510(k) Summary

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of 21 CFR 807.92.

510(k) Number: k112781

Purpose for Submission: Modification to PCR primer mix of the previously cleared xTAG® RVP (k112199) originally cleared under k063765 to improve reactivity to influenza A/H3 strains.

Measurand: 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

Type of Test: Qualitative nucleic acid multiplex test

Applicant: Luminex Molecular Diagnostics Inc.

Proprietary and Established Names: xTAG® Respiratory Viral Panel (RVP)

Regulatory Information:

Product Code	*Classification*	*Regulation Section*	*Review Panel*
OCC, OEM, OEP, NSU, JJH	Class II	21 CFR 866.3980 Respiratory viral panel multiplex nucleic acid assay	Microbiology (83)

Intended Use:
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 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.

xTAG RVP can also differentiate the hemagglutinin (HA) gene of some Influenza A subtypes H1 and H3 strains. Differentiation of Influenza A HA subtypes is based on both a positive result for the Influenza A matrix gene and an accompanying positive result for the Influenza A HA subtype H1 (circulating prior to the emergence of 2009 H1N1pdm) or Influenza A HA subtype H3. This device cannot differentiate the Influenza A HA subtype 2009 H1N1pdm by design, and may not be able to differentiate potential newly emerging Influenza A HA subtypes.

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.

Negative results do not preclude respiratory virus infection and should not be used as the sole basis for diagnosis, treatment or other patient management decisions.

The RVP assay cannot adequately detect Adenovirus species C, or serotypes 7a and 41. It is recommended that specimens found to be negative for Adenovirus after examination using RVP be confirmed by an alternate method (e.g., FDA cleared molecular test or cell culture). 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 HA subtype H3, subtype H1 (prior to the emergence of 2009 H1N1pdm), and when subtype 2009 H1N1pdm were the predominant Influenza A in circulation. When other Influenza A viruses are emerging, performance characteristics may vary.

If infection 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.

Indication(s) for use: Same as intended use.

Special conditions for use statement(s): N/A

Special instrument requirements: Luminex 100 or 200 instrument with IS or xPONENT software

Device Description:
The modified RVP is a PCR-based test system for detecting the presence / absence of viral DNA / RNA in clinical specimens. The modified device is the same as the predicate device, except for a reformulation of the PCR primer mix.

Substantial Equivalence Information:

a. Predicate device name(s): xTAG® Respiratory Viral Panel

b. Predicate 510(k) number(s): k063765, k081843, k091667 and k112199

c. Comparison with predicate:
The following table compares the modified xTAG® Respiratory Viral Panel with the xTAG® Respiratory Viral Panel (k063765, k081843, k091667, k112199).

