
- investigator involuntarily discontinues participation in study

10. STUDY DESIGN

10.1 STUDY DESIGN

This is a retrospective, multi-center, case series study to collect clinical data that will evaluate post-market Safety and Performance of the Q-Fix™ All- Suture Anchor System in the knee, shoulder and hip.

A minimum of 90 subjects and a maximum of 450 subjects in the United States who underwent surgery in the knee, shoulder or hip using the Q-Fix™ All- Suture Anchor System are planned to be enrolled into the study after the fulfilment of all inclusion and exclusion criteria.

Data from eligible subjects will have their data recorded on case report forms.

10.2 STUDY ENDPOINTS

10.2.1 Primary Endpoint

- Clinical success rate, defined as subjects without re-intervention at 6 months post- operative, as assessed by the surgeon

10.2.2 Secondary Endpoints

- Clinical success rate, defined as subjects without re-intervention at 12 months post- operative, as assessed by the surgeon
- VAS -pain
- ROM
- Clinical success rate in adolescents and young adults, defined as subjects ages 13-21 years of age without re-intervention at 6 and 12 months post-operative

10.2.3 Safety Endpoints

- Device-related re-intervention
- All adverse events (AEs) occurring from the time of surgery until revision or study completion
- Device related AEs and serious adverse events (SAE's)

10.3 METHODS USED TO MINIMIZE BIAS AND MAXIMIZE VALIDITY

10.3.1 Multiple Sites

Subject enrollment will be conducted using at least three sites for each indication with up to nine sites in total for the study. This will reduce the effect of observer bias that might arise at a particular clinical site. As well as maximize the range of subjects treated.

10.3.2 Retrospective Consecutive Enrollment

To minimize any potential for selection bias consecutive enrollment will be utilized to retrospectively enroll any subjects encountered that meet the inclusion/exclusion criteria.

10.3.3 Balanced Covariates

The inclusion/exclusion criteria will be generalizable and applicable to the widest possible subset of the population requiring arthroscopic or open surgery for soft tissue repair. These criteria will be uniformly applied so as to enroll a cohort of subjects with similar symptoms and clinical requirements. This should maximize the applicability to as many subjects with similar baseline characteristics and help to bolster external validity.

10.3.4 Subject Attrition

Subject attrition for the sample size has been accounted for in the estimate of the Confidence Interval so as to validate the analysis and most efficiently use the available subjects.

10.3.5 Pre-specification of Statistical Analysis

The primary outcome measure has been pre-specified as well as the type of statistical analysis to be performed to evaluate clinical success so as to minimize reporting bias. The details of the analysis will further be pre-specified in the Statistical Analysis Plan (SAP) so as minimize any threats to external validity and yield clinically relevant estimates of effects and precision.

11. STUDY PROCEDURES

11.1 VISITS AND EXAMINATIONS

11.1.1 Summary

For a summary of the required procedures by visit, refer to Table 11.1-1: Study Procedures by Visit.

Table 11.1-1: Study Procedures by Visit

Schedule of Events	Chart Review [1,2]		
	Screening	182 days post-op 6M (±91 Days)	365 days post-op 12M (± 91 Days)
Inclusion/Exclusion	X		
Case History Review***	X		
Implant Status[3]	X	X	X
VAS	X	X	X
ROM	X	X	X
Concomitant Medications, Procedures[4]	*	*	*
AE Assessment	*	*	*
Study Implant Disposition	*	*	*
Serious Adverse Event (SAE) / Adverse Device Effect (ADE) / Device Deficiency (DevD) Assessment	*	*	*
End of Study/Subject disposition	*	*	*

[1] Given the retrospective study design, data will be collected to the extent it is available.
[2] Informed consent/waiver of informed consent from the IRB must be obtained prior to retrospective data collection.

[3] Subjects who have undergone a revision procedure of the anchor will be considered terminated from the study from the date of the revision. Study related data will not be collected following the date of the revision.
[4] Any concomitant medications/ procedures associated with an AE, SAE or SADE will be recorded.
* If applicable
*** Review of subject demographics, medical history, operative, post-operative, discharge, and cumulative AE's occurring since date of surgery

11.1.2 Retrospective: Screening

Given the retrospective study design, data will be collected to the extent it is available.

