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Veritor™ System

For Rapid Detection of Flu A+B

Laboratory kit configured for testing liquid nasopharyngeal wash, aspirate and swab in transport media samples.

30
Determinations

BD Veritor™ System

For Rapid Detection of Flu A+B

Laboratory kit configured for testing liquid nasopharyngeal wash, aspirate and swab in transport media samples.

For *in vitro* diagnostic use only.

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, aspirate and swab in transport media samples from 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 nasopharyngeal (NP) washes/aspirates 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.

Performance characteristics for influenza A and B NP swabs in transport media were established during January through April of 2012 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, 2011-2012 Season, and Composition of the 2012-2013 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.

SUMMARY AND EXPLANATION

Influenza illness classically presents with sudden onset of fever, chills, headache, myalgias, and a non-productive cough. Epidemics of influenza typically occur during winter months with estimated 114,000 hospitalizations[1] and 36,000 deaths[2] per year in the U.S. Influenza viruses can also cause pandemics, during which rates of illness and death from influenza-related complications can increase dramatically.

Patients who present with suspected influenza may benefit from treatment with an antiviral agent especially if given within the first 48 hours of onset of illness. It is important to rapidly distinguish influenza A from influenza B in order to allow physicians a choice in selective antiviral intervention. Moreover, it is important to determine if influenza A or B is causing symptomatic disease in a particular institution (e.g., nursing home) or community, so that appropriate preventative intervention can be taken for susceptible individuals. It is therefore important to not only rapidly determine whether influenza is present, but also which type of influenza virus is present as severity and treatment can be different.[3]

Diagnostic tests available for influenza include rapid immunoassay, immunofluorescence assay, polymerase chain reaction (PCR), serology, and viral culture.[4-11] Immunofluorescence assays entail staining of specimens immobilized on microscope slides using fluorescent-labeled antibodies for observation by fluorescence microscopy.[6,12,13] Culture methods employ initial viral isolation in cell culture, followed by hemadsorption inhibition, immunofluorescence, or neutralization assays to confirm the presence of the influenza virus.[13-15]

The **BD Veritor** System for Rapid Detection of Flu A+B (also referred to as the **BD Veritor** System and **BD Veritor** System Flu A+B) is a chromatographic immunoassay to detect influenza A or B nucleoprotein antigens from respiratory specimens of symptomatic patients with a time to result of 10 minutes. The speed and simplified workflow of the **BD Veritor** System for Rapid Detection of Flu A+B makes it applicable as a "STAT" influenza A and B antigen detection test providing relevant information to assist with the diagnosis of influenza.

PRINCIPLES OF THE PROCEDURE

The **BD Veritor** System for Rapid Detection of Flu A+B is a chromatographic assay to qualitatively detect influenza A and B viral antigens in samples processed from respiratory specimens. When specimens are processed and added to the test device, influenza A or B viral antigens bind to anti-influenza antibodies conjugated to detector particles in the A + B test strip. The antigen-conjugate complex migrates across the test strip to the reaction area and is captured by the line of antibody on the membrane. A positive result for influenza A is determined by the **BD Veritor** System Reader when antigen-conjugate is deposited at the Test "A" position and the Control "C" position on the **BD Veritor** System Flu A+B assay device. A positive result for influenza B is determined by the **BD Veritor** System Reader when antigen-conjugate is deposited at the Test "B" position and the Control "C" position in the **BD Veritor** System Flu A+B assay device.

