510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

k120049

B. Purpose for Submission:

New Device

C. Measurand:

Influenza A and B nucleoprotein antigens in nasopharyngeal wash/aspirate samples

D. Type of Test:

Qualitative immunochromatogenic assay

E. Applicant:

Becton Dickenson and Company

F. Proprietary and Established Names:

BD Veritor System for Rapid Detection of Flu A+B

G. Regulatory Information:

1. Regulation section:

   21 CFR § 866.3330, Influenza Serological Reagents

2. Classification:

   Class I

3. Product code:

   GNX, Antigens, including CF controls, Influenza A, B, and C

4. Panel:

   Microbiology (83)

H. Intended Use:

1. Intended use(s):

The BD Veritor™ System for Rapid Detection of Flu A+B is a rapid chromatographic immunoassay for the direct and qualitative detection of influenza A and B viral nucleoprotein antigens from nasopharyngeal wash/aspirates of symptomatic patients. The BD Veritor System for Rapid Detection of Flu A+B is a differentiated test, such that influenza A viral antigens can be distinguished from influenza B viral antigens from a single processed sample using a single device. The test is to be used as an aid in the diagnosis of influenza A and B viral infections. A negative test is presumptive and it is recommended that these results be confirmed by viral culture or an FDA-cleared influenza A and B molecular assay. Negative test results do not preclude influenza viral infection and should not be used as the sole basis for treatment or other patient management decisions. The test is not intended to detect influenza C antigens.

Performance characteristics for influenza A and B were established during January through March of 2011 when influenza viruses A/2009 H1N1, A/H3N2, B/Victoria lineage, and B/Yamagata lineage were the predominant influenza viruses in circulation according to the *Morbidity and Mortality Weekly Report* from the CDC entitled "Update: Influenza Activity—United States, 2010-2011 Season, and Composition of the 2011-2012 Influenza Vaccine." Performance characteristics may vary against other emerging influenza viruses.

If infection with a novel influenza 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 the state or local health department for testing. Virus culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.

2. Indication(s) for use:

Same as Intended Use

3. Special conditions for use statement(s):

The device is for prescription use only

4. Special instrument requirements:

Requires the use of the BD Veritor System Reader

I. Device Description:

The BD Flu A+B test is a chromatographic assay to qualitatively detect influenza A and B viral nucleoprotein antigens in samples processed from respiratory specimens (nasopharyngeal wash/aspirates). The processed specimen is added to the test device where

influenza A or influenza B viral antigens bind to anti-influenza antibodies conjugated to detector particles on the A+B test strip. The antigen-conjugate complex migrates across the test strip to the reaction area and is captured by an antibody line on the membrane. Results are interpreted by the BD Veritor™ System Reader, a portable electronic device which uses a reflectance-based measurement method to evaluate the line signal intensities on the assay test strip, and applies specific algorithms to determine the presence or absence of any target analyte(s). A liquid crystal display (LCD) on the instrument communicates the results to the operator.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Quidel QuickVue Influenza A+B

2. Predicate 510(k) number(s):

   k053146

3. Comparison with predicate:

The BD Veritor™ System for Rapid Detection of Flu A+B was compared to the Quidel QuickVue Influenza A+B test (k053146).

Product Feature	BD Veritor™ System for Flu A+B	Quidel QuickVue Influenza A+B (k053146)

Intended Use	The BD Veritor™ System for Rapid Detection of Flu A+B is a rapid chromatographic immunoassay for the direct and qualitative detection of influenza A and B viral nucleoprotein antigens from nasopharyngeal wash/aspirates of symptomatic patients. The BD Veritor System for Rapid Detection of Flu A+B is a differentiated test, such that influenza A viral antigens can be distinguished from influenza B viral antigens from a single processed sample using a single device. The test is to be used as an aid in the diagnosis of influenza A and B viral infections. A negative test is presumptive and it is recommended that these results be confirmed by viral culture or an FDA-cleared influenza A and B molecular assay. Negative test results do not preclude influenza viral infection and should not be used as the sole basis for treatment or other patient management decisions. The test is not intended to detect influenza C antigens. Performance characteristics for influenza A and B were established during January through March of 2011 when influenza viruses A/2009 H1N1, A/H3N2, B/Victoria lineage, and B/Yamagata lineage were the predominant influenza viruses in circulation according to the *Morbidity and Mortality Weekly Report* from the CDC entitled "Update: Influenza Activity—United States, 2010-2011 Season, and Composition of the 2011-2012 Influenza Vaccine." Performance characteristics may vary against other emerging influenza viruses. If infection with a novel influenza 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 the state or local health department for testing. Virus culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens	The QuickVue® Influenza A+B test allows for the rapid, qualitative detection of influenza type A and type B antigens directly from nasal swab, nasopharyngeal swab, nasal aspirate, and nasal wash specimens. The test is intended for use as an aid in the rapid differential diagnosis of acute influenza type A and type B viral infections. The test is not intended to detect influenza C antigens. Negative results should be confirmed by cell culture; they do not preclude influenza virus infection and should not be used as the sole basis for treatment or other management decisions. The test is intended for professional and laboratory use.

