August 2, 2021

Neurolief Ltd.
℅ Janice Hogan
Partner
Hogan Lovells US LLP
1735 Market Street, Suite 2320
Philadelphia, Pennsylvania 19103

Re: K212106
Trade/Device Name: Relivion
Regulation Number: 21 CFR 882.5891
Regulation Name: Transcutaneous Electrical Nerve Stimulator To Treat Headache
Regulatory Class: Class II
Product Code: PCC
Dated: July 6, 2021
Received: July 6, 2021

Dear Janice Hogan:

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 (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 located 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.

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 803) for devices or postmarketing safety reporting (21 CFR 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 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 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,

Patrick Antkowiak
Acting 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

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*

Device Name
Relivion®

Indications for Use *(Describe)*

The Relivion® transcutaneous electrical nerve stimulator is indicated for the acute treatment of migraine with or without aura in patients 18 years of age or older. It is a prescription device to be self-used at home.

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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SPECIAL 510(k) SUMMARY

RELIVION®

Applicant Name: Neurolief Ltd.
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Contact Person: Michal Kedar-Datel
Clinical & Regulatory Affairs Director
Neurolief Ltd.
Tel: +972-9-3730288

Date Prepared: July 6, 2021

Trade Name: Relivion®

Classification Name: 21 CFR 882.5891 Transcutaneous electrical nerve stimulator to treat headache

Product Code: PCC

Classification: Class II

Classification Panel: Neurology

Predicate Device: Neurolief Ltd's Relivion® Device (K203419)

Intended Use/Indication for Use:

The Relivion® transcutaneous electrical nerve stimulator is indicated for the acute treatment of migraine with or without aura in patients 18 years of age or older. It is a prescription device to be self-used at home.

Device Description:

The modified Relivion® is an external non-invasive neurostimulator designed for transcutaneous electrical nerve stimulation. The modified Relivion® headset integrates three pairs of output electrodes which come in contact with the subject's scalp at the forehead and occiput. The electrodes deliver the stimulation pulses produced by the headset's stimulation unit to the subject's scalp. The frontal electrodes stimulate the trigeminal (supraorbital and supratrochlear) nerve branches and the posterior electrodes stimulate the greater occipital nerve branches.

The modified Relivion® includes single-use replaceable electrode pads that are positioned on-top of the electrodes prior to treatment and are wetted by the user before use, in order to provide proper conductivity between the electrodes and the scalp.

The modified Relivion® is powered by a rechargeable battery and the headset incorporates an on-board user interface that enables the user to activate/deactivate the device and to adjust the stimulation intensity. Upon treatment activation, the treatment automatically runs and ends after 60 minutes or alternatively, the user can stop the treatment when desired.

The modified Relivion® can communicate via a low energy Bluetooth link with the modified Relivion®'s dedicated mobile application on the patient's smartphone. The modified Relivion®'s mobile application is optional, and it is used by the patient to display the device status and provide indications and alerts. Additionally, the modified Relivion® mobile application also enables the patient to report their migraine headache status.

The main modification introduced in the Relivion® Device compared to the cleared predicate device (K203419) is an added optional Physician Interface that enables physicians to remotely follow-up on the patient's migraine attacks status and the treatments they performed using the Relivion device, based on the data transferred to it via the modified mobile application.

Both the modified Relivion®'s mobile application (for patients) and added physician interface (for physicians) are referred together as the optional "Patient Management Interface" (PMI) of the modified Relivion® Device.

Technological Characteristics:

The modified Relivion® treats migraines by stimulating the trigeminal and occipital nerve branches by a transcutaneous electrical nerve stimulation. Trigeminal and occipital electrical nerve stimulation induces neuromodulation of these nerve pathways and by that reduces pain associated with migraine and associated symptoms.

The modified Relivion® includes single-use, replaceable electrode pads that are positioned on-top of the headset electrodes and are wetted by the user before each use. Water releasing covers are located on the outer side of each back occipital electrode and are used to release moisture from the

electrode pads to the scalp in order to provide proper electrical conductivity between the electrodes and the scalp.

The modified Relivion® headset adjusts to various head sizes and contours and can be worn comfortably. The headset includes two flexible arms that penetrate under the hair layers while the headset is worn.

