510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY

I Background Information:

A 510(k) Number

K230917

B Applicant

Lumos Diagnostics, Inc.

C Proprietary and Established Names

FebriDx Bacterial / Non-bacterial Point-of-Care Assay

D Regulatory Information

Product Code(s)	Classification	Regulation Section	Panel
QXA	Class II	21 CFR 866.3230 - Device To Detect And Measure Non-Microbial Analytes To Aid In The Detection And Identification Of Localized Human Infections	MI - Microbiology

II Submission/Device Overview:

A Purpose for Submission:

To obtain a substantial equivalence determination for the FebriDx Bacterial/Non-bacterial Point-of-Care Assay.

B Measurand:

Myxovirus resistance protein A (MxA) and C-reactive protein (CRP)

C Type of Test:

Lateral flow immunochromatography

III Intended Use/Indications for Use:

A Intended Use(s):

See Indications for Use below.

B Indication(s) for Use:

The FebriDx Bacterial/Non-Bacterial Point-of-Care Assay is a qualitative visually read rapid immunoassay for the detection of human host response proteins, Myxovirus resistance protein A (MxA) and C-reactive protein (CRP) directly from fingerstick blood. FebriDx is indicated for use in patients aged 12-64 who present to urgent care or emergency care settings for evaluation of acute respiratory infection who have had symptoms for less than 7 days and within 3 days of fever onset.

FebriDx test results are intended to be used in conjunction with other clinical and diagnostic findings as an aid in the diagnosis of bacterial acute respiratory infection and differentiation from non-bacterial etiology. The assessment of whether a bacterial infection is present should always be based on consideration of all available information, and not based solely on the FebriDx test results. FebriDx test results are not intended to identify a specific pathogen or the severity of infection.

For in vitro diagnostic use

For prescription use only

C Special Conditions for Use Statement(s):

Rx - For Prescription Use Only

D Special Instrument Requirements:

None.

IV Device/System Characteristics:

A Device Description:

FebriDx is a 10-minute, point-of-care lateral flow assay that detects Myxovirus resistance protein A (MxA) and C-reactive protein (CRP) in patient fingerstick samples to aid in the evaluation of an infection in patients presenting with acute respiratory symptoms.

The single-use disposable FebriDx test includes a lateral flow test strip, a built-in retractable safety lancet, blood collection and transfer tube, and buffer delivery system.

B Principle of Operation:

The FebriDx test includes a built-in sample collection and transfer tube detects the presence of MxA and CRP in fingerstick blood specimens using lateral flow technology. A sample of the

fingerstick blood is added to the lateral flow test device followed by a running buffer that provides sufficient volume to activate the test. The running buffer contains leukocyte membrane lysing agents that release intracellular MxA to allow subsequent detection. The first pad in the device filters out the cellular material as well as intact red-blood cells. The filtered sample then contacts a pad that contains the reagents to adjust pH and reduce potential non-specific binding. Prior to reaching the test strip, free MxA and CRP migrate through a dried formulation of latex beads that have been further conjugated to antibodies specific for binding a particular analyte (MxA or CRP). As the analyte-antibody-bead complex continues to migrate across a porous nitrocellulose membrane, it can interact with one of three capture antibodies that are immobilized on the surface at distinct line positions, including the control line to verify that the sample flowed properly across the device. In the presence of a valid blue control line, the FebriDx test result may be interpreted as one of two different outcomes: the presence of a single black line in the result window indicates a positive bacterial infection result whereas a red line in the result window or the absence of any line in the result window indicates a nonbacterial etiology.

