Abbott

BinaxNOW™

INFLUENZA A & B CARD 2

with DIGIVAL™

BinaxNOW™ INFLUENZA A & B CARD 2 with DIGIVAL™

For use with nasal or nasopharyngeal swab specimens

For *in vitro* use only

℞ Only

CLIA Complexity: Waived

A Certificate of Waiver is required to perform this test in a CLIA Waived setting. To obtain CLIA waiver information and a Certificate of Waiver, please contact your state health department. Additional CLIA waiver information is available at the Centers for Medicare and Medicaid website at www.cms.hhs.gov/CLIA.

Failure to follow the instructions or modification to the test system instructions will result in the test no longer meeting the requirements for waived classification.

Intended Use

The BinaxNOW™ Influenza A & B Card 2 is an *in vitro* immunochromatographic assay for the qualitative detection of influenza A and B nucleoprotein antigens in nasopharyngeal (NP) swab and nasal swab specimens. It is intended to aid in the rapid differential diagnosis of influenza A and B viral infections. Negative test results are presumptive and should be confirmed by cell 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. BinaxNOW Influenza A & B Card 2 must be read by the DIGIVAL™.

Performance characteristics for influenza A were established during the 2015-2016 influenza season when influenza A/H3N2 and A/H1N1 pandemic were the predominant influenza A viruses in circulation. When other influenza A viruses are emerging, performance characteristics may vary.

If infection with a novel influenza A virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions for novel virulent Influenza viruses and sent to state or local health department for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.

Summary and Explanation of the Test

Influenza is a highly contagious, acute, viral infection of the respiratory tract. It is a communicable disease that is easily transmitted through the coughing and sneezing of aerosolized droplets containing live virus. Influenza outbreaks occur each year during the fall and winter months.[1] Type A viruses are typically more prevalent than type B viruses and are associated with most serious influenza epidemics, while Type B infections are usually milder.

Rapid diagnosis of influenza A and B has become more important due to the availability of effective antiviral therapy. Rapid diagnosis of influenza can lead to reduced hospital stays, antimicrobial use and cost of hospital care.[1]

The BinaxNOW Influenza A & B Card 2 provides a simple, rapid method for the diagnosis of influenza A and B using NP swab and nasal swab specimens. The easy-to-use format and rapid results allow for its use in "STAT" testing where it can provide information to assist with treatment and hospitalization decisions.

Principles of the Procedure

The BinaxNOW Influenza A & B Card 2 is an immunochromatographic membrane assay that detects influenza type A and B nucleoprotein antigens in respiratory specimens. Influenza specific antibodies and a control antibody are immobilized onto a membrane support as three distinct lines and combined with other reagents/pads to construct a test strip. This test strip is mounted inside a cardboard, book-shaped hinged test card.

Swab specimens require a sample preparation step, in which the sample is eluted off the swab into elution solution. Sample is added to the top of the test strip and the test card is closed. Test results will be interpreted at 15 minutes based on the presence or absence of Sample Lines. BinaxNOW Influenza A & B Card 2 test results must be read by the DIGIVAL.

The DIGIVAL is provided separately for result interpretation. The DIGIVAL enables direct data entry of User ID, Subject ID, and retention of test results, but is intended for result interpretation only.

Note: *Depending on the DIGIVAL setting selected, the BinaxNOW Influenza A & B Card 2 assay is either immediately inserted in the DIGIVAL for automatically timed assay development and result interpretation (Walk Away Mode) or placed on the counter or bench top for manual timed assay development and then placed in the DIGIVAL for result interpretation.*

Reagents and Materials

Materials Provided

22 Test Cards: A cardboard, book-shaped hinged test card containing the test strip

25 Transfer Pipettes: Fixed volume (100 µl) transfer pipettes used to transfer sample to the test cards.

1 Positive Control Swab: Inactivated influenza A and B viruses dried onto the swab.

1 Negative Control Swab: Inactivated *Streptococcus* Group A dried onto the swab.

22 Elution Solution 2 Vials: Vials containing elution solution used to prepare the Swab Specimens and Control Swabs for testing.

24 Nasal Swabs: Sterile swabs for use in the BinaxNOW Influenza A & B Card 2.

1 Product Insert

1 Procedure Card

Materials Required But Not Provided

- DIGIVAL
- Calibration Check Card (for use with the DIGIVAL)

Materials Recommended But Not Provided

- Clock, timer or stopwatch
- Nasopharyngeal (NP) Swabs

Precautions

1. For *in vitro* diagnostic use.
2. Federal Law restricts this device to sale by or on the order of a licensed practitioner.
3. Leave test card sealed in its foil pouch until just before use.
4. When using the DIGIVAL, to prevent tearing through the barcode, do not open the foil pouch prior to scanning or entering manually the Test Device ID.
5. Do not use kit past its expiration date.
6. Do not mix components from different kit lots.
7. Any labels or writing placed on the front of the card should be contained within the 2 lines provided on the right side of card face, to reduce interference with the DIGIVAL. Do not write on or cover the barcode on the front of the test card prior to inserting into the DIGIVAL.
8. The **WHITE** sample pad at the top of the test strip contains reagents that extract the target antigen from the virus. To ensure optimum performance, add the sample to the **TOP HALF** of this pad such that all of the sample volume absorbs into the pad.
9. Solutions used to make the control swabs are inactivated using standard methods. However, patient samples, controls, and test cards should be handled as though they could transmit disease. Observe established precautions against microbial hazards.
10. If infection with a novel influenza A virus is suspected based on current clinical and epidemiological screening criteria recommended by public health authorities, specimens should be collected with appropriate infection control precautions for novel virulent influenza viruses and sent to state or local health departments for testing. Viral culture should not be attempted in these cases unless a BSL 3+ facility is available to receive and culture specimens.[2]
11. **INVALID RESULTS** can occur when an insufficient volume of specimen is added to the test cards. To ensure delivery of an adequate volume, make certain that the lower shaft of the transfer pipette is full and does not contain air spaces before dispensing contents of the pipette onto the Sample Pad of the card. If air spaces are present, expel the specimen back into the container by squeezing the top bulb and redraw the specimen into the pipette. Use a new pipette if necessary.
12. All transfer pipettes and elution solution vials are single use items – do not use with multiple specimens.
13. Performance characteristics for influenza A were established when influenza A/H3 and A/H1 were the predominant influenza A viruses in circulation. When other influenza A viruses are emerging, performance characteristics may vary.
14. The elution solution packaged in this kit contains saline, detergents and preservatives that will inactivate cells and virus particles. Samples eluted in this solution are not suitable for culture.
15. Elution solution contains Triton® X-100 and Proclin® 300. Warning: may cause an allergic skin reaction, causes serious eye irritation.
16. Safety data sheets for this product are available upon request.
17. Follow your national, regional, and local ordinances accordingly for waste disposal regulations.
18. Care should be taken when handling the test to avoid potential contamination from debris such as lint, hair and other particulates as these may cause false results.
19. For result interpretation, DO NOT read results visually; results must be read by the DIGIVAL.