- Obtain informed consent, as required by the IRB, on and IRB approved ICF or a waiver of informed consent as detailed in Section 9.5

----- Do not proceed until consent has been obtained -----

- Screen the subject for protocol inclusion/exclusion criteria.
- Assign the subject a subject ID
- Collect the following retrospective data, to the extent is available in the subject's medical records, per CRF completion guidelines:
  - Case History Review (Review of subject demographics, medical history, operative, post-operative, discharge, and cumulative AE's occurring since date of surgery)
  - Implant status
  - VAS (pain) – preoperative if available
  - ROM - preoperative if available
- Implant Status CRF, if applicable
- Study Implant Disposition CRF, if applicable
- AE assessments- if applicable
- Concomitant medications/ procedures associated with an AE, SAE or SADE will be recorded- if applicable
- End of Study CRF, if applicable

11.1.3 Retrospective Data Collection: 6 Months Post-Operative (±91 Days)

Given the retrospective study design, data will be collected to the extent it is available

- VAS (pain) – post-operative if available

- ROM - post-operative-operative if available
- Implant Status CRF, if applicable
- Study Implant Disposition CRF, if applicable
- AE assessments- if applicable
- Concomitant medications/ procedures associated with an AE, SAE or SADE will be recorded- if applicable
- End of Study CRF, if applicable

11.1.4 Retrospective: 12 Months Post-Operative (±91 days)

- VAS (pain) – post-operative if available
- ROM- post-operative-operative if available
- Implant Status
- Study Implant Disposition CRF, if applicable
- AE assessments- if applicable
- Concomitant medications/ procedures associated with an AE, SAE or SADE will be recorded- if applicable
- End of Study CRF, if applicable

11.2 STUDY METHODS AND MEASUREMENTS

All Subjects

- VAS pain assessment*
- ROM assessment*

**Patient Reported Outcomes (PROs) are optional and used according to the Investigator's preference*

12. STATISTICAL DESIGN

An SAP will be written and finalized prior to database lock. The SAP will account for any changes or deviations from the projected analyses in this protocol.

12.1 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 quoted 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 9.3 (or later).

12.2 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 arthroscopic or open soft tissue repair using the Q-Fix™ All-Suture Anchor System i.e. subjects who only 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.

12.3 EFFICACY ANALYSIS

12.3.1 Analysis of Primary Endpoint(s)

Clinical success rate, defined as subjects without re-intervention at 6 months post-operative, as assessed by the surgeon:

The frequency of the subjects without re-intervention at 6 months together with percentage with a 95% CI will be reported. Clinical success rate for the entire sample, as well as by the position (i.e. the hip, shoulder and knee will be reported). This analysis will be carried out using the per protocol population as the primary analysis population with the safety population used for sensitivity analysis.

12.3.2 Analysis of Secondary Endpoint(s)

Clinical success rate, defined as subjects without re-intervention at 12 months post-operative, as assessed by the surgeon. The same type of analysis carried out on the primary endpoint would be implemented here as well.

Device-related re-intervention. All the above variables will be categorical in nature hence frequencies together with percentages will be tabulated for the entire sample as well as by the indication will be reported.

Clinical success rate on adolescents and young adults, defined as subjects ages 13-21 without re-intervention at 6 and 12 months post-operative, as assessed by the surgeon. The same type of analysis carried out on the primary endpoint would be implemented here as well.

Available data will be summarized and summary statistics tabulated.

12.4 SAFETY ANALYSES

All safety analyses will be conducted using the safety population. The number of incidences and number of subjects reporting all adverse events will be summarized both overall and by seriousness, severity,

relationship to study device and outcome. Incidences and number of subjects reporting device deficiencies will also be summarized. Further summaries of safety data may be described in the SAP.

13. SAMPLE SIZE JUSTIFICATION

Precision Analysis will be used to assess the overall proportion of success for the Q-Fix™ All-Suture Anchor System. Then assuming a 5% lost to follow-up rate after the first year, a minimum of 90 subjects will be enrolled (based on the inclusion/exclusion criteria) in order to complete 84 evaluable subjects. The 90 subjects will be enrolled to allow a minimum of 28 patients with each of the following indications to be recruited: Shoulder, Hip and Knee. Based on the results of the Byrd et al[25] study which showed an failure rate of 1.6% in the use of the Q-Fix™ All-Suture Anchor System, this number of subjects is sufficient to estimate the proportion of success rate to within 11% by use of the two-sided 95% confidence interval (based on an estimate of the rate of clinical success being 95%).