REAGENTS
The following components are included in the **BD Veritor** System for Rapid Detection of Flu A+B kit:

BD Veritor System Flu A+B Devices	30 devices	Foil pouched device containing one reactive strip. Each strip has two test lines of monoclonal antibody specific to either Flu A or Flu B influenza viral antigen and murine monoclonal control line antibodies.
RV Reagent C	30 tubes with 100 µL reagent	Detergent with < 0.1% sodium azide
300 µL Pipette	30 each	Transfer pipette
Control A+/B- Swab	1 each	Flu A Positive and Flu B Negative Control Swab, influenza A antigen (inactive recombinant nucleoprotein) with < 0.1% sodium azide
Control B+/A- Swab	1 each	Flu A Negative and Flu B Positive Control Swab, influenza B antigen (inactive recombinant nucleoprotein) with < 0.1% sodium azide

Materials Required But Not Provided: BD Veritor System Reader (Cat. No 256055), timer, vortex mixer, transport media (see Specimen Collection and Handling), distilled or deionized water, tube rack for specimen testing.

Warnings and Precautions:
1. For *in vitro* Diagnostic Use.
2. Test results are not meant to be visually determined. **All test results must be determined using the BD Veritor System Reader**.
3. 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 the 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.
4. Pathogenic microorganisms, including hepatitis viruses, Human Immunodeficiency Virus and novel influenza viruses, may be present in clinical specimens. "Standard Precautions"[16-19] and institutional guidelines should be followed in handling, storing and disposing of all specimens and all items contaminated with blood and other body fluids.
5. Dispose of used **BD Veritor** System test devices as biohazardous waste in accordance with federal, state and local requirements.
6. Reagents contain sodium azide, which is harmful if inhaled, swallowed or exposed to skin. Contact with acids produces very toxic gas. If there is contact with skin, wash immediately with plenty of water. Sodium azide may react with lead and copper plumbing to form highly explosive metal azides. On disposal, flush with a large volume of water to prevent azide build-up.
7. Do not use kit components beyond the expiration date.
8. Do not reuse the **BD Veritor** System test device.
9. Do not use the kit if the Control A+/B- swab and Control B+/A- swab do not yield appropriate results.
10. Wear protective clothing such as laboratory coats, disposable gloves and eye protection when specimens are assayed.
11. To avoid erroneous results, specimens must be processed as indicated in the assay procedure section.
12. 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.
13. Specific training or guidance is recommended if operators are not experienced with specimen collection and handling procedures.

Storage and Handling: Kits may be stored at 2–30°C. DO NOT FREEZE. Reagents and devices must be at room temperature (15–30°C) when used for testing.

SPECIMEN COLLECTION AND HANDLING
Specimen Collection and Preparation: Acceptable specimens for testing with the **BD Veritor** System for Rapid Detection of Flu A+B include nasopharyngeal (NP) washes, aspirates and swab specimens in transport media. It is essential that correct specimen collection and preparation methods be followed. Specimens obtained early in the course of the illness will contain the highest viral titers.

Inadequate specimen collection, improper specimen handling and/or transport may yield a false negative result; therefore, training in specimen collection is highly recommended due to the importance of specimen quality to accurate test results.

Specimen Transport Media: The following transport media have been tested and found to be compatible using moderate positive samples with the **BD Veritor** System for Rapid Detection of Flu A+B:

- M4RT, UTM, M4, M5, Amies Medium (liquid), Bartel ViraTrans™ Medium, Earle's Minimal Essential Medium (EMEM), Hank's Balanced Salt Solution, Normal Saline, Phosphate Buffered Saline (PBS).

For samples that are stored at 2–8°C for greater than 12 to 24 hours, it is recommended that only these media are used:

- M4RT, UTM, M4, M5, Amies Medium (liquid), Bartel ViraTrans Medium, Normal Saline, Phosphate Buffered Saline (PBS) and Hank's Balanced Salt Solution .

For samples that are stored frozen, it is recommended that Earle's Minimal Essential Medium not be used.

Other transport media may be utilized if an appropriate validation exercise is performed. **NOTE: Media containing lactalbumin (i.e., 0.5% or 1.0%) or any other transport media containing lactalbumin may not be compatible with the BD Veritor System for Rapid Detection of Flu A+B.**

Specimen Transport and Storage:
Freshly collected specimens should be processed and tested immediately. If necessary, specimens may be stored at 2–8°C for up to 72 hours. It is essential that correct specimen collection and preparation methods be followed. Do not centrifuge specimens prior to use, as the removal of cellular material may adversely affect test sensitivity.