Storage and Stability

Store kit at 2-30°C. The BinaxNOW Influenza A & B Card 2 kit and reagents are stable until the expiration dates marked on their outer packaging and containers.

Quality Control

Daily Quality Control:

The BinaxNOW Influenza A & B Card 2 has built-in procedural controls. For daily quality control, Abbott suggests that you record these controls for each test run.

Procedural Controls:

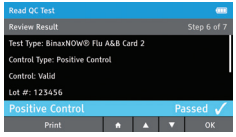
- An untested card has a blue line at the "Control" position. If the test flows and the reagents work, this blue line will always turn pink in a tested card.
- If the blue control line is not present on the test strip before use DO NOT use the test. Discard the test and use another test card from the test kit.
- The clearing of background color from the result window is a negative background control. The background color in the window should be light pink to white within 15 minutes.

External Positive and Negative Controls:

Good laboratory practice suggests the use of positive and negative controls to ensure that:

- Test reagents are working, and
- The test is correctly performed.

BinaxNOW Influenza A & B Card 2 kits contain Influenza A & B Positive and Viral Negative Control Swabs. The Influenza A and B Positive Control swab should generate a positive result for both Influenza A and B . When read by the DIGIVAL the positive result will be displayed as Passed.



These swabs will monitor the entire assay. Test these swabs with each new shipment received and once for each untrained operator. Other controls may be tested in order to conform with:

- local, state and/or federal regulations,
- accrediting groups, and/or,
- your lab's standard Quality Control procedures.

Refer to 42 CFR 493.1256 for guidance on proper QC practices (U.S. customers only).

If the correct control results are not obtained, do not report patient results. Contact Technical Service during normal business hours.

Specimen Collection and Handling

Use freshly collected specimens for optimal test performance. Inadequate specimen collection or improper sample handling/transport may yield a false-negative result.

Nasopharyngeal Swab

Use sterile rayon, foam or polyester flexible-shaft NP swabs to collect nasopharyngeal samples.

To collect a nasopharyngeal swab sample, carefully insert the swab into the nostril exhibiting the most visible drainage, or the nostril that is most congested if drainage is not visible. Pass the swab directly backwards without tipping the swab head up or down. The nasal passage runs parallel to the floor, not parallel to the bridge of the nose. Using gentle rotation, insert the swab into the anterior nare parallel to the palate advancing the swab into the nasopharynx, leave in place for a few seconds, and then slowly rotate the swab as it is being withdrawn.

To ensure proper collection, the swab should be passed a distance that is halfway of that from the nose to the tip of the ear. This is about half the length of the swab. **DO NOT USE FORCE** while inserting the swab. The swab should travel smoothly with minimal resistance; if resistance is encountered, withdraw the swab a little bit without taking it out of the nostril. Then elevate the back of the swab and move it forward into the nasopharynx.

Nasal Swab

For optimal performance, use the swabs provided in the test kit. Alternatively, sterile rayon, foam, polyester or HydraFlock® flocked (standard tip) solid shaft swabs can be used to collect nasal swab samples.

To collect a nasal swab sample, carefully insert the swab into the nostril exhibiting the most visible drainage, or the nostril that is most congested if drainage is not visible. Using gentle rotation, push the swab until resistance is met at the level of the turbinates (less than one inch into the nostril). Rotate the swab several times against the nasal wall then slowly remove from the nostril.

Note: *Puritan PurFlock Ultra® Flocked Swabs, Copan Regular Flocked Swabs and Calcium Alginate Swabs are not suitable for use in this assay.*

Sample Transport and Storage

Samples should be tested as soon as possible after collection. If swab specimens cannot be immediately eluted after collection, the swab is to be returned to its respective sheath and may be stored up to four (4) hours at room temperature. If the swab sample will be held longer than 4 hours, it must be refrigerated at 2-8 °C and tested within 24 hours from the time of sample collection.

Swab samples eluted in elution solution may be stored refrigerated at 2-8 °C and tested within 36 hours from the time of sample collection.

Allow all samples to warm to room temperature before testing in the BinaxNOW Influenza A & B Card 2. Swirl gently to mix before testing.

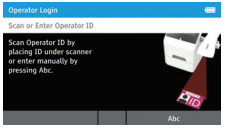
Test Procedure Using the DIGIVAL™

WARNING: INVALID RESULTS can occur when too little sample is added to the test. Be sure that the lower part of the transfer pipette is full and does not have any air spaces before you add the sample to the Sample Pad. If there are air spaces, put the sample back into the container by squeezing the top bulb. Redraw the sample from the bottom of the container into the pipette. Use a new pipette if needed.

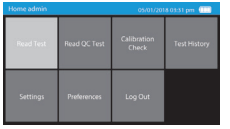
Part 1 -DIGIVAL™ Set Up

1. Turn on the DIGIVAL by pressing the power button. Wait for approximately 10 seconds for the instrument start up sequence. The DIGIVAL may be set to two different modes (Walk Away or Read Now). For full instructions on using the DIGIVAL please refer to the User Manual and Quick Start Guide.

2. Enter Operator ID by placing Operator ID barcode under scanner or entering manually with the keyboard. Enter Operator Password and confirm by pressing 'OK'.



