DE NOVO CLASSIFICATION REQUEST FOR iTEAR100 NEUROSTIMULATOR

REGULATORY INFORMATION

FDA identifies this generic type of device as:

Electromechanical tear stimulator. An electromechanical tear stimulator is a non-implantable device intended to increase tear production via mechanical stimulation.

NEW REGULATION NUMBER: 21 CFR 886.5305

CLASSIFICATION: Class II

PRODUCT CODE: QKV

BACKGROUND

DEVICE NAME: iTEAR100 Neurostimulator

SUBMISSION NUMBER: DEN190026

DATE DE NOVO RECEIVED: May 15, 2019

CONTACT: Olympic Ophthalmics, Inc.
400 NW Gilman Blvd #1370
Issaquah, WA 98027

INDICATIONS FOR USE

The iTEAR100 Neurostimulator is an electromechanical nerve stimulator device, indicated for temporary use (up to 30 days) to increase acute tear production during vibratory stimulation of the external nasal nerve in adults, under prescription of an eye care provider.

LIMITATIONS

The sale, distribution, and use of the iTEAR100 Neurostimulator is restricted to prescription use in accordance with 21 CFR 801.109.

Patient training is required on the proper use of the device before home use.

The safety and effectiveness of the iTEAR100 Neurostimulator for the treatment of dry eye disease or for the improvement in dry eye symptoms have not been established.

The device increases tear production during neurostimulation, i.e., tearing was assessed only during stimulation.

The clinical study was not designed to evaluate any changes in nerve sensitivity.

Clinical study results demonstrate a trend of decreased effectiveness (tear production) over time. The mechanism for this decrease has not been identified and was not analyzed as part of the study.

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

DEVICE DESCRIPTION

iTEAR100 Neurostimulator is a hand-held, portable electromechanical actuator intended to acutely increase tear production through vibratory stimulation of the external nasal nerve in patients. The device is battery-operated with a single vibratory tip. As the effective tip is pushed against the tissue, the beam deflects inward until it is deflected fully into the device. The device is comprised of a direct current vibration motor, vibrating beam(cantilever), a control circuit with micro SD card, tactile switch.

The motor is attached to a cantilever beam made from acrylonitrile butadiene styrene (ABS), a control circuit to charge the battery and deliver power to the motor, and a housing also made from ABS. The motor and cantilever beam move together to produce a linear vibration at the tip of the cantilever (oscillating tip). A lithium-ion rechargeable battery is supplied inside the device, and is not removable or replaceable. A micro USB port on the device allows for charging. The device is locked by firmware from use after a predetermined number of stimulation days has been triggered.

The frequency of operation without any force applied is approximately 270 Hz. The amplitude of movement is approximately 0.5 mm without force applied. In the optimal force range, the cantilever tip is depressed approximately 1 mm and the frequency is approximately 250 Hz. Below is a list of stimulation parameters for the device:

Parameter	**Control – In air**	**With Force**
Frequency	270 Hz	250 Hz
Amplitude	0.6 mm	Not tested
Acceleration (g)	50	5
Tip Retraction (maximum force) (100%)	<6N	N/A
Acoustic	<35 db	<35 db

Figure 1. iTEAR100 Neurostimulator

The device activates tear production through stimulation of the nasolacrimal reflex. Stimulation mechanically activates external nasal nerve and initiates the nasolacrimal reflex, resulting in tear secretion. To produce the intended effect, the vibratory tip of the device should be applied to the lateral aspect of the nose for several seconds.

