

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY AND INSTRUMENT COMBINATION TEMPLATE**

A. 510(k) Number:

k182874

B. Purpose for Submission:

New Device

C. Measurand:

Breath Nitric Oxide

D. Type of Test:

Quantitative, electrochemical sensor

E. Applicant:

Spirosure, Inc.

F. Proprietary and Established Names:

Fenom Pro™ Nitric Oxide Test

G. Regulatory Information:

1. Regulation section:

21 CFR 862.3080, Breath nitric oxide test system

2. Classification:

Class II

3. Product code:

MXA

4. Panel:

Clinical Chemistry (75)

H. Intended Use:

1. Intended use(s):

Refer to indications for use below.

2. Indication(s) for use:

Fenom Pro™ Nitric Oxide Test is a portable, non-invasive device to measure fractional exhaled nitric oxide (FeNO) in human breath. FeNO is increased in some airway inflammatory processes, such as asthma, and often decreases in response to anti-inflammatory treatment. Measurement of FeNO by Fenom Pro™ 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 therapeutic effect in patients with elevated FeNO levels. FeNO measurements are to be used as an adjunct to established clinical assessments. Fenom Pro™ is suitable for children, approximately 7-17 years, and adults 18 years and older.

Testing using the Fenom Pro™ should only be done in a point-of-care healthcare setting under professional supervision. Fenom Pro™ should not be used in critical care, emergency care or in anesthesiology.

3. Special conditions for use statement(s):

Fenom Pro™ may not be used by children under the age of approximately 7 years, including infants, as measurement requires patient cooperation. Fenom Pro™ may not be used by children under the age of 7 years, or by patients who are unable to understand and execute the instructions given by healthcare providers, as measurement requires patient cooperation.

Fenom Pro™ should not be used in critical care, emergency care, or in anesthesiology. All subjects should refrain from eating or drinking for at least 60 minutes before the FENOM test. Recent intake of nitrate rich food, such as lettuce, spinach, beets, walnuts, peanuts, and animal organs, can lead to increased FeNO levels .

Smoking reduces exhaled NO levels. Fenom Pro™ results obtained from subjects who smoke should only be considered after considering the subject's smoking history and the potential impact on NO levels.

For prescription use only.

4. Special instrument requirements:

None

I. Device Description:

The Fenom Pro™ Nitric Oxide Test (also referred to in short as Fenom Pro™) is a portable system for the non-invasive, quantitative measurement of the fraction of exhaled nitric oxide (NO) in expired human breath (FeNO).

The Fenom Pro™ Nitric Oxide Test is comprised of four major components (touch screen, handpiece, mouthpiece, breath conditioning cartridge). The main unit contains a touch screen interface for the use as well as houses the nitric oxide sensor and pneumatics needed to sample the patient's breath. The patient interfaces with Fenom through the mouthpiece which is attached to the handpiece. The handpiece is connected to the main unit via a breath tube. The handpiece contains a breath conditioning cartridge which prepares the breath sample from the patient for proper analysis in the main unit. Both the mouthpiece and the breath conditioning cartridge are consumables.

The mouthpiece is a single patient use, disposable component that contains an anti-bacterial/anti-viral filter. The mouthpiece has an ergonomically designed oval interface to the patient to aid in creating a proper seal during the breath maneuver.

The breath conditioning cartridge is designed to remove humidity from breath samples. It is intended to be used 20 times before being disposed. It contains desiccant beads conditioned to a low dew point to ensure proper sample conditioning over the useful life of the cartridge. The device keeps track of the number of uses on the cartridge as well as independently measures the humidity of the breath sample after the cartridge to verify the gas sample humidity is within the device requirement for proper FeNO analysis.

