K123620

510(k) Summary

FEB 1 1 2013

Modification of FilmArray® Respiratory Panel (RP)
to add an additional assay to detect Adenovirus

Introduction: According to the requirements of 21 CFR 807.92, the following information provides sufficient detail to understand the basis for a determination of substantial equivalence.

Submitted by:

BioFire Diagnostics, Inc.
390 Wakara Way
Salt Lake City, UT 84108

Telephone: 801-736-6354
Facsimile: 801-588-0507

Contact: Beth Lingenfelter, ext. 407

Date Submitted: November 21, 2012

Device Name and Classification:

Trade Name: FilmArray® Respiratory Panel (RP)

Regulation Number: 21 CFR 866.3980

Classification Name: Respiratory Viral Panel Multiplex Nucleic Acid Assay

Predicate Device:

FilmArray Respiratory Panel (RP) (K103175, K110764 and K120267)

Intended Use:

FilmArray® Respiratory Panel (RP) is a multiplexed nucleic acid test intended for use with the FilmArray Instrument for the simultaneous qualitative detection and identification of multiple respiratory viral and bacterial nucleic acids in nasopharyngeal swabs (NPS) obtained from individuals suspected of respiratory tract infections. The following organism types and subtypes are identified using the FilmArray RP: Adenovirus, Coronavirus 229E, Coronavirus HKU1, Coronavirus NL63, Coronavirus OC43, Human Metapneumovirus, Influenza A, Influenza A subtype H1, Influenza A subtype H3, Influenza A subtype H1-2009, Influenza B, Parainfluenza Virus 1, Parainfluenza Virus 2, Parainfluenza Virus 3, Parainfluenza Virus 4, Human

Rhinovirus/Enterovirus, Respiratory Syncytial Virus, *Bordetella pertussis*, *Chlamydophila pneumoniae*, and *Mycoplasma pneumoniae*. The detection and identification of specific viral and bacterial nucleic acids from individuals exhibiting signs and symptoms of a respiratory infection aids in the diagnosis of respiratory infection if used in conjunction with other clinical and epidemiological information. The results of this test should not be used as the sole basis for diagnosis, treatment, or other management decisions. Negative results in the setting of a respiratory illness may be due to infection with pathogens that are not detected by this test or, lower respiratory tract infection that is not detected by a nasopharyngeal swab specimen. Positive results do not rule out co-infection with other organisms: the agent(s) detected by the Film Array RP may not be the definite cause of disease. Additional laboratory testing (e.g. bacterial and viral culture, immunofluorescence, and radiography) may be necessary when evaluating a patient with possible respiratory tract infection.

Due to the small number of positive specimens collected for certain organisms during the prospective clinical study, performance characteristics for *Bordetella pertussis*, Coronavirus 229E, Coronavirus OC43, Influenza A H1, Influenza A H3, Influenza A H1-2009, Influenza B, *Mycoplasma pneumoniae*, Parainfluenza Virus 1, Parainfluenza Virus 2, and Parainfluenza Virus 4 were established primarily with retrospective clinical specimens. Performance characteristics for *Chlamydophila pneumoniae* were established primarily using contrived clinical specimens.

Due to the genetic similarity between Human Rhinovirus and Enterovirus, the FilmArray RP cannot reliably differentiate them. A positive FilmArray RP Rhinovirus/Enterovirus result should be followed-up using an alternate method (e.g., cell culture or sequence analysis).

The FilmArray RP assay for Coronavirus OC43 may cross-react with some isolates of Coronavirus HKU1. A dual positive result may be due to cross-reactivity or may indicate a co-infection.

Performance characteristics for Influenza A were established when Influenza A H1-2009, A H1, and A H3 were the predominant Influenza A viruses in circulation. Performance of detecting Influenza A may vary if other Influenza A strains are circulating or a novel Influenza A virus emerges. 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 departments for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.

Device Description:

The FilmArray RP System is a multiplex nucleic acid test system composed of the FilmArray instrument, the FilmArray software (preinstalled on a laptop computer) and the FilmArray RP pouch. The FilmArray RP reagent pouch contains freeze-dried reagents

to perform nucleic acid purification, reverse transcription, and nested, multiplex PCR with DNA melt analysis. The RP identifies 20 respiratory pathogens as shown in the following table.