Specimen Types	Nasopharyngeal wash/aspirates	Nasal swab, nasopharyngeal swab, nasal wash/aspirate
Assay Technology	Immunochromatographic	Immunochromatographic
Detection Format	An opto-electronic reader determines the line intensity at each of the spatially-defined test and control line positions, interprets the results using the scoring algorithm, and reports a positive, negative, or invalid result on the LCD screen based on pre-set thresholds.	Visual determination of presence or absence of pink-to-red Test Line and the appearance of a blue Procedural Control Line on the test strip indicate the presence of influenza A and/or B antigen.
Qualitative	Yes	Yes
Total Assay Time	Approximately 10 minutes	Less than 15 minutes
Control format	• Kit Flu A+/B− dry swab procedural control • Kit Flu B+/A− dry swab procedural control • Internal positive control • Internal negative control	• Kit Flu A+ control swab • Kit Flu B+ control swab • Kit Negative control swab • Internal control lines
Detection of Flu A and B viruses	Differentiated influenza A and influenza B	Differentiated influenza A and influenza B

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

Not Applicable

L. Test Principle:

The BD Flu A+B test is a chromatographic assay to qualitatively detect influenza A and B viral antigens (nucleoproteins) in nasopharyngeal wash/aspirates specimens. The patient specimen is mixed in a prefilled unitized tube containing RV Reagent C and added to the test device. RV Reagent C contains mucolytic agents that function to break down mucus in a patient specimen thereby exposing viral antigens and enhancing detection in the assay device. Processed specimens are expressed through a filter tip into a single sample well on the BD Flu A+B test device.

The processed specimen flows thru the test device where influenza A or influenza B viral antigens bind to anti-influenza antibodies conjugated to detector particles on the A+B test strip. The antigen-conjugate complex migrates across the test strip to the reaction area and is captured by an antibody line on the membrane. The assay utilizes a proprietary enhanced colloidal-gold particle at the test lines as the means for identifying the presence of influenza A or B viral antigens and requires the use of the BD Flu A+B Veritor System Reader.

The BD Flu A+B test devices are designed with five spatially-distinct zones including positive and negative control line positions, separate test line positions for the target analytes, and a background zone. The test lines for the target analytes are labeled on the test device as

'A' for flu A position, and 'B' for flu B position. The onboard positive control ensures the sample has flowed correctly and is indicated on the test device as 'C'. Two of the five distinct zones on the test device are not labeled. These two zones are an onboard negative control line and an assay background zone. The onboard negative control zone addresses non-specific signal generation and is not labeled on the test device. The remaining zone is used to measure the assay background and is also not labeled.

The BD Flu A+B assay incorporates an active negative control feature in each test to identify and compensate for sample-related, nonspecific signal generation. The BD Veritor™ System Reader uses a proprietary algorithm which subtracts nonspecific signal at the negative control line from the signal present at both the Flu A and Flu B test lines. If the resultant test line signal is above a pre-selected assay cutoff, the specimen is scored as positive. If the resultant test line signal is below the cutoff, the specimen is scored as negative. Use of the active negative control feature allows the BD Veritor™ System reader to correctly interpret test results that cannot be scored visually because the human eye is unable to accurately perform the subtraction of the nonspecific signal. The BD Veritor™ System Reader measures the amount of light reflected from various zones along the assay strip. The measurement of the assay background zone is an important factor during test interpretation as the reflectance is compared to that of the control and test zones. A background area that is white to light pink indicates the device has performed correctly. The instrument analyzes the reflectance data to provide the proper interpretation.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

The reproducibility of the BD Veritor System for Rapid Detection of Flu A+B test was evaluated at three clinical laboratory sites. The reproducibility panel was composed of 30 simulated influenza A or B samples. These included moderate positive samples, low positive samples (near the assay limit of detection), high negative samples (i.e., containing very low concentrations of virus such that positive results occur ~5% of the time) and negative samples. The results are summarized below.

Reproducibility Results – Percent of Flu A Positives				
Sample	**Site 1**	**Site 2**	**Site 3**	**Total**
High negative H1N1 A	3.3% (1/30) (95% C.I. 0.6%-16.7%)	0.0% (0/30) (95% C.I. 0.0%-11.3%)	0.0% (0/30) (95% C.I. 0.0%-11.3%)	1.1% (1/90) (95% C.I. 0.2%-6.0%)
Low positive H1N1 A	93.3% (28/30) (95% C.I. 78.7%-98.2%)	86.7% (26/30) (95% C.I. 70.3%-94.7%)	93.3% (28/30) (95% C.I. 78.7%-98.2%)	91.1% (82/90) (95% C.I. 83.4%-95.4%)
Moderate positive H1N1 A	100.0% (30/30) (95% C.I. 88.6%-100.0%)	96.7% (29/30) (95% C.I. 83.3%-99.4%)	100.0% (30/30) (95% C.I. 88.6%-100.0%)	98.9% (89/90) (95% C.I. 94.0%-99.8%)

