DE NOVO CLASSIFICATION REQUEST FOR MI-CHORD SYSTEM

REGULATORY INFORMATION

FDA identifies this generic type of device as:

> **Artificial chordae tendineae surgical replacement system.** An artificial chordae tendineae surgical replacement system is a standalone, prescription device consisting of nonabsorbable suture-based implant and suture placement device(s) that is used to replace mitral or tricuspid chordae tendineae in patients with atrioventricular valve insufficiency. The device includes clips or fasteners to secure the suture that are not embedded in the cardiac tissue. The system is used via surgical approach under direct visualization and not via transcatheter or percutaneous access.

NEW REGULATION NUMBER: 21 CFR 870.3490

CLASSIFICATION: Class II

PRODUCT CODE: SBK

BACKGROUND

DEVICE NAME: Mi-CHORD System

SUBMISSION NUMBER: DEN230069

DATE DE NOVO RECEIVED: September 29, 2023

SPONSOR INFORMATION: LSI Solutions, Inc.
7796 Victor-Mendon Rd.
Victor, NY 14564

INDICATIONS FOR USE

The Mi-CHORD System is indicated for the replacement of adult mitral chordae tendineae with the patient on cardiopulmonary bypass, with the heart either arrested or fibrillating, and the surgical field under direct visualization.

Direct visualization, in this context, requires that the surgeon is able to see the heart and target tissues in a bloodless field, with or without assistance from an operating telescope or videoscopy.

LIMITATIONS

The sale, distribution, and use of the Mi-CHORD System are restricted to prescription use in accordance with 21 CFR 801.109.

PLEASE REFER TO THE LABELING FOR A COMPLETE LIST OF WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS.

DEVICE DESCRIPTION

The Mi-CHORD™ System, shown in Figure 1, is a sterile, single use system, including the Mi-STITCH™ suturing device with its loaded LS-5™ expanded polytetrafluoro-ethylene (ePTFE) suture (Figure 2) and the Mi-KNOT™ device with its loaded Mi-KNOT™ titanium fastener (Figure 3).

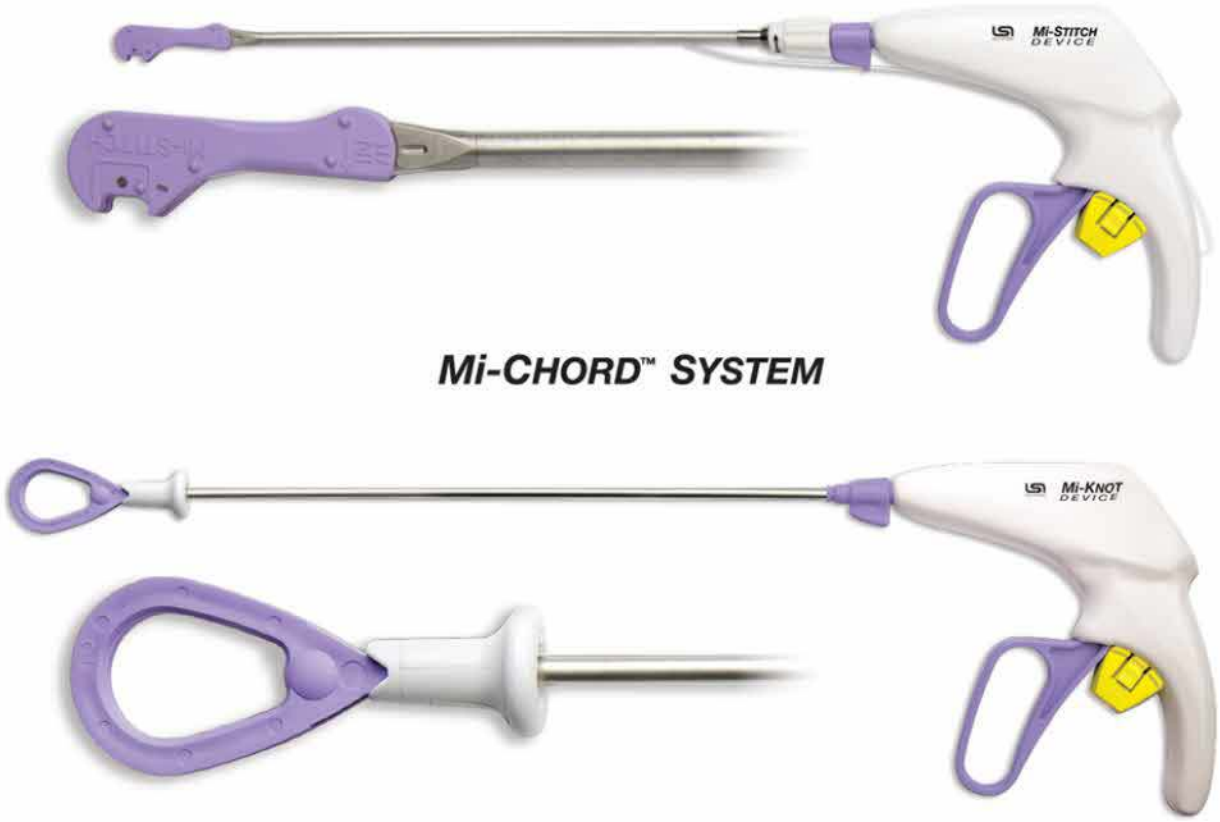

Figure 1: Mi-CHORD™ System

The Mi-CHORD™ System includes one Mi-STITCH™ Device, shown in Figure 2, which is loaded with one LS-5™ ePTFE suture. The lavender device tip ① of this device angulates and rotates to enable accurate positioning of its integrated tissue jaw ② for receiving tissue targeted for suture placement. Two curved needles ④ (shown partially advanced) emerge simultaneously from their protective compartments (not shown) to traverse the tissue jaw by