- For NP washes/aspirates, sample volumes of 1 to 3 mL are recommended. If transport medium is used, minimal dilution of specimen is preferred. Excessive wash volumes should be avoided as they may result in decreased test sensitivity.
- For NP swab specimens in transport media, minimal dilution of specimen is preferred and use of 1 mL or less of transport media is suggested for optimal test performance.

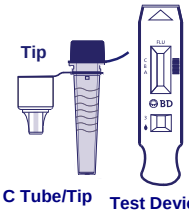
- Process specimens as described in “Test Procedure”.

PROCEDURE

Test Procedure

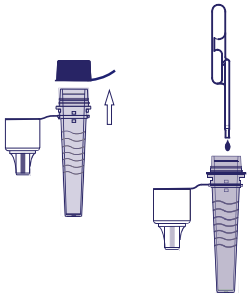
NOTES: Reagents, specimens and devices must be at room temperature (15–30°C) for testing. Thoroughly mix all specimens prior to removal of an aliquot for processing. Do not centrifuge specimens.

1. For each patient specimen and control swab, remove one **RV Reagent C** tube/tip and one **BD Veritor** System Flu A+B device from its foil pouch immediately before testing.
2. Label one **BD Veritor** System device and one **RV Reagent C** tube for each specimen and control to be tested.
3. Place the labeled **RV Reagent C** tube(s) in the designated area of the tube rack.

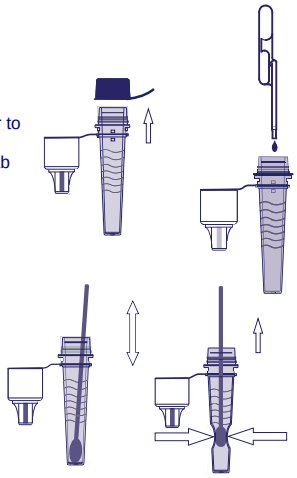


RV Reagent C Tube/Tip **Test Device**

4. Process the specimen or control as directed below:
   - **a. For NP washes, aspirates and swab specimens in transport media:**
     1. Vortex or thoroughly mix specimen. Do not centrifuge.
     2. Remove and discard the cap from the **RV Reagent C** tube corresponding to the sample to be tested.
     3. Using the transfer pipette, transfer 300 µL of specimen into the **RV Reagent C** tube. Discard pipette after use.



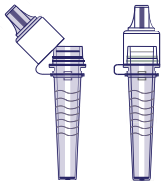
   - **b. For Kit Swab Controls:**
     1. Remove and discard the cap from the **RV Reagent C** tube corresponding to the sample to be tested.
     2. Using the transfer pipette add 300 µL of distilled or deionized water to the **RV Reagent C** tube.
     3. Insert the control swab into the tube and vigorously plunge the swab up and down in the fluid for a minimum of 15 seconds.
     4. Remove the swab while squeezing the sides of the tube to extract the liquid from the swab.



15 seconds

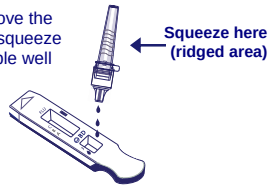
5. Press the attached tip firmly onto the **RV Reagent C** tube containing the processed specimen or control (threading/twisting not required).

   NOTE: Do not use tips from any other product, including other products from BD or other manufacturers.



6. Vortex or mix thoroughly.

7. Invert the **RV Reagent C** tube and hold the tube vertically (approximately one inch above the **BD Veritor** System Flu A+B device sample well). Holding the tube at the ridged area, squeeze gently allowing three (3) drops of the processed sample to be dispensed into the sample well of the appropriately labeled **BD Veritor** System Flu A+B device.

