April 14, 2020

Judy P. Ways, Ph. D.
Vice President, Regulatory Affairs
Lungpacer Medical USA, Inc.
260 Sierra Drive, Suite 116
Exton, PA 19341

Dear Dr. Ways:

This letter is in response to your request that the U.S. Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for the emergency use of the Lungpacer Diaphragm Pacing Therapy System[1] (hereafter "Lungpacer DPTS") to assist in weaning patients determined by their healthcare provider to be at high risk of weaning failure[2] off of breathing assistance machines requiring patient intubation (hereafter referred to as "ventilators," described in Section II), in healthcare settings during the Coronavirus Disease 2019 (COVID-19) pandemic for no more than 30 days[3].

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.[4] Pursuant to section 564 of the Act, and on the basis

[1] This EUA includes the emergency use of the Lungpacer Diaphragm Pacing Therapy System. In general, Diaphragmatic Pacing Simulator Systems function by means of either phrenic nerve stimulation, or by stimulation of the diaphragm using surgically implanted temporary electrodes to prevent Ventilator Induced Diaphragm Dysfunction (VIDD). These systems include any surgical tools needed for implantation, as well as 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 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. Modeling indicates that 30% of patients hospitalized will require critical care (invasive mechanical ventilation or ECMO). In those patients, the ventilator and bed demand will be 10 days in the ICU. If 40% of the time on ventilation is spent trying to wean off (4 days in this case) and the 64.5% reduction of that time with diaphragm pacing is applied, then this would mean that Lungpacer DPTS could shorten those 4 days to 2.6 days. This would effectively reduce the ventilator burden by 26% in the COVID-19 patients. Less time on the ventilator also decreases the risk of secondary pneumonia.

[3] Based on a review of the available scientific evidence, FDA believes that this authorized product may also help address concerns about ventilator availability in addition to helping treat patients.

[4] 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).

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 alternative products used as medical devices, during the COVID-19 outbreak, subject to the terms of any authorization issued under that section.[5]

There are no FDA approved, licensed, or cleared device treatments to assist in weaning patients off of ventilators. Based on bench testing and reported clinical experience, FDA has concluded that the Lungpacer DPTS may be effective at treating 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 the Lungpacer DPTS, 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 Lungpacer DPTS as described in the Scope of Authorization (Section II) of this letter for emergency use to assist in weaning patients off ventilators in healthcare settings 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 the Lungpacer DPTS may be effective for emergency use to treat patients by assisting in weaning patients off ventilators in healthcare settings 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 the Lungpacer DPTS for treating patients 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 the Lungpacer DPTS for emergency use to assist in weaning patients determined by their healthcare provider to be at high risk of weaning failure off of ventilators in healthcare settings during the COVID-19 pandemic for no more than 30 days.

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[5] 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.

[6] No other criteria of issuance have been prescribed by regulation under section 564(c)(4) of the Act.

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

The Lungpacer DPTS is a temporary, minimally invasive, percutaneously placed, transvenous phrenic nerve pacing system for treating patients on mechanical ventilation (MV). The device utilizes a temporarily placed, intravenous neurostimulation catheter and an external control system to activate the diaphragm muscle of patients on MV.

The Lungpacer DPTS is designed to operate in conjunction with MV to transvenously stimulate the left and/or right phrenic nerves to cause diaphragmatic contraction that may be sufficient to reverse diaphragm atrophy. Building or retaining diaphragm strength is intended to mitigate the effects of VIDD, allowing patients to wean from MV and regain the ability to breathe independently. Lungpacer DPTS is expected to allow more patients to recover from dependency on MV. The Lungpacer DPTS is designed to electrically stimulate the phrenic nerves of a patient through a temporary, disposable, indwelling multi-electrode stimulating catheter [the Lungpacer IntraVenous Electrode (LIVE) Catheter] that is attached by means of the Intermediate Cable to an external pulse generator called the Lungpacer Control Unit (LCU). Also connected to the LCU is the optional Handheld Controller that may be used as an alternative to the user interface touchscreen of the LCU to trigger the delivery of electrical charge to the electrodes of the LIVE Catheter. The Lungpacer DPTS uses a sequence of electrode stimulations to map the specific electrode combination that results in diaphragm stimulation, and stimulation is delivered by these specific electrodes. The main components of the Lungpacer DPTS are discussed below.

