510(K) SUMMARY

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

The assigned 510(k) number is: K141520

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DATE PREPARED
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TRADE NAME
Alere™ i Influenza A & B

COMMON NAME
Alere™ i flu, Alere™ i, Alere™ Influenza A & B

CLASSIFICATION NAME
Respiratory Viral Panel Multiplex Nucleic Acid Assay (per 21 CFR 866.3980)
Instrumentation for Clinical Multiplex Test Systems (per 21 CFR 862.2570)

CLASSIFICATION
Class II

PRODUCT CODE
OCC, OZE, OOI

PANEL
Microbiology (83)

PREDICATE DEVICE
IQuum Liat™ Influenza A/B Assay, K111387

DEVICE DESCRIPTION

Alere™ i Influenza A & B is a rapid, instrument-based isothermal test for the qualitative detection and differentiation of influenza A and influenza B from nasal swab specimens collected from patients presenting with signs and symptoms of respiratory infection. The Alere™ i Influenza A & B System utilizes isothermal nucleic acid amplification technology and is comprised of:

- Sample Receiver – single use, disposable containing the elution buffer
- Test Base – single use, disposable comprising two sealed reaction tubes, each containing a lyophilized pellet
- Transfer Cartridge – single use, disposable for transfer of the eluted sample to the Test Base, and
- Alere™ i Instrument – repeat use reader

The reaction tubes in the Test Base contain the reagents required for amplification of the target nucleic acid and an internal control. Alere™ i Influenza A & B utilizes a pair of templates (similar to primers) for the specific amplification of RNA from influenza A and B and a fluorescently labeled molecular beacon designed to specifically identify the amplified RNA targets. Alere™ i Influenza A & B is performed within the confinement of the Test Base, and no other part of the Alere™ i Instrument has contact with the sample during the amplification process. This minimizes the risk of instrument contamination and sample carry-over between measurements.

To perform the assay, the Sample Receiver and Test Base are inserted into the Alere™ i Instrument and the elution buffer is automatically heated by the instrument. The sample is added to the Sample Receiver and transferred via the Transfer Cartridge to the Test Base, resuspending the lyophilized pellet contained within the Test Base and initiating target amplification. Heating, mixing and detection by fluorescence is provided by the instrument, with results automatically reported.

Results are displayed by the Alere™ i Instrument separately for influenza A and influenza B. Results are also stored in an on-board archive and are assigned to a sample ID that has been entered into the Alere™ i Instrument by the operator, and the date/time the test was performed. Data can be retrieved and downloaded by the operator at any time after testing. An external Alere™ Universal Printer can be attached via USB to the Alere™ i Instrument to print test results.

INTENDED USE

The Alere™ i Influenza A & B assay performed on the Alere™ i Instrument is a rapid molecular *in vitro* diagnostic test utilizing an isothermal nucleic acid amplification technology for the qualitative detection and discrimination of influenza A and B viral RNA in nasal swabs from patients with signs and symptoms of respiratory infection. It is intended for use as an aid in the differential diagnosis of influenza A and B viral infections in humans in conjunction with clinical and epidemiological risk factors. The assay is not intended to detect the presence of influenza C virus.

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

Performance characteristics for influenza A were established during the 2012-2013 influenza season when influenza A/H3 and A/H1N1 pandemic were the predominant influenza A viruses 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 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.

TECHNOLOGICAL CHARACTERISTICS

Alere™ i Influenza A & B and the predicate device, IQuum Liat™ Influenza A/B Assay, have the same intended use, indications for use, and utilize similar basic principles of operation. They are both molecular tests for the qualitative detection of influenza A and B viral nucleic acid.

DEVICE COMPARISON

Alere™ i Influenza A & B was compared to the legally marketed predicate device, the IQuum Liat ™ Influenza A/B Assay.

