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510(k) SUMMARY

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92.

The assigned 510(k) number is: K053120

The purpose of this 510(k) submission is to expand the Analytical Reactivity claims of the currently 510(k) cleared BinaxNOW® Influenza A & B Test (510(k) #K041049).

SUBMITTER
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CONTACT PERSON
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DATE PREPARED
November 04, 2005

TRADE NAME
BinaxNOW® Influenza A & B Test

COMMON NAME
NOW® Flu A/B Test, NOW® Influenza A/B, NOW® Influenza A & B, Binax NOW® Influenza A & B, Binax NOW® Influenza A/B

CLASSIFICATION NAME
Antigen, CF (including CF Controls), Influenza Virus A, B, C (per 21 CFR 866.3330)

PREDICATE DEVICES
Binax NOW® Influenza A & B Test; K041049
Binax NOW® Flu A Test; K021649
Binax NOW® Flu B Test; K021646

DEVICE DESCRIPTION:
The BinaxNOW® Influenza A & B Test is an immunochromatographic membrane assay that uses highly sensitive monoclonal antibodies to detect influenza type A & B nucleoprotein antigens in nasopharyngeal specimens. These 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 device.

Swab specimens require a sample preparation step, in which the sample is eluted off the swab into elution solution or transport media. Nasal wash/aspirate samples require no preparation. Sample is added to the top of the test strip and the test device is closed. Test results are interpreted at 15 minutes based on the presence or absence of pink-to-purple colored Sample Lines. The blue Control Line turns pink in a valid assay.

INTENDED USE

The BinaxNOW® Influenza A & B Test is an *in vitro* immunochromatographic assay for the qualitative detection of influenza A and B nucleoprotein antigens in nasopharyngeal swab and nasal wash/aspirate specimens. It is intended to aid in the rapid differential diagnosis of influenza A and B viral infections. Negative test results should be confirmed by culture.

TECHNOLOGICAL CHARACTERISTICS

The Expanded Claim BinaxNOW® Influenza A & B Test is exactly the same as the currently 510(k) cleared BinaxNOW® Influenza A & B Test. Both tests use identical lateral flow immunochromatographic technology. Both tests are rapid immunoassays that employ specific antibodies immobilized onto a solid phase to capture and visualize influenza nucleoprotein antigens.

PERFORMANCE SUMMARY

CLINICAL STUDIES

BinaxNOW® Influenza A & B Test Performance vs. Cell Culture / DFA – Prospective Study

The performance of the BinaxNOW® Influenza A & B Test was compared to cell culture and/or DFA, and to the Binax NOW® Flu A Test and the Binax NOW® Flu B Test, in a prospective study conducted in 2004 outside the US. Nasopharyngeal (NP) swab and nasal wash / aspirate specimens, collected at multiple sites from children (less than 18 years of age) and adults (18 years or older) presenting with influenza-like symptoms, were evaluated in the Binax test at a central testing lab.

Forty-seven percent (47%) of the population tested was male, 53% female, 40% pediatric (< 18 years), and 60% adult (≥ 18 years). No differences in test performance were observed based on patient age or gender. There were no invalid tests reported.

One hundred and thirteen (113) NP swab specimens and 1 wash/aspirate specimen were tested. One hundred and eight (108) of the 114 samples tested were influenza negative by culture/DFA, and 6 samples were influenza positive. When compared to culture/DFA, the BinaxNOW® Test was 75% (3/4) sensitive and 100% (110/110) specific for detection of influenza A and 50% (1/2) sensitive and 100% (112/112) specific for detection of influenza B. There was 100% agreement between the BinaxNOW® Influenza A & B Test and the individual Flu A and Flu B Tests.

BinaxNOW® A & B Test specificity by sample type versus cell culture / DFA, including 95% confidence intervals, is listed below.

