

This guidance is intended to remain in effect until November 7, 2023, unless superseded by a revised final guidance before that date. For further information, refer to 88 FR 15417, March 13, 2023, available at <https://www.federalregister.gov/d/2023-05094>.

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**Enforcement Policy for
Extracorporeal Membrane
Oxygenation and Cardiopulmonary
Bypass Devices During the
Coronavirus Disease 2019
(COVID-19) Public Health
Emergency**

**Guidance for Industry and
Food and Drug Administration Staff**

April 2020

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health (CDRH)
Office of Product Evaluation and Quality (OPEQ)

Preface

Public Comment

This guidance is being issued to address the Coronavirus Disease 2019 (COVID-19) public health emergency. This guidance is being implemented without prior public comment because the Food and Drug Administration (FDA or the Agency) has determined that prior public participation for this guidance is not feasible or appropriate (see section 701(h)(1)(C) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and 21 CFR 10.115(g)(2)). This guidance document is being implemented immediately, but it remains subject to comment in accordance with the Agency's good guidance practices.

Comments may be submitted at any time for Agency consideration. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. Submit electronic comments to <https://www.regulations.gov>. All comments should be identified with the docket number FDA-2020-D-1138 and complete title of the guidance in the request.

Additional Copies

Additional copies are available from the FDA webpage titled "COVID-19-Related Guidance Documents for Industry, FDA Staff, and Other Stakeholders" *available at* <https://www.fda.gov/emergency-preparedness-and-response/mcm-issues/covid-19-related-guidance-documents-industry-fda-staff-and-other-stakeholders> and the FDA webpage titled "Search for FDA Guidance Documents" *available at* <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>. You may also send an e-mail request to CDRH-Guidance@fda.hhs.gov to receive a copy of the guidance. Please include the document number 20024 and complete title of the guidance in the request.

Questions

For questions about this document, contact Fernando Aguel, Assistant Director, Circulatory Support Devices at 301-796-6326 or fernando.aguel@fda.hhs.gov.

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Enforcement Policy for Extracorporeal Membrane Oxygenation and Cardiopulmonary Bypass Devices During the Coronavirus Disease 2019 (COVID- 19) Public Health Emergency

Guidance for Industry and Food and Drug Administration Staff

This guidance represents the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff or Office responsible for this guidance as listed on the title page.

I. Introduction

The Food and Drug Administration (FDA or Agency) plays a critical role in protecting the United States from threats such as emerging infectious diseases, including the Coronavirus Disease 2019 (COVID-19) pandemic. FDA is committed to providing timely guidance to support response efforts to this pandemic.

FDA is issuing this guidance to provide a policy to help expand the availability of devices used in extracorporeal membrane oxygenation (ECMO) therapy to address this public health emergency.

This policy is intended to remain in effect only for the duration of the public health emergency related to COVID-19 declared by the Department of Health and Human Services (HHS), including any renewals made by the HHS Secretary in accordance with section 319(a)(2) of the Public Health Service (PHS) Act.

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Given this public health emergency, and as discussed in the Notice in the *Federal Register* of March 25, 2020, titled “Process for Making Available Guidance Documents Related to Coronavirus Disease 2019,” available at <https://www.govinfo.gov/content/pkg/FR-2020-03-25/pdf/2020-06222.pdf>, this guidance is being implemented without prior public comment because FDA has determined that prior public participation for this guidance is not feasible or appropriate (see section 701(h)(1)(C) of the Federal Food, Drug, and Cosmetic Act (FD&C Act) and 21 CFR 10.115(g)(2)). This guidance document is being implemented immediately, but it remains subject to comment in accordance with the Agency’s good guidance practices.

In general, FDA’s guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency’s current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidance means that something is suggested or recommended, but not required.

II. Background

There is currently an outbreak of respiratory disease caused by a novel coronavirus. The virus has been named SARS-CoV-2 and the disease it causes has been named Coronavirus Disease 2019 (COVID-19). On January 31, 2020, HHS issued a declaration of a public health emergency related to COVID-19 and mobilized the Operating Divisions of HHS.¹ In addition, on March 13, 2020, the President declared a national emergency in response to COVID-19.²

FDA believes the policy set forth in this guidance may help address these urgent public health concerns by helping to expand the availability of devices used for extracorporeal membrane oxygenation (ECMO) therapy during this public health emergency.

