August 3, 2020

Mr. Ken Ryder
Senior Director, Global Regulatory Affairs
Abiomed, Inc.
22 Cherry Hill Drive
Danvers, MA 01923

Dear Mr. Ryder:

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 the Impella Left Ventricular (LV) Support Systems[1] intended for use by healthcare providers (HCP) in the hospital setting for providing temporary LV unloading and support to treat critical care[2] patients with confirmed Coronavirus Disease 2019 (COVID-19) infection who are undergoing extracorporeal membrane oxygenation (ECMO) treatment and who develop pulmonary edema while on veno-arterial (V-A) ECMO support or late cardiac decompensation from myocarditis while on veno-venous (V-V) ECMO support.

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 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.[4]

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[1] For purposes of this EUA, the term "Impella LV Support Systems" refers to the Impella 2.5, Impella CP, Impella CP with SmartAssist, Impella 5.0, and Impella 5.5 with SmartAssist Systems, which are a family of miniaturized percutaneous circulatory support systems for the left ventricle.
[2] For purposes of this EUA, "critical care" patients refer to patients in the intensive care unit (ICU) who have confirmed COVID-19 infection.
[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).
[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).

There are no FDA approved or cleared devices available for use by HCP in the hospital setting specifically for providing temporary LV unloading and support to treat COVID-19 patients on ECMO therapy who develop pulmonary edema or late cardiac decompensation from myocarditis requiring mechanical cardiac support to maintain hemodynamic stability and end-organ perfusion. Impella LV Support Systems are FDA-approved (PMA approval P140003) to provide temporary LV support in patients undergoing a percutaneous coronary intervention (PCI) procedure[5] or in cardiogenic shock.[6] COVID-19 patients may require V-A ECMO for circulatory support with oxygenation due to acute cardiopulmonary failure. However, in some patients, V-A ECMO alone does not provide sufficient LV unloading due to retrograde aortic perfusion, which can lead to LV overload and distension, resulting in pulmonary edema. The authorized emergency use of the Impella LV Support Systems can alleviate this problem by unloading the LV, thereby reducing the LV work, and fully emptying the LV in critical care patients with confirmed COVID-19 infection. In addition, COVID-19 patients may require V-V ECMO for pulmonary failure. Some of these patients suffer from LV decompensation from myocarditis, which may require additional mechanical circulatory support for systemic perfusion. For these patients, the Impella LV Support Systems may be effective at providing the necessary LV support for hemodynamic stability and end-organ perfusion. The conditions of pulmonary edema and late cardiac decompensation from myocarditis during ECMO therapy requiring temporary LV support are substantively different than the conditions of high-risk PCI and cardiogenic shock requiring temporary LV support for which the Impella LV Support Systems are FDA-approved to treat, and therefore, are unapproved uses. Based on the available information, including extrapolated data from the approved indications and reported clinical experience, FDA has concluded that the Impella LV Support Systems may be effective at providing temporary LV support for the treatment of pulmonary edema and late cardiac decompensation in critical care patients with confirmed COVID-19 infection as explained in Section II of this letter, and has therefore determined that the criteria for issuance under Section 564(c) of the Act are met.

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 Impella LV Support Systems, as described in the Scope of Authorization (Section II) and pursuant to the Conditions of Authorization (Section IV) of this letter.

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[5] More specifically, the Impella 2.5, Impella CP, and Impella CP with SmartAssist Systems are temporary (≤ 6 hours) ventricular support devices that are used during high-risk PCI performed in elective or urgent, hemodynamically stable patients with severe coronary artery disease when determined to be an appropriate therapeutic option. Use of the Impella 2.5 and Impella CP Systems in these patients may prevent hemodynamic instability, which can result from repeat episodes of reversible myocardial ischemia that occur during planned temporary coronary occlusions and may reduce peri- and post-procedural adverse events.

[6] The Impella 2.5, Impella CP, Impella CP with SmartAssist, Impella 5.0, and Impella 5.5 with SmartAssist Catheters, in conjunction with the Automated Impella Controller (collectively, "Impella System Therapy"), are temporary ventricular support devices intended for short term use (≤ 4 days for the Impella 2.5, Impella CP, and Impella CP with SmartAssist; and ≤ 14 days for the Impella 5.0 and Impella 5.5 with SmartAssist) to treat ongoing cardiogenic shock that occurs immediately (< 48 hours) following acute myocardial infarction or open heart surgery or in the setting of cardiomyopathy, including peripartum cardiomyopathy, or myocarditis as a result of isolated left ventricular failure that is not responsive to optimal medical management and conventional treatment measures (including volume loading and use of pressors and inotropes, with or without IABP [spell out]). The intent of Impella System Therapy is to reduce ventricular work and to provide the circulatory support necessary to allow heart recovery and early assessment of residual myocardial function.