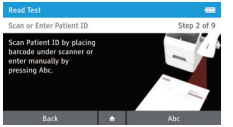
3. Tap 'Read Test' on the DIGIVAL menu, this starts the reading process.



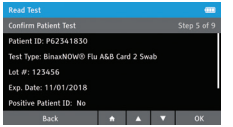
4. Enter Test Device ID by placing the barcode on the foil pouch under scanner or entering manually with the keyboard.

5. Enter Patient ID by placing Patient ID barcode under scanner or entering manually with the keyboard.

   Note: *Default is Patient ID only, see additional options in the DIGIVAL User Manual.*

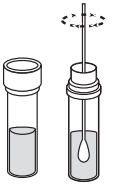


6. Confirm the data entry of Operator ID, Patient ID and Test Device ID on the screen then tap 'OK' to confirm.



Part 2 -Test Procedure

7. Elution Solution 2 vials are pre-filled. Twist off the vial cap.



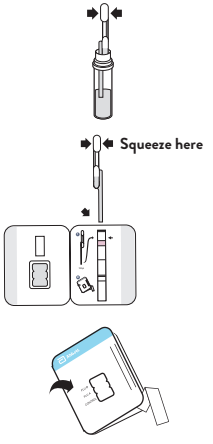
8. Put the swab to be tested in the vial. **Rotate the swab three (3) times in the liquid** while pushing vigorously against the bottom of the vial. Minimize bubbles.
9. **Push the swab against the side** of the vial and turn as you remove it from the vial. This removes sample from the swab. Discard the swab into a biohazard waste container.
10. Test the liquid sample (from the test vial) in the BinaxNOW Influenza A & B Card 2 as soon as possible.
11. Remove card from the foil pouch **just prior to testing** and lay flat on the work bench.

12. Fill pipette by firmly squeezing the top bulb and **then** placing pipette tip into sample. Slowly release bulb while tip is still in sample. This will pull liquid into the pipette. Make sure there are no air spaces in the lower part of the pipette.

    Note: *To ensure the correct volume of sample is added to the test card, the fixed volume pipette provided in the test kit must be used.*

13. See arrow on test card to find the **WHITE** sample pad at the top of the test strip. Add entire contents of pipette (100 µl) in a continuous flow to the **TOP HALF** of this pad by squeezing the top bulb such that all of the sample volume absorbs into this pad. **DO NOT** add sample to the pink/red colored pad. If the sample is added to the incorrect location on the test strip, the test should be discarded. Repeat the test using a new test device and ensure the sample is added to the correct location on the test strip.

14. Peel off adhesive liner from the right edge of the test card. Close and securely seal the card by pressing the right edge of the test card.

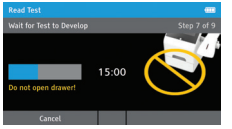


Part 3 -Reading the Results

15a. Read Now Mode: At the 15 minute read time open the DIGIVAL drawer, insert the BinaxNOW Influenza A & B Card 2 test into the drawer with the barcode and result window facing up and close the drawer.

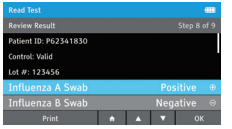
OR

15b. Walk Away Mode: Once the card is securely closed, immediately open the DIGIVAL drawer, insert the BinaxNOW Influenza A & B Card 2 test into the drawer with the barcode and result window facing up and close the drawer. The DIGIVAL will automatically time the test development and read the result at the read time.



16. WAIT until the result is displayed on the screen. **DO NOT OPEN THE DRAWER** until Test Results appear on the screen.

    Note: *Do not read test results before or after 15 minutes as they may not be correct.*

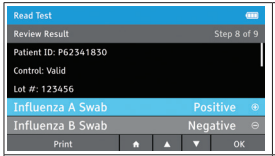
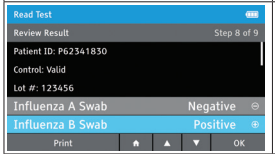
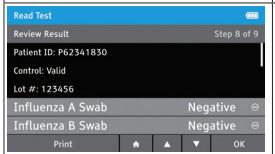
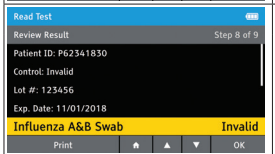
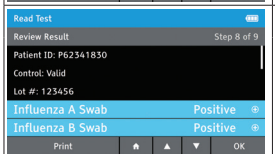


17. If using a Printer, tap "Print" to print test results.

18. Open the drawer, remove and discard the used BinaxNOW Influenza A & B Card 2 Test and close the drawer. The Home screen will automatically appear. **DO NOT REINSERT TEST DEVICE ONCE A RESULT HAS BEEN OBTAINED.**

Result Interpretation:

Results will be automatically displayed on the DIGIVAL screen. Results will be interpreted as positive or negative for Influenza A and Influenza B in addition to the procedural control line status.

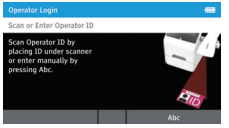
	Influenza A Positive/ Influenza B Negative Result
	Influenza A Negative/ Influenza B Positive Result
	Influenza A Negative/ Influenza B Negative Result
	Invalid Test Result If the test is invalid, another specimen should be collected and tested.
	Co-infection Result Co-infection with influenza A and B is very rare. A clinical specimen that generates positive results for both influenza A and B on the BinaxNOW Influenza A & B Card 2 Test should be considered an invalid result and another specimen should be collected and tested. If the test result is again positive for influenza A and B, the specimen should be re-tested by another method prior to reporting the results.

Procedure Using the DIGIVAL™ for QC Test

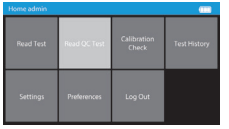
Part 1 -DIGIVAL™ Set Up

1. Turn on the DIGIVAL by pressing the power button. Wait for approximately 10 seconds for the instrument start up sequence. The DIGIVAL may be set to two different modes (Walk Away or Read Now). For full instructions on using the DIGIVAL please refer to Manual and Quick Start Guide.

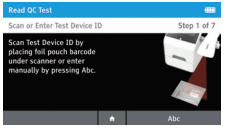
2. Enter Operator ID by placing Operator ID barcode under scanner or entering manually with the keyboard. Enter Operator Password and confirm by pressing 'OK'.



