



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

I Background Information:

A 510(k) Number

K251674

B Applicant

MGC Diagnostics Corporation

C Proprietary and Established Names

Fenom Flo™ FeNO Monitoring System

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
MXA	Class II	21 CFR 862.3080 - Breath Nitric Oxide Test System	CH - Clinical Chemistry

II Submission/Device Overview:

A Purpose for Submission:

New Device

B Measurand:

Breath Nitric Oxide

C Type of Test:

Quantitative, electrochemical sensor

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

Fenom Flo™ FeNO monitoring system 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 decreases in response to anti-inflammatory treatment. Fenom Flo™ measures fractional exhaled nitric oxide (FeNO) according to guidelines established by the American Thoracic Society.

Measurement of FeNO by Fenom Flo™ is a non-invasive quantitative 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 Flo™ is suitable for adults and children ages seven years and older.

Fenom Flo™ should be used in a point-of-care healthcare setting under professional supervision. Fenom Flo™ should not be used in critical care, emergency care, or anesthesiology.

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

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

Fenom Flo™ 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 Arugula, spinach, lettuce, radish, beetroot, chinese cabbage, turnips, cabbage, green beans, leek, spring onion, cucumber, carrots, potatoes, garlic, sweet pepper, green pepper, can lead to increased FeNO levels.

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

D Special Instrument Requirements:

Fenom Flo™ FeNO Monitoring System

IV Device/System Characteristics:

A Device Description:

Fenom Flo™ is a point-of-care (POC) breath analyzer that quantitatively measures fractional exhaled nitric oxide (NO) in expired human breath.

The device is a hand-held unit that houses a rechargeable lithium-ion battery, a nitric oxide (NO) sensor, and integrated pneumatics and electronics. The patient interfaces with the device through the mouthpiece which is attached to the handpiece. The mouthpiece is a single patient use, disposable component that contains an anti-bacterial/anti-viral filter. To measure the fraction of exhaled FeNO in human exhaled breath using the Fenom Flo™, the patient performs a breath maneuver by grasping the handpiece and exhaling into it. A graphical user interface (GUI) display assists the patient in keeping their breath flow rate within acceptable limits.

B Principle of Operation:

The candidate device utilizes digital electrochemical sensor technology to measure fractional exhaled nitric oxide (FeNO). The NO sensor produces an electrochemical potential difference between the electrodes of the sensor and is proportional to the amount of NO in the breath sample. The Fenom Flo device provides a digital readout of the fractional concentration of fractional exhaled nitric oxide (FeNO) in parts per billion (ppb).

C Instrument Description Information:

1. Instrument Name:

Fenom Flo™ FeNO Monitoring System

2. Specimen Identification:

There is no mechanism to identify the specimen, as it is analyzed at the point and time of collection. Results are stored in the order they are performed, cataloged by date and time. No patient information is entered or stored on the device.

3. Specimen Sampling and Handling:

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

4. Calibration:

The device is calibrated by the manufacturer; no calibration is required by operators.

5. Quality Control:

The device utilizes internal and external quality control procedures. For external quality control, two measurements (a positive and a negative control) are required to validate device performance. Quality control should be performed each day of device use.

V Substantial Equivalence Information:

A Predicate Device Name(s):

B Predicate 510(k) Number(s):
K213611

C Comparison with Predicate(s):

Device & Predicate Device(s):	<u>K251674</u>	<u>K213611</u>
Device Trade Name	Fenom Flo™	Fenom Pro
General Device Characteristic Similarities		
Intended Use/Indications For Use	Same	For the measurement of fractional exhaled nitric oxide (FeNO) in human breath.
Sample Type	Same	Exhaled human breath
Sensor type	Same	Amperometric Sensor Technology
Measurement Mode	Same	6-second and 10-second breath maneuver
General Device Characteristic Differences		
Measurement range	5-300 ppb NO	10-200 ppb NO
Limit of Detection	5 ppb	10 ppb
Analysis Time	Approximately 27 seconds	Approximately 30 seconds

VI Standards/Guidance Documents Referenced:

- ANSI AAMI ES60601-1:2005/(R)2012 & A1:2012 C1:2009/(R)2012 & A2:2010/(R)2012 (Cons. Text) [Incl. AMD2:2021] Medical electrical equipment - Part 1: General requirements for basic safety and essential performance (IEC 60601-1:2005, MOD).[Including Amendment 2 (2021)]
- ANSI AAMI IEC 60601-1-2:2014 [Including AMD 1:2021] Medical electrical equipment - Part 1-2: General requirements for basic safety and essential performance – Collateral Standard: Electromagnetic disturbances-Requirement and tests.
- ANSI AAMI ISO 14971: 2019 Medical devices - Applications of risk management to medical devices
- ISTA 3A2018 Packaged-Products for Parcel Delivery System Shipment 70 kg (150 lb) or Less

- CLSI EP05-A3 Evaluation of Precision of Quantitative Measurement Procedures; Approved Guideline - Third Edition
- AAMI TIR57:2016 Principles for medical device security - Risk management.

