



February 13, 2019

Spirosure, Inc.
% Erika Ammirati, President
Ammirati Regulatory Consulting
575 Shirlynn Court
Los Altos, CA 94022

Re: K182874
Trade/Device Name: Fenom Pro™ Nitric Oxide Test
Regulation Number: 21 CFR 862.3080
Regulation Name: Breath nitric oxide test system
Regulatory Class: Class II
Product Code: MXA
Dated: January 11, 2019
Received: January 15, 2019

Dear Erika Ammirati:

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/CombinationProducts/GuidanceRegulatoryInformation/ucm597488.htm>); 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 <http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm>.

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,


Kellie B. Kelm -S

for 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

Indications for Use

510(k) Number (if known)

K182874

Device Name

Fenom Pro™ Nitric Oxide Test

Indications for Use (Describe)

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.

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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510(k) SUMMARY

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92. The assigned 510(k) number is K182874. This document was

807.92 (a)(1): Name: Spirosure, Inc.
Address: 7020 Koll Center Parkway, Suite 110
Pleasanton, CA 94566

Phone: (925) 264-7720
Email: ryan@spirosure.com
Contact: Mr. Ryan Leard

Date of Preparation: October 11, 2018

807.92 (a)(2): Device name- trade name and common name, and classification

Trade name:
Fenom Pro™ Nitric Oxide Test

Common Name: Breath nitric oxide test system

Classification: 21 CFR Part 862.3080

807.92 (a)(3): Identification of the legally marketed predicate devices NIOX MINO (Aerocrine AB, Morrisville, NC), K072816

807.92 (a)(4): Device Description

Fenom Pro™ is a point-of-care breath analyzer that uses solid-state electrochemical technology to measure the fraction of exhaled nitric oxide (FeNO), a marker for airway inflammation, in human exhaled breath. Measurement of FeNO by Fenom Pro is a quantitative and non-invasive method to indicate therapeutic effects of anti-inflammatory pharmacological therapy in patients with elevated FeNO levels. Fenom Pro™ is suitable for children, approximately 7-17 years, and adults 18 years and older.

Fenom Pro uses solid state, potentiometric, sensor technology sensitive to nitric oxides (NO) compounds. The solid state sensor is fluidly 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. The visual and audible feedback is especially important during the FeNO measurement such that the user can modulate their breath speed within the flow parameters required by the American Thoracic Society (ATS) and the European Respiratory Society (ERS) standards.

Fenom Pro is comprised of four major components. 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.

807.92 (a)(5): Intended 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.

807.92 (a)(6): Technological Similarities and Differences to the Predicate

The following chart describes similarities and differences between Fenom Pro™ and the predicate.

Comparison	Subject Device Fenom Pro™ Nitric Oxide Test	Predicate Device NIOX MINO (K072816)
Intended 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.	NIOX MINO® 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 MINO according to guidelines for NO measurement established by the American Thoracic Society. Measurement of FeNO by NIOX MINO 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 MINO is suitable for children,

	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.	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 MINO is intended for prescription use and should only be used as directed in the NIOX MINO User Manual by trained healthcare professionals. NIOX MINO cannot be used with infants or by children approximately under the age of 7, as measurement requires patient cooperation. NIOX MINO should not be used in critical care, emergency care or in anesthesiology.
Class	Class II	Same
Regulation Number	21 CFR 862.3080	Same
Product Code	MXA	Same
FDA Branch	Toxicology/Chemistry (75)	Same
Result Type	Quantitative	Same
Test Locale	Point-of-Care, Professional	Same
Sample Type	Exhaled human breath	Same
Test Principle	Electrochemical sensor technology	Same
Sensor Calibration	Factory Calibrated	Same
Measurement Range	10-200ppb NO	5-300ppb NO
Detection Level	10ppb	5ppb
Analysis Time	approximately 30 seconds	approximately one minute
Power Supply	100-240V, ~50-60Hz	100-240V, ~47-63Hz

807.92 (b)(1): Brief Description of Nonclinical Data

Accuracy and Environmental Testing

Two devices were tested over three concentrations with five replicates each at 5 different environmental conditions for a total of 150 tests. The five different conditions tested are summarized in the table below.

