U.S. FOOD & DRUG ADMINISTRATION

May 1, 2020

Mary McNamara-Cullinane, RAC
Vice President, Regulatory Affairs
c/o Alira Health
1 Grant Street, Suite 400
Framingham, MA 01702

Dear Ms. McNamara-Cullinane:

This letter is in response to your request on behalf of Liberate Medical, LLC, that the U.S. Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for the emergency use of the VentFree Respiratory Muscle Stimulator[1] (hereafter "VentFree"), intended to be used by healthcare professionals (HCP) in healthcare settings to reduce disuse atrophy of the abdominal wall muscles, which may reduce the number of days of ventilator support in adult patients who require mechanical ventilation[2] (hereafter referred to as "ventilators," described in Section II), during the Coronavirus Disease 2019 (COVID-19) pandemic; use of the device is limited until successful weaning or for no more than 6 weeks, whichever comes first.

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.[3] 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, including

[1] This EUA includes the emergency use of the VentFree Respiratory Muscle Stimulator. In general, VentFree is used to apply a transcutaneous Neuromuscular Electrical Stimulation (NMES) to the abdominal wall muscles during a patient's expiratory phase of breathing. This stimulator system includes all of the components of the system that are needed for proper operation of the product (e.g., electrodes, power cord/supply, etc.).

[2] Patients at high risk of weaning failure include COVID-19 patients requiring ventilation and patients being mechanically ventilated for other high-risk conditions including post-cardiac and post-thoracic surgical procedures and medical intensive care unit (ICU) patients requiring prolonged ventilation. For these populations, transitioning patients off ventilators, when appropriate, may increase the availability of ventilators for use by patients during the COVID-19 pandemic. VentFree is intended to reduce breathing muscle atrophy and, in turn, may reduce the patient's time on mechanical ventilation. Based on a review of the available scientific evidence, FDA believes that this authorized product may also help address concerns about the current shortfall in ventilators by increasing ICU throughput for a given number of beds, ventilators, and staff via a reduction in the number of days on a ventilator.

[3] 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).

alternative products used as medical devices, due to shortages during the COVID-19 outbreak, subject to the terms of any authorization issued under that section.[4]

There are no FDA approved, licensed, or cleared device treatments to reduce disuse atrophy of the abdominal wall muscles, which may reduce the number of days of ventilator support in adult patients who require mechanical ventilation. Based on bench testing, a structured literature review, reported clinical experience from two randomized, controlled feasibility trials, six investigator initiated studies, and additional information about use of the VentFree outside the U.S.,[5] FDA has concluded that VentFree may be effective at treating adult patients during COVID-19 by helping wean patients off ventilators in healthcare settings, thereby reducing their risks of prolonged mechanical ventilation and increasing the availability of ventilators during the COVID-19 pandemic.

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 VentFree, 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 VentFree as described in the Scope of Authorization (Section II) of this letter for emergency use by HCP in healthcare settings to reduce disuse atrophy of the abdominal wall muscles, which may reduce the number of days of ventilator support in adult patients who require mechanical ventilation during the COVID-19 pandemic 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 VentFree may be effective for emergency use by HCP in healthcare settings to treat adult patients by reducing disuse atrophy of the abdominal wall muscles, which may reduce the number of days of ventilator support in patients who require mechanical ventilation during the COVID-19 pandemic, and that the known and potential benefits of the such products, for such use, outweigh the known and potential risks of such product; and,

3. There is no adequate, approved, and available alternative to the emergency use of VentFree for treating adult patients by reducing disuse atrophy of the abdominal wall

[4] 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).

