March 26, 2020

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

Re: K191830
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: February 25, 2020
Received: February 27, 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,

Vivek Pinto, PhD
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: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K191830

Device Name
gammaCore Sapphire

Indications for Use *(Describe)*
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.
• The preventive treatment of 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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Partner
Hogan Lovells US LLP
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Date of Submission:	**March 24, 2020**
Proprietary Name:	**gammaCore Sapphire**
Common Name:	**External vagal nerve stimulator for headache**
Classification Status:	**Class II**
Product Codes:	**PKR, QAK**
Predicate Device:	**gammaCore Sapphire, K182369**

Indications 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.
- The preventive treatment of 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 radio-frequency identification (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 1 to 6 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 migraine headache were collected from the PREMIUM study and the EVENT study. The PREMIUM study was a prospective, randomized, double-blind, sham-controlled, multicenter study in patients with episodic migraine conducted at 22 European sites from June 1, 2015, to November 21, 2017. It consisted of a 4-week run-in period of no study treatment, which was followed by a 12-week double-blind phase of randomly

assigned preventive treatment with nVNS or sham and a 24-week open-label phase during which all participants received nVNS therapy. Post hoc analysis of the modified intent-to-treat (mITT) population, which included subjects with ≥67% adherence per month, showed significant differences between groups in favor of nVNS for the study's primary endpoint, mean reduction in the number of migraine days per month (therapeutic gain, 0.74; *P*=0.043), as well as for headache days per month (therapeutic gain, 0.86; *P*=0.045) and acute medication days per month (therapeutic gain, 0.80; *P*=0.039). Response to treatment with nVNS during the double-blind period was maintained with further nVNS therapy during the open-label period. The sham device used in the PREMIUM study was recently proven to have activated the vagus nerve. This likely mitigated the therapeutic gain measured in the PREMIUM study. **Table 3** summarizes the key characteristics of the PREMIUM study.

Table 3. Key Characteristics of the PREMIUM Study

Test device	gammaCore R-30 (10015-00302)	
Study design	Randomized, sham-controlled, double-blind trial	
n	ITT	mITT
	332	278
Sites	22	
Trial duration (per subject)	10 months (1-month screening, 3-month randomization phase, and 6-month open-label phase)	
Treatment paradigm	Each treatment consisted of 2 consecutive 2-minute stimulations administered on the same side of the neck 3 times per day: (1) upon waking and (2, 3) 6 to 8 hours after the first and second daily treatments	
Primary efficacy endpoint	Mean reduction in the number of migraine days from the 4-week run-in period (baseline) to the last 4 weeks of the 12-week double-blind period	
Secondary efficacy endpoints	• Reductions in number of headache days • Subjects with ≥50% response rate	
Primary safety endpoint	Assessment of onset, type, severity, and frequency of adverse events (anticipated and unanticipated), including determination of device relatedness	
Key inclusion criteria	1. Between the ages of 18 and 75 years 2. Previously diagnosed as suffering from migraine with or without aura in accordance with the International Classification of Headache Disorders-3 Beta criteria 3. Experienced between 5 and 12 headache days per month (over the last 4 months) with at least 2 of the migraines lasting more than 4 hours 4. No use of any migraine prevention treatments and/or medications (including Botox® [onabotulinumtoxinA] injections) 5. Agreed to refrain from changing the type or dosage of any prophylactic medications for indications other than chronic migraine that in the opinion of the clinician might interfere with the study objectives (eg, antidepressants, anticonvulsants, beta-adrenergic blockers)	

