

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k081483

B. Purpose for Submission:

Request for removal of the requirement for culture confirmation of negative assay results for Influenza A, Influenza A subtypes H1 and H3, hMPV, and Rhinovirus. Addition of the bioMerieux EasyMag nucleic acid purification method.

C. Measurand:

See k063765

D. Type of Test:

See k063765

E. Applicant:

Luminex Molecular Diagnostics Inc.

F. Proprietary and Established Names:

xTAG™ Respiratory Viral Panel

Common Name: Respiratory Viral Panel (RVP) Multiplex Nucleic Acid Detection Assay

G. Regulatory Information:

1. Regulation section:
21 CFR 866.3980, Respiratory viral panel multiplex nucleic acid assay
2. Classification:
Class II
3. Product code:
OCC, OEM, OEP
4. Panel:
Microbiology (83)

H. Intended Use:

1. Intended use(s):

The xTAG™ Respiratory Viral Panel (RVP) is a qualitative nucleic acid multiplex test intended for the simultaneous detection and identification of multiple respiratory virus nucleic acids in nasopharyngeal swabs from individuals suspected of respiratory tract infections. The following virus types and subtypes are identified using RVP: Influenza A, Influenza A subtype H1, Influenza A subtype H3, Influenza B, Respiratory Syncytial Virus subtype A, Respiratory Syncytial Virus subtype B, Parainfluenza 1, Parainfluenza 2, and Parainfluenza 3 virus, Human Metapneumovirus, Rhinovirus, and Adenovirus. The detection and identification of specific viral nucleic acids from individuals exhibiting signs and symptoms of respiratory infection aids in the diagnosis of respiratory viral infection if used in conjunction with other clinical and laboratory findings. It is recommended that specimens found to be negative for Influenza B, Respiratory Syncytial Virus subtype A and B, Parainfluenza 1, Parainfluenza 2, Parainfluenza 3 and Adenovirus, after examination using RVP be confirmed by cell culture. Negative results do not preclude respiratory virus infection and should not be used as the sole basis for diagnosis, treatment or other management decisions. Positive results do not rule out bacterial infection, or co-infection with other viruses. The agent detected may not be the definite cause of disease. The use of additional laboratory testing (e.g. bacterial culture, immunofluorescence, radiography) and clinical presentation must be taken into consideration in order to obtain the final diagnosis of respiratory viral infection.

Due to seasonal prevalence, performance characteristics for Influenza A/H1 were established primarily with retrospective specimens.

The RVP assay cannot adequately detect Adenovirus species C, or serotypes 7a and 41. The RVP primers for detection of rhinovirus cross-react with enterovirus. A rhinovirus reactive result should be confirmed by an alternate method (e.g. cell culture).

Performance characteristics for Influenza A Virus were established when Influenza A/H3 and A/H1 were the predominant Influenza A viruses in circulation. When other Influenza A viruses are emerging, performance characteristics may vary. If infections with a novel Influenza A virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions for novel virulent Influenza viruses and sent to a state or local health department for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.

- 2. Indication(s) for use:
Same as Intended Use
- 3. Special conditions for use statement(s):
For prescription use only
- 4. Special instrument requirements:
Luminex[®] Instrument (100 IS and 200 systems)

I. Device Description:

See k063765

Materials Provided

See k063765

Reagents Required But Not Provided

Reagents required to perform testing with the device include **ancillary reagents** for which specific lots have been qualified by Luminex Molecular Diagnostics (LMD) and incorporated in the LMD quality system, for use with the xTAG[™] RVP. The xTAG[™] RVP product performance requires that only qualified ancillary reagent lots be used with the device. Any lots not specifically qualified by LMD for use with xTAG[™] RVP are not validated for use with this assay, and may cause erroneous results. To find an up to date list of Qualified Ancillary Reagents log onto Luminex website Support page https://oraweb.luminexcorp.com/OA_HTML/jtflogin.jsp and search “RVP”. Ancillary reagents should be used only according to the instructions for use contained in the RVP package insert. Any assay problems or failures that are suspected to involve ancillary reagents should be reported to Luminex Molecular Diagnostics Inc. The following is a list of ancillary reagents that are not supplied and are included in LMD’s reagent qualification program:

Ancillary Reagents Required BUT NOT supplied:

QIAGEN [®] OneStep RT-PCR Kit (5x QIAGEN OneStep RT-PCR Buffer, dNTP Mix and RNase-Free Water)
TaKaRa Taq [™] Hot Start Version (10X PCR Buffer and 2.5 mM TaKaRa dNTPS)
Phosphatase Alkaline, Shrimp

Exonuclease I
Bacteriophage Lambda DNA
Streptavidin, R-Phycoerythrin conjugate (SAPE)
E. coli phage MS 2
*Universal Transport Medium (UTM) Copan Innovations, Cat No 330C
*Distilled Water DNase/RNase-Free Water Invitrogen™ Corp, Cat No: 10977-015
*Nuclisens® miniMAG™ extraction Kit
*Nuclisens® EasyMag™ Extraction System
QIAamp® MiniElute® Virus Spin Kit

* these reagents are not part of the ancillary reagent qualification program

J. Substantial Equivalence Information:

1. Predicate device name(s):
xTAG™ RVP (Respiratory Viral Panel)
Common Name: Respiratory Viral Panel (RVP) Multiplex Nucleic Acid Detection Assay
2. Predicate 510(k) number(s):
k063765
3. Comparison with predicate:
See k063765

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

See k063765

L. Test Principle:

See k063765

Interpretation of Influenza A Results

See k063765

Reporting Influenza A Results

- Report negative test results for Influenza A as “Matrix gene target not detected, and hemagglutinin gene targets not detected. It is recommended that specimens found to be negative after examination using a respiratory viral panel nucleic acid detection assay be confirmed by cell culture. Negative results do not preclude respiratory virus infection and should not be used as the sole basis for diagnosis, treatment or other management decisions.”
- Report positive test results as “Influenza A positive, and (*where applicable*) hemagglutinin gene target (*specify hemagglutinin target detected, e.g. H1, or H3*). This result does not rule out co-infections with pathogens that were not screened for by RVP. A positive result for a hemagglutinin gene target does not identify a specific influenza A strain (e.g. H1N1). The agent detected may not be the definite cause of disease. Results should be used in conjunction with other clinical and laboratory findings.”
- Positive for type (i.e., influenza A), and negative or equivocal for subtype. In the event that RVP positively identifies the Flu A matrix gene target but fails to identify a hemagglutinin gene target (H1 or H3), the sample should be re-tested with RVP from the extraction step together with external controls for these two analytes. Extract prepared from the sample should be run in duplicate. In the case where the re-test on both replicates does not yield a positive type result for H1 or H3 and external controls are properly typed, further follow-up is required. A positive test result for Influenza A in the presence of a negative test result for an Influenza subtype (i.e., H1 or H3) necessitates immediate notification of appropriate

local, state or federal public health authorities to determine necessary measures for verification of results in accordance with the MMWR notice <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5613a4.htm> and <http://www.cste.org/ps/2007pdfs/novelfluannssjan10final23.pdf>), to determine whether the questionable Flu A specimen represents a novel strain of Influenza.

- A “No Call” due to an equivocal or invalid result as shown in Table 13.4.1-1, should not be reported but re-tested as per recommendations in Table 13.5-1. The re-test result should be considered the final RVP call for that analyte.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

See k063765

Reproducibility of the assay in the specimens near the clinical cutoff of the assay:

Reproducibility was assessed across 3 sites using replicates of samples containing viral material from culture-derived isolates in the matrix simulating intended use specimen type. The panel contained samples prepared to represent low positive (LP) and high negative (HN) analyte levels relative to the RVP cut-offs. Each simulated sample within the panel was divided into aliquots, blinded and stored frozen (-70°C) prior to testing. Thus, aliquots of the same blinded panel of samples were tested at the three different sites. Each site used a different extraction method (Site 1 used Biomérieux EasyMag™, Site 2 used Qiagen QIAamp® MiniElute®, and Site 3 used Biomérieux MiniMag™). For each of the 3 extraction methods evaluated, 2 aliquots of a given sample dilution were extracted per day, for each of 3 days (i.e. a total of six extractions per site). At each site, both extracts from a given day were assayed in singlicate on the same RVP run. Calls (Positive, Equivocal, Negative) generated for the viral analyte in question are summarized in Tables below.