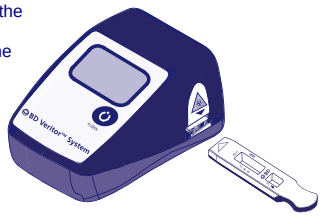


NOTE: Squeezing the tube too close to the tip may cause leakage.

8. After adding the sample, allow the test to run for 10 minutes before inserting into the reader.

9. When the test is ready, insert the **BD Veritor** System Flu A+B device into the **BD Veritor** System Reader. (The **BD Veritor** System Reader should be powered-on prior to use and will indicate when it is ready for insertion of the **BD Veritor** System device.)

   Follow the reader on-screen prompts to complete the procedure and obtain the test result.



Quality Control:
Quality control requirements must be performed in accordance with local, state and/or federal regulations or accreditation requirements and your laboratory's standard Quality Control procedures. Each **BD Veritor** System Flu A+B device contains both positive and negative internal/procedural controls:

1. The internal positive control validates the immunological integrity of the device, proper reagent function, and assures that the correct test procedure was followed.
2. The membrane area surrounding test lines functions as a background check on the assay device.

These positive and negative internal/procedural controls are evaluated by the **BD Veritor** System Reader after insertion of the **BD Veritor** System test device. The **BD Veritor** System Reader will prompt the operator should a quality issue occur. Failure of the internal/procedural controls will generate an invalid test result.

External Positive and Negative Controls:
Swab controls (Flu A positive/B negative and Flu B positive/A negative) are supplied with each kit. These controls provide additional quality control material to demonstrate positive or negative assay results using the **BD Veritor** System Reader and **BD Veritor** System test device. BD recommends that positive and negative controls be run once for:

- each new kit lot
- each new shipment of test kits
- each new operator
- as required by internal quality control procedures and in accordance with local, state and federal regulations or accreditation requirements.

If the kit controls do not perform as expected, do not test patient specimens. Contact BD Technical Services at 1-800-638-8663.

INTERPRETATION OF RESULTS

The **BD Veritor** System Reader instrument (purchased separately) must be used for all interpretation of test results. Operators should not attempt to interpret assay results directly from the test strip contained within the **BD Veritor** System Flu A+B assay device.

Reader Display	Interpretation
FLU A: + FLU B: -	Positive Test for Flu A (influenza A antigen present)
FLU A: - FLU B: +	Positive Test for Flu B (influenza B antigen present)
FLU A: - FLU B: -	Negative Test for Flu A and Flu B (no antigen detected)
RESULT INVALID	Result Invalid
CONTROL INVALID	Control line error

Invalid Test - If the test is invalid, the **BD Veritor** System Reader will display a "RESULT INVALID" or "CONTROL INVALID" result and the test or control must then be repeated.

REPORTING OF RESULTS

Positive Test Positive for the presence of influenza A or influenza B antigen. A positive result may occur in the absence of viable virus.

Negative Test Negative for the presence of influenza A and influenza B antigen. Infection due to influenza cannot be ruled-out because the antigen present in the sample may be below the detection limit of the test. 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.

Invalid Test Test result is inconclusive. Do not report results. Repeat the test.

