July 10, 2020

Mike Romaniw
EVP, Regulatory and Operations
o/b/o electroCore, Inc.
150 Allen Road, Suite 201
Basking Ridge, NJ 07920

Dear Mr. Romaniw:

This letter is in response to your request on behalf of electroCore, Inc. that the U.S. Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for the emergency use of the gammaCore Sapphire CV, intended for acute use at home or in a healthcare setting to treat adult patients with known or suspected COVID-19 who are experiencing exacerbation of asthma-related dyspnea and reduced airflow, and for whom approved drug therapies are not tolerated or provide insufficient symptom relief as assessed by their healthcare provider (HCP), by using non-invasive Vagus Nerve Stimulation (nVNS) on either side of the patient's neck.

On February 4, 2020, pursuant to section 564(b)(1)(C) of the Federal Food, Drug, and Cosmetic Act (the Act), the Secretary of the Department of Health and Human Services (HHS) determined that there is a public health emergency that has a significant potential to affect national security or the health and security of United States citizens living abroad, and that involves the virus that causes COVID-19.[1] Pursuant to section 564 of the Act, and on the basis of such determination, the Secretary of HHS then declared on March 24, 2020, that circumstances exist justifying the authorization of emergency use of medical devices during the COVID-19 outbreak, subject to the terms of any authorization issued under that section.[2]

There are no FDA approved or cleared devices for this intended use. Early reports of COVID-19 infections demonstrate a high level of aggressive, prolonged inflammation in the airways which will likely result in significant worsening of asthma symptoms in the large asthmatic population. While there are drug treatments available, the gammaCore Sapphire CV may provide benefits to some patients for whom standard drug therapy is unable to meet their needs. FDA has also determined that the available information also indicates that the gammaCore Sapphire CV may be an effective alternative for those who cannot tolerate beta agonists or for those whose exacerbations cannot be controlled with the limited use associated with standard inhaled

[1] U.S. Department of Health and Human Services, *Determination of a Public Health Emergency and Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3*. 85 FR 7316 (February 7, 2020).
[2] U.S. Department of Health and Human Services, *Declaration that Circumstances Exist Justifying Authorizations Pursuant to Section 564(b) of the Federal Food, Drug, and Cosmetic Act, 21 U.S.C. § 360bbb-3*, 85 FR 17335 (March 27, 2020).

treatments. As such, FDA has determined that standard drug therapy alternatives may not always be adequate, as set forth in Section I. In coming to these conclusions, FDA reviewed all available information, including data on the use of the gammaCore Sapphire CV on asthma patients, as well as data regarding the device's safety in clinical use for other indications.[3] The device was not studied in COVID-19 patients. Based on this evidence, FDA has made the conclusions described in Section I below.

Having concluded that the criteria for issuance of this authorization under section 564(c) of the Act are met, I am authorizing the emergency use of the gammaCore Sapphire CV, as described in the Scope of Authorization (Section II) and pursuant to the Conditions of Authorization (Section IV) of this letter.

## I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the gammaCore Sapphire CV as described in the Scope of Authorization (Section II) of this letter meets the criteria for issuance of an authorization under section 564(c) of the Act, because I have concluded that:

1. SARS-CoV-2, the virus that causes COVID-19, can cause a serious or life-threatening disease or condition, including severe respiratory illness, to humans infected by this virus;

2. Based on the totality of scientific evidence available to FDA, it is reasonable to believe that the gammaCore Sapphire CV may be effective for acute emergency use at home or in a healthcare setting to treat adult patients with known or suspected COVID-19 who are experiencing exacerbation of asthma-related dyspnea and reduced airflow, and for whom approved drug therapies are not tolerated or provide insufficient symptom relief as assessed by their HCP, by using non-invasive Vagus Nerve Stimulation (nVNS) on either side of the patients neck, and that the known and potential benefits of this product for such use outweigh the known and potential risks of such product; and,

3. There are no adequate, approved, and available device alternatives to the emergency use of the gammaCore Sapphire CV for such use.[4]