J. Substantial Equivalence Information:

1. Predicate device name(s):

NIOX MINO

2. Predicate 510(k) number(s):

k072816

3. Comparison with predicate:

| Item | Candidate Device Fenom Pro™ Nitric Oxide Test k182874 | Predicate NIOX MINO k072816 |
|-----------------------|---|-----------------------------------|
| Indications for Use | <p>Fenom Pro™ Nitric Oxide Test is a portable, non-invasive device to measure fractional exhaled nitric oxide (FeNO) in human breath. FeNO is increased in some airway inflammatory processes, such as asthma, and often decreases in response to anti-inflammatory treatment. Measurement of FeNO by Fenom Pro™ 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 therapeutic effect in patients with elevated FeNO levels. FeNO measurements are to be used as an adjunct to established clinical assessments. Fenom Pro™ is suitable for children, approximately 7-17 years, and adults 18 years and older.</p> <p>Testing using the Fenom Pro™ should only be done in a point-of-care healthcare setting under professional supervision. Fenom Pro™ should not be used in critical care, emergency care or in anesthesiology.</p> | Same |
| Intended Use Setting | Point-of-care healthcare setting under professional supervision | Same |
| User age | Children 7-17 years, and adults | Same |
| Measurement principle | Electrochemical sensor technology | Same |
| Calibration | Factory Calibrated | Same |
| Measurement range | 10 – 200 ppb | 5 – 300 ppb |

| Item | Candidate Device Fenom Pro™ Nitric Oxide Test k182874 | Predicate NIOX MINO k072816 |
|-----------------|---|-----------------------------------|
| Detection Limit | 10 ppb | 5 ppb |
| Analysis Time | ~30 sec. | ~60 sec. |

K. Standard/Guidance Document Referenced (if applicable):

CLSI EP05-A3, Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline – Third Edition.

CLSI EP06-A, Evaluation of the Linearity of Quantitative Measurement Procedures: A Statistical Approach; Approved Guideline.

CLSI EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures: Approved Guideline – Second Edition.

IEC 60601-1-2:2014 General requirements for basic safety and essential performance- Collateral standard: Electromagnetic compatibility- Requirements and tests and AIM 7351731 Medical Electrical Equipment and System Electromagnetic Immunity Test for RFID Readers.

L. Test Principle:

Fenom Pro™ Nitric Oxide Test uses solid-state electrochemical sensor technology sensitive to nitric oxide (NO) compounds. The solid state sensor is preceded by a reactive filter material that renders (oxidizes) potentially confounding species such as carbon monoxide (CO), ammonia (NH₄), and methanol (CH₄O) inactive, or inert, to the NO sensor. Fenom Pro™ provides visual and audible feedback during its use. A user performs a breath maneuver by exhaling into Fenom Pro™ Nitric Oxide Test, and the Fenom Pro™ Nitric Oxide Test graphical user interface (GUI) displays an indication of the user's breath flow rate, such that the user can modulate their breath flow rate to be within the acceptable limits. An electrochemical potential difference between the electrodes of the sensor develops and is proportional to the amount of NO in the gas sample.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Nitric oxide was mixed in a balance gas to simulate breath samples. Samples NO concentrations were determined using a chemiluminescence device calibrated against a NIST traceable NO tank. Fenom Pro™ Nitric Oxide Test results were collected by multiple operators over 5 operating days, 2 sessions per day, 4 runs per session with two replicates for each concentration, across five different devices using the

concentrations 10, 25, 75 and 200 ppb (N =400 per concentration). Repeatability is an estimated of variation within one test run in one day. Within-device precision is an estimate of variation between test runs and days. The repeatability and within-device precision over the five days was determined for each concentration as shown in the tables below:

Repeatability

| NO concentration | 10 ppb | 25 ppb | 75 ppb | 200 ppb |
|------------------|----------|----------|--------|---------|
| | SD (ppb) | SD (ppb) | CV (%) | CV (%) |
| Device 1 | 1.6 | 1.8 | 3.7 | 3.9 |
| Device 2 | 1.6 | 1.4 | 5.3 | 4.9 |
| Device 3 | 1.2 | 1.5 | 4.0 | 3.0 |
| Device 4 | 1.1 | 1.2 | 3.2 | 3.1 |
| Device 5 | 1.9 | 2.3 | 7.1 | 7.3 |

Within-device precision

| NO concentration | 10 ppb | 25 ppb | 75 ppb | 200 ppb |
|------------------|----------|----------|--------|---------|
| | SD (ppb) | SD (ppb) | CV (%) | CV (%) |
| Device 1 | 1.5 | 2.3 | 5.9 | 6.8 |
| Device 2 | 1.5 | 1.7 | 6.2 | 6.2 |
| Device 3 | 1.2 | 1.6 | 4.3 | 3.4 |
| Device 4 | 1.2 | 1.2 | 4.0 | 4.5 |
| Device 5 | 2.3 | 3.3 | 7.5 | 8.5 |

Clinical Precision

A multi-center, single visit, point-of care, inter-operator variability study was conducted to determine the repeatability of FeNO measured with the Fenom Pro™ Nitric Oxide Test. 3 different operators at each site instructed each subject to perform two valid Fenom Pro™ Nitric Oxide Test measurements. FeNO levels in this study were assessed for a total of 127 subjects at 4 different sites by a total of 12 operators.