Organisms Detected by the FilmArray Respiratory Panel

Viral Respiratory Pathogens
Adenovirus
Coronavirus 229E
Coronavirus HKU1
Coronavirus NL63
Coronavirus OC43
Human Metapneumovirus
Human Rhinovirus/Enterovirus
Influenza A
H1 subtype
H3 subtype
H1-2009 subtype
Influenza B
Parainfluenza Virus 1
Parainfluenza Virus 2
Parainfluenza Virus 3
Parainfluenza Virus 4
Respiratory Syncytial Virus
Bacterial Respiratory Pathogens
Bordetella pertussis
Chlamydophila pneumoniae
Mycoplasma pneumoniae

A test is initiated by loading Hydration Solution and an unprocessed patient nasopharyngeal swab (NPS) specimen (i.e., specimen mixed with Sample Buffer) into the FilmArray RP pouch. The pouch contains all of the reagents required for specimen testing and analysis in a freeze-dried format; the addition of Hydration Solution and specimen/Sample Buffer Mix rehydrates the reagents. After the pouch is prepared, the FilmArray software guides the user though the steps of placing the pouch into the instrument, scanning the pouch barcode, entering the sample identification, and initiating the run.

The FilmArray instrument contains a coordinated system of inflatable bladders and seal points, which act on the pouch to control the movement of liquid between the pouch blisters. When a bladder is inflated over a reagent blister, it forces liquid from the blister into connecting channels. Alternatively, when a seal is placed over a connecting channel it acts as a valve to open or close a channel. In addition, electronically controlled pneumatic pistons are positioned over multiple plungers in order to deliver the rehydrated reagents into the blisters at the appropriate times. Two Peltier devices control heating and cooling of the pouch to drive the reverse transcription reactions, the PCR reactions, and the melting curve analysis.

Nucleic acid extraction occurs within the FilmArray pouch using mechanical lysis and standard magnetic bead technology. After extracting and purifying nucleic acids from the

unprocessed sample, the FilmArray performs a nested multiplex PCR that is executed in two stages. During the first stage, the FilmArray performs a single, large volume, highly multiplexed reverse transcription PCR (rt-PCR) reaction. The products from first stage PCR are then diluted and combined with a fresh, primer-free master mix and a fluorescent double stranded DNA binding dye (LC Green®Plus, BioFire Diagnostics). This second master mix solution, is then distributed to each well of the array. Array wells contain sets of primers designed specifically to amplify sequences internal to the PCR products generated during the first stage PCR reaction. The second stage PCR, or nested PCR, is performed in singleplex fashion in each well of the array. At the conclusion of the 2nd stage PCR, the array is interrogated by melting curve analysis for the detection of signature amplicons denoting the presence of specific viral or bacterial targets. A digital camera placed in front of the second stage PCR captures fluorescent images of the PCR reactions in real time.

The FilmArray software automatically interprets the results of each DNA melting curve analysis and combines the data with the results of the internal pouch controls to provide a test result for each organism on the panel.

Substantial Equivalence:

The FilmArray RP is substantially equivalent to previously cleared FilmArray RP versions. The following tables compare the modified FilmArray RP to the previously cleared FilmArray RP (K103175, K110764 and K120267). The first table outlines the similarities between the two systems and the following table outlines the differences.

Similarities between the Modified Device and the Predicate.

Element	New Device: FilmArray Respiratory Panel	Predicate: FilmArray Respiratory Panel (K103175, K110764 and K120267)
Organisms Detected	Influenza A, Influenza A subtype H1, Influenza A subtype H3, Influenza A subtype H1-2009 Influenza B, Respiratory Syncytial Virus, Human Metapneumovirus, Adenovirus, Parainfluenza 1, Parainfluenza 2, Parainfluenza virus 3,Parainfluenza 4, Rhinovirus/Enterovirus, Coronavirus HKU1, Coronavirus NL63, Coronavirus 229E, Coronavirus OC43, *Mycoplasma pneumoniae*, *Chlamydophila pneumoniae*, and *Bordetella pertussis*.	Same
Analyte	RNA/DNA	Same
Technological Principles	Multiplex nucleic acid	Same
Specimen Types	Nasopharyngeal swabs	Same

Technological Principles	Nested multiplex RT-PCR followed by high resolution melting analysis to confirm identity of amplified product.	Same
Instrumentation	FilmArray Instrument	Same
Time to result	About 1 hour	Same
Test Interpretation	Automated test interpretation and report generation. User cannot access raw data.	Same
Sample Preparation Method	Sample Processing is automated in the FilmArray RP pouch.	Same
Reagent Storage	Reagents are stored at room temperature.	Same
Controls	Two controls are included in each reagent pouch to control for sample processing and both stages of PCR and melt analysis.	Same
User Complexity	Moderate/Low	Same

Differences between the Modified Device and the Predicate.