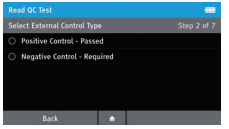
3. Tap 'Read QC Test' on the DIGIVAL menu. This starts the reading process.



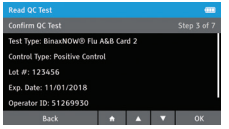
4. Enter Test Device ID by placing the barcode on the foil pouch under scanner or entering manually with the keyboard.



5. Select the positive or negative control to be tested and tap “OK” to continue.



6. Confirm the data entry of Operator ID, Test Type, Control Type and Test Device ID on the screen then tap ‘OK’ to confirm.

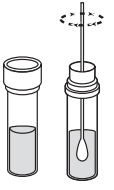


Part 2 -Test Procedure

7. Elution Solution 2 vials are pre-filled. Twist off the vial cap.

8. Put the swab to be tested in the vial. **Rotate the swab three (3) times in the liquid** while pushing vigorously against the bottom of the vial. Minimize bubbles.

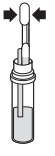
9. **Push the swab against the side** of the vial and turn as you remove it from the vial. This removes sample from the swab. Discard the swab into a biohazard waste container.



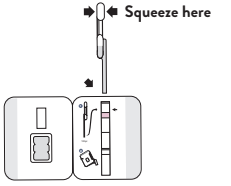
10. Test the liquid sample (from the test vial) in the BinaxNOW Influenza A & B Card 2 as soon as possible.

11. Remove card from the foil pouch **just prior to testing** and lay flat on the work bench.

12. Fill pipette by firmly squeezing the top bulb and **then** placing pipette tip into sample. Slowly release bulb while tip is still in sample. This will pull liquid into the pipette. Make sure there are no air spaces in the lower part of the pipette.



13. See arrow on test card to find the WHITE sample pad at the top of the test strip. Add entire contents of pipette (100 µl) **in a continuous flow** to the **TOP HALF** of this pad by squeezing the top bulb such that all of the sample volume absorbs into this pad. **DO NOT** add sample to the pink/red colored pad.



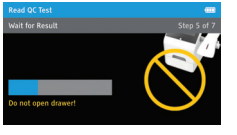
14. Peel off adhesive liner from the right edge of the test card. Close and securely seal the card by pressing the right edge of the test card.

Part 3 -Reading the Results

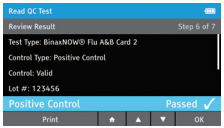
15a. Read Now Mode: At the 15 minute read time open the DIGIVAL drawer, insert the BinaxNOW Influenza A & B Card 2 test into the drawer with the barcode and result window facing up and close the drawer.

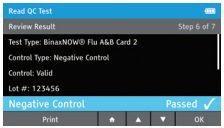
OR

15b. Walk Away Mode: Once the card is securely closed, immediately open the DIGIVAL drawer, insert the BinaxNOW Influenza A & B Card 2 test into the drawer with the barcode and result window facing up and close the drawer. The DIGIVAL will automatically time the test development and read the result at the read time.



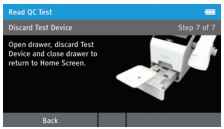
16. WAIT until the result is displayed on the screen. **DO NOT OPEN THE DRAWER** until Test Results appear on the screen.
Note: *Do not read test results before or after 15 minutes as they may not be correct.*





17. If using a Printer, tap 'Print' to print test results.

18. Open drawer, remove and discard the used BinaxNOW Influenza A & B Card 2 Test and close the drawer. The Home screen will automatically appear. **DO NOT REINSERT TEST DEVICE ONCE A RESULT HAS BEEN OBTAINED**.



Limitations

- A negative test result does not exclude infection with influenza A and/or B. Therefore, the results obtained with the BinaxNOW Influenza A & B Card 2 should be used in conjunction with clinical findings to make an accurate diagnosis. Additional testing is required to differentiate any specific influenza A subtypes, influenza B lineages or influenza strains, in consultation with state or local public health departments.
- The BinaxNOW Influenza A & B Card 2 detects both viable and non-viable influenza A and B. Test performance depends on antigen load in the specimen and may not correlate with cell culture performed on the same specimen.
- False negative results may occur if a specimen is improperly collected, transported or handled. False negative results may occur if low levels of viruses are present in the specimen.
- Performance of the BinaxNOW Influenza A & B Card 2 has not been established for monitoring antiviral treatment of influenza.
- Individuals who have received nasally administered influenza A vaccine may test positive in commercially available influenza rapid diagnostic tests for up to three days after vaccination.
- The assay performance was established during the 2015 to 2016 influenza season. The positive and negative predictive values may vary depending on the prevalence and population tested.
- This test has not been evaluated for patients without signs and symptoms of influenza infection.
- Puritan PurFlock Ultra® Flocked Swabs, Copan Regular Flocked Swabs and Calcium Alginate Swabs are not suitable for use in this assay.

Expected Values

The prevalence of influenza varies from year to year, with outbreaks typically occurring during the fall and winter months.[2] The rate of positivity found in influenza testing is dependent on many factors including the method of specimen collection, the test method used, geographic location, and the disease prevalence in specific localities. In the BinaxNOW Influenza A & B Card 2 multi center prospective clinical study (described in the "Clinical Study" section below), a total of 585 nasal or nasopharyngeal swab specimens were determined to be evaluable. The number and percentage of influenza A and influenza B positive cases per specified age group, as determined by the BinaxNOW Influenza A & B Card 2 assay with the DIGIVAL, are presented in the two tables below:

Influenza A Positives by the BinaxNOW™ Influenza A & B Card 2 Assay with the DIGIVAL™ per Age Group

Prospective Clinical Study During the 2015/2016 Influenza Season			
Age Group	**Number of Nasal or Nasopharyngeal Swab Specimens**	**Number of Influenza A Positives**	**Influenza A Positivity Rate**
<1 year	39	3	7.7%
1 to 5 years	119	23	19.3%
6 to 10 years	91	17	18.7%
11 to 15 years	39	10	25.6%
16 to 21 years	32	8	25.0%
>21 to 60 years	228	65	28.5%
>60 years	37	10	27.0%
Total	585	136	23.2%