Reproducibility Results – Percent of Flu A Positives				
Sample	**Site 1**	**Site 2**	**Site 3**	**Total**
High negative H3N2 A	16.7% (5/30) (95% C.I. 7.3%-33.6%)	3.3% (1/30) (95% C.I. 0.6%-16.7%)	0.0% (0/30) (95% C.I. 0.0%-11.3%)	6.7% (6/90) (95% C.I. 3.1%-13.8%)
Low positive H3N2 A	93.3% (28/30) (95% C.I. 78.7%-98.2%)	86.7% (26/30) (95% C.I. 70.3%-94.7%)	93.3% (28/30) (95% C.I. 78.7%-98.2%)	91.1% (82/90) (95% C.I. 83.4%-95.4%)
Moderate positive H3N2 A	100.0% (30/30) (95% C.I. 88.6%-100.0%)	100.0% (30/30) (95% C.I. 88.6%-100.0%)	96.7% (29/30) (95% C.I. 83.3%-99.4%)	98.9% (89/90) (95% C.I. 94.0%-99.8%)
Negatives	0.8% (1/120) (95% C.I. 0.1%-4.6%)	0.0% (0/120) (95% C.I. 0.0%-3.1%)	0.0% (0/119) (95% C.I. 0.0%-3.1%)	0.3% (1/359) (95% C.I. 0.0%-1.6%)

Reproducibility Results – Percent of Flu B Positives				
Sample	**Site 1**	**Site 2**	**Site 3**	**Total**
High negative B	3.3% (1/30) (0.6%,16.7%)	0.0% (0/30) (0.0%,11.3%)	0.0% (0/30) (0.0%,11.3%)	1.1% (1/90) (0.2%,6.0%)
Low positive B	90.0% (27/30) (74.4%,96.5%)	63.3% (19/30) (45.5%,78.1%)	82.8% (24/29) (65.5%,92.4%)	78.7% (70/89) (69.0%,85.9%)
Moderate positive B	96.7% (29/30) (83.3%,99.4%)	100.0% (30/30) (88.6%,100.0%)	100.0% (30/30) (88.6%,100.0%)	98.9% (89/90) (94.0%,99.8%)
Flu B Negatives	0.0% (0/210) (0%,1.8.0%)	0.0% (0/210) (0.0%,1.8%)	0.0% (0/210) (0.0%,1.8%)	0.0% (0/630) (0.0%,0.6%)

b. Linearity/assay reportable range:

Not Applicable

c. Traceability, Stability, Expected values (controls, calibrators, or methods):

Not Applicable

d. Detection limit:

All strains used to establish the analytical limit of detection were re-grown and re-titered. Serial 10-fold dilutions were made to determine the lowest detectable analyte level. Further characterization was carried out using a narrower range of dilutions.

The LoD was then determined as the concentration producing at least a 95% positivity rate. This concentration was tested using 20 or 60 replicates to define the LoD. The LoD data is shown in the table below.

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Type	Influenza Viral Strain	Calculated LOD ($TCID_{50}$/mL)	No. Positive / Total	% Positive
A	A/Brisbane/10/2007 H3N2	7.27×10^2	57/60	95%
A	A/Brisbane/59/2007 H1N1	3.30×10^2	57/60	95%
A	A/California/7/2009 H1N1	5.00×10^3	57/60	95%
A	A/Victoria/3/75 H3N2	3.11×10^3	59/60	98.3%
B	B/Brisbane/60/2008	7.42×10^3	58/60	96.7%
B	B/Florida/4/2006	1.30×10^3	58/60	96.7%
B	B/Lee/40	4.44×10^4	20/20	100%

e. Analytical specificity:

An analytical study to evaluate 51 microorganisms (36 bacteria, one yeast, and 14 viruses) for potential false positive reactions (cross-reactivity) with the BD Flu A+B test was done. Each of the bacteria (36) and yeast (1) were cultured on appropriate plated media. Bacteria and yeast were tested at a target concentration of approximately 10^7 CFU/mL, with the exception of *Staphylococcus aureus*, which was tested at a final concentration of 10^6 CFU/mL. The organisms were diluted if necessary with saline (10- to 100-fold) from stock in order to achieve the target concentration.

The 14 viruses were evaluated at concentrations of 10^3 to $10^{10}TCID_{50}$/mL and all viruses were tested at the stock concentration with the exception of Respiratory Syncytial Virus, which was diluted 10-fold from stock in saline.

All bacteria, yeast and viral frozen stock cultures were thawed and brought to room temperature prior to preparing target concentrations for testing. Three hundred (300) microliters of each organism suspension were added to the unitized tube of RV Reagent C and the attached filter tip was snapped in place. The sample was mixed and three drops of the suspension were added to the test well of a BD Flu A+B device. After 10 minutes at room temperature, the device was inserted into the BD Veritor™ System Reader for interpretation. All determinations were performed in triplicate with no cross reactivity observed for any of the tested organisms.