Element	**Modified Device: FilmArray Respiratory Panel**	**Predicate: FilmArray Respiratory Panel (K103175, K110764 and K120267)**
Limit of Detection for Adenovirus	100 $TCID_{50}$/mL	300 $TCID_{50}$/mL
Detection of Adenovirus Serotypes	Detects all serotypes with similar sensitivity	Detects Adenovirus species C serotype 2 and serotype 6 with reduced sensitivity.

Summary of Performance Data

Clinical Comparison

The original FilmArray RP was modified by the addition of a second Adenovirus assay. To demonstrate the performance of the modified FilmArray RP, a comparison study was performed by testing 222 de-identified archived nasopharyngeal swab (NPS) specimens collected between 2008 and 2011 throughout the United States (at least 8 geographically distinct locations) and Scotland (at least 1 location) with both the original FilmArray RP and the modified FilmArray RP. A total of 26 Adenovirus specimens were detected by the modified FilmArray RP, of these only 15 were detected by the original FilmArray RP, demonstrating a 73% greater detection rate by the modified FilmArray RP in this clinical comparison study. For the other 19 analytes on the panel, performance appeared to be equivalent between the original and modified FilmArray RP versions.

Performance Comparison of Modified FilmArray RP to Original FilmArray RP using Archived Specimens

Analyte	Positive Agreement				Negative Agreement			
	orig + mod +	orig + mod -	PPA	95% CI	orig - mod -	orig - mod +	NPA	95% CI
Adenovirus	15	0	100% (15/15)	78.2 – 100%	196	11 [a]	94.7% (196/207)	90.7 – 97.3%
CoV 229E	6	0	100% (6/6)	54.1 – 100%	216	0	100% (216/216)	98.3 – 100%
CoV HKU1	8	0	100% (8/8)	63.1 – 100%	214	0	100% (214/214)	98.3 – 100%
CoV NL63	15	1 [b]	93.8% (15/16)	69.8 – 99.8%	206	0	100% (206/206)	98.2 – 100%
CoV OC43	13	0	100% (13/13)	75.3 – 100%	208	1 [c]	99.5% (208/209)	97.4– 100%
hMPV	10	0	100% (10/10)	69.2 – 100%	209	3 [d]	98.6% (209/212)	95.9 – 99.7%
HRV/EV	57	4 [e]	93.4% (57/61)	84.0 – 98.2%	158	3 [e]	98.1% (158/161)	94.6 – 99.6%
Flu A	36	0	100% (36/36)	90.3 – 100%	184	1 [f]	99.5% (184/185)	97.0 – 100%
Flu A H1	9	0	100% (9/9)	66.4 – 100%	213	0	100% (213/213)	98.3 – 100%
Flu A H1 2009	15	0	100% (15/15)	78.2 – 100%	205	1 [f]	99.5% (205/206)	97.3 – 100%
Flu A H3	13	0	100% (13/13)	75.3 – 100%	209	0	100% (209/209)	98.3 – 100%
Flu B	10	0	100% (10/10)	69.2 – 100%	212	0	100% (212/212)	98.3 – 100%
RSV	21	0	100% (21/21)	83.9 – 100%	201	0	100% (201/201)	98.2 – 100%
PIV1	11	0	100% (11/11)	71.5 – 100%	211	0	100% (211/211)	98.3 – 100%

Analyte	Positive Agreement				Negative Agreement			
	orig + mod +	orig + mod -	PPA	95% CI	orig - mod -	orig - mod +	NPA	95% CI
PIV2	8	0	100% (8/8)	63.1 – 100%	214	0	100% (214/214)	98.3 – 100%
PIV3	18	0	100% (18/18)	81.5 – 100%	204	0	100% (204/204)	98.2 – 100%
PIV4	6	0	100% (6/6)	54.1 – 100%	214	2 [g]	99.1% (214/216)	96.7 – 99.9%
B. pertussis	25	1 [h]	96.2% (25/26)	80.4 – 99.9%	196	0	100% (196/196)	98.1 – 100%
C. pneumoniae	1	0	100% (1/1)	n/a	221	0	100% (221/221)	98.3 – 100%
M. pneumoniae	0	0	n/a	n/a	222	0	100% (222/222)	98.4 – 100%

orig = original FilmArray RP, mod = modified FilmArray RP, PPA = positive percent agreement, NPA = negative percent agreement, CI = confidence interval

[a] 10/11 of the additional AdV detections by the modified FilmArray RP were confirmed to contain Adenovirus by bi-directional sequence analysis; these Adenoviruses were identified by sequencing as serotypes C2, C5, C6, E4, and one undetermined serotype. One specimen could not be sequenced due to low analyte levels.