rotating about a circular engraved needle axle indicator ⑤. An embossed jaw width indicator ③ is provided to depict the jaw location and width when the tissue jaw may be embedded in tissue. Two needle caps ⑦ for subsequently engaging each corresponding needle tip are attached to the ends of a single strand of LS-5™ ePTFE suture ⑧. Each needle cap with its attached suture are held in specialized needle cap compartments ⑥, with alternating functions of suture pick-up or re-arming. An angulation indicator ⑨ depicting the direction and angulation of the device tip is embossed on the device tip located at the device tip hinge section where it intersects with the device shaft ⑩. The embossed arrow and word "IN" depict the direction the device tip moves when the white angulation knob ⑪ is turned clockwise; counterclockwise turning angles the tip in the direction opposite of the embossed arrow. The three embossed radial lines indicate the range of device tip angulation, which is approximately 30° in both directions. A lavender rotational knob ⑫ enables device shaft and device tip rotation through six distinct positions. The rotational knob includes an indicator fin ⑬ with an integrated eyelet that stabilizes the suture tube ⑭ with its indwelling LS-5™ ePTFE suture. Note the suture loop near the suture's midsection emerging from the suture tube above the white handle ⑰. A yellow lever stop ⑯ is located behind the lavender lever to restrict inadvertent squeezing during device handling prior to use. Simultaneous needle advancement across the tissue jaw is achieved by a single complete squeeze of the lavender lever ⑮. Release of the lavender lever retracts both needles with their engaged needle caps and pulls the suture ends back through the targeted tissue in the tissue jaw. With the next squeeze of the lever, in addition to advancing the needles, needle caps and suture ends back into their corresponding needle cap compartments, an internal mechanism also automatically alternates the device to its rearming function. The release of the lavender lever rotates the needles back to their protective compartments on the opposite side of the tissue jaw, while holding the needle caps and their suture ends in their needle cap compartments ready for pick-up in the subsequent tissue bite. The next lavender lever squeeze begins the alternating cycle again by advancing the bare needles towards the rearmed needle caps and suture ends, plus automatically alternating to the rearming function.

