April 9, 2020

MC3 Incorporated
Martha Rumford
Director RA/QA
2555 Bishop Circle W
Dexter, Michigan 48130

Re: K191935
Trade/Device Name: Nautilus Smart ECMO Module and Nautilus ECMO Oxygenator
Regulation Number: 21 CFR 870.4100
Regulation Name: Extracorporeal circuit and accessories for long-term respiratory/cardiopulmonary failure
Regulatory Class: Class II
Product Code: BYS
Dated: March 10, 2020
Received: March 11, 2020

Dear Martha Rumford:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. Although this letter refers to your product as a device, please be aware that some cleared products may instead be combination products. The 510(k) Premarket Notification Database located at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm identifies combination product submissions. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803) for devices or postmarketing safety reporting (21 CFR 4, Subpart B) for combination products (see https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820) for devices or current good manufacturing practices (21 CFR 4, Subpart A) for combination products; and, if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to https://www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance) and CDRH Learn (https://www.fda.gov/training-and-continuing-education/cdrh-learn). Additionally, you may contact the Division of Industry and Consumer Education (DICE) to ask a question about a specific regulatory topic. See the DICE website (https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Nicole Ibrahim, Ph.D.
Director
DHT2B: Division of Circulatory Support,
Structural and Vascular Devices
OHT2: Office of Cardiovascular Devices
Office of Product Evaluation and Quality
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K191935

Device Name
MC3 Nautilus(tm) Smart ECMO Module

Indications for Use *(Describe)*

The Nautilus(tm) Smart ECMO Module with integrated heat exchanger is intended to provide assisted long-term extracorporeal circulation and physiologic gas exchange (oxygenation and carbon dioxide removal) of the patient's blood for up to 48 hours in adult and pediatric adolescent patients with acute respiratory failure or acute cardiopulmonary failure, where other available treatment options have failed, and continued clinical deterioration is expected or the risk of death is imminent. The integrated heat exchanger is intended to heat or cool the blood as needed during use. Integrated fluid path pressure, temperature, and oxygen saturation monitoring is achieved by built-in sensor modules and display.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

CONTINUE ON A SEPARATE PAGE IF NEEDED.

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: 06/30/2020
See PRA Statement below.

510(k) Number *(if known)*
K191935

Device Name
MC3 Nautilus(tm) ECMO Oxygenator

Indications for Use *(Describe)*

The Nautilus(tm) ECMO Oxygenator with integrated heat exchanger is intended to provide assisted long-term extracorporeal circulation and physiologic gas exchange (oxygenation and carbon dioxide removal) of the patient's blood for up to 48 hours in adult and pediatric adolescent patients with acute respiratory failure or acute cardiopulmonary failure, where other available treatment options have failed, and continued clinical deterioration is expected or the risk of death is imminent. The integrated heat exchanger is intended to heat or cool the blood as needed during use.

Type of Use *(Select one or both, as applicable)*

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510(k) Summary

Sponsor Information:

Owner/Applicant/Submitter:	MC3 Incorporated 2555 Bishop Circle West Dexter, MI 48130 1-734-995-9089 Registration number: 3011468686
Contact Person:	Martha Rumford Director of RA/QA
Date Prepared:	4/5/2020

Device Names/Classification:

Device Trade Name:	Nautilus™ Smart ECMO Module Nautilus™ ECMO Oxygenator
Device Common Name:	Oxygenator, Long Term Support Greater Than 6 hours
Regulation Name:	Extracorporeal circuit and accessories for long-term respiratory/cardiopulmonary failure
Regulation Number:	21 CFR 870.4100
Product Code:	BYS
Predicate:	81 FR 7451, Feb. 12, 2016
Reference Devices:	Maquet Quadrox iD Oxygenator (K150267) CARDIOHELP System, Model CARDIOHELP-i (K133598)

Indications for Use:

The Nautilus™ ECMO Oxygenator with integrated heat exchanger is intended to provide assisted long-term extracorporeal circulation and physiologic gas exchange (oxygenation and carbon dioxide removal) of the patient's blood for up to 48 hours in adult and pediatric adolescent patients with acute respiratory failure or acute cardiopulmonary failure, where other available treatment options have failed, and continued clinical deterioration is expected or the risk of death is imminent. The integrated heat exchanger is intended to heat or cool the blood as needed during use.

