November 27, 2018

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

Re: K182369
Trade/Device Name: gammaCore Sapphire
Regulation Number: 21 CFR 882.8592
Regulation Name: External Vagal Nerve Stimulator For Headache
Regulatory Class: Class II
Product Code: PKR, QAK
Dated: August 30, 2018
Received: August 31, 2018

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/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm); 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 http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). 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 (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Timothy A. Marjenin -S

For Carlos L. Peña, PhD, MS
Director
Division of Neurological
and Physical Medicine Devices
Office of Device Evaluation
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)*
K182369

Device Name
gammaCore Sapphire

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:

- 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.
- The acute treatment of pain associated with migraine 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.

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5 510(K) SUMMARY

The following information is provided as required by 21 CFR §807.87 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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Establishment Registration Number: 3009060963

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Date of Submission:	**August 30, 2018**
Proprietary Name:	**gammaCore Sapphire**
Common Name:	**External vagal nerve stimulator for headache**
Classification Status:	**Class II**
Product Codes:	**PKR, QAK**
Primary Predicate Device:	**gammaCore Sapphire, K180538**
Reference Device:	**gammaCore-S, K173442**

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:

- 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.
- The acute treatment of pain associated with migraine 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 using the gammaCore Dispensing and Ordering Terminal (gammaCore DOT) 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 encoded RFID card is matched to a specific gammaCore device serial number residing in a database maintained by electroCore. The gammaCore DOT application, running on a Sony Xperia® tablet, 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 encoding algorithm is based on a seed-value pair of numbers specific to a device ID (unique device serial number) that is registered in the gammaCore DOT database. The gammaCore DOT application ensures that only legitimate seed values allow refilling/reloading of the device through validation of the prescription and seed values in the gammaCore DOT database using the unique device and patient IDs.

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.

Summary of Technological Characteristics:

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

Summary of Non-clinical Testing:

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

Summary of Clinical Data:

Clinical data demonstrating the safety and effectiveness of the gammaCore Sapphire for the prophylactic/preventive treatment of cluster headache were collected from a multicenter, randomized, controlled study that took place across 10 sites in Europe from November 23, 2012, to April 30, 2014. The study was designed to compare two parallel groups, standard of care (SoC) plus nVNS (active treatment) versus SoC alone (control). The study began with a 2-week run-in period, followed by a 4-week comparative period when the subjects were randomized 1:1 to either active treatment or control. The comparative period was followed by an open-label period during which all subjects received active treatment with gammaCore in addition to the SOC for 4 weeks.

Subject demographics were similar among the SoC plus nVNS and control groups that comprised the study population (Table 3).

Table 3. Subject Demographic Characteristics (safety population)

Characteristic	nVNS plus SoC (n=48)	Control (n=49)
Age, y, mean (SD)	45.4 (1.0)	42.3 (11.0)
Sex, no. (%) Male	34 (71)	33 (67)
Race, no. (%) Caucasian	48 (100)	49 (100)

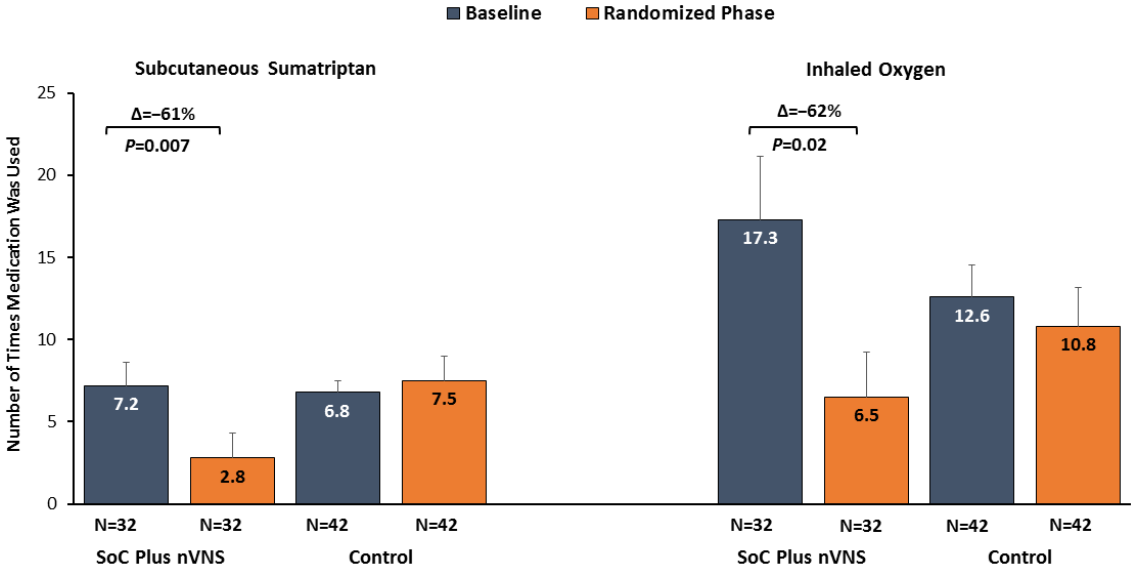
Abbreviations: nVNS, non-invasive vagus nerve stimulation; SD, standard deviation; SoC, standard of care.