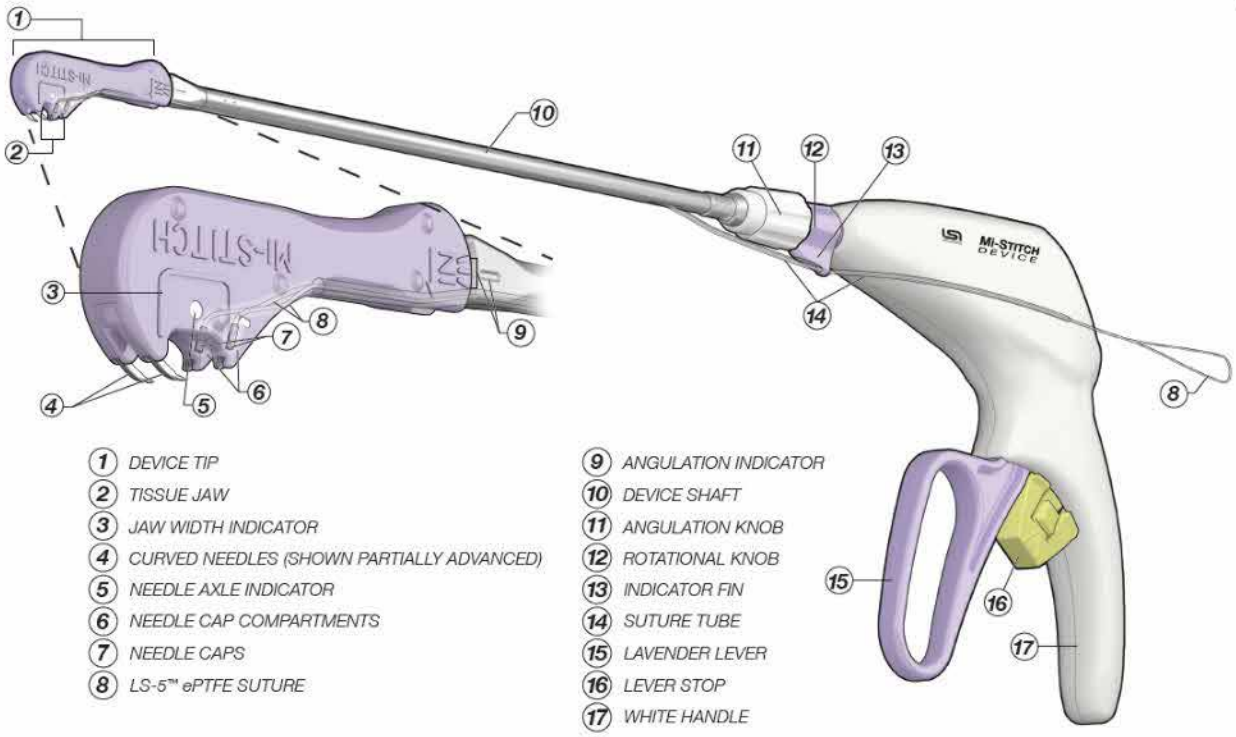

Figure 2: Mi-STITCH™ Device

The Mi-CHORD™ System also includes one Mi-KNOT™ Device, shown in Figure 3, which is loaded with a single Mi-KNOT™ fastener ①. Made from medical grade titanium, the Mi-KNOT™ fastener is a hollow sleeve with a rounded diamond-shaped base. A lavender target ②, (shown removed above) holds the loop shape of a wire snare ③. The wire snare passes through the Mi-KNOT™ fastener and is attached to a snare puller ④ knob. A suture slot ⑤ (not shown) in the device shaft ⑥, lies under the opening in the snare puller. The ends of LS-5™ ePTFE suture are passed through the wire snare and subsequently threaded into the titanium fastener. The snare puller is pulled up or retracted along the device shaft until it snaps onto the puller retainer ⑦ feature of the lavender knob ⑧, which also has an integrated indicator fin ⑨. The suture slot and the indicator fin are located on the same side of the device shaft. The subsequently crimped fastener and remnant trimmed suture tails bend slightly in the direction away from or opposite from the suture slot and indicator fin. By rotating the lavender knob and the device's white handle ⑩ the surgeon can ergonomically orient the direction of the suture tails. A yellow lever stop ⑪ is located behind the lavender lever ⑫ to restrict inadvertent squeezing of the lavender lever during device handling before crimping. The lever stop is removed by pinching its sides together and pulling it out of the handle. By squeezing the lavender lever, the Mi-KNOT™ Device crimps the Mi-KNOT™ fastener to fasten together segments of suture and trim away excess suture.

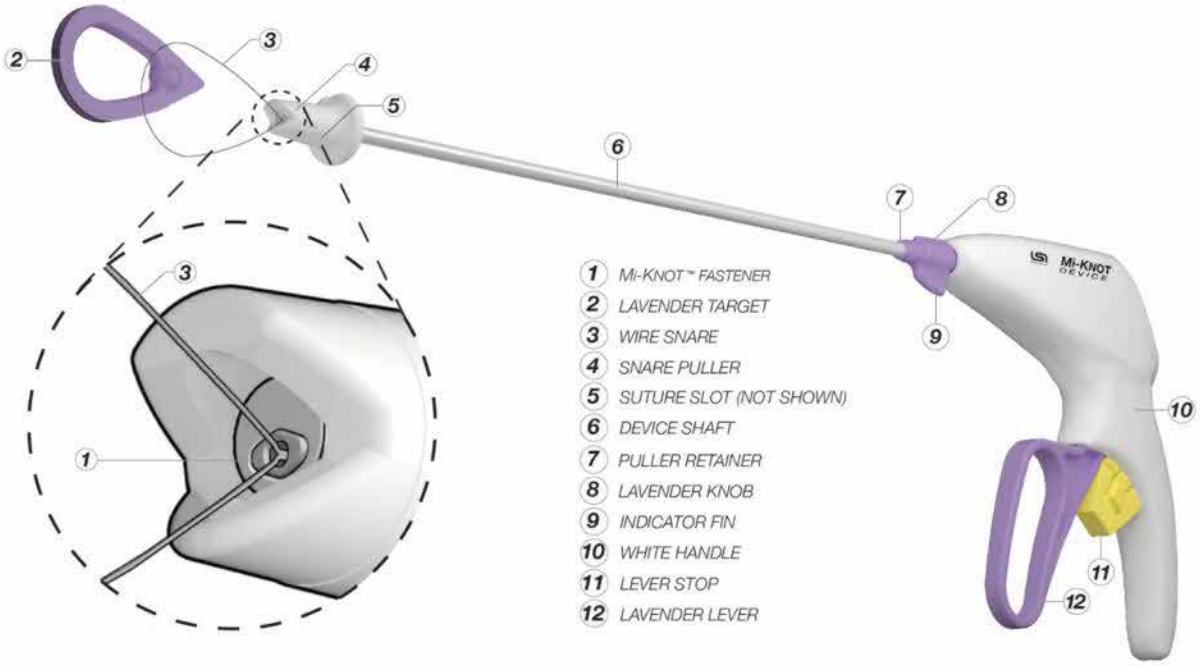

Figure 3: Mi-KNOT™ Device

SUMMARY OF NONCLINICAL/BENCH STUDIES

Nonclinical studies conducted for the Mi-CHORD™ System are summarized below.

BIOCOMPATIBILITY/MATERIALS

Components & Classification	The Mi-CHORD™ System is composed of four components. The Mi-STITCH™ Device and Mi-KNOT™ Device are external communicating devices with limited patient contact (≤ 24 hours). The LS-5™ ePTFE Suture and Mi-KNOT™ titanium fastener are implanted devices in permanent contact with circulating blood (> 30 days). Materials of the implanted components are listed in Table 1.

Table 1: Mi-CHORD™ Implant Component Materials

Name of Component	Material of Finished Component	Contact Duration
LS-5™ ePTFE Suture	expanded polytetrafluoro-ethylene (ePTFE)	Permanent patient contact
Mi-KNOT™ Fastener	Titanium (ASTM F67 Grade 1 or 2)	Permanent patient contact

Biocompatibility Assessment	A biological evaluation plan and assessment (BEP) was completed for the Mi-CHORD™ System according to the FDA Guidance for Industry, *Use of International Standard ISO 10993-1, "Biological evaluation of medical devices –*

	Part 1: Evaluation and testing within a risk management process," September 4, 2020, and ISO 10993-1:2018, *Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process*. Biocompatibility evaluation consisted of new testing and leveraging from prior 510(k) clearances (K100593, K163639, and K202551) for individual components which share similar materials and design features as the Mi-CHORD™ System components. The evaluated endpoints summarized below demonstrate that the Mi-CHORD™ System is biocompatible.