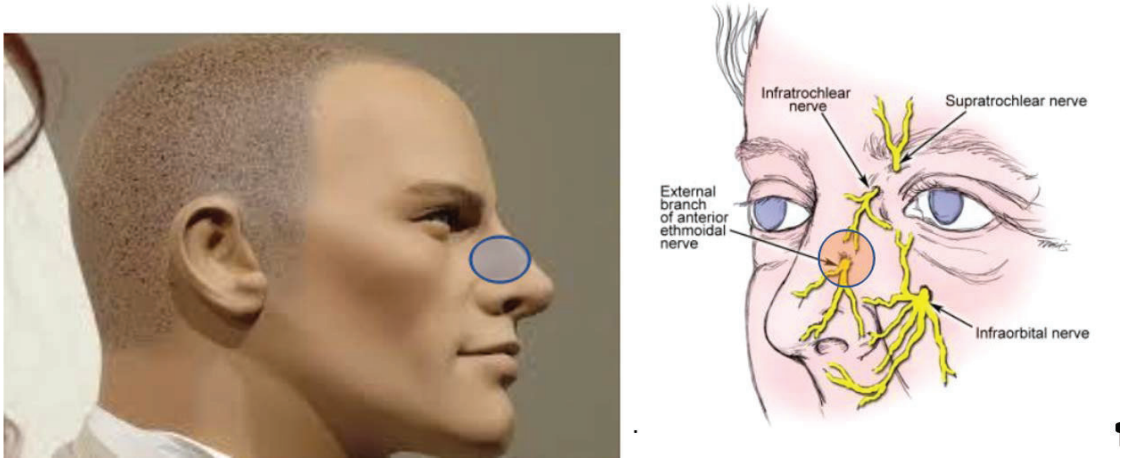


Figure 2 is a schematic showing correct use of the device

SUMMARY OF NONCLINICAL/BENCH STUDIES

BIOCOMPATIBILITY/MATERIALS

All patient contacting portions (all outer surfaces) of the device were assessed for cytotoxicity, skin irritation, and skin sensitization potential. Evaluation of these biocompatibility endpoints for devices that contact intact skin is consistent with recommendations in the June 2016 FDA Guidance, "Use of International Standard ISO 10993-1, "Biological evaluation of medical devices- Part 1: Evaluation and testing within a risk management process." These biocompatibility tests were performed per ISO 10993-5:2009 (MEM elution cytotoxicity) and ISO 10993-10:2010 (intracutaneous skin irritation, guinea pig maximization skin sensitization). For intracutaneous skin irritation and guinea pig maximization testing, both polar and non-polar

test article extracts were evaluated. For the intracutaneous skin irritation testing, observations were recorded to 72 hours after injection. For the guinea pig maximization testing, observations were made out to 72 hours after the challenge phase. Results demonstrated acceptable performance.

SHELF LIFE/STERILITY

The iTEAR100 Neurostimulator is provided non-sterile. Cleaning and maintenance instructions of the stimulator components of the device are included in the labeling.

ELECTROMAGNETIC CAPABILITY (EMC) AND ELECTRICAL SAFETY

Testing for the iTear100 device conformed to the following electromagnetic compatibility, electrical, mechanical, and thermal safety standards:

- ES 60601-1:2005/(R)2012. A1:2012, C1:2009/(R)2012 and A2:2010/(R)2012 (Consolidated Text) Medical Electrical Equipment - Part 1: General Requirements for Basic Safety And Essential Performance (IEC 60601-1:2005, MOD)
- IEC 60601-1-2 Edition 4.0 2014-02, Medical Electrical Equipment - Part 1-2: General Requirements for Basic Safety and Essential Performance - Collateral Standard: Electromagnetic Disturbances - Requirements and Tests 5-89
- 60601-1-6 Edition 3.1 2013-10 Medical Electrical Equipment - Part 1-6: General Requirements for Basic Safety and Essential Performance - Collateral Standard: Usability
- IEC 62133:2012 (Second Edition) 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

PERFORMANCE TESTING - BENCH

The sponsor has provided the test methods and results on multiple samples of their device for the following verification tests.
This testing is intended to address the risks of physical injury to the local muscles, nerves and skin due to repeated stimulation. Excessive acceleration, force, amplitude and frequency could all cause injury and or abrasions.

Test	Purpose	Method	Acceptance Criteria	Results
Acoustic Levels	To assess the acoustic output	Sound level meter in acoustic isolation chamber	(b)(4)	passed
Safeguards related to pressure/force against tissue	To assess force output performance when in operation	Load cell was lowered onto vibrating tip of device until tip depressed in housing		passed

Vibrational amplitude/ frequency	To assess the motion of the applicator tip of device	Use strobe to determine frequency and direct measurement of amplitude	passed
Thermal performance	To determine operating temperature of device	Thermocouples were applied to device and temperature measured with device in operation	passed
Use Life *	To assess fatigue of the cantilever	Cantilever deflection loading measured before and after life cycle test	passed

(b)(4)

*The sponsor has performed fatigue testing on their device for (b)(4) hours which simulates (b)(4) bilateral treatments. This resulted in no change in mechanical parameters or physical characteristics of the device.

