K991726

5/11/99 Revision

AUG 27 1999

510(k) SUMMARY OF SAFETY AND EFFECTIVENESS

Binax NOW® *Streptococcus pneumoniae* Urinary Antigen Test

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

Submitter:

Binax, Inc.
217 Read Street
Portland, Maine 04103

Attention: Pamela S. Angell
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Trade Name: Binax NOW® *Streptococcus pneumoniae* Urinary Antigen Test

Common Name: *Strep pneumo* ICT, Binax NOW® *Strep pneumo* test

Classification Name: *Streptococcus* spp. serological reagents (per 21 CFR 8660.3740)

Predicate Device: Wellcogen Bacterial Antigen Kit, 510(k) number K854852

Device Description: The Binax NOW® *Streptococcus pneumoniae* Urinary Antigen Test is an immunochromatographic membrane assay used to detect *Streptococcus pneumoniae (S. pneumoniae)* antigen in human urine. A test strip, containing gold-conjugated and immobilized anti-*S. pneumoniae* antibodies, and a swab well are mounted on opposite sides of a cardboard, book-shaped hinged test device. A swab is dipped into the urine to be tested and then inserted into the swab well. A single reagent is added to the swab well from a dropper bottle before closing the test device. Pneumococcal antigen present in the urine sample reacts to bind anti-*S. pneumoniae* conjugated antibody. The resulting antigen-conjugate complexes are captured by immobilized anti-*S. pneumoniae* antibody, forming the Sample Line. Immobilized goat anti-rabbit IgG captures excess visualizing conjugate, forming the Control Line.

510(k) SUMMARY OF SAFETY AND EFFECTIVENESS (Continued)

There are no transferring steps, the sample is contained, and results are available within 15 minutes.

Intended Use:

The Binax NOW® *Streptococcus pneumoniae* Urinary Antigen Test is an in vitro rapid immunochromatographic assay for the detection of *S. pneumoniae* antigen in urine specimens from patients with symptoms of pneumonia. It is intended to aid in the presumptive diagnosis of pneumococcal pneumonia in conjunction with culture and other methods.

Technological Characteristics:

Both the Binax NOW® *Streptococcus pneumoniae* Urinary Antigen and the Wellcogen Bacterial Antigen Tests are simple rapid tests with a visual result interpretation. Both use a solid phase coated with polyclonal antibody to detect *S. pneumoniae* antigen in human urine samples. However, the predicate device is a latex agglutination test employing antibody coated polystyrene beads that agglutinate in the presence of sufficient homologous antigen. The Binax NOW® *Streptococcus pneumoniae* Urinary Antigen Test is an immunochromatographic assay utilizing a colloidal gold conjugate and an antibody striped membrane to capture and visualize antigen.

Performance Summary:

The Binax NOW® *Streptococcus pneumoniae* Urinary Antigen Test is substantially equivalent to the predicate device, the Wellcogen Bacterial Antigen Test (K854852), for the detection of *S. pneumoniae* urinary antigen. The performance of the Binax NOW® *Streptococcus pneumoniae* Urinary Antigen Test was verified using freshly collected and characterized frozen urine specimens. Refer to attached **PERFORMANCE CHARACTERISTICS.**

Signed J. Georges Nitis Date 5/19/99

J. Georges Nitis, Ph.D., MBA
Director, Regulatory Affairs

510(k) SUMMARY OF SAFETY AND EFFECTIVENESS (Continued)

PERFORMANCE CHARACTERISTICS
BINAX NOW® *STREPTOCOCCUS PNEUMONIAE* URINARY ANTIGEN TEST

Analytic Sensitivity:
Twenty-three (23) of 83 known *Streptococcus pneumoniae* serotypes are responsible for at least 90% of serious pneumococcal infection worldwide.[1] Forty-four (44) isolates representing these 23 serotypes and one additional serotype were grown in culture and assayed in the Binax NOW® test at a concentration of 10^5 organisms/mL. One hundred percent (100%) were positive, indicating that the Binax NOW® test detects the most pathogenic *S. pneumoniae* serotypes.