Table 2: Biocompatibility Endpoints Evaluated

Mi-STITCH™ Device; Mi-KNOT™ Device (Limited patient contact)	**LS-5™ ePTFE Suture; Mi-KNOT™ Fastener (Permanent Implant)**
• Cytotoxicity: MEM Elution Test, L929 Cell Line • Sensitization: Guinea Pig Maximization Test • Irritation: Intracutaneous (Intradermal) Reactivity Test • Material Mediated Pyrogenicity: Rabbit Pyrogen Test • Acute Systemic Toxicity: Mouse Injection Test	• Cytotoxicity: MEM Elution Test, L929 Cell Line or MHLW Colony Formation Test on Extracts • Sensitization: Guinea Pig Maximization Test • Irritation: Intracutaneous (Intradermal) Reactivity Test • Material Mediated Pyrogenicity: Rabbit Pyrogen Test • Acute Systemic Toxicity: USP Systemic Toxicity Study in Mice – Extract or Mouse Injection Test • Subacute/Subchronic Toxicity • Chronic Toxicity • Implantation: Modified USP Muscle Implantation in Rabbits – 7 Day or 12 Week or 90 Day Subchronic Muscle Implantation (in rabbit) • Hemocompatibility: Partial Thromboplastin Time (PTT) • Hemocompatibility: Complement Activation C3a and SC5b-9 Assay • Hemocompatibility: Platelet and Leukocyte Counts • Hemocompatibility: ASTM Hemolysis – Direct Contact and Extract Method (GLP) • Genotoxicity

	• Carcinogenicity

SHELF LIFE/STERILITY

Sterility	Sterility testing conducted in accordance with the FDA Guidance for Industry, *Submission and Review of Sterility Information in Premarket Notification (510(k)) Submissions for Devices Labeled as Sterile*, January 21, 2016, demonstrates the Mi-CHORD™ System is provided sterile. The Mi-CHORD System was adopted into an existing, validated ethylene oxide (EtO) sterilization cycle (AAMI TIR28:2009). The sterilization cycle was assured by using the validated over kill (or the half-cycle) sterilization method qualified in accordance with ISO 11135:2014. Based on the validation results, a sterility assurance level (SAL) of at least 10^{-6} was achieved. The EO and ECH residuals of the Mi-CHORD™ System components were shown to meet the limits specified by ISO 10993-7:2008 following one routine full cycle sterilization.
Packaging	The packaging configuration for the Mi-CHORD™ System successfully met the packaging distribution testing qualifications, following 2X sterilization, simulated distribution consistent with ASTM D4169-16, and climatic conditioning cycles per ASTM F2825-18. The results of the testing demonstrate that the packaging design met the predetermined requirements, specifications, and acceptance criteria for packaging validation under typical distribution and climatic conditions, via the following testing: • Sterile barrier integrity via bubble leak testing in accordance with ASTM F2096; • Seal integrity via dye testing, visual inspection in accordance with ASTM F1929, ASTM F3039, and ASTM F1886; • Seal integrity via peel strength test in accordance with ASTM F1886 and ASTM F88/F88M; • Unit box integrity, labeling condition, product insert legibility, and device security via visual inspection.
Shelf Life	The shelf-life of the Mi-CHORD™ System has been established at 2 years based on real-time aging up to 2 years. Following 2X sterilization and real-time aging, the device packaging validation testing was repeated (except device securement) and functional tests listed below under "Performance Testing – Bench" which were deemed to be potentially affected by device aging were repeated. All tests passed.

PERFORMANCE TESTING - BENCH

The Mi-CHORD ™ System was subjected to a series of bench tests to assess its functional performance. These tests were performed on final sterilized product, as well as subjected to simulated distribution consistent with ASTM D4169-16 and climatic conditioning cycles per ASTM F2825-18 when required. The engineering bench testing summarized in Table 3 below demonstrate acceptable performance of the device for its intended use.

Table 3: Engineering Bench Testing Summary

Test	Test Purpose and Description
LS-5™ ePTFE Suture – Diameter and Material	The LS-5™ suture met specifications of (b)(4) diameter according to USP 42-NF37:2019 *<861> Sutures – Diameter*, suture is natural ePTFE, and material is monofilament nonabsorbable ePTFE.
LS-5™ ePTFE Suture – Tensile Knot Strength	Testing demonstrated that the LS-5™ suture exceeds performance requirements of non-absorbable surgical suture tensile knot strength as indicated in USP 42-NF37:2019 *<881> Sutures – Tensile Strength*.
LS-5™ ePTFE Suture – Needle Cap Attachment Strength	Testing demonstrated that the LS-5™ suture meets performance requirements of non-absorbable surgical suture for suture/needle (needle cap) pull-off force as indicated in USP 42-NF37:2019 *<871> Sutures – Needle Attachment*.
Mi-STITCH™ Orientation – Performance	Testing demonstrated that the Mi-STITCH™ device reliably allows for suture placement at different shaft orientations via device shaft rotation, by ensuring that the device functions equivalently at all the device's rotational detent positions.
Mi-STITCH™ Reliability – Implant Deployment	Testing demonstrated that the Mi-STITCH™ device reliably places a stitch when the device lever is squeezed and released by ensuring 1) a squeeze of the Mi-STITCH™ lever will actuate its dual curved needles simultaneously to drive through tissue, picking up a needle cap on each needle and 2) a release of the lever will pull the needles, needle caps, and suture back through the tissue.
Mi-STITCH™ Reliability – Multiple Deployment	Testing demonstrated that the Mi-STITCH™ device reliably picks up and resets the same set of needle caps multiple times by ensuring when the needle caps are on the needles, squeezing the lever again will cause the reset latch within the Mi-STITCH™ device to remove the needle caps from the needles and reset them into their corresponding needle cap compartments.
Mi-KNOT™ Orientation – Performance	Testing demonstrated that the Mi-KNOT™ device reliably allows for titanium fastener orientation via device shaft rotation.