<table>
<tr><td>Key exclusion criteria</td><td colspan="7">1. A history of aneurysm, intracranial hemorrhage, brain tumors, or significant head trauma
2. Known or suspected severe atherosclerotic cardiovascular disease, severe carotid artery disease (eg, bruits or history of transient ischemic attack or cerebrovascular accident), congestive heart failure, known severe coronary artery disease, or recent myocardial infarction
3. Uncontrolled high blood pressure
4. Current implantation of an electrical and/or neurostimulator device, including but not limited to a cardiac pacemaker or defibrillator, vagal neurostimulator, deep brain stimulator, spinal stimulator, bone growth stimulator, or cochlear implant
5. Current implantation of metal cervical spine hardware or a metallic implant near the gammaCore stimulation site</td></tr>
<tr><td rowspan="5">Subject baseline demographics</td><td rowspan="2">Device</td><td rowspan="2">Population</td><td colspan="2">Sex, No. (%)</td><td rowspan="2">Age, y, mean (SD)</td><td rowspan="2">Headache days, mean (SD)</td><td rowspan="2">Migraine days, mean (SD)</td></tr>
<tr><td>Female</td><td>Male</td></tr>
<tr><td rowspan="2">nVNS</td><td>ITT</td><td>142 (86.1)</td><td>23 (13.9)</td><td>43.5 (11.1)</td><td>8.9 (2.6)</td><td>7.9 (2.2)</td></tr>
<tr><td>mITT</td><td>119 (86)</td><td>19 (14)</td><td>43.9 (11)</td><td>8.9 (2.6)</td><td>8.1 (2.1)</td></tr>
<tr><td rowspan="2">Sham</td><td>ITT</td><td>138 (82.6)</td><td>29 (17.4)</td><td>41.4 (12.3)</td><td>9.1 (2.6)</td><td>8.1 (2.0)</td></tr>
<tr><td>mITT</td><td>115 (82)</td><td>25 (18)</td><td>41.8 (12)</td><td>9.0 (2.6)</td><td>8.1 (2.1)</td></tr>
<tr><td>Primary safety endpoint results</td><td colspan="7">• Preventive nVNS therapy was safe and well tolerated
• Across all study periods, the most common adverse device effects were rash, pain, erythema, discomfort at the application site, and dizziness
• No serious adverse device effects were reported during the study</td></tr>
<tr><td rowspan="4">Primary efficacy endpoint results</td><td colspan="2" rowspan="2">Population</td><td rowspan="2">n (nVNS/Sham)</td><td colspan="2">Mean change from baseline in no. of migraine days per month</td><td rowspan="2">Therapeutic gain</td><td rowspan="2">P value</td></tr>
<tr><td>nVNS</td><td>Sham</td></tr>
<tr><td colspan="2">ITT</td><td>165/167</td><td>-2.3</td><td>-1.8</td><td>-0.47</td><td>0.15</td></tr>
<tr><td colspan="2">mITT</td><td>138/140</td><td>-2.3</td><td>-1.5</td><td>-0.74</td><td>0.04</td></tr>
<tr><td>Control for medication use</td><td colspan="7">• The use of migraine prevention medication was not allowed
• Medications were allowed for the acute relief of migraine symptoms</td></tr>
</table>

Diener HC, Goadsby PJ, Ashina M, et al. Non-invasive vagus nerve stimulation (nVNS) for the preventive treatment of episodic migraine: the multicentre, double-blind, randomised, sham-controlled PREMIUM trial. *Cephalalgia*. 2019;39(12):1475-1487.
Abbreviations: ITT, intent-to-treat; mITT, modified intent-to-treat; nVNS, non-invasive vagus nerve stimulator; SD, standard deviation.

The EVENT study, a prospective, randomized, sham-controlled, multicenter pilot study for the prevention of chronic migraine, was conducted at 6 sites in the United States from October 2012 to April 2014. It consisted of a 4-week run-in phase of no study treatment, an 8-week double-blind phase of randomly assigned preventive treatment with nVNS or sham, and a 6-month open-label phase of nVNS treatment for all participants. The primary efficacy measure, mean change from baseline to month 2 in the number of headache days per month, was –1.4 in the nVNS group and –0.2 in the sham group. Continued nVNS use led to significant reductions from

baseline in the number of headache days per month during the open-label period. Among subjects who completed the study, the proportion who had a ≥50% reduction from baseline in the number of headache days per month increased with greater duration of treatment. Such findings suggest that the benefits of nVNS therapy may accrue over time. **Table 4** summarizes the key characteristics of the EVENT study.