Tested Conditions

Test Case	Test Case Description	Temperature (°C)	Relative Humidity (%RH)
1	Ambient Temp / Ambient Humidity	22°	37%
2	Low Temp / Low Humidity	15°	20%
3	High Temp / Low Humidity	30°	20%
4	Low Temp / High Humidity	15°	80%
5	High Temp / High Humidity	30°	80%

For each concentration, nitric oxide was mixed in a balance gas of simulated breath. Each concentration sample was measured using a chemiluminescence device calibrated against a NIST traceable NO tank. This measurement was used to calculate the device error for each replicate. The data are shown below.

Accuracy Study Summary

Test Case	Target Conc. (ppb)	Device	Actual Concentration (ppb)	Mean Score (ppb)	Std Dev Score (ppb)	Upper 95% Error Limit (ppb/%)	Lower 95% Error Limit (ppb/%)	Accuracy Acceptance Criterion	Pass/Fail
Ambient T/ Ambient RH	15	GP18	14.5	13.6	0.548	0.17ppb	-1.97ppb	+/-5ppb	Pass
Ambient T/ Ambient RH	15	GP35	14.5	12.8	1.095	0.44ppb	-3.84ppb	+/-5ppb	Pass
Ambient T/ Ambient RH	75	GP18	70.1	70	0.707	1.83%	-2.12%	+/-10%	Pass
Ambient T/ Ambient RH	75	GP35	70.1	70.2	0.837	2.48%	-2.20%	+/-10%	Pass
Ambient T/ Ambient RH	200	GP18	187.5	185	0.707	-0.59%	-2.07%	+/-10%	Pass
Ambient T/ Ambient RH	200	GP35	187.5	184.6	1.517	0.04%	-3.13%	+/-10%	Pass
High T/ High RH	15	GP18	14.5	16	1.225	3.90ppb	-0.90ppb	+/-5ppb	Pass
High T/ High RH	15	GP35	14.5	15.2	0.837	2.33ppb	-0.93ppb	+/-5ppb	Pass
High T/ High RH	75	GP18	70.1	68.8	1.643	2.74%	-6.45%	+/-10%	Pass
High T/ High RH	75	GP35	70.1	68.8	1.483	2.29%	-6.00%	+/-10%	Pass
High T/ High RH	200	GP18	187.5	182.8	2.683	0.30%	-5.31%	+/-10%	Pass
High T/ High RH	200	GP35	187.5	182	1.581	-1.28%	-4.59%	+/-10%	Pass
High T/ Low RH	15	GP18	14.5	15	1.000	2.46ppb	-1.46ppb	+/-5ppb	Pass
High T/ Low RH	15	GP35	14.5	14.6	0.894	1.85ppb	-1.65ppb	+/-5ppb	Pass
High T/ Low RH	75	GP18	70.1	68.8	0.837	0.48%	-4.19%	+/-10%	Pass
High T/ Low RH	75	GP35	70.1	69	0.707	0.41%	-3.55%	+/-10%	Pass
High T/ Low RH	200	GP18	187.5	183	1.414	-0.92%	-3.88%	+/-10%	Pass
High T/ Low RH	200	GP35	187.5	182.8	0.837	-1.63%	-3.38%	+/-10%	Pass
Low T/ High RH	15	GP18	14.5	14.8	1.304	2.85ppb	-2.25ppb	+/-5ppb	Pass
Low T/ High RH	15	GP35	14.5	14.8	0.447	1.17ppb	-0.57ppb	+/-5ppb	Pass
Low T/ High RH	75	GP18	70.1	70.8	1.304	4.64%	-2.65%	+/-10%	Pass
Low T/ High RH	75	GP35	70.1	69.4	0.894	1.50%	-3.50%	+/-10%	Pass
Low T/ High RH	200	GP18	187.5	184.6	1.342	-0.14%	-2.95%	+/-10%	Pass
Low T/ High RH	200	GP35	187.5	183.4	0.548	-1.61%	-2.76%	+/-10%	Pass
Low T/ Low RH	15	GP18	14.5	14	0.000	-0.5ppb	-0.5ppb	+/-5ppb	Pass
Low T/ Low RH	15	GP35	14.5	13.8	0.447	0.17ppb	-1.57ppb	+/-5ppb	Pass
Low T/ Low RH	75	GP18	70.1	68.2	1.095	0.35%	-5.77%	+/-10%	Pass
Low T/ Low RH	75	GP35	70.1	68.8	0.447	-0.60%	-3.10%	+/-10%	Pass
Low T/ Low RH	200	GP18	187.5	174.4	2.702	-4.16%	-9.81%	+/-10%	Pass
Low T/ Low RH	200	GP35	187.5	176.8	1.304	-4.34%	-7.07%	+/-10%	Pass