Consistent with previous studies of nVNS for the treatment of primary headache, nVNS was safe and well tolerated. The primary endpoint of the study was the change in mean number of CH attacks per week. The mean number of CH attacks per week was calculated as the sum of all attacks during the 2-week run-in period divided by 2 and as the sum of all attacks during the last 14 days of the randomized period divided

by 2. The change in mean number of attacks was calculated as the number of CH attacks per week during the randomized period (last 14 days) minus the number of CH attacks per week during the run-in period. Subjects treated with SoC plus nVNS had a significantly greater reduction in the number of cluster attacks per week versus the control arm (5.9 vs 2.1, respectively) for a mean therapeutic gain of 3.9 fewer attacks per week (95% CI: 0.5, 7.2; *P*=0.02). Higher 50% responder rates were also observed among subjects using SoC plus nVNS (40%) versus controls (8.3%) (*P*<0.001). SoC plus nVNS led to a reduction in the use of abortive medications from baseline to the last 2 weeks of the randomized phase (Figure 1). nVNS and SoC use was also associated with clinically meaningful improvements in the quality of life outcomes evaluated (Table 4). There was no change in CH duration or severity of acute attacks reported in this trial.

Figure 1. Abortive Medication Use (mITT Population)

Use of Sumatriptan and Oxygen: Baseline Versus the Last 2 Weeks of the Randomized Phase



Abbreviations: mITT, modified intent-to-treat; nVNS, non-invasive vagus nerve stimulation; SoC, standard of care.
Values are presented as means and were calculated from all subjects with evaluable data. Error bars denote standard error of the mean.

Table 4. Quality of Life Outcomes (ITT[a] and mITT Populations[b])

QoL Measures	Mean Change From Baseline to Randomized Phase		Mean Change From Baseline to Extension Phase	
ITT Population				
	SoC Plus nVNS (n=45)	**Control (n=48)**	**SoC Plus nVNS (n=45)**	**Control (n=48)**
EQ-5D-3L Index score	0.113[c]	−0.047	0.117	0.065
EQ-5D-3L VAS score	7.16	0.250	8.16	3.54
HIT-6 score	−2.29	−0.438	−2.62	−2.25
mITT Population				
	SoC Plus nVNS[d]	**Control[e]**	**SoC Plus nVNS[f]**	**Control[g]**
EQ-5D-3L Index score	0.145[h]	−0.049	0.155	0.078
EQ-5D-3L VAS score	9.20[i]	0.27	10.79	4.36
HIT-6 score	−2.78	−0.47	−3.28	−2.77

Abbreviations: ITT, intent-to-treat; HIT-6, 6-item Headache Impact Test; mITT, modified intent-to-treat; nVNS, non-invasive vagus nerve stimulation; QoL, quality of life; SoC, standard of care; VAS, visual analogue scale.
[a]For the ITT population, missing data were imputed to no change from baseline to the randomized phase or from baseline to the extension phase, respectively.
[b]All mITT calculations were performed for subjects with available data. No imputation for missing data was performed.
[c]*P*=0.011 versus control..
[d]Number of evaluated subjects in the SoC plus nVNS group was 35 for the EQ-5D-3L index score and the EQ-5D-3L VAS score and 37 for the HIT-6 score.
[e]Number of subjects evaluated in the control group was 46 for the EQ-5D-3L index score and the EQ-5D-3L VAS score and for the HIT-6 score:.
[f]Number of evaluated subjects in the SoC plus nVNS group was 34 for the EQ-5D-3L index score and the EQ-5D-3L VAS score and 36 for the HIT-6 score
[g]Number of evaluated subjects in the control group was 40 for the EQ-5D-3L index score and 39 for the EQ-5D-3L VAS score and the HIT-6 score..
[h]*P*=0.007 versus control.
[i]*P*=0.039 versus control.

nVNS was safe and well tolerated in both the randomized clinical trial as well as in the real-world study that supports this application. In the 2 months of treatment during the PREVA study, a similar proportion of participants in the SoC plus nVNS group and controls reported any AE. As with the studies supporting the currently cleared indications, the majority of AEs (>90%) were mild, transient, and self-limiting.

Clinical data demonstrating the safety and effectiveness of acute treatment of pain associated with migraine headache were provided in the gammaCore-S submission (K173442) and are applicable to the

gammaCore Sapphire. The gammaCore-S and gammaCore Sapphire have the same fundamental scientific technology and intended use. The devices do not differ in output, waveform, or treatment protocol.

Substantial Equivalence Discussion:

gammaCore Sapphire technology is identical to the device technology cleared under K180538. There have been no changes in the technological characteristics or intended use of the gammaCore Sapphire in the proposed Indications for Use Statement. The instructions for the device associated with acute treatment of episodic cluster headache do differ from those for preventive treatment of cluster headache and those for migraine headache; however, for all indications, use of more than 24 stimulations per day has not been formally evaluated and continues to be listed as a precaution in the labeling.

