K103209

Nanosphere

JAN 10 2011

510(k) Summary

This 510(k) Summary is being submitted in accordance with the requirements of SMDA 1900 and CFR 807.92.

510(k) numbers:	K103209: Verigene® Respiratory Virus Plus Nucleic Acid Test on the Verigene® System (RV+)
Summary preparation date:	December 28, 2010
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Proprietary names:	*For instrument:* Verigene® System *For the assay:* Verigene® Respiratory Virus Plus Nucleic Acid Test on the Verigene® System (RV+)
Common names:	*For the instrument:* Bench-top molecular diagnostics workstation *For the assay:* Respiratory viral panel multiplex nucleic acid assay Respiratory panel assay with sub-typing: – Flu A (H3, H1, 2009H1N1) – Flu B – RSV (RSV A, RSV B)
Regulatory information:	Regulation section: 866.3980 Respiratory viral panel multiplex nucleic acid assay Class II *Panel*: Microbiology (83) *Product Code*: OCC (Respiratory viral panel multiplex nucleic acid assay)

Comparison of RVNAT$_{SP}$ and RV+:	The instrumentation used with the **RVNAT$_{SP}$ (K092566)** and the **RV+** is identical. The Verigene® System utilized for both assays allows sample preparation, target amplification, and hybridization test and analysis using a single system. The **RVNAT$_{SP}$** and the **RV+** reagents and substrate have been modified to allow subtyping of Influenza A (H3, H1, 2009H1N1) and RSV (RSV A, RSV B). The safety and effectiveness of the Verigene® Respiratory Virus Plus Nucleic Acid Test on the Verigene System (**RV+**) are demonstrated with the analytical and methods comparison studies described below.
Device description:	The **RV+** is designed to identify virus-specific nucleic acids for Influenza A virus, Influenza A virus subtype H1, Influenza A virus subtype H3, Influenza A virus subtype 2009 H1N1, Influenza B virus, and respiratory syncytial virus (RSV A. RSV B). The RVNAT$_{SP}$ involves: 1) Sample Preparation – magnetic bead-based viral RNA extraction from nasopharyngeal swab specimens obtained from symptomatic patients; 2) Target Amplification – multiplex RT-PCR-based amplification of the eluted viral RNA targets to generate virus-specific amplicons; 3) Verigene Hybridization Test and Analysis – detection and identification of virus-specific amplicons by using gold nanoparticle probe-based technology. The entire **RV+** test is performed on the Verigene® System, which is a bench-top molecular diagnostics workstation that consists of two instruments, the **Verigene Processor *SP*** and the **Verigene Reader**. The Verigene Processor *SP* performs the assay steps on each sample by using a robotic pipettor to transfer and mix reagents within and between separate testing modules designed for nucleic acid extraction, target amplification, and the Verigene Hybridization Test. The Verigene Hybridization Test module is the same as in the original Verigene System with added modules for nucleic acid extraction and RT-PCR target amplification. Key functions of the Verigene Processor *SP* include: 1) Reading of the barcode identification label on inserted Test Consumables to maintain positive identification of patient samples throughout processing. 2) Facilitation of nucleic acid extraction, multiplex RT-PCR target amplification, and the Verigene Hybridization Test. 3) Real-time communication of test processing status to the Reader. The Verigene Reader is the same instrument as in the FDA-cleared RVNAT$_{SP}$. It is a free-standing instrument with a touch screen control panel and a wand-based barcode scanner. It utilizes a graphical user interface to guide the user through the process of ordering tests and reporting results. There are no serviceable parts and no user calibration is required. Interaction with the touch screen is minimized through barcode use. This instrument also serves as the reader of the Test Cartridges using advanced optics. The key functions of the Verigene Reader include: 1) Entry and tracking of specimen identification numbers via manual keyboard input or via barcode-reader wand. 2) Test selection for each specimen. 3) Automated transfer of specimen processing instructions on Test Cartridge-specific basis to linked Processor *SP* unit(s). A single Reader unit can control up to 32 Processor units. 4) Automated imaging and analysis of Test Cartridges. 5) Results display. 6) Results report generation. RV+ consumables within each single-use disposable test kit include: (i) Tip Holder Assembly; (ii) Extraction Tray; (iii) Amplification Tray; and (iv) RV+ Test Cartridge. The kit components are inserted into the corresponding module of the Verigene Processor *SP* prior to each test, and the sample is added to the Extraction Tray. Patient information is entered into the Reader to initiate the test procedure. 1) Tip Holder Assembly – The robotic pipettor picks up pipettes from the Tip Holder Assembly. The pipettes are used for mixing and transferring reagents within the test procedure.