Precision

The precision study was based on CLSI EP05-A3 (80 replicates per sample per device). Nitric oxide was mixed in a balance gas of simulated breath. Samples were measured using a chemiluminescence device calibrated against a NIST traceable NO tank. Data were collected from 5 devices over 5 operating days, 2 sessions per day, 4 runs per session with 2 replicates for each concentration, using the concentrations 10, 25, 75 and 200 ppb, by multiple operators. The data are shown below.

Analytical Precision Summary

	Repeatability			
	SD (ppb)	SD (ppb)	%CV	%CV
Bag ID	10 ppb	25 ppb	75 ppb	200 ppb
GammaPrime02	1.6	1.8	3.7%	3.9%
GammaPrime04	1.6	1.4	5.3%	4.9%
GammaPrime05	1.2	1.5	4.0%	3.0%
GammaPrime06	1.1	1.2	3.2%	3.1%
GammaPrime07	1.9	2.3	7.1%	7.3%

	Within-Device Precision			
	SD (ppb)	SD (ppb)	%CV	%CV
Bag ID	10 ppb	25 ppb	75 ppb	200 ppb
GammaPrime02	1.5	2.3	5.9%	6.8%
GammaPrime04	1.5	1.7	6.2%	6.2%
GammaPrime05	1.2	1.6	4.3%	3.4%
GammaPrime06	1.2	1.2	4.0%	4.5%
GammaPrime07	2.3	3.3	7.5%	8.5%

Linearity

Nitric oxide was mixed in a balance gas of simulated breath to obtain 8 NO concentration levels (5, 10, 15, 30, 50, 100, 150, 200 ppb). Samples were measured using a chemiluminescence device calibrated against a NIST traceable NO tank. Each concentration was tested in five replicates. Linearity was assessed across two devices. The linear regression of the device as compared to a reference measurement shall have a slope between 0.95 and 1.05 and r² values greater than 0.998.

Linearity

Device	Slope	Intercept	R ²
GammaPrime42	1.03	2.32	0.999
GammaPrime49	1.02	0.231	0.999
Combined	1.02	1.27	0.998

Limit of Detection

The limit of detection study was 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. Using the parametric option in CLSI-EP17-A2, the Limit of Detection (LoD) was calculated. The results are shown below.

Limit of Detection Study

Device	Limit of Detection (ppb)	Spec Requirement (ppb)	Pass/Fail
Device #1	1.8	≤10	Pass
Device #2	4.6	≤10	Pass

Interference Testing- other gasses

Sensor interference levels were tested in a laboratory setting. The applicable concentration of each substance was generated, the gas stream was fed to the sensor by a gas mixing system, and the sensor signal was measured. In the cases where test concentrations were higher than the minimum test concentrations, the sensor signals were scaled appropriately. Test gases were flowed at 100 ccm, and were exposed to the sensors for 25 seconds. The target was that the change in response to the interference gases at specified minimum or higher concentrations shall be equal to or less than the response of 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 ppm	10 ppb	3.7 ppb
Acetonitrile	150 ppb	100 ppb	120.8 ppb
Ammonia	1 ppm	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
Hydrogen Peroxide	500 ppm, balance air	1 ppm	4.0 ppb
Oxygen	21%	16%	-1.4 ppb

There were no observed interferences causing a response larger than a 4 ppb NO equivalent response for any of the substances except acetonitrile. Acetonitrile is only present in exhaled breath when someone has recently smoked^{1,2}. The ATS recommends that FeNO testing not be performed after smoking, and Fenom Pro is labeled in this manner.