[b] A single specimen was found to be positive for CoV NL63 when tested with the original RP pouch but not the modified RP pouch. The specimen had previously been identified as positive for *B. pertussis* and had not been tested for CoV NL63 by the source laboratory. This specimen previously tested using the original pouch was negative for CoV NL63 . There was insufficient specimen for discrepancy investigation. Low viral load is suspected to have caused this spurious result.

[c] The Coronavirus OC43 discrepancy was due to cross-reactivity between the OC43 assay and HKU1 virus that was detected in the RP modified pouch and not in the original RP pouch.

[d] 2/3 human Metapneumovirus discrepant specimens were confirmed by bi-directional sequence analysis. Low viral load is suspected to have prevented detection by sequencing for the other specimen.

[e] 0/7 Human Rhinovirus/Enterovirus discrepant specimens were confirmed by bi-directional sequence analysis. Low viral load is suspected to have prevented detection by sequencing .

[f] A single specimen containing Influenza A H1-2009 provided repeated equivocal results on the original RP pouch, but was detected by the modified pouch.

[g] Parainfluenza Virus 4 was confirmed in both discrepant specimens by bi-directional sequence analysis.

[h] *B. pertussis* was confirmed in the discrepant specimen by bi-directional sequence analysis.

To supplement the archived specimen data for low prevalence analytes and to provide additional Adenovirus performance data specifically for serotypes C2 and C6, a set of 44 contrived (spiked NPS) specimens (10 AdVC2, 10 AdVC6, 10 *C. pneumoniae*, and 14 *M. pneumoniae*) was tested with both the modified FilmArray RP and the original FilmArray RP. The analyte status of each contrived specimen was blinded to the users analyzing the specimens. The modified FilmArray RP detected all 20 Adenovirus-spiked specimens, while the original FilmArray RP detected none of the Adenovirus-spiked specimens. The modified FilmArray RP also detected another Adenovirus in the background of a specimen spiked with *C. pneumoniae*. Performance appeared to be equivalent between the modified FilmArray RP and the original FilmArray RP for *C. pneumoniae* and *M. pneumoniae*.

Clinical Comparison Data of Modified FilmArray RP to Original FilmArray RP for 44 Contrived Specimens

Analyte	Positive Agreement				Negative Agreement			
	orig + mod +	orig + mod -	PPA	95% CI	orig - mod -	orig - mod +	NPA	95% CI
Adenovirus (C2 and C6)	0	0	n/a	n/a	23	21[a]	52.3% (23/44)	36.7 – 67.5%
C. pneumoniae	8	1	88.9% (8/9)	51.8 – 99.7%	35	0	100% (35/35)	90.0 – 100%
M. pneumoniae	14	0	100% (14/14)	76.8 – 100%	30	0	100% (30/30)	88.4 – 100%

orig = original FilmArray RP, mod = modified FilmArray RP, PPA = positive percent agreement, NPA = negative percent agreement, CI = confidence interval

[a] In addition to ten specimens spiked with Adenovirus C6 and ten specimens spiked with Adenovirus C2, the modified FilmArray RP also detected an Adenovirus in the background of one specimen that had been spiked with *C. pneumoniae*. This detection was confirmed by bi-directional sequence analysis to be Adenovirus C2.

The Adenoviruses detected in archived specimens were categorized into serotype groups using bi-directional sequence analysis. Combining the archived and contrived specimen comparison data demonstrates improved detection of serotypes C2, C5, C6 and E4 by the modified FilmArray RP as compared to the original FilmArray RP.

Adenovirus Serotype Detections by the Modified FilmArray RP and the Original FilmArray RP in Archived and Contrived Specimens

Adenovirus (Serotyped by PCR)	Number of Adenovirus-positive Specimens (as Detected by Modified FilmArray RP)	Detections by Original FilmArray RP
AdVC1	8	8/8 (100%)
AdVC2	15[a]	2/15 (13%)
AdVC5	2	1/2 (50%)
AdVC6	16[a]	1/16 (6%)
AdVB3	1	1/1 (100%)
AdVE4	3	2/3 (67%)
AdV serotype unknown	2	0/2 (0%)

[a] Ten C2 specimens and ten C6 specimens were contrived by spiking these viruses into NPS specimens. One C2 was also detected and sequence confirmed in the background of a specimen spiked with *C. pneumoniae*.