## II. Scope of Authorization

I have concluded, pursuant to section 564(d)(1) of the Act, that the scope of this authorization is limited to the emergency use of the gammaCore Sapphire CV for acute use at home or in healthcare settings to treat adult patients with known or suspected COVID-19 who are experiencing exacerbation of asthma-related dyspnea and reduced airflow, and for whom approved drug therapies are not tolerated or provide insufficient symptom relief as assessed by their healthcare provider, using non-invasive VNS on either side of the patient's neck during the

[3] The gammaCore Sapphire CV was granted the European CE mark in 2011 (under the trade name gammaCore) for use in certain respiratory indications, including for the treatment or prevention of reactive airway disease, which includes asthma, bronchoconstriction, exercise induced bronchospasm, and COPD in adults.
[4] No other criteria of issuance have been prescribed by regulation under section 564(c)(4) of the Act.

COVID-19 pandemic. The gammaCore Sapphire CV may help patients with reduced airflow and dyspnea due to exacerbation of asthma from COVID-19 by potentially inhibiting airway constriction, resulting in smooth muscle relaxation and reducing the potential for the virus to induce such symptoms. Stimulation from the gammaCore Sapphire CV can be used on either side of the patient's neck. Each self-administered treatment should consist of two consecutive 2-minute stimulations (up to 24 stimulations in a 24-hour period) at the onset of respiratory distress or shortness of breath.

The gammaCore Sapphire CV is **not** intended for use:

- In patients with an active implantable medical device, such as a pacemaker, hearing aid implant, or any implanted electronic device;
- If the patient has a metallic device, such as a stent, bone plate, or bone screw, implanted at or near their neck;
- If the patient has an open wound, rash, infection, swelling, cut, sore, drug patch, or surgical scar(s) on their neck at the treatment location.

**Authorized Product**

The gammaCore Sapphire CV is a multiuse, handheld, rechargeable, portable, non-invasive vagus nerve stimulator consisting of a rechargeable battery, signal-generating and amplifying electronics, with a slide control switch for user/operator control of the signal amplitude (relative range, 0-40 continuous), an LED screen and auditory signal (to indicate device status), and a pair of stainless steel skin contact surfaces (referred to as the "stimulation surfaces"). A cap is provided to cover the stimulation surfaces when the device is not in use. A charging case and conductive electrode gel are also provided.

The gammaCore Sapphire CV produces a low-voltage electrical signal consisting of five 5000-Hz pulses that are repeated at a rate of 25 Hz. The waveform of the electric pulses approximates a sine wave with peak voltage limited to +/-30 Volts (24 Volts when against the skin of the neck) and a maximum output current of 60mA. The signal is transmitted through the skin of the neck to the vagus nerve. Each stimulation with the gammaCore Sapphire CV lasts 2 minutes.

The user applies the gammaCore Sapphire CV over the vagus nerve by holding the stimulation surfaces against the skin of the side of the neck. The user maintains an uninterrupted conductive path from the stimulation surfaces to the skin with the use of the provided conductive gel. The device may be operated by a HCP or by the patient (self-treatment). The device is capable of delivering multiple treatments (doses) to the patient. With each treatment, the device is active for 120 seconds before automatically stopping stimulation. The gammaCore Sapphire CV delivers up to 30 stimulations in a 24-hour period, starting when the device is turned on and the intensity level is increased above 3. Once the maximum daily number of stimulations has been reached, the device will not deliver any more stimulations until the following 24-hour period. The use of more than 24 stimulations per day has not been evaluated in controlled clinical trials. The user should not use more than 24 stimulations in a 24-hour period.