Microorganism Name	Concentration Tested	Cross Reactivity with Flu A	Cross Reactivity with Flu B
Bacteriodes fragilis	6.5×10^7 CFU/mL	No	No
Bordetella pertussis	5.0×10^7 CFU/mL	No	No
Candida albicans	3.5×10^7 CFU/mL	No	No
Chlamydia pneumoniae	$2.8 \times 10^6 TCID_{50}$/mL	No	No
Corynebacterium diphtherium	1.5×10^7 CFU/mL	No	No
Escherichia coli	1.5×10^7 CFU/mL	No	No
Fusobacterium nucleatum	1.2×10^7 CFU/mL	No	No
Haemophilus influenzae	1.5×10^7 CFU/mL	No	No
Haemophilus parainfluenzae	1.0×10^7 CFU/mL	No	No
Kingella kingae	5.0×10^7 CFU/mL	No	No
Klebsiella pneumoniae	1.5×10^7 CFU/mL	No	No
Lactobacillus sp.	1.5×10^7 CFU/mL	No	No
Legionella sp.	1.5×10^7 CFU/mL	No	No
Moraxella catarrhalis	5.0×10^7 CFU/mL	No	No
Mycobacterium tuberculosis	5.0×10^8 CFU/mL	No	No
Mycoplasma pneumoniae	5.0×10^7 CFU/mL	No	No
Neisseria gonorrhoeae	1.0×10^7 CFU/mL	No	No
Neisseria meningitidis	2.5×10^7 CFU/mL	No	No
Neisseria mucosa	2.0×10^7 CFU/mL	No	No
Neisseria sp.(Neisseria perflaus)	1.5×10^7 CFU/mL	No	No
Neisseria subflava	5.0×10^7 CFU/mL	No	No
Peptostreptococcus anaerobius	8.0×10^7 CFU/mL	No	No
Porphyromonas asaccharolyticus	5.0×10^7 CFU/mL	No	No
Prevotella oralis	5.0×10^7 CFU/mL	No	No
Propionibacterium acnes	2.0×10^7 CFU/mL	No	No
Proteus mirabilis	4.0×10^7 CFU/mL	No	No
Pseudomonas aeruginosa	5.0×10^7 CFU/mL	No	No
Serratia marcescens	4.0×10^7 CFU/mL	No	No
Staphylococcus aureus	5.0×10^6 CFU/mL	No	No
Staphylococcus epidermidis	3.0×10^7 CFU/mL	No	No
Streptococcus mutans	3.0×10^7 CFU/mL	No	No
Streptococcus pneumoniae	1.5×10^7 CFU/mL	No	No
Streptococcus pyogenes	2.0×10^7 CFU/mL	No	No
Streptococcus sp. Group C	4.0×10^7 CFU/mL	No	No
Streptococcus sp. Group G	2.5×10^7 CFU/mL	No	No
Streptococcus salivarius	2.3×10^7 CFU/mL	No	No
Veillonella parvula	1.5×10^7 CFU/mL	No	No

f. Inclusivity:

An analytical study to evaluate a panel of 52 influenza viral strains including 20 Influenza A strains and 32 Influenza B strains was conducted. These strains were selected to evaluate the reactivity and specificity of the BD Flu A+B. Influenza A and Influenza B viral stock strains were thawed to room temperature and diluted 100-fold with saline (with the exception of A/Moscow/10, which was diluted 10-fold). Three

hundred (300) microliters of each diluted viral suspension were added to the unitized tube containing RV Reagent C and the attached filter tip was snapped in place. The sample was mixed and three drops of the extracted sample were added to the test well of a BD Flu A+B device. After 10 minutes at room temperature the device was inserted into the BD Veritor™ System Reader for interpretation. All determinations were performed in triplicate. Triplicate test results were concordant for all strains evaluated. All Influenza A viruses and all Influenza B viruses were correctly detected by the test and no cross-reactivity was observed.

Influenza AViral Strain	Concentration Tested	Flu A Test Result	Flu B Test Result
A2/Aichi2/68 H3N2	1.58 x 106 $CEID_{50}$/mL	Positive	Negative
A/Brisbane/10/2007 H3N2	5.88×10^4 $TCID_{50}$/mL	Positive	Negative
A/Brisbane/59/2007 H1N1	7.63×10^4 $TCID_{50}$/mL	Positive	Negative
A/California/7/2009 H1N1 (2009 H1N1)	1.0×10^6 $TCID_{50}$/mL	Positive	Negative
A1/Denver/1/57 H1N1	8.89×10^6 $CEID_{50}$/mL	Positive	Negative
A/FM/1/47 H1N1	1.58×10^7 $CEID_{50}$/mL	Positive	Negative
A/Hong Kong/8/68 H3N2	8.89×10^6 $CEID_{50}$/mL	Positive	Negative
A/New Caledonia/20/1999	1.0×10^4 $TCID_{50}$/mL	Positive	Negative
A/New Jersey/8/76 H1N1	1.58×10^5 $CEID_{50}$/mL	Positive	Negative
A/NWS/33 H1N1	1.58×10^5 $CEID_{50}$/mL	Positive	Negative
A/Perth/16/2009 H3N2	1.0×10^7 $TCID_{50}$/mL	Positive	Negative
A/Port Chalmers/1/73 H3N2	1.58×10^6 $CEID_{50}$/mL	Positive	Negative
A/PR/8/34 H1N1	6.31×10^3 $TCID_{50}$/mL	Positive	Negative
A/Wisconsin/67/2005 H3N2	1.0×10^7 $TCID_{50}$/mL	Positive	Negative
A/Victoria/3/75 H3N2	8.89×10^5 $CEID_{50}$/mL	Positive	Negative
A/Weiss/43 H1N1	2.81×10^9 $CEID_{50}$/mL	Positive	Negative
A/Mal/302/54 H1N1	8.89×10^7 $CEID_{50}$/mL	Positive	Negative
A/WS/33 H1N1	1.58×10^4	Positive	Negative

	$CEID_{50}$/mL		
A/Moscow/10/99 H3N2	4.64×10^7 $TCID_{50}$/mL	Positive	Negative
A/Solomon Island/03/2006 H1N1	1.0×10^6 $TCID_{50}$/mL	Positive	Negative

Positive = presence of influenza A or B antigen
Negative = absence of influenza A or B antigen