The Nautilus™ Smart ECMO Module with integrated heat exchanger is intended to provide assisted long-term extracorporeal circulation and physiologic gas exchange (oxygenation and carbon dioxide removal) of the patient's blood for up to 48 hours in adult and pediatric adolescent patients with acute respiratory failure or acute cardiopulmonary failure, where other available treatment options have failed, and continued clinical deterioration is expected or the risk of death is imminent. The integrated heat exchanger is intended to heat or cool the blood as needed during use. Integrated fluid path pressure, temperature, and oxygen saturation monitoring is achieved by built-in sensor modules and display.

Device Description:

The Nautilus™ ECMO oxygenators are diffusion membrane oxygenators used in extracorporeal life support procedures to oxygenate blood, remove carbon dioxide and regulate blood temperature. Blood enters the device and passes through both the heat exchange membrane, where temperature is adjusted, and the gas transfer membrane, where oxygen is added and carbon dioxide is removed.

The Nautilus™ Smart ECMO Module device contains integrated sensors with an electronic touch screen display. The following measured parameters are visible on the electronic display: inlet pressure, inlet oxygen saturation, outlet pressure, outlet oxygen saturation, and outlet blood temperature. The difference between the inlet and outlet pressure, delta pressure, is calculated and also displayed on the screen. The touchscreen display allows users to set alarm limits for all measured parameters. The Nautilus™ Smart ECMO Module will alarm visually and audibly when the limits are exceeded.

The devices are single-use, nontoxic, non-pyrogenic, and not made from natural latex rubber materials.

Performance Evaluations:

Evaluation and testing was executed to demonstrate the substantial equivalence of the subject devices. Performance assessments for substantial equivalence were accomplished through bench and in vivo studies that included the following evaluations:

- Gas exchange
- Heat exchange
- Prime volume
- Coating coverage
- Low-flow clotting
- Hemolysis
- Integrity
- Operating Conditions
- In-vivo study

Smart Module Testing also included:

- Electrical Safety/EMC
- Sensor Accuracy
- Water Ingress Protection

Substantial Equivalence:

Substantial equivalence analysis includes both comparison to clinically-relevant Reference Devices and comparison to the Special Controls of FDA's final order, 81 FR 7451, Feb. 12, 2016 (Predicate). This is due to the fact that there has been no oxygenator device cleared under regulation 21 CFR 870.4100 to date, although ECMO has been well established clinically using currently marketed, state-of-the-art oxygenators.

Reference Device (Oxygenator): The subject oxygenator is comparable to the Maquet Quadrox iD Oxygenator in design, principles of operation, materials of construction, performance, and fundamental scientific technology.

Reference Device (Sensor Module): The sensor module functions are comparable to the Maquet CARDIOHELP System with regard to sensor accuracy and standards compliance.

Predicate: The Nautilus™ ECMO oxygenators meet all special controls required by 21 CFR 870.4100.

Special Controls met are:

- ***Technological Characteristics:*** Geometry and design parameters are consistent with the device's intended use in extracorporeal life support procedures. The subject device is designed to be compatible with other extracorporeal circuit devices and accessories.

- ***Biocompatibility:*** The subject device is demonstrated to be biocompatible for prolonged use in circulating blood in accordance with ISO 10993-1:2009 and in accordance with GLP (21 CFR 58).

- ***Sterility and Shelf-life:*** Testing demonstrates the sterility of the subject device as provided and that it maintains its sterility, integrity, durability, and reliability over the stated shelf-life of the device.

- ***Non-clinical Performance:*** Substantial equivalence is demonstrated by performance characteristics on the bench, mechanical integrity, electromagnetic compatibility, software, durability, reliability, and accuracy.