Mi-KNOT™ Reliability – Prior to Crimping	Testing demonstrated that the Mi-KNOT™ device reliably retains the uncrimped titanium fastener prior to crimping, without the fastener dislodging from the tip.
Mi-KNOT™ Usability – Suture Loading	Testing demonstrated that LS-5™ ePFTE suture is reliably able to be loaded through the loaded titanium fastener in the distal end of a Mi-KNOT™ device.
Mi-KNOT™ Reliability – Fastener Crimp	Testing demonstrated that a user of the Mi-KNOT™ device is reliably able to crimp a titanium fastener with one hand.
Mi-KNOT™ Reliability – Fastener Release	Testing demonstrated that the Mi-KNOT™ device reliably releases from a crimped fastener.
Mi-KNOT™ Reliability – Suture Cutting	Testing demonstrated that the Mi-KNOT™ device reliably trims the ePFTE suture tails and does not leave excess suture length.
LS-5™ ePTFE Suture Dynamic Creep Test	Dynamic Creep Testing of the ePTFE suture was performed to assess the total elongation of LS-5™ ePFTE Suture under supra-physiologic loading. Acceptance criteria for this testing was: After a minimum of 1000 test hours, the 95th-percentile with 95% Confidence upper bound of LS-5™ Creep performance will be less than or equal to the 95th-percentile with 95% Confidence upper bound of comparator product performance indicated for chordae replacement.
Mi-KNOT™ Fastener – Holding Strength	Testing demonstrated that the crimped Mi-KNOT™ titanium fastener reliably secures two strands of LS-5™ ePFTE suture with a designated minimum pull apart force.
Mi-KNOT™ Fastener – Post-crimp Inspection	Testing demonstrated that the crimped Mi-KNOT™ titanium fasteners have no sharp edges, are free of burrs, and are less than a pre-determined size specification to prevent patient tissue or native chordae abrasion *in situ*.
Mi-STITCH™ Verification & Validation Testing	Testing demonstrated that the Mi-STITCH™ device met all design specifications, including dimensional specifications, interaction with pre-loaded LS-5™ ePTFE suture, and mechanical requirements for usability and function under anticipated use conditions.
Mi-KNOT™ Verification & Validation Testing	Testing demonstrated that the Mi-KNOT™ device met all design specifications, including dimensional specifications, interaction with pre-loaded Mi-KNOT™ Fasteners, compatibility with LS-5™ ePTFE suture, and mechanical requirements for usability and function under anticipated use conditions.
Fastener-Suture Implant – Tissue Separation Force	Testing demonstrated that the replacement chord formed from LS-5™ ePTFE suture (placed by a Mi-STITCH™ device) and a crimped Mi-KNOT™ titanium fastener (placed by a Mi-KNOT™ device) will not pull through anchoring tissue at forces less than a physiologically relevant minimum

	mitral chordae force.
Fastener-Suture Interface (FSI) Accelerated Life Test	Fatigue of the replacement chord was evaluated in an accelerated life test. The testing validated the FSI portion of the replacement chord structure formed from LS-5™ ePTFE suture secured by a Mi-KNOT™ titanium fastener for use in the replacement of mitral chordae tendineae under simulating physiological cyclic loading conditions.
Fastener-Suture Interface (FSI) Durability	Durability of the FSI was evaluated with a 600 million cycle test where LS-5™ ePFTE suture test specimens secured with crimped Mi-KNOT™ titanium fasteners were cycled under clinically worst-case loading conditions for the duration of the test. The FSI samples were evaluated for suture fray or damage, Mi-KNOT™ Fastener integrity via pull-apart force after 600 million cycles, and suture slippage or pull-through. All test specimens passed acceptance criteria.
Mi-KNOT™ Fastener MRI Compatibility	Applicable testing demonstrates MRI compatibility of the Mi-KNOT™ titanium fastener. Test results show the Mi-KNOT™ fastener, will not present an additional risk or hazard to a patient in a MR field of 3-Tesla or less and under the MRI-related heating conditions.
Mi-KNOT™ Corrosion Resistance	Corrosion resistance of the implanted Mi-KNOT™ titanium fastener was assessed. Risk of corrosion was mitigated by leveraging testing and evidence from prior 510(k) clearances (K100593 and K202551) for titanium fasteners with identical materials and similar design as the Mi-KNOT™ Fastener.

PERFORMANCE TESTING – USABILITY &/OR ANIMAL

Simulated Use	Simulated use testing demonstrated the feasibility of using the device under worst-case clinical conditions. In testing, cardiothoracic surgeons were trained in the use of the system and completed a summative test to validate all critical procedural tasks (adjusting and positioning Mi-STITCH™ device tip over leaflet tissue, adjusting and positioning Mi-STITCH™ device tip over papillary muscle tissue, orienting the Mi-KNOT™ indicator fin and suture slot, Squeezing and holding the Mi-KNOT™ lever), as well as other non-critical procedural tasks. The usability testing models simulated mitral valve anatomy and indicated surgical access approaches and was performed under direct visualization with or without assistance by videoscopic endoscope. Usability testing demonstrated the feasibility of the Mi-CHORD™ System when operated by the intended users according to the Indication for Use under clinically-representative conditions.

SUMMARY OF CLINICAL INFORMATION

Overview

The Mi-CHORD™ System was supported by one outside the United States (OUS) single-center, single-cohort clinical trial to assess the feasibility of the Mi-CHORD™ System for mitral chordal replacement.

Objective:

To evaluate the Mi-CHORD™ System (Mi-STITCH™ and Mi-KNOT™ devices) for mitral valve repair in terms of operative times, echocardiographic outcomes, adverse events, and mortality in a single-center clinical safety and feasibility study. The study was initiated on August 3, 2021, and 1-year follow-up was completed on January 23, 2023.

Study Design:

Clinical, single-center safety and feasibility pilot trial. Prospective 12 patient cohort study, with 1-year postoperative follow-up.

Eligibility Criteria Summary:

All patients with severe primary mitral regurgitation with an indication for mitral valve repair according to the current guidelines with or without concomitant procedures were eligible for inclusion after a review of inclusion and exclusion criteria. A left ventricular function of more than 35%, a life expectancy of more than one year, a surgical risk of less than 8% (EuroScore II), a signed informed consent, and the willingness to perform the planned follow-up were the essential inclusion criteria. Patients with previous heart surgery, with a heavily calcified mitral valve annulus, with severe mitral valve stenosis, active endocarditis or myocarditis, as well as patients under 18 years of age, pregnant women, patients undergoing emergency surgery or patients who did not consent to the study had to be excluded from the study.