BinaxNOW® Influenza A & B Test Specificity vs. Cell Culture/DFA

	FLU A SPECIFICITY			
Sample	-/-	+/-	% Spec	95% CI
NP Swab	109	0	100%	97-100%
Wash/Aspirate	1	0	100%	16-99%
Overall	110	0	100%	97-100%

FLU B SPECIFICITY			
-/-	+/-	% Spec	95% CI
111	0	100%	97-100%
1	0	100%	16-99%
112	0	100%	97-100%

BinaxNOW® Influenza A & B Test Performance vs. Binax NOW® Flu A and Flu B Tests:

Performance of the BinaxNOW® Influenza A & B Test was compared to the current NOW® Flu A Test on 306 retrospective frozen clinical samples and to the NOW® Flu B Test on 303 retrospective frozen clinical samples. All clinical samples were collected from symptomatic patients at multiple physician offices, clinics and hospitals located in the Southern, Northeastern and Midwestern regions of the United States and from one hospital in Sweden. Fifty-three percent (53%) of the population tested was male, 47% female, 64% pediatric (< 18 years) and 36% adult (≥ 18 years). Nasal wash/aspirate specimens comprised approximately 57% of the samples tested, while NP swabs represented 42%. No differences in test performance were observed based on patient age and gender or based on sample type tested.

The BinaxNOW® Influenza A & B Test was 100% sensitive and 96% specific for detection of influenza A vs. the NOW® Flu A Test and 93% sensitive and 97% specific for detection of influenza B vs. the NOW® Flu B Test. Test performance by virus type (A vs. B), by sample type (swab vs. wash/aspirate), and overall, including 95% confidence intervals, is detailed in the following tables.

BinaxNOW® Influenza A & B Test vs. NOW® Flu A Test for Detection of Influenza A

	FLU A SENSITIVITY				FLU A SPECIFICITY			
Sample	+/+	-/+	% Sens	95% CI	-/-	+/-	% Spec	95% CI
NP Swab	30	0	100%	89-100%	96	1	99%	94-100%
Wash/Aspirate	47	0	100%	93-100%	123	9	93%	88-96%
Overall	77	0	100%	95-100%	219	10	96%	88-96%

BinaxNOW® Influenza A & B Test vs. NOW® Flu B Test for Detection of Influenza B

	FLU B SENSITIVITY				FLU B SPECIFICITY			
Sample	+/+	-/+	% Sens	95% CI	-/-	+/-	% Spec	95% CI
NP Swab	2	0	100%	29-99%	126	1	99%	96-100%
Wash/Aspirate	12	1	92%	66-98%	152	9	94%	90-97%
Overall	14	1	93%	70-98%	278	10	97%	94-98%

Binax NOW® Flu A and Flu B Test Performance vs. Cell Culture

Performance of the Binax NOW® Flu A and Flu B Tests was compared to cell culture on 373 prospective clinical samples collected as part of a multi-center study conducted during the 2002 Flu season at physician offices and clinics located in the Western and mid-Atlantic United States. Fifty-four percent (54%) of the population tested was male, 46% female, 90% pediatric (< 18 years) and 10% adult (≥ 18 years). Nasal wash/aspirates comprised 51% of the samples tested, while NP swabs represented 49%. No differences in performance were observed based on patient age and gender or based on sample type tested.

The Binax NOW® Flu A Test was 80% sensitive and 93% specific while the Binax NOW® Flu B Test was 65% sensitive and 97% specific when compared to cell culture. The performance of the two tests by sample type (swab vs. wash/aspirate) and overall, including 95% confidence intervals, is detailed in the following tables.

Binax NOW® Flu A Test vs. Cell Culture

	FLU A SENSITIVITY			
Sample	+/+	-/+	% Sens	95% CI
NP Swab	29	8	78%	62-88%
Wash/Aspirate	40	9	82%	69-90%
Overall	69	17	80%	71-87%

FLU A SPECIFICITY			
-/-	+/-	% Spec	95% CI
133	12	92%	86-95%
133	9	94%	89-97%
266	21	93%	89-95%

Binax NOW® Flu B Test vs. Cell Culture

	FLU B SENSITIVITY			
Sample	+/+	-/+	% Sens	95% CI
NP Swab	21	15	58%	42-73%
Wash/Aspirate	29	12	71%	56-83%
Overall	50	27	65%	54-75%

FLU B SPECIFICITY			
-/-	+/-	% Spec	95% CI
142	4	97%	93-99%
146	4	97%	93-99%
288	8	97%	95-99%

ANALYTICAL STUDIES

Analytical Sensitivity

The BinaxNOW® test limit of detection (LOD), defined as the concentration of influenza virus that produces positive BinaxNOW® test results approximately 95% of the time, was identified by evaluating different concentrations of inactivated Flu A/Beijing and inactivated Flu B/Harbin in the BinaxNOW® test.