Selected Analytic Studies

Limit of Detection

The analytical sensitivity or Limit of Detection (LoD) for Adenovirus was determined by testing limiting dilutions of quantified cultures with the modified FilmArray RP. LoD is defined as the lowest concentration at which the analyte is consistently detected (detection in ≥95% of samples tested). Simulated NPS sample matrix (cultured human cells in VTM) was spiked with Adenovirus and 20 replicates were tested at the estimated LoD concentration of 100 $TCID_{50}$/mL for each of four respiratory serotypes (AdVC1, AdVC2, AdVE4 and AdVC6). Adenovirus was detected in all 20 replicates for each

serotype and the system LoD for Adenovirus was reduced from 300 $TCID_{50}$/mL with the original panel to 100 $TCID_{50}$/mL in the modified panel.

Adenovirus Serotype	Modified FilmArray RP			Original FilmArray RP
	LoD ($TCID_{50}$/mL)	# Positive	% Positive	Estimated LoD ($TCID_{50}$/mL)
AdVC1	100	20/20	100.0%	300
AdVC2	100	20/20	100.0%	30,000
AdVE4	100	20/20	100.0%	300
AdVC6	100	20/20	100.0%	3,000,000

The LoD for all other analytes detected by the FilmArray RP was found to be equivalent between the original and modified panels by testing replicate samples at LoD level as well as bracketing levels.

Analytical Reactivity (Inclusivity)

The analytical reactivity of the modified FilmArray RP system was evaluated with an Adenovirus inclusivity panel representing 6 species (A-F) and 22 serotypes. These included both respiratory and non-respiratory adenovirus isolates. The modified FilmArray RP is designed to detect all respiratory species/serotypes of Adenovirus (B, C, and E). Detection of non-respiratory species (A, D, F and G) will vary. It is important to note that the presence of non-respiratory species of Adenovirus in clinical respiratory specimens is expected to be rare. Variable detection of these viruses by the FilmArray RP should have little to no impact on the clinical performance (sensitivity) of the system.

Samples were tested with both the original and modified panels at the Adenovirus LoD established for the modified panel (100 $TCID_{50}$/mL). If an Adenovirus isolate was not detected by the modified panel at LoD, testing was repeated at 10x LoD (1,000 $TCID_{50}$/mL). Testing above 10x LoD was not performed. Some reactivity with serotypes listed as Not Detected (ND) may be observed if present in a sample at high levels.

AdVB55 and AdVC57 are the only respiratory serotypes that were not evaluated for inclusivity. Available sequence information for these serotypes indicates a perfect match to FilmArray Adenovirus assay primers and efficient detection at 1x LoD is predicted.

Inclusivity Results for Adenovirus Respiratory Species/Serotypes Tested with the Original and Modified FilmArray RP

Species	Type	Isolate	Test Level	x LoD	Original FilmArray RP	Modified FilmArray RP
B	3	Zeptometrix #0810062CF	100 $TCID_{50}$/mL	1x	Detected	Detected
	7a	Zeptometrix #0810021CF	100 $TCID_{50}$/mL	1x	Detected	Detected
	7d2	Iowa/2001	100 $TCID_{50}$/mL	1x	Detected	Detected
	7h	Iowa/1999	100 $TCID_{50}$/mL	1x	Detected	Detected

Species	Type	Isolate	Test Level	x LoD	Original FilmArray RP	Modified FilmArray RP
	11	Wisconsin/2005	100 $TCID_{50}$/mL	1x	ND	Detected
	14	Missouri/2005	100 $TCID_{50}$/mL	1x	ND	Detected
	16	ATCC VR-17	100 $TCID_{50}$/mL	1x	Detected	Detected
	21	Missouri/2005	100 $TCID_{50}$/mL	1x	ND	Detected
	34	UIRF-Texas/2005	100 $TCID_{50}$/mL	1x	ND	Detected
	35	ATCC VR-718	100 $TCID_{50}$/mL	1x	ND	Detected
	50	ATCC VR-1602	100 $TCID_{50}$/mL	1x	ND	Detected
C	1	Zeptometrix #0810050CF	100 $TCID_{50}$/mL	1x	Detected	Detected [a]
	2	New York/2001	100 $TCID_{50}$/mL	1x	ND	Detected
		ATCC VR-846	100 $TCID_{50}$/mL	1x	ND	Detected
		Clinical isolate #266153	100 $TCID_{50}$/mL	1x	ND	Detected
		Clinical isolate #266161	100 $TCID_{50}$/mL	1x	ND	Detected
		Clinical isolate #266213	100 $TCID_{50}$/mL	1x	ND	Detected
	5	Zeptometrix #0810020CF	100 $TCID_{50}$/mL	1x	ND	Detected
	6	Colorado/2005	100 $TCID_{50}$/mL	1x	ND	Detected
		ATCC VR-6	100 $TCID_{50}$/mL	1x	ND	Detected
		Clinical isolate #274924	100 $TCID_{50}$/mL	1x	ND	Detected
		Clinical isolate #274948	100 $TCID_{50}$/mL	1x	ND	Detected
		Clinical isolate #275032	100 $TCID_{50}$/mL	1x	ND	Detected
E	4a	South Carolina/2004	100 $TCID_{50}$/mL	1x	Detected	Detected
	4p3	New Jersey/2005	100 $TCID_{50}$/mL	1x	Detected	Detected

