April 22, 2020

Frank Falcione
Senior VP Regulatory Affairs & Quality Assurance
ALung Technologies, Inc.
2500 Jane Street, Suite 1
Pittsburgh, PA 15203 USA

Dear Mr. Falcione:

This letter is in response to your request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for emergency use of ALung Technologies, Inc's Hemolung Respiratory Assist System ("Hemolung RAS," versions CR3 and CR4) to treat lung failure caused by Coronavirus Disease 2019 (COVID-19) when used as an adjunct to noninvasive or invasive mechanical ventilation to reduce hypercapnia and hypercapnic acidosis, and/or to maintain normalized levels of partial pressure of carbon dioxide (PCO2) and pH in patients suffering from acute, reversible respiratory failure for whom ventilation of CO_2 cannot be adequately, safely, or tolerably achieved.

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, including alternative products used as medical devices, during the COVID-19 outbreak, subject to the terms of any authorization issued under that Section.[2]

Hemolung RAS is not FDA-cleared or approved, and there are no FDA-approved or cleared device treatments for lung failure caused by COVID-19. *In vitro* and *in vivo* information was submitted to FDA in support of a U.S. clinical trial for the Hemolung RAS. Additional

[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 4, 2020) (accessible at https://www.fda.gov/media/135010/download).

[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).

information about clinical use of the Hemolung RAS outside the U.S.,[3] and additional biocompatibility, cytotoxicity, and performance testing were submitted for this EUA. Based on the information reviewed for the U.S. clinical trial, and this EUA, FDA believes that the Hemolung RAS has the potential to treat lung failure as an adjunct to noninvasive or invasive mechanical ventilation, to reduce hypercapnia and hypercapnic acidosis due to Coronavirus Disease 2019 (COVID-19), and/or to maintain normalized levels of partial pressure of carbon dioxide (PCO2) and pH in patients suffering from acute, reversible respiratory failure due to COVID-19 for whom ventilation of CO_2 cannot be adequately, safely, or tolerably achieved and, in turn, may provide clinical benefit.

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 Hemolung RAS, 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 Hemolung RAS, 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 Hemolung RAS may be effective in treating lung failure when used as described in the Scope of Authorization (Section II), and that the known and potential benefits of the Hemolung RAS for treating these patients, outweigh the known and potential risks; and

3. There is no adequate, approved, and available alternative to the emergency use of the Hemolung RAS to treat lung failure caused by COVID-19.[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 use of the Hemolung RAS device to treat lung failure due to COVID-19 when used as an adjunct to noninvasive or invasive mechanical ventilation in reducing hypercapnia and hypercapnic acidosis due to Coronavirus Disease 2019 (COVID-19), and/or maintaining normalized levels of partial pressure of carbon dioxide (PCO2) and pH in patients suffering from acute, reversible respiratory failure due to COVID-19 for whom ventilation of CO_2 cannot

[3] The Hemolung RAS received CE Mark for use in the EU in 2013 as well as post-market approvals for use in Canada and Australia.
[4] No other criteria of issuance have been prescribed by regulation under Section 564(c)(4) of the Act.

be adequately, safely, or tolerably achieved. The Hemolung RAS should not be used in patients with known sensitivity to heparin. The Hemolung 15.5 Fr Femoral Catheter[5] should not be used in patients with an inferior vena cava filter. The Hemolung RAS is not intended to provide therapeutic levels of oxygen.

The Authorized Hemolung RAS

The Hemolung RAS provides ultra-low flow, veno-venus extracorporeal carbon dioxide removal. The system requires central venous cannulation with a 15.5 French dual lumen catheter and operates with extracorporeal blood flows of 350 – 550 mL/min. The Hemolung RAS is intended to remove 30 – 50% of basal metabolic CO_2 production, but the Hemolung RAS is not intended to provide therapeutic levels of oxygenation.

The Hemolung RAS contains the following components:

- Hemolung Cartridge Kit with the Hemolung Cartridge and 7 Day Accessories Kit
- Hemolung 15.5 French Femoral Catheter Kit or Hemolung 15.5 French Jugular Catheter Kit
- Hemolung Catheter Insertion Kit
- Hemolung Spare Parts Kit
- Hemolung Controller

The Hemolung RAS requires the following components which are not provided but must be used in conjunction with the Hemolung RAS:

- Unfractionated heparin delivered through a peripheral intravenous (IV) line
- One liter of normal saline mixed with 1 Unit/mL of heparin for priming of the Hemolung circuit before starting therapy
- Lidocaine, suture, saline, sterile field prep for catheter insertion
- Ultrasound guidance for catheter insertion
- One liter of normal saline per day of therapy for flushing the Cartridge bearing

The above described Hemolung RAS, when labeled consistently with the labeling authorized by FDA, entitled “Hemolung CR4 Instructions for Use” or “Hemolung RAS Instructions for Use” (for the CR3 version of the device) (available at http://www.fda.gov/MedicalDevices/Safety/EmergencySituations/ucm161496.htm), together with the following product-specific information pertaining to emergency use, which is required to be made available to healthcare providers and healthcare facilities, respectively:

- Fact Sheet for Healthcare Providers: Hemolung RAS
- Fact Sheet for Patients: Hemolung RAS

[5] The Hemolung 15.5 Fr Femoral Catheter is one of two catheters included as a component of the Hemolung RAS.