Influenza B Viral Strain	Concentration Tested	Flu B Result	Flu A Result
B/Brazil/178/96	4.64×10^5 $TCID_{50}$/mL	Positive	Negative
B/Brisbane/60/2008	6.31×10^5 $TCID_{50}$/mL	Positive	Negative
B/Brisbane/72/97	1.0×10^6 $TCID_{50}$/mL	Positive	Negative
B/Canada/548/99	HA titer > 1.28	Positive	Negative
B/Egypt/00393/99	HA titer > 1.28	Positive	Negative
B/Florida/2/2006	2.15×10^5 $TCID_{50}$/mL	Positive	Negative
B/Florida/4/2006	2.15×10^5 $TCID_{50}$/mL	Positive	Negative
B/Fujian/93/97	1.58×10^7 $TCID_{50}$/mL	Positive	Negative
B/Fukushima/220/99	3.73×10^4 $TCID_{50}$/mL	Positive	Negative
B/GuangXi/547/98	4.64×10^6 $TCID_{50}$/mL	Positive	Negative
B/Hawaii/01/97	HA titer > 1.28	Positive	Negative
B/Hong Kong/5/72	8.89×10^4 $CEID_{50}$/mL	Positive	Negative
B/Hong Kong/219/98	HA titer 0.08	Positive	Negative
B/Johannesburg/5/99	1.58×10^6 $TCID_{50}$/mL	Positive	Negative
B/Lee/40	8.89×10^4 $CEID_{50}$/mL	Positive	Negative
B/Lisbon/03/96	HA titer > 0.08	Positive	Negative
B/Malaysia/2506/2004	1.0×10^6 $TCID_{50}$/mL	Positive	Negative
B/Maryland/1/59	2.81×10^3 $CEID_{50}$/mL	Positive	Negative
B/Ohio/1/05	2.68×10^6 $TCID_{50}$/mL	Positive	Negative
B/Ohio/11/96	HA titer > 0.16	Positive	Negative
B/Puerto Mont/10427/98	HA titer 0.08	Positive	Negative
B/Russia/69	3.9×10^3 $TCID_{50}$/mL	Positive	Negative
B/Shangdong/7/97	6.31×10^7 $TCID_{50}$/mL	Positive	Negative
B/Shanghai/04/97	1.58×10^7 $TCID_{50}$/mL	Positive	Negative
B/Shenzhen/135/97	6.31×10^6 $TCID_{50}$/mL	Positive	Negative
B/Sichuan/116/96	HA titer 0.64	Positive	Negative
B/Taiwan/2/62	2.81×10^3 $CEID_{50}$/mL	Positive	Negative
B/Victoria/504/00	4.64×10^6 $TCID_{50}$/mL	Positive	Negative
B/Yamanashi/166/98	1.95×10^5 $TCID_{50}$/mL	Positive	Negative
B/Yamanashi/16/88	1.95×10^5 $TCID_{50}$/mL	Positive	Negative
B/Jiangsu/10/2003	4.64×10^5 $TCID_{50}$/mL	Positive	Negative
B/Mass/3/66	1.58×10^6 $CEID_{50}$/mL	Positive	Negative

Positive = presence of influenza A or B antigen
Negative = absence of influenza A or B antigen

In addition, analytical inclusivity was also tested at dilutions much closer to the analytical limit

of detection on a subset of Influenza A and Influenza B strains. The table below summarizes the detection of three replicates at the indicated test level.

Type	Influenza Viral Strain	Stock Concentration ($CEID_{50}$/mL)	Concentration Tested	Result
A	A2/Aichi2/68 H3N2	1.58×10^8 $CEID_{50}$/mL	7.91×10^3 $CEID_{50}$/mL	Detected
A	A/Brisbane/10/2007 H3N2	7.63×10^6 $TCID_{50}$/mL	9.54×10^2 $TCID_{50}$/mL	Detected
A	A/Brisbane/59/2007 H1N1	5.88×10^6 $TCID_{50}$/mL	5.88×10^2 $TCID_{50}$/mL	Detected
A	A/California/7/2009 H1N1 (2009 H1N1)	1.0×10^8 $TCID_{50}$/mL	5.0×10^3 $TCID_{50}$/mL	Detected
A	A1/Denver/1/57 H1N1	8.89×10^8 $CEID_{50}$/mL	4.45×10^4 $CEID_{50}$/mL	Detected
A	A/FM/1/47 H1N1	1.0×10^9 $CEID_{50}$/mL	7.91×10^4 $CEID_{50}$/mL	Detected
A	A/Hong Kong/8/68 H3N2	8.89×10^8 $CEID_{50}$/mL	8.89×10^4 $CEID_{50}$/mL	Detected
A	A/New Caledonia/20/1999 H1N1	1.0×10^6 $TCID_{50}$/mL	5.0×10^3 $TCID_{50}$/mL	Detected
A	A/New Jersey/8/76 H1N1	1.58×10^7 $CEID_{50}$/mL	1.58×10^3 $CEID_{50}$/mL	Detected
A	A/NWS/33 H1N1	1.58×10^7 $CEID_{50}$/mL	1.58×10^4 $CEID_{50}$/mL	Detected
A	A/Perth/16/2009 H3N2	1.0×10^9 $TCID_{50}$/mL	1.0×10^6 $TCID_{50}$/mL	Detected
A	A/Port Chalmers/1/73 H3N2	1.58×10^8 $CEID_{50}$/mL	3.95×10^4 $CEID_{50}$/mL	Detected
A	A/PR/8/34 H1N1	6.31×10^5 $TCID_{50}$/mL	6.31×10^2 $TCID_{50}$/mL	Detected
A	A/Wisconsin/67/2005 H3N2	1.0×10^9 $TCID_{50}$/mL	2.5×10^5 $TCID_{50}$/mL	Detected
A	A/Victoria/3/75 H3N2	1.58×10^7 $CEID_{50}$/mL	8.89×10^1 $CEID_{50}$/mL	Detected
B	B/Brisbane/60/2008	6.31×10^7 $TCID_{50}$/mL	6.31×10^3 $TCID_{50}$/mL	Detected
B	B/Florida/4/2006	2.15×10^7 $TCID_{50}$/mL	2.15×10^3 $TCID_{50}$/mL	Detected
B	B/Hong Kong/5/72	1.58×10^7 $CEID_{50}$/mL	1.11×10^4 $CEID_{50}$/mL	Detected
B	B/Lee/40	1.58×10^7 $CEID_{50}$/mL	8.89×10^3 $CEID_{50}$/mL	Detected
B	B/Malaysia/2506/2004	1.0×10^8 $TCID_{50}$/mL	5.0×10^4 $TCID_{50}$/mL	Detected

