



July 1, 2025

Fasikl Incorporated
Zhen Zhang, Ph.D.
President
8500 Normandale Lake Blvd, Suite 400
Bloomington, Minnesota 55437

Re: K250096
Trade/Device Name: Felix NeuroAI System
Regulation Number: 21 CFR 882.5897
Regulation Name: External Upper Limb Tremor Stimulator
Regulatory Class: Class II
Product Code: QBC
Dated: June 24, 2025
Received: January 14, 2025

Dear Dr. Zhang:

We have reviewed your section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (the Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database available at <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm> identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Additional information about changes that may require a new premarket notification are provided in the FDA guidance documents entitled "Deciding When to Submit a 510(k) for a Change to an Existing Device" (<https://www.fda.gov/media/99812/download>) and "Deciding When to Submit a 510(k) for a Software Change to an Existing Device" (<https://www.fda.gov/media/99785/download>).

Your device is also subject to, among other requirements, the Quality System (QS) regulation (21 CFR Part 820), which includes, but is not limited to, 21 CFR 820.30, Design controls; 21 CFR 820.90, Nonconforming product; and 21 CFR 820.100, Corrective and preventive action. Please note that regardless of whether a change requires premarket review, the QS regulation requires device manufacturers to review and approve changes to device design and production (21 CFR 820.30 and 21 CFR 820.70) and document changes and approvals in the device master record (21 CFR 820.181).

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR Part 803) for devices or postmarketing safety reporting (21 CFR Part 4, Subpart B) for combination products (see <https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products>); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR Part 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR Parts 1000-1050.

All medical devices, including Class I and unclassified devices and combination product device constituent parts are required to be in compliance with the final Unique Device Identification System rule ("UDI Rule"). The UDI Rule requires, among other things, that a device bear a unique device identifier (UDI) on its label and package (21 CFR 801.20(a)) unless an exception or alternative applies (21 CFR 801.20(b)) and that the dates on the device label be formatted in accordance with 21 CFR 801.18. The UDI Rule (21 CFR 830.300(a) and 830.320(b)) also requires that certain information be submitted to the Global Unique Device Identification Database (GUDID) (21 CFR Part 830 Subpart E). For additional information on these requirements, please see the UDI System webpage at <https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/unique-device-identification-system-udi-system>.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to <https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems>.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (<https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance>) and CDRH Learn (<https://www.fda.gov/training-and-continuing-education/cdrh-learn>). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (<https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory->

[assistance/contact-us-division-industry-and-consumer-education-dice](#)) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Xiaorui Tang -S

for CDR Jitendra Virani
Assistant Director
DHT5B: Division of Neuromodulation and
Physical Medicine Devices
OHT5: Office of Neurological and
Physical Medicine Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known)

K250096

Device Name

The Felix™ NeuroAI™ Wristband

Indications for Use (Describe)

The Felix™ NeuroAI™ Wristband is indicated to aid in tremor-related functional limitations in the upper limbs in adults with essential tremor.

Type of Use (Select one or both, as applicable)

Prescription Use (Part 21 CFR 801 Subpart D)

Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

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**510(k) Summary
(K250096)**

1. Applicant Information:

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Bloomington, MN 55437
Phone: 612.470.3441

2. Contact Person:

Zhen Zhang, Ph.D.
President, Fasikl Inc.
8500 Normandale Lake Blvd, Suite 400
Bloomington, MN 55437

3. Device Information:

Trade Name:	Felix™ NeuroAI™ Wristband
Common Name:	External upper limb tremor stimulator
Classification Name:	External upper limb tremor stimulator (21 CFR 882.5897)
Device Class:	II
Product Code:	QBC

4. Predicate Device:

510(k) Number: K203288
Trade Name: Cala Trio
Manufacturer: Cala Health, Inc

5. Date Prepared:

June 24, 2025

6. Device Description:

Fasikl's Felix™ NeuroAI™ Wristband is a wrist-worn, noninvasive, transcutaneous neurostimulation system. It is intended to be used by adult patients with essential tremor (ET) on a daily basis to aid in tremor-related functional limitations in the upper limbs. The system continuously monitors tremor frequency and tremor amplitude and automatically adjusts stimulation settings. The Felix system consists of the following components: Felix wristband (NeuroAI™ stimulator with integrated strap and detachable connector band), disposable electrode band, wireless charger, and smartphone application. Figure 6.0 below provides the schematics of the Felix system.

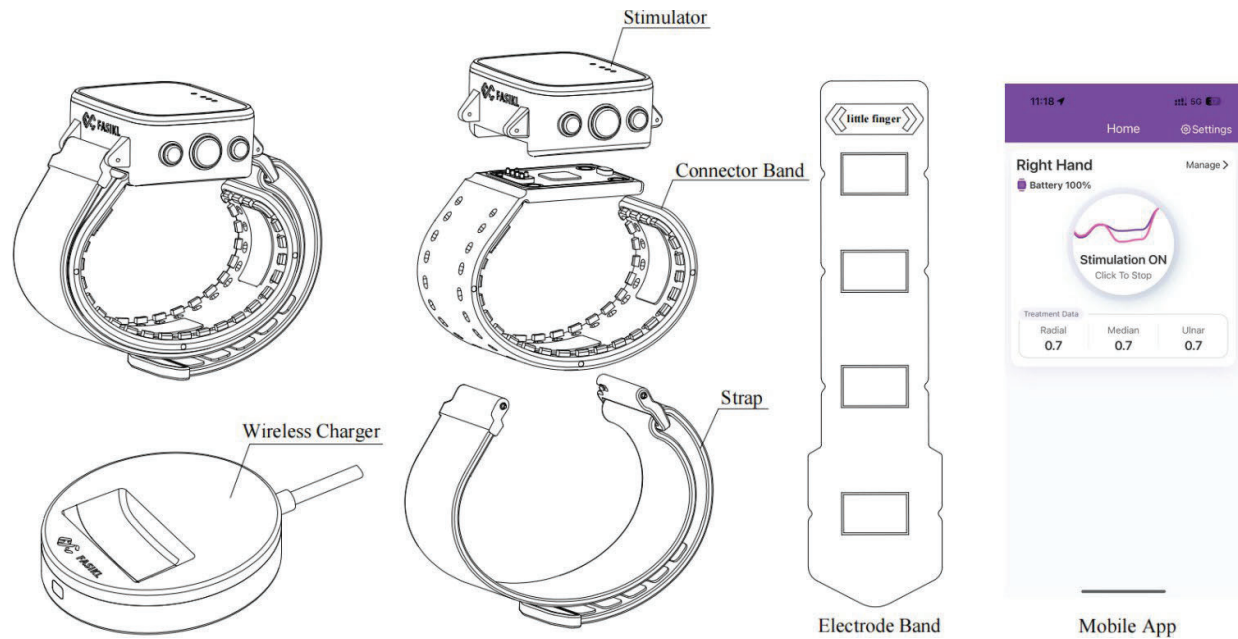


Figure 6.0: Felix NeuroAI System

6.1 NeuroAI Stimulator

The NeuroAI stimulator is a battery-powered and wrist-worn device that delivers transcutaneous electrical stimulation to the peripheral nerves in the wrist. The primary circuitry is a high-precision constant-current stimulator (CCS). It can generate biphasic stimulation pulses with current amplitude of up to 10mA and voltage compliance of 100V. The stimulation pulse-width, timing, and pattern are fully programmable with 1 μ s precision. The stimulator can support three output channels, which target three peripheral nerves accessible through the wrist area: the radial, median and ulnar nerves. Additional details regarding the output stimulation parameters are provided in Table 8.2 below.

The stimulator is equipped with a 6-axis inertial measurement unit (IMU) consisting of a 3-axis accelerometer and 3-axis gyroscope. The sensory data could be relayed wirelessly via Bluetooth Low Energy (BLE) to a smartphone and when applicable, further pushed to a cloud database for storage and further processing.

The stimulator has three side pushbuttons for simple controls such as on/off or adjusting stimulation amplitude. Other controls are done through the mobile device app.

