April 17, 2020

Erdie De Peralta
ExThera Medical Corporation
757 Arnold Drive, Suite B
Martinez, CA 94553

Dear Erdie De Peralta:

This letter is in response to ExThera Medical Corporation's request that the Food and Drug Administration (FDA) issue an Emergency Use Authorization (EUA) for emergency use of the Seraph 100 Microbind Affinity Blood Filter[1] device (also referred to as an extracorporeal blood purification (EBP) device) to treat patients 18 years of age or older with confirmed Coronavirus Disease 2019 (COVID-19) admitted to the intensive care unit (ICU) with confirmed or imminent respiratory failure to reduce pathogens and inflammatory mediators from the bloodstream, pursuant to Section 564 of the Federal Food, Drug, and Cosmetic Act (the Act) (21 U.S.C. §360bbb-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.[2] 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, due to shortages during the COVID-19 outbreak, pursuant to section 564 of the FD&C Act, subject to the terms of any authorization issued under that section.[3]

There are no FDA approved, licensed, or cleared device treatments for COVID-19. Based on bench performance testing and reported clinical experience, FDA has concluded that the Seraph 100 Microbind Affinity Blood Filter device may be effective at treating certain patients with confirmed COVID-19 by reducing various pathogens and inflammatory mediators from their blood. FDA believes, based on the totality of scientific evidence available, that the reduction of pathogens and pro-inflammatory mediators may provide clinical benefit.

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[1] Seraph Microbind Affinity Blood Filter device was granted European CE mark in July 2019 (CE0459) for the reduction of pathogens from the bloodstream as an adjunct to antibiotic treatment during bloodstream infections.
[2] 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).
[3] 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).

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 your device as described in the Scope of Authorization (Section II) of this letter, subject to the terms of this authorization.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the Seraph 100 Microbind Affinity Blood Filter device, as described in the Scope of Authorization (Section II) of this letter to treat patients 18 years of age or older with confirmed COVID-19 admitted to the ICU with confirmed or imminent respiratory failure, 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 Seraph 100 Microbind Affinity Blood Filter device may be effective in treating patients 18 years of age or older with confirmed COVID-19 admitted to the ICU with confirmed or imminent respiratory failure, and that the known and potential benefits of the Seraph 100 Microbind Affinity Blood Filter device, when used to treat such patients, outweigh the known and potential risks of the device; and

3. There is no adequate, approved, and available alternative to the emergency use of the Seraph 100 Microbind Affinity Blood Filter device for the treatment of these COVID-19 patients.[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 Seraph 100 Microbind Affinity Blood Filter device to reduce pathogens and inflammatory mediators, which may provide clinical benefit to such patients. For the purposes of this EUA, a patient with confirmed COVID-19 infection who is admitted to the ICU with confirmed or imminent respiratory failure is a patient 18 years of age or older who has any one of the following conditions:

a) Early acute lung injury (ALI)/early acute respiratory distress syndrome (ARDS); or
b) Severe disease, defined as:
    1) dyspnea,
    2) respiratory frequency $\geq$ 30/min,
    3) blood oxygen saturation $\leq$ 93%,
    4) partial pressure of arterial oxygen to fraction of inspired oxygen ratio < 300, and/or
    5) lung infiltrates > 50% within 24 to 48 hours; or

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

c) Life-threatening disease, defined as:
    1) respiratory failure,
    2) septic shock, and/or
    3) multiple organ dysfunction or failure.

Authorized Product

1. The Seraph 100 Microbind Affinity Blood Filter device is a sterile single-use, disposable column packed with ultra-high molecular weight polyethylene (UHMWPE) beads, which are surface-modified with non-leaching, end-point-attached heparin and is comprised of the following components and materials:

Component Description	**Materials of Construction**
Column Body and End Caps	Copolyester, DuraStar™ Polymer
End Plate	Hydrophilic porous polyethylene, pore size 90-130 microns
Adsorption media, beads	UHMWPE, particle size 300 microns
O-Ring	Medical grade Platinum cured silicone
End Point Attached Heparin	Heparin Sodium, USP
Adhesive	Two-part epoxy, Loctite

2. The Seraph 100 Microbind Affinity Blood Filter mechanism of function is as follows:

   The Seraph 100 Microbind Affinity Blood Filter device is an extracorporeal broad-spectrum sorbent hemoperfusion device that is designed to reduce bacteria, viruses, toxins, cytokines and other inflammatory mediators from whole blood. The Seraph 100 Microbind Affinity Blood Filter device is designed to share a form factor very similar to other blood filters, such as hemodialyzers or hemoperfusion filters, and therefore is compatible with hemodialysis systems that use industry standard bloodline connectors for ease of operation, training, and utility.

   The Seraph 100 Microbind Affinity Blood Filter device achieves its intended performance by relying on the natural affinity that many adsorbates (e.g., pathogens, toxins, and inflammatory mediators) have towards surface bound heparin. To achieve an efficient removal of pathogens and other adsorbates, the Seraph 100 Microbind Affinity Blood Filter device must present a high surface area of surface bound heparin. This is achieved by filling the device with heparin coated microparticles. Whole blood is then circulated through the Seraph 100 Microbind Affinity Blood Filter device to expose the pathogens and adsorbates to the heparin. The Seraph 100 Microbind Affinity Blood Filter device interacts with the pathogens and various inflammatory mediators via affinity adsorption. Heparin is comprised of many different potential specific binding sites that match chemical sequences of many inflammatory mediators, cytokines, and pathogens.

   Many microorganisms including bacteria, viruses and parasites attach to heparan sulfate receptors (glycosaminoglycans) on the surface of mammalian cells. Heparin is a similar glycosaminoglycan that has also been demonstrated to have binding sites for

microorganisms. The use of heparin-functional media creates a broad-spectrum device designed to reduce circulating pathogen from blood, regardless of drug resistance.