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

Analytical precision

The sponsor performed studies to evaluate the within-device precision and repeatability of the candidate device, based on CLSI EP05-A3. Data were collected using 5 candidate devices, over 5 operating days, 2 sessions per day, 4 runs per session with 2 replicates for each concentration, at concentrations of 10, 25, 75 and 200 ppb, by multiple operators. The repeatability and within-device precision over the five days was determined for each concentration.

Precision was evaluated for the 10-second mode and 6-second mode separately and the results are summarized in the tables below:

Precision Study Summary (6-second test)

Device	Repeatability				Within-device Precision			
	SD (ppb)	SD (ppb)	CV(%)	CV(%)	SD (ppb)	SD (ppb)	CV(%)	CV(%)
	10 ppb	25 ppb	75 ppb	200 ppb	10 ppb	25 ppb	75 ppb	200 ppb
200102	2.02	1.09	1.9%	0.7%	2.28	0.97	1.7%	0.6%
200111	1.13	1.64	1.9%	1.2%	1.13	1.42	1.7%	1.0%
200112	1.72	0.85	1.8%	0.6%	1.54	1.61	1.7%	0.6%
200113	1.34	1.0	1.6%	1.0%	1.26	1.16	1.5%	0.9%
200114	1.21	0.93	1.4%	0.5%	1.12	0.89	1.3%	0.5%

Precision Study Summary (10-second test)

Device	Repeatability				Within-device Precision			
	SD (ppb)	SD (ppb)	CV(%)	CV(%)	SD (ppb)	SD (ppb)	CV(%)	CV(%)
	10 ppb	25 ppb	75 ppb	200 ppb	10 ppb	25 ppb	75 ppb	200 ppb
200102	1.56	0.96	2.2%	1.0%	1.84	1.09	2.5%	1.0%
200111	1.05	1.55	2.5%	1.1%	0.95	1.75	2.4%	1.4%
200112	0.90	0.92	1.3%	1.3%	0.87	1.84	2.5%	1.5%
200113	0.99	1.0	1.2%	1.4%	1.75	0.99	1.1%	2.1%
200114	0.99	0.98	1.2%	1.4%	1.75	0.99	1.1%	2.1%

Clinical precision

The clinical precision of the candidate device was evaluated as part of a clinical study which included a total of 13 point of care sites. Across all sites, 22 healthcare providers (operators)

assisted with the data collection. Each of the 94 subjects provided duplicate samples using both the 6-second and 10-second measurement modes at each of two visits. The clinical precision results per mode and visit are summarized in the tables below:

10-second mode – visit 1

Median Concentrations	Number of subjects	Within Subject Mean SD (ppb)	95% CI for SD (ppb)	Within Subject Mean %CV	95% CI for %CV
≤ 10 ppb	0	N/A	N/A	N/A	N/A
>10 - ≤20 ppb	1	1.414	0.000, 0.000	7.86	0.00, 0.00
>20 - ≤30 ppb	6	1.414	0.832, 2.843	5.02	2.95, 10.09
>30 - ≤40 ppb	15	3.111	2.220, 4.652	9.13	6.52, 13.66
>40 - ≤50 ppb	13	1.904	1.326, 2.947	4.23	2.95, 6.55
> 50 ppb	59	4.231	3.556, 5.116	4.41	3.70, 5.33

10-second mode – visit 2

Median Concentrations	Number of subjects	Within Subject Mean SD (ppb)	95% CI for SD (ppb)	Within Subject Mean %CV	95% CI for %CV
≤ 10 ppb	5	0.990	0.553, 2.172	11.38	6.35, 24.96
>10 - ≤20 ppb	23	1.076	0.818, 1.476	6.73	5.12, 9.24
>20 - ≤30 ppb	21	1.179	0.885, 1.644	4.55	3.41, 6.34
>30 - ≤40 ppb	10	2.121	1.406, 3.532	5.99	3.97, 9.98
>40 - ≤50 ppb	9	3.064	1.987, 5.274	6.77	4.39, 11.65
> 50 ppb	26	3.291	2.541, 4.422	3.68	2.84, 4.95