Parameter	Alere™ i Influenza A & B	IQuum Liat ™ Influenza A/B Assay (K111387)
FDA Product Code	OCC, OZE, OOI	OCC, OOI
Assay Target	Influenza A, Influenza B	Same
Intended Use	Alere™ i Influenza A & B is a rapid, instrument-based, molecular *in vitro* diagnostic test utilizing isothermal nucleic acid amplification technology for the qualitative detection of influenza A and B viral nucleic acid in nasal swab specimens. It is intended to aid in the rapid differential diagnosis of influenza A and B viral infections in humans in conjunction with clinical and epidemiological risk factors. The assay is not intended to detect the presence of influenza C virus Negative results do not preclude influenza virus infection and should not be used as the sole basis for diagnosis, treatment or other patient management decisions. Performance characteristics for influenza A were established during the 2012-2013 influenza season when influenza A/H3 and A/H1N1 pandemic were the predominant influenza A viruses 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	The IQuum Liat™ Influenza A/B Assay performed on the Liat™ Analyzer is an automated multiplex real-time RT-PCR assay for the rapid *in vitro* qualitative detection and discrimination of influenza A virus and influenza B virus RNA in nasopharyngeal swab specimens from patients with signs and symptoms of respiratory infection in conjunction with clinical and epidemiological risk factors. The test is intended for use as an aid in the differential diagnosis of influenza A and influenza B in humans and is not intended to detect influenza C. Negative results do not preclude influenza virus infection and should not be used as the sole basis for treatment or other patient management decisions. Conversely, 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.

Parameter	Alere™ i Influenza A & B	IQuum Liat ™ Influenza A/B Assay (K111387)
	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 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.	
Intended Environment for Use	Professional use, in a medical laboratory or point-of-care	Professional use, in a medical laboratory
Instrumentation	Alere™ i Instrument	Liat ™ Analyzer
Self-Contained System	Integrated PC, Software, and Touch Screen Display	Same
Automated Assay	Yes. Sample preparation, amplification, detection, and result interpretation.	Same
Assay Information		
Sample Type	Nasal Swab	Nasopharyngeal Swab
Influenza A Viral Target	PB2 segment	Matrix Gene
Influenza B Viral Target	PA segment	Non-Structural Protein (NSP) Gene
Technology	Isothermal nucleic acid amplification for detecting the presence/absence of viral RNA in clinical specimens	RT-PCR for detecting the presence/absence of viral RNA in clinical specimens
Detection Method	Assay uses different reporter dyes for each target	Multiplex assay using different reporter dyes for each target
Internal Control	Yes	Yes
Result Interpretation	Automated	Same
Assay Result	Qualitative	Same
Time to Result	< 15 minutes	~20 minutes

PERFORMANCE SUMMARY

CLINICAL STUDY

Clinical performance characteristics of Alere™ i Influenza A & B were evaluated in a multi-site prospective study during the 2012-2013 flu season in the U.S. A total of eight investigational sites throughout the U.S. participated in the study. To be enrolled in the study, patients had to be presenting at the participating study centers with flu-like symptoms. Direct nasal swab specimens from patients with flu-like symptoms were collected and tested using the Alere™ i Influenza A & B at the eight study sites. Viral culture performed according to standard virology culture procedures, was utilized as the reference method for this study.

Two nasal swabs were collected from one nostril from each subject using standard collection methods. At all sites, one nasal swab was tested directly on Alere™ i Influenza A & B, according to product instructions. The other nasal swab was eluted in 3-mLof viral transport media (VTM). Six of the eight sites (Site 1, Site 4, Site 8, Site 10, Site 11, and Site 12) shipped nasal swab samples in VTM to a central testing laboratory for viral

culture testing. This central testing laboratory was located at Site 1, which also participated as a sample collection and Alere™ i Influenza A & B testing site. The nasal swab samples in VTM from Site 2 and Site 9 were cultured on site by a local laboratory.

External control testing, using Alere™ i Influenza A & B Positive and Negative Controls, was performed prior to sample testing each day and on each Alere™ i instrument the testing was performed, at all study sites.

All specimens generating discrepant Alere™ i Influenza A & B and viral culture results were investigated by testing using an FDA-cleared Influenza RT-PCR assay at a central testing laboratory located at Site 1.