Primary Safety Endpoints:

The primary safety endpoint is 30-day mortality.

Primary Effectiveness Endpoint:

The primary efficacy endpoint is implantation time (defined as the period from start of valve assessment until the completion of the repair; i.e., initiation of left atrial closure).

Secondary Endpoints:

The secondary safety endpoints are:

- Mortality at 6 and 12 months after surgery; and
- Number of serious adverse events (SAE) at 1, 6 and 12 months.

The secondary efficacy endpoints are:

- Procedural times (surgical time, aortic cross-clamp time, cardiopulmonary bypass time, valve repair time (from initial suturing to final knot securement);
- Placement of ePTFE sutures; and
- Echocardiographic evaluation of mitral regurgitation at 6 months follow-up.

Statistical Methods:
Descriptive statistical methods were used. Continuous variables are presented as mean ± standard deviation; skewed data as median and interquartile range [25th & 75th percentile].

Demographics:
A summary of the preoperative characteristics of the 12 enrolled subjects is provided below. Severe mitral regurgitation without mitral stenosis was present in all patients – classified as a Carpentier Type II valve pathology with excessive leaflet motion. Seven patients (58%) presented with isolated P2 prolapse, while three patients (25%) presented with prolapse of the P2 and the P3 segment, one patient (8%) showed isolated P1 prolapse, and one patient (8%) showed prolapse of the P1 and P2 segment. Ruptured chordae corresponding to the prolapsing segments were observed in 9 patients (75%).

Table 4: Clinical Subjects Demographics

Variables	Data (n=12)
Age (years)	66±12
Sex (male)	6 (50%)
BMI (kg/m²)	26.9±4.7
EuroSCORE II (%)	1.36% [0.71, 4.05]
Preoperative Creatinine (mg/dl)	0.94±0.2
NT-proBNP (pg/ml)	1249 [221, 2172]
NYHA	
I	3 (25%)
II	5 (41.7%)
III	4 (33.3%)
IV	0
Comorbidities	
Arterial Hypertonus	7 (58.3%)
Diabetes	1 (8.3%)
Smoking History	6 (50%)
Peripheral Vascular Disease	1 (8.3%)
AFIB History	5 (41.7%)
LVEF (%)	62±8
Preoperative Tricuspid regurgitation >3	2 (16.7%)

BMI= Body Mass Index, proBNP= b-type natriuretic peptide, NYHA= New York Heart Association, LVEF= Left Ventricular Ejection Fraction

Accountability:
The study was performed in compliance with the Helsinki Declaration after receiving a positive ethical vote from the local ethics committee of the Medical University of Vienna. Informed consent was obtained at least one-day before surgery in all patients. Data quality assurance was ensured by monitoring visits following GCP and the ISO 14155 standards.

All patients screened were enrolled into the study and completed follow up as planned. There was no subject discontinuation.

Results

Procedural:
All patients underwent mitral valve repair (MVr) with the study device system by one of two board-certified cardiac surgeons. One (n=3; 25%) or two (n=9; 75%) permanent ePTFE sutures for chordal replacement were implanted with the study device system; no other chordal replacements were performed in study patients. There was no distinguishable difference in the mean time to place the first ePTFE suture between open and minimally invasive cases (04:31 ± 02:48 minutes versus 05:44 ± 03:25 minutes) using the Mi-CHORD System. During the procedures, 27.6% of the total sutures implanted by the Mi-CHORD System were removed and replaced using another Mi-CHORD System to achieve better placement. Additional procedural results are shown below in Table 5.

Table 5: Mi-CHORD™ Procedure Results

Procedural Details	Values
Mini-Thoracotomy	33.3% (n=4)
Concomitant Procedure	58.3% (n=7)
Duration Surgery (min)	247±67
CBP (min)	128±48
ACC (min)	92±38
Valve Repair (min)	11±7
Number of Implanted Chords	2 [1,2]

A retrospective comparison to patients treated with conventional suture chordae replacement from the same single-center database was reported (n=39 comparator patients, from January 2009 to December 2021). For patients in the reference cohort, the average duration of surgery, cardiopulmonary bypass, and aortic cross-clamp times were 286±71, 175±61, and 117±39 minutes, compared to the times reported when using Mi-CHORD System (247±67, 128±48, and 92±38 minutes, respectively). Therefore, procedure times were nominally reduced with Mi-CHORD System compared to conventional methods; however, the times were not statistically analyzed.

There were no device failures. Final placement of ePTFE sutures was satisfactory in all patients. The median duration of stay at the intensive care unit was 1 day.

Safety:
There were no deaths at 30 days after the procedure (0% mortality). All subjects survived through 12-month follow-up. The mitral valve reoperation rate was 0%.

Effectiveness:
All patients (n=12) underwent echocardiography measurements preoperatively and at discharge, as well as 1-month, 6-month, and 12-month follow-up time points. Echocardiographic evaluation at discharge (n=12) revealed no residual MR in 11 patients (91.7%) and mild regurgitation in one patient (8.3%). At 6-month follow-up, eleven

patients (91.7%) presented with no residual MR, and one patient (8.3%) presented with trace MR. At 1 year, no MR was present in 7 (58.3%) patients, with trace in 2 patients (16.7%), mild in 2 patients (16.7%), and moderate in 1 patient (8.3%). The patient with moderate MR underwent transesophageal echocardiography, which revealed a cleft reopening in the posterior mitral leaflet and the implanted ePTFE suture with titanium fastener still in position; therefore, this patient's later-onset moderate MR is unlikely to be device-related. When compared to the reference cohort of patients treated with conventional suture chordae replacement, 28.6% of evaluable comparator patients (n=20) had recurrent moderate or greater MR at 1 year versus 8.3% of patients in the Mi-CHORD System treatment group.