Summary of Flu A and H3 calls in simulated Influenza A-H3 samples:

Virus / Titer	All Days (3 extraction days x 2 extractions per day)							
	Site	# Positive	# Equivocal	# Negative	25 th Percentile MFI	Median MFI	75 th Percentile MFI	%CV*
Flu A-H3 (Strain: A/Victoria/3/75 (H3N2), DHI Lot #121106)								
Flu A Low Positive (LP) (2 TCID ₅₀ per reaction)	Site 1	6 / 6	0 / 6	0 / 6	1531.38	1731.75	1969.25	29.25
	Site 2	6 / 6	0 / 6	0 / 6	1428.75	1746.75	1828.88	40.89
	Site 3	6 / 6	0 / 6	0 / 6	541.50	800.00	899.13	39.94
	Total	18 / 18	0 / 18	0 / 18	870.38	1463.00	1814.38	48.45
H3 Low Positive (LP) (200 TCID ₅₀ per reaction)		6 / 6	0 / 6	0 / 6	1679.00	1767.00	2017.75	14.89
	Site 2	6 / 6	0 / 6	0 / 6	1567.38	1718.25	1912.63	23.70
	Site 3	6 / 6	0 / 6	0 / 6	902.88	1077.25	1243.00	18.44
	Total	18 / 18	0 / 18	0 / 18	1256.00	1661.00	1793.75	30.04
Flu A High Negative (HN) (0.2 TCID ₅₀ per reaction)	Site 1	0 / 6	2 / 6	4 / 6	76.75	133.00	157.00	N/A**
	Site 2	0 / 6	6 / 6	0 / 6	180.00	192.50	200.88	N/A
	Site 3	0 / 6	0 / 6	6 / 6	12.63	40.00	66.25	N/A
	Total	0 / 18	8 / 18	10 / 18	56.75	133.00	176.25	N/A
H3 High Negative (HN) (2 TCID ₅₀ per reaction)	Site 1	0 / 6	0 / 6	6 / 6	64.25	68.00	73.25	N/A
	Site 2	0 / 6	0 / 6	6 / 6	100.00	119.50	127.75	N/A
	Site 3	0 / 6	0 / 6	6 / 6	15.13	32.50	49.50	N/A
	Total	0 / 18	0 / 18	18 / 18	46.88	68.00	95.50	N/A

* For reproducibility Tables, %CV = Standard Deviation / Mean*100

** For reproducibility Tables, N/A = not applicable.

Summary of Flu A and H1 calls in simulated Influenza A-H1 samples:

Virus / Titer	All Days (3 extraction days x 2 extractions per day)							
Flu A-H1 (Strain: A/PR/8/34 (H1N1), Zeptomatrix lot #303543)	Site	# Positive	# Equivocal	# Negative	25 th Percentile MFI	Median MFI	75 th Percentile MFI	%CV
Flu A Low Positive (LP) (0.02TCID ₅₀ per reaction)	Site 1	6	0	0	465.00	660.50	802.38	29.41
	Site 2	5	1	0	391.25	433.50	503.50	27.06
	Site 3	2	3	1	216.75	241.75	479.75	60.22
	Total	13 / 18	4 / 18	1 / 18	288.38	433.50	570.38	45.13
H1 Low Positive (LP) (0.06 TCID ₅₀ per reaction)	Site 1	6	0	0	1038.50	1151.50	1324.13	18.24
	Site 2	6	0	0	697.13	938.00	1088.13	36.99
	Site 3	6	0	0	666.88	890.50	933.00	33.31
	Total	18 / 18	0 / 18	0 / 18	826.63	990.5	1110.75	33.00
Flu A High Negative (HN) (0.001 TCID ₅₀ per reaction)	Site 1	0	0	6	37.75	59.00	83.63	N/A
	Site 2	0	0	6	92.38	98.00	101.75	N/A
	Site 3	0	0	6	4.00	10.25	22.50	N/A
	Total	0 / 18	0 / 18	18 / 18	20.50	59.00	94.13	N/A
H1 High Negative (HN) (0.004 TCID ₅₀ per reaction)	Site 1	0	1	5	58.00	95.50	135.25	N/A
	Site 2	0	3	3	102.50	136.00	175.50	N/A
	Site 3	0	0	6	22.50	50.25	77.25	N/A
	Total	0 / 18	4 / 18	14 / 18	52.50	87.00	140.00	N/A

