December 17, 2021

Bedfont Scientific Ltd
℅ Paul Dryden
ProMedic Consulting, LLC
131 Bay Point Dr. NE
St. Petersburg, Florida 33704

Re: K203695
Trade/Device Name: NObreath®
Regulation Number: 21 CFR 862.3080
Regulation Name: Breath Nitric Oxide Test System
Regulatory Class: Class II
Product Code: MXA
Dated: September 13, 2021
Received: September 14, 2021

Dear Paul Dryden:

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 and Part 809); 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,

Marianela Perez-Torres, Ph.D.
Deputy Director
Division of Chemistry
and Toxicology Devices
OHT7: Office of In Vitro Diagnostics
and Radiological Health
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: 06/30/2023
See PRA Statement below.

510(k) Number *(if known)*
K203695

Device Name
NObreath®

Indications for Use *(Describe)*

The NObreath® is a portable, non-invasive device for the measurement of Fractional Exhaled Nitric Oxide (FeNO) in human breath. The production of nitric oxide is often found to be increased in inflammatory conditions such as asthma. Measurement of FeNO by NObreath® is a method to measure the decrease in FeNO concentration in asthma patients that often occurs after treatment with anti-inflammatory pharmacological therapy, as an indication of the therapeutic effect in patients with elevated FeNO levels.

The fractional NO concentration in expired breath (FeNO), can be measured by NObreath® according to guidelines for NO measurement established by the American Thoracic Society.

NObreath® is intended for children, 7- 17 years, and adults 18 years and older. NObreath® 12 second test mode is for age 7 and up

NObreath® 10 second test mode is for ages 7-10 only who cannot successfully complete a 12 second test.

FeNO measurements provide the physician with means of evaluating an asthma patient's response to anti- inflammatory therapy, as an adjunct to the established clinical and laboratory assessments in asthma. The NObreath® cannot be used with infants or by children under the age of 7 as measurement requires patient cooperation.

NObreath® should not be used in critical care, emergency care or in anesthesiology.

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.

DO NOT SEND YOUR COMPLETED FORM TO THE PRA STAFF EMAIL ADDRESS BELOW.

The burden time for this collection of information is estimated to average 79 hours per response, including the time to review instructions, search existing data sources, gather and maintain the data needed and complete and review the collection of information. Send comments regarding this burden estimate or any other aspect of this information collection, including suggestions for reducing this burden, to:

Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."

Date Prepared: 13-Dec-21

Sponsor

Bedfont Scientific Ltd Station Road, Harrietsham
Maidstone, Kent, ME17 1JA, England

Sponsor Contact:

Louise Bateman
Quality and Regulatory Affairs Manager
Tel: +44 (0) 1622 851122

Submission Correspondent

ProMedic, LLC
131 Bay Point Dr. NE
St. Petersburg, FL 33704
Attn.: Paul Dryden

Proprietary or Trade Name: NObreath®

Common/Usual Name: Nitric Oxide Breath Test

Regulation Number: 21CFR 862.3080
Regulation Code: System, test, breath nitric oxide
Product Code: MXA
Regulatory Class: II

Predicate Device: Circassia AB NIOX VERO (K170983)

Device Description:

NObreath® is a portable system for the non-invasive, quantitative measurement of the fraction of exhaled nitric oxide (NO) in expired human breath (FeNO). The NObreath® system is comprised of the main unit with AC adapter, a rechargeable battery, an electrochemical NO sensor, disposable patient mouthpiece with filter. The device can connect to the PC via a standard USB cable or wirelessly via Bluetooth.

For testing, the patient inhales deeply and slowly exhales for 10 or 12 seconds through the patient filter. In approximately 12 seconds the NO concentration is displayed in parts per billion (ppb). Results are processed using dedicated software. The device has built-in system control procedures and a calibration to be performed every 12 months.

