June 19, 2020

Praxair, Inc.
% Sarah Fitzgerald
Senior Consultant, Quality and Regulatory Affairs
Emergo Global Consulting, LLC
2500 Bee Cave Road, Building 1, Suite 300
Austin, Texas 78746

Re: K201339
Trade/Device Name: The NOxBOXi Nitric Oxide Delivery System
Regulation Number: 21 CFR 868.5165
Regulation Name: Nitric Oxide Administration Apparatus
Regulatory Class: Class II
Product Code: MRN, MRO, MRP, MRQ, CCL
Dated: May 13, 2020
Received: May 20, 2020

Dear Sarah Fitzgerald:

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,

Todd Courtney
Assistant Director
DHT1C: Division of ENT, Sleep Disordered
Breathing, Respiratory and
Anesthesia Devices
OHT1: Office of Ophthalmic, Anesthesia,
Respiratory, ENT and Dental 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)*
K201339

Device Name
NOxBOXi Nitric Oxide Delivery System

Indications for Use *(Describe)*
NOxBOXi Nitric Oxide Delivery System is intended for use by healthcare professionals for the delivery and monitoring of a constant (user set) concentration of nitric oxide (NO) and the monitoring of NO2 and O2 in the inspiratory ventilator lines of a patient undergoing nitric oxide therapy (iNO).

The NOxBOXi Nitric Oxide Delivery System includes:
• The NOxBOXi head unit, which delivers NO gas while in the intelligent delivery mode.
• Continuous monitoring and alarms for NO, O2 and NO2.
• The integrated NOxMixer which provides a backup NO delivery capability that is intended to deliver a continuous flow of NO, mixed with O2, for iNO therapy and provides a continuous treatment option during transit and transfer conditions within hospitals.

The NOxBOXi Nitric Oxide Delivery System must only be used in accordance with the indications, contraindications, warnings and precautions described in the nitric oxide drug packaging inserts and labeling (currently neonates). Refer to this material prior to use.

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.

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Special 510(k) Summary

NOxBOXi Nitric Oxide Delivery System

1. Submission Sponsor

Praxair Distribution, Inc. (PDI)
10 Riverview Drive
Danbury, CT 06810 USA
Phone: (412) 874.3315
Dave Loflin
Director of Quality and FDA Regulations

2. Submission Correspondent

Emergo Global Consulting, LLC
2500 Bee Cave Road
Building 1, Suite 300
Austin, TX 78746
Office Phone: (512) 327.9997
Sarah Marie Fitzgerald, RAC
Senior Consultant, Quality and Regulatory Affairs

3. Date

June 18, 2020

4. Device Identification

Trade/Proprietary Name:	NOxBOXi Nitric Oxide Delivery System	
Classification Names:	Nitric Oxide administration apparatus, back-up and gas analyzers	
Common/Usual Name:	Nitric Oxide administration apparatus – primary	
	Nitric Oxide administration apparatus – backup	
	Nitric Oxide Analyzer	
	Nitrogen Dioxide Analyzer	
	Oxygen Gas Analyzer	
Classification Regulation and Product Code:	21 CFR 868.5165 – primary delivery system	MRN
Additional Regulations and Product Codes:	21 CFR 868.5165 – backup delivery system	MRO
	21 CFR 868.2380 – Nitric Oxide Analyzer	MRP
	21 CFR 868.2385 – Nitrogen Dioxide Analyzer	MRQ
	21 CFR 868.1720 – Oxygen Gas Analyzer	CCL
Device Class:	Class II	
Classification Panel:	Anesthesiology	

5. Legally Marketed Predicate Device

NOxBOXi Nitric Oxide Delivery System, K171696.

6. Device Description

The *NOxBOXi* Nitric Oxide Delivery System (*NOxBOXi*) simultaneously delivers Nitric Oxide (NO) medical gas, while monitoring Nitric Oxide, Nitrogen Dioxide and Oxygen levels in the inspiratory limb of a ventilator for patients undergoing inhaled Nitric Oxide Therapy.

The system is designed for use by healthcare professionals to administer treatment to patients undergoing inhaled Nitric Oxide (iNO) therapy. The *NOxBOXi* will deliver nitric oxide in a synchronous manner to a single patient.

An integrated component to the *NOxBOXi,* the *NOxMixer* is intended to deliver a continuous flow of Nitric Oxide from the *NOxBOXi*, mixed in line with Oxygen (O_2) for use in iNO therapy. The *NOxMixe*r will be used in conjunction with manually bagging a patient.

The *NOxBOXi* includes the *NOxBOXi* Head Unit, a *NOxFLOW* sample line, two NO feed hoses, two regulators (connector type dependent on the gas supplier), a test circuit, NO, O_2 & NO_2 monitors, power supply, drainage syringe, Operating Manual & Technical Guide.