A total of 612 nasal swab specimens were enrolled in this study. Of those, 27 nasal swab specimens did not meet eligibility criteria. A total of 585 direct nasal swab specimens were considered evaluable. Patient age and gender distribution for all the evaluable specimens is presented in the table below.

Age and Gender Distribution – Direct Nasal Swab Study

Age Group	Female	Male
<1 year	56	59
1 to 5 years	108	117
6 to 10 years	55	47
11 to 15 years	21	20
16 to 21 years	14	8
>21 to 60 years	51	20
>60 years	5	4
Total	310	275

Of the evaluable 585 specimens, Alere™ i Influenza A & B generated influenza A invalid results for 14 specimens and influenza B invalid results for 16 specimens, resulting in a total of 571 specimens for influenza A performance analysis and 569 specimens for influenza B performance analysis.

Compared to the viral culture reference method, the performance of Alere™ i Influenza A & B for influenza A and influenza B are presented in the two tables below.

Alere™ i Influenza A & B Influenza A Direct Nasal Swab Performance against Viral Culture

Alere™ i Influenza A & B – Flu A	Culture		
	Positive	Negative	Total
Positive	92	66[a]	158
Negative	2[b]	411	413
Total	94	477	571
Sensitivity: 92/94 97.9% (95%CI: 92.6%-99.4%)			
Specificity: 411/477 86.2% (95%CI: 82.8%-89.0%)			

[a] Flu A nucleic acid was detected in 58/66 False Positive specimens using an FDA-cleared molecular test

[b] Flu A nucleic acid was not detected in 1/2 False Negative specimens using an FDA-cleared molecular test

Alere™ i Influenza A & B Influenza B Direct Nasal Swab Performance against Viral Culture

Alere™ i Influenza A & B – Flu B	Culture		
	Positive	Negative	Total
Positive	74	17[a]	91
Negative	6[b]	472	478
Total	80	489	569
Sensitivity: 74/80 92.5% (95%CI: 84.6%-96.5%)			
Specificity: 472//489 96.5% (95%CI: 94.5%-97.8%)			

[a] Flu B nucleic acid was detected in 15/17 False Positive specimens using an FDA-cleared molecular test

[b] Flu B nucleic acid was not detected in 4/6 False Negative specimens using an FDA-cleared molecular test

Performance of Alere™ i Influenza A & B for the detection of influenza A and influenza B versus culture is presented in the table below stratified by patient age.

Nasal Swab Performance Obtained for Influenza A and Influenza B with the Alere™ i Influenza A & B in Comparison to Viral Culture – Stratified by Patient Age

	≤ 5 Years of Age (n = 332)		6 - ≤ 21 Years of Age (n = 162)		≥ 22 Years of Age (n = 77)	
Influenza Type	**Sensitivity 95% CI**	**Specificity 95% CI**	**Sensitivity 95% CI**	**Specificity 95% CI**	**Sensitivity 95% CI**	**Specificity 95% CI**
Flu A	98.3% (58/59) 91.0% - 99.7%	89.0% (243/273) 84.7% - 92.2%	100% (31/31) 89.0% - 100%	85.5% (112/131) 78.5% - 90.5%	75.0% (3/4) 30.1% - 95.4%	76.7% (56/73) 65.8% - 84.9%
Flu B	88.9% (32/36) 74.7% - 95.6%	98.0% (288/294) 95.6% - 99.1%	94.4% (34/36) 81.9% - 98.5%	96.8% (122/126) 92.1% - 98.8%	100% (8/8) 67.6% - 100%	89.9% (62/69) 80.5% - 95.0%

Alere™ i Influenza A & B detected one mixed influenza A and B infection in the prospective clinical evaluation. This sample tested positive for influenza B only by viral culture, but tested positive for influenza A only by an FDA cleared Influenza RT-PCR assay.

During the prospective clinical study, the initial invalid rate (before repeat testing per the product instructions) was 5.8% (34/585) (95% CI: 4.2% to 8.0%) for Flu A, and 3.6% (21/585) (95% CI: 2.4% to 5.4%) for Flu B. After repeat testing per the product instructions, the invalid rate was 2.4% (14/585) (95% CI: 1.4%, 4.0%) for Flu A, and 2.7% (16/585) (95% CI: 1.7%, 4.4%) for Flu B.