SOFTWARE

All components of the device are controlled/monitored by software, which is responsible for the functionality, user interface, safety checks and performance accuracy. The software is considered to be a moderate level of concern (LOC) because inadvertent software errors could result in injury to the patient.

The following device functions of the iTEAR100 Neurostimulator are controlled by the software:

1. Software detects the state of the switch and operate the vibration motor.
2. When in use the software modulates the motor on/off signal creating a stutter in the motor motion. This stuttering serves as a treatment duration indicator for the user.
3. Logs use data to memory SD Card.
4. Detect battery level.
5. Provide USB detect for charging. This disables the unit from being used when connected to USB.
6. LED control. LED is flashed signaling battery state.
7. Disable device after 30 Day of use

The submission contained all the elements of software documentation corresponding to the "Moderate" level of concern, as outlined in the FDA guidance document "Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices." Adequate documentation describing the software/firmware, software specifications, architecture design, software development environment, traceability, revision level history, unresolved anomalies and cybersecurity provide the foundation that the software will operate in a manner as described in the specifications. Hazard analysis was performed to characterize software risks including device malfunction, measurement related errors and cybersecurity. The submission included verification and validation (V&V) testing to address the potential hazards with satisfactory results.

SUMMARY OF CLINICAL INFORMATION

Two clinical studies, CLP-OO2 and CLP-OO7, were completed with the iTEAR100 Neurostimulator™ and are discussed below.

CLP-OO2 Study

CLP-OO2 was a prospective, open-label, single-arm, multi-center (8 US sites), 2-stage study. The first stage of this pivotal trial included 30 days of follow-up while using the device at home and included all enrolled subjects. After 30 days, subjects were given the option to participate in an additional 150 days of follow-up while using the device (180 days of follow-up in total). The subject was provided a take-home device to perform the study treatment per the instructions for use. It was recommended that subjects use the study device on each side of the nose for 30 seconds on each side twice per day for the 30-day follow-up period. In the extended follow up, subjects were asked to use the device at least once every other day for the 150 days in the extended follow-up period.

Below are the inclusion and exclusion criteria:

Inclusion Criteria

1. Twenty-one (21) years of age or older
2. Schirmer test with anesthetic of (b)(4) in at least one eye
3. Ability to produce tears upon training with (b)(4) change in Schirmer score compared to baseline in at least one eye (the technique for this assessment is provide below)
4. In the opinion of the investigator, subject is in good general health and free of any condition that could impair study participation or ocular evaluation
5. Subject is willing and able to give written informed consent and commits to comply with study requirements

Exclusion Criteria

1. Sjogren's syndrome or other rheumatologic condition
2. Intraocular surgery within 6 months of Visit 1
3. Intraocular or periocular injection within 6 months of Visit 1
4. Used intranasal neurostimulation within two months of Visit 1 or plans to use it during the study
5. Lid function abnormalities
6. Any acute infectious or non-infectious ocular condition of the anterior or posterior segments in either eye within 30 days of Visit 1
7. Diseases/conditions of ocular surface associated with clinically significant scarring/destruction of conjunctiva/cornea
8. Subject has any of the following conditions:
   - History of facial nerve palsy
   - History of neuromuscular disorder
   - Uncontrolled ocular or systemic disease
   - Other clinically significant local skin condition (e.g., skin infection) at target treatment site
9. Participation in any clinical trial with a new active substance or a new device within 30 days of Visit 1 (with the exception of the devices to be used in the study described herein).

