

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE**

A. 510(k) Number:

k090301

B. Purpose for Submission:

To obtain a SE determination for this Premarket notification submission.

C. Measurand:

Methicillin Resistant *Staphylococcus aureus* (MRSA)

D. Type of Test:

Detection of penicillin-binding protein2a (PBP2a) present in MRSA

E. Applicant:

Binax, Inc.

F. Proprietary and Established Names:

BinaxNOW® PBP2a Test

G. Regulatory Information:

1. Regulation section:

21 CFR 866.1640

2. Classification:

Class II

3. Product code:

MYI

4. Panel:

Microbiology

H. Intended Use:

1. Intended use(s):

The BinaxNOW[®] PBP2a Test is a qualitative, *in vitro* immunochromatographic assay for the rapid detection of penicillin-binding protein 2a (PBP2a) present in methicillin-resistant *Staphylococcus aureus* (MRSA). The test is performed directly on blood culture samples positive for *S. aureus*.

The BinaxNOW[®] PBP2a Test is not intended to diagnose MRSA nor to guide or monitor treatment for MRSA infections. Subculturing positive blood cultures is necessary to recover organisms for susceptibility testing or epidemiological typing.

2. Indication(s) for use:

The BinaxNOW[®] PBP2a Test is a qualitative, *in vitro* immunochromatographic assay for the rapid detection of penicillin-binding protein 2a (PBP2a) present in methicillin-resistant *Staphylococcus aureus* (MRSA). The test is performed directly on blood culture samples positive for *S. aureus*.

The BinaxNOW[®] PBP2a Test is not intended to diagnose MRSA nor to guide or monitor treatment for MRSA infections. Subculturing positive blood cultures is necessary to recover organisms for susceptibility testing or epidemiological typing.

3. Special conditions for use statement(s):

For Prescription use only.

4. Special instrument requirements:

Not applicable

I. Device Description:

The BinaxNOW[®] PBP2a Test is a cardboard, book-shaped hinged test device containing the test strip.

The kit consists of

Reagent 1: Clear alkaline solution

Reagent 2: Clear blue alkaline solution and blue pH indicator solution

Reagent 3: Clear, slightly acidic solution containing buffer and pictures

J. Substantial Equivalence Information:

1. Predicate device name(s):

Mueller Hinton Agar w/4% NaCl w/antibiotics (Remel)

Oxoid PBP2' Latex Agglutination test

2. Predicate K number(s):

K850291

k011710

3. Comparison with predicate:

Similarities			
Item	Device	PBP2' Latex Agglutination test	Mueller Hinton Agar w/4% NaCl w/antibiotics
Intended Use	Detect methicillin resistance from <i>S. aureus</i>	Same	Same
Mode of Detection	PBP2a	PBP2a	Resistance to penicillinase-resistant penicillin (i.e. oxacillin)
Isolates	<i>S. aureus</i>	Same	Same

Differences			
Item	Device	PBP2' Latex Agglutination test	Mueller Hinton Agar w/4% NaCl w/antibiotics
Technology	Immuno-chromatographic membrane assay	Latex agglutination	Agar dilution
Detection mechanism	Dipstick	Sensitized latex	Agar with antibiotic (i.e. oxacillin)
Specimen type	Directly from blood culture containing <i>S. aureus</i>	<i>S. aureus</i> colonies	<i>S. aureus</i> colonies
Reading method	Visual read at 10 minutes after elution	Visual read within 3 minutes after extraction	24 hrs incubation

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

Not applicable

L. Test Principle:

The BinaxNOW® PBP2a Test is a rapid immunochromatographic membrane assay that uses highly sensitive monoclonal antibodies to detect the PBP2a protein directly from blood cultures which have been identified as being positive for *S. aureus*. These antibodies and a control antibody are immobilized onto a test strip as two distinct lines and combined with other reagents/pads. This test strip is mounted inside a cardboard, book-shaped hinged test device.

Specimens are aliquots from blood cultures which have been identified as positive for *S. aureus*. After the sample is prepared, it is added to the sample pad at the top of the test strip and the device is closed. Results are read at 10 minutes.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Reproducibility study was done at three sites, tested by two operators in duplicates for five days.

10 x (2) duplicates x 2 operators x 5 days x 3 sites= 600

Reproducibility was >95%.

b. *Linearity/assay reportable range:*

Not applicable

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

The controls for the BinaxNOW® PBP2a Test are:

1. Built-in positive and negative procedural controls with each testing strip

A. The appearance of a blue line at the “control line” position can be considered an internal positive procedural control. If capillary flow has occurred, this line will always appear.