Wireless Bluetooth Low Energy (BLE) is used as a means of communication between the monitor and FeNOchart™ software running on a PC. The FeNOchart™ software is a charting program that retrospectively collects data from the NObreath® monitor when it is not monitoring. It is not time critical, there are no alarms

Principles of Operation:
The measurement principle is based on American Thoracic Society guidelines (ATS/ERS Recommendations for Standardized Procedures for the Online and Offline Measurement of Exhaled Lower Respiratory Nitric Oxide and Nasal Nitric Oxide, 2005. Am J Respir Crit Care Med. 2005;171:912-930). The last fraction of the exhalation is evaluated for average NO concentration. NO is measured using electrochemical detection.

Indications for Use:
The NObreath® is a portable, non-invasive device for the measurement of Fractional Exhaled Nitric Oxide (FeNO) in human breath. The production of nitric oxide is often found to be increased in inflammatory conditions such as asthma. Measurement of FeNO by NObreath® is a method to measure the decrease in FeNO concentration in asthma patients that often occurs after treatment with anti-inflammatory pharmacological therapy, as an indication of the therapeutic effect in patients with elevated FeNO levels.

The fractional NO concentration in expired breath (FeNO), can be measured by NObreath® according to guidelines for NO measurement established by the American Thoracic Society.

NObreath® is intended for children, 7- 17 years, and adults 18 years and older. NObreath® 12 second test mode is for age 7 and up

NObreath® 10 second test mode is for ages 7-10 only who cannot successfully complete a 12 second test.

FeNO measurements provide the physician with means of evaluating an asthma patient's response to anti-inflammatory therapy, as an adjunct to the established clinical and laboratory assessments in asthma. The NObreath® cannot be used with infants or by children under the age of 7 as measurement requires patient cooperation.

NObreath® should not be used in critical care, emergency care or in anesthesiology.

Patient Population:
NObreath® is intended for children, 7- 17 years, and adults 18 years and older.
NObreath® 12 second test mode is for age 7 and up
NObreath® 10 second test mode is for ages 7-10 only who cannot successfully complete a 12 second test.

Environments of Use:
Point-of-care healthcare setting under professional supervision.

Table 1 - Table of the Similarities and Differences of Predicate vs. Proposed Device

	Proposed Bedfont NObreath® Nitric Oxide test	Predicate Circassia NIOXVERO
510(k)		K170983
Procode	MXA – Breath nitric oxide test system CFR – 862-3080	MXA – Breath nitric oxide test system CFR – 862-3080
Indications for Use	The NObreath® is a portable, non-invasive device for the measurement of Fractional Exhaled Nitric Oxide (FeNO) in human breath. The production of nitric oxide is often found to be increased in inflammatory conditions such as asthma. Measurement of FeNO by NObreath® is a method to measure the decrease in FeNO concentration in asthma patients that often occurs after treatment with anti-inflammatory pharmacological therapy, as an indication of the therapeutic effect in patients with elevated FeNO levels. The fractional NO concentration in expired breath (FeNO), can be measured by NObreath® according to guidelines for NO measurement established by the American Thoracic Society. Measurement of FeNO by NObreath® is a quantitative, non-invasive, simple and safe method to measure the decrease in FeNO concentration in asthma patients that often occurs after treatment with anti- inflammatory pharmacological therapy, as an indication of the therapeutic effect in patients with elevated FeNO levels. NObreath® is intended for children, 7- 17 years, and adults 18 years and older. NObreath® 12 second test mode is for age 7 and up	NIOX VERO® measures Nitric Oxide (NO) in human breath. Nitric Oxide is frequently increased in some airway inflammatory processes such as asthma. The fractional NO concentration in expired breath (FeNO), can be measured by NIOX VERO according to guidelines for NO measurement established by the ATS. Measurement of FeNO by NIOX VERO is a quantitative, non-invasive, simple and safe method to measure the decrease in FeNO concentration in asthma patients that often occurs after treatment with anti- inflammatory pharmacological therapy, as an indication of the therapeutic effect in patients with elevated FeNO levels. NIOX VERO is suitable for children, 7- 17 years, and adults 18 years and older. NIOX VERO 10 second test mode is for age 7 and up. NIOX VERO 6 second test mode is for ages 7-10 only who cannot successfully complete a 10 second test. FeNO measurements provide the physician with means of evaluating an asthma patient's response to anti-inflammatory therapy, as an adjunct to the established clinical and laboratory assessments in asthma. The NIOX VERO is intended for prescription use and should only be