Optional accessories include 4 separate *NOxKITs* (22mm, 15mm, 12 mm, & 10mm), one way valve for HFOV (High Frequency Oscillatory Ventilation), bagging kits (hyperinflation & self-inflating) and circuit reducers (22f – 15m).

This submission is for the addition of compatibility claims for specific ventilators and is not related to product changes. There are no changes to the indications for use of the product and there are no significant design changes.

7. Indication for Use Statement

NOxBOXi Nitric Oxide Delivery System is intended for use by healthcare professionals for the delivery and monitoring of a constant (user set) concentration of nitric oxide (NO) and the monitoring of NO_2 and O_2 in the inspiratory ventilator lines of a patient undergoing nitric oxide therapy (iNO).

The *NOxBOXi* Nitric Oxide Delivery System includes:

- The *NOxBOXi* head unit, which delivers NO gas while in the intelligent delivery mode.
- Continuous monitoring and alarms for NO, O_2 and NO_2.
- The integrated *NOxMixer* which provides a backup NO delivery capability that is intended to deliver a continuous flow of NO, mixed with O_2, for iNO therapy and provides a continuous treatment option during transit and transfer conditions within hospitals.

The *NOxBOXi* Nitric Oxide Delivery System must only be used in accordance with the indications, contraindications, warnings and precautions described in the nitric oxide drug packaging inserts and labeling (currently neonates). Refer to this material prior to use.

8. Substantial Equivalence Discussion

The following table compares the *NOxBOXi* to the predicate device with respect to intended use, technological characteristics and principles of operation.

Comparison of Characteristics With Changes From Device Cleared in K171696

	Subject: NOxBOXi Nitric Oxide Delivery System	Predicate: NOxBOXi Nitric Oxide Delivery System	Comparison
510(k) Number	K201339	K171696	N/A
Manufacturer	Praxair Distribution, Inc.		No Change
Regulatory & Indications for Use			
Product Code	MRN, MRO, MRP, MRQ, CCL		No Change
Regulation Numbers	21 CFR 868.5165, .2380, .2385, .1720		No Change
Regulation Name	Nitric Oxide administration apparatus, back-up and gas analyzers		No Change
Indications for Use	NOxBOXi Nitric Oxide Delivery System is intended for use by healthcare professionals for the delivery and monitoring of a constant (user set) concentration of nitric oxide (NO) and the monitoring of NO_2 and O_2 in the inspiratory ventilator lines of a patient undergoing nitric oxide therapy (iNO). **The NOxBOXi Nitric Oxide Delivery System includes:** • The NOxBOXi head unit, which delivers NO gas while in the intelligent delivery mode. • Continuous monitoring and alarms for NO, O_2 and NO_2. • The integrated NOxMixer which provides a backup NO delivery capability that is intended to deliver a continuous flow of NO, mixed with O_2, for iNO therapy and provides a continuous treatment option during transit and transfer conditions within hospitals. The NOxBOXi Nitric Oxide Delivery System must only be used in accordance with the indications, contraindications, warnings and precautions described in the nitric oxide drug packaging inserts and labeling (currently neonates). Refer to this material prior to use.		No Change
Technical			
NO administration	NO blended with O_2 in the patient's inhalation circuit		No Change
NO flow rate (sample flow rate)	225 ml/min		No Change
NO concentration provided	0.0 TO 80ppm		No Change
NO monitor	Yes		No Change
O_2 monitor	Yes		No Change
Monitoring accuracy	NO & NO_2 - +/- 2% or 0.2ppm		No Change
NO_2 monitor & alarm	Yes		No Change
Battery Backup capability	4 hours without AC power		No Change