V Substantial Equivalence Information:

A Predicate Device Name(s):
Synovasure Alpha Defensin Lateral Flow Test Kit

B Predicate 510(k) Number(s):
DEN180032

C Comparison with Predicate(s):

Device & Predicate Device(s):	K230917	DEN180032
Device Trade Name	FebriDx Bacterial/Non-bacterial Point-of-Care Assay	Synovasure Alpha Defensin Lateral Flow Test Kit
General Device Characteristic Similarities		
Intended Use/Indications For Use	The FebriDx Bacterial/Non-bacterial Point-of-Care Assay is a qualitative visually read rapid immunoassay for the detection of human host response proteins, Myxovirus resistance protein A (MxA) and C-reactive protein (CRP) directly from fingerstick blood. FebriDx is indicated for use in patients aged 12-64 who present to urgent care or	The Synovasure Alpha Defensin Lateral Flow Test Kit is a qualitative visually read immunochromatographic assay for the detection of human host response proteins, Alpha Defensins 1-3, in the synovial fluid of adults with a total joint replacement who are being evaluated for revision surgery. The Synovasure Alpha Defensin Lateral Flow Test Kit results are intended to be used in conjunction

	emergency care settings for evaluation of acute respiratory infection who have had symptoms for less than 7 and within 3 days of fever onset. FebriDx test results are intended to be used in conjunction with other clinical and diagnostic findings as an aid in the diagnosis of bacterial acute respiratory infection and differentiation from non-bacterial etiology. The assessment of whether a bacterial infection is present should always be based on consideration of all available information, and not based solely on the FebriDx test results. FebriDx test results are not intended to identify a specific pathogen or the severity of infection.	with other clinical and diagnostic findings as an aid in the diagnosis of periprosthetic joint infection (PJI). The Synovasure Alpha Defensin Lateral Flow Test Kit is not intended to identify the etiology or severity of a PJI.
Intended User	Same	Professional Use
Test Type	Same	Visually read lateral flow immunochromatographic assay
Result Output	Same	Qualitative
Analyte	Same	Host biomarkers of infection
General Device Characteristic Differences		
Measurand	MxA and CRP	Human alpha defensins 1-3
Sample type	Fingerstick blood	Synovial fluid
Sample volume	5 µL	15 µL

VI Standards/Guidance Documents Referenced:

1. ISO 10993-1 Fifth edition 2018-08 Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process
2. ISO 15223-1 Fourth Edition 2021-07 Medical Devices - Symbols To Be Used With Medical Device Labels, Labelling, And Information To Be Supplied - Part 1: General Requirements
3. CLSI EP07, Third Edition, Interference Testing in Clinical Chemistry
4. CLSI EP12-A2, User Protocol for Evaluation of Qualitative Test Performance
5. CLSI EP17-A2, Evaluation of Detection Capability for Clinical Laboratory Measurement Procedures
6. CLSI EP18-A2, Risk Management Techniques to Identify and Control Laboratory Error Sources
7. CLSI EP25-A, Evaluation of Stability of In Vitro Diagnostic Reagents

VII Performance Characteristics (if/when applicable):

A Analytical Performance:

1. Precision/Reproducibility:

A reproducibility study was conducted across three sites with two operators at each site. Spiked whole blood sample panels for the precision and reproducibility studies were prepared using the pre-determined FebriDx C5 and C95 concentrations. A description of each panel member is included in Table 1 below.

Table 1. Reproducibility Study Panel Members

Panel Member	C-Reactive Protein Concentration	Myxovirus Resistance Protein A Concentration
P1	C5	C95
P2	C95	C5
P3	C95	C95
P4	C95	120 ng/mL
P5	150 µg/mL	C95
P6	0	0

A total of 540 determinations were performed by untrained operators at the point of care settings across three different sites over five contiguous days during a two-week period. The study demonstrates overall reproducibility among three lots of material, among three separate sites, and among six separate users. On each day of testing, the Positive and Negative External Controls were run by one individual to ensure the appropriate results were produced. All External Controls tests produced the expected results. Reproducibility study results are summarized below.

