February 12, 2021

Electrocore, Inc.
Mike Romaniw
VP, Quality Assurance & Regulatory Affairs
150 Allen Road, Suite 201
Basking Ridge, New Jersey 07920

Re: K203546
Trade/Device Name: gammaCore Sapphire
Regulation Number: 21 CFR 882.5892
Regulation Name: External vagal nerve stimulator for headache
Regulatory Class: Class II
Product Code: PKR, QAK
Dated: December 2, 2020
Received: December 4, 2020

Dear Mike Romaniw:

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
Assistant Director (Acting)
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: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*

Not yet known

Device Name

gammaCore Sapphire Non-invasive Vagus Nerve Stimulator

Indications for Use *(Describe)*

gammaCore Sapphire (non-invasive vagus nerve stimulator) is intended to provide non-invasive vagus nerve stimulation (nVNS) on the side of the neck. gammaCore is indicated for:

- The preventive treatment of migraine headache in adolescent (age 12 and older) and adult patients.
- The acute treatment of pain associated with migraine headache in adolescent (age 12 and older) and adult patients.
- Adjunctive use for the preventive treatment of cluster headache in adult patients.
- The acute treatment of pain associated with episodic cluster headache in adult patients.

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.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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510(K) SUMMARY

The following information is provided as required by 21 CFR §807.92 for the electroCore gammaCore Sapphire 510(k) premarket notification. In response to the Safe Medical Devices Act of 1990, the following is a summary of the information upon which the substantial equivalence determination is based.

Applicant: electroCore, Inc.
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Date of Submission:	**February 12, 2021**
Proprietary Name:	**gammaCore Sapphire**
Common Name:	**External vagal nerve stimulator for headache**
Classification Status:	**Class II**
Product Codes:	**PKR, QAK**
Predicate Device:	**gammaCore Sapphire, K191830**

Indication for Use: The gammaCore Sapphire Non-invasive Vagus Nerve Stimulator is intended to provide non-invasive vagus nerve stimulation (nVNS) on the side of the neck. The gammaCore Sapphire device is indicated for:

- The preventive treatment of migraine headache in adolescent (age 12 and older) and adult patients.
- The acute treatment of pain associated with migraine headache in adolescents (age 12 and older) and adult patients.
- Adjunctive use for the preventive treatment of cluster headache in adult patients.
- The acute treatment of pain associated with episodic cluster headache in adult patients.

Device Description: The gammaCore Sapphire (gammaCore) is a multiuse, handheld, rechargeable, portable device consisting of a rechargeable battery and signal-generating and amplifying electronics, with a slide control switch for user/operator control of the signal amplitude (relative range, 0-40 continuous).

The gammaCore Sapphire:

- Includes a charging station incorporated into the "clam shell" storage case connected to a power adapter for charging of the device as necessary by the end user.
- Provides visible (light and display) and audible (beep) feedback regarding device and stimulation status.
- Allows for multiple stimulations or doses; each stimulation or dose lasts 120 seconds, after which the device automatically turns off unless turned off earlier by the user/operator.
  Note: One dose is defined as one stimulation cycle lasting 120 seconds (2 minutes).
- Delivers up to a fixed number of doses within a 24-hour period; once the maximum daily number of doses has been reached, the device will not deliver any more doses until the following 24-hour period.
- Indicates on the display the number of remaining doses available in a 24-hour period.

The device will be provided to the patient/user with an initial 10-, 31-, or 93-day RFID card on the basis of the healthcare provider's prescription. Additional (refill/reload) cards will be provided in response to a user/patient request based on a prescription from his or her healthcare provider. The refill/reload RFID cards will be programmed by electroCore or its authorized agent. This is a specialized application for dispensing the device therapy.

When a 10-, 31-, or 93-day refill/reload card is requested by a patient/user (in accordance with a prescription from a healthcare provider) for a unique device serial number, an RFID card is encoded with the appropriate dosage according to the prescription. The gammaCore RFID card loading application uses a proprietary encoding algorithm to encrypt the therapy days and doses per day on the refill/reload RFID card using near field communication (NFC) protocols.

The encoded refill/reload RFID card is then provided to the user/patient who requested the refill/reload of the device, along with one to six additional tubes of conductive gel (the number of conductive gel tubes provided is based on the 10-, 31-, or 93-day refill/reload being provided). On receipt of the RFID card, the user/patient refills/reloads his or her gammaCore device by placing the RFID card across the face of the device (with the device turned on). The device will display "rd" and the "refill" icon as the device reads the RFID card. The device will signal (beeping twice) when it has been loaded with the programmed doses. The device will now be ready for use as treatment. The RFID card can be used for only one refill/reload; upon completion of the device refill/reload, the card can be thrown away.