6.2 Connector band

The connector band magnetically snaps into the stimulator's back. It provides electrical connections between the stimulator and the electrode band. The user will be fitted with a connector band from different sizes (S1, M1, M2, M3, L1, and L2), depending on their hand's anatomy.

6.3 Electrode band

The user will be fitted with an electrode band matching the connector band. The electrode band sticks to the wrist and provides a direct interface with the user's body. It electrically connects to the connector band via metalized contacts on the top. The electrode band is for one-time use and should be replaced daily or when the gel is no longer sticky.

6.4 Wireless Charger

The user can charge the Felix device by placing the simulator sideways (the side with buttons facing up) onto the charger base. The charger can be used with any standard USB 2.0 port with at least a 5V/1A power rating. An AC adapter may be provided separately.

6.5 Smartphone App

The app has full control over the stimulator, including starting/stopping stimulation, selecting stimulation parameters, and changing stimulation mode. It connects to the stimulator via Bluetooth (BLE). Real-time IMU data is streamed from the stimulator to the app via BLE. The app can communicate with a secure cloud database to store IMU data. In Artificial Intelligence (AI) closed-loop stimulation mode, the app will communicate with a secure cloud computing services for AI to determine the best stimulation setting for the user continuously and control the stimulator accordingly. The stimulation intensity will always stay below the threshold set by the user such that it will not cause discomfort or muscle contraction.

6.6 AI algorithm

The sole purpose of the AI algorithm is to control the stimulation state of the Felix device. It is NOT intended to be used for any diagnostic purposes and has no interpretable outputs. It automatically determines whether to turn stimulation on or off and at what stimulation intensity, based on measurements of the effects of stimulation on the severity of hand tremor (as assessed by the built-in accelerometer).

7. Indications for Use:

The FelixTM NeuroAITM Wristband is indicated to aid in tremor-related functional limitations in the upper limbs in adults with essential tremor.

8. Comparison to Predicate Device:

8.1. Intended Use/Indications for Use Comparison

The subject device and the predicate have the same intended use. Specifically, both devices are for transcutaneous stimulation for upper limb tremor related symptoms in essential tremor patients. The differences in indications for use are discussed in the table below and do not raise new questions of safety and effectiveness. Clinical data has been provided to support the modified indications for use.

8.2. Technological Characteristics

The subject device has similar technological characteristics and principles of operation as the predicate device. Both devices deliver electrical stimulation to the wrist. Both have a stimulator with on-board motion sensors that detach from the connecting band, in addition to electrodes embedded in the band that produce biphasic rectangular waveforms with a similar phase and pulse durations. In addition, both devices have embedded firmware that allow for control of device calibration, stimulation delivery, and measurement of tremors. Both devices are also provided non-sterile.

While there are some differences between the two devices in terms of technology (e.g. user interface, stimulation features, closed loop technology, as well as the energy source and device design), these differences do not raise new questions of safety and effectiveness. The differences in stimulation are shown not to impact safety or effectiveness of the device as determined by clinical evidence. Table 8.2 below provides technical comparison of the subject device and the predicate device.

TABLE 8.2: TECHNICAL COMPARISON OF THE SUBJECT DEVICE AND THE PREDICATE DEVICE

	Felix NeuroAI Wristband (Subject device)	Cala Trio K203288 (Predicate device)	Discussion of Differences
Regulation/ Product Code	882.5897 QBC	882.5897 QBC	Same
Intended Use	External stimulator designed to aid in tremor symptom relief of the upper limb.	External stimulator designed to aid in tremor symptom relief of the upper limb.	Same Per 21 CFR 88.5897, the Felix NeuroAI system and the predicate devices are prescription use devices that stimulate the upper limb to aid in tremor symptom relief of the upper limbs.
Indications for Use	The Felix NeuroAI TM Wristband is indicated to aid in tremor-related functional limitations in the upper limbs in adults with essential tremor.	Cala Trio device is indicated to aid in the temporary relief of hand tremors in the treated hand following stimulation in adults with essential tremor.	Different The predicate Cala device is limited to temporary relief of hand tremor. In contrast, the Felix NeuroAI Wristband provides closed-loop stimulation which allows for aiding in tremor-related functional limitations while the device is worn. This change in indication does not constitute a new intended use and clinical data has been provided to support the modified indications for use. The subject device indication also specified upper limb tremor while the predicate device is limited to hand tremor. <ul style="list-style-type: none"> The difference in the indication associated with “location/region” of symptom relief in the upper limb vs. hand does not change the intended use of the device which is to “aid in tremor symptom relief of the upper limb”.

	Felix NeuroAI Wristband (Subject device)	Cala Trio K203288 (Predicate device)	Discussion of Differences
			<ul style="list-style-type: none"> To aid in tremor-related functional relief in the upper limbs in the subject device is based on the clinical study results for the outcome measure of TETRAS mADL. The TETRAS mADL includes activities of daily living that involve the entire upper limb (e.g. feeding with a spoon, hygiene, dressing, pouring, carrying food trays, using keys). <p>The predicate device specifies that the treatment effect is specific to the “treated hand”. In contrast, the subject device does not limit the treatment effect to the treated hand.</p> <ul style="list-style-type: none"> This difference in the indication is supported by the clinical study which allowed participants the option of unilateral stimulation or bilateral stimulation. For unilateral stimulation, the wrist worn was decided by the investigator and patient. Unlike the primary endpoint for the predicate device (e.g. Isaacson et al., 2020¹¹) which evaluated tremor in the dominant arm, the primary endpoint for the clinical study for the subject device did not specify the hand that was being evaluated. Instead, the primary endpoint captured improvements in activities of daily living which involved tasks that are generally considered to be bimanual (e.g. working, hygiene, dressing). In all of these subtasks, participants using the Felix device reported significantly greater improvements as compared to

¹ Isaacson SH et al. Prospective Home-use Study on Non-invasive Neuromodulation Therapy for Essential Tremor. Tremor Other Hyperkinet Mov (N Y). 2020 Aug 14;10:29. doi: 10.5334/tohm.59. PMID: 32864188; PMCID: PMC7427656.

	Felix NeuroAI Wristband (Subject device)	Cala Trio K203288 (Predicate device)	Discussion of Differences
			<p>participants in the sham control arm.</p> <ul style="list-style-type: none"> The TETRAS mADL is a composite of ADL and PS items. ADL items are not associated with a particular limb. All TETRAS PS times were assessed by limb except for handwriting which was evaluated in the dominant limb. For the Felix group, there were significant changes in TETRAS PS ratings from baseline pre-stimulation to 90 days. This observation was consistent for both the stimulated and non-stimulated limb. <p>Compared to the predicate device, the subject device does not include the phrase “following stimulation”. The subject device provides transcutaneous stimulation based on an AI algorithm, which delivers the stimulation when the algorithm believes it is needed. As such, unlike the predicate device, the subject device can provide continuous aid in tremor symptom relief of the upper limbs when the device is worn.</p>
Design	Stimulator with on-board motion sensors that detach from the strap and the connector band.	Stimulator with on-board motion sensors that is detachable from wristband	<p>Similar</p> <ul style="list-style-type: none"> The difference in component attachment does not raise new questions of safety or effectiveness of the device. Per 21 CFR 882.5897(b)(1)(iii), stimulated use testing of sensor performance and software verification and validation of the device design was conducted.