B	B/Maryland/1/59	2.81 X 10^5 $CEID_{50}$/mL	3.51 x 10^2 $CEID_{50}$/mL	Detected
B	B/Taiwan/2/62	2.81 X 10^5 $CEID_{50}$/mL	2.81 x 10^2 $CEID_{50}$/mL	Detected

g. *Interfering substances:*

An analytical study to evaluate a total of 43 substances including whole blood, prescription medications and over-the-counter (OTC) medications commonly taken to relieve flu symptoms was carried out. These substances were tested for potential interference with the BD Flu A+B test. To screen for potential interference, Influenza A (flu A/PR/8/34) and Influenza B (flu B/Lee/40) positive samples were prepared to yield a final concentration corresponding to a moderate positive (~5 times LoD). Test interference may be seen in the form of a false positive result with Influenza A or Influenza B negative samples or a false negative result with an Influenza A or Influenza B positive sample. Of the 43 substances tested in this study, none exhibited interference with the BD Veritor™ System for Rapid Detection of Flu A+B test.

The FluMist® is made from attenuated live Flu virus and although the concentration tested was non-interfering, it is possible when tested with higher concentrations that an Influenza A and/or Influenza B false positive may occur. Therefore, the following statement is included in the Warnings and Precautions section of the product package insert: "FluMist® is made from attenuated live Flu virus and although the concentration tested (1%) was non-interfering, it is possible when tested with higher concentrations that an influenza A and/or influenza B false positive may occur."

Substance	Concentration Tested	Interference with Flu A Result	Interference with Flu B Result
Whole Blood	2%	No	No
4-Acetamidophenol	10 mg/mL	No	No
Acetylsalicylic acid	20 mg/mL	No	No
Albuterol	0.083 mg/mL	No	No
Amantadine	500 ng/mL	No	No
Ayr Saline Nasal Gel	10 mg/mL	No	No
Beclomethasone	500 ng/mL	No	No
Budesonide	500 ng/mL	No	No
Chlorpheniramine maleate	5 mg/mL	No	No
Dextromethoraphan	10 mg/mL	No	No
Diphenhydramine HCl	5 mg/mL	No	No
Dexamethasone	10 mg/mL	No	No
Fexofenadine	500 ng/mL	No	No
FluMist®	1%	No	No
Flunisolide	500 ng/mL	No	No

Fluticasone	500 ng/mL	No	No
Guaiacol Glyceryl Ether	20 mg/mL	No	No
Ibuprofen	10 mg/mL	No	No
Loratidine	100 ng/mL	No	No
Menthol Throat Lozenges	10 mg/mL	No	No
Mometasone	500 ng/mL	No	No
Mupirocin	500 ng/mL	No	No
Oxymetazoline	0.05 mg/mL	No	No
Osteltamivir	500 ng/mL	No	No
Phenylephrine	1 mg/mL	No	No
Pseudoephedrine HCl	20 mg/mL	No	No
Purified Mucin Protein	1 mg/mL	No	No
Ribavirin	500 ng/mL	No	No
Rimantadine	500 ng/mL	No	No
Tobramycin	500 ng/mL	No	No
Triamcinolone	500 ng/mL	No	No
Zanamivir	1 mg/mL	No	No
Antiseptic Mouthwash (CVS)	5%	No	No
Cool Mint Listerine Antiseptic	5%	No	No
Scope Outlast Mouthwash	5%	No	No
Ibuprofen Concentrated Drops	25%	No	No
Pedia Care Drops for infants	25%	No	No
Triaminic infants drops	25%	No	No
Infants Advil concentrated Drops	25%	No	No
Nasal Spray	10%	No	No
Nasal Spray	10%	No	No
Nasal Spray	10%	No	No
Homeopathic Allergy Medicine	10 mg/mL	No	No

2. Comparison studies:

   a. Method comparison with predicate device:

   Not Applicable

   b. Matrix comparison:

   An additional matrix comparison study was conducted to address concerns regarding matrix effects on the assay's sensitivity. The matrix effect study was designed using two influenza viruses (A/California/7/2009 and B/Brisbane/60/2008) which were serially diluted in saline and in a negative pooled wash/aspirate matrix to levels close to the reported LoD. Each virus dilution was tested 20 times. The results of the study show there were no significant differences in the LoD between the two matrices.