[a] The initial test of AdVC1 with the modified FilmArray RP pouch was invalid due to a control failure. Adenovirus was detected on the retest.

Inclusivity Results for Non-Respiratory Adenovirus Species/Serotypes Tested with the Original and Modified FilmArray RP

Species	Type	Isolate	Test Level	x LoD	Original FilmArray RP	Modified FilmArray RP
A	12	ATCC VR-863	1,000 $TCID_{50}$/mL	10x	ND	ND
	18	ATCC VR-19	1,000 $TCID_{50}$/mL	10x	ND	ND
	31	Zeptometrix #0810073CF	1,000 $TCID_{50}$/mL	10x	Detected	Detected
D	8	Zeptometrix #0810069CF	100 $TCID_{50}$/mL	1x	ND	Detected
	20	Zeptometrix #0810115CF	100 $TCID_{50}$/mL	1x	Detected	Detected
	37	Zeptometrix #0810119CF	100 $TCID_{50}$/mL	1x	Detected [a]	Detected
F	40	Zeptometrix #0810084CF	1,000 $TCID_{50}$/mL	10x	ND	ND
	41	Indiana/2004	100 $TCID_{50}$/mL	1x	Detected	Detected [b]

[a] The initial test of AdVD37 at 1x LoD in the original FilmArray RP pouch was negative. Adenovirus was detected on the retest.
[b] The initial test of AdVF41 at 1x LoD in the modified FilmArray RP pouch was negative. Adenovirus was detected on the retest.

Analytical Specificity (Cross-reactivity and Exclusivity)

The potential for cross-reactivity with organisms detected by the FilmArray RP was evaluated by testing simulated NPS samples containing high concentrations of respiratory panel viruses and bacteria (tens to thousands-fold higher than LoD) with the modified panel. No cross-reactivity was observed.

NOTE: Although not observed in this study, the Coronavirus OC43 assay may cross-react with certain strains of Coronavirus HKU1 when present in the sample at high concentrations.

Results of Cross-reactivity Testing with the Modified FilmArray RP – RP Organisms

Analyte	Type / Strain / ID	Test Concentration	Multiple of LoD Tested
Adenovirus	AdVC1	1.00E+05 $TCID_{50}$/mL	1,000x
Coronavirus	229E ATCC VR-740	5.67E+03 $TCID_{50}$/mL	1,418x
	HKU1 Clinical specimen	1.34E+08 RNA copies/mL	70 x
	NL63 NR-470	5.67E+03 TCID50/mL	1,134x
	OC43 ATCC VR-759	7.30E+04 $TCID_{50}$/mL	122x
Human Metapneumovirus	Type A1 - hMPV-16 IA10-2003	8.17E+03 $TCID_{50}$/mL	4,085x
Human Rhinovirus /	Echovirus 6	3.40E+06 $TCID_{50}$/mL	113x

Analyte	Type / Strain / ID	Test Concentration	Multiple of LoD Tested
Enterovirus	Rhinovirus 1A	5.67E+03 TCID50/mL	5,670x
Influenza A H1N1	A/Brisbane/59/07	1.00E+05 $TCID_{50}$/mL	500x
Influenza A H1-2009	A/SwineNY/03/2009	8.40E+05 $TCID_{50}$/mL	840x
Influenza A H3N2	A/Wisconsin/67/2005	8.17E+03 $TCID_{50}$/mL	1634x
Influenza B	B/FL/04/06	1.67E+04 $TCID_{50}$/mL	278x
Parainfluenza Virus	Type 1	1.39E+04 $TCID_{50}$/mL	28x
	Type 2	1.67E+04 $TCID_{50}$/mL	1,670x
	Type 3	1.00E+05 $TCID_{50}$/mL	10,000x
	Type 4a	5.67E+03 $TCID_{50}$/mL[a]	1.13x
Respiratory Syncytial Virus	Type A	1.39E+04 $TCID_{50}$/mL	6,950x
Bordetella pertussis	A639	1.00E+06 CFU/mL	250x
Chlamydophila pneumoniae	TW183	2.42E+05 copies/mL	.81x
Mycoplasma pneumoniae	M129	1.88E+05 TCID50/mL	6,267x

[a] Highest test concentration possible based on the concentration of virus in the stock culture fluid.