	Felix NeuroAI Wristband (Subject device)	Cala Trio K203288 (Predicate device)	Discussion of Differences
	Wrist-worn band with four electrodes embedded in the band: three nerve electrodes of 4 cm ² and one return/common electrode of 10.5 cm ²	Wrist-worn band with three 4.84 cm ² electrodes embedded in the band that targets the median and radial nerves of a patient's wrist.	<p style="text-align: center;">Similar</p> <ul style="list-style-type: none"> • Changes in the electrode size and number do not raise new questions of safety and effectiveness. Non-clinical testing (e.g. biocompatibility, performance testing, electrical safety testing) was used to support that safety and effectiveness of the electrodes. • Additionally, targeting the additional ulnar nerve does not raise new question of safety or effectiveness. Clinical data is provided to support the ability of the device to meet the proposed indication.
	USB-powered wireless charging base that connects to any standard USB 2.0 port with at least 5V/1A power rating	AC-powered base station for recharging the stimulator Base Station includes an LTE antenna that provides connection and data transfer to cloud system which supports device operations such as device assistance and maintenance	<p style="text-align: center;">Different</p> <p>The difference in the charging component does not raise new questions of safety and effectiveness. Testing per AAMI/ANSI ES 60601-1 was conducted to support electrical safety of the device and charging base.</p>
	Embedded firmware and Smartphone application for control of device calibration, stimulation delivery, and device function.	Embedded firmware control of device calibration, stimulation delivery, and device function	<p style="text-align: center;">Similar</p> <p>Verification and validation testing was conducted to support compatibility across the device components and to ensure that the software meets the device design specification. Cybersecurity testing was provided to support the use of Smartphone.</p>

	Felix NeuroAI Wristband (Subject device)	Cala Trio K203288 (Predicate device)	Discussion of Differences
	<p>Device sensors (triaxial accelerometer, triaxial gyroscope) measure tremor motion and hand orientation</p>	<p>Device sensors (triaxial accelerometer) measure tremor motion</p>	<p>Similar</p> <p>The addition of orientation measurement does not raise new questions of safety or effectiveness of the device. Per special controls 21 CFR 882.5897(b)(1)(iii), verification and validation testing of sensor performance and associated algorithms were conducted.</p>
Features	<ul style="list-style-type: none"> • Set-up calibration • Stimulation intensity control • Therapy available on demand • Different stimulation modes: fixed stimulation and AI-adjusted stimulation • Continuous monitoring of tremor power. 	<ul style="list-style-type: none"> • Set-up calibration • Stimulation intensity control • Therapy available continuously or on demand 	<p>Similar</p> <p>The predicate device has the same features as the subject device which enables the user to setup and control therapy. Addition of fixed and AI-algorithm adjusted stimulation does not raise new question of safety and effectiveness. The safety and effectiveness of the stimulation paradigm of the subject device is supported through clinical data.</p>

	Felix NeuroAI Wristband (Subject device)	Cala Trio K203288 (Predicate device)	Discussion of Differences
User Interface	<ul style="list-style-type: none"> Smartphone app guides device setup, calibration, operation, and usage information. Three buttons on the device housing allow user control of the stimulation amplitude. 	<p>Stimulator display guides device setup, operation, and usage information.</p> <p>Three buttons on the device housing allows user control of the stimulation amplitude and device calibration</p>	<p>Similar</p> <p>The difference in the user interface does not raise new questions of safety or effectiveness.</p> <p>The addition of smartphone app's interface does not impact safety or effectiveness.</p> <p>Clinical evidence demonstrates that the difference in the user interface does not impact the safety or effectiveness of the device</p>
Prescription or OTC	Prescription	Prescription	Same
Sterility	Non-sterile	Non-sterile	Same
Materials	Biocompatible wrist band	Biocompatible wrist band	<p>Similar</p> <p>Differences in patient contacting materials does not raise new questions of safety and effectiveness. Biocompatibility assessments for all patient contacting components have been provided to support safety of device.</p>
Energy Source	Permanent 3.7V Lithium-Ion rechargeable battery	Permanent 3.8V Lithium-Ion rechargeable battery	<p>Similar</p> <p>The difference in battery voltage does not raise new questions of safety or effectiveness. The battery complies with IEC 62133-2 standard.</p>
Frequency of Use	The device is used as needed by the patient	The device is used as needed by the patient	<p>Similar</p> <p>Clinical evidence demonstrates that the frequency of use does not impact the safety or effectiveness of the device</p>
Band Use Life	Electrode band is for one-time use and should be replaced daily or when the gel is no longer sticky. Connector band should be replaced every 6 months.	90 days	<p>Different</p> <p>The difference in band use-life does raise new questions of safety or effectiveness. The Ag/AgCl electrode with wet-gel backing is standard for TENS stimulators.</p>

	Felix NeuroAI Wristband (Subject device)	Cala Trio K203288 (Predicate device)	Discussion of Differences
Principle of Operation	Apply transcutaneous stimulation to the peripheral nerves of the wrist to provide tremor relief	Apply transcutaneous stimulation to the peripheral nerves of the wrist to provide tremor relief	Same
Output Modes	3 alternative channels	2 alternating channels	Similar The number of channels that deliver stimulation does not raise new questions of safety and effectiveness. Evidence from clinical data is used to support the safety and effectiveness of an additional channel for stimulation.
Output	Current Regulated	Current Regulated	Same
Housing Materials	Plastic Velcro Straps (Nylon) Connector band: soft silicone and conductive silicone contacts	Plastic Velcro Straps (Nylon)	Similar Similar materials are used for the housing material in both devices. Biocompatibility assessment, verification and validation testing, and electrical and EMC testing have been conducted to support the safety and effectiveness of the device.
Waveform	Biphasic	Biphasic	Same
Shape	Rectangular	Rectangular	Same
Maximum Output Voltage (volts)	5 @ 500Ω	4 @ 500Ω ²	Different Clinical evidence demonstrates that the difference in maximum output voltage does not impact safety or effectiveness of the device

² Based on 510k Summary for the Cala device in K222237 (which used Cala Trio as the predicate device): https://www.accessdata.fda.gov/cdrh_docs/pdf22/K222237.pdf

	Felix NeuroAI Wristband (Subject device)	Cala Trio K203288 (Predicate device)	Discussion of Differences
	100 @ 10kΩ	80 @ 10kΩ	
Maximum Output Current (mA)	10 @ 500Ω	8 @ 500Ω	Different Clinical evidence demonstrates that the difference in maximum output current does not impact safety or effectiveness of the device
	9 @ 10kΩ	8 @ 10kΩ	
Duration of primary (depolarizing) phase (µsec)	300	300	Same
Pulse Duration (µsec)	650	650	Same
Frequency (Hz)	Pulse-to-pulse interval is uniformly randomized from 2ms – 18ms (56 – 500 Hz) for individual pulse, with a mean of 10ms (100Hz).	150	Same
Symmetrical phases?	Yes	Yes	Same
Phase Duration (µS)	300 each phase	300 each phase	Same
Net Charge (µC)	0 @500Ω	0 @500Ω	Same
Maximum Phase Charge (µC)	3 @ 500Ω	2.4 @ 500Ω	Different Clinical evidence demonstrates that the differences in maximum phase charge does not impact safety or effectiveness of the device

	Felix NeuroAI Wristband (Subject device)	Cala Trio K203288 (Predicate device)	Discussion of Differences
Maximum Current Density (mA/cm², r.m.s.)	0.61 @ 500Ω	0.5 @ 500Ω ³	Different Clinical evidence demonstrates that the difference in maximum current density does not impact safety or effectiveness of the device
Maximum Average Current (mA) (average absolute value)	0.6 @ 500Ω	0.72 @ 500Ω	Different Clinical evidence demonstrates that the difference in maximum average current does not impact safety or effectiveness of the device
Maximum Average Power Density (mW/cm²)	0.75 @ 500Ω	0.59 @ 500Ω	Different Clinical evidence will be provided to demonstrate that the difference in maximum average power density does not impact safety or effectiveness of the device. Additionally, the maximum average power density is lower than the 0.25W/cm ² threshold to reduce the risk of thermal burns ⁴ .