1 Analysis of exhaled breath from smokers, passive smokers and non-smokers by solid phase microextraction gas chromatography/mass spectrometry. Buszewski B, Ulanowska A, Ligor T, Denderz N, Amann A. Biomed Chromatogr. 2009 May;23(5):551-6. doi: 10.1002/bmc.1141.

2 Quantification of acetonitrile in exhaled breath and urinary headspace using selected ion flow tube mass spectrometry. Abbott S.M., Elder J.B., Spinel P., Smith D. International Journal of Mass Spectrometry, Vol. 228, Issues 2-3, 2003 August 15, Pages 655-665.

Interference Testing- Exogenous Substances

A study was performed with seven commonly used oral substances (see below). A minimum of 10 volunteers per substance determined their baseline Fenom Pro levels, ingested or used the substance, and then repeated their Fenom Pro measurements 10 minutes and 60 minutes after the exposure. The 10-minute data were for interest, only. For non-interference to be validated, the mean differences between 60 minutes and baseline values needed to be within 5 ppb. Further, the lower and upper 95% confidence intervals around the means needed to pass through zero.

#	Exogenous Compound
1	Alcohol Free Mouthwash
2	Caffeinated Soda
3	Caffeine Free Soda
4	Menthol Lozenge
5	Mouthwash with Alcohol
6	Non-Menthol Lozenge
7	Toothpaste

The data indicated that Fenom Pro was not impacted by any of the substances at 60 minutes.

Summary Data Pre and Post Exogenous Exposure

Exposure	Test description	Mean difference	Mean difference <5ppb	Lower 95%	Upper 95%	95% CI includes zero
Alcohol Free Mouthwash	PRE	0.0				
	60 Min	-0.8	PASS	-3.5	1.9	PASS
Caffeinated Soda	PRE	0.0				
	60 Min	-3.0	PASS	-6.2	0.2	PASS
Caffeine Free Soda	PRE	0.0				
	60 Min	-1.7	PASS	-6.9	3.5	PASS
Menthol Lozenge	PRE	0.0				
	60 Min	0.9	PASS	-1.0	2.8	PASS
Mouthwash with Alcohol	PRE	0.0				
	60 Min	-1.2	PASS	-7.4	5.0	PASS
Non-Menthol Lozenge	PRE	0.0				
	60 Min	0.8	PASS	-1.9	3.5	PASS
Toothpaste	PRE	0.0				
	60 Min	-1.8	PASS	-4.0	0.5	PASS

807.92 (b)(2): Brief Description of Clinical Data

In one study, the clinical precision, as it relates to user bias of Fenom Pro, was evaluated in a mixed study population of 127 subjects- including 44 pediatric subjects (ages 5-17 years) and 83 adults. Subjects were asked to obtain two Fenom Pro measurements with the assistance of three health care professionals (HCPs), for a total of six Fenom Pro evaluations per subject. Both subjects and HCPs completed ease-of-use questionnaires after the testing.

The objective of the evaluation was to confirm there is no user bias for Fenom Pro. The maximum mean bias observed was only 1.2 ppb between pairs of HCPs. Very high quantitative agreement was demonstrated between HCPs by Deming regression, correlation, and all bias analyses as shown in the table below.

	Slope	Y-Intercept	Pearson R
HCP 1 v HCP 2	0.9775	0.4455	0.9937
	95% CI: 0.9473 to 1.008	95% CI: -0.53 to 1.42	95% CI: 0.9910 to 0.9955
HCP 2 vs HCP 3	0.9815	0.6193	0.9945
	95% CI: 0.9467 to 1.0160	95% CI: -0.080 to 2.04	95% CI: 0.9923 to 0.9962
HCP 1 v HCP 3	0.9584	1.098	0.9873
	95% CI: 0.9169 to 0.9999	95% CI: -0.36 to 2.55	95% CI: 0.9819 to 0.9910

The within subject precision was also assessed from this study population and is presented below in three tables: the first for the whole study population (n=127), second the pediatric population (n=44), and third those aged ≥ 18 (n=83).