	2) Extraction Tray – Nucleic acids are extracted from the sample by using magnetic bead-based methods within the Extraction Tray. Each Tray contains reagents for a single extraction procedure. A robotic pipette transfers reagents to designated wells within the Extraction Tray to affect the steps of lysis, capture of nucleic acids onto the magnetic beads, washing, and eluting the isolated nucleic acids from the magnetic beads. 3) Amplification Tray – The isolated nucleic acids are amplified by using multiplex RT-PCR within the Amplification Tray. Each Tray contains reagents for a single multiplex RT-PCR procedure. A robotic pipette transfers the reagents to a specific well within the Amplification Tray. A set thermal profile is then initiated to perform all of the amplification related steps including UDG-based decontamination, reverse transcription, and multiplex PCR in a single tube. Upon completion, an aliquot of the amplified sample is mixed with hybridization buffer containing the virus specific mediator probes. The sample is then transferred to the Test Cartridge. 4) RV+ Test Cartridge for Verigene Hybridization Test – The virus-specific and subtype-specific amplicons are detected and identified within a Test Cartridge by using specific nucleic acid probes in conjunction with gold nanoparticle probe-based detection technology. Each Test Cartridge is a self-contained, laboratory consumable that consists of two parts. The upper housing of each cartridge is called the "reagent pack" and contains reservoirs filled with the detection reagents. When in place with the 'substrate holder', the reagent pack creates an air-tight hybridization chamber surrounding the region of the substrate containing a target-specific capture array. As each step of the test is completed, old reagents are moved out of the hybridization chamber and new reagents are added from the reagent pack via microfluidic channels and pumps. Once the test is complete, the Test Cartridge is removed from the Verigene Processor *SP* unit and the reagent pack is snapped off and discarded. The remaining slide is now ready for imaging and analysis in the Verigene Reader. 5) End-point detection on the Verigene Reader: The test slide is inserted into the Verigene Reader wherein it is illuminated along its side. The gold-silver aggregates at the test sites scatter the light, which is in turn captured by a photosensor. The relative intensity arising from each arrayed test site is tabulated. Net signals, defined as the absolute signal intensities with background signals subtracted, are compared with thresholds determined by negative controls within the slide in order to arrive at a decision regarding the presence or absence of target. These results are linked to the test and patient information entered at the beginning of each test session to provide a comprehensive results file.
Intended use:	The **Verigene® Respiratory Virus Plus Nucleic Acid Test on the Verigene® System (RV+)** is a qualitative nucleic acid multiplex test intended to simultaneously detect and identify multiple respiratory virus nucleic acids in nasopharyngeal (NP) swab specimens from individuals with signs and symptoms of respiratory tract infection. The following virus types and subtypes are identified using the RV+: Influenza A, Influenza A subtype H1, Influenza A subtype H3, 2009 H1N1, Influenza B, Respiratory Syncytial Virus (RSV) subtype A, and RSV subtype B. The test is not intended to detect Influenza C virus. Detecting and identifying 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. Negative results for Influenza A, Influenza B, or RSV do not preclude influenza virus or RSV infection and should not be used as the sole basis for diagnosis, treatment, or 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. The use of additional laboratory testing and clinical presentation must be considered in order to obtain the final diagnosis of respiratory viral infection. Performance characteristics for Influenza A Virus were established when Influenza A/H3, A/H1, and 2009 H1N1 were the predominant Influenza A viruses circulating. These characteristics may vary when other Influenza A viruses are emerging. 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 used specifically 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.