Influenza B Positives by the BinaxNOW™ Influenza A & B Card 2 Assay with the DIGIVAL™ per Age Group

Prospective Clinical Study During the 2015/2016 Influenza Season			
Age Group	**Number of Nasal or Nasopharyngeal Swab Specimens**	**Number of Influenza B Positives**	**Influenza B Positivity Rate**
<1 year	39	1	2.6%
1 to 5 years	119	7	5.9%
6 to 10 years	91	15	16.5%
11 to 15 years	39	4	10.25%
16 to 21 years	32	7	21.8%
>21 to 60 years	228	15	6.6%
>60 years	37	5	13.5%
Total	585	54	9.2%

Performance Characteristics

Clinical Study:

Clinical performance characteristics of BinaxNOW Influenza A & B Card 2 with the DIGIVAL were evaluated in a multi-site prospective study during the 2015-2016 flu season in the U.S. A total of twelve (12) investigational sites throughout the U.S. participated in the study. To be enrolled in the study, patients had to be presenting at the participating study centers with flu-like symptoms. Either two nasopharyngeal swabs or two nasal swabs were collected from one nostril from each patient with flu-like symptoms using standard collection methods and tested using the BinaxNOW Influenza A & B Card 2 assay with the DIGIVAL. An FDA cleared influenza real-time Polymerase Chain Reaction (RT-PCR) assay was utilized as the comparator method for this study.

At all sites, one nasal or nasopharyngeal swab was eluted in elution solution and the other swab was eluted in 1 mL of Viral Transport Media (VTM). The swab eluted in elution solution was tested on BinaxNOW Influenza A & B Card 2, according to product instructions. All twelve (12) sites shipped the VTM sample to a central testing laboratory for RT-PCR.

External control testing, using BinaxNOW Influenza A & B Card 2 Positive and Negative Controls, was performed prior to sample testing each day, at all study sites.

A total of 645 Subjects were enrolled in this study. Of those, 60 swab samples did not meet eligibility criteria due to protocol deviations (sample handling or storage errors or Subject withdrawal). A total of 585 nasal or nasopharyngeal swab specimens were considered evaluable. Patient age and gender distribution for all the evaluable specimens is presented in the table below.

Age and Gender Distribution

Age Group	Female	Male
<1 year	18	21
1 to 5 years	57	62
6 to 10 years	45	46
11 to 15 years	21	18
16 to 21 years	18	14
>21 to 60 years	143	85
>60 years	25	12
Total	327	258

Of the evaluable 585 specimens, BinaxNOW Influenza A & B Card 2 with the DIGIVAL generated invalid results with the DIGIVAL for 20 specimens, resulting in a total of 565 specimens for performance analysis.

Compared to the comparator method, the performance of BinaxNOW Influenza A & B Card 2 with the DIGIVAL for influenza A and influenza B are presented in the two tables below.

Influenza A Performance with BinaxNOW™ Influenza A & B Card 2 with the DIGIVAL™ Against the Comparator Method

BinaxNOW™ Influenza A & B Card 2 – Flu A	Comparator Method		
	Positive	**Negative**	**Total**
Positive	113	23	136
Negative	21	408	429
Total	134	431	565
Sensitivity: 84.3% (113/134), 95%CI: (77.2%-89.5%)			
Specificity: 94.7% (408/431), 95%CI: (92.1%-96.4%)			

Influenza B Performance with BinaxNOW™ Influenza A & B Card 2 with the DIGIVAL™ Against the Comparator Method

BinaxNOW™ Influenza A & B Card 2 – Flu B	Comparator Method		
	Positive	**Negative**	**Total**
Positive	51	3	54
Negative	6	505	511
Total	57	508	565
Sensitivity: 89.5% (51/57), 95%CI: (78.9%-95.1%)			
Specificity: 99.4% (505/508), 95%CI: (98.3%-99.8%)			

During the prospective clinical study, the invalid rate was 3.4% (20/585) (95% CI: 2.2% to 5.2%). The invalid rate includes 19 results that were positive for both influenza A and B.

Analytical Studies:

Reproducibility

A reproducibility study of BinaxNOW Influenza A & B Card 2 with the DIGIVAL was conducted by operators from three (3) sites using panels of blind coded specimens containing negative, high negative (below the limit of detection), low positive (at the limit of detection), and moderate positive (above the limit of detection) influenza A and B viral samples. Virus dilutions were prepared using one influenza A strain and one influenza B strain in Viral Transport Media (VTM). The concentrations of the viral stocks (in $TCID_{50}$/mL) were determined by standard virologic method prior to inactivation by the vendors.

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

Participants tested the sample panels over five (5) different days. The percent agreement with expected results, across the three sites, for the influenza A moderate positive, low positive, and high negative samples were 100% (90/90), 100% (90/90) and 96.6% (86/89), respectively. The percent agreement with expected result for the influenza B moderate positive, low positive, and high negative samples were 100% (90/90), 100% (89/89) and 97.8% (88/90), respectively. All of the true negative samples (90) generated negative test results.

Site-To-Site Qualitative Results – Percent Agreement with Expected Results

Sample Type		Site 1	Site 2	Site 3	Overall % Agreement with Expected Results
Influenza A	Moderate Positive	100% (30/30)	100% (30/30)	100% (30/30)	**100% (90/90)**
	Low Positive	100% (30/30)	100% (30/30)	100% (30/30)	**100% (90/90)**
	High Negative	100% (29/29)[1]	93.3% (28/30)	96.7% (29/30)	**96.6% (86/89)**
Influenza B	Moderate Positive	100% (30/30)	100% (30/30)	100% (30/30)	**100% (90/90)**
	Low Positive	100% (30/30)	100% (30/30)	100% (29/29)[2]	**100% (89/89)**
	High Negative	100% (30/30)	93.3% (28/30)	100% (30/30)	**97.8% (88/90)**
True Negative		100% (30/30)	100% (30/30)	100% (30/30)	**100% (90/90)**

[1] One sample generated an invalid result and was not re-tested.
[2] One sample generated a positive Flu A and Flu B result, was considered invalid and was not re-tested.