I. Criteria for Issuance of Authorization

I have concluded that the emergency use of the Impella LV Support Systems, 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 disease 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 Impella LV Support Systems may be effective when used by HCP in the hospital setting for providing temporary LV unloading and support to treat critical care patients with confirmed COVID-19 infection who are undergoing ECMO treatment and who develop pulmonary edema while on V-A ECMO support or late cardiac decompensation from myocarditis while on V-V ECMO support, and that the known and potential benefits of the Impella LV Support System, for such use, outweigh the known and potential risks; and,

3. There is no adequate, approved, and available alternative to the emergency use of the Impella LV Support Systems for critical care patients undergoing ECMO treatment for COVID-19 who develop pulmonary edema while on V-A ECMO support or late cardiac decompensation from myocarditis while on V-V ECMO support.[7]

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 Impella LV Support Systems by HCP in the hospital setting for providing temporary (≤ 4 days for Impella 2.5, Impella CP, and Impella CP with SmartAssist; and ≤ 14 days for Impella 5.0 and Impella 5.5 with SmartAssist) LV unloading and support to treat critical care patients with confirmed COVID-19 infection who are undergoing ECMO treatment who develop pulmonary edema while on V-A ECMO support or late cardiac decompensation from myocarditis while on V-V ECMO support. The Impella LV Support Systems are not intended for use to treat patients with the following conditions:

- Mural thrombus in the left ventricle;
- Presence of a mechanical aortic valve or heart constrictive device;
- Aortic valve stenosis/calcification (equivalent to an orifice area of 0.6 cm^2 or less);
- Moderate to severe aortic insufficiency (echocardiographic assessment graded as ≥ +2);
- Severe peripheral arterial disease precluding placement of the Impella System;
- Significant right heart failure;

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

- Combined cardiorespiratory failure;
- Presence of an Atrial or Ventricular Sepal Defect (including post-infarct VSD);
- Left ventricular rupture; or
- Cardiac tamponade.

The Authorized Impella LV Support Systems

The Impella LV Support Systems are a family of minimally invasive, miniaturized percutaneous circulatory support systems for the left ventricle.

Each Impella LV Support System is comprised of the following components:

- An Impella LV Catheter and its accessories as follows:
    - An Impella 2.5 introducer kit (K934901, Merit Medical) used to gain arterial access for the Impella 2.5 Catheter and contains: peel-away introducer, dilator, 18 G Seldinger needle, 12 cc syringe, 0.035 inch access guidewire (K914138, Lake Region Medical);
    - An Impella CP introducer kit (K192769), Abiomed, Inc., or K122084, Oscor Medical) used to gain arterial access for the Impella CP or Impella CP with Smart Assist Catheter and contains: two 14 Fr (13 cm and 25 cm) peel-away introducers, 8 Fr, 10 Fr, 12 Fr, and 14 Fr dilators, 0.035 inch access guidewire (K914138, Lake Region Medical);
    - A 0.018 inch, 260 cm placement guidewire (K011084, Lake Region Medical) used for the placement of the Impella 2.5, Impella 5.0, Impella 5.5 with Smart Assist, Impella CP Catheter, or Impella CP with Smart Assist Catheter; and
    - An Impella axillary insertion kit used to facilitate placement of the Impella Catheters via the axillary artery and contains a 23 Fr diameter x 6 cm length peel-away introducer (K122084, Oscor Inc.), two (2) graft locks used to attach a graft onto the introducer, an 8 Fr silicone-coated lubrication dilator.
- The Automatic Impella Controller (AIC)
- The Impella Purge Cassette
- A reusable cart for the AIC

The Impella LV Support Systems require the use of the following components and materials, which are not provided with the authorized product but are commonly used in the hospital setting, as described in the authorized Impella LV Support Systems Instructions for Use:

- 5-8 Fr introducer for initial femoral vein access (Product Code DYB, 21 CFR 870.1340, Catheter introducer)
- Standard 0.035”x175 cm J-tip guidewire (Product Code DQX, 21 CFR 870.1330, Catheter guide wire)
- Diagnostic catheter (Abiomed recommends a 5 Fr pigtail without side holes. Product Code DQO, 21 CFR 870.1200, Diagnostic intravascular catheter)
- Dextrose solution (typically 5% dextrose in water with 25 or 50 International Units (IU)/milliliter (mL) of heparin) used as the purge fluid

- If using the axillary insertion kit, 10 mm x 20 cm Hemashield Platinum vascular graft (K052302, Boston Scientific) or 10 mm x 30 cm Gelweave vascular graft (K162794, Terumo)

The above described Impella LV Support Systems are authorized to be accompanied with labeling, entitled:

- "Impella Ventricular Support Systems for Use During Cardiogenic Shock and High-Risk PCI - Impella 2.5, , Impella 5.0, Impella CP, Impella LD (cardiogenic shock only), Impella 2.5 and Impella CP (High-Risk PCI) Instructions for Use and Clinical Reference Manual,"
- "Impella CP with SmartAssist for Use During Cardiogenic Shock and High-Risk PCI - Instructions for Use and Clinical Reference Manual," and
- "Impella 5.5 with SmartAssist for Use During Cardiogenic Shock - Instructions for Use and Clinical Reference Manual."