- ***In vivo Evaluation:*** In vivo evaluation demonstrates the subject device's performance over a long-term duration of use in a biologic test system. In addition to in-vivo study, a summary was prepared that described the initial real-world clinical experience of the device with the first records of clinical ECMO cases entered sequentially into the ELSO registry.

- ***Labeling:*** The Instructions for Use includes a detailed summary of the non-clinical evaluations pertinent to the device's use in an extracorporeal circuit. Adequate instructions are included with respect to installation, circuit setup, maintenance during a procedure, changeout, adverse effects, and performance characteristics relevant to compatibility among different devices and accessories in the circuit.

ECMO Performance Evidence

- ***Long-term Bench Gas Exchange testing***

Gas transfer testing of the MC3 Nautilus oxygenator device and competitive heparin coated oxygenators was executed for the comparative evaluation of oxygen and carbon dioxide transfer, and blood path pressure drop performance over an extended duration of use. Testing was performed in accordance with the ISO standard for blood-gas exchangers (ISO 7199:2016), using bovine blood at determined time points over a full range of operating variables, simulating a use duration of 14 days by circulating bovine plasma between test points . MC3 Nautilus oxygenators from accelerated age populations were tested. Nautilus had comparable or better oxygen and carbon dioxide transfer rates and pressure drop performance as a heparin coated state-of-the art device, over 14-days of use.

- ***In-Vivo Study in Sheep***

A 96 hour animal study was conducted to evaluate the safety and performance of Nautilus during extracorporeal membrane oxygenation (ECMO) for long term use. Target ACT during this study was 180-220 sec. The study was conducted on a total of 15 sheep. Ten of the 15 sheep were used specifically to evaluate the Nautilus at either 2 or 5 lpm, and 5 control animals were studied at 2 l/min with a state of the art heparin coated device. After 4 days, there were no clots in any location in the Nautilus device and oxygenator functionality was confirmed.

- ***Clinical information (Real World Evidence)***

The purpose of the Real World Evidence (RWE) study was to collect and summarize the initial real world performance of the Nautilus™ when used as part of an ECMO/ECLS system in patients. Data were voluntarily entered into the ELSO registry.

Data were collected on patients at 7 centers in 4 countries. The cases reported demonstrate experience with the Nautilus™ in a diverse set of ECMO conditions, including multiple ECMO centers, venovenous and venoarterial support, and a typical variety of primary indications for ECMO support.

The average duration of ECMO support was 378.5 hours (15.8 days), with a range of 17 to 1271 hours (52.9 days). The average Nautilus™ use duration is comparable to the typical length of ECMO support reported in the literature.

The most common complication reported was circuit exchange in twenty percent of patients, of which one exchange was attributed to diminished performance after 12 days; one exchange was due to hemolysis not attributed to the Nautilus™; and two exchanges were electively exchanged.

Fifteen percent of patients had reports of hemolysis complications, of which none was directly attributed to the Nautilus™. One hemolysis complication was reported to have occurred after 27 days of operation, another was reported prior to Nautilus™ use while operating on a different oxygenator, and one was attributed to patient condition (sepsis) and pump clotting.

Ten percent of patients had reports of blood infections on ECMO, which is similar to the rate of infections (11%) previously reported by others.1

One patient suffered a CNS infarction event (5%), and another patient, a CNS hemorrhage. There were no reports of circuit clotting, air in the circuit, or mechanical failure.

Conclusion:

MC3 Incorporated concludes the Nautilus™ Oxygenators are substantially equivalent to the Predicate by the meeting the special controls (81 FR 7451, Feb 12, 2016) and have demonstrated to have performed comparably to clinical Reference devices with respect to intended use, design, materials of construction, principles of operation, performance, and specifications.

[1]Daniel Brodie, et al "Extracorporeal Life Support for Adults With Respiratory Failure And Related Indications A Review" JAMA August 13, 2019.