[5] The VentFree received CE Mark for use in the EU in 2019.

muscles, which may reduce the number of days of ventilator support in patients who require mechanical ventilation during the COVID-19 pandemic.[6]

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 use of VentFree for emergency use by HCP to treat adult patients by reducing disuse atrophy of the abdominal wall muscles, which may reduce the number of days of ventilator support in patients who require mechanical ventilation in healthcare settings during the COVID-19 pandemic. Treatment is recommended until successful weaning or for no more than 6 weeks, whichever comes first. The VentFree is not intended to be used with demand type implanted pacemaker or defibrillator, electrical stimulation over pregnant uterus, on a patient with recent abdominal surgery with open abdominal wounds, on open or damaged skin, or on patients under 18 years of age. In addition, the VentFree should not be used as a replacement for a mechanical ventilator. The VentFree electrodes and flow sensor should not be shared between patients, but may be reused on the same patient. Electrodes should only be placed on the abdomen in compliance with the directions for use. Electronic monitoring equipment (such as ECG and ECG alarms) may not operate properly when electrical stimulation is in use.

Under this EUA, "ventilators include any breathing assistance machine requiring patient intubation that are cleared, approved, or authorized[7] under the Act or are otherwise distributed and used consistent with FDA policy.[8]

Authorized Product

VentFree Respiratory Muscle Stimulator is a muscle stimulator that applies transcutaneous neuromuscular electrical stimulation to the abdominal wall muscles during the expiratory phase of breathing. It is recommended for use in two 30-minute sessions per day (one in the morning and one in the afternoon/evening), 5 days per week, for 6 weeks or until a patient is weaned from mechanical ventilation (MV), whichever occurs sooner.

VentFree uses non-invasive, transcutaneous, Neuromuscular Electrical Stimulation (NMES) to cause the abdominal wall muscles to contract in synchrony with exhalation. During NMES, small electrical pulses are applied to motor nerves supplying a muscle to elicit a contraction. As NMES does not require patient cooperation, therapy can begin during the early phase of mechanical ventilation while patients are sedated or delirious.

The VentFree device consists of the VentFree stimulator or control unit, a flow sensor, and electrodes. The control unit controls the general device, stimulation hardware and peripheral handling. The flow rate through the flow sensor is measured using a differential

[6] No other criteria of issuance have been prescribed by regulation under section 564(c)(4) of the Act.
[7] On March 24, 2020, FDA issued an EUA authorizing certain ventilators, anesthesia gas machines modified for use as ventilators, and positive pressure breathing devices modified for use as ventilators. Devices authorized by this EUA at https://www.fda.gov/media/136423/download can be found in Appendix B at https://www.fda.gov/media/136528/download.
[8] Available at https://www.fda.gov/media/136318/download.

pressure transducer in the controller board. The flow sensor is connected in series with the patient's airway path to the ventilator to provide measurement of the patient's breathing. The microcontroller inside the control unit reads the output of the flow sensor and generates a stimulation trigger during the patient's breath cycle according to the proprietary stimulation trigger algorithm. Stimulation is then applied to the patient through the dual channel electrodes connecting the patient to the stimulator.

The flow sensor is a variable orifice type pneumotachograph which measures bi-directional flow, proximal to the patient's airway. It uses a variable orifice design to produce a differential pressure signal that is proportional to the flow rate of air running through the flow sensor. Flexible tubing attached to the flow sensor transmits the differential pressure signal to a pressure sensor inside the Controller Board. It is designed to be placed between the patient's endotracheal tube and the Y-piece of the patient circuit. It can also be connected to a face mask or a mouthpiece. The electrodes consist of four rectangular stimulation electrodes (VentFree electrodes (Model A) or Axelgaard electrodes (Model B)) and are used to deliver bilateral stimulation to the abdominal wall muscles.