The modified Relivion® headset incorporates an on-board user interface and can communicate via a low energy Bluetooth link with the modified Relivion®'s dedicated mobile application on the patient's smartphone. The user interface and mobile app display the device status and provides indications and alerts, in addition to an optional Physician Interface that enables physicians to remotely follow-up on the patient's migraine attacks status and treatments performed with the Relivion device.

Performance Data:

Neurolief conducted several performance tests to demonstrate that the modified Relivion® device complies with performance standards and that it functions as intended.

Performance - Bench Testing: The modified Relivion® device underwent performance testing for the modifications introduced, including software validation and device verification tests. It was successfully verified that the modified Relivion® output parameters meet the product's specifications.

Software Testing: The PMI software was also subject to verification and validation testing, and results demonstrated that the modified Mobile Application and added Physician Interface perform as intended. Cybersecurity risks were also identified and addressed.

Because the modification to the device impacted only the software, no further testing was required.

Substantial Equivalence:

The following table compares the modified Relivion® device to its predicate device with respect to intended use, technological characteristics and principles of operation, providing detailed information regarding the basis for the determination of substantial equivalence.

Table 1: Neurolief, Ltd.'s Modified Relivion® Substantial Equivalence

Parameter	Neurolief Ltd.'s Relivion® (Subject Device)	Neurolief Ltd.'s Relivion® (Predicate)	Comparison
General Characteristics			
510(k) number	Pending	K203419	N/A
Classification	21 CFR § 882.5891	21 CFR § 882.5891	Same
Product Code	PCC	PCC	Same
Product Class	Class II	Class II	Same
Regulation Name	Transcutaneous Electrical Nerve Stimulator to Treat Headache	Transcutaneous Electrical Nerve Stimulator to Treat Headache	Same
Indications for Use	The Relivion® transcutaneous electrical nerve stimulator is indicated for the acute treatment of migraine with or without aura in patients 18 years of age or older. It is a prescription device to be self-used at home.	The Relivion® transcutaneous electrical nerve stimulator is indicated for the acute treatment of migraine with or without aura in patients 18 years of age or older. It is a prescription device to be self-used at home.	Same
Technology	Transcutaneous Electrical Nerve Stimulator	Transcutaneous Electrical Nerve Stimulator	Same
Invasiveness	Non-Surgical	Non-Surgical	Same
Electrode Locations	Forehead and Occiput	Forehead and Occiput	Same
Nerves over which electrodes are placed	Supratrochlear and supraorbital branches of the trigeminal nerve bilaterally and the occipital nerves	Supratrochlear and supraorbital branches of the trigeminal nerve bilaterally and the occipital nerves	Same
Energy	Electric	Electric	Same
Power Source	Rechargeable Li-Po 3.7 V Battery	Rechargeable Li-Po 3.7 V Battery	Same
Software-controlled	Yes, 1 fixed program	Yes, 1 fixed program	Same
Constant Current	Yes	Yes	Same
Constant Voltage	No	No	Same
Software Function	Controls the output of the device and device indicators	Controls the output of the device and device indicators	Same
Timer Settings	Yes	Yes	Same

Parameter	Neurolief Ltd.'s Relivion® (Subject Device)	Neurolief Ltd.'s Relivion® (Predicate)	Comparison
Patient override control method	On/Off button	On/Off button	Same
Button Types	On/Off Button and buttons to adjust intensity of electrical stimulus	On/Off Button and buttons to adjust intensity of electrical stimulus	Same
Functional features	Visual and auditory indicators inform the user when the device is on vs. off and help them troubleshoot if it is not working properly (e.g., indicates if device is active/non-active, low battery indication and if electrical connection between device and skin is unacceptable)	Visual and auditory indicators inform the user when the device is on vs. off and help them troubleshoot if it is not working properly (e.g., indicates if device is active/non-active , low battery indication and if electrical connection between device and skin is unacceptable)	Same
Bluetooth Capable	Yes	Yes	Same
Associated Mobile Application (for patients)	Yes	Yes	Similar Both devices include an optional mobile app to display device status, treatment duration, and battery status, with the modified device application also enabling patients to report their migraine headache status, this feature does not alter the therapeutic effect.
Associated Physician Interface (for physicians)	Yes	No	Different The modified device has an optional a ssocia ted Physician Interface that enables physicians to remotely follow-up on the patient's migraine attacks status and treatments performed with the Relivion device, this feature does not alter the therapeutic effect.
Max leakage current	None (battery operated)	None (battery operated)	Same