The potential for the FilmArray RP system to cross-react with non-FilmArray RP organisms was evaluated by testing an exclusivity panel consisting of 26 bacteria, 6 viruses, and 1 yeast. These organisms were selected based on their relatedness to FilmArray RP organisms, clinical relevance (cause respiratory symptoms or represent nasopharyngeal flora), or high prevalence within the population (e.g. Herpes Simplex Virus). Negative sample matrix was spiked with bacteria or fungi at a concentration of 10^6 CFU/mL and viruses at a concentration between 10^4 - 10^5 $TCID_{50}$/mL, or the highest concentration possible. The modified FilmArray RP system did not cross-react with the exclusivity panel organisms.

Results of Exclusivity Testing with the Modified FilmArray RP – Non-RP Organisms

Virus	Strain / Isolate
Bocavirus	Clinical Specimen
Cytomegalovirus (CMV)	AD-169 (VR-538)
Epstein-Barr Virus (EBV)	B95-8
Herpes Simplex Virus	Type 1
Measles Virus	Edmonston
Mumps	Zeptometrix # 0810079CF
Yeast	**Strain / Isolate**
Candida albicans	Zeptometrix #0801504
Bacterium	**Strain / Isolate**

Bordetella bronchiseptica	clinical isolate
Bordetella holmesii	F061
Bordetella parapertussis	A747
Chlamydia trachomatis	D-UW3
Corynebacterium diptheriae	ATCC14779
Escherichia coli	O157:H7
Haemophilus influenzae	MinnA
Lactobacillus acidophilus	Type strain
Lactobacillus plantarum	17-5
Legionella longbeacheae	Long Beach 4
Legionella micdadei	Tatlock
Legionella pneumophilia	Philadelphia
Moraxella catarrhalis	Ne 11 (type strain)
Mycobacterium tuberculosis	H37Ra-1
Mycoplasma hominis	ATCC 23114
Mycoplasma genitalium	ATCC 33530
Neisseria elongata	type strain
Neisseria gonorrhoeae	ATCC 700825
Neisseria meningitidis	M1027 (type strain)
Pseudomonas aeruginosa	Zeptometrix #0801519
Staphylococcus aureus	COL
Staphylococcus epidermidis	RP62A
Streptococcus pneumoniae	type 59
Streptococcus pyogenes	Zeptometrix #0801512
Streptococcus salivarius	ATCC 13419
Ureaplasma urealyticum	ATCC 27618

Competitive Interference

Interference testing was performed by preparing simulated NPS samples with a combination of two respiratory viruses, with one being Adenovirus. The competing viruses were selected based on the dominant Adenovirus co-infections documented in the FilmArray RP Clinical Evaluation. In total, five different virus combinations (co-infections) were evaluated with each virus tested at a low level (LoD for organism) and at a high or competing level (~ 5,000 – 100,000 $TCID_{50}$/mL).

The modified FilmArray RP demonstrated improved detection of Adenoviruses compared to detection in the original panel. This is consistent with the improved analytical sensitivity and reactivity for Adenovirus in the modified panel. There were no signs of interference or inaccurate results with competing organisms in a sample.

Results for Adenovirus Co-infection Samples Tested with the Original and Modified FilmArray RP

Sample	LoD Virus	Competing Virus	Original FilmArray RP Result	Modified FilmArray RP Result
1a	AdVC1	HRV	Adenovirus Human Rhinovirus/Enterovirus	Adenovirus Human Rhinovirus/Enterovirus
1b	HRV	AdVC1	Adenovirus Human Rhinovirus/Enterovirus	Adenovirus Human Rhinovirus/Enterovirus
2a	AdVC5	hMPV	- Human Metapneumovirus	Adenovirus Human Metapneumovirus
2b	hMPV	AdVC5	Adenovirus Human Metapneumovirus	Adenovirus Human Metapneumovirus
3a	AdVC6	RSV	- Respiratory Syncytial Virus	Adenovirus Respiratory Syncytial Virus
3b	RSV	AdVC6	- Respiratory Syncytial Virus	Adenovirus Respiratory Syncytial Virus
4a	AdVB7h	AdVE4p3	Adenovirus	Adenovirus
4b	AdVE4p3	AdVB7h	Adenovirus	Adenovirus
5a	AdVC2	AdVB21	Adenovirus	Adenovirus
5b	AdVB21	AdVC2	Adenovirus	Adenovirus