III. Scope

Extracorporeal circuits and accessories for long-term respiratory/cardiopulmonary failure, including devices used for ECMO therapy, are a system of devices and accessories regulated under 21 CFR 870.4100 that provide assisted extracorporeal circulation and physiologic gas exchange of the patient’s blood for more than 6 hours. Cardiopulmonary bypass devices are regulated under multiple other regulations also under 21 CFR Part 870, Subpart E – Cardiovascular Surgical Devices, but are only for uses less than or equal to 6 hours. The classification regulations and associated product codes are listed in Table 1 and Table 2:

¹ Secretary of Health and Human Services Alex M Azar, Determination that a Public Health Emergency Exists. (Jan. 31, 2020), available at <https://www.phe.gov/emergency/news/healthactions/phe/Pages/2019-nCoV.aspx>.

² Proclamation on Declaring a National Emergency Concerning the Novel Coronavirus Disease (COVID-19) Outbreak (Mar. 13, 2020), available at <https://www.whitehouse.gov/presidential-actions/proclamation-declaring-national-emergency-concerning-novel-coronavirus-disease-covid-19-outbreak/>.

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Table 1 – ECMO devices

Classification Regulation	Device Type	Product Code³	Device Classification
21 CFR 870.4100	Extracorporeal System for Long-Term Respiratory / Cardiopulmonary Failure	QJZ	II
21 CFR 870.4100	Oxygenator, Long Term Support Greater Than 6 Hours	BYS	II
21 CFR 870.4100	Dual Lumen ECMO Cannula	PZS	II

Table 2 – Cardiopulmonary bypass devices, accessories, and components

Classification Regulation	Device Type	Product Code	Device Classification
21 CFR 870.4200	Accessory Equipment, Cardiopulmonary Bypass	KRI	I
21 CFR 870.4205	Detector, Bubble, Cardiopulmonary Bypass	KRL	II
21 CFR 870.4210	Cannula, Arterial, Cardiopulmonary Bypass (CPB), Embolism Protection	NCP	II
21 CFR 870.4210	Catheter, Cannula and Tubing, Vascular, Cardiopulmonary Bypass	DWF	II
21 CFR 870.4210	Cardiopulmonary Bypass Catheter Kit	OEU	II
21 CFR 870.4220	Console, Heart-Lung Machine, Cardiopulmonary Bypass	DTQ	II
21 CFR 870.4230	Defoamer, Cardiopulmonary Bypass	DTP	II
21 CFR 870.4240	Heat-Exchanger, Cardiopulmonary Bypass	DTR	II
21 CFR 870.4240	Cardioplegia Solution Administration Kit	OET	II
21 CFR 870.4250	Controller, Temperature, Cardiopulmonary Bypass	DWC	II
21 CFR 870.4260	Filter, Blood, Cardiopulmonary Bypass, Arterial Line	DTM	II
21 CFR 870.4270	Filter, Blood, Cardiotomy Suction Line, Cardiopulmonary Bypass	JOD	II

³ For more information see the Product Classification Database at <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPCD/classification.cfm>.

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21 CFR 870.4280	Filter, Prebypass, Cardiopulmonary Bypass	KRJ	II, exempt
21 CFR 870.4290	Adaptor, Stopcock, Manifold, Fitting, Cardiopulmonary Bypass	DTL	II, exempt
21 CFR 870.4300	Gas Control Unit, Cardiopulmonary Bypass	DTX	II
21 CFR 870.4310	Gauge, Pressure, Coronary, Cardiopulmonary Bypass	DXS	II
21 CFR 870.4320	Generator, Pulsatile Flow, Cardiopulmonary Bypass	JOR	III
21 CFR 870.4330	Monitor, Blood-Gas, On-Line, Cardiopulmonary Bypass	DRY	II
21 CFR 870.4340	Monitor and/or Control, Level Sensing, Cardiopulmonary Bypass	DTW	II, exempt
21 CFR 870.4350	Oxygenator, Cardiopulmonary Bypass	DTZ	II
21 CFR 870.4360	Pump, Blood, Cardiopulmonary Bypass, Non-Roller Type	KFM	II
21 CFR 870.4370	Pump, Blood, Cardiopulmonary Bypass, Roller Type	DWB	II
21 CFR 870.4380	Control, Pump Speed, Cardiopulmonary Bypass	DWA	II
21 CFR 870.4390	Tubing, Pump, Cardiopulmonary Bypass	DWE	II
21 CFR 870.4400	Reservoir, Blood, Cardiopulmonary Bypass	DTN	II
21 CFR 870.4400	CPB Check Valve, Retrograde Flow, In-line	MJJ	II
21 CFR 870.4400	Valve, Pressure Relief, Cardiopulmonary Bypass	MNJ	II
21 CFR 870.4400	Reservoir, Blood, Cardiopulmonary Bypass, Exempt	PTN	II, exempt
21 CFR 870.4410	Sensor, Blood-Gas, In-Line, Cardiopulmonary Bypass	DTY	II
21 CFR 870.4420	Sucker, Cardiomy Return, Cardiopulmonary Bypass	DTS	II, exempt
21 CFR 870.4430	Suction Control, Intracardiac, Cardiopulmonary Bypass	DWD	II, exempt