14. ADVERSE EVENTS AND DEVICE DEFICIENCIES

Adverse Events (AE) related to the study implant, or procedure including Adverse Device Effects (ADE), Serious Adverse Device Effects (SADE), Unanticipated Serious Adverse Device Effect (USADE), and Device Deficiencies (DevD) occurring from the time of the surgery until revision or study completion must be recorded on the appropriate CRF and reported. If the event is known to have been previously reported to Smith & Nephew, this must be noted on the CRF. After consent, in addition to all events related to the implant or the procedure, all serious adverse events (SAE), regardless of causality, must be recorded on the appropriate CRF and reported to the Sponsor and IRB if necessary. Events leading to a revision should be reported at all times regardless of causality.

Adverse Device Effects (ADE) occurring after study completion will be handled as product complaints reportable by the Sponsor and will not be entered into the study database.

14.1 DEFINITIONS

The categories of adverse events are shown in table 14.1-1. The definitions for each of these categories are given in the subsequent sections (see reference within the table).

Table 14.1-1: Categories of Adverse Event

<table>
<tr><th></th><th>NOT DEVICE- RELATED</th><th colspan="2">DEVICE- OR PROCEDURE-RELATED</th></tr>
<tr><td>NON-SERIOUS</td><td>ADVERSE EVENT
(AE) (SEE 14.1.1)</td><td colspan="2">ADVERSE DEVICE EFFECT
(ADE) (SEE 14.1.2)</td></tr>
<tr><td rowspan="3">SERIOUS</td><td rowspan="3">SERIOUS ADVERSE EVENT
(SAE)
(SEE 14.1.3)</td><td colspan="2">SERIOUS ADVERSE DEVICE EFFECT
(SADE) (SEE 14.1.3)</td></tr>
<tr><td>ANTICIPATED</td><td>UNANTICIPATED</td></tr>
<tr><td>ANTICIPATED SERIOUS ADVERSE DEVICE EFFECT
(ASADE) (SEE 14.1.4)</td><td>UNANTICIPATED SERIOUS ADVERSE DEVICE EFFECT
(USADE) (SEE 14.1.4)</td></tr>
</table>

14.1.1 Adverse Event

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

14.1.2 Adverse Device Effect

An 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.

An ADE is further categorized depending on whether the criteria in section 14.1.3 and 14.1.4 are met.

14.1.3 Serious Adverse Events and Serious Adverse Device Effects

An AE or ADE is considered a SAE or 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.

14.1.4 Anticipated/Unanticipated Serious Adverse Device Effect

An 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.

14.1.5 Severity

The severity of every AE will be assessed by the Investigator 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.

14.1.6 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.

14.2 REPORTING PROCEDURES

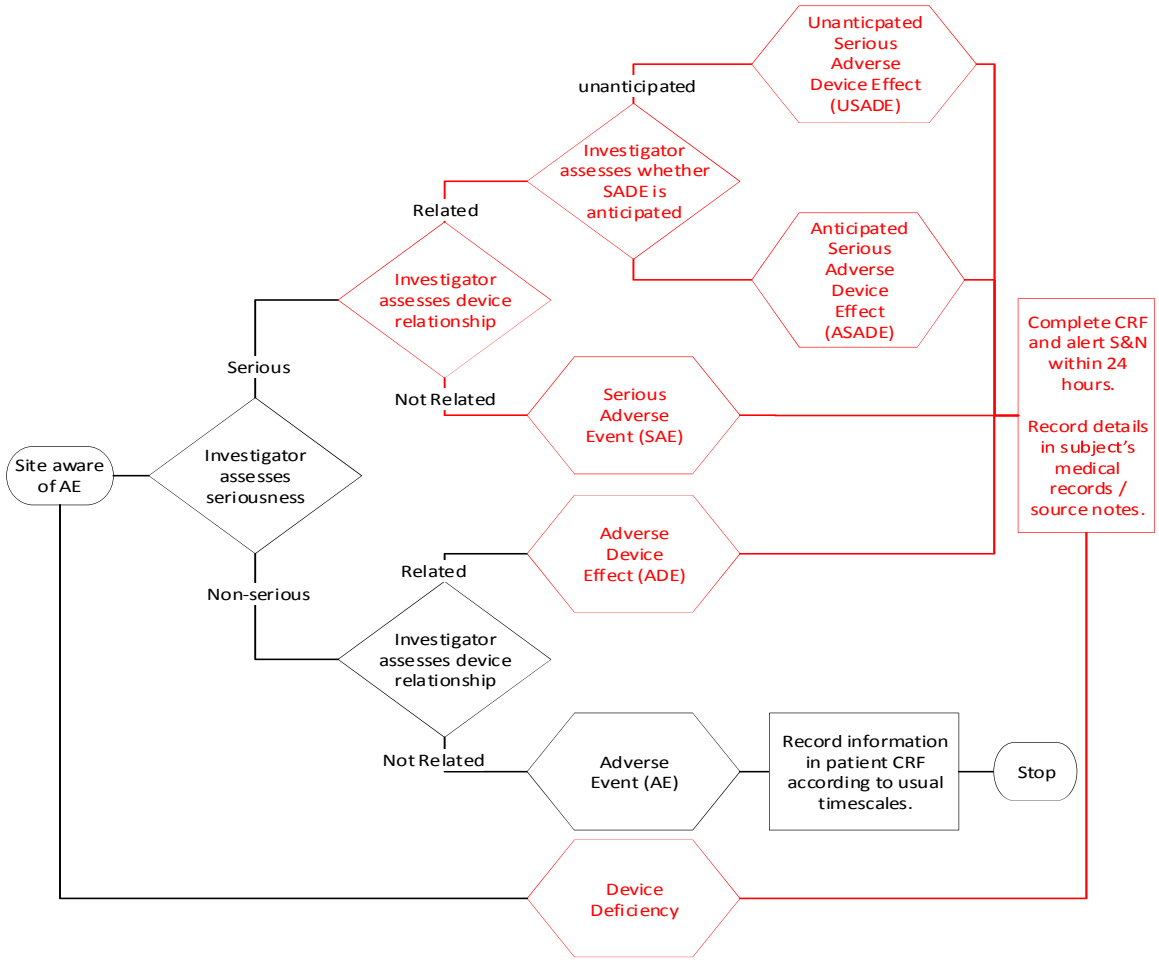
AEs of any kind and DevDs will be recorded in the applicable CRF and source notes. The Investigator will evaluate all AEs for relationship to the device and procedure, if applicable, seriousness, and severity.