Table 1: Comparison between Modified (New) Device and Predicate

Item	**Modified Device (k112781) xTAG® RVP**	**Predicates (k063765, k081483, k091667, k112199) xTAG® RVP**
Manufacturer	Luminex Molecular Diagnostics	Luminex Molecular Diagnostics
Specimen Types	Nasopharyngeal swabs	Nasopharyngeal swabs
Amplification Method	Multiplex end point RT-PCR	Multiplex end point RT-PCR
Test Format	Multiplex bead-based universal array sorting on Luminex 100/200 instrument	Multiplex bead-based universal array sorting on Luminex 100/200 instrument
Detection Method	Fluorescence based	Fluorescence based
Quality Control	Internal Control (E. coli phage MS2), Run Control (bacteriophage Lambda DNA), rotating analyte control and negative controls	Internal Control (E. coli phage MS2) and Run Control (bacteriophage Lambda DNA), rotating analyte control and negative controls
Results	Qualitative	Qualitative
Instrument	LX100 or LX200 with xMAP system (IS or xPONENT)	LX100 or LX200 with xMAP system (IS or xPONENT)
Intended Use	Same as predicate	See above
Targets Reported	Influenza A, Influenza A subtype H1, Influenza A subtype H3, Influenza B, Respiratory Syncytial Virus A, Respiratory Syncytial Virus B, Parainfluenza 1, Parainfluenza 2, Parainfluenza 3, Human Metapneumovirus, Rhinovirus, and Adenovirus	Influenza A, Influenza A subtype H1, Influenza A subtype H3, Influenza B, Respiratory Syncytial Virus A, Respiratory Syncytial Virus B, Parainfluenza 1, Parainfluenza 2, Parainfluenza 3, Human Metapneumovirus, Rhinovirus, and Adenovirus
Sample Preparation	QIAGEN QIAamp MinElute, Biomérieux NucliSENS® EasyMag®, and Biomérieux MiniMag™	QIAGEN QIAamp MinElute, Biomérieux NucliSENS® EasyMag®, and Biomérieux MiniMag™
Amplification Enzyme	xTAG® OneStep Enzyme Mix and ancillary reagent TaKaRa Taq™ Hot Start	xTAG® OneStep Enzyme Mix and ancillary reagent TaKaRa Taq™ Hot Start
Primer Mixes	Two primer mixes (1 for PCR and 1 for TSPE). Modified PCR primer mix	Two primer mixes (1 for PCR and 1 for TSPE)
Software	xTAG Data Analysis Software RVP (US)	xTAG Data Analysis Software RVP (US)

Standards/Guidance Documents referenced (if applicable):

Table 2: Guidance Documents

	Title	Date
1	Class II Special Controls Guidance: Respiratory Viral Panel Multiplex Nucleic Acid Assay	Oct. 9, 2009
2	Class II Special Control Guidance Document: Testing for Detection and Differentiation of Influenza A Virus Subtypes Using Multiplex Assays	Oct. 9, 2009
3	Guidance (Draft) for Establishing the Performance Characteristics of In Vitro Diagnostic Devices for the Detection or Detection and Differentiation of Influenza Viruses	Feb. 15, 2008
4	Guidance for In Vitro Diagnostic Devices to Detect Influenza A Viruses: Labeling and Regulatory Path	May 1, 2007
5	Class II Special Controls Guidance: Reagents for Detection of Specific Novel Influenza A Viruses	Mar. 22, 2006
6	Class II Special Control Guidance Document: "Testing for Human Metapneumovirus (hMPV) Using Nucleic Acid Assays"	Oct. 9, 2009
7	Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices	May 11, 2005
8	Guidance document for Format for Traditional and Abbreviated 510(k)s	Aug. 12, 2005

Table 3: Standards

	Standards No.	Recognition Number (FDA)	Standards Title	Date
1	MM13-A	7-191	Collection, Transport, Preparation and Storage of Specimens	03/18/2009
2	MM03-A2	7-132	Molecular Diagnostic Methods for Infectious Diseases (2nd edition)	09/09/2008
3	EP12-A2	7-152	User Protocol for Evaluation of Qualitative Test Performance (2nd edition)	09/09/2008
4	ISO14971	5-40	Medical devices - Application of risk management to medical devices	09/12/2007

Test Principle:
Same as predicate

Performance Characteristics:

Analytical Performance:
Precision/Reproducibility: Same as predicate.

Limit of Detection (LoD):

The LoD for Influenza A subtype H3 was determined using two strains of influenza A comparing results of the predicate for these analytes to those of the modified device (see Table 4).

Table 4: Comparison of (LoD) for Influenza A H3 between Modified and Original RVP

Strain ID	Analyte	Modified xTAG® RVP		Original xTAG® RVP	
		$TCID_{50}$/mL (at estimated LoD)	Average MFI from 22 replicates at LoD	$TCID_{50}$/mL (at estimated LoD)	Average MFI from 22 replicates at LoD
A/Victoria/3/75	Flu A Matrix	0.4768	1806.84	0.4768	1776.05
	Flu A H3	0.4768	974.36	7.629	1219.64
A/Perth/16/2009	Flu A Matrix	0.1347	1225.16	0.5388*	2796.07
	Flu A H3	0.1347	706.39	8.621	1441.16

*Note: This LoD level was achieved with 22 out of 22 replicates making the correct Flu A Matrix POS call. At 0.1347 $TCID_{50}$/mL (one dilution below 0.5388 $TCID_{50}$/mL level), 18 out of 22 replicates made the correct Flu A Matrix POS call with the original xTAG® RVP assay. The remaining 4 replicates displayed MFI values of 226, 295, 249, 219, just below the cut-off, thus generating "No Call" results for Flu A Matrix.