Table 2. Reproducibility Study Results for Each Analyte Band – By Site

Sample	% Agreement with Expected Results									
	Site 1		Site 2		Site 3		Overall			
	MxA	CRP	MxA	CRP	MxA	CRP	MxA	95% CI	CRP	95% CI
P1 MxA C95 CRP C5	100% (30/30)	80% (24/30)	70% (21/30)	90% (27/30)	93.3% (28/30)	83.3% (25/30)	87.8% (79/90)	79.4-93	84.4% (76/90)	75.6-90.5
P2 MxA C5 CRP C95	100% (30/30)	100% (30/30)	90% (27/30)	100% (30/30)	73.3% (22/30)	100% (30/30)	87.8% (79/90)	79.4-93	100% (90/90)	95.1-100
P3 MxA C95 CRP C95	100% (30/30)	100% (30/30)	90% (27/30)	100% (30/30)	100% (30/30)	100% (30/30)	96.7% (87/90)	90.7-98.9	100% (90/90)	95.1-100
P4 MxA High CRP C95	100% (30/30)	100% (30/30)	100% (30/30)	100% (30/30)	100% (30/30)	100% (30/30)	100% (90/90)	95.1-100	100% (90/90)	95.1-100
P5 MxA C95 CRP High	100% (30/30)	100% (30/30)	90% (27/30)	100% (30/30)	93.3% (28/30)	100% (30/30)	94.4% (85/90)	87.7-97.6	100% (90/90)	95.1-100
P6 MxA Neg CRP Neg	100% (30/30)	100% (30/30)	90% (27/30)	100% (30/30)	100% (30/30)	100% (30/30)	100% (87/90)	90.7-98.9	100% (90/90)	95.1-100

Lower than expected MxA reactivity was observed for the P1 panel member at site 2. Further analysis of the data indicated that the majority of the discrepant results observed in the reproducibility study were obtained from just one user at site 2 and another user at site 3. Users should ensure they follow the assay instructions to avoid potential erroneous results.

The same results are presented below when interpreting individual cartridge results for each replicate against the expected band reactivities.

Table 3. Reproducibility Study Results Final Interpretation – By Site

Sample	% Agreement with Expected Results				
	Site 1	Site 2	Site 3	Overall	95% CI
P1	80% (24/30)	70% (21/30)	76.7% (23/30)	75.6% (68/90)	65.8-83.3
P2	100% (30/30)	90% (27/30)	73.3% (22/30)	87.8% (79/90)	79.4-93.0
P3	100% (30/30)	90% (27/30)	100% (30/30)	96.7% (87/90)	90.7-98.9
P4	100% (30/30)	100% (30/30)	100% (30/30)	100% (90/90)	95.9-100
P5	100% (30/30)	90% (27/30)	93.3% (28/30)	94.4% (85/90)	87.7-97.6
P6	100% (30/30)	90% (27/30)	100% (30/30)	96.7% (87/90)	90.7-98.9

Additional analyses evaluated potential variability between different FebriDx cartridge lots. The results are summarized in Table 4 below.

Table 4. Reproducibility Study Results Final Interpretation – By Lot

Sample	% Agreement with Expected Results		
	Lot 1	Lot 2	Lot 3
P1	75% (27/36)	80.5% (29/36)	66.7% (12/18)
P2	83.3% (30/36)	91.7% (33/36)	88.9% (16/18)
P3	100% (36/36)	100% (36/36)	83.3% (15/18)
P4	100% (36/36)	100% (36/36)	100% (18/18)
P5	91.7% (33/36)	94.4% (34/36)	100% (18/18)
P6	100% (36/36)	100% (36/36)	83.3% (15/18)

The reproducibility study results are acceptable and support use of the device in appropriate clinical settings with users trained in the use of the FebriDx test.

2. Linearity:
   Not applicable

3. Analytical Specificity/Interference:

   Interfering Substance Study

   Two sets of spiked whole blood samples were prepared that separately contained either C95 concentrations of MxA and CRP or C5 concentrations of MxA and CRP. Sample panels were tested by a trained operator prior to using them in the study to confirm the expected reactivity. Both sets of samples were further spiked with the interferents listed in Table 5 below and evaluated on the FebriDx device by three operators in triplicate to assess any potential interference effect.