ADEs, SAEs, and DevDs will be submitted/entered into the CRF and reported to the Sponsor within 24 hours of the Investigator being informed about the event (Figure 14.2-1). For ADEs and DevDs, 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 the sponsor 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.

All SAEs and ADEs 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 of AEs according to the IRB requirements.

Depending on the nature of the AE, the Sponsor 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 the Sponsor and should be forwarded as soon as it becomes available. In certain cases, the Sponsor also may request a letter from the Investigator that summarizes the events related to the case.

Figure 14.2-1: Evaluation and Reporting of AE and DevD



Reference the Investigator Site File Sponsor Contact Information Sheet to report SAEs, unanticipated ADEs and SADEs, anticipated SADEs, and DevDs.

14.3 FOLLOW-UP OF SUBJECTS WITH ADVERSE EVENTS

For subjects who are experiencing an ongoing unresolved AE at the time of their study completion or early discontinuation from the study, it is recommended that the Investigator 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.

14.3.1 Ongoing Adverse Events at Study Discontinuation

Adverse events which are **related** to a study procedure or 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.
Adverse events which are **not related** to a study procedure or 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.

15. INVESTIGATOR OBLIGATIONS

The Principal Investigator (PI) will comply with the commitments outlined in the in the Statement of Investigator and with GCP, and all applicable regulatory requirements as outlined in Appendix 23.2 of this protocol.

16. SPONSOR AND MONITOR RESPONSIBILITIES

The Sponsor will designate a monitor to conduct the appropriate site visits at the appropriate intervals. The clinical investigation will be monitored to ensure that: the rights and wellbeing of the subjects are protected; the reported data are accurate, complete, and verifiable from the source documents; and the study is conducted in compliance with the currently approved protocol, with GCP regulations, and with applicable regulatory requirements.

Detailed monitoring requirements will be documented within the Clinical Monitoring Plan for this study.

16.1 SITE QUALIFICATION VISIT

A site qualification visit may be performed by the Sponsor prior to the execution of a clinical agreement to ensure that all Investigators have the appropriate training, staff, facilities, and resources to adequately conduct the study.

16.2 SITE INITIATION VISIT

A site initiation visit to provide training on the specifics of the study, site obligations and expectations of study conduct will be performed by the Sponsor or qualified person designated by the Sponsor following the execution of the Clinical Trial Agreement (CTA) and documented IRB approval.

16.3 SPONSOR AUDITS AND REGULATORY INSPECTION

Quality Assurance auditors, whether an employee of the Sponsor or its designee, may evaluate study conduct at the study sites. These parties must have access to any and all study reports and source documentation, regardless of location and format.