Predicate devices:	Two cleared predicate devices were utilized: the Verigene® Respiratory Virus Nucleic Acid Test ($RVNAT_{SP}$; K092566) and the Prodesse ProFAST+ assay (K101855). The $RVNAT_{SP}$ is a multiplex *in vitro* diagnostic test for the rapid and qualitative detection and discrimination of Influenza A Virus, Influenza B Virus, and Respiratory Syncytial Virus (RSV). The ProFAST+ is a multiplex Real Time RT-PCR *in vitro* diagnostic test for the qualitative detection and discrimination of seasonal Influenza A/H1, seasonal Influenza A/H3 and 2009 H1N1 Influenza viral nucleic acids isolated and purified from nasopharyngeal (NP) swab specimens from human patients with signs and symptoms of respiratory.

Comparison between the Cleared and the New Systems

Feature	Verigene RV+ Subject Device	Verigene RVNAT SP Predicate 1	Prodesse ProFAST+ Predicate 2
510(k) #	K103209	K092566	K101855
Regulation	866.3980	866.3980	866.3332
Product Codes	OCC	OCC; NSU	OQW
Device Class	Class II	Class II	Class II
Intended Use	The Verigene® Respiratory Virus Plus Nucleic Acid Test (RV+) on the Verigene® System is a qualitative nucleic acid multiplex test intended to simultaneously detect and identify multiple respiratory virus nucleic acids in nasopharyngeal (NP) swab specimens from individuals with signs and symptoms of respiratory tract infection. The following virus types and subtypes are identified using the RV+: Influenza A, Influenza A subtype H1, Influenza A subtype H3, 2009 H1N1, Influenza B, Respiratory Syncytial Virus (RSV) subtype A, and RSV subtype B. The test is not intended to detect Influenza C virus. Detecting and identifying 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.	The Verigene® Respiratory Virus Nucleic Acid Test ($RVNAT_{SP}$) is a qualitative multiplex *in vitro* diagnostic test for the detection and identification of Influenza A Virus, Influenza B Virus, and Respiratory Syncytial Virus (RSV) nucleic acids purified from nasopharyngeal swab specimens obtained from patients symptomatic for viral upper respiratory infection.	The Prodesse ProFAST+ Assay is a multiplex Real Time RT-PCR *in vitro* diagnostic test for the qualitative detection and discrimination of seasonal Influenza A/H1, seasonal Influenza A/H3 and Influenza A/2009 H1N1 Influenza viral nucleic acids isolated and purified from nasopharyngeal (NP) swab specimens from human patients with signs and symptoms of respiratory infection in conjunction with clinical and epidemiological risk factors.
Targets	Influenza A Influenza A/H1 Influenza A/H3 Influenza A/2009 H1N1 Influenza B RSV A RSV B	Influenza A Influenza B RSV	Influenza A/H1 Influenza A/H3 Influenza A/2009 H1N1