In addition, a Bluetooth® feature will be enabled to facilitate diagnostics of any devices returned by patients/users to the manufacturer, to allow determination of the number of days the device was used and/or the number of doses, as well as any days/doses remaining on the device. The Bluetooth feature will not be accessible to the patient/user; it is accessible only to the device manufacturer.

The subject device delivers the same energy and maintains the same operational characteristics as the gammaCore Sapphire device cleared in K191830. No changes in design or manufacturing process have been made that could affect device functionality. All functional aspects of the device remain the same as K191830, including the strength and nature of the device outputs.

Summary of Technological Characteristics:

There are no changes to the technological characteristics of the gammaCore Sapphire for this expanded labeling.

Summary of Non-clinical Testing:

There are no changes to the technological characteristics of the gammaCore Sapphire for this expanded labeling; no additional non-clinical or performance testing is required.

Summary of Clinical Data:

gammaCore Sapphire is the same as the predicate device and no technological changes have occurred. Thus, clinical testing was not conducted for this premarket notification, nor was required to support the safety and performance of the gammaCore Sapphire for the expanded Intended Use/Indications for Use population. Please refer to:

- K173442 for further information regarding the multicenter, randomized, double-blind, parallel-group, sham-controlled clinical study (PRESTO) supporting the safety and effectiveness of gammaCore Sapphire for the acute treatment of pain associated with migraine headache.
- K191830 for further information regarding the prospective, randomized, sham-controlled, multicenter studies (PREMIUM and EVENT studies) supporting the safety and effectiveness of gammaCore Sapphire for the preventive treatment of migraine headache.

Clinical data to support use of gamma Core Sapphire for preventive and acute treatment of migraine headache in the adolescent population has been extrapolated from clinical data in adult populations for the same indication. In addition to extrapolation of adult data, a small study was performed evaluating the use of gamma Core Sapphire in the acute treatment of migraine in adolescent population. As described in Grazzi et al[1], in nine (9) adolescents, 46.8% of treated migraine attacks were considered successfully treated and did not require any rescue medication. No device-related adverse events were observed. These results are consistent with those seen in adults and further supports the safety and effectiveness of the gamma Core Sapphire device in adolescents.

[1] Grazzi L, Egeo G, Liebler E, Padovan AM, Barbanti P. Non-invasive vagus nerve stimulation (nVNS) as symptomatic treatment of migraine in young patients: a preliminary safety study. Neurol Sci. 2017 May;38(Suppl 1):197-199. doi: 10.1007/s10072-017-2942-5. PMID: 28527086.

Substantial Equivalence Discussion:

gammaCore Sapphire technology is identical to the device technology cleared under K191830. There have been no changes in the technological characteristics or intended use of the gammaCore Sapphire. Therefore, there are no new issues of safety or effectiveness, thus, the subject gammaCore Sapphire is substantially equivalent to the predicate gammaCore Sapphire device.

Summary:

Table 1 establishes the substantial equivalence of the subject device to that of the predicate device.

Table 1. Substantial Equivalence Comparison Table

	gammaCore Sapphire (Predicate Device)	gammaCore Sapphire (Subject Device)	Substantial Equivalence
510(k) Number	K191830	TBD	
Intended Use	The gammaCore Sapphire is a device that provides non-invasive vagus nerve stimulation (nVNS) when applied to the side of the neck. This is a mild electrical stimulation of the vagus nerve, which runs through the neck and carries information to the central nervous system. Each stimulation with gammaCore lasts 2 minutes. The patient controls the stimulation strength.	The gammaCore Sapphire is a device that provides non-invasive vagus nerve stimulation (nVNS) when applied to the side of the neck. This is a mild electrical stimulation of the vagus nerve, which runs through the neck and carries information to the central nervous system. Each stimulation with gammaCore lasts 2 minutes. The patient controls the stimulation strength.	Same; no change in intended use
Indication for Use	The gammaCore Sapphire is indicated for: • The preventive treatment of cluster headache (CH) in adult patients. • The acute treatment of pain associated with episodic cluster headache (eCH) in adult patients. • The acute treatment of pain associated with migraine headache in adult patients. • The preventive treatment of migraine headache in adult patients.	The gammaCore Sapphire is indicated for: • The preventive treatment of cluster headache (CH) in adult patients. • The acute treatment of pain associated with episodic cluster headache (eCH) in adult patients. • The acute treatment of pain associated with migraine headache in adolescents (age 12 and older) and adult patients. • The preventive treatment of migraine headache in adolescent (age 12 and older) and adult patients.	Clinical data from the adult population has been fully extrapolated to support the expanded labeling for use of gammaCore Sapphire in adolescent patients for the preventive and acute treatment of migraine headache. Questions of safety or effectiveness have been addressed in the supporting data.
Rx vs OTC	Prescription use	Prescription use	No change