In addition, the limit of detection study compared the LoD of the modified xTAG® RVP assay with the original xTAG® RVP assay for all targets in the RVP panel using one strain for each target (Table 5). For each strain, 20 replicates of the dilutions at the estimated LoD level and at least the two bracketing levels were tested.

Table 5: Summary of Limit of Detection (LoD) for the non-H3 Targets

Analyte	Strain ID	Dilution Levels (L1 and L3 are at 4 fold below and above the estimated LOD, respectively)	Original xTAG® RVP			Modified xTAG® RVP		
			$TCID_{50}$/mL (at estimated LoD)	Average MFI from 20 replicates at LoD	No. of POS Calls from 20 replicates	$TCID_{50}$/mL (at estimated LoD)	Average MFI from 20 replicates at LoD	No. of POS Calls from 20 replicates
Flu A Matrix	Solomon Island/3/2006	L1	1.91E+00	3464.9	20	1.91E+00	2914.9	20
		L2 (LOD Level)	4.77E-01	3059.4	20	4.77E-01	2099.6	19
		L3	1.19E-01	229.8	2	1.19E-01	209.9	1
Flu A H1	Solomon Island/3/2006	L1	1.91E+00	944.3	20	1.91E+00	721.9	19
		L2 (LOD Level)	4.77E-01	857.1	20	4.77E-01	492.9	19
		L3	1.19E-01	72.7	0	1.19E-01	74.2	0
Influenza B	Brisbane/33/08	L1	7.82E-01	1872.8	20	7.82E-01	2101.9	20
		L2 (LOD Level)	1.96E-01	923.9	20	1.96E-01	753.1	20
		L3	4.89E-02	187.5	2	4.89E-02	206.4	2
RSV A	Long	L1	7.63E-02	2473.4	20	7.63E-02	2694.7	20
		L2 (LOD Level)	1.91E-02	595.4	20	1.91E-02	595.9	20
		L3	4.77E-03	159.4	0	4.77E-03	212.3	1
RSV B	Wash/18537/62	L1	4.88E+00	2820.2	20	4.88E+00	3604.8	20
		L2 (LOD Level)	1.22E+00	923.5	20	1.22E+00	921.2	20
		L3	3.05E-01	202.0	2	3.05E-01	337.8	12
hMPV	CDC Isolate	L1	1.60E+00	5844.5	20	1.60E+00	6284.475	20
		L2 (LOD Level)	4.00E-01	1395.625	20	4.00E-01	1494.4	20
		L3	1.00E-01	345.5	14	1.00E-01	466.125	16
Para-1	C-35	L1	3.91E-01	2188.2	20	3.91E-01	2062.5	20
		L2 (LOD Level)	9.77E-02	865.7	20	9.77E-02	749.5	20
		L3	2.44E-02	164.8	4	2.44E-02	240.9	6
Para-2	Greer	L1	7.63E-01	5113.1	20	7.63E-01	5889.8	20
		L2 (LOD Level)	1.91E-01	4238.5	20	1.91E-01	5340.9	20
		L3	4.77E-02	467.0	14	4.77E-02	675.3	15
Para-3	Zeptometrix 0810016CF	L1	1.00E+01	3206.1	20	1.00E+01	2524.6	20
		L2 (LOD Level)	2.51E+00	729.5	20	2.51E+00	1148.5	20
		L3	6.27E-01	38.8	0	6.27E-01	8.3	0
Adenovirus	Type 1	L1	4.07E+01	1272.1	20	4.07E+01	737.8	20
		L2 (LOD Level)	1.02E+01	494.1	20	1.02E+01	468.3	19
		L3	2.54E+00	193.6	2	2.54E+00	158.6	0
Rhinovirus	Type 54	L1	3.00E-02	3052.7	20	3.00E-02	3773.0	20
		L2 (LOD Level)	7.50E-03	1006.6	20	7.50E-03	1387.2	20
		L3	1.88E-03	399.6	13	1.88E-03	366.3	13