The table below shows the intra-subject precision of Fenom Pro™ Nitric Oxide Test measurements within six different measurement ranges.

| Median Concentrations | N* | Within Subject Mean SD | 95% CI for SD | Within Subject Mean CV (%) | 95% CI for CV |
|------------------------------|-----------|-------------------------------|----------------------|-----------------------------------|----------------------|
| 10 to <20 | 13 | 2.19 | 1.57, 3.61 | 14.23% | 10.21%, 23.49% |
| 20 to <30 | 30 | 2.44 | 1.94, 3.28 | 10.11% | 8.05%, 13.59% |
| 30 to <40 | 29 | 2.71 | 2.15, 3.66 | 8.11% | 6.44%, 10.97% |
| 40 to <50 | 11 | 4.74 | 3.31, 8.31 | 10.98% | 7.67%, 19.27% |
| >=50 | 44 | 5.57 | 4.60, 7.05 | 5.94% | 4.91%, 7.52% |

*Number of subjects, each providing two measurements.

An additional clinical precision evaluation, conducted with subjects under corticosteroid therapy, is provided in section 3.c.

b. Linearity/assay reportable range:

Nitric oxide was mixed to create simulated breath gas to obtain 8 NO concentration levels ranging from 5-200 ppb (5, 10, 15, 30, 50, 100, 150, 200 ppb). Samples NO concentrations were determined using a chemiluminescence device calibrated against a NIST traceable NO tank. Five replicates were obtained with the Fenom Pro™ Nitric Oxide Test at each level, using two Fenom Pro™ Nitric Oxide Test devices.

| Linearity | | | |
|------------------|--------------|------------------|----------------------|
| Device | Slope | Intercept | R² |
| Device 1 | 1.03 | 2.32 | 0.999 |
| Device 2 | 1.02 | 0.231 | 0.999 |

Effects of extreme temperature, relative humidity.

The effects of temperature, relative humidity (RH) were assessed using the following conditions: 15°C/20% RH, 15°C/80% RH, 30°C/20% RH, 30°C/80% RH, and ambient conditions at 22°C/37% RH. For each sample, nitric oxide was mixed in a balance gas of simulated breath and the concentration of NO was determined using a NO Gas Analyzer. Each concentration sample was measured using 2 Fenom Pro™ devices, with each concentration tested in five replicates per device per test condition. The results support the claimed operating conditions for the Fenom Pro™ Nitric Oxide Test: 15°C-30°C, 20-80% RH .

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

The Fenom Pro™ Nitric Oxide Test is manufacturer calibrated and does not require calibration by the user.

The device is pre-programmed to allow a defined number of tests for the nitric oxide sensor. Stability study results were provided to support the sensor life of 250 tests or 50 hours of use, whichever comes first. Replacement of the sensor is done by the manufacturer.

The breath conditioning cartridge is a replacement part of the device. Stability study results were provided to support the claimed cartridge shelf life of 3 months. Once installed, each cartridge is pre-programmed to allow a defined number of tests (12 hours of use or 20 uses, whichever comes first).

The shelf-life for the mouthpiece is 24 months. The mouthpiece is a single patient use, disposable component that contains an anti-bacterial/anti-viral filter.

d. *Detection limit:*

The limit of detection for the Fenom Pro™ Nitric Oxide Test was determined based on CLSI EP17-A2. Two devices were tested at 0 ppb (60 replicates), 5 ppb (30 replicates) and 10 ppb (30 replicates) over three days. Nitric oxide samples were mixed in a balance gas of simulated breath. The limit of detection was calculated using the parametric option in CLSI EP17-A2, using the following formulas: $LoB = \mu_B + 1.645 \sigma_B$ and $LoD = LoB + 1.645 \sigma_S$. The results of the limit of detection analysis support the claimed detection limit of 10 ppb.

e. *Analytical specificity:*

Endogenous substance interference

Interference testing was performed using simulated breath having 15, 30, and 50 ppb NO. Five sensors were used to evaluate endogenous interference. The substances and concentrations tested are summarized in the table below. A substance was defined as non-interfering if the response at the tested concentration was within ± 4 ppb NO.