This guidance is limited to devices in Table 1 and Table 2 that are intended to pump blood or oxygenate blood by:

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1. Moving the blood to a component that pumps/oxygenates the blood;
2. Controlling pump speed;
3. Controlling or monitoring gas flow for the circuit; or
4. Controlling the temperature of the blood.

This guidance does not apply to devices intended only for extracorporeal carbon dioxide removal because such devices may not oxygenate the blood at clinically meaningful levels. Manufacturers of such devices may, however, consider requesting an Emergency Use Authorization (EUA)⁴ described in section IV.B of this document.

IV. Policy

As a sudden acute respiratory syndrome, COVID-19 can trigger acute respiratory failure and/or acute cardiopulmonary failure. Under such conditions, long-term extracorporeal oxygenation (i.e., extracorporeal oxygenation for greater than 6 hours) can be an important tool for treating patients, and FDA recognizes the importance and utility of increased availability of extracorporeal oxygenation devices for patients during the COVID-19 public health emergency. The FDA-cleared or FDA-approved cardiopulmonary bypass devices identified in Table 2 are technologically capable of being used for ECMO therapy, providing extracorporeal oxygenation for longer than 6 hours. Therefore, to facilitate expanded availability of devices to perform ECMO therapy to treat COVID-19 patients, FDA does not intend to object to limited modifications to the indications, and design of FDA-cleared or FDA-approved ECMO devices and cardiopulmonary bypass devices listed in Table 1 and Table 2 during the declared public health emergency where such modification does not create an undue risk, as described in more detail below, without prior submission of a premarket notification under section 510(k) of the FD&C Act and 21 CFR 807.81⁵ or submission of a Premarket Approval Application (PMA) Supplement under section 515 of the FD&C Act and 21 CFR 814.39.⁶ As a general best practice, because cardiopulmonary bypass circuit systems might incorporate multiple components, it is recommended that compatibility between components (e.g., flow rates, coatings, intended patient population) be considered prior to configuring the circuit for clinical use.

⁴ For more information about FDA's EUA process, please see FDA's Guidance, "Emergency Use Authorization of Medical Products and Related Authorities", available at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities>.

⁵ For further guidance on modifications that trigger the requirement that a manufacturer submit a new premarket notification (510(k)) to FDA, refer to "Deciding When to Submit a 510(k) for a Change to an Existing Device: Guidance for Industry and Food and Drug Administration Staff," <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/deciding-when-submit-510k-change-existing-device>.

⁶ For further guidance on modifications that trigger the requirement that a manufacturer submit a PMA supplement to FDA, refer to "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process," available at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/modifications-devices-subject-premarket-approval-pma-pma-supplement-decision-making-process>.

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A. Modifications to FDA-cleared or FDA-approved Indications or Design

For the duration of the public health emergency, FDA does not intend to object to modifications to the indications or design of FDA cleared or approved devices listed in Table 1 and Table 2 without prior submission of a premarket notification or premarket approval application supplement where the modification does not create an undue risk in light of the public health emergency. FDA currently believes a modification does not create such undue risk in the following scenarios:

1. For cardiopulmonary bypass devices, changes to the device's indications to include use of the device in an ECMO circuit to treat patients who are experiencing acute respiratory failure and/or acute cardiopulmonary failure;
2. For cardiopulmonary bypass devices, changes to the device's indications regarding use of the device for longer than 6 hours in an ECMO circuit; or
3. For both cardiopulmonary bypass devices and ECMO devices, changes to the dimension(s) of cannulae, tubing, filters, connectors, or other accessories to support use in an ECMO circuit that do not affect the flow rate of blood throughout the circuit.