These documents are available at https://www.fda.gov/medical-devices/emergency-situations-medical-devices/emergency-use-authorizations), together with the following product-specific information pertaining to emergency use, which is required to be made available to HCP and patients, respectively:

- Fact Sheet for Healthcare Providers: Emergency Use of Impella Left Ventricular Support Systems During the COVID-19 Outbreak
- Fact Sheet for Patients: Emergency Use of Impella Left Ventricular Support Systems During the COVID-19 Outbreak

The above described product, when accompanied with the Instructions for Use (identified above) and the two Fact Sheets (collectively 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 Impella LV Support Systems when used 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 authorized Impella LV Support Systems may be effective 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 Impella LV Support Systems, 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 Impella LV Support Systems 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 III). 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 Impella LV Support Systems described above is authorized for use by HCP in the hospital setting for providing temporary (≤ 4 days for Impella 2.5, Impella CP, and Impella CP with SmartAssist; and ≤ 14 days for Impella 5.0 and Impella 5.5 with SmartAssist) LV unloading and support to treat critical care patients with confirmed COVID-19 infection who are undergoing ECMO treatment and who develop pulmonary edema while on V-A ECMO support or late cardiac decompensation from myocarditis while on V-V ECMO support.

III. Conditions of Authorization

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

Abiomed, Inc., as Sponsor of the Authorized Product

A. Abiomed, Inc. must comply with the labeling requirements under 21 CFR Part 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. Abiomed, Inc. must comply with 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 devices

C. Abiomed, Inc. will make the authorized product available with authorized labeling. Abiomed, Inc. may request changes to the authorized labeling. Such changes require review and concurrence from Office of Health Technology 2 (OHT2)/Office of Product Evaluation and Quality (OPEQ)/Center for Devices and Radiological Health (CDRH).

D. Abiomed, Inc. may request changes to the Scope of Authorization (Section II in this letter) of the authorized Impella LV Support Systems. Such requests will be made by Abiomed, 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).

E. Abiomed, Inc. may request changes to any components or materials. Such requests will be made in consultation with and require concurrence of OHT2/OPEQ/CDRH.

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

G. Abiomed, Inc. will notify FDA of any authorized distributor(s)[8] of the Impella LV Support Systems, 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.

Abiomed, Inc. and any Authorized Distributor(s)

H. Abiomed, Inc. and authorized distributors will distribute the authorized product with the authorized labeling only to healthcare facilities with HCP who are adequately equipped, trained, and capable of using the Impella LV Support Systems according to the authorized labeling.

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

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

K. Through a process of inventory control, Abiomed, Inc. and authorized distributors will maintain records of the healthcare facilities to which they distribute the Impella LV Support Systems and the number of each product they distribute.

L. Abiomed, 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. Abiomed, 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 product must make available to patients the accompanying Patient Fact Sheet and make available to the HCP the accompanying Healthcare Provider Fact Sheet.

O. Healthcare facilities using the authorized product must make Abiomed, Inc., and FDA

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

aware of any adverse events under 21 CFR Part 803.

P. Healthcare facilities will ensure HCP using authorized product are adequately equipped, trained, and capable, and will maintain records of device usage.

Conditions Related to Advertising and Promotion

Q. All descriptive printed matter, including advertising and promotional materials relating to the use of the authorized Impella LV Support Systems 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 product may represent or suggest that this product is safe or effective when used by HCP in the hospital setting for providing temporary (≤ 4 days for Impella 2.5, Impella CP, and Impella CP with SmartAssist; and ≤ 14 days for Impella 5.0 and Impella 5.5 with SmartAssist) LV unloading and support to treat critical care patients with confirmed COVID-19 infection who are undergoing ECMO treatment and who develop pulmonary edema while on V-A ECMO support or late cardiac decompensation from myocarditis while on V-V ECMO support.

S. All descriptive printed matter, including advertising and promotional materials relating to the authorized use of the Impella LV Support Systems shall clearly and conspicuously state that:

- The authorized Impella LV Support Systems have neither been cleared or approved for the authorized indication for use (Section II of this letter);
- The Impella LV Support Systems have been authorized for the above emergency use by FDA under an EUA; and,
- The Impella LV Support Systems have 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.

IV. Duration of Authorization

This EUA will be effective until the declaration that circumstances exist justifying the authorization of the Impella LV Support Systems 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