| Substance | Concentration tested | Concentration expected in exhaled breath | Sensor interference, equivalent to ppb NO |
|-------------------|----------------------|--|---|
| Acetaldehyde | 150 ppb | 100 ppb | 0.8 ppb |
| Acetone | 5,000 ppb | 10 ppb | 3.7 ppb |
| Acetonitrile | 150 ppb | 100 ppb | 120.8 ppb |
| Ammonia | 1,000 ppb | 0.5 ppb | 1.9 ppb |
| Carbon Dioxide | 8% vol | 8% vol | 2.6 ppb |
| Carbon Monoxide | 50 ppm | 50 ppm | 1.5 ppb |
| Ethanol | 165 ppm | 165 ppm | -0.2 ppb |
| Hydrogen | 50 ppm | 50 ppm | 0.5 ppb |
| Hydrogen Sulfide | 5 ppm | 1 ppm | -2.0 ppb |
| Isoprene | 1.5 ppm | 1 ppm | 2.3 ppb |
| Oxygen | 21% | 16% | -1.4 ppb |
| Hydrogen Peroxide | 500 ppm | 1ppb | 4.0 ppb |
| Nitrogen Dioxide | 13 ppb | 0ppb | 19.2 ppb |

Exogenous substance interference

A clinical study was performed to investigate the influence of common orally consumed or used exogenous substances on FeNO results measured with Fenom Pro™ Nitric Oxide Test. Each subject performed one baseline measurement before the exogenous substance was introduced and one measurement 60 minutes post exposure or consumption. All subjects refrained from eating or drinking for 60 minutes before the FeNO testing. The results of the study are shown below and support that there is no significant effect of these exogenous substances on the

measurement of FeNO by Fenom Pro™ Nitric Oxide Test, if users allow one hour to pass before a FeNO measurement. The device labeling recommends that no food or beverage be consumed, and no smoking be done, for at least one hour before taking an FeNO measurement.

| Exogenous Substance | # of Subjects | Mean difference (ppb) | 95% Confidence Intervals (ppb) |
|------------------------|---------------|-----------------------|--------------------------------|
| Alcohol Free Mouthwash | 12 | -0.8 | [-3.5, 1.9] |
| Caffeinated Soda | 11 | -3.0 | [-6.2, 0.2] |
| Caffeine Free Soda | 10 | -1.7 | [-6.9, 3.5] |
| Menthol Lozenge | 15 | 0.9 | [-1.0, 2.8] |
| Mouthwash with Alcohol | 10 | -1.2 | [-7.4, 5.0] |
| Non-Menthol Lozenge | 10 | 0.8 | [-1.9, 3.5] |
| Toothpaste | 12 | -1.8 | [-4.0, 0.5] |

f. Assay cut-off:

Not applicable.

2. Comparison studies:

a. Method comparison with predicate device:

Not applicable. A clinical study was conducted to validate the clinical performance of the Fenom Pro™ Nitric Oxide Test (see section 3.c.).

b. Matrix comparison:

Not applicable.

3. Clinical studies:

a. Clinical Sensitivity:

Not applicable.

b. Clinical specificity:

Not applicable.

c. Other clinical supportive data (when a. and b. are not applicable):

A multi-center, open label, non-randomized, prospective, single cohort study was

conducted to evaluate FeNO measured with the Fenom Pro™ Nitric Oxide Test, spirometry, and asthma symptoms in adult and pediatric subjects with uncontrolled asthma before and after corticosteroid treatment. A total of 82 males and females from 7 to 79 years of age with uncontrolled asthma (not taking asthma controller medications) and elevated FeNO were enrolled at 10 sites and completed the study according to the protocol. The demographic data for the subjects are presented below.