LIMITATIONS OF THE PROCEDURE

- Failure to follow the Test Procedure may adversely affect test performance and/or invalidate the test result.
- The contents of this kit are to be used for the qualitative detection of influenza type A and B antigens from NP wash, aspirate and swab in transport media specimens.
- The **BD Veritor** System for Rapid Detection of Flu A+B is capable of detecting both viable and non-viable influenza particles. The **BD Veritor** System for Rapid Detection of Flu A+B performance depends on antigen load and may not correlate with other diagnostic methods performed on the same specimen.
- Results from the **BD Veritor** System for Rapid Detection of Flu A+B test should be correlated with the clinical history, epidemiological data and other data available to the clinician evaluating the patient.
- A false-negative test result may occur if the level of viral antigen in a sample is below the detection limit of the test or if the sample was collected or transported improperly; therefore, a negative test result does not eliminate the possibility of influenza A or influenza B infection, and should be confirmed by viral culture or an FDA-cleared influenza A and B molecular assay.
- Positive test results do not rule out co-infections with other pathogens.
- Positive test results do not identify specific influenza A virus subtypes.
- Negative test results are not intended to rule out other non-influenza viral or bacterial infections.
- Children tend to shed virus for longer periods of time than adults, which may result in differences in sensitivity between adults and children.
- Positive and negative predictive values are highly dependent on prevalence rates. Positive test results are more likely to represent false positive results during periods of little/no influenza activity when disease prevalence is low. False negative test results are more likely during peak influenza activity when prevalence of disease is high.
- This device has been evaluated for use with human specimen material only.
- Monoclonal antibodies may fail to detect, or detect with less sensitivity, influenza A viruses that have undergone minor amino acid changes in the target epitope region.
- The analytical reactivity of this device has not been established for avian or swine origin influenza strains other than those included in the "strain reactivity" tables.
- The performance characteristics of this test with specimens from humans infected with H5N1 or other avian influenza viruses are unknown.
- The performance of this test has not been evaluated for use in patients without signs and symptoms of respiratory infection.
- The **BD Veritor** System Reader reports dual positive influenza A and influenza B results as "Result Invalid." Specimens generating a "Result Invalid" should be retested. Upon retesting, if the specimen produces a "Result Invalid" the user may want to consider other methods to determine whether the sample is positive or negative for influenza virus.

EXPECTED VALUES

The rate of positivity observed in respiratory testing will vary depending on the method of specimen collection, handling/transport system employed, detection method utilized, the time of year, age of the patient, geographic location and most importantly, local disease prevalence.

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.

The overall prevalence observed with an FDA-cleared influenza A and B molecular assay in the U.S. during the 2011-2012 clinical study was 31.7% for influenza A and 4.5% for influenza B. At the clinical sites located in Japan, the prevalence observed with the same FDA-cleared influenza A and B molecular assay was 0% for influenza A and 89 % for influenza B.

PERFORMANCE CHARACTERISTICS

Explanation of Terms:

PPA: Positive Percent Agreement = a / (a+c) × 100%

NPA: Negative Percent Agreement = d / (b+d) × 100%

P: Positive

N: Negative

C.I.: Confidence Interval

	Comparator Method	
New Test Method	P	N
P	A	B
N	C	D
Total	(a+c)	(b+d)

Clinical Performance NP Washes/Aspirates 2010-2011:

Performance characteristics for the **BD Veritor** System for Rapid Detection of Flu A+B test were established using NP wash/aspirate specimens 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. Five specimens were not evaluable because of data reconciliation issues, an additional 13 were excluded because of insufficient sample volume for reference method testing and 13 samples were excluded as “Result Invalid” (for an invalid rate of 0.9% [13/1484]).

The prospective specimens consisted of NP 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).

The performance is presented in Table 1 below.

Table 1: Summary of the Performance of the BD Veritor System for Rapid Detection of Flu A+B Test Compared to PCR for All NP 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" and one sample was excluded as "Result Invalid" (for an invalid rate of 0.4% [1/250]). The retrospective specimens consisted of NP 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 NP 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%)			

Clinical Performance NP Swabs in Transport Media 2011-2012; U.S. and Japan Combined
Performance characteristics for the **BD Veritor** System for Rapid Detection of Flu A+B test were established using NP swabs in transport media in multi-center studies conducted at six clinical trial sites located in geographically diverse areas within the United States and five clinical sites in Japan using a total of 292 samples.

The combined results are presented in Table 3 below.