	NObreath® 10 second test mode is for ages 7-10 only who cannot successfully complete a 12 second test. FeNO measurements provide the physician with means of evaluating an asthma patient's response to anti-inflammatory therapy, as an adjunct to the established clinical and laboratory assessments in asthma. The NObreath® cannot be used with infants or by children under the age of 7 as measurement requires patient cooperation. NObreath® should not be used in critical care, emergency care or in anesthesiology.	used as directed in the NIOX VERO User Manual by trained healthcare professionals. NIOX VERO cannot be used with infants or by children under the age of 7 as measurement requires patient cooperation. NIOX VERO should not be used in critical care, emergency care or in anesthesiology
Intended Users	Trained medical personnel	Trained medical personnel
Target Population	Children, 7-17 years, and adults 18 years and older	Children, 7-17 years, and adults 18 years and older
Environments of use	Point of care healthcare settings	Point of care healthcare settings
Results type	Quantitative	Quantitative
Technology	Electrochemical sensor technology	Electrochemical sensor technology
Sensor Calibration	Every 12 months or factory calibrated sensor replacement	Factory calibrated
Measurement Range	5-500 ppb NO	5-300 ppb NO
Limit of Detection	5 ppb	5 ppb
Analysis time	12 sec	25 sec
Patient sampling	12 sec - adults 10 sec – 7-17 yrs	10 sec adults 6 sec – 7-17 yrs
Accuracy	$\pm$ 5 ppb of measured value $\leq$ 50 ppb $\pm$ 10% of measured value > 50 ppb	$\pm$ 5 ppb of measured value $\leq$30 ppb $\pm$ 10% ppb of measured value >30 ppb
Altitude	Up to 6300 feet	Not listed
Precision	$\pm$ 5 ppb of measured value $\leq$ 50 ppb $\pm$ 10% of measured value > 50 ppb	<3 ppb of measured value < 30 ppb $\leq$10% ppb of measured value >30 ppb
Patient interface	Mouthpiece with integral filter	Mouthpiece

	Proposed Bedfont NObreath® Nitric Oxide test	Predicate Circassia NIOXVERO
Standards used for testing	ANSI / AAMI /ES 60601-1:2005+A1:2012 IEC 60601-1-2:2014 AIM Standard 7351731: 2017 ISO 10993-5, -10 ISO 18562-1, -3	AAMI ANSI ES 60601-1: 2005 +A1: 2012 IEC 60601-1-6 CLSI EP5-A2 Vol 24 No. 25 CLSI EP6-A vol 23, no. 16

Substantial Equivalence Rationale
The Bedfont NObreath® is substantially equivalent to the predicate device because:

Indications –
- The NObreath® is a portable nitric oxide test for measuring FeNO.

Discussion – The indications for use are similar to the predicate K170983.

Environment of Use –
- Both devices have the same environments of use

Discussion – The environments of use and personnel are similar to the predicate.

Technology –
- The technology is electrochemical sensor technology.

Discussion – This technology is equivalent for both devices.

Non-clinical Testing Summary -

Biocompatibility of Materials – the following testing was performed:
- Cytotoxicity
- Sensitization
- Irritation / intracutaneous reactivity
- Acute Systemic toxicity
- Material Mediated Pyrogenicity
- ISO 18562 testing: Gas emission VOC, PM2.5 and PM10
- Inorganic gases – CO, CO_2, Ozone

Discussion – The materials in contact were found non-cytotoxic, non-sensitizers, non-irritants, and passed systemic toxicity and pyrogenicity.