The results from this LoD study indicate that the modified xTAG® RVP is equivalent to that of the original xTAG® RVP for all target calls.

Carryover Contamination Limit of Blank (LoB): Same as predicate

Analytical Specificity (Reactivity, Cross-Reactivity and Competitive Inhibition):

A total of 48 potentially cross-reactive pathogens (bacterial and viral) were assessed in replicates with RVP. Each replicate underwent a single EasyMag (bioMerieux NucliSENS®) extraction prior to testing.

Table 6: Bacterial pathogens assessed as potential cross-reactive species in the RVP Assay

Organism	Strain	Titer Tested	Titer Units	Analyte, Results Positive (+) or Negative (-) for Reactivity											
				Flu A matrix	Flu A H1	Flu A H3	Flu B	Para 1	Para 2	Para 3	RSV A	RSV B	Rhinovirus	Metapneumovirus	Adenovirus
Bordetella pertussis	NEQAS 1505	13.66	Ct*	-	-	-	-	-	-	-	-	-	-	-	-
Corynebacterium glutamicum	Type strain 534 [NCIB 10025]	6.00×10^5	cfu/mL	-	-	-	-	-	-	-	-	-	-	-	-
Escherichia coli	ATCC 8739	5.60×10^5	cfu/mL	-	-	-	-	-	-	-	-	-	-	-	-
Haemophilus influenzae	Type b (Zeptometrix 0801680)	2.63×10^5	cfu/mL	-	-	-	-	-	-	-	-	-	-	-	-
Lactobacillus casei	03 [7, IAM 12473, Orland L-323, R.P. Tittsler 303]	6.00×10^8	cfu/mL	-	-	-	-	-	-	-	-	-	-	-	-
Legionella pneumophila	ATCC 33152	15.42	Ct*	-	-	-	-	-	-	-	-	-	-	-	-
Moraxella (Branhamella) catarrhalis	Ne 11	5.00×10^4	cfu/mL	-	-	-	-	-	-	-	-	-	-	-	-
Mycobacterium avium subsp. avium	ATCC 15769	2.50×10^4	cfu/mL	-	-	-	-	-	-	-	-	-	-	-	-
Mycobacterium intracellulare	ATCC 13209	2.50×10^4	cfu/mL	-	-	-	-	-	-	-	-	-	-	-	-
Mycoplasma pneumoniae	M129	5.63×10^6	$TCID_{50}$/mL	-	-	-	-	-	-	-	-	-	-	-	-
Neisseria elongata subsp. elongata	NCTC 10660	2.50×10^4	cfu/mL	-	-	-	-	-	-	-	-	-	-	-	-
Neisseria meningitides	Zeptometrix 0801511	3.37×10^5	cfu/mL	-	-	-	-	-	-	-	-	-	-	-	-
Pseudomonas aeruginosa	ATCC15442	4.00×10^8	cfu/mL	-	-	-	-	-	-	-	-	-	-	-	-
Staphylococcus aureus	Zepto 0801638	4.00×10^8	cfu/mL	-	-	-	-	-	-	-	-	-	-	-	-
Staphylococcus epidermidis	ATCC 12228	4.00×10^5	cfu/mL	-	-	-	-	-	-	-	-	-	-	-	-
Streptococcus pneumoniae	Type 59	15.95	Ct	-	-	-	-	-	-	-	-	-	-	-	-
Streptococcus pyogenes	ATCC 51500	$2.0. \times 10^5$	cfu/mL	-	-	-	-	-	-	-	-	-	-	-	-
Streptococcus salivarius	75 [NCTC 8618]	6.00×10^5	cfu/mL	-	-	-	-	-	-	-	-	-	-	-	-

Ct = Ct value obtained from testing by a qPCR assay at 10^{-1} dilution. An undiluted sample was tested in the cross-reactivity study.*

These bacterial pathogens did not cross-react or interfere with any viral target probed by RVP in either the original or modified device.