Twelve (12) different operators each interpreted 2 devices run at each concentration for a total of 24 determinations per level. The following results identify a concentration of 1.03×10^2 ng/ml as the LOD for Flu A/Beijing and 6.05×10^1 ng/ml for Flu B/Harbin.

Influenza A/Beijing		
Concentration (ng/ml)	# Detected	% Detected
1.03×10^2 (LOD)	23/24	96
5.60×10^1 (Cutoff)	*	50
3.27×10^1 (High Neg)	4/24	17
True Negative	0/24	0

Influenza B/Harbin		
Concentration (ng/ml)	# Detected	% Detected
6.05×10^1 (LOD)	23/24	96
2.42×10^1 (Cutoff)	11/24	46
1.51×10^1 (High Neg)	6/24	25
True Negative	0/24	0

*Linear regression was used to calculate a line equation, which was then used to project the cutoff concentration of Flu A/Beijing.

To demonstrate comparable analytical sensitivity of the BinaxNOW® Influenza A & B Test and the individual NOW® Flu A and Flu B Tests, the Flu A and B cutoff levels identified above were evaluated in the NOW® Flu A and Flu B Tests.

The A/Beijing cutoff sample detected 50% of the time in the BinaxNOW® Influenza A & B Test was also detected 50% (12/24) of the time in the NOW® Flu A Test when tested by six (6) operators interpreting a total of 24 devices. Likewise, the B/Harbin cutoff sample detected 46% of the time in the BinaxNOW® Influenza A & B Test was detected 10% (4/40) of the time in the NOW® Flu B Test when tested by ten (10) operators interpreting 40 devices.

These data demonstrate that the analytical sensitivity of the BinaxNOW® Influenza A & B Test is equivalent or better than that of the individual NOW® Flu A and B Tests.

Avian Influenza (H5N1) Analytical Reactivity Testing

The two (2) live avian influenza (H5N1) strains isolated from humans listed below tested positive in the BinaxNOW® Influenza A & B Test at concentrations ranging from 10^2-10^4 $TCID_{50}$/ml.

Avian Influenza Strain	Concentration
A/Hong Kong/156/97	1.3×10^2
A/Vietnam/1194/04	1.0×10^4

Reactivity Testing

The seven (7) live influenza A strains and five (5) live influenza B strains listed below tested positive in the BinaxNOW® Influenza A & B Test at concentrations ranging from 10^2-10^6 $CEID_{50}$/ml. Although the specific influenza strains causing infection in humans can vary year to year, all contain the conserved nucleoproteins targeted by the BinaxNOW® test.[1]

Influenza Strain	ATCC #
Flu A/WS/33	VR-825
Flu A/NWS/33	VR-219
Flu A/Hong Kong/8/68	VR-544
Flu A/Aichi/2/68	VR-547
Flu A/New Jersey/8/76	VR-897
Flu A/Mal/302/54	VR-98
Flu A/Port Chalmers/1/73	VR-810
Flu B/Lee/40	VR-101
Flu B/Brigit	VR-786
Flu B/Russia/69	VR-790
Flu B/Hong Kong/5/72	VR-791
Flu B/R75	VR-789

Analytic Specificity (Cross-Reactivity)

To determine the analytical specificity of the BinaxNOW® Influenza A & B Test, 36 commensal and pathogenic microorganisms (27 bacteria, 8 viruses and 1 yeast) that may be present in the nasal cavity or nasopharynx were tested. All of the following microorganisms were negative when tested at concentrations ranging from 10^4 to 10^8 $TCID_{50}$/ml (viruses), 10^7 to 10^8 organisms/ml (bacteria) and 10^6 organisms/ml (yeast).