Specimen	Nasopharyngeal swabs in sample matrix	Nasopharyngeal swabs in sample matrix	Nasopharyngeal swabs in sample matrix
Nucleic Acid Isolation	Automated internal extraction of nucleic acids performed on the Processor SP using silica coated magnetic beads and chaotropic salts.	Automated internal extraction of nucleic acids performed on the Processor SP using silica coated magnetic beads and chaotropic salts.	External isolation of nucleic acids on the Roche MagNA Pure LC System and bioMerieux NucliSENS easyMAG.
Quality control	Internal procedural quality controls: IC1 – inhibition control; IC2 – process control; internal positive and negative controls; external positive controls	Internal procedural quality controls: PC1 (IC1) – inhibition control; PC2 (IC2) – process control; internal positive and negative controls; external positive controls	Influenza positive RNA transcript control and an internal RNA control provided
Amplification method	Internal multiplexed RT-PCR performed within the Amplification Module on the Processor SP	Internal multiplexed RT-PCR performed within the Amplification Module on the Processor SP	Real Time RT-PCR detection
	M-MLV Reverse Transcriptase	M-MLV Reverse Transcriptase	M-MLV Reverse Transcriptase
Pipetting	Pipetting module to automate fluid transfer steps	Pipetting module to automate fluid transfer steps	Mostly manual
Detection Method	Verigene Test (hybridization) is performed in the hybridization module housed in the Processor SP of the Verigene® System by using single-use Test Cartridges	Verigene Test (hybridization) is performed in the hybridization module housed in the Processor SP of the Verigene® System by using single-use Test Cartridges	In the Cepheid Smartcycler II instrument, the amount of fluorescence at a given cycle is dependent on the amount of amplification products present at the time
Decision algorithm	Target-specific signal intensities are compared to a signal threshold and ratioed against positive and negative controls for a decision.	Target-specific signal intensities are compared to a signal threshold and ratioed against positive and negative controls for a decision.	Fluorescent intensity is monitored during each PCR cycle by the real-time instrument. A specific number of cycles are defined as a threshold for presence or absence of a target.
Results	Positive or negative qualitative results	Positive or negative qualitative results	Positive or negative qualitative results
Reader	Provides the user interface, controls the Processor SP, performs image analysis, and provides results.	Provides the user interface, controls the Processor SP, performs image analysis, and provides results.	Not applicable
Software	A custom embedded software application running under the Micro-C/OS real-time operating system. Additional software programming to control the Extraction and Amplification Modules.	A custom embedded software application running under the Micro-C/OS real-time operating system. Additional software programming to control the Extraction and Amplification Modules.	Not applicable

Performance Characteristics of the RV+ Test

Analytical and methods comparison studies to establish the performance of the test on the Verigene System were performed.

A. Analytical Studies for the RV+ Test - Overview

In order to establish analytical performance characteristics of the RV+, various analytical studies were conducted by following recommendations delineated in FDA Guidance Documents. The studies included Analytical Sensitivity Determination, Analytical Reactivity Studies, Analytical Specificity Studies, Interference Studies, Competitive Inhibition Studies, Carry-Over/Cross-Contamination Studies, Fresh-vs-Frozen Comparison Studies, and Assay Design and Cut-Off Determination. The results from these studies supported a claim of safety and effectiveness and support the proposed labeling of the RV+.

B. Methods Comparison Studies for the RV+ Test

A Methods Comparison study was conducted at three sites. The study was conducted under IRB supervision.

The Verigene System, including the Verigene Processor *SP*, the Verigene Reader, the Verigene Respiratory Virus Plus Nucleic Acid Test Cartridges (RV+), Amplification Trays and Extraction Trays used in the methods comparison studies were identical to the devices intended for market with respect to their functional features and reagent composition.

Clinical samples for methods comparison study were collected prospectively at three collection hospital sites during the 2008-2009 and 2009-2010 respiratory seasons. Each site saved prospectively-collected residual specimens that were then de-identified on-site, frozen at -70°C, and shipped on dry ice to Nanosphere. Nanosphere stored the specimens at -70°C, labeled the specimens with a random number generated unique identifier while removing the collection site identifier, and shipped the specimens to the testing sites overnight on dry ice. The sites stored the specimens at -70°C before and after testing.

One thousand and twenty-two (1022) prospectively-collected specimens were tested at the three external study sites. All tests were performed by laboratory personnel using the RV+ on the Verigene System. The Influenza A, Influenza B and RSV results in the methods comparison study were compared to results obtained for the samples using culture-based methods confirmed with a FDA-cleared DFA test. Influenza A subtyping and RSV subtyping results were compared to results obtained for the specimens utilizing bi-directional sequencing. Discordant results were resolved utilizing bi-directional sequencing and/or the NAAT. Seven (7) samples that were deemed discrepant for the RV+ test compared to culture/DFA were tested on the NAAT for further clarification of results.