Subject demographics

| | | N (82 total) | % |
|-------------|------------------------|--------------|------|
| Sex | Males | 46 | 56.1 |
| | Females | 36 | 43.9 |
| Age (years) | < 18 (Children) | 37 | 45.1 |
| | ≥ 18 (Adults) | 45 | 54.9 |
| Race | Caucasian | 60 | 73.2 |
| | African American | 13 | 15.9 |
| | Asian | 4 | 4.9 |
| | Two or more races | 1 | 1.2 |
| | Other | 4 | 4.9 |
| Ethnicity | Hispanic or Latino | 19 | 23.2 |
| | Not Hispanic or Latino | 62 | 75.6 |
| | Unknown/Not Provided | 1 | 1.2 |

Clinical Precision:

Each subject provided replicate FeNO measurements at Visit 1 (baseline) and Visit 2 (after approximately two weeks of corticosteroid therapy). The results are summarized in the below tables:

Visit 1

| Median NO concentration | N* | Within Subject Mean SD (ppb) | 95% CI for SD (ppb) | Within Subject Mean CV (%) | 95% CI for CV (%) |
|-------------------------|----|------------------------------|---------------------|----------------------------|-------------------|
| 10 to ≤ 20 | 6 | 1.28 | 0.8, 3.14 | 7.09 | 4.43, 17.40 |
| 20 to ≤ 30 | 5 | 4.97 | 2.98, 14.30 | 20.78 | 12.45, 59.75 |
| 30 to ≤ 40 | 5 | 2.04 | 1.22, 5.86 | 5.76 | 3.45, 16.55 |
| 40 to ≤ 50 | 13 | 3.03 | 2.18, 5.01 | 6.76 | 4.85, 11/16 |
| 50 to <75 | 23 | 3.69 | 2.86, 5.23 | 6.23 | 4.82, 8.82 |
| 75 to <100 | 12 | 6.39 | 4.53, 10.85 | 7.35 | 5.20, 12.47 |
| ≥100 | 18 | 4.37 | 3.28, 6.54 | 3.09 | 2.32, 4.63 |

*Number of subjects

Visit 2

| Median concentration | N* | Within Subject Mean SD (ppb) | 95% CI for SD (ppb) | Within Subject Mean CV (%) | 95% CI for CV (%) |
|----------------------|----|------------------------------|---------------------|----------------------------|-------------------|
| <10 | 2 | 0.29 | 0.13, 9.38 | 3.48 | 1.55, 111.03 |
| 10 to ≤ 20 | 12 | 1.18 | 0.83, 2.00 | 7.71 | 5.46, 13.08 |
| 20 to ≤ 30 | 20 | 1.88 | 1.43, 2.75 | 7.48 | 5.69, 10.93 |
| 30 to ≤ 40 | 18 | 1.81 | 1.36, 2.71 | 5.23 | 3.93, 7.85 |
| 40 to ≤ 50 | 11 | 2.23 | 1.56, 3.92 | 5.21 | 3.64, 9.15 |
| 50 to <75 | 15 | 2.93 | 2.15, 4.63 | 4.87 | 3.56, 7.68 |
| 75 to <100 | 3 | 5.22 | 2.72, 32.79 | 6.40 | 3.33, 40.25 |
| ≥100 | 1 | 2.41 | - | 1.69 | - |

*Number of subjects

Clinical Accuracy

Using the Fenom Pro™ Nitric Oxide Test, FeNO was measured in all subjects at baseline and after 2 weeks of corticosteroid treatment (follow-up). Testing was performed by 42 trained technicians. At study entry, the adult subjects (≥ 18 years of age) had FeNO levels > 30 ppb and children subjects (< 18 years of age) had FeNO levels > 25 ppb. The changes in FeNO (Mean ± SD) in these patients are summarized in the below table.

| | Baseline FeNO (ppb) | Follow-up FeNO (ppb) | Change (ppb) | p-value* |
|-----------------------|---------------------|----------------------|--------------|----------|
| All subjects (N = 82) | 81.8 ± 49.2 | 39.5 ± 24.5 | -42.3 ± 45.5 | < 0.0001 |

*p-value for statistical significance of change vs baseline.

FeNO and various asthma outcome measures [Asthma Control Questionnaire (ACQ/pACQ (pediatric ACQ)), and Forced Expiratory Volume at 1 second (FEV1)] are presented in Tables below. The majority of subjects showed improvement in FEV1 (66.7%) and ACQ/pACQ (78.6%) and a decrease in FeNO levels at visit 2, as compared to their baseline measurements taken at visit 1.