Table 4. Key Characteristics of the EVENT Study

Test device	gammaCore-150 (10007-00305)	
Study design	Randomized, sham-controlled, double-blind trial	
n	ITT	PP
	59	49
Sites	6	
Trial duration (per subject)	9 months (1-month screening, 2-month randomization phase, and 6-month open-label phase)	
Treatment paradigm	Each treatment consisted of two 2-minute self-administered stimulations delivered 5 to 10 minutes apart to the right side of the neck at 3 prespecified times every day: (1) within 1 hour of awakening; (2) 6 to 8 hours after the first treatment; and (3) 6 to 8 hours after the second treatment	
Primary efficacy endpoint	Change in the mean number of headache days at the end of month 2 of the randomized phase compared with baseline	
Secondary efficacy endpoint	Severity of each headache day	
Primary safety endpoint	Assessment of the onset, type, severity, and frequency of adverse events (anticipated and unanticipated), including the determination of device relatedness	
Key inclusion criteria	1. Between the ages of 18 and 65 years 2. Previously diagnosed as suffering from migraine with or without aura in accordance with the International Classification of Headache Disorders-2 criteria 3. Experienced at least 15 headache days per month (over the last 3 months) 4. No use of any migraine prevention treatments and/or medications (including Botox® [onabotulinumtoxinA] injections) 5. Agreement to refrain from changing the type or dosage of any prophylactic medications for indications other than chronic migraine that in the opinion of the clinician might interfere with the study (eg, antidepressants, anticonvulsants, beta-adrenergic blockers)	
Key exclusion criteria	1. A history of aneurysm, intracranial hemorrhage, brain tumors, or significant head trauma 2. Known or suspected severe atherosclerotic cardiovascular disease, severe carotid artery disease (eg, bruits or history of transient ischemic attack or cerebrovascular accident), congestive heart failure, known severe coronary artery disease, or recent myocardial infarction 3. Uncontrolled high blood pressure 4. Current implantation of an electrical and/or neurostimulator device, including but not limited to cardiac pacemaker or defibrillator, vagal neurostimulator, deep brain stimulator, spinal stimulator, bone growth stimulator, or cochlear implant 5. Current implantation of metal cervical spine hardware or a metallic implant near the gammaCore stimulation site	

<table>
<tr><td rowspan="6">Subject baseline demographics</td><td rowspan="2">Device</td><td rowspan="2">Population</td><td colspan="2">Sex, No. (%)</td><td rowspan="2">Age, y, mean (SD)</td><td rowspan="2">Headache days, mean (SD)</td></tr>
<tr><td>Female</td><td>Male</td></tr>
<tr><td rowspan="2">nVNS</td><td>ITT</td><td>26 (87)</td><td>4 (13)</td><td>40.5 (14.2)</td><td>20.8 (5.0)</td></tr>
<tr><td>PP</td><td>22 (85)</td><td>4 (15)</td><td>42.0 (14.4)</td><td>22.7 (6.0)</td></tr>
<tr><td rowspan="2">Sham</td><td>ITT</td><td>27 (93)</td><td>2 (7)</td><td>38.8 (11.1)</td><td>22.3 (4.9)</td></tr>
<tr><td>PP</td><td>22 (96)</td><td>1 (4)</td><td>39.3 (11.1)</td><td>25.2 (5.0)</td></tr>
<tr><td>Primary safety endpoint results</td><td colspan="6">• nVNS had a benign tolerability profile that was generally similar to that of the sham treatment
• Most adverse events were mild or moderate and transient
• The most commonly reported adverse events were upper respiratory tract infections and gastrointestinal symptoms</td></tr>
<tr><td rowspan="4">Primary efficacy endpoint results</td><td colspan="2" rowspan="2">Population</td><td rowspan="2">n (nVNS/Sham)</td><td colspan="2">Mean change from baseline in no. of migraine days per month</td><td rowspan="2">Therapeutic gain</td><td rowspan="2">P value</td></tr>
<tr><td>nVNS</td><td>Sham</td></tr>
<tr><td colspan="2">ITT</td><td>30/29</td><td>-1.4</td><td>-0.2</td><td>-1.2</td><td>0.56</td></tr>
<tr><td colspan="2">PP</td><td>26/23</td><td>-2.0</td><td>-0.1</td><td>-1.9</td><td>0.44</td></tr>
<tr><td>Control for medication use</td><td colspan="6">• The use of migraine prevention medication was not allowed
• Medications were allowed for the acute relief of migraine symptoms</td></tr>
</table>