Additional echocardiographic results are summarized in Table 6 below.

Table 6: Echocardiographic Results

Echocardiographic Measurements	Preoperative	Discharge	1-month Follow-up	6-month Follow-up	12-month Follow-up
LV ejection fraction (%)	60±7	54±7[c]	62±6	61±7	62±5
LA diameter (mm)	48±3[a]	53±6[d]	50±5[g]	47±6	48±5
LVEDD (mm)	49±5[b]	46±6[e]	44±5[h]	45±4	46±6
MV mean pressure gradient (mmHg)	-	3.2±1.2[f]	3.2±1.3	3.1±1.2	2.9±1.4
MR					
0 (None)	0	11 (92%)	8 (67%)	11 (92%)	7 (58%)
≤ 1 (Trace)	0	0	2 (17%)	1 (8%)	2 (8%)
≤ 2 (Mild)	0	1 (8%)	2 (17%)	0	2 (8%)
≥ 3 (Moderate, Severe)	12 (100%)	0	0	0	1 (8.3%)
TR ≥ 3	3 (25%)	0	1 (8.3%)	0	0

Adverse Events:
Over the 12-month follow-up, there were 49 adverse events (AE) reported in 12 patients and 6 serious adverse events (SAE) reported in 6 patients. Postoperative atrial fibrillation or flutter was present in 9 (75%) patients, with two requiring electrical cardioversion. None of the AEs or SAEs were judged to be device-related by the principal investigator.

Conclusions
In the presented OUS single-center, single-cohort clinical trial to assess the feasibility of the Mi-CHORD™ System for mitral chordal replacement, 12 patients underwent mitral valve repair using the Mi-CHORD™ System.

Results demonstrated that the Mi-CHORD™ System can be used successfully through median sternotomy and minimally invasive access as a standalone procedure or with concomitant procedures. The number of suture-fastener implants may be selected by the surgeon per patient anatomy (1 or 2 replacement chordae were implanted) and procedure times are reasonable. Satisfactory repair was obtained in all patients without any device-related AEs or SAEs. All subjects survived through 1-year, with 100% of patients at 6 months and 92% of patients at 12 months showing mild or lower MR, suggesting durable mitral valve repair using the Mi-CHORD™ System.

Pediatric Extrapolation

In this De Novo request, existing clinical data were not leveraged to support the use of the device in a pediatric patient population.

LABELING

The Mi-CHORD™ System labeling consists of Instructions for Use, Patient Implant Card, and packaging labels. The labeling satisfies the requirements of 21 CFR 801.109 for prescription devices.

The labeling addresses:

- Patient population that the device is intended to treat;
- The recommended training for safe use of the device;
- Instruction describing how to perform the surgical chordae replacement procedure;
- Requirement for surgical access and visualization of the tissues to be treated;
- Identification of the maximum number of deployments and actuations for each device(s);
- A shelf-life

The Instructions for Use also includes the Indications for Use; a description of the device; warnings, precautions, and contraindications for use of the Mi-CHORD™ System; MRI Safety information; and a prescription statement. PLEASE REFER TO THE LABELING FOR A COMPLETE LIST OF WARNINGS, PRECAUTIONS AND CONTRAINDICATIONS.

The Mi-CHORD™ System Patient Implant Card identifies the device, manufacture contact information, product number, UDI and device lot information, MRI Safety information, and space to enter the patient's name, the health institution name, and date of implant.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with an artificial chordae tendineae surgical replacement system and the measures necessary to mitigate these risks.

Table 7: Identified Risks to Health and Mitigation Measures

Risks to Health	Mitigation Measures
Infection	Sterilization validation Shelf life testing Labeling
Adverse tissue reaction	Biocompatibility evaluation
Failure to deploy suture and/or anchor correctly (i.e. partial deployment, tangle,	*In vivo* performance testing Non-clinical performance testing Simulated use testing

Risks to Health	Mitigation Measures
un-crimped, unable to cut/leave excess suture)	Shelf life testing Labeling
Abnormal leaflet motion and/or coaptation, relapse of valvular regurgitation, loss of function	*In vivo* performance testing Labeling
Leaflet tearing; papillary muscle tearing	*In vivo* performance testing Non-clinical performance testing Labeling
Embolic events: thromboembolic; device emboli	*In vivo* performance testing Biocompatibility evaluation Labeling
Mechanical injury to coronary arteries or proximal tissues (e.g. native chordae)	*In vivo* performance testing Non-clinical performance testing Simulated use testing Labeling
Needle penetration through cardiac conduction system leading to postoperative arrythmias, including atrial fibrillation and heart block	*In vivo* performance testing Simulated use testing Labeling

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the artificial chordae tendineae surgical replacement system use is subject to the following special controls:

(1) *In vivo* evaluation of the device must demonstrate that the device performs as intended under anticipated conditions of use. Testing must:
   (i) Demonstrate that the device performs as intended for atrioventricular valve repair;
   (ii) Demonstrate that the technology and techniques can be performed by the intended user population; and
   (iii) Evaluate all adverse events, including device malfunctions, tissue or vessel damage, unanticipated surgical interventions, and relapse of atrioventricular valve regurgitation.

(2) Simulated use testing must demonstrate the feasibility of device implantation and translatability to clinical use under worst-case clinical conditions, considering indicated anatomies, surgical access, and visualization.