ANALYTICAL STUDIES

ANALYTICAL SENSITIVITY

Alere™ i Influenza A & B limit of detection (LoD) in natural nasal swab matrix was determined by evaluating different concentrations of 3 strains of influenza A and 2 strains of influenza B virus in Alere™ i Influenza A & B. Three strains of influenza A virus representing each of the three common currently or recently circulating influenza A subtypes (i.e., A/H1N1, A/H3N2 seasonal, and A/H1N1 pandemic (pdm)) and two strains of influenza B virus representing each of the two influenza B genetic lineages (i.e., Victoria and Yamagata) were included in this study.

Presumed negative natural nasal swab specimens were eluted in UTM. Swab elutes were combined and mixed thoroughly to create a clinical matrix pool to be used as the diluent. Each influenza virus strain was diluted in this natural nasal swab matrix pool to generate virus dilutions for testing. The vender provided virus strains were re-titered and the concentrations (in $TCID_{50}$/mL) were determined by standard virologic method. The concentration for each dilution (in genome equivalents/mL) was also assessed using laboratory developed and validated influenza A and influenza B quantitative real-time PCR assays.

Contrived nasal swab specimens were prepared by coating 10 microliters of each virus dilution onto the swab. The contrived swab samples were tested according to product instructions.

The LoD for each influenza strain tested was determined as the lowest virus concentration that was detected ≥ 95% of the time (i.e., concentration at which at least 19 out of 20 replicates tested positive).

The confirmed LoDs in natural nasal swab matrix for each influenza strain tested are presented in the table below:

Limit of Detection (LoD) Study Results – Natural Nasal Swab Matrix

Influenza Strain	Influenza A Subtype or Influenza B Genetic Lineage	LoD ($TCID_{50}$/mL)	LoD ($TCID_{50}$/Swab)*	LoD (Genome Equivalents/mL)	LoD (Genome Equivalents/Swab)*
A/Puerto Rico/8/34	A/H1N1	1.88×10^5	1.88×10^3	4.22×10^6	4.22×10^4
A/Perth/16/2009	A/H3N2	8.60×10^2	8.60×10^0	7.91×10^4	7.91×10^2
A/California/7/2009	A/2009 H1N1 pdm	1.25×10^4	1.25×10^2	5.20×10^6	5.20×10^4
B/Malaysia/2506/2004	B Victoria lineage	1.90×10^3	1.90×10^1	7.24×10^4	7.24×10^2
B/Bangladesh/3333/2007	B Yamagata lineage	5.55×10^2	5.55×10^0	7.36×10^4	7.36×10^2

*Note: 10 ul of each virus dilution was coated onto a swab

REACTIVITY TESTING

An analytical reactivity (inclusivity) study was performed to determine whether the Alere™ i Influenza A & B assay is able to detect a variety of influenza A and B strains that represent temporal and geographic diversity.

Vender provided stocks of influenza A and B strains were diluted in UTM to generate virus dilutions for testing. The concentration (in $TCID_{50}$/mL, $CEID_{50}$/mL, or EID_{50}/mL) for each strain was determined by standard virologic method. The concentration for each dilution (in genome equivalents/mL) was also assessed using laboratory developed and validated influenza A and influenza B quantitative real-time PCR assays.

Contrived swab specimens were prepared by coating 10 microliters of virus dilution onto each swab. The contrived swab samples were tested according to product instructions.

The starting dilution concentration selected for testing in this study was higher than the established LoDs in the Limit of Detection study. Each starting dilution per virus strain was tested in triplicates initially. If the initial testing concentration tested positive for all three replicates, the strain was further diluted 10-fold and tested in triplicates until at least one out three replicates generated a negative result. When a negative result was obtained, additional 2-fold dilutions were tested, starting from the highest dilution that produced 100% (3/3) positive results. A concentration level was considered "reactive/positive" in this study for all but one strain tested (i.e., B/Texas/06/2011 – see footnote "c" under the table below) if all three replicates generated a positive result for the expected influenza virus.