Table 5. Interference Testing Results

Test Substance	Concentration	Interference?
Acetaminophen	15.6 mg/dL	No
Acetylsalicylic acid	3 mg/dL	No
Alcohol	789 mg/dL	No
Azithromycin	1.11 mg/dL	No
Bilirubin (Conjugated)	40 mg/dL	No
Bilirubin (Unconjugated)	0.4 mg/dL	No
Biotin	3500 ng/mL	No
Caffeine	10 mg/dL	No

Celecoxib	0.879 mg/dL	No
Cetririzine HCL	0.435 mg/dL	No
Dextromethorphan	1.56 ug/dL	No
Doxycycline	1.8 mg/dL	No
Furosemide	1.59 mg/dL	No
HAMA	8000 ng/mL	No
Hemoglobin	1000 mg/dL	No
Ibuprofen	21.9 mg/dL	No
Imipenem	18 mg/dL	No
Levofloxacin	3.6 mg/dL	No
Loratadine	0.5 mg/dL	No
Nicotine	0.097 mg/dL	No
Oxymetazoline HCL	0.09 mg/dL	No
Phenylephrine	0.003 mg/dL	No
Prednisolone	0.120 mg/dL	No
Protein (total)	9 g/dL	No
Rheumatoid Factor	1000 IU/mL	Yes
Salmeterol	6.03 µg/dL	No
Tiotropium	4.80 ng/dL	No
Triglycerides	1500 mg/dL	No
Vancomycin	12 mg/dL	No

Initial testing with Rheumatoid Factor at 1000 IU/mL demonstrated interference with CRP band interpretation. Only 5/9 replicates exhibited expected results for samples that contained either C5 or C95 concentrations of CRP in the presence of Rheumatoid Factor. This interferent was diluted and interference testing was repeated until no interference effect was observed. Potential interference with MxA results was also observed at Rheumatoid Factor concentrations below 1000 IU/mL. No interference for either analyte was observed at concentrations below 50 IU/mL.

Hook Effect Study

To assess whether a hook effect exists for the FebriDx test device, samples containing MxA and CRP at the concentrations described in the table below were evaluated and individual band reactivity for both MxA and CRP was assessed.

Table 6. Hook Effect Study Samples

Panel Member	MxA (ng/mL)	CRP (µg/mL)
1	700	1000
2	600	800
3	500	600
4	400	500
5	200	250
6	100	125
7	50	62.5
8	0	0

All evaluated specimens were reactive for both MxA and CRP. No hook effect was identified for CRP concentrations up to 1000 µg/mL and MxA concentrations up to 700 ng/mL.

4. Assay Reportable Range:

Not applicable.

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

Controls

The FebriDx test has built-in procedural controls represented by a blue control line.

External controls should be used to demonstrate that the reagents and assay perform properly. External controls (one positive and one negative) are not supplied with the FebriDx test kit (i.e. box of 25 devices) but are available separately from Lumos Diagnostics. External controls should be used, as consistent with good laboratory practices, to verify test performance. The negative external control is composed of buffered solution containing a preservative. The positive external control is composed of buffered stabilizing solution containing preservative and recombinant MxA and CRP proteins near the LoD for each analyte (55.6 ng/mL and 22.9 ug/mL for MxA and CRP, respectively).

Reagent Stability

Protocols for evaluation of real-time stability, transport stability, and in-use stability of the FebriDx test cartridge as well as real-time stability of the external control materials were reviewed and found to be acceptable.

6. Detection Limit:

The limit of detection (LoD) for the individual CRP and MxA bands on the FebriDx test were determined on two lots of FebriDx assay cartridges with two (2) operators. A series of whole blood samples spiked with MxA and CRP analytes at concentrations spanning the assay range were blinded to test operators, tested, and read to determine the LoD concentration (C95) and a high negative concentration (C5). Results for each reagent lot are described separately below in Tables 7-10. In accordance with CLSI EP17-A2, the highest observed value from each individual lot was chosen as the corresponding C5 or C95 value.

Table 7. LoD Study results Lot 1 - MxA

Sample	[MxA] (ng/mL)	% Positive (n/N)
1	0	0% (0/20)
2	10	0% (0/20)
3	15	0% (0/20)
4	20	15% (3/20)
5	25	50% (0/20)

6	30	75% (15/20)
7	35	90 (18/20)
8	40	95% (19/20)
9	45	100% (20/20)
10	60	100% (20/20)

Probit analysis identified C5, C50, and C95 MxA concentrations of 18.71, 26.68, and 38.05, respectively for Lot 1.