B. The clearing of the background color from the result window is a negative background control. In comparison to the color of the control line, the background color in the window should be white within 10 minutes.

2. The recommended QC organisms are the following

Positive control: Methicillin-resistant *Staphylococcus aureus* BAA44
 Negative control: Methicillin-sensitive *Staphylococcus aureus*
 ATCC25923

Quality control data was compiled across all four sites and all QC results were acceptable. The overall expected results were greater than 95%.

d. *Detection limit:*

The analytical limit of detection of the BinaxNOW[®] PBP2a Test in ATCC strain BAA44 using 1/10 diluted saline suspension inoculum is 2.5×10^7 cells/mL.

Bacterial Concentration/mL	Number Detected	% Detection
3.33×10^7	20/20	100
2.5×10^7	19/20	95
4.94×10^6	13/20	65
2.19×10^6	3/20	15
Whole Blood	0/20	0

An additional study using the same dilution as the initial study has been performed to determine the LoD in CFU/mL. Results of the study are presented in the table below

Organism	ID#	Concentration (CFU/mL)
<i>S. aureus</i> (USA100)	NRS658	5.8×10^5
<i>S. aureus</i> (USA100)	NRS660	1.64×10^6
<i>S. aureus</i> (USA300)	NRS643	1.66×10^6
<i>S. aureus</i> (USA300)	NRS647	6.2×10^5
<i>S. aureus</i>	ATCC-29737	5.3×10^5
<i>S. aureus</i>	ATCC-29213	7.0×10^5
<i>S. aureus</i>	ATCC-BAA44	4.7×10^5
<i>S. aureus</i>	ATCC-33592	9.9×10^5

The concentrations for the 1/10 diluted saline suspension inoculum in this study ranged from 4.7×10^5 to 1.66×10^6 CFU/mL.

e. *Analytical specificity:*

Analytical Reactivity

The Analytical Reactivity study included 60 well characterized MRSA strains from Network on Antimicrobial Resistance in *Staphylococcus aureus* (NARSA) and American Type Culture Collection (ATCC) and tested using

the BinaxNOW[®] PBP2a Test which provided expected results. There were 38 MRSA strains from NARSA included in the study representing Pulse-Field Types (PFT) USA100, USA200, USA300, USA400, USA500, USA600, USA700, and USA800.

Cross Reactivity

Cross Reactivity Study was performed on 32 methicillin-susceptible *Staphylococcus aureus* (MSSA), 38 *Staphylococcal* strains (other than *S. aureus*) and 100 non-*Staphylococcal* strains. All strains tested negative in the BinaxNOW[®] test except *Cryptococcus neoformans* and *Staphylococcus sciuri*. A limitation statement will be included in the package insert regarding the unexpected results of *Cryptococcus neoformans* and *Staphylococcus sciuri* on the BinaxNOW[®] PBP2a.

Interfering Substances

There was no interference observed with the 20 substances such as medications, human and blood components, and supplements normally found in blood culture bottle media.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

The clinical study was conducted in 2008-09 at four geographically diverse hospital laboratories within the US. A total of 199 *S. aureus* samples were evaluated with the BinaxNOW[®] PBP2a Test and compared to standard methods used routinely by the laboratories: Cefoxitin (30 µg) disc diffusion, Oxacillin (1 µg) disc diffusion and automated antimicrobial susceptibility test systems.

The table below presents BinaxNOW[®] PBP2a Test performance by reference method. Because each sample was tested on more than one reference method, there are more observations in this table (n=317) than the total number of samples (n=199).

BinaxNOW® PBP2a Test Performance vs. Reference Methods

Reference Method	Positive Agreement (95% CI)	Negative Agreement (95% CI)
Cefoxitin (30 µg) disc diffusion	96.9% (62/64) (89.3 - 99.1%)	100.0% (67/67) (94.6 - 100.0%)
Oxacillin (1 µg) disc diffusion	96.5% (55/57) (88.1 - 99.0%)	100.0% (58/58) (93.8 - 100.0%)
Automated Antimicrobial Susceptibility Test System	97.6% (41/42) (87.7 - 99.6%)	100.0% (29/29) (88.3- 100.0%)

b. Matrix comparison:

Not Applicable

3. Clinical studies:

a. Clinical Sensitivity:

Not Applicable

b. Clinical specificity:

Not Applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not Applicable

4. Clinical cut-off:

Not Applicable

5. Expected values/Reference range:

Not Applicable

N. Proposed Labeling:

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

O. Conclusion:

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