Study Visits were performed at Baseline (Day 0), Follow-up Call (day 3), Day 14, Day 30, Day 90, Day 180. Study Visits were performed at Baseline (Day 0), Follow-up Call (day 3), Day 14, Day 30, Day 90, Day 180. Clinical assessments included:

- Corrected distance visual acuity (Baseline, Day 30, Day 180)
- Corneal and conjunctival staining (Baseline, Day 14, Day 30, Day 90, Day 180)
- Schirmer test (Baseline, Day 14, Day 30, Day 90, Day 180)
- Neurological exam (Baseline, Day 30, Day 180)
- Adverse event recording (all visits)

The primary endpoint was statistically significant improvement from baseline to Day 30 on the Schirmer Index (SI). Briefly, anesthesia was applied, followed by placement of the Schirmer strip in the subject's eye and measurement of the distance a subject's tears traveled along it. After 5 minutes, iTEAR100 stimulation was applied for 30 seconds on each side (with the strip in place), and the was re-measured 5 minutes afterward. The SI is the difference between the 2 measurements (pre- and post- stimulation). Subjects were allowed to maintain medication regimens if the regimens were considered to be stable and unlikely to change over the course of 180 days. Subjects were chosen based on their ability at day 0 to respond to neurostimulation and the company recommends a trial in the office prior to writing a prescription.
The study enrolled 108 subjects, of which 101 subjects completed the 30 days of follow-up. Eighty (80) subjects agreed to continue in the extended follow-up phase of the study, of which 58 reached the final 180-day endpoint. Demographic data and subject accountability data for the study are provided below:

Table 1- Demographic Characteristics

		n
Sex	F	82
	M	26
Age	<30	6
	30-50	18
	50-70	60
	>70	24
Ethnicity	Hispanic/Latino	5
	Not Hispanic/Latino	101
	NA	2
Race	White	87
	Black	2
	Other	3
	NA	16
	All	**108**