	gammaCore Sapphire (Predicate Device)	gammaCore Sapphire (Subject Device)	Substantial Equivalence
510(k) number	K191830	TBD	
Migraine Treatment recommendation	**Acute treatment of migraine:** 120-second stimulation cycle, 2 bilateral stimulations up to 3 times a day **Preventive treatment of migraine:** 120-second stimulation cycle, 2 consecutive stimulations on either side of the neck as follows: • First daily treatment: within 1 hour of waking • Second daily treatment: 4-6 hours after the first daily treatment • Third daily treatment: within 1 hour before going to sleep	**Acute treatment of migraine:** 120-second stimulation cycle, 2 bilateral stimulations up to 3 times a day **Preventive treatment of migraine:** 120-second stimulation cycle, 2 consecutive stimulations on either side of the neck as follows: • First daily treatment: within 1 hour of waking • Second daily treatment: 4-6 hours after the first daily treatment • Third daily treatment: within 1 hour before going to sleep	No change in treatment protocol for adolescents compared to adults.
Patient- contacting materials	SS, ABS-PC, SignaGel electrode gel	SS, ABS-PC, SignaGel electrode gel	No change in materials
Electrical classification	UL 60601-1 Class III Type BF Applied Part	UL 60601-1 Class III Type BF Applied Part	No change in classification
Waveform/frequency	Sinusoidal wave, symmetrical biphasic 5000-Hz pulses at a rate of 25 Hz	Sinusoidal wave, symmetrical biphasic 5000-Hz pulses at a rate of 25 Hz	No change in waveform or frequency
Maximum output	30V (peak), 60 mA(peak)	30V (peak), 60 mA(peak)	No change in outputs
Load impedance	450-550 ohms	450-550 ohms	No change in impedance
Power supply	3V LiFePo4 battery	3V LiFePo4 battery	No change in power supply voltage
Service life	3 Years from date of manufacture	3 Years from date of manufacture	No change in service life
Controls	Control slide Increase slide up/decrease slide down	Control slide Increase slide up/decrease slide down	No change in circuitry or controls of the subject and predicate devices
Output regulation	Device software and control slide	Device software and control slide	

	gammaCore Sapphire (Predicate Device)	gammaCore Sapphire (Subject Device)	Substantial Equivalence
Device status display	LED screen	LED screen	Differences between the subject device and reference device represent changes in the user interface. These changes do not impact the safety or effectiveness of the device.
Battery charger	Qi-compatible wireless charger in clam shell storage case	Qi-compatible wireless charger in clam shell storage case	
RFID refill/reload capability	Allows refilling/reloading of the number of days/doses for which the device can provide treatment; allows for continued use of same device for extended periods of time	Allows refilling/reloading of the number of days/doses for which the device can provide treatment; allows for continued use of same device for extended periods of time	
Device diagnostics, Bluetooth	Provides for diagnostics by manufacturer of returned devices, including number of days device was used, number of doses delivered, and remaining days/doses	Provides for diagnostics by manufacturer of returned devices, including number of days device was used, number of doses delivered, and remaining days/doses	
Start-up	Yes	Yes	No change in available alarm signals
Session complete	Yes	Yes	
Errors/depleted battery	Yes	Yes	
No doses left	Yes	Yes	
Expired/no days left	Yes	Yes	
Start-up (powered on)	Light on	Light on	No change to display/message in the subject and predicate devices Differences between the subject device and reference device represent changes in the user interface. These changes do not impact the safety or effectiveness of the device.
Unit ready (powered on)	LED doses remaining for 24-hr period	LED doses remaining for 24-hr period	
Dose complete	LED days and doses remaining and last amplitude	LED days, doses remaining, and last amplitude	
Errors/depleted battery	E# display	E# display	
No doses remaining	LED doses 00	LED doses 00	

	gammaCore Sapphire (Predicate Device)	gammaCore Sapphire (Subject Device)	Substantial Equivalence
Expired/no days left	LED doses/days remaining	LED doses/days remaining	
Low battery	LED display battery charge indicator	LED display battery charge indicator	
Reloading error	LED display if refill process fails	LED display if refill process fails	
Card error	LED display if refill card fails	LED display if refill card fails	

Conclusion:

The gammaCore Sapphire device is the same as the predicate device and no technological or intended use changes have occurred. Therefore, no new issues of safety or effectiveness are raised. Thus, gammaCore Sapphire is substantially equivalent to the predicate device.