Analytic Specificity (Cross-Reactivity):
To demonstrate the immunologic specificity of the Binax NOW® test, 144 potential cross-reactants were grown in culture and tested in the Binax NOW® test. The cross-reactant panel included organisms associated with pneumonia as well as those likely to be found in the urogenital tract as normal flora or as a result of urinary tract infection. The Binax NOW® test does not cross-react with 143 of the 144 organisms when tested at concentrations of 10^6 to 10^9 CFU/mL. The single positive organism, *Streptococcus mitis*, is an expected cross-reactant as is shares the antigen against which the Binax NOW® test is directed. *Streptococcus mitis* is associated with endocarditis, not pneumonia, and is not likely to appear with any frequency in the population intended to be tested with the NOW® test.[1a]

Clinical Sensitivity and Specificity:
The Binax NOW® *Streptococcus pneumoniae* Urinary Antigen Test was evaluated in both prospective and retrospective clinical studies.

In the retrospective study, 35 urine specimens from blood culture positive pneumococcal pneumonia patients and 338 urine specimens from presumed *S. pneumoniae* negative patients were evaluated in the NOW® test. Of the presumed negative urines, 28 were collected from bacteremic patients, 4 from patients with empyema, 53 from patients with pneumonia, 153 from patients with urinary tract infections, and 100 from patients with no known infection. Binax NOW® test performance, calculated using standard methods, was 86% sensitivity, 94% specificity, and 93% overall accuracy. Ninety-five percent (95%) confidence intervals are listed below.

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[1] Refer to Product Insert reference number 9.
[1a] Howard, B.J., Clinical & Pathogenic Microbiology, 2nd ed. 1994. Mosby-Year Book Inc., St. Louis, MO., pg 267.

510(k) SUMMARY OF SAFETY AND EFFECTIVENESS

PERFORMANCE CHARACTERISTICS (Continued)
BINAX NOW® *STREPTOCOCCUS PNEUMONIAE* URINARY ANTIGEN TEST

		Blood Culture +	Blood Culture -
NOW® Result	+	30	21
	-	5	317

Sensitivity	=	86%	(70.9% - 93.9%)
Specificity	=	94%	(90.9% - 96.0%)
Accuracy	=	93%	(89.9% - 95.1%)

In a separate multi-center prospective study, 215 urine specimens from either hospitalized or out-patients presenting with lower respiratory symptoms or sepsis and from patients otherwise suspected of pneumococcal pneumonia were tested in the NOW® test. The confirmatory blood specimen was collected within 24 hours of the urine sample and then cultured. NOW® test performance versus blood culture, calculated using standard methods, was 90% sensitivity, 76% specificity, and 78% overall accuracy. Ninety-five percent (95%) confidence intervals are listed below.

		Blood Culture +	Blood Culture -
NOW® Result	+	28	45
	-	3	135

Sensitivity	=	90%	(74.6% - 96.4%)
Specificity	=	75%	(69.3% - 81.5%)
Accuracy	=	77%	(71.9% - 83.0%)

Interfering Substances:

The Binax NOW® test was found not to cross-react with potentially interfering substances present in urine. Nineteen (19) urine specimens with elevated levels of white blood cells, red blood cells, protein, and/or glucose, 5 urines with high turbidity, and 5 urines normal with respect to each of these parameters were assayed in the Binax NOW® test. Twenty-eight (28) specimens were negative. The single invalid test, produced by a specimen with elevated red blood cells, could not be interpreted due to the extreme coloration of the test membrane.

Pneumococcal Vaccine:

The impact of *S. pneumoniae* vaccine on Binax NOW® test performance was evaluated. Urines were collected from 49 volunteers both before and after immunization with the Lederle Pnu-Immune® 23 vaccine. All study participants tested negative in the Binax NOW® test before vaccination. Thirteen percent (13%) tested positive within 30 hours of being vaccinated, but again tested negative

510(k) SUMMARY OF SAFETY AND EFFECTIVENESS

PERFORMANCE CHARACTERISTICS (Continued)
BINAX NOW® *STREPTOCOCCUS PNEUMONIAE* URINARY ANTIGEN TEST

within 48 hours of vaccination. Binax NOW® test product labeling includes a limitation stating that *S. pneumoniae* vaccine may cause false positive results in the Binax NOW® test in the 48 hours following vaccination. It is recommended that the Binax NOW® test not be administered within 5 days of receiving the *S. pneumoniae* vaccine.