	Subject: NOxBOXi Nitric Oxide Delivery System	Predicate: NOxBOXi Nitric Oxide Delivery System	Comparison
Manual bagging & back up system	NOxMIXER®		No Change
NO dosing range in manual mode	0 - 185ppm on 800ppm cylinders		No Change
NO dosing Accuracy in manual mode	± 20% or 2 ppm, whichever is the greater for NO doses from 5 - 80 ppm (800 ppm drug cylinder) and O2 flow rates of 5 - 14 L/min * +/-40% or 4 ppm, whichever is the greater; for NO doses from 0 to < 5 ppm or > 80 to 185 ppm (800 ppm drug cylinder) and O2 flow rates of 2 to < 5 L/min or > 14 to 25 L/min		No Change
NO flow in manual mode	Adjustable 50 – 600 mL/min of NO/N2		No Change
O2 flow range in manual bagging mode	2 to 25 L/min of O2		No Change
Oxygen inlet pressure	3.5 – 4.5 bar		No Change
NO delivery pressure	1.65bar from manual control valve		No Change
Manual bagging & back up system	NOxMIXER®		No Change
Dimensions	65 mm (W) X 185 mm (H) x 60.8 mm (D)		No Change
Pre-use set up time	Instant set-up		No Change
Monitoring during manual bagging	Yes		No Change
Alarms active during bagging	Yes		No Change
Stand alone vs Built-in	Built-in		No Change
Can be used as a back-up function	Yes		No Change
Back-up accuracy	± 20% or 2 ppm, whichever is the greater for NO doses from 5 - 80 ppm (800 ppm drug cylinder), * +/-40% or 4 ppm, whichever is the greater; for NO doses from 0 to < 5 ppm or > 80 to 185 ppm (800 ppm drug cylinder)		No Change
Ventilator Compatibility			
Compatible Ventilators	Various models from the following manufacturers: • Bunnel • Carefusion • Carefusion / SensorMedics • Drägerwerk • Fisher & Paykel Healthcare • Hamilton Medical • Maquet • Newport (Covidien) • Philips Respironics • Puritan Bennett (Covidien) • Smiths Medical • Vapotherm	Various models from the following manufacturers: • Bunnel • Carefusion • Carefusion / SensorMedics • Drägerwerk • (N/A) • Hamilton Medical • Maquet • Newport (Covidien) • Philips Respironics • Puritan Bennett (Covidien) • Smiths Medical • Vapotherm	Equivalent; testing shows no new questions raised regarding safety and effectiveness

9. Non-Clinical and Usability Performance Data

NOxBOXi has been verified and validated to ensure that it meets its functional, performance, and usability specifications and requirements. The device has been tested in compliance to international standards and US FDA guidance documents including the following:

- FDA guidance "Use of International Standard ISO 10993-1, "Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process" (K171696)
- FDA guidance "Premarket Notification Submissions for Nitric Oxide Delivery Apparatus, Nitric Oxide Analyzer and Nitrogen Dioxide Analyzer" including accuracy of NO delivery, response of NO delivery to external perturbations and user changes, purity of NO drug delivery, acceptable / minimal production of NO_2, NO analyzer accuracy, NO_2 analyzer accuracy, control of excess NO_2, backup testing, and compatibility testing (effects on ventilator functionality) of ventilators listed in the product labeling, as applicable (K171696 and K201339)
- FDA guidance "Content of Premarket Submissions for Software Contained in Medical Devices" (K171696)
- FDA guidance "Applying Human Factors and Usability Engineering to Medical Devices." (K171696)
- ISO 10993-1: Biological Evaluation of Medical Devices Part 1: Evaluation and Testing Within a Risk Management Process (K171696)
- ISO 10993-5: Biological Evaluation of Medical Devices Part 5: Tests for In Vitro Cytotoxicity (K171696)
- ISO 10993-10: Biological Evaluation of Medical Devices Part 10: Tests for Irritation and Skin Sensitization (K171696)
- IEC 60601-1: Medical Electrical Equipment – Part 1: General Requirements for Basic Safety and Essential Performance (K171696)
- IEC 60601-1-2: Medical Electrical Equipment – Part 1-2: General Requirements for Basic Safety and Essential Performance – Collateral Standard: Electromagnetic Disturbances – Requirements and Tests (K171696)
- IEC 62366: Medical Devices – Application of Usability Engineering to Medical Devices (K171696)
- ISO 80601-2-55: Medical Electrical Equipment – Part 2-55: Particular Requirements for the Basic Safety and Essential Performance of Respiratory Gas Monitors (K171696)
- IEC 62304: Medical Device Software – Software Life Cycle Processes (K171696)
- ISO 15223-1: Medical Devices – Symbols to be Used With Medical Device Labels, Labelling, and Information to be Supplied – Part 1: General Requirements (K171696)

Additionally, gases delivered through the NOxBOXi system were analyzed for the presence of volatile organic compounds (VOC) and particulate matter. Measurement of the resulting VOC concentrations resulted in levels that were three orders of magnitude below OSHA permissible exposure levels. Particulate testing determined that the gas delivered by the NOxBOXi system

contained particulate levels well below the EPA's maximum limits for total suspended particulates. (K171696)

Testing for this submission was limited to the aspects that could be affected by including compatibility with additional ventilators. No additional usability testing was conducted for this submission. No clinical testing was required to support substantial equivalency of this medical device.

10. Conclusions/Statement of Substantial Equivalence

This submission is for the addition of compatibility claims for specific ventilators and is not related to product changes. There are no changes to the indications for use of the product and there are no significant design changes. The above-described non-clinical data support the substantial equivalence of the device and the compatibility with additional ventilators. The NOxBOXi passed all testing and no different questions of safety or effectiveness were raised. The information provided within this premarket notification supports substantial equivalence to the predicate device.