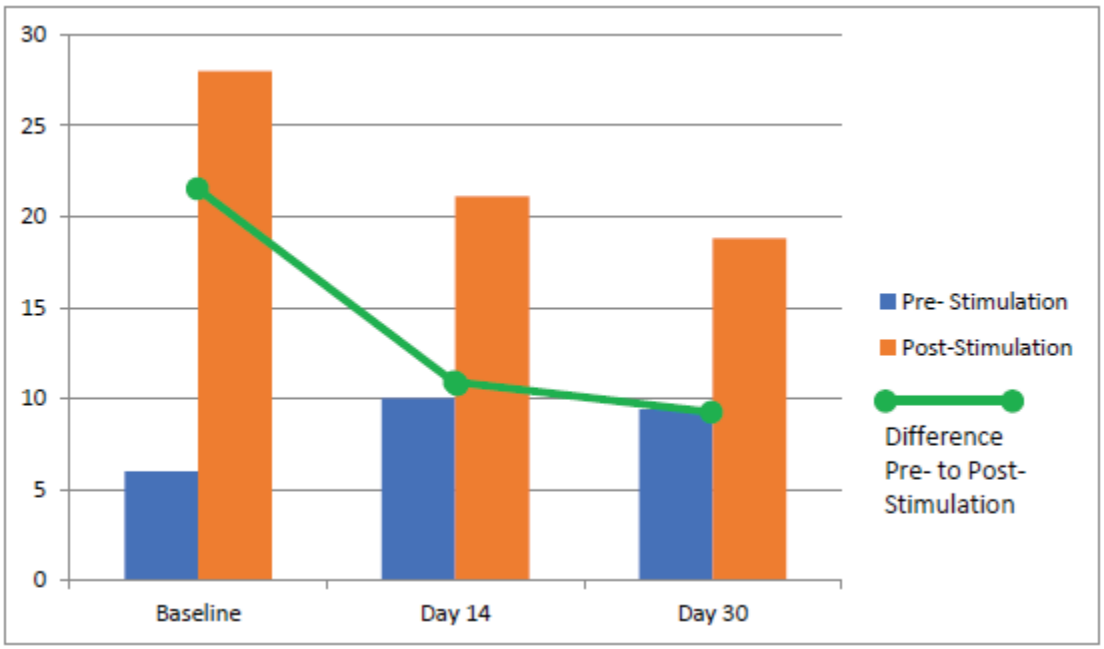
Table 2 - Subject Accountability

	Main Study				Optional Extended Follow-up: At Day 30, 80 subjects chose to enroll in the extended follow-up	
	Baseline	**Day 3 (call)**	**Day 14**	**Day 30**	**Day 90**	**Day 180**
Theoretical	108	108	108	108	80	80
Death	0	0	0	0	0	0
Withdrawal (cumulative)	0	0	4	6	6	9
Lost to Follow Up (cumulative)	0	0	1	1	7	13
Missing	0	1	2	0	0	0
Expected	108	108	104	102	74	71
Actual[A]	108	103	97	88	51	40
Actual[B]	108	107	101	101	67	58
% Follow Up Actual[A]	100%	95.4%	89.8%	81.5%	63.8%	50.0%
% Follow Up Actual[B]	100%	99.1%	93.5%	93.5%	83.8%	72.5%

Expected is equal to Theoretical minus Deaths minus Withdrawals
Actual[A] is all subjects with data available for primary endpoint and within window
Actual[B] is all subjects with data available for primary endpoint
Follow-up Actual[A] is equal to Actual[A] divided by Theoretical.
Follow-up Actual[B] is equal to Actual[B] divided by Theoretical.

The stimulated Schirmer's test score was greater than the unstimulated test score at each visit during the 30-day follow-up period (Table 3). There was also an increase in the pre-stimulation Schirmer score during the course of the study.

Table 3 - Change in tear production (Schirmer score)



Safety information for the entire 180-day follow-up period is provided below.

Table 4 - Ophthalmic Adverse Events

Event Description	Day to AE	Duration (days)	Severity	Impact of Device	Action Taken
Inflammation due to Schirmer strip	13	14	Mild	No change	Drug Rx
Blurred vision	1	232*	Mild	No Change	New Contact Lenses
Eye Floater	92	1	Mild	No Change	None
Corneal Medicamentosa	91	60	Mild	No change	Decrease artificial tear usage
Corneal Neovascularization	180	21	Moderate	No change	None
Dry Eye Pain	2	19	Mild	No change	Artificial Tears
Eyelid irritation due to Schirmer strip	0	1	Mild	No change	None
Stye on lower lid OD	1		Mild	No change	Drug Rx
Vitreous Hemorrhage OS	64	16	Mild	Discontinued	None
Severe itching and sensitive eyes papillae OU	5	8	Moderate	Discontinued	Drug Rx
Eye infection OU	55	7	Mild	No change	None
Eye infection OU	74	8	Mild	No change	None
Eye infection OU	95	0	Mild	No change	None
Corneal Abrasion due to Schirmer strip		23	Moderate	No change	Drug Rx
Sjogren's syndrome	30	Ongoing	Mild	No change	Referred to rheumatologist

*The cause of the blurry vision was poor contact lens fit and the days to resolution represents the time of the phone call inquiry that was made outside the study follow-up period, since the subject could not recall the exact date of the new lens fitting.

There were 2 events that were definitely related to the device: one event described as headache, sneezing, and ticking sensation (onset at 1 day from study enrollment); the other was described as intermittent nose soreness (onset at 85 days from study enrollment). There were 7 events that were possibly related to the device (Table 5).

Table 5 - Adverse Events Possibly Related to Device

Event Description	Day to AE	Duration (days)	Severity	Impact of Device	Action Taken
Inflammation due to Schirmer strip	13	14	Mild	No change	Drug Rx
Blurred vision	1	232*	Mild	No Change	New Contact Lenses
Eye Floater	92	1	Mild	No Change	None
Corneal Medicamentosa	91	60	Mild	No change	Decrease artificial tear usage
Corneal Neovascularization	180	21	Moderate	No change	None
Dry Eye Pain	2	19	Mild	No change	Artificial Tears
Eyelid irritation due to Schirmer strip	0	1	Mild	No change	None
Stye on lower lid OD	1		Mild	No change	Drug Rx
Vitreous Hemorrhage OS	64	16	Mild	Discontinued	None
Severe itching and sensitive eyes papillae OU	5	8	Moderate	Discontinued	Drug Rx
Eye infection OU	55	7	Mild	No change	None
Eye infection OU	74	8	Mild	No change	None
Eye infection OU	95	0	Mild	No change	None
Corneal Abrasion due to Schirmer strip		23	Moderate	No change	Drug Rx
Sjogren's syndrome	30	Ongoing	Mild	No change	Referred to rheumatologist

*The cause of the blurry vision was poor contact lens fit and the days to resolution represents the time of the phone call inquiry that was made outside the study follow-up period, since the subject could not recall the exact date of the new lens fitting.