FeNO / Symptoms / FEV1 Comparison Table (all subjects)

| Measurement Variables | % Change Baseline to Follow-Up | p-value* |
|----------------------------|--------------------------------|----------|
| FeNO | -51.4% | < 0.0001 |
| Symptoms (ACQ/pACQ scores) | -49.5% | < 0.0001 |
| Spirometry (FEV1) | +7.7% | < 0.0001 |

FeNO / Symptoms / FEV1 Comparison Table (Adults ≥18)

| Measurement Variables | % Change Baseline to Follow-Up | p-value* |
|-----------------------|--------------------------------|----------|
| FeNO | -50.7% | < 0.0001 |

| | | |
|----------------------------|--------|----------|
| Symptoms (ACQ/pACQ scores) | -49.0% | < 0.0001 |
| Spirometry (FEV1) | +9.8% | < 0.0001 |

FeNO / Symptoms / FEV1 Comparison Table (Children <18)

| Measurement Variables | % Change Baseline to Follow-Up | p-value* |
|----------------------------|--------------------------------|----------|
| FeNO | -52.3% | < 0.0001 |
| Symptoms (ACQ/pACQ scores) | -50.3% | < 0.0001 |
| Spirometry (FEV1) | 5.2% | < 0.0001 |

*p-value for statistical significance of change vs baseline.

The relationship between the percent change in FeNO and the percent change in pre- and post-bronchodilator FEV1 from visit 1 to visit 2 was investigated. The magnitude of the FeNO change and degree of improvements in ACQ and FEV1 are different because the scale and precision of these metrics varies. The data presented in the table below indicate that FEV1 and symptom score (ACQ) are different metrics and are not directly correlated with FeNO as determined by Fenom Pro™ Nitric Oxide Test.

| Correlation between change in FENO and change in FEV1 and ACQ in the ITT population (adults and children combined) | | |
|--|----------------------|--------|
| | | FeNO |
| Change in FEV ₁ | R-square correlation | -0.14 |
| | P-value | 0.2161 |
| Change in asthma symptom score (ACQ) | R-square correlation | 0.21 |
| | P-value | 0.0637 |

4. Clinical cut-off:

Not applicable.

5. Expected values/Reference range:

The expected values are provided from the literature. In the labeling the sponsor states, “Given that physiological and environmental factors can affect FeNO levels, in clinical practice, ‘healthy’ FeNO levels need to be established on an individual basis. However, most healthy individuals will have NO levels in the range 5-35 ppb (children slightly lower 5-25 ppb) when measured at 50 mL/s. (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).”

N. Instrument Name:

Fenom Pro™ Nitric Oxide Test

O. System Descriptions:

1. Modes of Operation:

A user will perform a breath maneuver by exhaling into Fenom Pro™ Nitric Oxide Test, and the Fenom Pro™ Nitric Oxide Test graphical user interface (GUI) will display an incentive or indication of the user's breath flow rate, such that the user can modulate their breath flow rate to be within the acceptable limits recommended by the ATS and ERS guidelines.

The Fenom Pro™ Nitric Oxide Test device evaluates the breath maneuver and determines if the breath maneuver was performed according to the ATS and ERS guidelines with regards to breath flow rate and duration. The breath sample is presented through the reactive filter that transforms interferent species into inert species for the sensor and then fluidly presents the gas sample to the sensor. An electrochemical potential difference between the electrodes of the sensor develops and is proportional to the amount of NO in the gas sample.

Does the applicant's device contain the ability to transmit data to a computer, webserver, or mobile device?

Yes _____ or No _____

Does the applicant's device transmit data to a computer, webserver, or mobile device using wireless transmission?

Yes _____ or No _____

2. Software:

FDA has reviewed applicant's Hazard Analysis and software development processes for this line of product types:

Yes _____ or No _____

3. Specimen Identification:

The patient performs the test in real-time and is identified by patient name.

4. Specimen Sampling and Handling:

The user obtains a breath sample by having the subject exhale into the device.

5. Calibration:

The manufacturer performs calibration for each Fenom Pro™ Nitric Oxide Test device. No calibration is required by the operator.

6. Quality Control:

Fenom Pro™ Nitric Oxide Test provides internal controls as well as an External Quality Control program for the user to verify the reliability of measurements.

The External Quality Control (QC) program consists of two parts: One positive control from a qualified staff member with a stable FeNO value providing a normal biological FeNO sample and a negative control consisting of a NO free gas sample which is generated by the device from ambient air.