The Alere™ i Influenza A & B assay detected all strains tested at the concentrations indicated in the table below:

Analytical Reactivity Study Results

Influenza Strain	Influenza A Subtype or Influenza B Genetic Lineage	Test Concentration (in $TCID_{50}$ or Genome Equivalents, unless indicated otherwise)				Flu A Result (n=3, unless indicated otherwise)	Flu B Result (n=3, unless indicated otherwise)
		$TCID_{50}$/mL	$TCID_{50}$/Swab*	Genome Equivalents/ mL	Genome Equivalents/Swab*		
A/New Caledonia/20/1999[a]	A/H1N1	9.19×10^5	9.19×10^3	4.09×10^6	4.09×10^4	+	-
A/New Jersey/8/76[a]	A/H1N1	3.41×10^1	3.41×10^{-1}	1.52×10^5	1.52×10^3	+	-

A/Brisbane/59/2007[a]	A/H1N1	2.11×10^{4}	2.11×10^{2}	3.39×10^{5}	3.39×10^{3}	+	-
A/WSN/33[a]	A/H1N1	2.11×10^{2}	2.11×10^{0}	2.43×10^{5}	2.43×10^{3}	+	-
A/Port Chalmers/1/73	A/H3N2	4.22×10^{4}	4.22×10^{2}	1.31×10^{6}	1.31×10^{4}	+	-
A/Hong Kong/8/68	A/H3N2	7.03×10^{0}	7.03×10^{-2}	2.70×10^{5}	2.70×10^{3}	+	-
A/Aichi/2/68	A/H3N2	2.08×10^{5}	2.08×10^{3}	7.47×10^{6}	7.47×10^{4}	+	-
A/Victoria/3/75	A/H3N2	3.68×10^{5}	3.68×10^{3}	3.39×10^{6}	3.39×10^{4}	+	-
A/Wisconsin/67/2005	A/H3N2	6.81×10^{4}	6.81×10^{2}	2.57×10^{6}	2.57×10^{4}	+	-
A/Brisbane/10/2007	A/H3N2	3.16×10^{2}	3.16×10^{0}	3.37×10^{5}	3.37×10^{3}	+	-
A/Texas/50/2012	A/H3N2	2.50×10^{0}	2.50×10^{-2}	6.35×10^{3}	6.35×10^{1}	+	-
A/Victoria/361/2011	A/H3N2	1.56×10^{1}	1.56×10^{-1}	3.53×10^{5}	3.53×10^{3}	+	-
A/California/4/2009	A/H1N1 (pdm)	1.47×10^{4}	1.47×10^{2}	1.07×10^{6}	1.07×10^{4}	+	-
A/Maryland/04/2011	A/H1N1 (pdm)	7.88×10^{4}	7.88×10^{2}	3.81×10^{6}	3.81×10^{4}	+	-
A/New York/18/2009	A/H1N1 (pdm)	1.25×10^{2}	1.25×10^{0}	9.16×10^{5}	9.16×10^{3}	+	-
A/Anhui/1/2013 (Inactivated)[a]	A/H7N9 (Detected in China in 2013)	4.00×10^{6} EID_{50}/mL	4.00×10^{4} EID_{50}/Swab	1.72×10^{6}	1.72×10^{4}	+	-
A/Indiana/10/2011[a]	A/H3N2v	2.00×10^{8} EID_{50}/mL	2.00×10^{6} EID_{50}/Swab	2.00×10^{6}	2.00×10^{4}	+	-
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
B/Lee/40	Victoria Lineage	5.00×10^{1} $CEID_{50}$/mL	5.00×10^{-1} $CEID_{50}$/Swab	5.40×10^{4}	5.40×10^{2}	-	+
B/Victoria/504/2000	Victoria Lineage	1.19×10^{3}	1.19×10^{1}	8.29×10^{4}	8.29×10^{2}	-	+
B/Nevada/03/2011	Victoria Lineage	1.75×10^{3}	1.75×10^{1}	1.13×10^{5}	1.13×10^{3}	-	+
B/Montana/05/2012	Victoria Lineage	9.00×10^{1}	9.00×10^{-1}	2.55×10^{4}	2.55×10^{2}	-	+
B/Maryland/1/59	Yamagata Lineage	8.51×10^{2}	8.51×10^{0}	1.13×10^{5}	1.13×10^{3}	-	+
B/Russia/69[b]	Yamagata Lineage	4.44×10^{1}	4.44×10^{-1}	2.96×10^{6}	2.96×10^{4}	-	+
B/Wisconsin/01/2010[c]	Yamagata Lineage	3.68×10^{4}	3.68×10^{2}	1.16×10^{6}	1.16×10^{4}	-	+
B/Massachusetts/2/2012	Yamagata Lineage	6.25×10^{1}	6.25×10^{-1}	2.28×10^{5}	2.28×10^{3}	-	+
B/Texas/06/2011[c]	Yamagata Lineage	2.89×10^{5}	6.25×10^{3}	2.00×10^{6}	2.00×10^{4}	-	+