LIVE Catheter

The LIVE Catheter is a sterile (ethylene oxide), single-use, disposable device designed to resemble a typical polyurethane central venous catheter. The LIVE Catheter consists of a polyurethane catheter shaft with a tapered atraumatic tip. There are two arrays of electrodes, proximal for targeting the left phrenic nerve and distal for targeting the right phrenic nerve. An extension line is connected to the catheter shaft at the catheter manifold and forms a continuous lumen between the female luer on the extension line and the catheter tip. This lumen is used for guidewire insertion as well as for fluid delivery when the guidewire is removed. All the electrode leads pass through a Primary Cable and terminate at an electrical connector. The catheter manifold at the junction between the catheter shaft, extension line, and Primary Cable has tabs for sutures to secure the catheter in position.

[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.

When placed in a patient, the LIVE Catheter runs from the left subclavian insertion point, lateral to the left phrenic nerve, towards the right phrenic nerve and the superior vena cava. The manifold of the catheter sits outside the patient's body where it is secured to the skin using sutures or another suitable method to reduce or prevent catheter movement. The catheter is then connected to the LCU via the Intermediate Cable.

To accommodate the geometric variability in the anatomies of patients, the LIVE Catheter will be available in three effective lengths: 19 cm, 21 cm, and 23 cm.

The catheter contains nineteen (19) platinum/iridium electrodes with individual stainless-steel conductors arranged in two arrays. The left (proximal) array is designed to deliver stimulation to the left phrenic nerve, and the right (distal) array is designed to deliver stimulation to the right phrenic nerve.

The left (proximal) electrode array consists of twelve (12) platinum/iridium electrodes that are designed to deliver stimulation to the left phrenic nerve. The right (distal) electrode array consists of six (6) platinum/iridium electrodes that are designed to deliver stimulation to the right phrenic nerve. One electrode (number 19) is present but unused in this version of the device system. The difference in the number of electrodes in the left electrode array versus the right electrode array is a design feature intended to accommodate varying anatomical geometries, in particular the distance between the two phrenic nerves.

Lungpacer Control Unit (LCU)
The LCU is a reusable electromedical device that is used with the LIVE Catheter and Intermediate Cable to provide phrenic nerve stimulation. The LCU is contained within a sheet metal box mounted to an off-the-shelf pole cart with touchscreen monitor mounted above it. A plastic bin is attached to the pole below the LCU Electronics Box for convenient storage of the Intermediate Cable and the Handheld Controller. Stimulation from the LCU is routed via the Intermediate Cable and the Primary Cable to electrode combinations on the LIVE Catheter, where the electrode combinations are selected by the LCU software and user feedback. The most suitable right electrode combination and left electrode combination (i.e., those combinations that stimulate the phrenic nerves with the lowest charge) are identified via a mapping process and are used to deliver cyclic trains of electrical charge to cause diaphragm contraction. The optional Handheld Controller may be connected to the LCU to facilitate remote triggering of electrical charge delivery to the LIVE Catheter electrodes.

Intermediate Cable:
The Intermediate Cable is a multiconductor cable designed to connect the LCU to the LIVE Catheter. The Intermediate Cable is the means of connectivity between the LIVE Catheter and the LCU for stimulation delivery. The Intermediate Cable is a reusable component supplied non-sterile and not intended for sterilization.

The above described product, when labeled consistently with the labeling authorized by FDA, referred to as the sponsor's developed Instructions for Use and entitled:

- "Lungpacer Diaphragm Pacing Therapy System Instructions for Use"

- "Lungpacer Live Catheter Kit Instructions for Use"
- "Lungpacer Intermediate Cable Instructions for Use"
- "Lungpacer Handheld Controller Instructions for Use"

(available at https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations) is authorized to be distributed under this EUA, despite the fact that it does not meet requirements otherwise required by applicable federal law.

In addition, the authorized Lungpacer DPTS must be accompanied by the following information pertaining to the emergency use, which is required to be made available to healthcare providers and patients:

- Fact Sheet for Healthcare Providers: Emergency Use of the Lungpacer Diaphragm Pacing Therapy System During the COVID-19 Pandemic
- Fact Sheet for Patients: Emergency Use of the Lungpacer Diaphragm Pacing Therapy System During the COVID-19 Pandemic

The sponsor's developed Instructions for Use (identified above) and the two Fact Sheets are referred to as "authorized labeling." Lungpacer Medical, Inc. may request changes to the authorized labeling. Such requests will require concurrence of the Office of Health Technology 1, Office of Product Evaluation and Quality, Center for Devices and Radiological Health (OHT1/OPEQ/CDRH).