9. Non-Clinical Performance Data:

The following performance data were provided to demonstrate safety and efficacy in support of substantial equivalence determination:

9.1 Software verification and validation testing

Software verification and validation testing was conducted and documentation provided as recommended by the FDA Guidance for Industry and FDA Staff, entitled “Content of Premarket Submissions for Device Software Functions” issued on June 2023. Verification and validation testing includes:

- Code inspections
- Unit level testing
- Integration level testing
- System level testing
- ML/AI Algorithm Verification Testing

³ Based on 510k Summary for a more recent Cala device clearance K222237 (which used Cala Trio as the predicate device): https://www.accessdata.fda.gov/cdrh_docs/pdf22/K222237.pdf

⁴ FDA Guidance: Guidance Document for Powered Muscle Stimulator 510(k) (issued on June 9, 1999): <https://www.fda.gov/media/71804/download>

Felix NeuroAI Wristband uses a control algorithm to set the controller output variable associated with the stimulation to treat tremor of the upper limb. As such, the device meets the definition of a physiologic closed-loop control system and was evaluated and conforms to FDA recognized consensus standard:

- IEC 60601-1-10 Edition 1.2 2020-07: General requirements for basic safety and essential performance – Collateral Standard: Requirements for the development of physiologic closed-loop controllers.

9.2 Bench Performance Testing

Table 9.2 Special Control Bench Testing Summary

Test Name	Test scope	Special Control per 21 CFR 882.5897(b)
Stimulation Test	Test the pulse width, amplitude, rising time, falling time, pulse interval, current adjustment step value, and charge balancing, and observe whether the waveform meets the design input requirements.	1i
Electrode Band Adhesion and Impedance Test	Verify that the adhesion and impedance performance of the Electrode band meets the requirements specified by FASIKL.	1ii
Gel Electrode Current distribution Test	The objective of the test is to measure the current distribution on the surface of the gel electrodes for the Felix-G1 watch device	1ii
IMU Test	Test the accuracy of the vibration frequency and acceleration values recorded by the Felix device to meet the design requirements.	1iii

9.3 Electromagnetic Compatibility (EMC)/ Electrical Safety Testing/Wireless

- IEC 60601-1: Medical electrical equipment - Part 1: General requirements for basic safety and essential performance
- IEC 60601-1-2: Medical electrical equipment - Part 1-2: General requirements for basic safety and essential performance - Collateral Standard: Electromagnetic disturbances - Requirements and tests
- IEC 60601-1-11: Medical electrical equipment - Part 1-11: General requirements for basic safety and essential performance - Collateral Standard: Requirements for medical electrical equipment and medical electrical systems used in the home healthcare environment
- IEC 60601-2-10: Particular requirements for the basic safety and essential performance of nerve and muscle stimulators

- IEC 62133-2: Secondary cells and batteries containing alkaline or other non-acid electrolytes - Safety requirements for portable sealed secondary cells and for batteries made from them for use in portable applications - Part 2: Lithium systems
- IEEE/ANSI USEMCSC C63.27-2021: American National Standard for Evaluation of Wireless Coexistence.

9.4 Biocompatibility

A biocompatibility assessment was conducted on all skin contacting components. Testing was conducted in accordance with FDA’s guidance entitled “Use of International Standard ISO 10993-1, Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process”. All test results demonstrated acceptable biocompatibility for the patient contacting components.

9.5 Shelf-life and service life

The shelf-life of the device and various components were evaluated and found to meet the design specifications of the device. Durability testing was also conducted to evaluate the service life of the device components.

10. Clinical Testing

10.1. Clinical Study Design

10.1.1. Study Overview

The TRANQUIL study was a prospective, randomized, sham-controlled, double-blinded, multi-center, multi-region clinical trial (MRCT). Eight (8) sites in the US and four (4) sites outside the US (in China) participated in the study. Patients who met all the inclusion and none of the exclusion criteria after screening were randomized in a 2:1 ratio to either the Felix group or the sham stimulation group. The Felix group received the Felix device while the participants in the Sham group received a device that was identical to that of the Felix device, however it did not deliver any electrical stimulation. Instead, the sham device generated a brief vibration alert from inside the stimulator case and randomly vibrated throughout the day, averaging one vibration alert every five minutes.

During the baseline visit, patients first went through pre-stimulation assessments and then were fitted with the Felix or the sham device(s). Sites and patients jointly determined whether to perform unilateral stimulation or bilateral stimulation, and which side to wear the device for unilateral stimulation. Patients were stimulated for 40 minutes and went through post-stimulation assessments and device training before being discharged from the baseline clinic visit. After discharge, patients were strongly encouraged to use the device as much as possible during waking hours every day. The patient's tremor was evaluated during follow-up visits scheduled for 14 days, 30 days, 60 days, and 90 days after the baseline evaluation.

Patients and raters assessing the effectiveness endpoints were blinded to the treatment assignment until the end of the 90-day visit. Safety was assessed using adverse event data collected during the study.

10.1.2. Key Inclusion Criteria:

1. At least 18 years of age.
2. A clinical diagnosis of ET by a movement disorder specialist.
3. For the dominant hand, a tremor severity score of 2 or higher as measured by one of the six Tremor Research Group Essential Tremor Rating Assessment Scale (TETRAS) Performance Subscale (PS) tasks: forward outstretch, lateral wing beating, kinetic, spiral drawing, handwriting, and dot approximation, and a total score of 7 or higher. If applicable, this must be met while the patient is on ET treatment.
4. Stable dosage of anti-tremor medications, if applicable, for 30 days prior to study entry.
5. Stable dosage of antidepressant medications, if applicable, for 90 days prior to study entry.
6. Familiar with operating a touch-screen smartphone and connecting to Wi-Fi internet at home.

10.1.3. Key Exclusion Criteria:

1. Prior limb amputation or any known symptomatic peripheral neuropathy condition of the involved upper extremity.
2. Prior surgical intervention for ET such as deep brain stimulation or thalamotomy.
3. Moderate to severe alcohol use disorder (AUD) as per Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-5) (the presence of at least 4 symptoms or more).
4. Any current drug abuse.
5. Current unstable epileptic conditions with a seizure within 6 months of study entry.
6. Other possible causes of tremor such as drug-induced tremor, enhanced physiological tremor, dystonia, and Parkinson's disease.
7. Pregnant or nursing subjects and those who plan pregnancy during the course of the study.
8. Swollen, infected, inflamed areas, or skin eruptions, open wounds, or cancerous lesions of skin at the stimulation site.
9. Known allergy to adhesive bandages.
10. Botulinum Toxin injection for hand tremor within 4 months prior to study enrollment.

10.1.4. Study Endpoints

10.1.4.1. Primary Effectiveness Endpoint

Change in TETRAS modified Activities of Daily Living (mADL) score from baseline pre-stimulation to Day 90, Superiority of Felix versus Sham stimulation. The TETRAS mADL score is a composite sum of items 2 to 11 of the TETRAS ADL subscale and items 6 (bilateral) and 7 (dominant hand) of the TETRAS performance subscale (PS). These items are listed below. TETRAS mADL score is calculated as the sum of all 12 items and ranges from 0 to 52.

- TETRAS ADL items (patient rating based on the prior week, each item is rated on a scale from 0 to 4, representing increasing difficulty in doing the activity due to tremor, from normal to severely abnormal/cannot perform the activity):
 - Feeding with a spoon
 - Drinking from a glass
 - Hygiene
 - Dressing
 - Pouring
 - Carrying food trays, plates or similar items
 - Using keys
 - Writing
 - Working (if patient is retired, ask as if they were still working. If the patient is a housewife, ask the question as it relates to housework)
 - Overall disability with the most affected task (name task, e.g. using computer mouse, writing, etc.)
- TETRAS PS items (physician rating, each item is rated on a scale from 0 to 4, representing increasing severity of tremor, from normal to severe):
 - Archimedes spirals (both hands, rated separately)
 - Handwriting (dominant hand)

10.1.4.2. Key Secondary Effectiveness Endpoints:

- Change in TETRAS mADL score from baseline pre-stimulation to 14 days, 30 days, and 60 days.
- TETRAS Performance Subscale (items 1, 4 and 8) at baseline pre-stimulation, baseline post-stimulation, 30 days, 90 days
- TETRAS Performance Subscale (items 6 and 7) at baseline pre-stimulation, baseline post-stimulation, 14 days, 30 days, 60 days, 90 days.
- TETRAS Dominant Hand Score at baseline pre-stimulation, baseline post-stimulation, 30 days, 90 days. Defined as the total scores of TETRAS Performance Subscale for the dominant hand (items 4, 6, 7 and 8)
- Clinical Global Impression of Improvement (CGI-I) baseline post-stimulation, 30 days, 90 days
- Patient Global Impression of Improvement (PGI-I) at baseline post-stimulation, 14 days, 30 days, 60 days, 90 days
- Quality of Life in Essential Tremor Questionnaire (QUEST) at baseline pre-stimulation, 90 days