16.4 CLOSE-OUT VISIT

A study close-out visit will be performed by the Sponsor or designee to retrieve and account for all remaining clinical data and to resolve outstanding queries. During study close-out, the monitor will review investigator files to ensure required documents and records are on file, confirm the disposition of any other ancillary items used for the study, and review regulatory requirements regarding records retention and IRB/IEC reporting requirements.

17. 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

18. CONFIDENTIALITY OF THE STUDY

The confidentiality of this study and associated documents is governed by the terms of the CTA.

19. STATEMENTS OF COMPLIANCE

This clinical study will be performed in compliance with the ethical principles of the Declaration of Helsinki; International Organization for Standardization (ISO) 14155: Clinical investigation of medical devices – Good Clinical Practice (GCP); and the International Council for Harmonisation (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.

20. END OF 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), then this will be undertaken according to the Standard Operating Procedures (SOP) of the Sponsor.

21. PUBLICATION POLICY

21.1 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

21.2 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. In accordance, Smith & Nephew will consider requests to share individual (deidentified) 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 the Sponsor. To gain access, data requestors will need to sign a data access agreement.

22. REFERENCES

1. Fitzgerald GK, Axe MJ, Snyder-Mackler L. A decision-making scheme for returning patients to high-level activity with nonoperative treatment after anterior cruciate ligament rupture. Knee surgery, sports traumatology, arthroscopy: official journal of the ESSKA. 2000; 8(2):76-82.
2. Kim SH, Ha KI, Kim SH. Bankart repair in traumatic anterior shoulder instability: open versus arthroscopic technique. Arthroscopy: the journal of arthroscopic & related surgery: official publication of the Arthroscopy Association of North America and the International Arthroscopy Association. Sep 2002; 18(7):755-763.
3. Arciero RA, Wheeler JH, Ryan JB, McBride JT. Arthroscopic Bankart repair versus nonoperative treatment for acute, initial anterior shoulder dislocations. Am J Sports Med. Sep-Oct 1994; 22(5):589-594.
4. Kerin C, Hopgood P, Banks A. Delayed repair of the quadriceps using the Mitek anchor system: a case report and review of the literature. The Knee. 2006; 13(2):161-163.
5. Lemos SE, Ebramzedeh E, Kvitne RS. A New Technique In Vitro Suture Anchor Fixation Has Superior Yield Strength to Bone Tunnel Fixation for Distal Biceps Tendon Repair. The American Journal of Sports Medicine. 2004; 32(2):406-410.
6. Maniscalco P, Bertone C, Rivera F, Bocchi L. A new method of repair for quadriceps tendon ruptures. A case report. Panminerva medica. Sep 2000; 42(3):223-225.
7. Richards DP, Barber FA. Repair of quadriceps tendon ruptures using suture anchors. Arthroscopy: The Journal of Arthroscopic & Related Surgery. 2002; 18(5):556-559.
8. Efird C, Traub S, Baldini T, et al. Knotless single-row rotator cuff repair: a comparative biomechanical study of 2 knotless suture anchors. Orthopedics. Aug 2013; 36(8):e1033-1037.
9. Agrawal V. Clinical Outcomes of the JuggerKnot Soft Anchor for Shoulder Repair. Biomet webpage: Form No. BMET0230.0 Rev111512. 2012.
10. McKenzie B, Moore C. Mechanical performance of the SUTUREFIX Ultra soft suture anchor for shoulder labral repair. Bone&JointScience. 2014.