There were no significant differences observed within run (replicates tested by one operator), between run (five different days), between sites (three sites), or between operators (six operators).

Analytical Sensitivity (Limit of Detection)

BinaxNOW Influenza A & B Card 2 with the DIGIVAL limit of detection (LOD) was determined by evaluating different concentrations of five (5) strains of influenza A and three (3) strains of influenza B virus. Pre-screened negative natural nasal swab specimens were eluted in 1 X PBS. Swab elutes were combined and mixed thoroughly to create a clinical matrix pool to be used as the diluent. Each influenza virus strain was diluted in this natural nasal swab matrix pool to generate virus dilutions for testing. The vendor provided virus strains were re-titered and the concentrations (in $TCID_{50}$/mL) were determined by standard virologic method.

Contrived nasal swab samples were prepared by coating 10 microliters of each virus dilution onto the swab. The contrived swab samples were tested after elution in elution solution according to the test procedure.

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

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

Limit of Detection (LOD) Study Results

Strain	Concentration $TCID_{50}$/mL	% Detected
A/Anhui/13 (H7N9) – Inactivated*	1:1500	95%
A/Indiana/10/11 (H3N2v)	3.67×10^{1}	95%
A/California/7/2009 (H1N1)	5.94×10^{3}	95%
A/Perth/16/2009 (H3N2)	1.68×10^{4}	95%
A/Puerto Rico/8/34 (H1N1)	3.16×10^{4}	95%
B/Massachusetts/02/12 (Yamagata)	1.47×10^{6}	95%
B/Nevada/03/2011 (Victoria)	9.72×10^{3}	95%
B/Malaysia/2506/2004	4.27×10^{3}	95%

Note: *10µl of each virus dilution was coated onto a swab.*
*The LOD is reported as a dilution factor from the inactivated stock. The concentration of the virus stock prior to inactivation was $10^{10.9}$ EID_{50}/mL.

Analytical Reactivity:

An analytical reactivity (inclusivity) study was performed to determine whether the BinaxNOW Influenza A & B Card 2 with the DIGIVAL is able to detect a variety of influenza A and B strains that represent temporal and geographic diversity.

Vendor provided stocks of influenza A and influenza B were diluted in elution solution to generate virus dilutions for testing. The virus strains were re-titered and the concentrations (in $TCID_{50}$/mL) were determined by standard virologic methods.

Contrived swab samples were prepared by coating 10 microliters of virus dilution onto each swab. The contrived swab samples were tested according to the test procedure.

The starting dilution concentration selected for testing in this study was of a high concentration in order to generate a strong positive result. Each starting dilution per virus strain was tested in triplicates initially. If the initial testing concentration tested positive for all three replicates, the strain was further diluted 10-fold and tested in triplicates until at least one out of three replicates generated a negative result. When a negative result was obtained, additional 2-fold dilutions were tested, starting from the highest dilution that produced 100% (3/3) positive results.

The BinaxNOW Influenza A & B Card 2 assay detected all strains tested (3/3) at the concentrations indicated in the table below.

Analytical Reactivity Study Results

Influenza Strain	Influenza A Subtype or Influenza B Genetic Lineage	Concentration $TCID_{50}$/mL
A/Brisbane/59/2007	A/H1N1	8.35×10^{1}
A/California/4/2009	A/H1N1 (pdm)	3.68×10^{3}
A/Maryland/04/2011	A/H1N1 (pdm)	1.07×10^{2}
A/New Caledonia/20/1999	A/H1N1	2.08×10^{2}
A/New Jersey/8/1976	A/H1N1	1.04×10^{1}
A/New York/18/2009	A/H1N1 (pdm)	1.41×10^{2}
A/Solomon Islands/3/2006	A/H1N1	5.28×10^{1}
A/WSN/33	A/H1N1	5.00×10^{2}
A/Texas/018/2014	A/H1N1	7.90×10^{3}
A/Texas/002/2014	A/H1N1	1.70×10^{3}
A/Aichi/2/68	H3N2	7.90×10^{3}
A/Brisbane/10/2007	H3N2	3.68×10^{0}
A/Hong Kong/8/68	H3N2	2.41×10^{1}
A/Port Chalmers/1/73	H3N2	1.58×10^{4}
A/Texas/50/2012	H3N2	1.06×10^{0}
A/Victoria/3/75	H3N2	1.58×10^{1}
A/Victoria/361/2011	H3N2	2.11×10^{0}
A/Wisconsin/67/2005	H3N2	2.63×10^{1}
B/Bangladesh/3333/2007	Yamagata Lineage	2.11×10^{5}
B/Brisbane/60/2008	Victoria Lineage	3.41×10^{5}
B/Florida/04/2006	Yamagata Lineage	2.97×10^{5}
B/Lee/40	Victoria Lineage	6.81×10^{3}
B/Maryland/1/59	Yamagata Lineage	7.90×10^{4}
B/Montana/05/2012	Victoria Lineage	2.51×10^{6}
B/Ohio/1/2005	Victoria Lineage	3.40×10^{3}
B/Russia/69	Yamagata Lineage	5.93×10^{5}
B/Texas/06/2011	Yamagata Lineage	1.47×10^{6}
B/Victoria/304/2006	Victoria Lineage	1.58×10^{5}
B/Victoria/504/2000	Victoria Lineage	6.81×10^{4}
B/Wisconsin/01/2010	Yamagata Lineage	1.45×10^{4}

Annual Analytical Reactivity

An annual review of the BinaxNOW Influenza A & B Card 2 with the DIGIVAL performance was conducted by testing contemporary strains of human influenza virus supplied by the CDC.

The viral stocks were diluted in elution solution to generate virus dilutions for testing. Contrived swab samples were prepared by coating 50µl of the virus dilution onto each swab. The contrived swab samples were tested according to the test procedure. For each viral strain included in the panel, all dilutions were tested until a level that produced 100% negative results for two consecutive dilutions on all 5 replicates at each level was obtained.