10.1.4.3. Safety Endpoints:

- Adverse events (AEs) and serious adverse events (SAEs)
- Adverse device effects (ADEs) and serious adverse device effects (SADEs)
- Unanticipated adverse device effect (UADE) and unanticipated serious adverse device effect (USADE)

10.2. Statistical Considerations

10.2.1. Analysis populations

- **Intent to Treat (ITT) set:** the ITT analysis set is defined as patients who have been randomized. In accordance with the ITT principle, subjects will be kept in their originally assigned treatment group.
- **Modified Intent to Treat (mITT) set:** it is the dataset that includes all the patients who have been randomized and have gone through at least 1 day of at-home treatment.
- **Per-Protocol Set (PPS):** it refers to a subset of the ITT subjects who complete the evaluation of primary performance endpoint without major protocol deviation affected the evaluation of primary performance endpoint.

The primary analysis of the primary endpoint was based on the ITT population.

10.2.2. Missing Data Handling

In the prespecified primary analysis, patients with missing data were excluded from the analysis. This analysis is unbiased for the ITT population under the assumption that all patients with missing primary endpoint data are Missing-Completely-At-Random (MCAR), which is a “strong assumption, unlikely to hold in many missing data settings that are not under the control of the investigators in clinical trials”⁵. This analysis is presented in Section 10.3.4, Table 10.3.4.1.

A supplementary *post-hoc* primary analysis was performed (Table 10.3.4.2) which imputed data under more clinically reasonable assumptions; this analysis is viewed by the Agency as more clinically relevant and interpretable and was regarded as the primary scientific evidence for demonstrating the device’s substantially equivalent effectiveness to the predicate. The prespecified primary analysis of Table 10.3.4.1 which excluded subjects with missing data was considered supportive. Missing data were imputed using a mixed-effect model for repeated measures (MMRM) under the following assumptions:

- Patients who withdrew from the study due to adverse events were assumed to be missing not at random (MNAR) and their treatment effect at 90 days were assumed to be zero.
- Other patients with missing data were assumed to be missing at random (MAR). The imputation for missing data was inherent in the statistical models.

10.2.3. Safety Analysis

Adverse events were summarized according to the latest MedDRA coding dictionary. Safety analysis was based on the ITT population

10.2.4. Blinding

A blinding assessment was performed at the end of the randomized phase (90-day visit). Patients were asked to guess which treatment arm they were assigned to, which were compared to the actual assignment.

10.3. Study Results

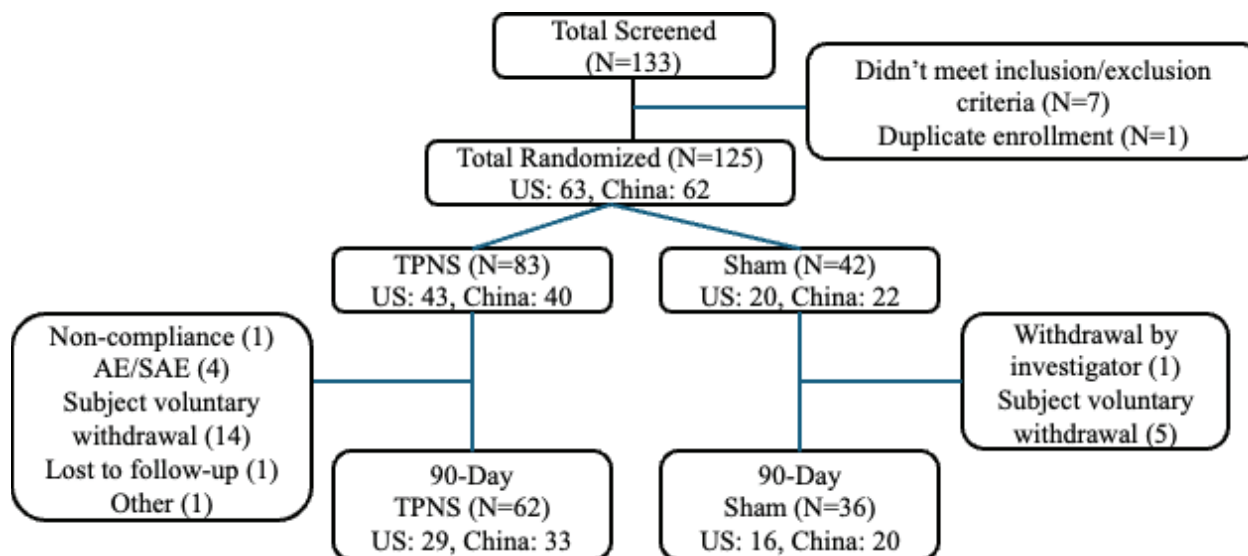
Results from the mITT and PPS populations were similar to the ITT population, therefore only the ITT results were summarized below.

⁵ National Research Council (US) Panel on Handling Missing Data in Clinical Trials. The Prevention and Treatment of Missing Data in Clinical Trials. Washington (DC): National Academies Press (US); 2010.

10.3.1. Subject Disposition

Details of subject disposition were shown in Figure 10.3.1. In summary, 133 subjects were screened, 125 subjects were enrolled and randomized. A total of 83 patients were randomized to the Felix group, of which 21 subjects discontinued within 90 days. A total of 42 patients were randomized to the sham stimulation group, of which 6 subjects discontinued within 90 days.

Figure 10.3.1 Subject disposition



10.3.2. Baseline Patient Information

Baseline patient information was shown in Table 10.3.2 below. The average age of subjects in the Felix group and the sham stimulation group was 63.8 ± 13.88 vs. 67.2 ± 11.37 years, respectively. There were 44 female subjects (53.0%) vs. 18 female subjects (42.9%) in the two groups, respectively. The average BMI of two groups was 26.1 ± 4.69 vs. 25.4 ± 4.45 kg/m², respectively. The average duration of essential tremor (ET) in the Felix group was 11.3 ± 12.8 years, compared to 11.6 ± 13.9 years in the sham stimulation group. Prior to participating in the study, 45 subjects (54.2%) in the Felix group and 21 subjects (50.0%) in the sham group received treatment for ET. Anti-tremor medications were used by 33 subjects (39.8%) in the Felix group and 17 subjects (40.5%) in the sham group, while antidepressant medications were used by 13 subjects (15.7%) and 4 subjects (9.5%), respectively. Baseline TETRAS performance score, which was a screening criterion, was 12.3 ± 3.1 in the Felix group and 12.9 ± 3.1 in the sham group.

Table 10.3.2. Demographics and Clinical Characteristics of Participants at Baseline

	Felix (N=83)	Sham (N=42)
Age (years), mean \pm SD (range)	63.8 \pm 13.9 (20, 86)	67.2 \pm 11.4 (35, 88)
Female sex, n (%)	44 (53.0)	18 (42.9)
BMI (kg/m ²), mean \pm SD (range)	26.1 \pm 4.7 (18.0, 41.3)	25.4 \pm 4.4 (15.1, 36.6)
Duration of ET (years), mean \pm SD (range)	11.3 \pm 12.8 (0, 56.0)	11.6 \pm 13.9 (0, 49.9)
Prior ET treatment, n (%)	45 (54.2)	21 (50.0)
Current ET medication, n (%)	33 (39.8)	17 (40.5)
Family history of ET, n (%)	42 (50.6)	26 (61.9)
Current antidepressant medication, n (%)	13 (15.7)	4 (9.5)
TETRAS performance score, mean \pm SD (range)	12.3 \pm 3.1 (5.5, 22.5)	12.9 \pm 3.1 (7.0, 19.0)

10.3.3. Device Usage

Device usage during the study was summarized in Table 10.3.3 below. The average total wearing days were 69.0 ± 31.44 and 75.7 ± 26.08 days in the Felix and the sham group, respectively. Patients wore the device 8.6 ± 2.39 hours daily in the Felix group and 9.5 ± 2.73 hours in the sham group. 98.8% of subjects in the Felix group chose unilateral stimulation and 1.2% chose bilateral. 95.2% of subjects in the sham group chose unilateral stimulation and 4.8% chose bilateral. 89.2% of subjects in the Felix group stimulated their dominant hand and 10.8% stimulated the non-dominant hand. In the sham group, 95.2% stimulated their dominant hand and 4.8% stimulated the non-dominant hand.