Parameter	Neurolief Ltd.'s Relivion® (Subject Device)	Neurolief Ltd.'s Relivion® (Predicate)	Comparison
Electrodes	Relivion® electrode	Relivion® electrode	Same
Indicator display: Unit functioning	Yes	Yes	Same
Low battery indicator	Yes	Yes	Same
Standards: IEC 60601-1	Yes	Yes	Same
IEC 60601-1-2	Yes	Yes	Same
IEC 60601-1-6	Yes	Yes	Same
IEC 60601-1-11	Yes	Yes	Same
IEC 60601-2-10	Yes	Yes	Same
IEC 62366	Yes	Yes	Same
Weight	90 gr	90 gr	Same
Dimensions	209mm x 128mm x 39mm	209mm x 128mm x 39mm	Same
Housing materials	Plastic PA + Silicone	Plastic PA + Silicone	Same
Maximum Time Device Used	60 minutes	60 minutes	Same
Net Charge (µC) per pulse	0	0	Same
Pulse Duration (µsec)	850	850	Same
Frequency (Hz)	80	80	Same
Maximum output voltage (V): @500 ohms @2000 ohms @10000 ohms	3 front electrodes / 6 back electrodes 12 front electrodes / 24 back electrodes 60 front electrodes / 100 back electrodes	3 front electrodes / 6 back electrodes 12 front electrodes / 24 back electrodes 60 front electrodes / 100 back electrodes	Same
Maximum output current (mA): @500 ohms @2000 ohms @10000 ohms	6 front electrodes /12 back electrodes 6 front electrodes /12 back electrodes 6 front electrodes /10 back electrodes	6 front electrodes /12 back electrodes 6 front electrodes /12 back electrodes 6 front electrodes /10 back electrodes	Same

Parameter	Neurolief Ltd.'s Relivion® (Subject Device)	Neurolief Ltd.'s Relivion® (Predicate)	Comparison
Max Phase Amplitude	6 mA front electrodes/ 12 mA back electrodes; with a load of a 4.7 uF capacitor parallel with 2.2K ohms resistance	6 mA front electrodes/ 12 mA back electrodes; with a load of a 4.7 uF capacitor parallel with 2.2K ohms resistance	Same
Maximum phase charge (µC) @500Ω	4.8	4.8	Same
Maximum Current Density, (mA/cm², r.m.s.) @500Ω	1.93 front electrodes/ 2.78 back electrodes	1.93 front electrodes/ 2.78 back electrodes	Same
Maximum Average Power Density, (W/cm²) @500Ω	0.0000116 front electrodes / 0.000034 back electrodes	0.0000116 front electrodes / 0.000034 back electrodes	Same
Maximum Average Current (average absolute value, mA) @500Ω	0.38 front electrodes / 0.76 back electrodes	0.38 front electrodes / 0.76 back electrodes	Same
Phase rise time	5 µS	5 µS	Same
Modulation Options **Amplitude** **Frequency** **Duration**	0- 12 mA Fixed @ 80 Hz 330- 400 µS	0- 12 mA Fixed @ 80 Hz 330- 400 µS	Same
Phase decay time	2 µS	2 µS	Same
Ramp Modulations **Ramp Up** **Ramp Down**	Manually Manually	Manually Manually	Same

As described in the comparison table above, the subject modified Relivion® and the predicate Relivion® device (K203419) share the same intended use and indications, technological characteristics, and same principles of operation. The minor differences in the technological characteristics do not alter the overall therapeutic effect of the device. Any differences between the modified Relivion® and its predicate (K203419) were carefully evaluated through performance testing. The modified Relivion® device underwent performance testing, including bench testing and software validation testing. These performance tests confirmed that the modified Relivion® complies with the same special controls and the same consensus and performance standards, on which FDA based its clearance of the company's Relivion® device (K203419). These tests demonstrated that the differences in the technological characteristics between the subject and predicate device do not adversely impact performance and that the subject modified Relivion® is substantially equivalent to its predicate device (K203419).

Conclusions:

Therefore, based on the same intended use, indications, technological characteristics, and same principles of operation, the modified Relivion® device is substantially equivalent to its predicate device.