6-second mode – visit 1

Median Concentrations	Number of subjects	Within Subject Mean SD (ppb)	95% CI for SD (ppb)	Within Subject Mean %CV	95% CI for %CV
≤ 10 ppb	0	N/A	N/A	N/A	N/A
>10 - ≤20 ppb	0	N/A	N/A	N/A	N/A
>20 - ≤30 ppb	7	1.010	0.618, 1.903	3.68	2.25, 6.94
>30 - ≤40 ppb	15	1.650	1.177, 2.467	4.72	3.37, 7.06
>40 - ≤50 ppb	11	1.607	1.085, 2.602	3.71	2.51, 6.01
> 50 ppb	60	3.677	3.095, 4.439	4.02	3.38, 4.85

6-second mode – visit 2

Median Concentrations	Number of subjects	Within Subject Mean SD (ppb)	95% CI for SD (ppb)	Within Subject Mean %CV	95% CI for %CV
≤ 10 ppb	3	0.707	0.327, 2.153	7.44	3.44, 22.66
>10 - ≤20 ppb	24	1.591	1.216, 2.167	10.07	7.70, 13.72
>20 - ≤30 ppb	19	1.228	0.909, 1.746	4.81	3.56, 6.83
>30 - ≤40 ppb	12	1.827	1.254, 2.887	5.35	3.68, 8.46
>40 - ≤50 ppb	9	1.728	1.121, 2.975	3.89	2.52, 6.69
> 50 ppb	27	2.933	2.276, 3.918	3.41	2.64, 4.55

2. Linearity:

The sponsor performed studies to evaluate the linearity performance of the candidate device. Nitric oxide was mixed to create simulated breath gas to obtain nine NO concentration levels ranging from 5-300 ppb (5, 10, 15, 30, 50, 100, 150, 200, and 300 ppb). Five replicates were obtained at each level, and ten candidate devices were evaluated in both the 6-second and the 10-second modes. The range of slope, intercept, and R² values obtained are listed in the tables below.

	Range of Slopes	Range of Intercepts	R ²
6-second mode	0.99 – 1.01	-0.67 – 0.23	1.00
10-second mode	0.99 – 1.02	-0.93 – -0.12	1.00

Effect of extreme temperature and relative humidity

The sponsor performed a study to evaluate the effects of extreme temperature and humidity conditions on the performance of the candidate device. Two devices were tested in an environmentally controlled chamber at the four corners of temperature and humidity extremes (15-35°C and 20-90%RH) at three NO concentrations (15, 75, and 200 ppb) in air with 5 replicates at each combination of temperature and humidity:

Test Case	Temperature (°C)	Relative Humidity (%RH)
low temperature/low humidity	15°	20%
high temperature/low humidity	35°	20%
low temperature/high humidity	15°	90%
high temperature/high humidity	35°	90%

The results support the claimed operating conditions for the candidate device of 15°C-35°C and 20-90% RH.

3. Analytical Specificity/Interference:

Interference from endogenous compounds and exogenous substances

The sponsor performed a study to evaluate potential interference from endogenous compounds and exogenous substances. A substance was defined as non-interfering if the response at the tested concentration was within ± 4 ppb NO.

The following endogenous compounds were tested at the concentrations listed below and showed no interference:

Substance	Concentration Tested
Acetaldehyde	923 ppb
Acetone	102 ppm
Acetonitrile	500 ppm
Ammonia	100 ppm
Carbon Dioxide	8% by volume
Carbon Monoxide	249 ppm

Substance	Concentration Tested
Ethanol	1000 ppm
Hydrogen	480 ppb
Hydrogen Peroxide	500 ppm
Hydrogen Sulfide	5 ppm
Isoprene	1.5 ppm
Nitrogen Dioxide	1 ppm
Oxygen	100% by volume

Exogenous substances

The sponsor also performed a study at a single site by testing FeNO levels after use of seven common substances that are orally consumed or utilized and could potentially interfere with the device. Each subject performed one baseline measurement before the exogenous substance was introduced, one measurement 10 minutes post exposure or consumption, and one measurement 60 minutes post exposure or consumption. All subjects refrained from eating or drinking for 60 minutes prior to the baseline testing. The results of the study are shown below. The device labeling recommends that no food or beverage be consumed, and no smoking be done, for at least one hour before taking a FeNO measurement.