The above described gammaCore Sapphire CV is authorized to be accompanied with the "Instructions for Use for gammaCore Sapphire CV," (available at https://www.fda.gov/medical-

devices/coronavirus-disease-2019-covid-19-emergency-use-authorizations-medical-devices/respiratory-assist-devices-euas), together with the following product-specific information pertaining to emergency use, which is required to be made available to HCPs and patients:

- Fact Sheet for Healthcare Providers: Emergency Use of the gammaCore Sapphire CV During the COVID-19 Pandemic
- Fact Sheet for Patients: Emergency Use of the gammaCore Sapphire CV During the COVID-19 Pandemic

The "Instructions for Use for gammaCore Sapphire CV" and the two Fact Sheets are referred to as "authorized labeling." The above described gammaCore Sapphire CV, when accompanied with the described labeling is authorized to be distributed to and used under this EUA, despite the fact that it does not meet certain requirements otherwise required by federal law.

I have concluded, pursuant to section 564(d)(2) of the Act, that it is reasonable to believe that the known and potential benefits of the authorized gammaCore Sapphire CV, when used consistent with the Scope of Authorization of this letter (Section II), outweigh the known and potential risks of such products.

I have concluded, pursuant to section 564(d)(3) of the Act, based on the totality of scientific evidence available to FDA, it is reasonable to believe that the gammaCore Sapphire CV may be effective for acute use at home or in a healthcare setting to treat adult patients with known or suspected COVID-19 who are experiencing exacerbation of asthma-related dyspnea and reduced airflow, and for whom approved drug therapies are not tolerated or provide insufficient symptom relief as assessed by their HCP, by using non-invasive Vagus Nerve Stimulation (nVNS) on either side of the patients neck and that the known and potential benefits of this product for such use outweigh the known and potential risks of such product; when used consistent with the Scope of Authorization of this letter (Section II), pursuant to section 564(c)(2)(A) of the Act.

FDA has reviewed the scientific information available to FDA, including the information supporting the conclusions described in Section I above, and concludes that the authorized gammaCore Sapphire CV, as described in the Scope of Authorization of this letter (Section II), meets the criteria set forth in section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of the authorized gammaCore Sapphire CV under this EUA must be consistent with, and may not exceed, the terms of this letter, including the Scope of Authorization (Section II) and the Conditions of Authorization (Section IV). Subject to the terms of this EUA and under the circumstances set forth in the Secretary of DHS's determination described above and the Secretary of HHS's corresponding declaration under section 564(b)(1), the gammaCore Sapphire CV is authorized to be used and distributed as set forth in this EUA.

**III. Waiver of Certain Requirements**

Pursuant to Section 564(e)(3) of the Act, with respect to the emergency use of a product for which an authorization under this section is issued, FDA may waive or limit, to the extent appropriate given the circumstances of the emergency, requirements regarding good manufacturing practice otherwise applicable to the manufacture, processing, packing, or holding of products subject to regulations under this Act, including such requirements established under section 520(f)(1). FDA grants that waiver, including the quality system requirements under 21 CFR Part 820.

## IV. Conditions of Authorization

Pursuant to section 564 of the Act, I am establishing the following conditions on this authorization:

### electroCore, Inc. as Sponsor of Authorized Product

A. electroCore, Inc. will make the gammaCore Sapphire CV available with the authorized labeling. electroCore, Inc. may request changes to the authorized labeling. Such changes require review and concurrence from Office of Health Technology 1 (OHT1)/Office of Product Evaluate and Quality (OPEQ)/Center for Devices and Radiological Health (CDRH).

B. electroCore, Inc. may request changes to the Scope of Authorization (Section II in this letter) of the authorized gammaCore Sapphire CV. Such requests will be made by electroCore, Inc., in consultation with OHT1/OPEQ/CDRH, and require concurrence of the Office of Counterterrorism and Emerging Threats (OCET)/Office of the Chief Scientist (OCS)/Office of the Commissioner (OC) and OHT1/OPEQ/CDRH.

C. electroCore, Inc. must comply with the labeling requirements under 21 CFR 801 Subpart A (general labeling provisions) and 21 CFR 801.109 (labeling for prescription devices), as well as those described in Section II of this letter, Scope of Authorization.