Table 10.3.3 Device Usage Summary

	Felix (N=83)	Sham (N=42)
Total Usage (Days), mean \pm SD	69.0 ± 31.4	75.7 ± 26.1
Daily Usage (Hours), mean \pm SD	8.6 ± 2.4	9.5 ± 2.7
Stimulation		
Unilateral	82 (98.8%)	40 (95.2%)
Bilateral	1 (1.2%)	2 (4.8%)
Stimulated Hand		
Dominant	74 (89.2%)	40 (95.2%)
Non-dominant	9 (10.8%)	2 (4.8%)

10.3.4. Primary Effectiveness Endpoint

Results of the prespecified primary effectiveness analysis are shown in Table 10.3.4. The average TETRAS mADL scores of subjects in the Felix group and the sham stimulation group were 29.9 ± 7.26 and 29.5 ± 7.80 ($P=0.7708$) at baseline pre-stimulation, respectively. The average TETRAS mADL scores of subjects in two groups at 90 days were 22.7 ± 8.81 and 27.0 ± 9.20 , respectively. The average TETRAS mADL score differences (90 days-baseline pre-stimulation) in the two groups were -6.9 ± 5.96 vs. -2.7 ± 4.12 , respectively.

The difference of the average of the paired difference in the TETRAS mADL scores between 90 days follow-up and baseline pre-stimulation in two groups was -4.2 , the 95% confidence interval was $[-6.2, -2.2]$, the p-value was less than 0.0001, which was less than a pre-specified one-sided superiority alpha of 0.025. The primary effectiveness endpoint was met, and Felix was shown to be superior to sham in change in TETRAS mADL score from baseline pre-stimulation to 90 days.

Table 10.3.4.1 Primary Effectiveness Endpoint (Patients with Non-missing Primary Endpoint Data)

				Difference (90 days- baseline pre- stimulation)		Difference [95% CI]	P-value
		Felix (N=83)	Sham (N=42)	Felix (N=83)	Sham (N=42)		
Visit							
Baseline pre- stimulation	n	83	42				
	Mean (SD)	29.9 (7.26)	29.5 (8.00)				
90 days	n	62	36	62	36		
	Mean (SD)	22.7 (8.81)	27.0 (9.20)	-6.9 (5.96)	-2.7 (4.12)	-4.2 [-6.2, -2.2]	<0.0001

Using the missing data imputation method described in section 10.2.2 above, the imputed primary endpoint results were shown in Table 10.3.4.2 below. The difference of the average of the paired difference in the TETRAS mADL scores between 90 days follow-up and baseline pre-stimulation in two groups was -3.4, the 95% confidence interval was [-5.6, -1.2], the p-value was 0.0032. The primary effectiveness endpoint was met based in MMRM imputed data.

Table 10.3.4.2 Primary Effectiveness Endpoint (MMRM Imputation)

Felix (N=83)	Sham (N=42)	Difference [95% CI]	P-value
-6.3 [-7.6, -5.0]	-2.9 [-4.7, -1.1]	-3.4 [-5.6, -1.2]	0.0032

10.3.5 Secondary Effectiveness Endpoint

Results for secondary effectiveness endpoints are reported descriptively below, since the study was not statistically powered for these endpoints, and these endpoints were not subjected to prospective statistical control of type-I error. These analyses are intended to provide additional support for and further explicate the primary finding.

10.3.5.1. Components of the Primary Effectiveness Endpoint

The components of the primary effectiveness endpoint of change in TETRAS mADL from baseline pre-stimulation to 90 days based on patients with non-missing primary endpoint data are shown in Table 10.3.5.1 below.

Table 10.3.5.1 Components of the Primary Effectiveness Endpoint (Patients with Non-missing Primary Endpoint Data)

			Difference (90 days-baseline pre-stimulation)			
			Felix (N=83)	Sham (N=42)	Felix (N=83)	Sham (N=42)
Visit						
TETRAS ADL score (Items 2-11)	Baseline pre-stimulation	n	83	42		
		Mean (SD)	23.42 (5.94)	22.73 (6.61)		
	90 days	n	62	36	62	36
		Mean (SD)	17.63 (7.07)	21.06 (7.20)	-5.47 (5.35)	-1.53 (3.73)
TETRAS PS score (Items 6 and 7)	Baseline pre-stimulation	n	83	42		
		Mean (SD)	6.47 (2.00)	6.90 (2.39)		
	90 days	n	62	36	62	36
		Mean (SD)	5.04 (2.29)	5.94 (2.47)	-1.40 (1.53)	-1.13 (1.55)

10.3.5.2. Change in TETRAS mADL score over time

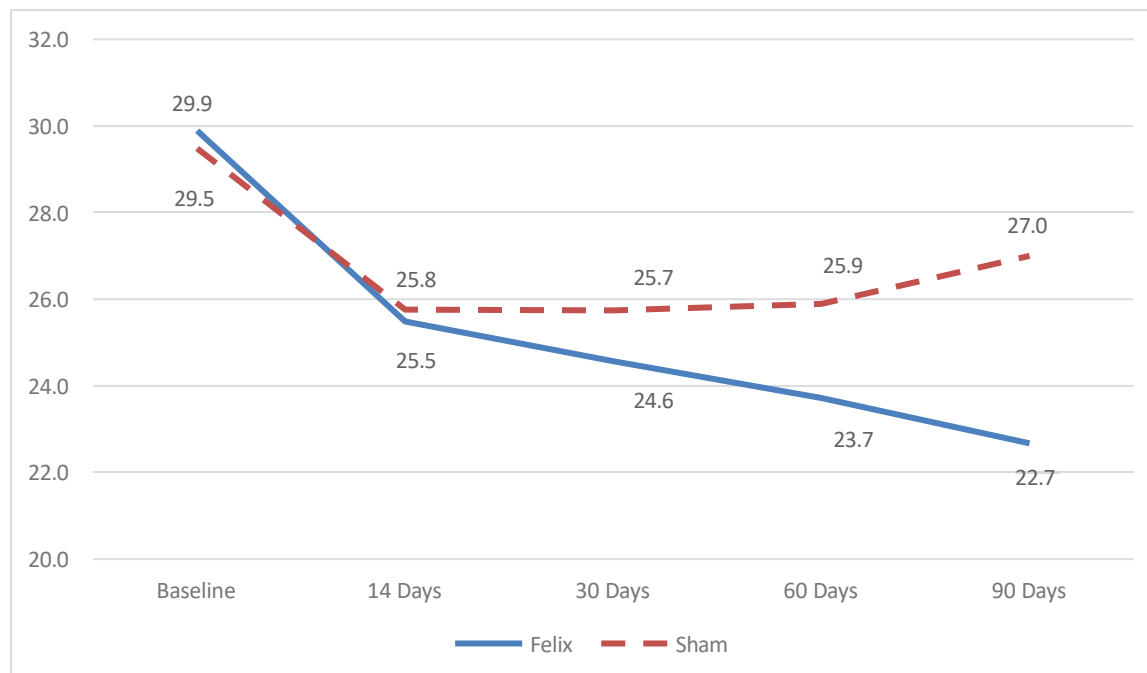
Change in TETRAS mADL score overtime based on patients with non-missing primary endpoint data was presented in Table 10.3.5.2.1. TETRAS mADL score over time were shown in Figure 10.3.5.2.1.