Table 7: Viral pathogens assessed as potential cross-reactive species in the RVP Assay

Organism	Strain	Titer Tested	Titer Units	Analyte, Results Positive (+) or Negative (-) for Reactivity											
				Flu A matrix	Flu A H1	Flu A H3	Flu B	Para 1	Para 2	Para 3	RSV A	RSV B	Rhinovirus	Metapneumovirus	Adenovirus
Flu A H1 (Seasonal)	A/New Caledonia/20/99	5.00×10^3	$TCID_{50}$/mL	+	+	-	-	-	-	-	-	-	-	-	-
Influenza B	B/Russia/69	3.16×10^6	$TCID_{50}$/mL	-	-	-	+	-	-	-	-	-	-	-	-
Influenza B	B/Mass/3/66	3.16×10^7	$TCID_{50}$/mL	-	-	-	+	-	-	-	-	-	-	-	-
Parainfluenza 1	C-35	1.58×10^5	$TCID_{50}$/mL	-	-	-	-	+	-	-	-	-	-	-	-
Parainfluenza 2	Greer	5.00×10^5	$TCID_{50}$/mL	-	-	-	-	-	+	-	-	-	-	-	-
Parainfluenza 3	C-243	5.00×10^4	$TCID_{50}$/mL	-	-	-	-	-	-	+	-	-	-	-	-
Parainfluenza 4A	Unknown	4.17×10^5	$TCID_{50}$/mL	-	-	-	-	-	-	-	-	-	-	-	-
Parainfluenza 4B	Unknown	2.45×10^5	$TCID_{50}$/mL	-	-	-	-	-	-	-	-	-	-	-	-
RSV A	Long	5.00×10^4	$TCID_{50}$/mL	-	-	-	-	-	-	-	+	-	-	-	-
RSV B	Wash/18537/62	1.00×10^4	$TCID_{50}$/mL	-	-	-	-	-	-	-	-	+	-	-	-
Enterovirus (Echo 13)	Del Carmen	5.00×10^7	$TCID_{50}$/mL	-	-	-	-	-	-	-	-	-	+	-	-
Enterovirus (Coxsackie B)	Unknown	5.00×10^6	$TCID_{50}$/mL	-	-	-	-	-	-	-	-	-	+	-	-
Enterovirus Type 68	Fermon	1.00×10^6	$TCID_{50}$/mL	-	-	-	-	-	-	-	-	-	+	-	-
Enterovirus Type 69	Toluca-1	2.00×10^4	$TCID_{50}$/mL	-	-	-	-	-	-	-	-	-	+	-	-
Rhinovirus	Strain 1A	1.26×10^5	$TCID_{50}$/mL	-	-	-	-	-	-	-	-	-	+	-	-
Rhinovirus	Type 60	5.00×10^7	$TCID_{50}$/mL	-	-	-	-	-	-	-	-	-	+	-	-
HMPV	CAN97-83 (CDC Isolate 26583)	5.00×10^3	$TCID_{50}$/mL	-	-	-	-	-	-	-	-	-	-	+	-
Adenovirus	Type 1, Adenoid 71	5.00×10^5	$TCID_{50}$/mL	-	-	-	-	-	-	-	-	-	-	-	+
Adenovirus	Type 1	4.17×10^6	$TCID_{50}$/mL	-	-	-	-	-	-	-	-	-	-	-	+
Adenovirus	Type 7A	5.37×10^8	$TCID_{50}$/mL	-	-	-	-	-	-	-	-	-	-	-	+
Coronavirus 229E	229E	5.00×10^6	$TCID_{50}$/mL	-	-	-	-	-	-	-	-	-	-	-	-
Coronavirus NL63	NL63	5.00×10^5	$TCID_{50}$/mL	-	-	-	-	-	-	-	-	-	-	-	-
Coronavirus OC43	OC43	5.00×10^6	$TCID_{50}$/mL	-	-	-	-	-	-	-	-	-	-	-	-
Varicella Zoster virus	Isolate A	1.86×10^4	$TCID_{50}$/mL	-	-	-	-	-	-	-	-	-	-	-	-
Measles virus	Unknown	1.26×10^6	$TCID_{50}$/mL	-	-	-	-	-	-	-	-	-	-	-	-
Cytomegalovirus	AD-169	9.55×10^6	$TCID_{50}$/mL	-	-	-	-	-	-	-	-	-	-	-	-
Epstein-Barr virus	B95-8	3.00×10^9	cp/mL	-	-	-	-	-	-	-	-	-	-	-	-
Mumps virus	N/A (Zeptometrix)	7.57×10^4	$TCID_{50}$/mL	-	-	-	-	-	-	-	-	-	-	-	-
Mumps virus	N/A (Cultured from parotid swab)	16.36	Ct	-	-	-	-	-	-	-	-	-	-	-	-
Herpes simplex virus	McIntyre	1.45×10^{10}	$TCID_{50}$/mL	-	-	-	-	-	-	-	-	-	-	-	-