11. Barber FA, Herbert MA. Cyclic loading biomechanical analysis of the pullout strengths of rotator cuff and glenoid anchors: 2013 update. Arthroscopy: the journal of arthroscopic & related surgery: official publication of the Arthroscopy Association of North America and the International Arthroscopy Association. May 2013; 29(5):832-844.
12. Galland A, Airaudi S, Gravier R, Le Cann S, Chabrand P, Argenson JN. Pullout strength of all suture anchors in the repair of rotator cuff tears: a biomechanical study. International orthopaedics. Oct 2013; 37(10):2017-2023.
13. Goschka AM, Hafer JS, Reynolds KA, et al. Biomechanical comparison of traditional anchors to all-suture anchors in a double-row rotator cuff repair cadaver model. Clin Biomech (Bristol, Avon). Jun 14 2015.
14. Mazzocca AD, Chowaniec D, Cote MP, et al. Biomechanical evaluation of classic solid and novel all-soft suture anchors for glenoid labral repair. Arthroscopy: the journal of arthroscopic & related surgery: official publication of the Arthroscopy Association of North America and the International Arthroscopy Association. May 2012; 28(5):642-648.
15. Agrawal V, Pietrzak WS. Triple labrum tears repaired with the JuggerKnot soft anchor: Technique and results. Int J Shoulder Surg. Jul-Sep 2015; 9(3):81-89.
16. Brown CA, Hurwit D, Behn A, Hunt KJ. Biomechanical comparison of an all-soft suture anchor with a modified Brostrom-Gould suture repair for lateral ligament reconstruction. Am J Sports Med. Feb 2014; 42(2):417-422.
17. Hirzinger C, Resch H, Schauer J. A perilunate dislocation with the hand in a 90° radial deviation. Sports Orthopaedics and Traumatology Sport-Orthopädie-Sport-Traumatologie. 2015.
18. Prasathaporn N, Kuptniratsaikul S, Kongrukgreatiyos K. Arthroscopic Lateral Meniscus Root Repair with Soft Suture Anchor Technique. Arthroscopy techniques. 2013; 2(4):e479-e482.
19. Koga H, Muneta T, Yagishita K, et al. Arthroscopic centralization of an extruded lateral meniscus. Arthrosc Tech. Dec 2012; 1(2):e209-212.

20. Matsuda DK, Gupta N, Burchette RJ, Sehgal B. Arthroscopic surgery for global versus focal pincer femoroacetabular impingement: are the outcomes different? Journal of Hip Preservation Surgery. 2015:hnv010.
21. IFUs. 62526.en_A, 62529.en_A, and 62533.en_A.
22. ISO 14155:2011 Clinical investigation of medical devices for human subjects – good clinical practice.
23. ISO 14155:2011 Clinical investigation of medical devices for human subjects – good clinical practice.
24. 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
25. Byrd, J.W. Thomas, Kays S, et al. Acetabular All-Suture Anchor for Labral Repair: Incidence of Intraoperative Failure due to Pullout. Arthroscopy: The Journal of Arthroscopic & Related Surgery, Volume 34, Issue 4, April 2018, Pages 1217-1218
26. U.S. Department of Health and Human Services (HHS) Code of Federal Regulation Title 45 Part 46 (45 CFR 46) Revised January 15, 2009

23. APPENDICES

23.1 INSTRUCTIONS FOR USE

Always refer to the Q-Fix™ All-Suture Anchor System IFU.

23.2 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: informed consent may be given by the legally authorized representative 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.

23.3 PROTOCOL AMENDMENT #1

- **General Purpose**

The purpose for this amendment is to:

1) Decrease age limit to ≥13 years to include adolescents as it was determined that the Q-Fix™ anchor is being used by sites in adolescents; it is important to obtain information on the safety and performance in the adolescent population as well as in adults. A secondary objective is added so that an analysis may be done on adolescents and young adults ages 13-21 years of age. As this retrospective study is granted a waiver of informed consent for adults, it is requested for adolescents as well.

2) Increase enrollment maximum to 450 subjects to allow for the enrollment of adolescents and additional Q-Fix™ MINI subjects (150 maximum per joint type.)

3) Revise the timeline to account for the enrollment of adolescents; this amendment is not expected to affect the overall study duration.

4) Include both open and arthroscopic surgeries in the study as it was determined that sites used the Q-Fix™ anchor in both arthroscopic and open soft tissue repair surgeries; it is important to obtain safety and performance data for both types of surgery. Also clarified that as the study is collecting real world safety data, use in knee, shoulder, and hip may be collected beyond the indications for use.

5) Clarify that another enrollment date may be used if agreed upon by Investigators and site, as long as a bias is not introduced using this date. In addition, the enrollment start date for Q-Fix™ MINI may be different than the start date for the 1.8 and 2.8mm Q-Fix™ anchors to ensure that the data is collected on all 3 sizes of the Q-Fix™ anchor.

- **Rationale**

The rationale for the changes is as follows:

1) From the screening and enrollment logs provided by the sites to the Sponsor, individuals <18 years old are receiving Q-Fix™ anchors, but this population is not included per the current

eligibility criteria. A goal of this post-market study is to determine the safety and performance of the Q-Fix™ anchor in populations that are receiving the Q-Fix™ anchor, so by not including adolescents, this study is unable to analyze whether the anchor is safe and performs well in a population that physicians are already using the Q-Fix™ anchor in: individuals aged 13 to 17 years old. A secondary exploratory analysis will be conducted on adolescents and young adults ages 13-21 years of age. Given that the current processes for this retrospective study will not change, it is requested that a waiver of consent be extended to include the adolescent population as well the adult population.