Headache and dizziness were the most common related events reported in the study. Seven (7) of the 9 related adverse events were considered mild, 1 was considered moderate, and 1 was considered severe. Most related events were transient and resolved within approximately 1 week. After a single device treatment, one subject experienced continuous nausea, dizziness,

lightheaded and headache for 30-day duration. The subject was instructed to seek neurological evaluation, stop device use, and discontinue from the study. This adverse event was considered to be a serious unanticipated adverse event, possibly related to the device. Four subjects experienced a loss of 2 lines or more in visual acuity during treatment. For 3 of the 4 subjects, loss of visual acuity was attributed to fluctuations in the disease, and/or the fact that subjects were asked not to use artificial tears or other treatments when follow-up visits were scheduled. Pinhole correction and manifest refraction was not attempted or used for any of these subjects. The subjects' vision returned to baseline or 20/20 as fast as 2 weeks for 1 subject and within 180 days for the other 2 subjects. The last subject experienced a loss of visual acuity when the 30 day follow-up visit was performed without correction, but demonstrated no change in visual acuity when the exam was performed with correction, at 180 days. Therefore, this subject's change in visual acuity was attributed to a lack of correction at the 30 day visit. All 4 subjects' vision returned to baseline during the follow-up period. The investigators believed that the alterations in vision were due to temporary worsening of dry eye disease, however, causality could not be definitively determined due to limitations in the study design.

CLP-OO7 Study

CLP-OO7 was a multi-center, nonsignificant-risk, prospective, double-masked, randomized, sham controlled, single visit clinical trial that enrolled 60 subjects. The sham group received an iTEAR100 Neurostimulator device which looked identical to and made noise similar to a fully functional device but had a tip that did not vibrate. All subjects received cross-over treatment with the active device at the conclusion of the study procedures. Regardless of whether they were using the sham or active device, subjects were instructed to apply the device tip against the skin of the nose at the junction of the nasal cartilage and the nasal bone. The application duration was 30 seconds or less for each side of the nose.

The inclusion and exclusion criteria are provided below:

Inclusion Criteria

1. 18 years of age or older;
2. Willing and able to provide an English language written informed consent;
3. Able to safely use the study device and be free of any condition that, in the opinion of the investigator, could impair study participation.

Exclusion Criteria

1. Presence of clinically significant nasal/facial skin conditions (e.g., infection, ulceration, wound);
2. Under arrest or was otherwise in custody;
3. Presence of any other condition, which in the judgment of the principal investigator would prevent a potential subject from safely completing the study or tolerating device use, such as mental illness, dementia, severe agitation, etc.).

No study-mandated tests were required for enrollment. The schedule of assessments and procedures for the study is shown in the table below.

Table 6 – Clinical Assessments

Assessment	Schedule
	Screening/Day 0[a]
Eligibility screening & IC	X
OSDI questionnaire	X
Demographic information	X
Focused DES history	X
Baseline nasal skin exam & facial neurological exam	X
Baseline visual acuity (OS)	X
Baseline slit lamp examination (SLE) with emphasis on corneal edema (OS)	X
Baseline blood pressure (BP), heart rate (HR), pulse oximetry	X
Baseline Schirmer's test (OD)	X
Baseline meibomian gland expression score (OS)	X
Randomization & experimental device training/treatment[b]	X
Repeat Schirmer's test (OD) *with new Schirmer strip* during device treatment[b,c]	X
Repeat BP, HR, pulse oximetry during Schirmer's test (at 2.5 & 5 min)[b]	X
Repeat nasal skin exam & facial neurological exam	X
Repeat visual acuity (OS)	X
Repeat SLE with emphasis on corneal edema (OS)	X
Repeat meibomian gland expression score (OS)	X
Cross-over treatment with fully active iTEAR device & qualitative assessment of response	X
PI usability survey	X
Subject usability survey	X
Record adverse events	X

[a] Screening and Day 0 were the same
[b] Second investigator to perform; initial investigator was out of the room
[c] Device treatment begins immediately after placement of Schirmer's test strip

The primary endpoint of this study was the mean within-subject change in the Schirmer's test score post vs. pre neurostimulation in the active treatment vs. sham groups in the primary analysis population (i.e., subjects with baseline Schirmer's test score ≤10mm). The replacement Schirmer technique was used for this study, under which a Schirmer strip is applied to the subject's eye to assess pre-stimulation tear production, and then a second strip is inserted to assess post-stimulation tear production.