Summary of Clinical Precision for FeNO measurements, Age group = ALL (n=127)

Median Concentrations	N	Within Subject		Within Subject	
		Mean SD	95% CI for SD	Mean CV (%)	95% CI for CV
0 to <10	0	-	-	-	-
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%

Summary of Clinical Precision for FeNO measurements, Age group <18yrs (n=44)

Median Concentrations	N	Within Subject		Within Subject	
		Mean SD	95% CI for SD	Mean CV (%)	95% CI for CV
0 to <10	0	-	-	-	-
10 to <20	6	2.51	1.57, 6.16	14.70%	9.18%, 36.06%
20 to <30	8	2.60	1.72, 5.29	10.84%	7.17%, 22.07%
30 to <40	6	2.55	1.59, 6.25	7.25%	4.52%, 17.77%
40 to <50	4	6.38	3.62, 23.78	13.89%	7.87%, 51.77%
≥ 50	20	5.74	4.36, 8.38	6.27%	4.77%, 9.16%

Summary of Clinical Precision for FeNO measurements, Age group ≥ 18 yrs (n=83)

Median Concentrations	N	Within Subject		Within Subject	
		Mean SD	95% CI for SD	Mean CV (%)	95% CI for CV
0 to <10	0	-	-	-	-
10 to <20	7	1.91	1.23, 4.21	13.83%	8.91%, 30.46%
20 to <30	22	2.38	1.83, 3.40	9.85%	7.57%, 14.07%
30 to <40	23	2.75	2.13, 3.89	8.34%	6.45%, 11.80%
40 to <50	7	3.80	2.45, 8.36	9.32%	6.00%, 20.52%
≥ 50	24	5.43	4.22, 7.61	5.66%	4.40%, 7.94%

HCPs and subjects generally indicated favorable responses for the features of the device via their questionnaires. For the subject group, favorable impressions of the system were recorded approximately 93% of time; for the HCP group, favorable impressions of the system were recorded approximately 96% of time.

Clinical Precision was also assessed from a study that closely embodies the clinical use condition, where each subject provided replicate (n = 2) FeNO measurements at Visit 1 (baseline) and Visit 2 (after approximately two weeks of high dose corticosteroid therapy). The data were analyzed by median FeNO scores within FeNO concentration subgroups across the reporting range for the device. The table below presents the whole study population (n=82), but data were also sub-grouped by age range: 5 to 17 years (n=37), and ≥ 18 years (n=45). The clinical imprecision was less than 5ppb by mean standard deviation for FeNO values below 50ppb, and %CVs for FeNO values greater than 50ppb were maintained at less than 10%, unless the sample size was small, across all subgroups.

Summary of Clinical Precision of FeNO Measurements by Visit

Age Group	Visit	Median Concentrations	N	Within Subject		Within Subject	
				Mean SD	95% CI for SD	Mean CV (%)	95% CI for CV
All	Visit 1 (Baseline)	0 to <10	0	-	-	-	-
		10 to <20	6	1.28	0.80, 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%
	Visit 2	0 to <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%	

Age Group	Visit	Median Concentrations	N	Within Subject Mean SD	95% CI for SD	Within Subject Mean CV (%)	95% CI for CV
5 to 17	Visit 1 (Baseline)	0 to <10	0	-	-	-	-
		10 to <20	2	0.27	0.12, 8.67	1.63%	0.73%, 51.98%
		20 to <30	4	5.54	3.14, 20.66	23.45%	13.29%, 87.40%
		30 to <40	2	2.82	1.26, 89.96	7.34%	3.27%, 234.17%
		40 to <50	5	4.52	2.71, 13.00	10.23%	6.13%, 29.42%
		50 to <75	11	4.13	2.88, 7.24	7.04%	4.92%, 12.36%
		75 to <100	3	16.31	8.49, 102.54	18.73%	9.75%, 117.75%
		≥100	10	4.57	3.14, 8.34	3.31%	2.28%, 6.05%
	Visit 2	0 to <10	1	0.20	-	2.78%	-
		10 to <20	7	1.33	0.86, 2.93	8.28%	5.33%, 18.23%
		20 to <30	11	1.48	1.04, 2.60	5.88%	4.11%, 10.32%
		30 to <40	7	1.43	0.92, 3.15	4.00%	2.58%, 8.81%
		40 to <50	1	1.59	-	3.19%	-
		50 to <75	8	2.83	1.87, 5.76	4.71%	3.12%, 9.59%
		75 to <100	1	3.50	-	3.97%	-
		≥100	1	2.41	-	1.69%	-