Exogenous Interference Results – 6 Second Tests

Exogenous Gas Substance	n	Mean Difference (ppb)	95% Confidence Intervals (ppb)
Mint without Menthol	14	2.2	[16, 26]
Mint with Menthol	14	1.9	[17, 28]
Toothpaste	14	-0.3	[16, 29]
Mouthwash with Alcohol	14	-2.0	[14, 25]
Alcohol Free Mouthwash	14	-3.0	[15, 29]
Caffeinated Soda	15	-1.0	[18, 29]
Caffeine Free Soda	13	2.5	[16, 29]

Exogenous Interference Results – 10 Second Tests

Exogenous Gas Substance	n	Mean Difference (ppb)	95% Confidence Interval (ppb)
Mint without Menthol	19	1.2	[17, 25]
Mint with Menthol	17	-0.8	[18, 29]
Toothpaste	17	0.3	[18, 33]
Mouthwash with Alcohol	16	-2.1	[14, 24]
Alcohol Free Mouthwash	16	0.4	[18, 29]
Caffeinated Soda	16	-0.8	[17, 27]
Caffeine Free Soda	16	0.7	[15, 26]

Effect of altitude

The sponsor performed a study to evaluate the effect of altitude on the candidate device. Three devices were tested using both 6-second and 10-second modes at 25, 50, and 200 ppb NO in seven replicates each at 330 feet (the nominal condition) and at 6550 feet. The results were found acceptable to support that the candidate device functions as intended at altitudes up to the claimed altitude of 6550 feet.

4. Assay Reportable Range:

The results of the sponsor's detection limit and linearity studies support the claimed measuring range of 5-300 ppb FeNO.

5. Traceability, Stability, Expected Values (Controls, Calibrators, or Methods):

Calibration stability

The manufacturer performs calibration for each Fenom Pro device. No calibration is required by the user.

6. Detection Limit:

The sponsor provided data collected with both the 6-second and 10-second modes that supported the claimed detection limit of 5 ppb.

7. Assay Cut-Off:

Not applicable.

8. Accuracy (Instrument):

Please see Comparison Studies section below.

9. Carry-Over:

The sponsor performed a study to evaluate the potential for carryover from a high concentration FeNO sample to a subsequent sample. Five devices were evaluated using both the 6-second and 10-second modes and the FeNO concentrations applied to assess carryover ranged from approximately 10 to 200 ppb. The results showed no carryover effect.

B Comparison Studies:

1. Method Comparison with Predicate Device:

Not applicable. A clinical study was conducted to validate the clinical performance of the candidate device.

2. Matrix Comparison:

Not applicable. The assay can be run using breath samples only.

C Clinical Studies:

1. Clinical Sensitivity:

See Other Clinical Supportive Data

2. Clinical Specificity:

See Other Clinical Supportive Data

3. Other Clinical Supportive Data (When 1. and 2. Are Not Applicable):

The sponsor provided the results of a study incorporating both the 6-second and 10-second tests to evaluate the clinical accuracy of the candidate device. A total of 94 patients (53 adults 18 years of age and older and 41 children ages 7 – 17) participated in the study where measurements for FeNO, spirometry, and asthma control questionnaires (ACQ) were completed at baseline (Visit 1) and two weeks later (Visit 2) after therapeutic agents were administered. The study included data from a total of 13 sites, and 22 healthcare providers (operators) assisted with the data collection.

The American Thoracic Society (ATS) defines elevated FENO as >25 ppb for adults and > 20 ppb for children. The initial (visit 1) FENO inclusion criteria for this study were >30 ppb for adults and >25 ppb for children.

A meaningful change in F150 FENO 10-s is defined as > 20% for initial FENO values >50 ppb and > 10 ppb for initial FENO values <50 ppb. Among pediatric subjects, 80% showed a meaningful decline in FENO. Among adult subjects, 80.0% showed a meaningful decline in FeNO. Overall results showed a mean FeNO change of -30.15 ppb (-37.94%) with a mean SD of 34.90 ppb.

The decline in FeNO after 2 weeks of corticosteroid therapy resulted in the following changes in subjective and objective asthma measures.

- ACQ: Mean ACQ score fell by 54.5% % after corticosteroids
- FEV1: There was a mean FEV1 change of 6.8 % after corticosteroids

D Clinical Cut-Off:

Not applicable

E Expected Values/Reference Range:

The sponsor states the following in the labeling: The fractional NO concentration in expired breath can be measured by the Fenom Flo device according to guidelines for NO measurement established by the American Thoracic Society (ATS).

F Other Supportive Instrument Performance Characteristics Data:

Not applicable

VIII Proposed Labeling:

The labeling supports the finding of substantial equivalence for this device.

IX Conclusion:

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