2) In order to enroll adolescents, as well as Q-Fix™ MINI anchors, the study maximum is increased from 360 to 450 subjects (150 subjects per indication). As the sites will be enrolling subjects that were originally excluded, this number is enough to include all adolescents that were previously excluded per the site Screening Logs.
3) In order to enroll adolescents, data collection is increased from 12 to 16 months. Follow-up is expected to take shorter than originally planned; therefore, the overall timeline for the study remains at 2.5 years.
4) Physicians are already using the Q-Fix™ anchor in both open and arthroscopic surgeries. In order to adequately describe the safety and performance of the Q-Fix™ anchor post-market, it is important to include both surgery types. A protocol waiver to include these individuals was already granted by all IRBs; therefore, the protocol is being revised to capture this information, as well as clarifying that the Q-Fix™ is indicated for use in soft tissue repair (not just instability). Additionally, clarified that as the study is collecting retrospective real world safety and performance data, sites may provide data on use in the shoulder, knee, or hip that is not listed in the indications for use.
5) The wording on the statement for enrolling subjects is not clear and there has been confusion in interpreting this line by the sites: “To eliminate the potential for bias, Investigators will consecutively screen subjects by date of surgery, starting with subjects that have undergone arthroscopic tissue repair with Q-Fix™ All-Suture Anchor system in the past 12 months as of the

IRB approval date." Biostatisticians confirmed that the goal of that statement was to ensure that sites were not selecting records to prevent bias, and therefore this was broadened to include that a start date may be agreed upon by the Site and Sponsor. In addition, as the Q-Fix™ MINI anchor was released later than the 1.8mm and 2.8mm Q-Fix™ anchors, to ensure enrollment of MINI anchors, a more recent date will need to be used by the sites to specifically target Q-Fix™ MINI subjects.

- **Effect on Study Status**

These changes does not affect subjects that are already enrolled and does not affect the Case Report Forms. Current enrollment is 106 hip subjects, 99 shoulder subjects, and 24 knee subjects across all 5 sites that are participating in the study. If approval is received to enroll adolescents, the Statistical Analysis Plan will be revised to include adolescents to reflect the change in Secondary Endpoints. This change is not expected to affect the overall timeline of 2.5 years, however, enrollment is expected to require 16 months rather than 12 months and follow-up was decreased from 6 months to 2 months.

- **Details**

Section	Current Text 26JUN2018 Version 1.0	Revised Text 05SEP2019 Version 2.0
Heading	Version: 1.0 26JUN2018	Version: 2.0 05SEP2019
1.1 Protocol Signature Page	I have read the attached protocol entitled "Safety and Performance of Q-Fix™ All-Suture Anchor System", version 1.0, dated 26June2018, and agree to abide by all provisions set forth herein. I have read the attached protocol entitled "Safety and Performance of Q-Fix™ All-Suture Anchor System", version 2.0, dated 05SEP2019, and agree to abide by all provisions set forth herein. I agree to comply with the Investigator's Obligations stipulated in Section 15.0 of the protocol.	I have read the attached protocol entitled "Safety and Performance of Q-Fix™ All-Suture Anchor System", version 2.0, dated 05SEP2019, and agree to abide by all provisions set forth herein. I have read the attached protocol entitled "Safety and Performance of Q-Fix™ All-Suture Anchor System", version 2.0, dated 05SEP2019, and agree to abide by all provisions set forth herein. I agree to comply with the Investigator's Obligations stipulated in Section 15.0 of the protocol.
1.2 Sponsor Approval	Head of Global Clinical Operations	Shirley Mak-Parisi, Regional Operations Manager

	Head of Global Clinical Strategy	Stephan Mangin, Clinical Strategy Lead
	Head of Global Biostatistics	Alan Rossington, Head of Global Biostatistics
	Medical Affairs Representative	Luca Orlandini, Medical Affairs Representative
2. Synopsis Sample Size	A total minimum sample size of 90 subjects is proposed with a maximum of 360 subjects (depending on market share) for approved joint indications. Maximum 120	A total minimum sample size of 90 subjects is proposed with a maximum of 450 subjects (depending on market share) for approved joint indications. Maximum 150
2. Synopsis Inclusion Criteria	1. Subject has undergone arthroscopic instability repair with Q-Fix™ All-Suture Anchor System	1. Subject has undergone arthroscopic or open soft tissue repair with Q-Fix™ All-Suture Anchor System 2. Subject was ≥ 13 of age at time of