Summary:

Table 5 establishes the substantial equivalence of the subject device to that of the predicate device.

Table 5. Substantial Equivalence Comparison Table

	gammaCore Sapphire (Subject Device)	gammaCore Sapphire (Primary Predicate)	gammaCore-S (Reference Device)	Substantial Equivalence
510(k) number	TBD	K180538	K173442	
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 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-S is a device that provides 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.	No change in intended use
Indication for use	The gammaCore Sapphire is indicated for: • Adjunctive use 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 gammaCore Sapphire is indicated for the acute treatment of pain associated with eCH in adult patients	The gammaCore-S device is indicated for the acute treatment of pain associated with eCH and migraine headache in adult patients	The expansion of the indication does not alter the intended therapeutic effect or otherwise create a new intended use, as explained previously. Supported by clinical data in Section 20 of this submission.
Rx vs OTC	Prescription use only	Prescription use only	Prescription use only	No change

	gammaCore Sapphire (Subject Device)	gammaCore Sapphire (Primary Predicate)	gammaCore-S (Reference Device)	Substantial Equivalence
Treatment recommendation	Preventive treatment of CH: 120-second stimulation cycle, 3 consecutive stimulations- on either side of the neck as follows: o First daily treatment: within 1 hour of waking o Second daily treatment: at least 7-10 hours after the first daily treatment Acute treatment of eCH: 120-second stimulation cycle, 3 consecutive stimulations up to 8 times a day Acute treatment of migraine: 120-second stimulation cycle, 2 bilateral stimulations up to 3 times a day	Acute treatment of eCH: 120-second stimulation cycle, 3 consecutive stimulations up to 8 times a day	Acute treatment of eCH: 120-second stimulation cycle, 3 consecutive stimulations up to 8 times a day Acute treatment of migraine: 120-second stimulation cycle, 2 bilateral stimulations up to 3 times a day	Change in treatment protocol to reflect different forms of primary headache
Patient-contacting materials	SS, ABS-PC, SignaGel® electrode gel	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	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	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)	30V (peak), 60 mA(peak)	No change in outputs
Load impedance	450-550 ohms	450-550 ohms	450-550 ohms	No change in impedance
Power supply	3V LiFePo4 battery	3V LiFePo4 battery	3V LiFePo4 battery	No change in power supply voltage

	gammaCore Sapphire (Subject Device)	gammaCore Sapphire (Primary Predicate)	gammaCore-S (Reference Device)	Substantial Equivalence
Service life	3 Years from date of manufacture	3 Years from date of manufacture	3 Years from date of manufacture	No change in service life
Device circuitry				
Controls	Control slide Increase slide up/decrease slide down	Control slide Increase slide up/decrease slide down	Increase (+) and decrease (-) push buttons	No change in circuitry or controls of 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.
Output regulation	Device software and control slide	Device software and control slide	Device software and push buttons	
Device status display	LED screen	LED screen	LCD screen	
Battery charger	Qi-compatible wireless charger in clam shell storage case	Qi-compatible wireless charger in clam shell storage case	Not applicable	
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	Not applicable	
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	Not applicable	

	gammaCore Sapphire (Subject Device)	gammaCore Sapphire (Primary Predicate)	gammaCore-S (Reference Device)	Substantial Equivalence
Audible signals/alarms				
Start-up	Yes	Yes	Yes	No change in available alarm signals
Session complete	Yes	Yes	Yes	
Errors/depleted battery	Yes	Yes	Yes	
No doses left	Yes	Yes	Yes	
Expired/no days left	Yes	Yes	Yes	
Visual indicators/status				
Start-up (powered on)	Light 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	Light on/LCD amplitude “0”	
Dose complete	LED days and doses remaining and last amplitude	LED days, doses remaining, and last amplitude	Light off/LCD days, doses remaining, and last amplitude	
Errors/depleted battery	E# display	E# display	LCD “Err”/flashing light	
No doses remaining	LED doses 00	LED doses 00	Flashing light/LCD number of doses remaining	
Expired/no days left	LED doses/days remaining	LED doses/days remaining	Flashing light/LCD days remaining	
Low battery	LED display battery charge indicator	LED display battery charge indicator	No light/LCD display “Lo”	
Reloading error	LED display if refill process fails	LED display if refill process fails	Not applicable	
Card error	LED display if refill card fails	LED display if refill card fails	Not applicable	

Conclusion:

There have been no changes in the technological characteristics or intended use of the gammaCore Sapphire. Clinical data demonstrating the safety and effectiveness of acute treatment of pain associated with migraine headache were provided previously for gammaCore-S in submission K173442 and are applicable to the gammaCore Sapphire. The addition of the preventive treatment of cluster headache to the Indications for Use does not raise new or different questions of safety or effectiveness compared to those raised with the predicate device. Therefore, the presented information demonstrates that the subject device is substantially equivalent to the predicate device.