The safety of the device was evaluated by the incidence of device-related adverse events and serious adverse events, as well as changes in the following measures:

- Best corrected Snellen distance visual acuity (VA);
- Ophthalmic exam with emphasis to determine the presence of corneal edema;
- Nasal skin examination and facial neurologic examination;
- Hemodynamic parameters (blood pressure, heart rate, pulse oximetry).

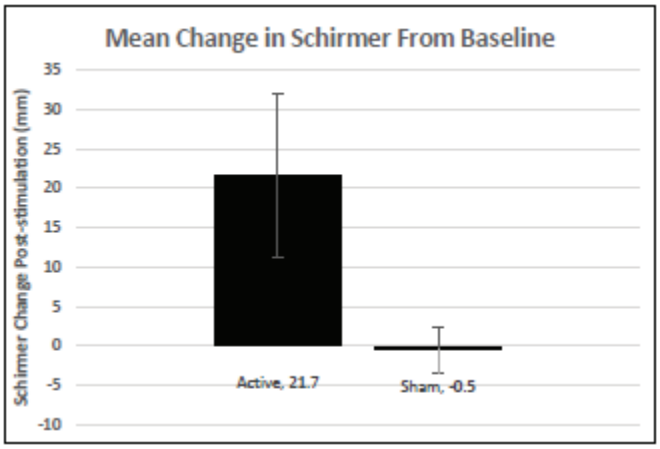
Below are the study demographics:

Table 8 – Baseline Demographics

Summary[a]	Randomized Treatment		All Subjects (N=60)
	Active (N=28)	Sham (N=32)	
Sex, n (%)			
Female	16 (57.1%)	24 (75.0%)	40 (66.7%)
Male	12 (42.9%)	8 (25.0%)	20 (33.3%)
Age (Years)			
Mean (SD)	49.7 (15.99)	50.0 (16.25)	49.9 (16.00)
Median	51	50	51
Min, Max	24, 79	21, 77	21, 79
Ethnicity, n (%)			
Hispanic or Latino	3 (10.7%)	7 (21.9%)	10 (16.7%)
Not Hispanic or Latino	25 (89.3%)	25 (78.1%)	50 (83.3%)
Race, n (%)			
Asian	5 (17.9%)	7 (21.9%)	12 (20.0%)
Black	2 (7.1%)	1 (3.1%)	3 (5.0%)
Caucasian	18 (64.3%)	21 (65.6%)	39 (65.0%)
Other	3 (10.7%)	3 (9.4%)	6 (10.0%)
Subjects using Eye Treatment, n (%)	21 (75.0%)	25 (78.1%)	46 (76.7%)

Each randomized subject underwent all study assessments, thus subject accountability was 100%. In the primary analysis population, there was a statistically significant increase in Schirmer's test scores in the active group (mean within-subject change pre- to post-stimulation = 21.7mm) compared to sham (mean within-subject change pre- to post-stimulation = -0.5mm) with a between group difference of 22.2mm (SD 2.61) favoring the active device, as shown in in the figure below. The bars included in the figure show the standard deviation for the mean change reported, which indicates the degree of variability for the with-in subject change scores.

Figure 9 – Schirmer's Test Score Change in Active Compared to Sham Groups



There were no device-related adverse events or serious adverse events reported in this study. One unrelated adverse event involved a near-syncopal episode that occurred following the administration of topical proparacaine anesthetic to the subject's right eye prior to placement of the baseline Schirmer's test strip. The subject was randomized but had not received treatment with either a sham or an active study device. She was terminated from any further study participation and was monitored by the investigator at the site until her symptoms had resolved. Additionally, there were no observed significant changes in post vs. pre-test visual acuity, corneal edema, facial neurologic examinations, or hemodynamic parameters.