	2. Subject was ≥ 18 of age at time of surgery	surgery
2. Synopsis Study Duration	12 months for subject enrollment 6 months for follow-up	16 months for subject enrollment 2 months for follow-up
2. Synopsis Secondary Endpoints		Clinical success rate in adolescents and young adults, defined as subjects ages 13-21 years of age without re-intervention at 6 and 12 months post-operative
4. Table of Contents and throughout protocol	Original sections and page numbers	Updated sections and page numbers
5.1 Background	Non-absorbable, soft suture anchors have recently been introduced for use in arthroscopic soft tissue to bone reattachment. Suture anchors are continuously evolving to improve anchor strength and to facilitate arthroscopic procedures.	Non-absorbable, soft suture anchors have recently been introduced for use in arthroscopic or open soft tissue to bone reattachment. Suture anchors are continuously evolving to improve anchor strength and to facilitate arthroscopic or open procedures.
8.1.1 Indications	**Note**: Foot, ankle, elbow, hand and wrist indications are not included in	**Note**: Foot, ankle, elbow, hand and wrist indications are not included in the above list as data will not be collected. As the

	the above list as data will not be collected.	study is collecting real world data retrospectively, data may be collected on the shoulder, knee, or hip beyond the indications listed above.
9.1 Subject Population	To eliminate the potential for bias, Investigators will consecutively screen subjects by date of surgery, starting with subjects that have undergone arthroscopic instability repair with Q-Fix™ All-Suture Anchor system in the past 12 months as of the IRB approval date.	To eliminate the potential for bias, Investigators will consecutively screen subjects by date of surgery, starting with subjects that have undergone arthroscopic or open soft tissue repair with Q-Fix™ All-Suture Anchor system in the past 12 months as of the IRB approval date, or using another date as agreed upon by the Investigators and site. In addition, to ensure enrollment of Q-Fix MINI subjects, a different enrollment start date may be selected to enroll Q-Fix MINI subjects only.
9.2 Inclusion Criteria	1. Subject has undergone arthroscopic or open soft tissue repair with Q-Fix™ All-Suture Anchor System 2. Subject was ≥ 13 of age at time of surgery	1. Subject has undergone arthroscopic or open soft tissue repair with Q-Fix™ All-Suture Anchor System 2. Subject was ≥ 13 of age at time of surgery
9.5 Informed Consent		If the subject is an adolescent ages 13-17 years old, a signed adolescent informed consent form will be required of the

		subject as well as a signed parental informed consent form of a parent or guardian.
10.1 Study Design	A minimum of 90 subjects and a maximum of 360 subjects in the United States who underwent surgery in the knee, shoulder or hip using the Q-Fix™ All- Suture Anchor System are planned to be enrolled into the study after the fulfilment of all inclusion and exclusion criteria.	A minimum of 90 subjects and a maximum of 450 subjects in the United States who underwent surgery in the knee, shoulder or hip using the Q-Fix™ All- Suture Anchor System are planned to be enrolled into the study after the fulfilment of all inclusion and exclusion criteria.
10.2.2 Secondary Endpoints		Clinical success rate in adolescents and young adults, defined as subjects ages 13-21 years of age without re-intervention at 6 and 12 months post-operative
10.3.3 Balanced Covariates	The inclusion/exclusion criteria will be generalizable and applicable to the widest possible subset of the population suffering from arthroscopic instability.	The inclusion/exclusion criteria will be generalizable and applicable to the widest possible subset of the population requiring arthroscopic or open surgery for soft tissue repair.
12.2 Analysis Populations	**Safety Population (SAF):** This includes all subjects who enroll in the study who had previously undergone arthroscopic repair using the Q-Fix™	**Safety Population (SAF):** This includes all subjects who enroll in the study who had previously undergone arthroscopic or open soft tissue repair using the Q-Fix™

	All-Suture Anchor System i.e. subjects who only provide retrospective data.	All-Suture Anchor System i.e. subjects who only provide retrospective data.
12.3.2 Analysis of Secondary Endpoint(s)		Clinical success rate on adolescents and young adults, defined as subjects ages 13-21 without re-intervention at 6 and 12 months post-operative, as assessed by the surgeon. The same type of analysis carried out on the primary endpoint would be implemented here as well.