Annual analytical reactivity testing data can be found at:
https://www.globalpointofcare.abbott/us/en/product-details/binaxnow-influenza-a-and-b-2.html

Analytical Specificity (Cross-Reactivity):

To determine the analytical specificity of BinaxNOW Influenza A & B Card 2 with the DIGIVAL, 58 commensal and pathogenic microorganisms (41 bacteria, 16 viruses and 1 yeast) that may be present in the nasal cavity or nasopharynx were tested, with results read by the DIGIVAL. All of the following microorganisms were negative when tested at concentrations ranging from 10^3 to 10^{10} cells/mL or CFU/mL or IFU/mL (bacteria), 10^4 to 10^8 $TCID_{50}$/mL or $CEID_{50}$/mL (viruses), and 10^8 cells/mL (yeast).

Bacteria	Viruses	Yeast
Acinetobacter calcoaceticus	Adenovirus type 1	*Candida albicans*
Bacteroides fragilis	Adenovirus type 7	
Bordetella pertussis	Cytomegalovirus[6]	
Chlamydia pneumoniae	Human Coronavirus OC43	
Corynebacterium diptheriae	Human Coronavirus 229E[6]	
Enterococcus faecalis	Enterovirus/Coxsackievirus B4	
Escherichia coli	Human Cytomegalovirus strain AD-169[6]	
Gardnerella vaginalis	Human metapneumovirus	
Haemophilus influenzae	Rhinovirus type 1A	
Haemophilus parainfluenza	Measles virus, strain Edmonston	
Klebsiella pneumoniae	Mumps virus, strain Enders	
Lactobacillus casei	Parainfluenza virus 1	
Lactobacillus plantarum	Parainfluenza virus 2	
Legionella pneumophilia	Parainfluenza virus 3	
Listeria monocytogenes[1]	Respiratory Syncytial virus, type B, strain 18537	
Moraxella/Branhamella catarrhalis	Epstein Barr virus, strain P-3	
Mycobacterium avium		
Mycobacterium intracellulare		
Mycobacterium tuberculosis		
Mycoplasma pneumoniae[5]		
Neisseria gonorrhoeae		
Neisseria meningitidis		
Neisseria mucosa[2]		
Neisseria sicca[3]		
Neisseria subflava		
Peptostreptococcus anaerobius		
Proteus mirabilis		
Proteus vulgaris		
Pseudomonas aeruginosa		
Serratia marcescens[4]		
Staphylococcus aureus		
Staphylococcus epidermidis		
Streptococcus mutans		
Streptococcus pneumoniae		
Streptococcus salivarius		
Streptococcus sanguinis		
Streptococcus Group A		
Streptococcus sp. Gp. B		
Streptococcus sp. Gp. C		
Streptococcus sp. Gp. F		
Streptococcus sp. Gp. G		

[1] Flu A positive result obtained at 7.23×10^9 cells/mL; concentration diluted to 7.23×10^8 cells/mL and generated a negative result.
[2] Flu A positive result obtained at 9.4×10^9 cells/mL; concentration diluted to 9.4×10^8 cells/mL and generated a negative result.
[3] Flu A positive result obtained at 1.0×10^{10} cells/mL; concentration diluted to 1.0×10^9 cells/mL and generated a negative result.
[4] Flu A positive result obtained at 6.5×10^8 cells/mL; concentration diluted to 6.5×10^7 cells/mL and generated a negative result.
[5] *Mycoplasma pneumonia* 10^3 was the maximum cfu/mL that could be achieved for growth.
[6] Viruses were tested at concentrations lower than the recommended 10^5 pfu/ml, reflect the stock concentration received from the vendor. Viral stocks were tested at the highest achievable titer allowed by the vendor stock concentration.

Interfering Substances:

The following substances, naturally present in respiratory specimens or that may be artificially introduced into the nasal cavity or nasopharynx, were evaluated with BinaxNOW Influenza A & B Card 2 with the DIGIVAL at the concentrations listed below and were found not to affect test performance.

Substance	Concentration
Mucin	2% (w/v)
Whole Blood	1% (v/v)
Sinus Buster Nasal Spray	20% (v/v)
NeoSynephrine Cold & Sinus Extra Strength Spray	20% (v/v)
Zicam Extreme Congestion Relief	20% (v/v)
4-acetamidophenol	203 µg/mL
Acetylsalicylic acid (aspirin)	652 µg/mL
Albuterol	399 ng/mL
Chlorpheniramine	142 ng/mL
Dexamethasone	0.8 mg/mL
Dextromethorphan	1 µg/mL
Diphenhydramine	5 µg/mL
Doxylamine Succinate	232 ng/mL
Ephedrine	276 ng/mL
Flunisolide	6.8 ng/mL
Guaiacol glycerol ether (pseudoephedrine)	3.58 ng/mL
Mupirocin	12 mg/mL
Oxymetazoline	0.6 mg/mL
Phenylephrine	12 mg/mL
Relenza	284 ng/mL
Rebetol	4.4 µg/mL
Rimantadine	0.28 ng/mL
Tamiflu	1.102 µg/mL
Tobramycin	2.4 mg/mL
Triamcinolone	40 µg/mL

Inhibition by other Microorganisms

BinaxNOW Influenza A & B Card 2 with the DIGIVAL test performance in the presence of non-influenza respiratory pathogens was evaluated. Vendor provided stocks of influenza A and B strains were diluted in clinical contrived matrix to approximately 2 times the limit of detection. Contrived influenza A and B positive swab specimens were prepared by coating 10 microliters of virus dilution onto each swab. The following non-influenza viruses were tested (3/3) at the concentration provided in the table below and were found not to affect test performance.

Virus Panel	Concentration ($TCID_{50}$/mL)
Adenovirus Type 1	4.51×10^5
Rhinovirus Type 1A	4.51×10^6
Respiratory Syncytial Virus, Type B, Strain 18537	2.54×10^4

Inhibition by High Levels of Influenza A and B

BinaxNOW Influenza A & B Card 2 with the DIGIVAL test performance in the presence of high levels of influenza A and B was evaluated. Vendor provided stocks of influenza A and B strains were diluted in clinical contrived matrix to approximately 2 and 20 times the limit of detection. Contrived influenza A and B positive swab specimens were prepared by coating 10 microliters of virus dilution onto each swab. To create the co-infection swabs, diluted influenza A (at a concentration approximately 20 times the LoD) was added to the near LoD Flu B swab. Likewise, diluted influenza B (at a concentration approximately 20 times the LoD) was added to the near LoD Flu A swab. No impact on test performance was observed.