Age Group	Visit	Median Concentrations	N	Within Subject Mean SD	95% CI for SD	Within Subject Mean CV (%)	95% CI for CV
≥18	Visit 1 (Baseline)	0 to <10	0	-	-	-	-
		10 to <20	4	1.78	1.01, 6.65	9.83%	5.57%, 36.62%
		20 to <30	1	2.70	-	10.11%	-
		30 to <40	3	1.52	0.79, 9.54	4.70%	2.45%, 29.55%
		40 to <50	8	2.11	1.39, 4.29	4.59%	3.04%, 9.35%
		50 to <75	12	3.30	2.33, 5.59	5.49%	3.89%, 9.33%
		75 to <100	9	3.09	2.08, 5.91	3.55%	2.40%, 6.80%
		≥100	8	4.12	2.72, 8.38	2.80%	1.85%, 5.70%
	Visit 2	0 to <10	1	0.39	-	4.18%	-
		10 to <20	5	0.96	0.57, 2.75	6.91%	4.14%, 19.86%
		20 to <30	9	2.36	1.60, 4.53	9.44%	6.37%, 18.08%
		30 to <40	11	2.05	1.43, 3.60	6.02%	4.21%, 10.56%
		40 to <50	10	2.30	1.58, 4.19	5.42%	3.73%, 9.89%
		50 to <75	7	3.05	1.97, 6.73	5.05%	3.25%, 11.12%
		75 to <100	2	6.07	2.71, 193.82	7.62%	3.40%, 243.16%
		≥100	0	-	-	-	-

In a third study, Fenom Pro was evaluated to show clinical efficacy; the study was designed to demonstrate that the device can be used successfully to monitor changes in fractional exhaled nitric oxide in uncontrolled asthma patients when therapeutic agents are administered. Specifically, the intent was to show that there is a significant concordance between Fenom Pro and other established asthma-related outcome measures.

A total of 82 subjects (37 five to 17 years of age and 45 aged 18 and older) with uncontrolled asthma participated in a longitudinal study where measurements for FeNO, spirometry, and asthma questionnaires were completed at baseline (Visit 1) and two weeks later (Visit 2) after therapeutic agents were administered. The data demonstrated that significant differences between the two visits were achieved for all three modalities, and therefore concordance between Fenom Pro and the established asthma-related outcome measures.

The results of Passing-Bablok regressions are summarized in the table below for the key asthma condition assessments of FEV1 and ACQ/pACQ that show concordance. Note that two subject records did not have asthma symptom scores available thus study population for the correlations dropped to n=80.

Parameter	FeNO vs. FEV1	FeNO vs. ACQ/pACQ
N in comparison	80	80
Slope point estimate	-0.0017	0.0089
Slope 95% CI	-0.0032 to 0.0000	0.0014 – 0.0148
Y-intercept point estimate	0.0956	-0.5018
Y-intercept 95% CI	0.0091 – 0.1250	-0.7432 to -0.1848
Kendall's Tau point estimate	-0.1599	0.1931
Kendall's Tau 95% CI	-0.3003 to -0.0126	0.0468 – 0.3312
Kendall's Tau p-value	<i>0.0370</i>	<i>0.0125</i>

807.92 (b)(3): Conclusions from Nonclinical and Clinical Data

The conclusions drawn from the analytical and clinical data demonstrate that the device is safe and effective for its intended use.