The original and modified xTAG® RVP assays did not generate non-specific positive calls for these viral strains with the following exceptions (where a contaminated sample is suspected in each instance since the result was observed in both the original and modified devices): Flu A H1 (Seasonal) demonstrated some signal for the run control near the cutoff (lambdoid DNA);

Parainfluenza 3 demonstrated a low-level influenza A signal; Enterovirus (Echo 13) and Enterovirus (Coxsackie B) showed an Adenovirus signal; and Adenovirus (Type 1, Adenoid 71) showed an H3 (but not influenza A matrix) signal.

For the reactivity study, the initial stocks were diluted to approximately 2x to 3x the LoD established for the two reference strains in the LoD study. At least three replicates per strain were evaluated starting from the extraction step with both original and modified xTAG® RVP assays. Both were able to successfully detect all five H3 strains tested (see Table 8).

Table 8: Influenza A Subtype H3 Strains Tested in the Reactivity Study

A/Port Chalmers/1/73
A/Hong Kong/8/68
A2/Aichi2/68
A/Alice
MRC2

The following four additional strains were identified from the clinical sample data set in the accuracy study (Table 9).

Table 9: Influenza A Subtype H3 Strains Tested in the Accuracy Study

A/District of Columbia/WRAIR0301/2010(H3N2)
A/Texas/NHRC0001/2011(H3N2)
A/South Carolina/AF2724/2011(H3N2)
A/Iasi/47326/2010(H3N2)

Eight additional strains representing other cleared analytes were tested in the analytical reactivity study (Table 10). The initial stocks were diluted to approximately 3 times the LoD established for reference strains. Three replicates per strain were evaluated with both original and modified xTAG® RVP assays. Both devices were able to successfully detect all eight strains tested.

Table 10: Additional Strains Tested in the Reactivity Study

Flu A H1	A/New Caledonia/20/99 (H1N1)
Flu B	B/Malaysia/2506/04
RSV A	AUS/A2/61
RSV B	B WV/14617/'85
Parainfluenza 3	C-243
Rhinovirus	Type 39
hMPV	Type 8, strain Peru6-2003 B2
Adenovirus	Type 3

Competitive Inhibition Study

The combinations of analytes tested in the competitive inhibition study are listed in Table 11. Each analyte was tested at two different concentrations, High Positive (HP, approximately at 1.3 to 4-fold dilution of the original stock) and Low Positive (LP, approximately at 2 to 4 times LoD for that analyte). The results show that the modifications made to the device did not inhibit the detection of the competing analytes. The performance of the Original and Modified devices was equivalent. All expected positive calls were present.