3. Clinical studies:

Performance characteristics for the BD Veritor System for Rapid Detection of Flu A+B test were established in multi-center clinical studies conducted at two U.S. trial sites and one Hong Kong trial site during the 2010-2011 respiratory season. A total of 1502 prospective specimens (1002 in the U.S and 500 in Hong Kong) were evaluated using the BD Veritor System for Rapid Detection of Flu A+B test and PCR. One specimen was not evaluated because the study protocol was not followed and two specimens were collected from the same individual; four specimens were excluded from the analyses because raw instrument data differed from the records in the case report forms; an additional 13 were excluded due to insufficient sample volume for reference method testing; and 13 samples were excluded due to invalid results "Result Invalid" (for an invalid rate of 0.9% [13/1484]). The prospective specimens consisted of nasopharyngeal washes and aspirates from symptomatic patients. 49% of the samples were from females and 51% from males. 56.6% were from patients less than or equal to 5 years of age. 21.9% of the patients tested were in the 6-21 year age group, 5.7% were from 22-59 years of age and 15.8% were obtained from people greater than or equal to age 60 (the patient age was not provided for 0.1% of samples). The performance of the BD Veritor System for Rapid Detection of Flu A+B test was compared to an FDA-cleared Influenza A and B molecular assay (PCR).

An additional 263 frozen retrospective specimens were evaluated with the BD Veritor System for Rapid Detection of Flu A+B test. Twelve samples were excluded because there was insufficient sample volume for reference method testing. One sample was excluded as a PCR "Unresolved." and one sample was "Result Invalid" for an invalid rate of 0.8% (2/249). The retrospective specimens consisted of nasopharyngeal washes and aspirates from symptomatic patients. 44.9% of the samples were from females and 55.1% from males. 87.5% were from patients less than or equal to 5 years of age.

For testing specimens with the BD Veritor Flu A+B test, sites were instructed to follow the procedures outlined in the draft package insert. Briefly, 300 µl of the nasal wash/aspirate specimen is inserted into the prefilled unitized tube containing RV Reagent C. After mixing, RV Reagent C tube is inverted and squeezed gently on the half of the tube away from the tip, allowing three drops of processed specimen to be dispensed into the sample well of the appropriately labeled BD Veritor Flu A + B device. After 10 minutes at room temperature the device was inserted into the BD Veritor™ System Reader for interpretation. For kit control swabs, transfer 300 µl of distilled or deionized water into the RV Reagent C tube. Insert the control swab and vigorously plunge the swab up and down in the fluid for a minimum of 15 seconds. Remove the swab while squeezing the sides of the tube to extract the liquid from the swab. Press the attached cap onto the Reagent C tube and vortex or mix thoroughly. Invert the RV Reagent C tube and, holding the tube vertically (approximately one inch above the BD Veritor System Flu A+B device sample well), squeeze gently on the half of the tube away from the tip, allowing three drops of the processed specimen to be dispensed into the sample well of the appropriately labeled BD Veritor System Flu A+B device.

The reference method was performed following the package insert of an FDA-cleared

molecular Influenza A and B assay. Briefly, nucleic acids were extracted from specimens using the indicated extraction system according to the package insert. An internal control (IC) was added to each specimen prior to extraction in order to monitor for inhibitors of PCR present in the extracted samples. Amplification was carried out for 50 cycles using the indicated instrument according to the assay procedure described in the package insert. Interpretation of PCR results for all specimens and controls was determined using the device software and according to the protocol outlined in the package insert.

The clinical specimen types used in the evaluation of clinical performance were nasopharyngeal washes/aspirates. Test results were analyzed based on positive and negative Influenza A or B results with the BD Flu A+B assay. The data were tabulated using reference method (an FDA-cleared Influenza A and B molecular assay) results to categorize the BD Flu A+B test results into the following categories:

1. True Positive: Any BD Flu A+B test result which exhibits a positive result and has a paired reference method positive result shall be deemed a true positive.

2. False Positive: Any BD Flu A+B test result which exhibits a positive result but the paired reference method is negative shall be deemed a false positive.

3. True Negative: Any BD Flu A+B test result which exhibits a negative result for which reference method is negative shall be deemed a true negative.

4. False Negative: Any BD Flu A+B test result that exhibits a negative result but for which the reference method is positive shall be deemed false negative.

Table 1: Summary of the Performance of the BD Veritor System for Rapid Detection of Flu A+B Test Compared to PCR for All Prospectively Collected Nasopharyngeal Wash/Aspirate Specimens – All Sites

	Reference PCR		
Clinical kit: BD Flu A	P	N	Total
P	224	29	253
N	46	1172	1218
Total	270	1201	1471
Reference Method: PCR PPA: 83.0% (95% C.I. 78.0%- 87.0%) NPA: 97.6% (95% C.I. 96.6%- 98.3%)			

	Reference PCR		
Clinical kit: BD Flu B	P	N	Total
P	74	3	77
N	17	1377	1394
Total	91	1380	1471
Reference Method: PCR PPA: 81.3% (95% C.I. 72.1%- 88.0%) NPA: 99.8% (95% C.I. 99.4%- 99.9%)			

An additional 263 frozen retrospective specimens were evaluated with the BD Veritor System for Rapid Detection of Flu A+B test. Twelve samples were excluded because there was insufficient sample volume for reference method testing. One sample was excluded as a PCR "Unresolved." Although the BD Veritor System reports dual positive samples as "Result Invalid", these samples (N=1) are included in the PPA/NPA

calculation for an invalid rate of 0.4% (1/249). The retrospective specimens consisted of nasopharyngeal washes and aspirates from symptomatic patients; 44.9% of the samples were from females and 55.1% from males; 87.5% were from patients less than or equal to 5 years of age. The performance is presented in Table 2 below.