The age distribution of the 1022 samples tested during the methods comparison study is presented below.

Age Distribution in the RV+ Methods Comparison Study

Age Categorization (yrs)	Number of Subjects	Proportion (%)
0-2	269	26.3%
3-5	118	11.5%
6-11	147	14.4%
12-18	124	12.1%
19-64	297	29.1%
≥ 65	67	6.6%
All Ages	1022	100%

During the methods comparison study, across all three sites, there were a total of 25 processing errors (2.4%=25/1022) ("pre-analysis error" [pre-ae] results). There were 34 initial "no call" results (3.3%=34/1022). Both the "no call" and "pre-ae" specimens were repeated and only 2 resulted in a final "no call" result (0.2%=2/1022).

Combined results for the method comparison study across the three sites are presented below. They reflect the results after all "no call" results were repeated per the protocol and the proposed package insert guidance. Results from the RV+ were initially compared to results from culture-based - DFA methods and the NAAT test. Bi-directional sequencing was used to subtype Influenza A, differentiate RSV A and RSV B, and for discordant testing. The tables show results for Influenza A, Influenza B, and RSV both compared to culture-based methods and the NAAT and after resolution using sequencing. RSV A and RSV B results are shown after resolution by sequencing.

Percent positive and negative agreement for each table are provided as well as the lower and upper two-sided 95% confidence limits that were calculated using the exact binomial method.

Influenza A and subtyping results for all three sites combined:

Influenza A Results: RV+ vs. Culture/DFA

INFA		Culture/DFA			
		Positive	Negative	Total	Total
RV+	Positive	311 [a, c]	48 [b]	359	Sensitivity = 98.7% (96.8%-99.5%) 95% CI
	Negative	4 [d, e, f]	659	663	Specificity = 93.2% (91.1%-94.8%) 95% CI
	Total	315	707	1022 [g]	

[a] 1 specimen was positive for Influenza A by both culture and **RV+**. No sub-typing was observed on the **RV+** result. Also, the specimen failed subtype sequencing for H1, H3 and 2009 H1N1. [b] 4 specimens were Influenza A positive by **RV+**. No sub-typing was observed on the **RV+**. All 4 specimens were culture negative and failed sequencing. [c] 1 specimen was Influenza A/H1 by **RV+** and positive for Influenza A by culture. Sequencing resulted in a positive result for Influenza A/2009H1N1. [d] 1 specimen was negative by **RV+** for Flu A and positive for Flu B. Initial culture/DFA of the specimen was Flu A positive. By sequencing, the specimen was positive for Flu B and negative for Flu A. By NAAT and upon repeat culture/DFA, the specimen was positive for Flu B and negative for Flu A and RSV. [e] 1 specimen was negative for Flu A and positive for RSV B by **RV+**. By initial culture/DFA, the specimen was Flu A positive. By sequencing the specimen was positive for RSV B and negative for Flu A. By NAAT and upon repeat culture/DFA the specimen was positive for RSV and negative for Flu A and Flu B. [f] 2 specimens were negative by **RV+** but Flu A positive by culture. By sequencing both specimens were negative for Flu A. Both specimens were negative for Flu A (and negative for Flu B and RSV B) by NAAT. [g] 5 specimens failed sequencing or were not subtyped by the **RV+** assay and are not included in the Subtyping Tables.