Change from baseline pre-stimulation to 14 days, 30 days, and 60 days in the Felix vs. the sham stimulation group were -4.4 ± 4.24 vs. -3.5 ± 5.05 , -5.1 ± 4.40 vs. -3.5 ± 4.80 , and -6.0 ± 4.98 vs. -3.3 ± 4.12 , respectively. Treated effect of the sham group plateaued at 14 days while the treatment effect of the Felix group continued to improve over time.

Table 10.3.5.2.1 Change in TETRAS mADL Score over Time (Patients with Non-missing Primary Endpoint Data)

Visit		Difference (90 days-baseline pre-stimulation)			
		Felix (N=83)	Sham (N=42)	Felix (N=83)	Sham (N=42)
Baseline pre-stimulation	n	83	42		
	Mean (SD)	29.9 (7.26)	29.5 (8.00)		
14 days	n	74	38	74	38
	Mean (SD)	25.5 (8.13)	25.8 (8.56)	-4.4 (4.23)	-3.5 (5.05)
30 days	n	67	38	67	38
	Mean (SD)	24.6 (7.42)	25.7 (9.02)	-5.1(4.39)	-3.5 (4.80)
60 days	n	64	35	64	35
	Mean (SD)	23.7 (8.03)	25.9 (9.40)	-6.0 (4.98)	-3.3 (4.12)
90 days	n	62	36	62	36
	Mean (SD)	22.7 (8.81)	27.0 (9.20)	-6.9 (5.96)	-2.7 (4.12)

Figure 10.3.5.2.1 TETRAS mADL Score over Time (Patients with Non-missing Primary Endpoint Data)



Change in TETRAS mADL score overtime based on MMRM imputation was presented in Table 10.3.5.2.2, which showed a similar trend as seen in the complete data analysis.

Table 10.3.5.2.2 Change in TETRAS mADL Score over Time (MMRM Imputation)

Visit	Difference (90 days-baseline pre-stimulation)	
	Felix (N=83)	Sham (N=42)
14 days	-4.3 [-5.3, -3.2]	-3.5 [-5.0, -2.1]
30 days	-5.0 [-6.1, -4.0]	-3.6 [-5.0, -2.1]
60 days	-5.7 [-6.9, -4.6]	-3.2 [-4.8, -1.7]
90 days	-6.3 [-7.6, -5.0]	-2.9 [-4.7, -1.1]

10.3.5.3. Other Secondary Effectiveness Endpoints

Results of other secondary effectiveness endpoints at 90 days were presented in Table 10.3.5.3 for patients with non-missing data for each assessment timepoint. The study was not statistically powered for these secondary endpoints, and their analysis did not involve prospective Type I error control.

For clinical global impression of improvement (CGI-I), the number (percentage) of patients achieved any improvement (including very much improved, much improved and minimally improved) at 90 days in the Felix vs. the sham stimulation group was 43 (69.4%) vs. 16 (44.4%), respectively. A higher percentage of patients in the Felix group achieved any improvement at 90 days than that of the sham stimulation group.

For patient global impression of improvement (PGI-I), the number (percentage) of patients achieved any improvement (including very much improved, much improved and minimally improved) at 90 days in the Felix vs. the sham stimulation group was 42 (67.7%) vs. 18 (50.0%), respectively. A higher percentage of patients in the Felix group achieved any improvement at 90 days than that of the sham stimulation group.

The total score of the QUEST questionnaire included communication score, work and finances score, hobbies and leisure score, physical and psychosocial score, and less score indicates more improvement of patients' life quality in ET.

Total scores of QUEST at baseline pre-stimulation and 90 days in the Felix vs. the sham stimulation group were 32.1 ± 16.78 vs. 31.6 ± 17.79 and 24.6 ± 14.71 vs. 28.1 ± 17.25 , respectively. The average change of total scores from 90 days to baseline pre-stimulation in two groups was -6.0 ± 10.77 vs. -3.4 ± 7.87 .

Table 10.3.5.3 Other Secondary Effectiveness Endpoints

			Felix (N=83)	Sham (N=42)
Endpoint	Visit			
CGI-I	90 Days	n	62	36
		Very much improved	2 (3.2%)	0
		Much improved	11 (17.7%)	4 (11.1%)
		Minimally improved	30 (48.4%)	12 (33.3%)
		No change	19 (30.6%)	20 (55.6%)
		Any improvement	43 (69.4%)	16 (44.4%)
PGI-I	90 Days	n	62	36
		Very much improved	1 (1.6%)	0
		Much improved	11 (17.7%)	4 (11.1%)
		Minimally improved	30 (48.4%)	14 (38.9%)
		No change	20 (32.3%)	15 (41.7%)
		Minimally worse	0	1 (2.8%)
		Much worse	0	1 (2.8%)
		Very much worse	0	1 (2.8%)
		Any improvement	42 (67.7%)	18 (50.0%)
QUEST Total Score	Baseline	n	83	42
		Mean (SD)	32.1 (16.78)	31.6 (17.79)
	90 Days	n	62	36
		Mean (SD)	24.6 (14.71)	28.1 (17.25)
	Difference	n	62	36
		Mean (SD)	-6.0 (10.77)	-3.4 (7.87)

10.3.5.4. Responder Analysis of the Primary Effectiveness Endpoint

Two responder analyses of the primary effectiveness endpoint on patients with non-missing primary endpoint data were performed.

The first responder analysis was performed using two different cut-offs for TETRAS mADL, with thresholds corresponding to the average TETRAS mADL change at 90-days among subjects who were rated as “minimally improved” on CGI-I (-5.58) or PGI-I (-6.19) assessments. Responder rate was calculated for each treatment group by the proportion of patients with change in TETRAS mADL scores by 90 days equal or less than the corresponding cut-off, i.e., more improvement. The results were summarized

in Table 10.3.5.4.1. The responder rate for the CGI-I cut-off was 61.3% in the Felix group and 16.7% in the sham group. The responder rate for the PGI-I cut-off was 59.7% in the Felix group and 11.1% in the sham group. The Felix group had higher responder rate than the sham group in the primary effectiveness endpoint.

Table 10.3.5.4.1 Responder Analysis of the Primary Effectiveness Endpoint (TETRAS mADL) at 90-days for Patients with Non-missing Primary Endpoint Data based on CGI-I/PGI-I

Anchor	Cut-off	Felix Responder Rate (N=62)	Sham Responder Rate (N=36)
CGI-I	-5.58	61.3% (38/62)	16.7% (6/36)
PGI-I	-6.19	59.7% (37/62)	11.1% (4/36)

The second responder analysis was performed based on the relative reduction in TETRAS mADL score at or above 10%, 20%, and 30% from baseline pre-stimulation to 90 days. As shown in Table 10.3.5.4.2 below, the responder rate for 10% relative reduction was 71.0% in the Felix group and 38.9% in the sham group. The responder rate for 20% relative reduction was 61.3% in the Felix group and 25.0% in the sham group. The responder rate for 30% relative reduction was 35.5% in the Felix group and 19.4% in the sham group. At each level of improvement, the Felix group had a higher responder rate than the sham group in the primary effectiveness endpoint.

Table 10.3.5.4.2 Responder Analysis of the Primary Effectiveness Endpoint (TETRSS mADL) at 90-days for Patients with Non-missing Primary Endpoint Data based on Relative Reduction

Relative Reduction in TETRAS mADL	Felix Responder Rate (N=62)	Sham Responder Rate (N=36)
≥10%	71.0% (44/62)	38.9% (14/36)
≥20%	61.3% (38/62)	25.0% (9/36)
≥30%	35.5% (22/62)	19.4% (7/36)

10.4. Adverse Events

Table 10.4.1 provided an overall summary of adverse events. During the study, 47.0% of subjects in the Felix group and 9.5% of subjects in the sham stimulation group experienced adverse events. Details of adverse events were provided in Table 10.4.2. Serious adverse events occurred in 2.4% of subjects in both groups. The difference between the two groups was mainly due to adverse device effects (ADEs), which occurred in 33.7% of subjects in the Felix group and 4.8% of subjects in the sham stimulation group. Details of ADEs were summarized in Table 10.4.3.