Table 8. LoD Study Results for Lot 1 - CRP

Sample	[CRP] (µg/mL)	% Positive (n/N)
1	0	0% (0/20)
2	7	0% (0/20)
3	9	30% (6/20)
4	11	40% (8/20)
5	13	50% (10/20)
6	15	70% (14/20)
7	17	100% (20/20)
8	19	100% (20/20)
9	25	100% (20/20)
10	40	100% (20/20)

Probit analysis identified C5, C50, and C95 CRP concentrations of 8.53, 11.89, and 16.56, respectively for Lot 1.

Table 9. LoD Study results Lot 2 - MxA

Sample	[MxA] (ng/mL)	% Positive (n/N)
1	0	0% (0/20)
2	10	0% (0/20)
3	15	0% (0/20)
4	20	20% (4/20)
5	25	55% (11/20)
6	30	60% (12/20)
7	35	70% (14/20)
8	40	100% (20/20)
9	45	100% (20/20)
10	60	100% (20/20)

Probit analysis identified C5, C50, and C95 MxA concentrations of 18.78, 26.75, and 38.10, respectively.

Table 10. LoD Study Results for Lot 2 - CRP

Sample	[CRP] (µg/mL)	% Positive (n/N)
1	0	0% (0/20)
2	7	0% (0/20)
3	9	10% (2/20)
4	11	45% (9/20)
5	13	75% (15/20)
6	15	85% (17/20)
7	17	100% (20/20)
8	19	100% (20/20)
9	25	100% (20/20)
10	40	100% (20/20)

Probit analysis identified C5, C50, and C95 CRP concentrations 8.72, 11.64, and 15.54, respectively.

Based on the results of the LoD testing across each test cartridge lot, the overall LoD for MxA was established as 40 ng/mL and the LoD for CRP was established as 16.6 µg/mL.

7. Assay Cut-Off:

Not applicable.

B Comparison Studies:

1. Method Comparison with Predicate Device:

Not applicable.

2. Matrix Comparison:

The FebriDx test is intended to be utilized with freshly collected fingerstick specimens. Due to difficulties obtaining sufficient quantities of this sample matrix, venous whole blood was utilized for the analytical studies described above. To support the use of venous whole blood as a surrogate matrix for fingerstick blood in analytical studies, a study was conducted to demonstrate equivalent LoD for both analytes across both sample matrices of the FebriDx device. Specifically, a matched series of samples was prepared in both venous and fingerstick blood by spiking MxA and CRP to various concentrations and then testing them across 20 replicates of each dilution. The results of the samples for each matrix were fit to a 4-parameter logistic curve and this curve was used to determine the C5 and C95 values for the FebriDx test using either venous blood or fingerstick blood as the sample matrix. Additional confirmatory testing was performed with another 20 replicates at the C5 and C95 concentrations to confirm the values. No significant differences in LoD were observed between fingerstick and venous sample matrices. This data supported the use of venous whole blood matrix in analytical studies and is not intended to support a venous whole blood claim

C Clinical Studies:

1. Clinical Sensitivity:

A prospective multi-center blinded clinical trial (DISRUPT, ClinicalTrials.gov identifier: NCT02018198) was conducted in the United States (U.S.) to evaluate the clinical performance of FebriDx. Patients presenting to a primary care provider, urgent care clinic or Emergency Department with signs/symptoms of acute respiratory infection (ARI) and a recent fever were screened for eligibility. Separately, additional healthy subjects (the asymptomatic cohort) were enrolled in an all comer fashion across the same study sites to evaluate the reference range of the FebriDx device. FebriDx testing for all enrolled patients was conducted by users at the point of care.

A patient's final diagnosis (i.e., clinical truth) was based on results of a clinical reference algorithm in conjunction with adjudication by two independent expert reviewers who had the ability to accept or override the results of the clinical reference algorithm based on the review of available data for each participant. The clinical experts had access to clinical data as well as microbiological results and laboratory tests. Additionally, standard of care tests ordered for the evaluation of acute respiratory infection by treating clinicians were captured, recorded, and made available to the reviewers.

The demographic characteristics of the DISRUPT study populations are described in Table 11 below.