Influenza A Subtype H3 Results: RV+ vs. Culture/DFA/Sequencing

INFA/H3		Culture/DFA/Sequencing			
		Positive	Negative	Total	Total
RV+	Positive	108	0	108	Sensitivity = 100% (96.6%-100%) 95% CI
	Negative	0	909	909	Specificity = 100% (99.6%-100%) 95% CI
	Total	108	909	1017	

Influenza A Subtype H1 Results: RV+ vs. Culture/DFA/Sequencing

INFA/H1		Culture/DFA/Sequencing			
		Positive	Negative	Total	Total
RV+	Positive	39	1[c]	40	Sensitivity = 100% (91.0%-100%) 95% CI
	Negative	0	977	977	Specificity = 99.9% (99.4%-100%) 95% CI
	Total	39	978	1017	

Influenza A Subtype 2009 H1N1 Results: RV+ vs. Culture/DFA/Sequencing

INFA/2009 H1N1		Culture/DFA/Sequencing			
		Positive	Negative	Total	Total
RV+	Positive	206	0	206	Sensitivity = 99.5% (97.3%-99.9%) 95% CI
	Negative	1[c]	810	811	Specificity = 100% (99.5%-100%) 95% CI
	Total	207	810	1017	

Influenza B results for all three sites combined:

Influenza B Results: RV+ vs. Culture/DFA

INFB		Culture/DFA			
		Positive	Negative	Total	Total
RV+	Positive	43	3 [a, b]	46	Sensitivity = 100% (91.8%-100%) 95% CI
	Negative	0	976	976	Specificity = 99.7% (99.1%-99.9%) 95% CI
	Total	43	979	1022	

[a] 1 specimen was positive for Influenza B by **RV+** and negative for Influenza B by culture/DFA. This specimen was tested by NAAT assay and found to be positive for Influenza B. Specimen was positive for Influenza B by sequencing and upon repeat culture/DFA. [b] 2 specimens were positive for Influenza B by **RV+** and negative for Influenza B by culture. Both specimens were positive for Influenza B by sequencing.

Influenza RSV and subtyping results for all three sites combined:

RSV Results: RV+ vs. Culture/DFA

RSV		Culture/DFA			
		Positive	Negative	Total	Total
RV+	Positive	104	5 [a, d]	109	Sensitivity = 97.2% (92.1%-99.0%) 95% CI
	Negative	3 [b, c]	910	913	Specificity = 99.5% (98.7%-99.8%) 95% CI
	Total	107	915	1022 [e]	

[a] 1 specimen was positive for RSV B by **RV+** and by sequencing but negative for RSV by culture/DFA. Specimen was positive for RSV by NAAT and upon repeat culture/DFA. [b] 1 specimen was negative for RSV by **RV+** and by sequencing but positive for RSV by culture and NAAT assay. [c] 2 specimens were negative for RSV by **RV+** and positive for RSV by culture. The specimens were negative for RSV by NAAT assay and failed sequencing. [d] 4 specimens were positive for RSV A or RSV B by **RV+** but negative by culture: 1 was positive for RSV A and 3 were positive for RSV B by **RV+** and by sequencing. [e] 3 specimens failed subtype sequencing and are not included in the Subtyping Tables.

RSV Subtype A Results: RV+ vs. Culture/DFA/Sequencing

RSV A		Culture/DFA/Sequencing			
		Positive	Negative	Total	Total
RV+	Positive	57 [f]	0	57	Sensitivity = 100% (93.7%-100%) 95% CI
	Negative	0	962	962	Specificity = 100% (99.6%-100%) 95% CI
	Total	57	962	1019	

[f] 1 specimen was positive for both RSV A and RSV B (dual infection) by **RV+** and was culture positive for RSV. By sequencing specimen was positive for both RSV A and RSV B.

RSV Subtype B Results: RV+ vs. Culture/DFA/Sequencing

RSV B		Culture/DFA/Sequencing			
		Positive	Negative	Total	Total
RV+	Positive	53 [f]	0	53	Sensitivity = 100% (93.2%-100%) 95% CI
	Negative	0	966	966	Specificity = 99.9% (99.6%-100%) 95% CI
	Total	53	966	1019	

[f] 1 specimen was positive for both RSV A and RSV B (dual infection) by **RV+** and was culture positive for RSV. By sequencing specimen was positive for both RSV A and RSV B.