Table 11. Analyte Combinations Tested in the Competitive Inhibition Study

Count	Analyte 1	Concentration	Analyte 2	Concentration
1	Flu A H3, strain A/Victoria/3/75	HP	RSV A, strain Long	LP
2	Flu A H3, strain A/Victoria/3/75	LP	RSV A, strain Long	HP
3	Flu A H3, strain A/Victoria/3/75	HP	RSV B, strain Wash/18537/62	LP
4	Flu A H3, strain A/Victoria/3/75	LP	RSV B, strain Wash/18537/62	HP
5	Flu A H3, strain A/Victoria/3/75	HP	Rhinovirus, Type 54	LP
6	Flu A H3, strain A/Victoria/3/75	LP	Rhinovirus, Type 54	HP
7	Flu A H3, strain A/Victoria/3/75	HP	hMPV 5, Peru3-2003 B1	LP
8	Flu A H3, strain A/Victoria/3/75	LP	hMPV 5, Peru3-2003 B1	HP
9	Flu A H3, strain A/Victoria/3/75	HP	Adenovirus, Type 1	LP
10	Flu A H3, strain A/Victoria/3/75	LP	Adenovirus, Type 1	HP

No differences between the modified and the original xTAG® RVP were observed in reactivity, cross-reactivity or competitive inhibition studies.

Clinical Comparison Studies (Accuracy)

The accuracy study evaluated the positive agreement and negative agreement between the original and modified xTAG® RVP devices. Table 12 shows the list of analytes tested by both the original and modified xTAG® RVP Assays.

Table 12: Analytes Tested

Human Influenza A
Human H1 seasonal subtype of Influenza A
Human H3 subtype of Influenza A
Influenza B
RSV A
RSV B
Human Metapneumovirus
Rhinovirus / Enterovirus
Parainfluenza 1
Parainfluenza 2
Parainfluenza 3
Adenovirus

A total of 369 retrospectively collected left-over clinical samples (nasopharyngeal swabs) obtained primarily from the 2010-2011 influenza season were collected from 14 clinical sites in the United States and Canada. To preserve the confidentiality of the subjects, clinical specimens were individually numbered so the identity of the subject could not be readily ascertained by the investigator or any other individual associated with the study. Nucleic acid extraction was performed either by the clinical site or at Luminex Molecular Diagnostics (LMD), using one of the following methods: BioMerieux EasyMAG, BioMerieux MiniMAG or QIAGEN MinElute Viral Spin Kit, as directed in the instructions for use of the original device. Extracted samples were stored frozen at a temperature of -70°C until used in the study.

All Flu A matrix positive samples (158) from either the original or modified xTAG® RVP device were bi-directionally sequenced for Flu A subtype H3. 132 of the 158 samples were found to be Flu A H3 sequence positive (see Table 13), leaving 26 samples that were Flu A H3 sequence negative. Four out of these 26 Flu A H3 sequencing negative samples were H1 positive by both the original RVP and the modified RVP assays. Three samples out of the 26 did not have adequate sample left over and therefore could not be sequenced. The remaining 19 samples (4+3+19=26) were sequenced with an in-house designed set of 2009 H1N1pdm primers and the majority of these samples (13) were 2009 H1N1pdm positive.

Table 13: Positive agreement for Influenza A H3 Target, Modified xTAG® RVP against Sequencing

		95% CI	
Sequencing POS for H3	132 Samples	Lower	Upper
Modified xTAG® RVP POS	121 Samples		
Percent Positive Agreement (TP/TP+FN)	121/132=91.7%	87.82%	96.91%

Positive agreement and negative agreement for each analyte were evaluated between the original and modified xTAG RVP devices (see Table 14).