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 professional and patient labeling are adequate and meet the requirements of 21 CFR 801.109. The labels summarize the clinical trial results that characterized the probable benefit and the identified risks of the device, including tissue damage, pain, headache, and discomfort. Both guides contain requirements for use by prescription only and proper patient training, Indications for Use, contraindications, device description, technical parameters, warnings, precautions, potential complications, instructions for use (including an explanation of all user-interface components and information regarding proper device placement), recommended stimulation schedule, instructions for device maintenance/cleaning, summary of clinical trials, information related to electromagnetic compatibility, language to direct end users to contact the device manufacturer and MedWatch if they experience any adverse events with this device, expected service life, disposal & replacement, environmental operating conditions, electrical specifications, and symbols & markings.

RISKS TO HEALTH

The table below identifies the risks to health that may be associated with use of an electromechanical tear stimulator and the measures necessary to mitigate these risks.

Table 9 – Identified Risks to Health and Mitigation Measures

Identified Risks	Mitigation Measures
Tissue damage due to overstimulation/understimulation or mechanical injury, device breakage	Clinical performance testing Non-clinical performance testing Software verification, validation, and hazard analysis Labeling
Adverse tissue reaction	Biocompatibility evaluation Labeling
Electrical shock or burn	Electrical, thermal, and mechanical safety testing Software verification, validation, and hazard analysis Labeling
Interference with other devices	Electromagnetic compatibility (EMC) testing Software verification, validation, and hazard analysis Labeling
Pain, headache, or discomfort	Clinical performance testing Non-clinical performance testing
Insufficient tear production	Clinical performance testing

SPECIAL CONTROLS

In combination with the general controls of the FD&C Act, the electromechanical tear stimulator is subject to the following special controls:

1. Clinical performance testing under anticipated conditions of use must evaluate tear production and all adverse events, including tissue damage, pain, headache, and discomfort.

2. Non-clinical performance testing must demonstrate that the device performs as intended under anticipated conditions of use. The following must be conducted:
    a. An assessment of mechanical output specifications including vibration amplitude and frequency, pressure and force, and acoustic (noise level) properties;
    b. Mechanical safety testing to validate safeguards related to the pressure aspects of the device; and
    c. Use life testing.

3. Performance data must demonstrate the electrical safety, thermal safety, and electromagnetic compatibility (EMC) of all electrical components of the device.

4. All patient-contacting components of the device must be demonstrated to be biocompatible.

5. Software verification, validation and hazard analysis must be performed.

6. Physician and patient labeling must include:
    a. A detailed summary of the device's technical parameters;

b. Instructions for use, including an explanation of all user-interface components and information regarding proper device placement;
c. Information related to electromagnetic compatibility classification;
d. Instructions on how to clean and maintain the device;
e. A summary of the clinical performance testing conducted with the device;
f. Language to direct end users to contact the device manufacturer and MedWatch if they experience any adverse events with this device; and
g. Information on how the device operates and the typical sensations experienced during treatment.

BENEFIT-RISK DETERMINATION

The risks of the device are based on non-clinical laboratory data, as well as data collected in clinical trials described above. The device exhibited an acceptable safety profile for up to 30 day use in the clinical studies which were conducted. One device-related serious adverse event was observed; this event resolved without treatment. Non-serious device-related adverse events were few in number and all were self-limited.

The probable benefits of the device are also based on nonclinical laboratory data, as well as data collected in clinical trials. Compared to a sham control, the device was shown to provide a statistically significant increase in acute tear production during a single stimulation. Results from an additional clinical study suggest that a temporary increase in acute tear production may be seen in response to repeated device stimulation up to 30 days.

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, the probable benefits outweigh the probable risks for the iTEAR100 Neurostimulator. The device provides benefits, and the risks can be mitigated by use of general controls and the identified special controls.

CONCLUSION

The De Novo request for the iTEAR100 Neurostimulator is granted and the device is classified as follows:

Product Code: QKV
Device Type: Electromechanical tear stimulator
Class: II
Regulation Number: 21 CFR 886.5305