Summary of Flu B calls in simulated Influenza B samples:

Virus / Titer	All Days (3 extraction days x 2 extractions per day)							
Flu B (Strain: B/Malaysia/2506/04)	Site	# Positive	# Equivocal	# Negative	25 th Percentile MFI	Median MFI	75 th Percentile MFI	%CV
Low Positive (LP) (0.001 TCID ₅₀ per reaction)	Site 1	6 / 6	0 / 6	0 / 6	1272.00	1440.00	1684.13	20.83
	Site 2	6 / 6	0 / 6	0 / 6	1009.00	1258.00	1528.00	41.44
	Site 3	6 / 6	0 / 6	0 / 6	918.75	1036.50	1201.50	18.78
	Total	18 / 18	0 / 18	0 / 18	1034.25	1263.00	1528.00	31.11
High Negative (HN) (0.00002 TCID ₅₀ per reaction)	Site 1	0 / 6	0 / 6	6 / 6	18.50	22.00	26.25	N/A
	Site 2	0 / 6	1 / 6	5 / 6	76.63	93.25	120.38	N/A
	Site 3	0 / 6	0 / 6	6 / 6	4.00	31.00	81.25	N/A
	Total	0 / 18	1 / 18	17 / 18	18.50	55.00	90.88	N/A

Summary of hMPV calls in simulated hMPV samples:

Virus / Titer	All Days (3 extraction days x 2 extractions per day)							
hMPV (CAN 97-83; in-house)	Site	# Positive	# Equivocal	# Negative	25 th Percentile MFI	Median MFI	75 th Percentile MFI	%CV
Low Positive (LP) (0.002 TCID ₅₀ per reaction)	Site 1	6 / 6	0 / 6	0 / 6	662.38	701.25	757.38	82.67
	Site 2	5 / 6	1 / 6	0 / 6	377.25	601.50	742.50	63.98
	Site 3	6 / 6	0 / 6	0 / 6	538.88	646.00	690.50	24.50
	Total	17 / 18	1 / 18	0 / 18	523.88	662.00	757.38	69.75
High Negative (HN) (0.0001 TCID ₅₀ per reaction)	Site 1	0 / 6	0 / 6	6 / 6	20.25	30.00	55.13	N/A
	Site 2	0 / 6	0 / 6	6 / 6	76.00	82.00	89.13	N/A
	Site 3	0 / 6	0 / 6	6 / 6	31.75	46.00	54.63	N/A
	Total	0 / 18	0 / 18	18 / 18	30.00	59.00	80.00	N/A

Summary of RSV A calls in simulated RSV A samples:

Virus / Titer	All Days (3 extraction days x 2 extractions per day)							
RSV A (Strain: A2, Zeptomatrix lot 303544)	Site	# Positive	# Equivocal	# Negative	25 th Percentile MFI	Median MFI	75 th Percentile MFI	%CV
Low Positive (LP) (10 TCID ₅₀ per reaction)	Site 1	6 / 6	0 / 6	0 / 6	2171.38	3150.00	3990.63	40.60
	Site 2	6 / 6	0 / 6	0 / 6	1004.00	1291.25	1442.00	32.56
	Site 3	6 / 6	0 / 6	0 / 6	834.00	1193.00	1507.00	64.94
	Total	18 / 18	0 / 18	0 / 18	1067.00	1509.25	2721.13	65.22
High Negative (HN) (0.8 TCID ₅₀ per reaction)	Site 1	1 / 6	2 / 6	3 / 6	110.50	144.00	158.00	N/A
	Site 2	1 / 6	2 / 6	3 / 6	104.00	145.25	255.50	N/A
	Site 3	0 / 6	0 / 6	6 / 6	21.50	25.50	39.25	N/A
	Total	2 / 18	4 / 18	12 / 18	52.00	111.00	153.88	N/A