*Note: 10 ul of each virus dilution was coated onto a swab

[a] Although this test has been shown to detect A/H1N1 (pre-2009 pandemic), A/H7N9 (detected in China in 2013) and A/H3N2v viruses cultured from positive human respiratory specimens, the performance characteristics of this device with clinical specimens that are positive for the A/H1N1 (pre-2009 pandemic), A/H7N9 (detected in China in 2013) and A/H3N2v viruses have not been established.

[b] Influenza B/Russia/69 lowest level in which 3/3 replicates were positive is approximately 40 to 150 x the LoD (as comparing to the Genome Equivalents/Swab values generated in the LoD with simulated clinical matrix study testing B/Malaysia/2506/2004 and B/Brisbane/60/2008, respectively). A polymorphism within segment PA of the Influenza B genome was identified at a position which is 4 nucleotides from the 3'-end of template 2. This G to A polymorphism results in a G/C (product/template) match to an A/C (product/template) mismatch. An A/C mismatch is determined to be moderately destabilizing, and coupled to its position only 4 nucleotides from the 3'-end of the template 2 recognition region, its impact on annealing is potentially great. The frequency of this G to A polymorphism is determined to be very low. In analyzing the strains present in the NCBI Influenza Virus Resource database from 2/2005 to 3/2014 (N=986), no strains contained this polymorphism, suggesting that it has not been circulating for an extended period of time.

[c] Influenza B/Wisconsin/01/2010 lowest level in which 3/3 replicates were positive is approximately 15 to 60 x the LoD, and Influenza B/Texas/06/2011 lowest level in which at least 1/3 replicates were positive is approximately 25 to 100 x the LoD (as comparing to the Genome Equivalents/Swab values generated in the LoD with simulated clinical matrix study testing B/Malaysia/2506/2004 and B/Brisbane/60/2008, respectively). A single G to A polymorphism within segment PA of the Influenza B genome was identified at a position which is 5 nucleotides from the 3'-end of the molecular beacon annealing region in both strains. The G to A polymorphism results in a C/G match to a C/A mismatch between the molecular beacon and product 1. The C/A mismatch is determined to be moderately destabilizing that can significantly reduce assay sensitivity. An assessment of what impact this polymorphism would have on the melting temperature (Tm) of the molecular beacon/product 1 annealing was performed and the results showed a Tm drop from 62.3°C to 55.6°C, just below the assay running temperature. This suggests that annealing would occur, but at a greatly reduced level, with a concomitant loss of assay sensitivity. The frequency of this G to A polymorphism is found at a frequency of approximately 5% within the NCBI Influenza Virus Resource database covering the time frame from 2/2005 through 3/2014.

ANALYTICAL SPECIFICITY (CROSS-REACTIVITY)

To determine the analytical specificity of Alere™ i Influenza A & B, 53 commensal and pathogenic microorganisms (37 bacteria, 15 viruses and 1 yeast) that may be present in the nasal cavity or nasopharynx were tested. All of the following microorganisms were negative when tested at concentrations ranging from

10^8 to 10^{10} cells/mL, CFU/mL or IFU/mL (bacteria), 10^4 to 10^8 $TCID_{50}$/mL or $CEID_{50}$/mL (viruses), and 10^8 cells/mL (yeast).