(3) Non-clinical performance testing data must demonstrate that the device performs as intended under anticipated conditions of use. The following performance characteristics must be tested:

(i) Verification of diameters, tensile strengths, and bond or joint strengths of sterile suture components;
(ii) Ability to orient the device appropriately to prevent damage to surrounding tissue structures;
(iii) Consistency and reliability of implant deployment to achieve the desired treatment effect, including implant locations, leaflet tethering, and implant fixation;
(iv) Mechanical integrity (e.g., tensile strength, fatigue or creep, bond failure) of the implant and placement devices to function under anticipated loading conditions;
(v) Assessment of implant-tissue separation force;
(vi) Durability of the implant;
(vii) Compatibility of the implant in a magnetic resonance environment, if the implant contains magnetic or metallic materials; and
(viii) Corrosion assessment, if the implant contains metal components.

(4) The patient-contacting components of the device must be demonstrated to be biocompatible.

(5) Performance data must validate the sterility of the patient-contacting components of the device.

(6) Performance data must support the shelf-life of the device by demonstrating continued sterility, package integrity, and device functionality over the labeled shelf life.

(7) Labeling must include the following:
(i) The recommended training for safe use of the device;
(ii) A precaution to use clinical judgment in selecting patients eligible for atrioventricular valve surgery and suitable for the device;
(iii) A precaution to maintain direct visualization of the tissues to be treated during use of the device;
(iv) Identification of the maximum number of deployments and actuations for each device(s); and
(v) A shelf life.

BENEFIT-RISK DETERMINATION

The Mi-CHORD™ System is indicated for the replacement of adult mitral chordae tendineae with the patient on cardiopulmonary bypass, with the heart either arrested or fibrillating, and the surgical field under direct visualization. In general, the risks and benefits of the Mi-CHORD™ System are expected to be similar to those observed with established techniques for surgical replacement of chordae tendineae using suture.

The probable risks of the device are based on nonclinical laboratory studies, as well as data collected in an OUS feasibility clinical study as described above. There are known difficulties and risks associated with mitral valve repair procedures using conventional surgical technology

and techniques. Some selected risks are outlined below, which are inherent risks for the Mi-CHORD™ System due to similarity of technique:

- Residual MR
- Systolic anterior motion of the mitral valve
- Occlusion or injury of the left circumflex artery
- Postoperative arrythmias, including atrial fibrillation and heart block
- Surgical site bleeding and infection
- Acute renal insufficiency
- Respiratory insufficiency
- Thromboembolic events
- Vascular injury
- Mortality

Clinical investigation of the Mi-CHORD™ System to treat severe MR subjects with a 12-month follow-up demonstrated 0% mortality through the follow-up period. There were no device failures reported in the clinical study. The risk of improper suture placement was mitigated in that 27.6% of total implanted sutures were removed and replaced to achieve better placement without compromising patient outcomes. Over the 12-month follow-up, there were 49 adverse events (AE) reported in 12 patients and 6 serious adverse events (SAE) reported in 6 patients. No valve thrombosis, endocarditis, or pacemaker implantation occurred in the postoperative course. Postoperative atrial fibrillation or flutter was present in 9 (75%) patients, with two requiring electrical cardioversion, which is an anticipated risk of mitral valve surgery.

The probable benefits of the device are also based on nonclinical laboratory studies, as well as data collected in an OUS feasibility clinical study as described above. Probable benefits of the device include reduction of mitral regurgitation and reduced procedural time. Nonclinical bench testing demonstrated the device met all design specifications and feasibility of open access or minimally invasive approach with or without videoscopic assistance. The nonclinical results were confirmed in clinical study, in which the Mi-CHORD™ System was successfully used to treat severe MR patients through median sternotomy and minimally invasive access. Satisfactory repair was obtained in all patients without any device-related AEs or SAEs. There were no mitral valve reoperations through 1 year. All (100%) of patients at 6 months and 92% of patients at 12 months demonstrated mild or lower MR, suggesting durable mitral valve repair using the Mi-CHORD™ System.

Additional factors to be considered in determining the probable risks and benefits for the Mi-CHORD™ System include that treatment of the Mi-CHORD™ System is similar to current surgical, suture-based mitral valve chordae tendineae replacement. Nonclinical and clinical data gathered for the Mi-CHORD™ System informed the Instruction for Use to provide detailed instruction to surgeons to mitigate possible risks. However, limitations of the submitted clinical study are that the trial design was single-center and single-arm for 12 patients with up to 12-month follow-up, which may limit the ability to identify and mitigate unknown risks. Furthermore, the small number of investigators in the study (2 surgeons) may not be representative of likely real-world users of the device. As a result, an additional probable risk is that surgeon experience with conventional techniques and their experience with the device may

affect clinical results. It is also important to note that manual surgical techniques are not precluded by use of the Mi-CHORD™ System, should device failure occur or should manual suture placement be preferred with a particular case.

Overall, the known or probable risks are considered minimal or are not thought to be meaningfully different than risks associated with conventional surgical repair techniques. Therefore, the probable benefits outweigh the risks when taking into account these considerations.

Patient Perspectives

This submission did not include specific information on patient perspectives for this device.

Benefit/Risk Conclusion

In conclusion, given the available information above, for the following indication statement:

> The Mi-CHORD System is indicated for the replacement of adult mitral chordae tendineae with the patient on cardiopulmonary bypass, with the heart either arrested or fibrillating, and the surgical field under direct visualization.
>
> Direct visualization, in this context, requires that the surgeon is able to see the heart and target tissues in a bloodless field, with or without assistance from an operating telescope or videoscopy.

The probable benefits outweigh the probable risks for the Mi-CHORD™ System. The device provides benefits and the risks can be mitigated by the use of general controls and the identified special controls.

CONCLUSION

The De Novo request for the Mi-CHORD™ System is granted and the device is classified as follows:

> Product Code: SBK
> Device Type: Artificial chordae tendineae surgical replacement system
> Regulation Number: 21 CFR 870.3490
> Class: II