3. The following device settings have been validated for operation of the Seraph 100 Microbind Affinity Blood Filter device:

Blood Priming Volume	160 mL
Maximum Blood Flow Rate	350 mL/min
Minimum Blood Flow Rate	100 mL/min
Maximum Pressure Limit	1,138 mmHg
Priming Fluid	Physiologic Saline

Additional treatment information has been provided in the Seraph 100 Microbind Affinity Blood Filter Instructions for Use, which is authorized under this EUA.

The Seraph 100 Microbind Affinity Blood Filter device, when labeled consistently with the labeling authorized by FDA entitled "Seraph 100 Microbind Affinity Blood Filter Instructions for Use" (available at https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations), which may be revised in consultation with, and with concurrence of, the Division of Renal, Gastrointestinal, Obesity and Transplant Devices (DHT3A)/Office of GastroRenal, ObGyn, General Hospital and Urology Devices (OHT3)/Office of Product Evaluation and Quality (OPEQ)/Center for Devices and Radiological Health (CDRH), is authorized under the terms and conditions of this EUA, despite the fact that it does not meet certain requirements otherwise required by applicable federal law.

The Seraph 100 Microbind Affinity Blood Filter device is authorized to be accompanied by the following product-specific 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 Seraph 100 Microbind Affinity Blood Filter for COVID-19
- Fact Sheet for Patients: Emergency Use of Seraph 100 Microbind Affinity Blood Filter for COVID-19

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 Seraph 100 Microbind Affinity Blood Filter device, when used to treat patients 18 years of age or older with confirmed COVID-19 infection admitted to the ICU with confirmed or imminent respiratory failure, as described in the Scope of Authorization of this letter (Section II), outweigh the known and potential risks of this 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 Seraph 100 Microbind Affinity Blood Filter device may be effective in treating COVID-19, when used as described in 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 Seraph 100 Microbind Affinity Blood Filter device, when used 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 product 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 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 Seraph 100 Microbind Affinity Blood Filter device, with the required labeling set forth in this section (Section II), is authorized to treat patients 18 years of age or older with confirmed COVID-19 infection admitted to the ICU with confirmed or imminent respiratory failure, by reducing pathogens and inflammatory mediators.

III. Waiver of Certain FDA 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:

ExThera Medical Corporation

A. ExThera Medical Corporation 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, 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. ExThera Medical Corporation may request changes to the authorized labeling and fact sheets. Such requests will be made in consultation with, and require concurrence of, DHT3A/OHT3/OPEQ/CDRH.

C. ExThera Medical Corporation may request changes to the components and materials. Such requests will be made in consultation with, and require concurrence of, DHT3A/OHT3/OPEQ/CDRH.

D. ExThera Medical Corporation may request changes to the Scope of Authorization (Section II in this letter) of your product. Such requests will be made in consultation with and require concurrence of DHT3A/OHT3/OPEQ/CDRH and Office of Counterterrorism and Emerging Threats (OCET)/Office of the Chief Scientist (OCS)/Office of the Commissioner (OC).

E. ExThera Medical Corporation may request the addition of other instruments and associated software for use with your product. Such requests will be made in consultation with, and require concurrence of, DHT3A/OHT3/OPEQ/CDRH.

F. ExThera Medical Corporation 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. Adverse events of which the ExThera Medical Corporation becomes aware will be reported to FDA.

G. ExThera Medical Corporation is 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.

H. ExThera Medical Corporation will notify FDA of any authorized distributor(s) of the product, including the name, address, and phone number of any authorized distributor(s), and provide authorized distributor(s) with a copy of this EUA.

ExThera Medical Corporation and Authorized Distributor(s)[5]

I. ExThera Medical Corporation and authorized distributor(s) will make the Seraph 100 Microbind Affinity Blood Filter devices available with the authorized labeling and fact sheets, described in the Scope of Authorization (Section II) of this letter.

J. ExThera Medical Corporation and authorized distributor(s) will make available on their website(s) the Seraph 100 Microbind Affinity Blood Filter Instructions for Use, Fact Sheet for Healthcare Providers, and the Fact Sheet for Patients.

K. ExThera Medical Corporation 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.

L. Through a process of inventory control, ExThera Medical Corporation and authorized distributor(s) will maintain records of the healthcare settings to which they distribute the Seraph 100 Microbind Affinity Blood Filter device and number of Seraph 100 Microbind Affinity Blood Filter devices they distribute.

M. ExThera Medical Corporation 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.

[5] "Authorized Distributor(s)" are identified by the sponsor in EUA requests as an entity allowed to distribute the product.

Conditions Related to Advertising and Promotion

N. All descriptive printed matter, including advertising and promotional materials, relating to the use of the Seraph 100 Microbind Affinity Blood Filter device 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.

O. No descriptive printed matter, including advertising or promotional materials, relating to the use of Seraph 100 Microbind Affinity Blood Filter device may represent or suggest that such products are safe or effective for the prevention or treatment of COVID-19.

P. All descriptive printed matter, including advertising and promotional materials, relating to the use of Seraph 100 Microbind Affinity Blood Filter device clearly and conspicuously shall state that:

- the Seraph 100 Microbind Affinity Blood Filter device has neither been cleared or approved for the indication to treat patients with COVID-19 infection;
- the Seraph 100 Microbind Affinity Blood Filter device has been authorized by FDA under an EUA;
- the Seraph 100 Microbind Affinity Blood Filter device is authorized only for the duration of the declaration that circumstances exist justifying the authorization of the emergency use of the Seraph 100 Microbind Affinity Blood Filter device 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 Seraph 100 Microbind Affinity Blood Filter device during the COVID-19 outbreak 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