Table 3: Summary of the Performance of the BD Veritor System for Rapid Detection of Flu A+B Test Compared to PCR for NP Swabs in Transport Media - U.S. and Japan Combined

	Reference PCR		
Clinical kit: BD Flu A	P	N	Total
P	52	6	58
N	12	222	234
Total	64	228	292
Reference Method: PCR PPA: 81.3% (95% C.I. 70.0% - 88.9%) NPA: 97.4% (95% C.I. 94.4% - 98.8%)			

	Reference PCR		
Clinical kit: BD Flu B	P	N	Total
P	77	2	79
N	13	200	213
Total	90	202	292
Reference Method: PCR PPA: 85.6% (95% C.I. 76.8% - 91.4%) NPA: 99.0% (95% C.I. 96.5% - 99.7%)			

Clinical Performance NP Swabs in Transport Media 2011-2012; U.S
Performance characteristics for the **BD Veritor** System for Rapid Detection of Flu A+B test were established using NP swabs in transport media in multi-center studies conducted at six clinical trial sites located in geographically diverse areas within the United States. A total of 217 prospective specimens were evaluated using the **BD Veritor** System for Rapid Detection of Flu A+B test and PCR. Two specimens could not be evaluated because of data reconciliation issues, one was eliminated because of an invalid control reading and 13 were excluded because the PCR results were unresolved.

The specimens consisted of NP swabs in transport media from symptomatic patients. 55.8% of the samples were from females and 44.2% from males. 16.1% were from patients less than or equal to 5 years of age, 25.3% were from patients 6-21 years of age, 47.5% were from patients 22-59 years of age and 11.1% were obtained from patients greater than or equal to 60 years of age.

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).

The results are presented in Table 4 below.

Table 4: Summary of the Performance of the BD Veritor System for Rapid Detection of Flu A+B Test Compared to PCR for NP Swabs in Transport Media – U.S.

	Reference PCR		
Clinical kit: BD Flu A	P	N	Total
P	52	6	58
N	12	131	143
Total	64	137	201
Reference Method: PCR PPA: 81.3% (95% C.I. 70.0% - 88.9%) NPA: 95.6% (95% C.I. 90.8% - 98.0%)			

	Reference PCR		
Clinical kit: BD Flu B	P	N	Total
P	7	0	7
N	2	192	194
Total	9	192	201
Reference Method: PCR PPA: 77.8% (95% C.I. 45.3% - 93.7%) NPA: 100% (95% C.I. 98.0% - 100%)			

Clinical Performance NP Swabs in Transport Media 2011-2012; Japan
Performance characteristics for the **BD Veritor** System for Rapid Detection of Flu A+B test were established using NP swabs in transport media in multi-center studies conducted at five clinical trial sites in Japan. A total of 93 prospective specimens were evaluated using the **BD Veritor** System for Rapid Detection of Flu A+B test and PCR. Two specimens were excluded as the results were undetermined with the comparator assay.

The specimens consisted of NP swabs in transport media from symptomatic patients. 49.5% of the samples were from females and 50.5% from males. 31.2% were from patients less than or equal to 5 years of age, 63.4% were from patients 6-21 years of age and 5.4% were from patients 22-59 years of age (there were no specimens from patients greater than or equal to 60 years of age).

The results are presented in Table 5 below.

Table 5: Summary of the Performance of the BD Veritor System for Rapid Detection of Flu A+B Test Compared to PCR for NP Swabs in Transport Media – Japan.

	Reference PCR		
Clinical kit: BD Flu A	P	N	Total
P	0	0	0
N	0	91	91
Total	0	91	91
Reference Method: PCR No Data for PPA Calculation NPA: 100% (95% C.I. 95.9% - 100%)			

	Reference PCR		
Clinical kit: BD Flu B	P	N	Total
P	70	2	72
N	11	8	19
Total	81	10	91
Reference Method: PCR PPA: 86.4% (95% C.I. 77.3% - 92.2%) NPA: 80.0% (95% C.I. 49.0% - 94.3%)			