Bacteria

Acinetobacter calcoaceticus
Bacteroides fragilis
Bordetella pertussis
Chlamydia pneumoniae
Corynebacterium diphtheriae
Enterococcus faecalis
Escherichia coli
Gardnerella vaginalis
Haemophilus influenzae
Klebsiella pneumoniae
Lactobacillus casei
Lactobacillus plantarum
Legionella pneumophila
Listeria monocytogenes
Moraxella/Branhamella catarrhalis
Mycobacterium avium
Mycobacterium intracellulare
Mycobacterium tuberculosis
Mycoplasma pneumoniae
Neisseria gonorrhoeae
Neisseria meningitidis
Neisseria sicca
Neisseria subflava
Proteus vulgaris
Pseudomonas aeruginosa
Serratia marcescens
Staphylococcus aureus
Staphylococcus epidermidis
Streptococcus, Group A
Streptococcus, Group B
Streptococcus, Group C
Streptococcus, Group F
Streptococcus, Group G
Streptococcus mutans
Streptococcus pneumoniae
Streptococcus salivarius
Streptococcus sanguinis

Viruses

Adenovirus type 1
Adenovirus type 7
Human Coronavirus OC43
Human Coronavirus 229E
Enterovirus/Coxsackievirus B4
Human Cytomegalovirus (CMV) (Herpes V)
Epstein Barr Virus
Human metapneumovirus
Measles (Edmonston)
Mumps (Enders)
Parainfluenza 1
Parainfluenza 2
Parainfluenza 3
Respiratory Syncytial Virus type B
Rhinovirus type 1A

Yeast

Candida albicans

INTERFERING SUBSTANCES

The following substances, naturally present in respiratory specimens or that may be artificially introduced into the nasal cavity or nasopharynx, were evaluated with Alere™ i Influenza A & B at the concentrations listed below and were found not to affect test performance.

Substance	Concentration
Mucin	20 µg/mL
Whole Blood	50 µl/mL
Sinus Buster Nasal Spray	200 µl/mL
NeoSynephrine Cold & Sinus Extra Strength Spray	200 µl/mL

Zicam Extreme Congestion Relief	200 µl/mL
4-acetamidophenol	200 µg/mL
Acetylsalicylic acid	650 µg/mL
Albuterol	400 ng/mL
Chlopheniramine	145 ng/mL
Dexamethasone	0.80 mg/mL
Dextromethorphan	1 µl/mL
Diphenhydramine	5 µg/mL
Doxylamine Succinate	236 ng/mL
Ephedrine	237 ng/mL
Flunisolide	6.8 ng/mL
Guaiacol glycerol ether	3.5 ng/mL
Mupirocin	12 mg/mL
Oxymetazoline	0.6 mg/mL
Phenylephrine	12 mg/mL
Rebetol	4.5 µg/mL
Relenza	282 ng/mL
Rimatadine	282 ng/mL
Tamiflu	1.1 µg/mL
Tobryamycin	2.43 mg/mL
Triamcinolone	40 µg/mL

REPRODUCIBILITY

A reproducibility study of Alere™ i Influenza A & B was conducted by operators from three sites using panels of blind coded specimens containing negative, high negative (below the limit of detection), low positive (at the limit of detection), and moderate positive (above the limit of detection) influenza A and B viral samples.

Virus dilutions were prepared using one influenza A strain and one influenza B strain in Universal Transport Medium (UTM). The concentrations of the viral stocks (in $TCID_{50}$/mL) were determined by standard virologic method prior to inactivation by the venders. The concentration for each dilution (in genome equivalents/mL) was also assessed using laboratory developed and validated influenza A and influenza B quantitative real-time PCR assays.

Contrived nasal swab specimens were prepared by coating 10 microliters of each virus dilution onto the swab. The contrived swab samples were tested according to product instructions.