The above described VentFree is authorized to be accompanied with labeling entitled, "VentFree Respiratory Muscle Stimulator User Manual- Model A" and "VentFree Respiratory Muscle Stimulator User Manual- Model B," as appropriate (available at https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations), and together with the following product-specific information pertaining to emergency use, which is required to be made available to HCP and patients:

- Fact Sheet for Healthcare Providers: Emergency Use of the VentFree Respiratory Muscle Stimulator During the COVID-19 Pandemic
- Fact Sheet for Patients: Emergency Use of the VentFree Respiratory Muscle Stimulator During the COVID-19 Pandemic

The above described product, when accompanied by the User Manuals (identified above) and the two Fact Sheets (referred to as "authorized labeling") is authorized to be distributed 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 VentFree, when used consistently 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, that it is reasonable to believe that the authorized VentFree may be effective for emergency use by HCP in healthcare settings to treat adult patients by reducing disuse atrophy of the abdominal wall muscles, which may reduce the number of days of ventilator support in adult patients who require mechanical ventilation during the COVID-19 pandemic when used consistently 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 VentFree, when used for emergency use by HCP in healthcare settings to reduce disuse atrophy of the abdominal wall muscles, which may reduce the number of days of ventilator support in adult patients who require mechanical ventilation during the COVID-19 pandemic (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 VentFree 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), VentFree 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 sections 520(f)(1). FDA grants that waiver, including the quality system requirements under 21 CFR 820.

IV. Conditions of Authorization

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

Liberate Medical, LLC as Sponsor of Authorized Product

A. Liberate Medical, LLC will make the VentFree available with authorized labeling. Liberate Medical, LLC may request changes to the authorized labeling. Such changes require review and concurrence from OHT1/OPEQ/CDRH.

B. Liberate Medical, LLC may request changes to the Scope of Authorization (Section II in this letter) of the authorized VentFree. Such requests will be made by Liberate Medical, LLC, 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. Liberate Medical, LLC 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.

As such, compliance with unique device identification regulations (see Subpart B of 21 CFR Part 801) is not required under this EUA.

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

E. Liberate Medical, LLC will notify FDA of any authorized distributor(s)[9] of the VentFree, 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. Liberate Medical, LLC may request changes to any components or materials. Such requests will be made in consultation with and require concurrence of OHT1/OPEQ/CDRH.

Liberate Medical, LLC, and any Authorized Distributor(s)

G. Liberate Medical, LLC, and any authorized distributors will distribute the authorized VentFree with the authorized labeling only to healthcare facilities with HCP who are adequately equipped, trained, and capable of using the VentFree according to the criteria set forth by Liberate Medical, LLC.

H. Liberate Medical, LLC, and any authorized distributors will make authorized labeling available on their websites.

I. Authorized distributors will make Liberate Medical, LLC aware of any adverse events of which they become aware.

J. Through a process of inventory control, Liberate Medical, LLC and any authorized distributors will maintain records of the healthcare facilities to which they distribute the VentFree and the number of each product they distribute.

K. Liberate Medical, LLC 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.

L. Liberate Medical, LLC 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.

[9] "Authorized Distributor(s)" are identified by Liberate Medical, LLC in an EUA submission as an entity allowed to distribute the device.

Healthcare Facilities

M. Healthcare facilities using the authorized VentFree must make available to patients the authorized Patient Fact Sheet and make available to HCP the authorized Healthcare Provider Fact Sheet.

N. Healthcare facilities using VentFree must make Liberate Medical, LLC and FDA aware of any adverse events under 21 CFR Part 803.

O. Healthcare facilities will ensure HCP using VentFree are adequately equipped, trained, capable, and will maintain records of device usage.

Conditions Related to Printed Materials, Advertising and Promotion

P. All descriptive printed matter, including advertising and promotional materials relating to the use of the authorized VentFree 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.

Q. No descriptive printed matter, including advertising or promotional materials relating to the use of the authorized VentFree may represent or suggest that this product is safe or effective for the prevention or treatment of COVID-19.

R. All descriptive printed matter, including advertising and promotional materials relating to the use of the authorized VentFree shall clearly and conspicuously state that:

- VentFree has neither been cleared or approved for the indication for use by HCP to treat adult patients by reducing disuse atrophy of the abdominal wall muscles, which may reduce the number of days of ventilator support in patients who require mechanical ventilation in healthcare settings during the COVID-19 pandemic;

- VentFree has been authorized for the above emergency use by FDA under an EUA; and,

- VentFree 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,

_____

RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

Enclosures