Reproducibility

The reproducibility of the **BD Veritor** System for Rapid Detection of Flu A+B test was evaluated at three clinical laboratory sites in 2010-2011. 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 panel was tested by two operators at each site for five consecutive days. 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%)
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) (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 B	90.0% (27/30) (95% C.I. 74.4%-96.5%)	63.3% (19/30) (95% C.I. 45.5%-78.1%)	82.8% (24/29) (95% C.I. 65.5%-92.4%)	78.7% (70/89) (95% C.I. 69.0%-85.9%)
Moderate positive B	96.7% (29/30) (95% C.I. 83.3%-99.4%)	100.0% (30/30) (95% C.I. 88.6%-100.0%)	100.0% (30/30) (95% C.I. 88.6%-100.0%)	98.9% (89/90) (95% C.I. 94.0%-99.8%)
Negatives	0.0% (0/210) (95% C.I. 0%-1.8.0%)	0.0% (0/210) (95% C.I. 0.0%-1.8%)	0.0% (0/210) (95% C.I. 0.0%-1.8%)	0.0% (0/630) (95% C.I. 0.0%-0.6%)

Analytical Studies

Analytical Sensitivity (Limit of Detection)

The limit of detection (LOD) for the **BD Veritor** System for Rapid Detection of Flu A+B test was established for a total of 7 influenza strains: 4 influenza A and 3 influenza B. The LOD for each strain represents the lowest concentration producing a positivity rate of ≥95% based on testing 20 to 60 replicates.

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%

$TCID_{50}$/mL = 50% Tissue Culture Infectious Dose

Strain Reactivity with Influenza A and B Viruses

The **BD Veritor** System for Rapid Detection of Flu A+B test was evaluated using a panel of 52 influenza strains. All influenza A strains showed positive Flu A test results and negative Flu B test results. Conversely, all of the influenza B strains showed positive Flu B test results and negative Flu A test results.

Influenza A Viral Strains
A/Aichi/2/68
A/Brisbane/10/2007
A/Brisbane/59/2007
A/California/7/2009
A/Denver/1/57
A/FM/1/47
A/Hong Kong/8/68
A/New Caledonia/20/1999
A/New Jersey/8/76
A/NWS/33
A/Perth/16/2009
A/Port Chalmers/1/73
A/PR/8/34
A/Wisconsin/67/2005
A/Victoria/3/75
A/Weiss/43
A/Mal/302/54
A/WS/33
A/Moscow/10/99
A/Solomon Island/03/2006

Influenza B Viral Strains
B/Brazil/178/96
B/Brisbane/60/2008
B/Brisbane/72/97
B/Canada/548/99
B/Egypt/00393/99
B/Florida/2/2006
B/Florida/4/2006
B/Fujian/93/97
B/Fukushima/220/99
B/GuangXi/547/98
B/Hawaii/01/97
B/Hong Kong/5/72
B/Hong Kong/219/98
B/Jiangsu/10/2003
B/Johannesburg/5/99
B/Lee/40
B/Lisbon/03/96
B/Malaysia/2506/2004
B/Maryland/1/59
B/Mass/3/66
B/Ohio/1/05
B/Ohio/11/96
B/Puerto Mont/10427/98
B/Russia/69
B/Shangdong/7/97
B/Shanghai/04/97
B/Shenzhen/135/97
B/Sichuan/116/96
B/Taiwan/2/62
B/Victoria/504/00
B/Yamanashi/166/98
B/Yamagata/16/88

Analytical Specificity (Cross Reactivity)

The **BD Veritor** System for Rapid Detection of Flu A+B test was evaluated with a total of 51 microorganisms. The 37 bacteria and yeast were tested at a target concentration of approximately 10^7 CFU/mL (CFU – Colony Forming Units) with the exception of *Staphylococcus aureus,* which was tested at a final concentration of 10^6 CFU/mL. The 14 viruses were evaluated at concentrations of 10^3 to 10^{10} $TCID_{50}$/mL. Of the 51 microorganisms tested, none showed cross-reactivity in either the Flu A or Flu B tests.