Table 14: Clinical Comparison of Modified xTAG® RVP and Original xTAG® RVP

Analyte	Positive Percent Agreement (PPA)	Confidence Interval	Negative Percent Agreement (NPA)	Confidence Interval
Influenza A	98.09% (154/157)	94.52% - 99.60%	99.06% (210/212)	96.63% - 99.89%
Influenza A H1	100% (4/4)	39.76% - 100.00%	100% (365/365)	98.99% - 100.00%
Influenza A H3	100% (80/80)	95.49% – 100.00%	85.47% (247/289)	80.87% – 89.32%
Influenza B	100% (30/30)	88.43% - 100.00%	100% (339/339)	98.92% - 100.00%
RSV A	100% (23/23)	85.18% - 100.00%	99.71% (345/346)	98.40% - 99.99%
RSV B	96.30% (26/27)	81.03% - 99.91%	100% (342/342)	98.93% - 100.00%
Parainfluenza 1	100% (6/6)	54.07% - 100.00%	99.72% (362/363)	98.47% - 99.99%
Parainfluenza 2	100% (8/8)	63.06% - 100.00%	99.72% (360/361)	98.47% - 99.99%
Parainfluenza 3	100% (24/24)	85.75% - 100.00%	100% (345/345)	98.94% - 100.00%
hMPV	96.43% (27/28)	81.65% - 99.91%	100% (341/341)	98.92% - 100.00%
Rhinovirus	92.16% (47/51)	81.12% - 97.82%	99.69% (317/318)	98.26% - 99.99%
Adenovirus	100% (5/5)	47.82% - 100.00%	100% (364/364)	98.99% - 100.00%

Clinical Cut-off: Not applicable.

Expected values/ reference range: Not applicable.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration

10903 New Hampshire Avenue
Silver Spring, MD 20993

Luminex Molecular Diagnostics, Inc.
c/o Ms. Lubna Syed
Director, Regulatory Affairs
439 University Avenue, Suite 900
Toronto, Ontario, M5G 1Y8, CANADA

FEB 17 2012

Re: k112781
Trade Name: xTAG®Respiratory Viral Panel (RVP)
Regulation Number: 21 CFR 866.3980
Regulation Name: Respiratory Viral Panel Multiplex Nucleic Acid Assay
Regulatory Class: Class II
Product Code: OCC, OEM, OEP, NSU, JJH
Dated: December 19, 2011
Received: December 22, 2011

Dear Ms. Syed:

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. 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.

If your device is classified (see above) into class II (Special Controls), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. 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 Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820). This letter

will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (301) 796-5450. 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 the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html.

Sincerely yours,

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): k112781

Device Name: xTAG® Respiratory Viral Panel (RVP)

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 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.

xTAG RVP can also differentiate the hemagglutinin (HA) gene of some Influenza A subtypes H1 and H3 strains. Differentiation of Influenza A HA subtypes is based on both a positive result for the Influenza A matrix gene and an accompanying positive result for the Influenza A HA subtype H1 (circulating prior to the emergence of 2009 H1N1pdm) or Influenza A HA subtype H3. This device cannot differentiate the Influenza A HA subtype 2009 H1N1pdm by design, and may not be able to differentiate potential newly emerging Influenza A HA subtypes.

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.

Negative results do not preclude respiratory virus infection and should not be used as the sole basis for diagnosis, treatment or other patient management decisions.

The RVP assay cannot adequately detect Adenovirus species C, or serotypes 7a and 41. It is recommended that specimens found to be negative for Adenovirus after examination using RVP be confirmed by an alternate method (e.g., FDA cleared molecular test or cell culture). 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 HA subtype H3, subtype H1 (prior to the emergence of 2009 H1N1pdm), and when subtype 2009 H1N1pdm were the predominant Influenza A in circulation. When other Influenza A viruses are emerging, performance characteristics may vary.

If infection 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.

Prescription Use ___X___ (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of *In Vitro* Diagnostic Device Evaluation and Safety (OIVD)

Tamara Feldblum

Division Sign-Off
Office of *In Vitro* Diagnostic Device
Evaluation and Safety

510(k) K112781