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 Lungpacer DPTS, 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 Lungpacer DPTS may be effective for emergency use in treating patients by assisting in weaning patients off ventilators in healthcare settings 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 Lungpacer DPTS, when used for emergency use to assist in weaning patients off ventilators in healthcare settings 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 Lungpacer DPTS 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 Lungpacer DPTS is authorized to be used and distributed as set forth in this EUA.

III. Waiver of Certain Requirements

I am waiving applicable current good manufacturing practice requirements, including the quality system requirements under 21 CFR Part 820 with respect to the design, manufacture, packaging, labeling, storage, and distribution of the authorized Lungpacer DPTS that is used in accordance with this EUA.

IV. Conditions of Authorization

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

Lungpacer Medical, Inc. as Sponsor of Authorized Product

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

B. Lungpacer Medical, Inc. may request changes to the Scope of Authorization (Section II in this letter) of the authorized Lungpacer DPTS. Such requests will be made by Lungpacer Medical, 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. Lungpacer Medical, 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. As such, compliance with unique device identification regulations (see Subpart B of 21 CFR Part 801) is not required under this EUA.

D. All descriptive printed matter relating to the use of the authorized Lungpacer DPTS shall be consistent with the authorized labeling. No descriptive printed matter relating to the use of the authorized Lungpacer DPTS may represent or suggest that this product is safe or effective for the prevention or treatment of COVID-19.

E. Lungpacer Medical, Inc. will have process in place for reporting adverse events of which they become aware to FDA under 21 CFR Part 803.

F. Lungpacer Medical, Inc. will notify FDA of any authorized distributor(s)[9] of the Lungpacer DPTS, including the name, address, and phone number of any authorized

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

distributor(s), and provide authorized distributor(s) with a copy of this EUA and any updates.

G. Lungpacer Medical, Inc. may request changes to any components or materials. Such requests will be made in consultation with and require concurrence of OHT1/OPEQ/CDRH.

Lungpacer Medical, Inc., and any Authorized Distributor(s)

H. Lungpacer Medical, Inc., and authorized distributors will distribute the authorized Lungpacer DPTS with the authorized labeling only to healthcare facilities with healthcare providers who are adequately equipped, trained, and capable of using the Lungpacer DPTS according to the criteria set forth by Lungpacer Medical, Inc.

I. Lungpacer Medical, Inc., and authorized distributors will make authorized labeling available on their websites.

J. Authorized distributors will make Lungpacer Medical, Inc. aware of any adverse events of which they become aware.

K. Through a process of inventory control, Lungpacer Medical, Inc. and authorized distributors will maintain records of the healthcare facilities to which they distribute the Lungpacer DPTS and the number of each product they distribute.

L. Lungpacer Medical, Inc. and 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.

M. Lungpacer Medical, 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

N. Healthcare facilities using the authorized Lungpacer DPTS must make available to patients the accompanying Patient Fact Sheet and make available to healthcare providers the accompanying Healthcare Provider Fact Sheet.

O. Healthcare facilities using the Lungpacer DPTS must make Lungpacer Medical, Inc. aware of any adverse events.

P. Healthcare facilities will ensure healthcare providers using the Lungpacer DPTS are adequately equipped, trained, capable, and will maintain records of device usage.

Conditions Related to Advertising and Promotion

Q. All advertising and promotional descriptive printed matter relating to the use of the authorized Lungpacer DPTS 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 advertising or promotional descriptive printed matter relating to the use of the authorized Lungpacer DPTS may represent or suggest that this product is safe or effective for the prevention or treatment of COVID-19.

S. All advertising and promotional descriptive printed matter relating to the use of the authorized Lungpacer DPTS shall clearly and conspicuously state that:

- The Lungpacer DPTS has neither been cleared or approved for the indication to assist in weaning patients off ventilators in healthcare settings during the COVID-19 pandemic;
- The Lungpacer DPTS has been authorized for the above emergency use by FDA under an EUA;
- The Lungpacer DPTS 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,

Denise M. Hinton -S3

Digitally signed by Denise M. Hinton -S3
Date: 2020.04.14 22:40:01 -04'00'

RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

Enclosures