There was no serious adverse device effect and no unanticipated serious adverse device effect. 2 subjects in the Felix group experienced unanticipated adverse device effect, including 1 case of mild nausea and 1 case of worsening of pre-existing arthritis in the thumb.

Table 10.4.1 Overall Adverse Events Summary

	Felix (N=83)	Sham (N=42)
Adverse event	39 (47.0%)	4 (9.5%)
Serious adverse event	2 (2.4%)	1 (2.4%)
Adverse device effect	28 (33.7%)	2 (4.8%)
Serious adverse device effect	0	0
Unanticipated adverse device effect	2 (2.4%)	0
Unanticipated serious adverse device effect	0	0

Table 10.4.2 Adverse Events

	Felix (N=83)	Sham (N=42)
Injury, poisoning and procedural complications	7 (8.4%)	0
Contusion	2 (2.4%)	0
Buttock injury	1 (1.2%)	0
Cartilage injury	1 (1.2%)	0
Fall	1 (1.2%)	0
Head injury	1 (1.2%)	0
Limb injury	1 (1.2%)	0
Neck injury	1 (1.2%)	0
General disorders and administration site conditions	6 (7.2%)	2 (4.8%)
Medical device site joint erythema	2 (2.4%)	0
Medical device site rash	2 (2.4%)	0
Chest discomfort	1 (1.2%)	0
Fatigue	1 (1.2%)	0
Medical device site pruritus	1 (1.2%)	0
Chest pain	0	1 (2.4%)
Influenza like illness	0	1 (2.4%)
Medical device site reaction	0	1 (2.4%)
Infections and infestations	5 (6.0%)	2 (4.8%)
Urinary tract infection	1 (1.2%)	1 (2.4%)
Influenza	1 (1.2%)	0
Nasopharyngitis	1 (1.2%)	0
Papilloma viral infection	1 (1.2%)	0
Respiratory tract infection	1 (1.2%)	0
Bronchitis	0	1 (2.4%)
Musculoskeletal and connective tissue disorders	5 (6.0%)	1 (2.4%)
Arthralgia	1 (1.2%)	0
Arthritis	1 (1.2%)	0
Limb discomfort	1 (1.2%)	0
Muscular weakness	1 (1.2%)	0
Temporomandibular pain and dysfunction syndrome	1 (1.2%)	0
Myofascitis	0	1 (2.4%)
Gastrointestinal disorders	4 (4.8%)	0
Abdominal distension	1 (1.2%)	0
Constipation	1 (1.2%)	0

Nausea	1 (1.2%)	0
Toothache	1 (1.2%)	0
Skin and subcutaneous tissue disorders	22 (26.5%)	1 (2.4%)
Skin irritation	2 (2.4%)	0
Rash	19 (22.9%)	1 (2.4%)
Erythema	1 (1.2%)	0
Cardiac disorders	2 (2.4%)	0
Atrial fibrillation	1 (1.2%)	0
Cardiac flutter	1 (1.2%)	0
Surgical and medical procedures	2 (2.4%)	0
Carpal tunnel decompression	1 (1.2%)	0
Spinal fusion surgery	1 (1.2%)	0
Eye disorders	1 (1.2%)	0
Retinal detachment	1 (1.2%)	0
Metabolism and nutrition disorders	1 (1.2%)	0
Hyperglycaemia	1 (1.2%)	0
Nervous system disorders	1 (1.2%)	0
Muscle contractions involuntary	1 (1.2%)	0
Respiratory, thoracic and mediastinal disorders	1 (1.2%)	0
Dyspnoea	0	1 (0.8%)

Table 10.4.3 provided a summary of all adverse device effects, which was mainly driven by skin irritation. 31.3% of subjects in the Felix group and 4.8% in the sham group experienced skin irritations during the study. Moderate skin irritations occurred in 3.6% of subjects in the Felix group and 4.8% in the sham group. Mild skin irritations occurred in 28.9% of subjects in the Felix group and none in the sham group. Symptoms of skin irritations include redness, itchiness, and swelling. Most of the skin irritations did not require any treatment. Treatment of skin irritations included anti-histamine, corticosteroids, antibiotics, anti-inflammatory in the form of spray, ointment, or cream, i.e., topical treatment. Other isolated ADEs included arthralgia, worsening of arthritis, limb discomfort, muscular weakness, nausea, and involuntary muscle contraction in the Felix group, and arthralgia in the sham group.

Table 10.4.3 Adverse Device Effect

	Felix (N=83)	Sham (N=42)
Skin irritation (redness, itchiness, swelling)	26 (31.3%)	2 (4.8%)
Moderate skin irritation	3 (3.6%)	2 (4.8%)
Requiring topical treatment	3 (3.6%)	2 (4.8%)
Not requiring treatment	0	0
Mild skin irritation	24 (28.9%)	0
Requiring topical treatment	4 (4.8%)	0
Not requiring treatment	20 (24.1%)	0
Other isolated events	6 (7.2%)	0
Arthralgia	1 (1.2%)	0
Worsening of arthritis in thumb	1 (1.2%)	0
Limb discomfort	1 (1.2%)	0
Muscular weakness	1 (1.2%)	0
Nausea	1 (1.2%)	0
Involuntary muscle contractions	1 (1.2%)	0

Table 10.4.4 provided further details on skin irritations. For the Felix group, 12% of the patients had skin irritations that were resolved and 19.3% of patients had ongoing/recurring skin irritations. For the sham group, 4.8% of the patients had ongoing/recurring skin irritations. For the Felix group, the average time to the first skin irritation was 24.4 days and the range was 0 to 88 days. Two patients in the Felix group were excluded in this calculation because of missing adverse event start date. There were two skin irritations in the sham group, one on day 15 and the other on day 86.

Table 10.4.4 Adverse Device Effect

	Felix (N=83)	Sham (N=42)
Number of Patients with Skin Irritation	26 (31.3%)	2 (4.8%)
Skin Irritation Resolved	10 (12.0%)	0
Skin Irritation Ongoing/Recurring	16 (19.3%)	2 (4.8%)
Number of Days to First Irritation Statistics		
Mean (SD)	24.4 (25.45)	50.5 (50.20)
Median	14.5	50.5
Q1, Q3	3.5, 38.0	15.0, 86.0
Min, Max	0, 88	15, 86

10.5. Blinding Assessment

A blinding assessment was conducted via a survey prior to unblinding at the 90-day visit. The results were summarized in Table 10.5 below. In the Felix group (N=62), 64.5% believed they were assigned to Felix and 35.5% believed they were assigned to sham. In the sham stimulation group (N=36), 36.1% believed they were assigned to Felix and 63.9% believed they were assigned to sham. The main reason for patients' guesses was treatment effect or the lack thereof.

Table 10.5 Blinding Assessment at 90 Days

	Felix	Sham
Guess of treatment group	(N=83)	(N=42)
Felix group	40 (64.5%)	13 (36.1%)
Sham Stimulation group	22 (35.5%)	23 (63.9%)
Reason for the Guess		
Treatment effect of the device	24 (53.3%)	11 (40.7%)
Lack of treatment effect of the device	13 (28.9%)	14 (51.9%)
Someone told me	1 (2.2%)	0
Other (Can feel or notice stimulation sensation from watch)	1 (2.2%)	0
Other (Effective)	0	1 (3.7%)
Other (Feel the stimulus)	1 (2.2%)	0
Other (I felt as though the severity of my tremors got worse.)	0	1 (3.7%)
Other (Just guessing)	1 (2.2%)	0
Other (Patient didn't think about the placement (randomization) group.)	1 (2.2%)	0
Other (She feels like she's being treated)	1 (2.2%)	0
Other (The shock got early on)	1 (2.2%)	0
Other (no difference, no effect as before on device)	1 (2.2%)	0

11. Substantial Equivalence Conclusion

The results from the non-clinical performance data and clinical study data demonstrated that the difference in indication for use statement and technological difference between the Felix™ NeuroAI™ Wristband and the predicate raises no new question of safety or effectiveness for the intended use.