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-002

FEB 1 1 2013

BioFire Diagnostics, Inc.
C/O Beth Lingenfelter, M.S.
390 Wakara Way
Salt Lake City, UT 84108

Re: k123620
Trade/Device Name: FilmArray® Respiratory Panel (RP)
Regulation Number: 21 CFR 866.3980
Regulation Name: Respiratory Viral Panel Multiplex Nucleic Acid Assay
Regulatory Class: Class II
Product Code: OCC, OEM, OOU, OEP, OTG, OQW, OOI, OZZ, OZY, OZX
Dated: November 21, 2012
Received: November 23, 2012

Dear Ms. Lingenfelter:

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 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 Part 801); 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 regulation (21 CFR Parts 801 and 809), please contact the Office of *In Vitro* Diagnostics and Radiological Health 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

Sally 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

Indications for Use

510(k) Number (if known): K123620

Device Name: FilmArray® Respiratory Panel (RP)

FilmArray® Respiratory Panel (RP) is a multiplexed nucleic acid test intended for use with the FilmArray Instrument for the simultaneous qualitative detection and identification of multiple respiratory viral and bacterial nucleic acids in nasopharyngeal swabs (NPS) obtained from individuals suspected of respiratory tract infections. The following organism types and subtypes are identified using the FilmArray RP: Adenovirus, Coronavirus 229E, Coronavirus HKU1, Coronavirus NL63, Coronavirus OC43, Human Metapneumovirus, Influenza A, Influenza A subtype H1, Influenza A subtype H3, Influenza A subtype H1-2009, Influenza B, Parainfluenza Virus 1, Parainfluenza Virus 2, Parainfluenza Virus 3, Parainfluenza Virus 4, Human Rhinovirus/Enterovirus, Respiratory Syncytial Virus, *Bordetella pertussis*, *Chlamydophila pneumoniae*, and *Mycoplasma pneumoniae*. The detection and identification of specific viral and bacterial nucleic acids from individuals exhibiting signs and symptoms of a respiratory infection aids in the diagnosis of respiratory infection if used in conjunction with other clinical and epidemiological information. The results of this test should not be used as the sole basis for diagnosis, treatment, or other management decisions. Negative results in the setting of a respiratory illness may be due to infection with pathogens that are not detected by this test or, lower respiratory tract infection that is not detected by a nasopharyngeal swab specimen. Positive results do not rule out co-infection with other organisms: the agent(s) detected by the FilmArray RP may not be the definite cause of disease. Additional laboratory testing (e.g. bacterial and viral culture, immunofluorescence, and radiography) may be necessary when evaluating a patient with possible respiratory tract infection.

Due to the small number of positive specimens collected for certain organisms during the prospective clinical study, performance characteristics for *Bordetella pertussis*, Coronavirus 229E, Coronavirus OC43, Influenza A H1, Influenza A H3, Influenza A H1-2009, Influenza B, *Mycoplasma pneumoniae*, Parainfluenza Virus 1, Parainfluenza Virus 2, and Parainfluenza Virus 4 were established primarily with retrospective clinical specimens. Performance characteristics for *Chlamydophila pneumoniae* were established primarily using contrived clinical specimens.

Due to the genetic similarity between Human Rhinovirus and Enterovirus, the FilmArray RP cannot reliably differentiate them. A positive FilmArray RP Rhinovirus/Enterovirus result should be followed-up using an alternate method (e.g., cell culture or sequence analysis).

The FilmArray RP assay for Coronavirus OC43 may cross-react with some isolates of Coronavirus HKU1. A dual positive result may be due to cross-reactivity or may indicate a co-infection.

Performance characteristics for Influenza A were established when Influenza A H1-2009, A H1, and A H3 were the predominant Influenza A viruses in circulation. Performance of detecting Influenza A may vary if other Influenza A strains are circulating or a novel Influenza A virus emerges. 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 departments 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* Diagnostics and Radiological Health (OIR)

Tamara Feldblyum

Division Sign-Off

Office of In Vitro Diagnostics and Radiological Health

510(k) K123620