FDA currently believes that modifications like the ones described below would create an undue risk:

1. Changes to the coating of a device; or,
2. Other changes that might negatively impact the gas transfer/exchange properties of the cleared device such as:
 - a) Changes to the dimension of the fiber used for gas exchange;
 - b) Changes to the type of fiber or membrane used for gas exchange; or,
 - c) Changes to the surface area of the fiber mat.

FDA recommends that labeling for modified devices include the following elements, where these elements are not already required by regulation. FDA is making these labeling recommendations to help users better understand the device modifications:

1. A clear description of the available data on the device's new indications or design characteristics related to ECMO, including:
 - a) Device performance (e.g. flow rates for which the device is compatible and pressure drop information (if applicable));
 - b) Summary of durability testing;
 - c) Summary of animal and clinical performance, if available; and
 - d) Potential risks.
2. A prominent and exhaustive list of clinical signs or observations that suggest device change-out is necessary regardless of the time the device has been in use;
3. Information on use conditions;
4. A clear distinction delineating FDA-cleared or FDA-approved indications from those that

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are not FDA-cleared or FDA-approved; and,

5. A general statement about changes that have not been cleared or approved by FDA.

FDA recommends any modifications be designed, evaluated, and validated in accordance with FDA recognized standards,⁷ including (as applicable):

- ANSI/AAMI/ISO 7199: 2016: *Cardiovascular Implants and Artificial Organs - Blood-Gas exchangers (Oxygenators)*
- ASTM F1841-97: 2017: *Standard Practice for Assessment of Hemolysis in Continuous Flow Blood Pumps*
- ISO 18242: 2016: *Cardiovascular Implants and Extracorporeal Systems – Centrifugal Blood Pumps*
- ASTM F1830-97: 2017: *Standard Practice for Selection of Blood for In Vitro Evaluation of Blood Pumps*
- ANSI/AAMI ES 60601-1:2005/(R)2012 and A1: 2012, C1:2009/(R)2012 and A2:2010/(R)2012: *Medical Electrical Equipment – Part 1: General Requirements for Basic Safety and Essential Performance*
- IEC 60601-1-2: 2014: *Medical Electrical Equipment Part 1-2: General Requirements for Basic Safety and Essential Performance – Collateral Standard: Electromagnetic Disturbances – Requirements and Tests*
- ISO 10993-1: 2018: *Biological Evaluation of Medical Devices — Part 1: Evaluation and Testing Within a Risk Management Process*

Manufacturers must document changes to their device in their device master record and change control records and make this information available to FDA, if requested, consistent with 21 CFR 820.30 and 21 CFR 820.180.

For the current edition of the FDA-recognized standard(s) referenced in this document, see the [FDA Recognized Consensus Standards Database](#).⁸ For more information regarding use of consensus standards in regulatory submissions, refer to FDA guidance titled “[Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices](#).”⁹

B. FDA’s Intended Approach for EUAs for Cardiopulmonary Bypass/ECMO Devices

FDA recommends that healthcare personnel use devices that are FDA-cleared for delivering ECMO therapy under 21 CFR 870.4100 (Table 1) when available, followed by devices designed for cardiopulmonary bypass and cleared or approved by FDA under the regulations referenced in Table 2. FDA recognizes that there may be concerns about the availability of such devices during the

⁷ <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm>.

⁸ <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm>.

⁹ <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/appropriate-use-voluntary-consensus-standards-premarket-submissions-medical-devices>.

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COVID-19 pandemic, and therefore, to help support the wider availability of devices for patients in need of ECMO in the United States for the duration of the public health emergency, FDA is interested in interacting with manufacturers of ECMO devices, or manufacturers of cardiopulmonary bypass devices seeking indications greater than 6 hour use to be used for ECMO, that are not currently legally marketed in the U.S. FDA intends to work interactively with these manufacturers through its EUA process.

FDA would find it helpful if such manufacturers (whether foreign or domestic) send FDA the following information to CDRH-NonDiagnosticEUA-Templates@fda.hhs.gov. FDA believes this information will be valuable in assessing whether the device would be able to meet the EUA requirements. FDA believes that companies may already have information available to help support an EUA request for ECMO or modified use of cardiopulmonary bypass, such as the information outlined below. FDA will expeditiously review this information, and other required information, to determine if an EUA can be issued.