Electrical, EMC, EMI testing –

- The candidate device was evaluated per ANSI/AAMI/ES 60601-1, IEC 60601-1-2 and AIM Standard 7351731: 2017 and the device performed as intended and met the requirements.

Discussion – The proposed device met the requirements of the standards.

Bench testing –

- Bench testing including analytical performance testing such as precision and linearity was performed to verify the performance to specifications of the proposed device. Testing includes IEC 60601-1, IEC 60601-1-2, software verification and system verification.

Discussion – Upon completion of the tests, the candidate device was found to have met its performance requirements.

Clinical testing –

Two clinical studies were performed:

- **Clinical precision**

In one of the studies conducted, the clinical precision, as it relates to user bias of the NObreath®, was evaluated in a mixed study population of 76 participants - including 24 paediatric participants (ages 7-17 years) and 52 adults (18 years +). Participants were asked to obtain two NObreath® measurements with the assistance of three health care professionals (HCPs), for a total of six NObreath® evaluations per participant.

The clinical precision study was designed to capture the accuracy and precision of the NObreath device, therefore FeNO values acquired by subjects covered potential FeNO values which would be observed in clinical practice. The within subject precision* was assessed from this study population and is presented in the table below:

Median Concentrations	N	Within Subject Mean SD (ppb)	Within Subject Mean CV (%)	95% CI for CV (%)
0 to <10	10	0.8034172	13.35%	7.85%; 18.85%
10 to <20	21	1.2430966	9.18%	6.73%; 11.64%
20 to <30	23	0.9720727	4.17%	2.48%; 5.85%
30 to <40	5	1.2279205	3.65%	1.3%; 6%
40 to <50	5	1.3867462	3.17%	0.23%; 6.1%
>=50	12	1.4078969	1.89%	1.29%; 2.48%

*Three subjects in the clinical precision study had a large variation between the measurements. One subject was from median concentration bin of >= 50 ppb and two subjects were from the median concentration bin of 40 to <50 ppb. The %CV for these subjects was 10.24%, 21.54%, and 14.17%. This table excludes data from these three subjects.

- **Clinical efficacy**

A second study also evaluated the clinical efficacy of the NObreath®;

A total of 186 patients (n= 95 18+ and n=91 7 to 17 years of age) participated in a longitudinal study where measurements for FeNO, spirometry, and asthma control questionnaires were completed at baseline (Visit 1) and two weeks later (Visit 2) after therapeutic agents were administered.

For those with elevated initial FeNO defined by ATS >25ppb for adults and >20ppb for children (total n=139),there was a fall in mean FeNO measured by NObreath® in patients with elevated FeNO levels for combined adult and paediatric treatment population (n=139).

Results showed a mean change of -13.7 ppb (-27.7%) with a mean SD of 17.8.

The Decline in FeNO was accompanied by the following changes in subjective and objective asthma measures.
The following secondary outcome measures showed the following after 2 weeks of corticosteroid therapy that accompanied the fall in FeNO described above.

ACQ:
Mean ACQ score fell by -29.7% after corticosteroids

FEV1:
There was a mean FEV1 change of 10.1% after corticosteroids

Discussion of Differences

The differences between the subject and predicate device include:

- Broader detection range 5-500 ppb vs. 5-300 ppb. This does not affect performance or safety.
- Slightly longer measurement time for adults and pediatric vs. predicate. This difference does not introduce any new concerns of safety and effectiveness.
- Replacement factory calibrated sensor or factory calibration vs. at the factory. This is a convenience feature for the user.
- Performance specifications were similar.

The differences do not raise any new concerns of safety or effectiveness and thus the subject device can be considered to be substantially equivalent to the predicate.

Substantial Equivalence Conclusion:
The sponsor has demonstrated through performance testing, design and features and non-clinical and clinical testing that the proposed device is substantially equivalent to the predicate device.