Table 11. Demographic Information of DISRUPT Study Cohorts

Characteristics	Acute Respiratory Infection Cohort Overall % (Proportion)	Asymptomatic Cohort Overall % (Proportion)
Sex		
Male	44.2% (230/520)	44.7% (76/170)
Female	55.8% (290/520)	55.3% (94/170)
Age		
Median (IQR)	32.0 (23.0, 48.0)	38.0 (19.0, 69.0)
1-21 years	20.8% (108/520)	31.2% (53/170)
22- 64 years	71.7% (373/520)	31.8% (54/170)
65+	7.5% (39/520)	37.1% (63/170)
Race		
American Indian	0.4% (2/520)	0
Asian	2.7% (14/520)	1.2% (2/170)
Black	21.2% (110/520)	17.1% (29/170)
Other	7.1% (37/520)	2.4% (4/170)
Pacific Islander	0.2% (1/520)	0
Unknown	0	0
White	68.5% (356/520)	79.4% (135/170)
Ethnicity		
Hispanic	18.7% (97/520)	12.4% (21/170)

Not Hispanic	80.6% (419/520)	87.6% (149/170)
Declined to Answer	0.8% (4/520)	0
Comorbidities		
Asthma	11.3% (59/520)	10.6% (18/170)
Cancer	0	4.7% (8/170)
Cystic Fibrosis	0.2% (1/520)	0
Congesitve Heart Failure	1.3% (7/520)	1.2% (2/170)
COPD	3.3% (17/520)	1.2% (2/170)
Diabetes	4.6% (24/520)	10.0% (17/170)
Indwelling Vascular Catheter	0.2% (1/520)	0
Chronic Lung Disease	0.6% (3/520)	0
Autoimmune Disease	0.4% (2/520)	N/A[1]
Hepatitis B	0	N/A[1]
Hepatitis C	0.4% (2/520)	N/A[1]
Osteomyelitis	0.4% (2/520)	N/A[1]
Active Tuberculosis	0.4% (2/520)	N/A[1]

[1]These conditions were considered exclusion criteria for the asymptomatic cohort and were thus not collected.

Of the total enrolled participants in the ARI cohort, 14.0% (73/520) were classified as bacterial, and 81.3% (423/520) were considered as a non-bacterial etiology (e.g., either non-infectious or a viral infection) by the comparator clinical reference algorithm that incorporated pathogen detection testing as well as measures of host immune response in conjunction with clinical adjudication by two independent reviewers who were blinded to FebriDx device results. In the event that the two clinical medical experts disagreed, one additional independent expert served as the arbitrator between the two conflicting opinions and a majority opinion, determined by independent review, served to assign a final clinical diagnosis.

A final diagnosis could not be determined by the clinical reference algorithm/adjudication due to insufficient laboratory evidence (e.g., samples lost in transit, thawed in transit, not labelled correctly and thus not tested) for 4.6% (24/520) participants. These subjects were excluded from the performance analysis. The expert panel agreed with classification assigned by the algorithm in 93.3% (463/496) of the adjudicated cases.

Results from the DISRUPT study are summarized in Table 12 and Table 13 below.

Table 12. DISRUPT Study FebriDx Results versus Clinical Comparator

FebriDx Result	Adjudicated Clinical Reference Algorithm Result			
	Bacterial	Non-bacterial	Unknown	Total
Bacterial	68	49	7	124
Non-bacterial	5	374	17	396
Invalid	0	0	0	0
Total	73	423	24	520

Table 13. FebriDx Performance Summary – DISRUPT Study

	Bacterial Infection
PPA [95% CI]	93.2% (68/73) [84.9-97.0%]
NPA [95% CI]	88.4% (374/423) [85.0-91.1%]
PPV [95% CI]	58.1% (68/117) [49.1-66.7%]
NPV [95% CI]	98.7% (374/379) [96.9-99.4%]

Positive and negative controls were performed every day of enrollment, with every new lot or shipment and with every first-time test-operator. Prior to performing testing on study participants, 100% of positive and negative controls were read as positive and negative, respectively. A small percentage of controls (0.8%, 10/1205) required repeat testing due to operator error (insufficient buffer delivered caused by weak pressure when pushing the buffer release button and invalid readings).