Reproducibility:

A blind study of the Binax NOW® test was conducted at 3 separate sites using a panel of coded specimens containing negative, low positive, moderate positive and high positive urine controls. Participants performed testing on 3 different days. 99.4% of the 359 samples tested were correctly interpreted.

Quality Control:

The ability of the Binax NOW® Test procedural control to indicate test failure was evaluated when 3 operators each ran 20 kit controls in a panel of 20 devices, 9 of which had been rendered inoperative. The number of defective devices and the defect itself were not apparent to the operator. 100% (60/60) of the devices were correctly interpreted as positive, negative, or invalid.

Preliminary Stability:

Preliminary stability studies of the Binax NOW® *Streptococcus pneumoniae* Urinary Antigen Test and kit controls are ongoing. Test results are consistent with other Binax 510(k) cleared ICT products. A minimum shelf life of one year is anticipated.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

AUG 27 1999

Ms. Pamela S. Angell
Program Manager
Binax, Inc.
217 Read Street
Portland, Maine 04103

Re: K991726
Trade Name: Binax Now® *Streptococcus pneumoniae* Urinary Antigen Test
Regulatory Class: II
Product Code: GTZ
Dated: August 18, 1999
Received: August 23, 1999

Dear Ms. Angell:

We have reviewed your Section 510(k) notification of intent to market the device referenced above and we 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). 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 (Premarket Approval), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 895. A substantially equivalent determination assumes compliance with the Current Good Manufacturing Practice requirements, as set forth in the Quality System Regulation (QS) for Medical Devices: General regulation (21 CFR Part 820) and that, through periodic QS inspections, the Food and Drug Administration (FDA) will verify such assumptions. Failure to comply with the GMP regulation may result in regulatory action. In addition, FDA may publish further announcements concerning your device in the Federal Register. Please note: this response to your premarket notification submission does not affect any obligation you might have under sections 531 through 542 of the Act for devices under the Electronic Product Radiation Control provisions, or other Federal laws or regulations.

Under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88), this device may require a CLIA complexity categorization. To determine if it does, you should contact the Centers for Disease Control and Prevention (CDC) at (770) 488-7655.

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

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801 and additionally 809.10 for in vitro diagnostic devices), please contact the Office of Compliance at (301) 594-4588. Additionally, for questions on the promotion and advertising of your device, please contact the Office of Compliance at (301) 594-4639. Also, please note the regulation entitled, "Misbranding by reference to premarket notification"(21 CFR 807.97). Other general information on your responsibilities under the Act may be obtained from the Division of Small Manufacturers Assistance at its toll-free number (800) 638-2041 or (301) 443-6597, or at its internet address "http://www.fda.gov/cdrh/dsma/dsmamain.html".

Sincerely yours,

Steven Gutman

Steven I. Gutman, M.D, M.B.A.
Director
Division of Clinical
Laboratory Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

Enclosure

APPENDIX B

INDICATIONS FOR USE FORM

510(k) Number (if known): K991726

Device Name: Binax NOW® *Streptococcus pneumoniae* Urinary Antigen Test

Indications For Use:

The Binax NOW® *Streptococcus pneumoniae* Urinary Antigen Test is a rapid immunochromatographic assay for the detection of *Streptococcus pneumoniae* in human urine as an adjunct to culture for the presumptive diagnosis of pneumococcal pneumonia. It is intended for *in vitro* diagnostic use.

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

Concurrence of CDRH, Office of Device Evaluation (ODE)

Woody Dubois
(Division Sign-Off)
Division of Clinical Laboratory Devices
510(k) Number K991726

Prescription Use X
(Per 21 CFR 801.109)

OR Over-The-Counter Use _____

(Optional Format 1-2-96)