Bacteriodes fragilis
Bordetella pertussis
Candida albicans
Chlamydia pneumoniae
Corynebacterium diphtherium
Escherichia coli
Fusobacterium nucleatum
Haemophilus influenzae
Haemophilus parainfluenzae
Kingella kingae
Klebsiella pneumoniae
Lactobacillus sp.
Legionella sp.
Moraxella catarrhalis
Mycobacterium tuberculosis
Mycoplasma pneumoniae
Neisseria gonorrhoeae
Neisseria meningitides
Neisseria mucosa
Neisseria sp.*(Neisseria perflaus)*
Neisseria subflava
Peptostreptococcus anaerobius
Porphyromonas asaccharolyticus
Prevotella oralis
Propionibacterium acnes
Proteus mirabilis
Pseudomonas aeruginosa
Serratia marcescens
Staphylococcus aureus
Staphylococcus epidermidis
Streptococcus mutans
Streptococcus pneumoniae
Streptococcus pyogenes
Streptococcus sp. Group C
Streptococcus sp. Group G
Streptococcus salivarius
Veillonella parvula

Adenovirus, type 1
Adenovirus, type 7
Cytomegalovirus
Enterovirus
Epstein Barr Virus
HSV Type 1
Human Coronavirus OC43
Human Coronavirus 2229E
Human metapneumovirus (HMPV-27 A2)
Human Parainfluenza
Measles virus
Mumps virus
Respiratory syncytial virus
Rhinovirus

Interfering Substances

Various substances were evaluated with the **BD Veritor** System for Rapid Detection of Flu A+B test. These substances included whole blood (2%) and various medications. No interference was noted with this assay for any of the substances tested.

Substance	Concentration
4-Acetamidophenol	10 mg/mL
Acetylsalicylic acid	20 mg/mL
Albuterol	0.083 mg/mL
Amantadine Hydrochloride	500 ng/mL
Ayr Saline Nasal Gel	10 mg/mL
Beclomethasone	500 ng/mL
Budesonide	500 ng/mL
Chlorpheniramine maleate	5 mg/mL
Dexamethasone	10 mg/mL
Dextromethorphan	10 mg/mL
Diphenhydramine HCl	5 mg/mL
Fexofenadine	500 ng/mL
FluMist	1%
Flunisolide	500 ng/mL
Fluticasone	500 ng/mL
Four OTC nasal sprays	10 %
Four OTC throat drops	25 %
Guaiacol Glyceryl Ether	20 mg/mL
Homeopathic Allergy Medicine	10 mg/mL
Ibuprofen	10 mg/mL
Loratidine	100 ng/mL
Menthol Throat Lozenges	10 mg/mL
Mometasone	500 ng/mL
Mupirocin	500 ng/mL
Oseltamivir	500 ng/mL
Oxymetazoline	0.05 mg/mL
Phenylephrine	1 mg/mL
Pseudoephedrine HCl	20 mg/mL
Purified Mucin Protein	1 mg/mL
Ribavirin	500 ng/mL
Rimantadine	500 ng/mL
Three OTC mouthwashes	5 %
Tobramycin	500 ng/mL
Triamcinolone	500 ng/mL
Whole Blood	2%
Zanamivir	1 mg/mL

Of the 44 substances tested in this study, none exhibited interfering reactions when tested with influenza A and influenza B positive samples. Based on the data, the substances tested at the indicated concentration levels did not interfere with the **BD Veritor** System for Rapid Detection of Flu A+B test.

AVAILABILITY

Cat. No.	Description
256041	**BD Veritor™** System for Rapid Detection of Flu A+B, 30 tests
256055	**BD Veritor™** System Reader
256051	**BD Veritor™** System Flu A+B Control Swab Set, 10 pairs of swabs

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Manufacturer


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