C. Reproducibility/Precision Studies for the RV+ Test

The Reproducibility/Precision study was conducted at three sites (two external and one internal) to investigate the inter-laboratory reproducibility of the **RV+**. The reproducibility panels (see Table below) were developed by using 6 unique virus strains that together represented all of the analytes in the **RV+**. The 6 virus strains were combined to generate combinations such that each virus strain was represented at 3 levels: HN- High Negative, LP - Low Positive, and MP - Moderate Positive. For two of the unique samples, virus strains were combined as in the case of INFA/H3 and RSVA and Influenza B and RSV B. For the Reproducibility/Precision study, the Test Panel comprised the 12 unique samples in duplicate for a total of 24 samples. The Test Panel samples were then divided equally into Panel A (12 samples) and Panel B (12 samples).

Viral Panel	Virus Strain	Level	Samples
A	INFB + RSVB	High Negative	1
			2
		Low Positive	3
			4
		Moderate Positive	5
			6
	INFA/2009H1N1-MT	High Negative	7
			8
		Low Positive	9
			10
		Moderate Positive	11
			12
B	INFA/H1-MT	High Negative	1
			2
		Low Positive	3
			4
		Moderate Positive	5
			6
	INFA/H3 + RSVA	High Negative	7
			8
		Low Positive	9
			10
		Moderate Positive	11
			12

At the two external study sites, Test Panel A and Test Panel B were tested on separate days. Testing each day involved 2 operators testing the same Test Panel in two replicate runs. Both Test Panels A and B were tested for a total testing period of six non-consecutive days.

The internal site ran a 12-day precision study and utilized the same four unique samples at the three levels. The complete Test Panel (Test Panel A and B) was tested separately by two operators each day. The precision study was run for a total testing period of 12 non-consecutive days. The cumulative results from the Reproducibility/Precision Studies are summarized. Data is presented for each individual site and then combined to provide collective results. The Table contains the agreement between the expected results and the obtained results for each virus strain in the Test Panel. These are grouped further based on their concentration levels (MP, LP, and HN). NOTE: Though some samples in the Test Panels contained combinations of viruses, results are stratified by individual virus strains.

Reproducibility Study Results – Agreement to Specific Panel Member

Site		Site 1	Site 2	Site 3	All 3 Sites		
Specific Panel Member	Level	Agreement	Agreement	Agreement	Total Agreement	% Agreement	95% CI
INFA/H1-MT	MP	12/12	12/12	46/48[1,2]	70/72	97.2%	90.4% - 99.2%
	LP	12/12	12/12	48/48	72/72	100%	94.9% - 100%
	HN	11/12[3]	12/12	48/48	71/72	98.6%	92.5% - 99.8%
INFA/H3	MP	12/12	12/12	48/48	72/72	100%	94.9% - 100%
	LP	12/12	12/12	47/48[4]	71/72	98.6%	92.5% - 99.8%
	HN	12/12	12/12	48/48	72/72	100%	94.9% - 100%
INFA/2009H1N1-MT	MP	12/12	12/12	48/48	72/72	100%	94.9% - 100%
	LP	12/12	12/12	48/48	72/72	100%	94.9% - 100%
	HN	12/12	12/12	47/48[5]	71/72	98.6%	92.5% - 99.8%
INFB	MP	12/12	12/12	48/48	72/72	100%	94.9% - 100%
	LP	12/12	12/12	48/48	72/72	100%	94.9% - 100%
	HN	12/12	11/12[a]	48/48	71/72	98.6%	92.5% - 99.8%
RSVA	MP	12/12	12/12	48/48	72/72	100%	94.9% - 100%
	LP	12/12	12/12	46/48[b,4]	70/72	97.2%	90.4% - 99.2%
	HN	12/12	12/12	48/48	72/72	100%	94.9% - 100%
RSVB	MP	12/12	12/12	48/48	72/72	100%	94.9% - 100%
	LP	11/12[c]	12/12	47/48[d]	70/72	97.2%	90.4% - 99.4%
	HN	11/12[e]	12/12	48/48	71/72	98.60%	92.5% - 99.8%