Silberstein SD, Calhoun AH, Lipton RB, et al. Chronic migraine headache prevention with noninvasive vagus nerve stimulation: the EVENT study. *Neurology.* 2016;87(5):529-538.
Abbreviations: ITT, intent-to-treat; nVNS, non-invasive vagus nerve stimulator; PP, per-protocol; SD, standard deviation.

Consistent with results from previous trials, nVNS was shown to be safe and well tolerated in both the PREMIUM and EVENT studies. No serious device-related adverse events (AEs) were reported, and no new safety concerns for nVNS use in the intended population were apparent.

Substantial Equivalence Discussion:

gammaCore Sapphire technology is identical to the device technology cleared under K182369. 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 the dosing for the prevention of migraine headache differ from those for preventive or acute treatment of cluster headache and those for the acute treatment of 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 (Predicate Device)	Substantial Equivalence
510(k) number	TBD	K182369	
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.	No change in intended use
Indications 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 preventive treatment of migraine headache in adult patients	The gammaCore Sapphire is indicated for: • Adjunctive use for the preventive treatment of CH in adult patients • The acute treatment of pain associated with eCH in adult patients • The acute treatment of pain associated with 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 this submission.
Rx vs OTC	Prescription use only	Prescription use only	No change

	gammaCore Sapphire (Subject Device)	gammaCore Sapphire (Predicate Device)	Substantial Equivalence
Treatment recommendation	**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 **Preventive treatment of CH**: 120-second stimulation cycle, 3 consecutive stimulations on either side of the neck as follows: • First daily treatment: within 1 hour of waking • Second daily treatment: 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	**Preventive treatment of CH**: 120-second stimulation cycle, 3 consecutive stimulations on either side of the neck as follows: • First daily treatment: within 1 hour of waking • Second daily treatment: 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	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	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

	gammaCore Sapphire (Subject Device)	gammaCore Sapphire (Predicate Device)	Substantial Equivalence
Maximum output	30 V (peak), 60 mA (peak)	30 V (peak), 60 mA(peak)	No change in outputs
Load impedance	450-550 ohms	450-550 ohms	No change in impedance
Power supply	3-V LiFePo4 battery	3-V 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 device.
Output regulation	Device software and control slide	Device software and control slide	
Device status display	LED screen	LED screen	
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	

	gammaCore Sapphire (Subject Device)	gammaCore Sapphire (Predicate Device)	Substantial Equivalence
Expired/no days left	Yes	Yes	
Start-up (powered on)	Light on	Light on	No change to display/message in the subject and predicate device.
Unit ready (powered on)	LED doses remaining for 24-hour period	LED doses remaining for 24-hour period	
Dose complete	LED days, 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	
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	

Abbreviations: ABS-PC, acrylonitrile-butadiene-styrene polycarbonate; LED, light-emitting diode; OTC, over the counter; RFID, radio-frequency identification; Rx, prescription; SS, stainless steel; TBD, to be determined.

Conclusion:

There have been no changes in the technological characteristics or intended use of the gammaCore Sapphire. The addition of the preventive treatment of migraine 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.