Bacteria	Viruses	Yeast
Acinetobacter	Adenovirus	*Candida albicans*
Bordetella pertussis	Coronavirus	
Enterococcus faecalis	Coxsackie B4	
Escherichia coli	Cytomegalovirus (CMV)	
Gardnerella vaginalis	Parainfluenza 1	
Haemophilus influenzae	Parainfluenza 2	
Klebsiella pneumoniae	Parainfluenza 3	
Lactobacillus casei	Respiratory Syncytial Virus (RSV)	
Legionella pneumophila		
Listeria monocytogenes		
Moraxella catarrhalis		
Neisseria gonorrhoeae		
Neisseria meningitidis		
Neisseria sicca		
Neisseria subflava		
Proteus vulgaris		
Pseudomonas aeruginosa		
Serratia marcescens		
Staphylococcus aureus		
Staphylococcus aureus (Cowan protein A producing strain)		
Staphylococcus epidermidis		
Streptococcus, Group A		
Streptococcus, Group B		

Streptococcus, Group C
Streptococcus, Group F
Streptococcus mutans
Streptococcus pneumoniae

Interfering Substances

The following substances, naturally present in respiratory specimens or that may be artificially introduced into the nasal cavity or nasopharynx, were evaluated in the BinaxNOW® Influenza A & B Test at the concentrations listed and were found not to affect test performance. Whole blood (1%) did not interfere with the interpretation of negative BinaxNOW® test results, but did interfere with the interpretation of Flu A LOD positive samples. Therefore, visibly bloody samples may not be appropriate for use in this test.

Substance	Concentration
1 OTC mouthwash	20%
3 OTC nasal sprays	15%
3 OTC throat drops	15%
2 OTC throat sprays	20%
4-acetamidophenol	10 mg/ml
Acetylsalicylic acid	15 mg/ml
Albuterol	20 mg/ml
Chlorpheniramine	5 mg/ml
Dextromethorphan	10 mg/ml
Diphenhydramine	5 mg/ml
Guaiacol glycerol ether	20 mg/ml
Oxymetazoline	0.05%
Phenylephrine	50 mg/ml
Phenylpropanolamine	20 mg/ml
Rebetol	500 ng/ml
Relenza	20 mg/ml
Rimantadine	500 ng/ml
Synagis	0.1 mg/ml
Tamiflu	50 mg/ml

Transport Media

The following transport media were tested in the BinaxNOW® Influenza A & B Test as negative samples (no virus present) and after inoculation with the LOD levels of Influenza A & B. Media did not impact BinaxNOW® test performance, with the media alone testing negative in the NOW® test and media inoculated with LOD Influenza A & B testing positive on the appropriate test line in BinaxNOW® test.

Amies Media
Hank's Balanced Salt Solution
M4 Media
M4-RT Media
M5 Media
Stuart's Media
Saline

Reproducibility

A blind study of the BinaxNOW® Influenza A & B Test was conducted at 3 separate sites using panels of blind coded specimens containing negative, low positive, and moderate positive samples. Participants tested each sample multiple times on 3 different days. There was 97% (242/250) agreement with expected test results, with no significant differences within run (replicates tested by one operator), between run (3 different days) or between sites (3 sites).

Signed R M Calnan Date 04-NOV-2005

Rita Calnan
Director of Quality & Regulatory Affairs

1) Dowdle, W.R, Kendal, A.P., and Noble, G.R. 1980. Influenza Virus, p 836-884. Manual of Clinical Microbiology, 3rd edition, In Lennette, et. Al (ed.). American Society for Microbiology, Washington, D.C.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

NOV 3 0 2005

Ms. Angela Drysdale
Clinical Affairs Specialist
Binax, Inc.
10 Southgate Road
Portland, Maine 04103

Re: k053126
Trade/Device Name: BinaxNOW® Influenza A & B Test
Regulation Number: 21 CFR 866.3330
Regulation Name: Influenza Virus Serological Reagents
Regulatory Class: Class II
Product Code: GNX
Dated: November 4, 2005
Received: November 7, 2005

Dear Ms. Drysdale:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (240)276-0484. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html

Sincerely yours,

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

STATEMENT OF INDICATIONS FOR USE

510(k) Number (if known): K053126

Device Name: BinaxNOW® Influenza A & B Test

Indications For Use:

The BinaxNOW® Influenza A & B Test is an *in vitro* immunochromatographic assay for the qualitative detection of influenza A and B nucleoprotein antigens in nasopharyngeal (NP) swab and nasal wash/aspirate specimens. It is intended to aid in the rapid differential diagnosis of influenza A and B viral infections. Negative test results should be confirmed by culture.

PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use ✓ OR Over-The-Counter Use _____

(Per 21 CFR 801.109)
(Optional Format 1-2-96)

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K053126