Expected Calls: [a]One (1) INFB + RSVB HN detected Influenza B. [b]One (1) INFA/H3 + RSVA LP sample detected Influenza A and H3 but did not detect RSV A. [c]One (1) INFB + RSVB LP sample detected Influenza B but did not detect RSV B. [d]One INFB + RSVB LP sample detected Influenza B but did not detect RSV B. [e]One INFB + RSVB HN sample detected RSV B but did not detect Influenza B. Additional Positive Calls: [1]One (1) INFA/H1-MT MP sample detected both Influenza A and H1 as expected, but also detected H3 which was unexpected. [2]One (1) INFA/H1-MT MP sample detected both Influenza A and H1 as expected, but also detected H3, Flu B and RSV A which was unexpected. [3]One (1) INFA/H1-MT HN sample detected Influenza A, but did not detect H1 which was expected as this is a high negative sample. However, RSV A was also detected which was unexpected. [4]One INFA/H3 + RSVA LP sample detected both Influenza A, H3 and RSV A as expected for a low positive sample, but also detected 2009H1N1 which was not expected. [5]One INFA/2009H1N1-MT HN sample did not detect Influenza A and 2009H1N1 which was expected as this is a high negative sample. However, Influenza B and RSV B were also detected which was not expected. NOTE: All the samples with additional positive calls gave the expected results for the intended virus; there were no mis-calls. The source of the additional positives is likely cross-contamination artifacts during the Test Panel preparation.

There were 14 "No Calls" and 2 "pre-analytical errors" in the study. These 16 samples were repeat tested successfully. In this study the "No Call" rate was 1.6% (14/864) and the "pre-analysis error" failure rate was 0.2% (2/864). Out of the 864 samples tested, the percent agreement for all panel members for the combined sites ranged from 97.2%-100% (95% CI range from 90.3% - 99.7% to 95.0% - 100.0%, respectively).

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

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JAN 10 2011

Re: K103209
Trade/Device Name: Verigene Respiratory Virus Plus Nucleic Acid Test (RV+)
Regulation Number: 21 CFR§ 866.3980
Regulation Name: Respiratory viral panel multiplex nucleic acid assay
Regulatory Class: Class II
Product Code: OCC; NSU
Dated: December 23, 2010
Received: December 27, 2010

Dear Dr. Shipp:

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

JAN 10 2011

510(k) Number (if known): ____ K103209_____

Device Name: Verigene® Respiratory Virus Plus Nucleic Acid Test (RV+)

The Verigene® Respiratory Virus Plus Nucleic Acid Test (RV+) on the Verigene® System is a qualitative nucleic acid multiplex test intended to simultaneously detect and identify multiple respiratory virus nucleic acids in nasopharyngeal (NP) swab specimens from individuals with signs and symptoms of respiratory tract infection. The following virus types and subtypes are identified using the RV+: Influenza A, Influenza A subtype H1, Influenza A subtype H3, 2009 H1N1, Influenza B, Respiratory Syncytial Virus (RSV) subtype A, and RSV subtype B. The test is not intended to detect Influenza C virus. Detecting and identifying 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.

Negative results for Influenza A, Influenza B, or RSV do not preclude influenza virus or RSV infection and should not be used as the sole basis for diagnosis, treatment, or 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. The use of additional laboratory testing and clinical presentation must be considered in order to obtain the final diagnosis of respiratory viral infection.

Performance characteristics for Influenza A Virus were established when Influenza A/H3, A/H1, and 2009 H1N1 were the predominant Influenza A viruses circulating. These characteristics may vary when other Influenza A viruses are emerging.

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 used specifically 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.

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)

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

Concurrence of CDRH, Office of In Vitro Diagnostic Devices (OIVD)

510(k) K103209