November 30, 2017

Circassia AB
William Sammons
Manager, Global Regulatory Affairs
Hansellisgatan 13
SE-754 50 Uppsala, Sweden

Re: K170983
Trade/Device Name: NIOX VERO
Regulation Number: 21 CFR 862.3080
Regulation Name: Breath nitric oxide test system
Regulatory Class: Class II
Product Code: MXA
Dated: October 19, 2017
Received: October 23, 2017

Dear William Sammons:

This letter corrects our substantially equivalent letter of November 22, 2017.

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. 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); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); 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 http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

For comprehensive regulatory information about medical devices and radiation-emitting products, including information about labeling regulations, please see Device Advice (https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/) and CDRH Learn (http://www.fda.gov/Training/CDRHLearn). 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 (http://www.fda.gov/DICE) for more information or contact DICE by email (DICE@fda.hhs.gov) or phone (1-800-638-2041 or 301-796-7100).

Sincerely,

Courtney H. Lias -S

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
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: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
K170983

Device Name
NIOX VERO

Indications for Use *(Describe)*
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 American Thoracic Society.

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 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.

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."

510(k) SUMMARY

The assigned 510(k) number is: K170983

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SDMA 1990 and 21 CFR 807.92.

Preparation Date: 22 Nov 2017

510(k) Applicant:
Circassia AB
Hansellisgatan 13
SE-754 50 Uppsala
Sweden
Phone: +46-8-629-0780
Fax: +46-8-629-0781

Contact Person: Susanne Parks

Global Director Regulatory Affairs & Quality Assurance

Trade Name: NIOX VERO®

Common Name: Airway Inflammation Monitor

Classification Name: System, Test, Breath Nitric Oxide
Regulatory Class: Class II
Product Code: MXA
CFR Section: 21 CFR 862.3080

Predicate Device: NIOX VERO® Airway Inflammation Monitor
510(k) Clearance Number: K150233

Class II under 21 CFR 862.3080, Product Code MXA

Device Description

NIOX VERO is a portable system for the non-invasive, quantitative measurement of the fraction of exhaled nitric oxide (NO) in expired human breath (FeNO). NO levels increase during allergic airway inflammation. Measurement of changes in FeNO concentration is used in evaluating a patient's response to anti-inflammatory therapy, as an adjunct to established clinical and laboratory assessments.

The NIOX VERO system is comprised of the NIOX VERO unit with AC adapter, a rechargeable battery, an electrochemical NO sensor, disposable patient filters, and an exchangeable handle containing an internal NO scrubber filter. The NIOX Panel is an optional PC application for operation of the NIOX VERO from a PC and access to electronic medical record systems. The device can connect to the PC via a standard USB cable or wirelessly via Bluetooth.

The patient empties their lungs, inhales deeply through the patient filter to total lung capacity and then slowly exhales for 10 seconds. A 6 second mode is available for children aged 7 – 10 who cannot perform a 10 second exhalation. In approximately one minute, the NO concentration is displayed in parts per billion (ppb).

The NIOX VERO unit includes a sampling and gas conditioning system and a man-machine interface (MMI). The instrument controls the inhaled sample appropriately via the electronics and software program. Filtering of inhaled air eliminates contamination from ambient NO levels. A built-in flow control keeps exhalation standardized at 50 ml/s so that it is standardized for all patients. The sample enters an electromechanical sensor and interacts with an electrolyte. A chemical reaction takes place where electrons are generated proportional to the number of NO molecules.

Results are processed using dedicated software. In order to verify the device's performance and reliability of measurements, there are built-in system control procedures and a Quality Control procedure to be performed on a daily basis.

Intended Use/Indications for Use

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 American Thoracic Society.

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 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.

Technological Characteristics Compared to Predicate

	Subject **NIOX VERO®**	**Predicate** **NIOX VERO®**
Trade Name	**10 s and 6s Measurement Modes**	**10 Measurement Mode**
510(k) Number	K170983	K150233
Regulatory Class	Class II	Class II
Regulation Number	21 CFR 862.3080	21 CFR 862.3080
Product Code	MXA	MXA

Indications for Use	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 American Thoracic Society. 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 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	NIOX VERO measures Nitric Oxide (NO) in human breath. Nitric Oxide is frequently increased in some 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 American Thoracic Society. 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, approximately 7 - 17 years, and adults 18 years and older. 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 used as directed in the NIOX VERO User Manual by trained healthcare professionals. NIOX VERO cannot be used with infants or by children approximately under the age of 7, as measurement requires patient cooperation. NIOX VERO should not be used in critical care, emergency care or in anesthesiology.

	anesthesiology.	
Analytical limits at low levels, (limit of detection)	Identical to predicate	5 ppb
Precision	Identical to predicate	< 3 ppb of measured value for values < 30 ppb < 10% of measured value for values ≥30 ppb
Accuracy	Identical to predicate	±5 ppb for measured values ≤ 30ppb or 10% of measured value for values > 30 ppb.
Measurement Range	Identical to predicate	5 - 300 ppb
Linearity, reportable range	Identical to predicate	Squared correlation coefficient $r^2 \geq 0.998$, slope 0.95 – 1.05, intercept ±3ppb
Measurement Mode	, 10s mode for patients 7 to 17 and for adults age 18 and over; 6s measurement mode for patients 7 to 10 only	10s measurement mode for patients 7 to 17

The scope of this 510(k) application is the activation of the existing 6s measurement mode on the predicate device. The 6s measurement mode was present in the previously cleared device, but not activated for the US market. The 6s measurement mode is used to aid the performance of patients that are younger and unable to successfully achieve a 10s breath sample for testing purposes.

Performance Testing:

Performance testing was repeated for the NIOX VERO device in 6s mode. The 6s exhalation mode is technically identical to the standard 10s exhalation mode for which all other verification and validation is made, except for the timing counter that controls how long time the patient should exhale into the device. When bench testing is performed, certified calibration gas of approximately 200 ppb is mixed with nitrogen gas in a gas mixer, connected with the NIOX VERO instrument, to produce 5ppb, 25 ppb and 75ppb. 200ppb is produced directly from the gas bottle.

The precision, accuracy, and linearity bench testing was repeated with the NIOX VERO in 6s mode. All results were found to be within specifications for the original NIOX VERO performance specifications.

Clinical Testing:

This 510(k) submission supports the use of an alternative 6s mode to the currently approved 10 second test for use in children aged 7 to 10.

The evidence to support use of the 6 second mode is demonstrated by the clinical study conducted and provided in the submission.

<u>AER-047 Use of 6s in ages 7 to 10 years</u>

A randomized, single-center, single-visit, point-of-care clinical validation study was conducted in 43 male and female subjects age 7 to 10 years. Data supports use of 6s mode in children under age of 10.

Conclusions:

The updated NIOX VERO has the same intended use as the predicate device and the Indications for Use have been updated to reflect the 6s mode usage. The device modifications do not affect the device's fundamental scientific technology, clinical performance, hardware or software as the functionality was previously implemented in the predicate, but not activated in the US market.

Performance bench testing was repeated in the 6s mode to demonstrate that the use of the NIOX VERO in 6s mode does not change the fundamental performance properties of the device and the new measurement mode is as safe and effective as the predicate 10s mode.

Clinical testing has been performed to demonstrate that the NIOX VERO in 6s mode for patients between the ages of 7 and 10 years old is substantially equivalent to 10s mode use in this patient population. The patient ages for the 6s mode are ages 7 - 10 year age range. This data supports substantial equivalence and the changes to the NIOX VERO Indications for Use to support this new measurement mode.