CLIA Waiver Studies

As part of the prospective study testing nasopharyngeal or nasal swabs eluted in elution solution (as described in the Performance Characteristics section above) the accuracy of BinaxNOW Influenza A & B Card 2 with the DIGIVAL was evaluated when used by operators who had no laboratory experience and who were representative of CLIA waived testing sites (intended users). The study was conducted at twelve (12) CLIA waived sites with 36 intended users participating. No training on the use of the test was provided to the operators. A total of 642 Subjects were enrolled in this study. Of those, 33 swab samples did not meet eligibility criteria due to protocol deviations (sample handling or storage errors or Subject withdrawal). A total of 609 nasal or nasopharyngeal swab specimens were considered evaluable. The prospectively collected samples, described above were supplemented with testing swab samples prepared with archived respiratory specimens that were obtained from patients with influenza-like symptoms and were confirmed positive or negative by an FDA cleared assay for influenza A and influenza B. A total of 105 swabs (65 swabs positive for influenza B, 20 swabs positive for influenza A and 20 swabs negative for both influenza A and influenza B) were tested. The supplemental samples were blind-coded and randomized and the testing was incorporated into the daily workflow at each testing site.

Overall, 714 swab specimens were tested by intended users at CLIA waived sites with BinaxNOW Influenza A & B Card 2 with the DIGIVAL, and the results were compared to an FDA cleared molecular-based comparator method. Of the evaluable 714 specimens, BinaxNOW Influenza A & B Card 2 with the DIGIVAL generated invalid results for 21 specimens, resulting in a total of 693 specimens for performance evaluation.

The positive percent agreement (PPA) and the negative percent agreement (NPA) between the BinaxNOW Influenza A & B Card 2 with the DIGIVAL and the comparator method, for all specimens combined, are presented in the tables below, including the 95% confidence intervals (95% CI).

Influenza A Performance with BinaxNOW™ Influenza A & B Card 2 with the DIGIVAL™ Against the Comparator Method

BinaxNOW™ Influenza A & B Card 2 – Flu A	Comparator Method		
	Positive	Negative	Total
Positive	141	23	164
Negative	21	508	529
Total	162	531	693
PPA: 87.0% (141/162) 95%CI: (81.0%-91.4%)			
NPA: 95.7% (508/531) 95%CI: (93.6%-97.1%)			

Influenza B Performance with BinaxNOW™ Influenza A & B Card 2 with the DIGIVAL™ Against the Comparator Method

BinaxNOW™ Influenza A & B Card 2 – Flu B	Comparator Method		
	Positive	Negative	Total
Positive	116	3	119
Negative	6	568	574
Total	122	571	693
PPA: 95.1% (116/122) 95%CI: (89.7%-97.7%)			
NPA: 99.5% (568/571) 95%CI: (98.5%-99.8%)			

During this study, the invalid rate was 2.9% (21/714) (95% CI: 1.9% to 4.5%). The invalid rate includes 19 results that were positive for both influenza A and B.

Sample Studies with Near the Limit of Detection

A study was conducted to evaluate the performance of BinaxNOW Influenza A & B Card 2 with the DIGIVAL with weakly reactive samples when used by untrained users. Randomized blind-coded panels, containing negative, low positive (targeted at the limit of detection {LOD} or assay cutoff), and high negative (below the LOD) influenza A and influenza B specimens, were tested with BinaxNOW Influenza A & B Card 2 at three (3) CLIA waived sites (300 tests in total). Six untrained users at the CLIA waived sites participated in the study. The panel testing was conducted over a minimum of 16 days, and the testing was integrated into the users' daily work flow. The performance of BinaxNOW Influenza A & B Card 2 with samples near the assay cutoff in the hands of untrained users is shown below.

Influenza A and B Testing of Samples near the Assay Cutoff (LOD)

	Untrained Users	
Sample Type	**% Detection**	**95% CI**
Flu A Low Positive (near LOD)	96.7% (58/60)	88.6%, 99.1%
Flu B Low Positive (near LOD)	100.0% (60/60)	94.0%, 100%
Flu A High Negative (below LOD)[1]	100.0% (60/60)	94.0%, 100%
Flu B High Negative (below LOD)[1]	96.7% (58/60)	88.6%, 99.1%
True Negative[1]	100.0% (60/60)	94.0%,100%

[1]Percent Detection correlates to the detection of negative results.

Using risk analysis as a guide, flex studies were conducted on BinaxNOW Influenza A & B Card 2 with the DIGIVAL. The testing evaluated numerous sources of potential human errors and environmental factors that could affect the accuracy of results, including those related to sample handling, reagent handling, extremes of operational conditions, and the operation of the DIGIVAL. The studies demonstrated that the test and the DIGIVAL are robust to the usage variation and environmental factors that may be encountered.

Symbols

℞ Only	
Prescription Only	Hazard Pictogram. See Precautions.

Ordering and Contact Information

Reorder numbers:

575-000: BinaxNOW Influenza A & B Card 2 - 22 Test Kit
575-080: BinaxNOW Influenza A & B Card 2 Control Swab Kit

Technical Support
Advice Line

Further information can be obtained from your distributor, or by contacting Technical Support on:

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2. "Updated Interim Guidance for Laboratory Testing of Persons with Suspected Infection with Avian Influenza A (H5N1) Virus in the United States" CDC Health Alert, June 7, 2006. http://www.phppo.cdc.gov/HAN/ArchiveSys/ViewMsgV.asp?AlertNum=00246

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CE IVD

IN575000 Rev.4 2024/02
SAP: 40005311

Abbott
BinaxNOW
Influenza A & B 2
DIGIVAL, CLIA

PI - US

Size:

8 in x 5.5 in

Printed Colors

CMYK

Incoming Inspection Colors (For Reference Only)

Colors below are not used for printing

PMS 2995 U
Primary Blue

PMS 303 U
Dark Blue

PMS 297 U
Light Blue

PN: IN575000
Rev: 4
SAP: 40005311

Date of Last Revision:
4.3 2024/02/28