The above described product, when accompanied with the described labeling is authorized to be distributed under this EUA, despite the fact that it does not meet certain requirements otherwise required by applicable 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 Hemolung RAS when used and labeled consistently with the Scope of Authorization of this letter (Section II), outweigh the known and potential risks of such product.

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 Hemolung RAS may be effective for treatment of lung failure when used as described in this Section (the Scope of Authorization, 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 of this letter, and concludes that the authorized Hemolung RAS, as described in this Section, the Scope of Authorization (Section II)), meets the criteria set forth in Section 564(c) of the Act concerning safety and potential effectiveness.

The emergency use of the Hemolung RAS 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 and conditions of this EUA and under the circumstances set forth in the Secretary of HHS's determination under Section 564(b)(1)(C) described above and the Secretary of HHS's corresponding declaration under Section 564(b)(1), the Hemolung RAS is authorized for use as described above.

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(e) of the Act, I am establishing the following conditions on this authorization:

<u>ALung Technologies, Inc., as Sponsor of the Authorized Product</u>

A. ALung Technologies, 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.

B. ALung Technologies, Inc., will make the Hemolung RAS available with authorized labeling. ALung Technologies, Inc. may request changes to the authorized labeling. Such changes require review and concurrence from OHT2/OPEQ/CDRH.

C. ALung Technologies, Inc. may request changes to the Scope of Authorization (Section II in this letter) of the authorized Hemolung RAS. Such requests will be made by ALung Technologies, Inc., in consultation with and require concurrence of OHT2/OPEQ/CDRH and the Office of Counterterrorism and Emerging Threats (OCET)/Office of the Chief Scientist (OCS)/Office of the Commissioner (OC).

D. ALung Technologies, Inc. will notify FDA of any authorized distributor(s)[6] of the Hemolung RAS, 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.

E. ALung Technologies, Inc. may request changes to the components and materials. Such requests will be made in consultation with, and require concurrence of, DHT2/OHT2/OPEQ/CDRH

F. ALung Technologies, Inc. will have a process in place to collect information on the performance of their products and for reporting adverse events of which they become aware to FDA under 21 CFR Part 803. ALung Technologies, Inc. will establish a process to collect adverse event information from healthcare facility customers. Adverse events of which the ALung Technologies, Inc. becomes aware will be reported to FDA.

<u>ALung Technologies, Inc. and any Authorized Distributors(s)</u>

G. ALung Technologies, Inc. and authorized distributor(s) will make the Hemolung RAS available with authorized labeling only to healthcare facilities with healthcare providers who are adequately equipped, trained, and capable of using the Hemolung RAS according to the Scope of Authorization (Section II) of this EUA.

H. ALung Technologies, Inc. and authorized distributor(s) will make authorized labeling available on their websites.

I. Authorized distributors will make ALung Technologies, Inc. aware of any adverse

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

events of which they become aware.

J. Through a process of inventory control, ALung Technologies, Inc. and authorized distributor(s) will maintain records of the healthcare settings to which they distribute the Hemolung RAS and the number of each product they distribute.

K. ALung Technologies, Inc. and authorized distributor(s) are authorized to make available additional information relating to the emergency use of the authorized Hemolung RAS that is consistent with, and does not exceed, the terms of this letter of authorization.

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

Healthcare Facilities

M. Healthcare facilities using the authorized Hemolung RAS must make available to patients the accompanying Fact Sheet for Patients and make available to healthcare providers the accompanying Fact Sheet for Healthcare Providers as well as the instructions for use entitled “Hemolung CR4 Instructions for Use” and “Hemolung RAS Instructions for Use”.

N. Healthcare facilities using the Hemolung RAS must make ALung Technologies, Inc. and FDA aware of any adverse events under 21 CFR Part 803.

O. Healthcare facilities will ensure healthcare providers using the Hemolung RAS are adequately equipped, trained, and capable of device usage.

Conditions Related to Advertising and Promotion

P. All descriptive printed matter, including advertising and promotional materials, relating to the use of the authorized Hemolung RAS shall be consistent with the authorized Fact Sheets and 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 Hemolung RAS 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 Hemolung RAS shall clearly and conspicuously state that:

- The Hemolung RAS has not been FDA cleared or approved;

- The Hemolung RAS has been authorized for the above emergency use by FDA under an EUA;

- This device is authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of the Hemolung RAS 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 of the emergency use of the Hemolung RAS during the COVID-19 pandemic 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: 2020.04.22 22:15:42 -04'00'

RADM Denise M. Hinton
Chief Scientist
Food and Drug Administration

Enclosures