The labeling states that QC Users must be over 18 years of age, non-smoker, no known airway diseases or chronic cold, preferably no allergies or asthma, and stable FeNO values between 10-40 ppb. The device has built in QC rules and the user will see the Passed or Failed instructions after the daily QC is performed.

The process consists of performing four QC measurements, one per day, within 7 days. The negative control result must be <10ppb. The positive control result must be with process control limits for control charts with subgroup size one as defined in "Understanding Statistical Process Control" by Donald L. Wheeler and David S. Chambers. The control limits are established as follows: the most recent result (V0) is compared to a rolling average (AVG) and the prior result (V1). The control limit is a multiple of the rolling absolute range (RAR), which is the average difference of successive results. The control limits are:

$$|V_0 - AVG| \leq RAR * 2.66, \text{ or } 5\text{ppb, whichever is greater}$$
$$|V_0 - V_1| \leq RAR * 3.268, \text{ or } 5\text{ppb, whichever is greater}$$

When the QC has passed both criteria, the device is ready for clinical use. A QC test must be performed each day of use. If the QC tester does not perform a QC test in 30 days, the qualification is suspended and the QC tester needs to re-qualify.

P. Other Supportive Instrument Performance Characteristics Data Not Covered In The "Performance Characteristics" Section above:

Analytical Accuracy

An accuracy study was performed to compare performance of the Fenom Pro™ Nitric Oxide Test device to a chemiluminescence device calibrated against a NIST traceable NO tank. Four Fenom Pro™ Nitric Oxide Test devices were tested over six concentrations (10 ppb, 25 ppb, 75 ppb, 100 ppb, 200 ppb, and 300 ppb) with ten replicates each for a total of 240 tests. For each concentration, nitric oxide was mixed in a balance gas of simulated breath.

The results of the study are shown below:

| | Mean Bias (%) | | | | | |
|----------|-----------------------|----------------------|---------------|----------------|----------------|----------------|
| | 10 ppb | 25 ppb | 75 ppb | 100 ppb | 200 ppb | 300 ppb |
| Device 1 | -1.1 ppb (-11.0 %) | -2.6 ppb (-10.4%) | -0.5 | 1.1 | -6.4 | -2.5 |
| Device 2 | -0.7 ppb (-7.0%) | -1.6 ppb (-6.4%) | -5.4 | -2.7 | -7.7 | -5.0 |
| Device 3 | 3.2 ppb (32.0%) | 3.0 ppb (12.0%) | -0.1 | -1.5 | -4.6 | -5.2 |
| Device 4 | -0.9 ppb (-9.0%) | -1.2 ppb (-4.8%) | -7.0 | -4.6 | -7.3 | -3.2 |

Electrical Safety testing

The sponsor provided documentation describing conformity assessment to the relevant electrical safety standard (IEC 60601-1).

Electromagnetic Compatibility testing

The sponsor provided documentation describing conformity assessment to the relevant EMC standard IEC 60601-1-2:2014

Biocompatibility testing

Fenom PRO Nitric Oxide Test device will be contacting patient’s gas pathway via air. In addition, the mouthpiece component will have direct surface contact. The contact duration is limited (<24 hours). Based on the intended patient contact types and duration, the sponsor provided demonstrated acceptable cytotoxicity, intracutaneous reactivity, sensitization, and acute systemic toxicity for the device.

Effects of extreme temperature, relative humidity.

The operating conditions for the device is 15°C-30°C, 20-80% RH. The effects of temperature, relative humidity (RH) were assessed using the following conditions: 15°C/20% RH, 15°C/80% RH, 30°C/20% RH, 30°C/80% RH, and ambient conditions at 22°C/37% RH. For each sample, nitric oxide was mixed in a balance gas of simulated breath and the concentration of NO was determined using a NO Gas Analyzer. Each concentration sample was measured using 2 Fenom Pro™ devices, with each concentration tested in five replicates per device per test condition. The readings from the candidate device meet the acceptance criteria of within +/-5 ppb at 15 ppb, and +/-10% at 75 and 200ppb. The results support the recommended operating conditions of 5°C-30°C (59°F to 86 °F), 20-80% RH.

Effects of altitude

The sponsor also tested device performance at the following atmospheric pressure range of 106 to 92 kPa, equivalent to -1500 feet to +2500 feet above sea level, and show that the device performance are not affected. The labeling states the operation condition of the device is from Sea level to 6500 ft.

Q. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Parts 801 and 809, as applicable.

R. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.