For current ECMO device manufacturers or cardiopulmonary bypass manufacturers seeking to utilize their device for over 6 hours for ECMO whose product(s) are not currently marketed in the U.S., FDA recommends providing the following information:

- a) General information such as your contact information, name and place of business, email address, and contact information for a U.S. agent (if any), in addition to general information about the device such as the proprietary or brand name, model number, and marketing authorization in your country (or region).
- b) A copy of the product labeling.
- c) Whether the device currently has marketing authorization in another regulatory jurisdiction such as the European CE Mark, Australian Register of Therapeutic Goods (ARTG) Certificate of Inclusion, Health Canada License, or Shonin approval from the Ministry of Health, Labour, and Welfare in Japan. When providing this information, you should include a copy of the marketing authorization letter or certificate and also include any relevant corresponding information such as the certificate of conformity.
- d) A summary of performance data available for long term use of the device (e.g., gas exchange, reliability, thrombogenicity).
- e) Whether the device has been designed, evaluated, and validated in accordance with the applicable FDA recognized standards identified in Section IV.A above.
- f) Whether the device is manufactured in compliance with 21 CFR Part 820, ISO 13485: *Medical Devices – Quality Management Systems – Requirements for Regulatory Purposes*, or an equivalent quality system, and the manufacturer or importer has documentation of such.
- g) Whether the device is designed with a power supply that is compatible with United States voltage, frequency, and plug type standards or is accompanied by an appropriate power supply adapter for use in the United States.

FDA will acknowledge receipt of the information provided and intends to work interactively with these manufacturers to facilitate distribution of their products through an Emergency Use

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Authorization in the United States.¹⁰ In addition, where appropriate under the circumstances, FDA will notify the manufacturer that it does not intend to object to the distribution and use of the device while the manufacturer is preparing, and FDA is reviewing, the EUA request. Manufacturers who are unable to provide all the above information are still eligible for EUA consideration and should engage with FDA through the pre-EUA process.

For any ECMO or cardiopulmonary bypass device issued an EUA, FDA will include appropriate conditions of authorization in accordance with the mandatory conditions outlined in section 564 of the FD&C Act. Although this is a case-by-case determination, based on current information and experience, we will likely include the following conditions:

- Appropriate conditions designed to ensure that health care professionals administering the device are informed—
 - that FDA has authorized the emergency use of the device;
 - of the significant known and potential benefits and risks of the emergency use of the device, and of the extent to which such benefit and risks are unknown; and
 - of the alternatives to the device that are available, and of their benefits and risks.
- Appropriate conditions designed to ensure that individuals to whom the device is administered are informed—
 - that FDA has authorized the emergency use of the device;
 - of the significant known and potential benefits and risks of the emergency use of the device, and of the extent to which such benefit and risks are unknown; and
 - of the option to accept or refuse use of the device, of the consequence, if any, of refusing use of the device, and of the alternatives to the device that are available and of their benefits and risks.
- Appropriate conditions for the monitoring and reporting of adverse events associated with the emergency use of the device. FDA intends to include conditions that are consistent with those promulgated under 21 CFR Part 803.
- For manufacturers of the device, appropriate conditions concerning recordkeeping and reporting, including records access by FDA, with respect to emergency use of the device.

C. Additional Helpful Resources

The following online resources may be helpful for consideration when pursuing these design changes:

¹⁰ For more information about FDA’s EUA process, please see FDA’s Guidance, “Emergency Use Authorization of Medical Products and Related Authorities”, available at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities>.

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- [Guidance for Cardiopulmonary Bypass Oxygenator 510\(k\) Submissions; Final Guidance for Industry and FDA Staff](#)¹¹
- [Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process" – Guidance for Industry and Food and Drug Administration Staff](#)¹²
- [Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices – Guidance for Industry and FDA Staff](#)¹³
- [Content of Premarket Submissions for Management of Cybersecurity in Medical Devices – Guidance for Industry and Food and Drug Administration Staff](#)¹⁴

¹¹ <https://www.fda.gov/medical-devices/guidance-documents-medical-devices-and-radiation-emitting-products/cardiopulmonary-bypass-oxygenators-510k-submissions-final-guidance-industry-and-fda-staff>.

¹² <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/use-international-standard-iso-10993-1-biological-evaluation-medical-devices-part-1-evaluation-and>.

¹³ <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-content-premarket-submissions-software-contained-medical-devices>.

¹⁴ <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/content-premarket-submissions-management-cybersecurity-medical-devices-0>.