D. electroCore, Inc. will have a process in place for reporting adverse events of which they become aware to FDA under 21 CFR Part 803. electroCore, Inc. will establish a process to collect adverse event information from healthcare facility customers and patients.

E. electroCore, Inc. is the current sole distributor of the gammaCore Sapphire CV. electroCore, Inc. will notify FDA of any future authorized distributor(s)[5] of the gammaCore Sapphire CV, including the name, address, and phone number of any authorized distributor(s), and provide authorized distributor(s) with a copy of this EUA and any updates.

F. electroCore, Inc. may request changes to any materials, components, parts, or accessories. Such requests will be made in consultation with and require concurrence

[5] "Authorized Distributor(s)" are identified by electroCore, Inc. in an EUA submission as an entity allowed to distribute the device.

of OHT1/OPEQ/CDRH.

**electroCore, Inc., and any Authorized Distributor(s)**

G. electroCore, Inc., and any authorized distributors will make the authorized labeling available on their websites.

H. Authorized distributors will make electroCore, Inc. aware of any adverse events of which they become aware.

I. Through a process of inventory control, electroCore, Inc. and any authorized distributors will maintain records of the healthcare facilities to which they distribute the gammaCore Sapphire CV and the number of each product they distribute.

J. electroCore, Inc. and any authorized distributor(s) are authorized to make available additional information relating to the emergency use of the product that is consistent with, and does not exceed, the terms of this letter of authorization.

K. electroCore, Inc. and authorized distributor(s) will ensure that any records associated with this EUA are maintained until otherwise notified by FDA. Such records will be made available to FDA for inspection upon request.

**Healthcare Facilities and Healthcare Providers**

L. Healthcare facilities using the authorized gammaCore Sapphire CV must make available to patients the authorized Patient Fact Sheet and make available to HCP the authorized Healthcare Provider Fact Sheet.

M. Healthcare facilities using the gammaCore Sapphire CV must make electroCore, Inc. and FDA aware of any adverse events pursuant to 21 CFR Part 803.

N. Healthcare facilities will ensure HCP using the gammaCore Sapphire CV are adequately equipped, trained, capable, and will maintain records of device usage.

O. Healthcare facilities will ensure that HCP adequately train patients for whom the device is prescribed, provide patients the appropriate authorized labeling, and maintain records of patients prescribed the device.

P. HCPs will ensure the patient is adequately trained on the proper use of the gammaCore Sapphire CV.

**Conditions Related to Printed Materials, Advertising and Promotion**

Q. All descriptive printed matter, including advertising and promotional materials, relating to the use of the authorized gammaCore Sapphire CV shall be consistent with the

authorized labeling, as well as the terms set forth in this EUA and the applicable requirements set forth in the Act and FDA regulations.

R. No descriptive printed matter, including advertising or promotional materials, relating to the use of the authorized gammaCore Sapphire CV may represent or suggest that this product is safe or effective for the prevention or treatment of asthma exacerbated by COVID-19.

S. All descriptive printed matter, including advertising and promotional materials, relating to the use of the authorized gammaCore Sapphire CV shall clearly and conspicuously state that:

- The gammaCore Sapphire CV has neither been cleared nor approved for acute use at home or in healthcare settings to treat adult patients with known or suspected COVID-19 who are experiencing exacerbation of asthma-related dyspnea and reduced airflow, and for whom approved drug therapies are not tolerated or provide insufficient symptom relief as assessed by their healthcare provider, using non-invasive VNS on either side of the patient's neck;

- The gammaCore Sapphire CV has been authorized for the above emergency use by FDA under an EUA; and,

- The gammaCore Sapphire CV has been authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of medical devices under section 564(b)(1) of the Act, 21 U.S.C. § 360bbb-3(b)(1), unless the authorization is terminated or revoked sooner.

**V. Duration of Authorization**

This EUA will be effective until the declaration that circumstances exist justifying the authorization is terminated under section 564(b)(2) of the Act or the EUA is revoked under section 564(g) of the Act.

Sincerely,

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RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

Enclosures