The DISRUPT study was not adequately powered to evaluate differences in performance among different age groups or between specific races or ethnicities. Results from the FebriDx test should be interpreted with other clinical and diagnostic findings and the presence of a bacterial respiratory infection should not be determined based on FebriDx test results alone.

Table 14. FebriDx Test Performance – DISRUPT Study, Stratified by Race

Bacterial Infection Performance	Patient Race		
	Black	White	Other
PPA [95% CI]	75.0% (6/8) [40.9-92.9%]	94.8% (55/58) [85.9-98.2%]	100% (7/7) (64.6-100%)
NPA [95% CI]	89.0% (89/100) [81.4-93.7%]	87.7% (242/276) [83.3-91.1%]	91.5% (43/47) [80.1-96.6%]

Additionally, clinical performance of the FebriDx device has not been established in pediatric patients younger than 12 years old or in elderly patients above 64 years old. The FebriDx test should not be used in these patient populations. These populations may be at increased risk of severe complications from undiagnosed respiratory infections, and differences in the immune response among these age groups could contribute to differences in assay performance.

FebriDx test performance in the DISRUPT study stratified by patient age is summarized in Table 15 below.

Table 15. FebriDx Test Performance – DISRUPT Study, Stratified By Patient Age

Bacterial Infection Performance	Patient Age Range		
	1-21 years old	22-64 years old	65+ years old
PPA [95% CI]	100.0% (13/13) [77.2-100.0%]	92.3% (48/52) [81.8-97.0%]	87.5% (7/8) [52.9-97.8%]
NPA [95% CI]	95.7% (88/92) [89.3-98.3%]	86.7% (260/300) [82.4-90.1%]	83.9% (26/31) [67.4-92.9%]

Cumulatively, the data from the DISRUPT study support device performance in patients aged 12-64 years old and a determination of substantial equivalence.

2. Clinical Specificity:

   See Clinical Sensitivity section C.1 above.

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

   Not applicable.

D Clinical Cut-Off:

Not applicable.

E Expected Values/Reference Range:

Expected Values

The results from a prospectively enrolled study cohort of 520 individuals with signs and symptoms of Acute Respiratory infection are summarized in Table 16 below.

Table 16. Expected Values of FebriDx Test in DISRUPT study

FebriDx Result	Adjudicated Clinical Reference Algorithm Result			
	Bacterial	Non-bacterial	Unknown	Total
Bacterial	68	49	7	124
Non-bacterial	5	374	17	396
Invalid	0	0	0	0
Total	73	423	24	520

The predictive value of FebriDx test results will depend upon the prevalence of bacterial infections in the population. Users should evaluate FebriDx test results in conjunction with other clinical and diagnostic findings.

Reference Range Study

The clinical study included evaluation of 170 asymptomatic patients who were not suspected of having an infection. The cohort included 44.7% male and 55.3% female participants with a diverse ethnic background. The mean age of participants was 43.5 years and ranged from 3 to 87 years of age. The study enrolled participants in each of three age groups; 31.2% (53/170) of participants were children/adolescents (1 - 21 years); 31.8% (54/170) were adults (22-64 years); and 37.1% (63/170) were elderly (65+ years). Participants presented without signs/symptoms of acute respiratory infection at the time of enrollment. Individual asymptomatic individuals were subjected to FebriDx testing and the same clinical comparator methods described above. Results are summarized in Table 17 below.

Table 17. FebriDx Performance in the Asymptomatic Cohort – DISRUPT Study

FebriDx Result	Adjudicated Clinical Reference Algorithm Result			
	Bacterial	**Non-bacterial**	**Unknown**	**Total**
Bacterial	1	3	0	4
Non-bacterial	0	157	9	166
Invalid	0	0	0	0
Total	1	160	9	170

Clinical Truth could not be determined by the clinical reference algorithm/adjudication due to insufficient laboratory evidence (e.g., samples lost in transit, thawed in transit, not labelled correctly and thus not tested) for 5% (9/170) participants.

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.