Table 2: Summary of the Performance of the BD Veritor System for Rapid Detection of Flu A+B Test Compared to PCR for Retrospective Nasopharyngeal Wash/Aspirate Specimens

	Reference PCR		
Clinical kit: BD Flu A	P	N	Total
P	58	2	60
N	5	184	189
Total	63	186	249
Reference Method: PCR PPA: 92.1% (95% C.I. 82.7%- 96.6%) NPA: 98.9% (95% C.I. 96.2%- 99.7%)			

	Reference PCR		
Clinical kit: BD Flu B	P	N	Total
P	29	2	31
N	10	208	218
Total	39	210	249
Reference Method: PCR PPA: 74.0% (95% C.I. 58.9%- 85.4%) NPA: 99.0% (95% C.I. 96.6%-99.7%)			

Invalid rates for the BD Flu A+B POC assay while running patient specimens were 13/1484 or 0.9%. Invalid rates were calculated from the specimen data as the number of invalid results divided by the total number of tests.

4. Clinical cut-off**:**

   Not applicable

5. Expected values/Reference range:

   The overall prevalence observed with an FDA-cleared Influenza A and B molecular assay in the U.S. during the 2010-2011 clinical study was 23.9 % for Influenza A and 7.5% for influenza B. At the clinical site located in Hong Kong, the prevalence observed with the same FDA-cleared Influenza A and B molecular assay was 7.2% for influenza A and 3.4% for influenza B.

N. Instrument Name:

BD Veritor System Reader

O. System Descriptions:

1. Modes of Operation:

The Veritor System Reader is a small, battery powered, bench top instrument that is used to read the Veritor lateral flow test cassette. After the extracted patient sample has been added to the test cassette, the test is developed at room temperature for 10 minutes. The cassette is then placed into the reader where it is scanned. The cassette is divided into distinct zones where the analyzer reads the negative background, positive control, and the Influenza A and B specific zones. The reader applies an algorithm to determine the background of the test as well as the specific signal from the A or B test zones. The reader has a finite number of reads and will prompt the end-user as the total reads approaches the lifetime of the unit.

2. Software:

   The Veritor System Reader is the identical instrument that has been reviewed and cleared with the 510(k) BD influenza A and B assay k112277. FDA has reviewed applicant's instrument Hazard Analysis and software development processes for this instrument and for this analyte. Please refer to decision summary for k112277.

   Yes __ X___ or No _____

3. Specimen Identification:

   Not Applicable

4. Specimen Sampling and Handling:

   Not Applicable

5. Calibration:

   The Veritor Reader is not configurable by the end user and is designed to have a finite lifetime based on number of tests performed or shelf life from date of manufacture. Device calibration is not required, however, a verification device is provided with the reader to QC the device function.

6. Quality Control:

   Each BD Flu A+B test strip is designed with spatially-distinct zones containing a positive and negative internal controls. The positive control zone ensures that the sample has flowed correctly, and the negative control zone serves to monitor non-specific signal generation. The BD Veritor™ System Reader determines the line intensity at each of the spatially-defined control zones and utilizes specific algorithms to determine the presence or absence of any target analyte. The BD Veritor™ System Reader must be used to read the BD Flu A+B test devices, as these devices cannot be interpreted visually by the user.

   In addition to the two internal controls, each BD Flu A+B kit contains the following external controls:

1. Control A+/B- is a dry swab control that contains inactivated recombinant influenza A nucleoprotein antigen and is tested in a similar manner as patient specimens and is used as an external control. A positive flu A test result and a negative flu B test result on the reader LCD display confirm that the operator performed the test correctly.

2. Control B+/A- is a dry swab control that contains inactivated recombinant influenza B nucleoprotein antigen and is tested in a similar manner as patient specimens and is used as an external control. A positive flu B test result and a negative flu A test result on the reader LCD display confirm that the operator performed the test correctly.

The BD Flu A+B device is to be read only by the instrument and cannot be read manually. At a minimum, the external dry swab controls should be run as a quality control procedure for each new lot and new shipment received. Controls should be tested in accordance with local, state and/or federal regulations or accreditation requirements and the standard Quality Control procedures. A BD Veritor System Verification Cartridge is also included with the reader. This allows the user to perform a functional test on the reader. Upon completion the reader will display QC Pass or QC Fail. If the reader has passed QC with the Verification Cartridge, it may be used to test specimens; QC failure requires contacting technical assistance. If desired, appropriate reagent performance and proper testing technique may also be determined by using specimens qualified as positive or negative for the influenza A or B virus. The user is instructed not to use the BD Flu A+B test if control A+/B- and control B+/A- do not yield appropriate results.

P. Other Supportive Instrument Performance Characteristics Data Not Covered in the "Performance Characteristics" Section above:

Not Applicable

Q. Proposed Labeling:

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

R. Conclusion:

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