Participants tested each sample multiple times on five different days. The percent agreement with expected results for the influenza A moderate positive, low positive, and high negative samples were 100% (90/90), 100 % (90/90) and 70% (63/90), respectfully. The percent agreement with expected result for the influenza B moderate positive, low positive, and high negative samples were 100% (90/90), 92% (83/90) and 90% (81/90), respectfully. All of the true negative samples (90) generated negative test results. There were no significant differences observed within run (replicates tested by one operator), between run (five different days), between sites (three sites), or between operators (six operators).

The Reproducibility Study site-to-site qualitative results (agreements with expected results) are presented in the table below:

Reproducibility Study Site-To-Site Qualitative Results

Sample Category	SITE						Overall Percent Agreement and 95% CI	
	Site 1		Site 2		Site 3			
	Percent Agreement	Count	Percent Agreement	Count	Percent Agreement	Count		
HN[1] Influenza A	66.7%	20/30	80.0%	24/30	63.3%	19/30	70.0% (63/90)	(59.9%, 78.5%)
LP Influenza A	100%	30/30	100%	30/30	100%	30/30	100% (90/90)	(95.9%, 100%)
MP Influenza A	100%	30/30	100%	30/30	100%	30/30	100% (90/90)	(95.9%, 100%)
HN[1] Influenza B	86.7%	26/30	100%	30/30	83.3%	25/30	90.0% (81/90)	(82.1%, 94.6%)
LP Influenza B	93.3%	28/30	86.7%	26/30	96.7%	29/30	92.2% (83/90)	(84.8%, 96.2%)
MP Influenza B	100%	30/30	100%	30/30	100%	30/30	100% (90/90)	(95.9%, 100.0%)
TN	100%	30/30	100%	30/30	100%	30/30	100% (90/90)	(95.9%, 100%)

[1]Percent Agreement correlates to the percent of negative results.

Signed ____________________________ Date ____________

Angela Drysdale
VP, Regulatory & Clinical Affairs – Infectious Disease
Alere Scarborough, Inc.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

June 13, 2014

Alere Scarborough, Inc.
Angela Drysdale
Vice President, Regulatory and Clinical Affairs – Infectious Disease
10 Southgate Road
Scarborough, ME 04074

Re: K141520
Trade/Device Name: Alere™ i Influenza A&B
Regulation Number: 21 CFR 866.3980
Regulation Name: Respiratory Viral Panel Multiplex Nucleic Acid Assay
Regulatory Class: II
Product Code: OCC, OZE, OOI
Dated: June 06, 2014
Received: June 09, 2014

Dear Ms. Drysdale:

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. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of

medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR 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/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Uwe Scherf -S for

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of In Vitro Diagnostics and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES Food and Drug Administration **Indications for Use**	Form Approved: OMB No. 0910-0120 Expiration Date: January 31, 2017 *See PRA Statement below.*

510(k) Number *(if known)*
K141520

Device Name
Alere™ i Influenza A&B

Indications for Use *(Describe)*
The Alere™ i Influenza A & B assay performed on the Alere™ i Instrument is a rapid molecular in vitro diagnostic test utilizing an isothermal nucleic acid amplification technology for the qualitative detection and discrimination of influenza A and B viral RNA in nasal swabs from patients with signs and symptoms of respiratory infection. It is intended for use as an aid in the differential diagnosis of influenza A and B viral infections in humans in conjunction with clinical and epidemiological risk factors. The assay is not intended to detect the presence of influenza C virus
Negative results do not preclude influenza virus infection and should not be used as the sole basis for diagnosis, treatment or other patient management decisions.

Performance characteristics for influenza A were established during the 2012-2013 influenza season when influenza A/H3 and A/H1N1 pandemic were the predominant influenza A viruses 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 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.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

Tamara V. Feldblyum -S
2014.06.12 09:27:31 -04'00'

This section applies only to requirements of the Paperwork Reduction Act of 1995.

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Department of Health and Human Services
Food and Drug Administration
Office of Chief Information Officer
Paperwork Reduction Act (PRA) Staff
PRAStaff@fda.hhs.gov

"An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB number."