Summary of RSV B calls in simulated RSV B samples:

Virus / Titer	All Days (3 extraction days x 2 extractions per day)							
RSV B (Strain: B WV/14617/ '85 [B-1 wild type], ATCC)	Site	# Positive	# Equivocal	# Negative	25 th Percentile MFI	Median MFI	75 th Percentile MFI	%CV
Low Positive (LP) (0.1 TCID ₅₀ per reaction)	Site 1	6 / 6	0 / 6	0 / 6	639.75	818.50	962.38	45.96
	Site 2	5 / 6	1 / 6	0 / 6	474.00	602.00	814.75	45.05
	Site 3	6 / 6	0 / 6	0 / 6	609.50	735.50	968.75	29.21
	Total	17 / 18	1 / 18	0 / 18	556.75	683.00	926.13	41.49
High Negative (HN) (0.0008 TCID ₅₀ per reaction)	Site 1	0 / 6	1 / 6	5 / 6	61.50	91.75	110.75	N/A
	Site 2	0 / 6	0 / 6	6 / 6	72.63	87.00	100.63	N/A
	Site 3	0 / 6	0 / 6	6 / 6	22.25	39.75	56.13	N/A
	Total	0 / 18	1 / 18	17 / 18	53.13	71.75	95.00	N/A

Summary of Para 1 calls in simulated Parainfluenza-1 samples:

Virus / Titer	All Days (3 extraction days x 2 extractions per day)							
Para 1 (Strain: C-35, DHI Lot 081006B)	Site	# Positive	# Equivocal	# Negative	25 th Percentile MFI	Median MFI	75 th Percentile MFI	%CV
Low Positive (LP) (100 TCID ₅₀ per reaction)	Site 1	5 / 6	0 / 6	1 / 6	863.00	924.50	1099.25	50.83
	Site 2	5 / 6	1 / 6	0 / 6	347.13	502.75	633.63	65.52
	Site 3	5 / 6	0 / 6	1 / 6	769.50	798.25	848.38	73.11
	Total	15 / 18	1 / 18	2 / 18	482.88	798.25	940.25	63.02
High Negative (HN) (2 TCID ₅₀ per reaction)	Site 1	0 / 6	0 / 6	6 / 6	35.00	45.00	64.75	n/a
	Site 2	0 / 6	0 / 6	6 / 6	68.00	83.00	95.75	n/a
	Site 3	0 / 6	0 / 6	6 / 6	2.13	11.50	20.50	n/a
	Total	0 / 18	0 / 18	18 / 18	21.50	52.00	70.88	n/a

Summary of Para 2 calls in simulated Parainfluenza-2 samples:

Virus / Titer	All Days (3 extraction days x 2 extractions per day)							
Para 2 (Strain: Greer, DHI Lot 062706)	Site	# Positive	# Equivocal	# Negative	25 th Percentile MFI	Median MFI	75 th Percentile MFI	%CV
Low Positive (LP) (6 TCID ₅₀)	Site 1	6 / 6	0 / 6	0 / 6	600.25	726.50	1116.00	44.73
	Site 2	3 / 6	1 / 6	2 / 6	179.00	308.50	387.75	83.16

per reaction)	Site 3	5 / 6	1 / 6	0 / 6	453.50	595.50	910.00	50.25
	Total	14 / 18	2 / 18	2 / 18	332.75	544.50	930.75	59.26
High Negative (HN) (0.4 TCID ₅₀ per reaction)	Site 1	0 / 6	1 / 6	5 / 6	54.50	69.00	112.38	N/A
	Site 2	0 / 6	0 / 6	6 / 6	78.50	86.50	96.38	N/A
	Site 3	0 / 6	0 / 6	6 / 6	18.25	52.50	67.63	N/A
	Total	0 / 18	1 / 18	17 / 18	51.50	73.25	96.38	N/A

Summary of Para 3 calls in simulated Parainfluenza-3 samples:

Virus / Titer	All Days (3 extraction days x 2 extractions per day)							
Para 3 (Strain: C-243, DHI Lot 052506)	Site	# Positive	# Equivocal	# Negative	25th Percentile MFI	Median MFI	75th Percentile MFI	%CV
Low Positive (LP) (0.2 TCID ₅₀ per reaction)	Site 1	4 / 6	2 / 6	0 / 6	293.88	405.50	543.00	43.89
	Site 2	3 / 6	3 / 6	0 / 6	239.50	291.00	348.50	54.53
	Site 3	3 / 6	2 / 6	1 / 6	200.00	285.00	461.88	50.45
	Total	10 / 18	7 / 18	1 / 18	236.00	327.00	482.63	47.44
High Negative (HN) (0.02 TCID ₅₀ per reaction)	Site 1	0 / 6	0 / 6	6 / 6	21.25	22.25	27.38	N/A
	Site 2	0 / 6	0 / 6	6 / 6	63.88	70.75	75.00	N/A
	Site 3	0 / 6	0 / 6	6 / 6	6.25	19.00	25.75	N/A
	Total	0 / 18	0 / 18	18 / 18	21.25	27.50	62.38	N/A

Summary of Rhino calls in simulated Rhinovirus samples:

Virus / Titer	All Days (3 extraction days x 2 extractions per day)							
Rhinovirus (Type 54: ATCC)	Site	# Positive	# Equivocal	# Negative	25th Percentile MFI	Median MFI	75th Percentile MFI	%CV
Low Positive (LP) (0.0006 TCID ₅₀ per reaction)	Site 1	6 / 6	0 / 6	0 / 6	775.25	906.50	972.50	27.97
	Site 2	6 / 6	0 / 6	0 / 6	512.00	670.00	769.50	33.92
	Site 3	6 / 6	0 / 6	0 / 6	827.38	1215.25	1283.25	30.47
	Total	18 / 18	0 / 18	0 / 18	666.00	827.00	1049.38	35.55
High Negative (HN) (0.00004 TCID ₅₀ per reaction)	Site 1	0 / 6	0 / 6	6 / 6	36.25	50.00	54.75	N/A
	Site 2	0 / 6	0 / 6	6 / 6	78.75	94.00	96.88	N/A
	Site 3	0 / 6	0 / 6	6 / 6	24.88	67.50	121.75	N/A
	Total	0 / 18	0 / 18	18 / 18	36.25	60.75	96.88	N/A

Summary of Adeno Calls in simulated Adenovirus samples:

Virus / Titer	All Days (3 extraction days x 2 extractions per day)							
Adenovirus (cultured patient isolate – Species C)	Site	# Positive	# Equivocal	# Negative	25th Percentile MFI	Median MFI	75th Percentile MFI	%CV
Low Positive (LP) (0.8 TCID ₅₀ per reaction)	Site 1	6 / 6	0 / 6	0 / 6	865.63	925.25	992.75	9.52
	Site 2	5 / 6	0 / 6	1 / 6	708.75	834.00	905.63	44.23
	Site 3	6 / 6	0 / 6	0 / 6	758.88	971.00	1204.50	41.80
	Total	17 / 18	0 / 18	1 / 18	813.63	888.25	1007.50	36.16
High Negative (HN) (0.05 TCID ₅₀ per reaction)	Site 1	0 / 6	2 / 6	4 / 6	121.00	126.75	178.63	N/A
	Site 2	2 / 6	3 / 6	1 / 6	162.75	225.00	303.75	N/A
	Site 3	1 / 6	3 / 6	2 / 6	146.75	222.00	263.50	N/A
	Total	3 / 18	8 / 18	7 / 18	124.50	189.00	259.00	N/A

Analytical Sensitivity

See k063765

Reactivity

See k063765

Analytical Specificity

See k063765

Carry-over/Contamination

See k063765

2. Comparison studies:

See k063765

3. Clinical studies:

See k063765 – all three recommended extraction methods (Biomérieux EasyMag™, Qiagen QIAamp® MiniElute®, and Biomérieux MiniMag™) were evaluated in the prospective clinical study.

4. Clinical cut-off:

See k063765

5. Expected values/Reference range:

See k063765

N. Proposed Labeling:

The labeling is sufficient and it satisfies the requirements of 21 CFR Part 809.10.

O. Conclusion:

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