

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

A. 510(k) Number:

K091766

B. Purpose for Submission:

To determine substantial equivalence for the Clearview[®] Exact PBP2a Test, Model 891-000

C. Measurand:

Penicillin-binding protein 2a (PBP2a) in isolates of methicillin-resistant *Staphylococcus aureus* (MRSA)

D. Type of Test:

The Clearview[®] Exact PBP2a test is a rapid immunochromatographic membrane assay that uses monoclonal antibodies to detect the PBP2a protein directly from *Staphylococcus aureus* isolates.

E. Applicant:

Binax, Inc

F. Proprietary and Established Names:

Clearview[®] Exact PBP2a Test. Model 891-000

G. Regulatory Information:

1. Regulation section:

CFR 866.1640

2. Classification:

II

3. Product code:

MYI - System, Test, Genotypic Detection, Resistant Markers,
Staphylococcus colonies

4. Panel:

83, Microbiology

H. Intended Use:

1. Intended use:

The Clearview[®] Exact PBP2a Test is a qualitative, *in vitro* immunochromatographic assay for the detection of penicillin-binding protein 2a (PBP2a) in isolates identified as *Staphylococcus aureus*, as an aid in detecting methicillin-resistant *Staphylococcus aureus* (MRSA). The Clearview[®] Exact PBP2a Test is not intended to diagnose MRSA nor to guide or monitor treatment for MRSA infections.

2. Indications for use:

The Clearview[®] Exact PBP2a Test is a qualitative, *in vitro* immunochromatographic assay for the detection of penicillin-binding protein 2a (PBP2a) in isolates identified as *Staphylococcus aureus*, as an aid in detecting methicillin-resistant *Staphylococcus aureus* (MRSA). The Clearview[®] Exact PBP2a Test is not intended to diagnose MRSA nor to guide or monitor treatment for MRSA infections.

3. Special conditions for use statement(s)

Prescription use only

4. Special instrument requirements:

Not applicable

I. Device Description:

The Clearview[®] Exact PBP2a Test is a rapid immunochromatographic membrane assay that uses monoclonal antibodies to detect the PBP2a protein directly from bacterial isolates. These antibodies and a control antibody are immobilized onto a nitrocellulose membrane as two distinct lines and combined with a sample pad, a blue conjugate pad, and an absorption pad to form a test strip.

Isolates are sampled directly from the culture plate and eluted into an assay tube containing Reagent 1. Reagent 2 is then added and the dipstick is placed in the assay tube. Results are read visually at 5 minutes.

Materials Provided in Clearview[®] Exact PBP2a Test Kit

- Test Strips (x 25): A dipstick covered with a clear, plastic overlay with directional arrows to indicate testing position
- Reagent 1 (x1): A clear blue alkaline solution (irritant) – 6 mL
- Reagent 2 (x1): A clear, slightly acidic solution containing sodium azide, buffer and proteins – 2.5 mL
- Assay Tubes
- Test Rack

Materials required but not provided

- Clock, timer or stopwatch, applicator sticks (for *S. aureus* isolates)
- 1 µl inoculating loops (for CoNS isolates)
- Vortex mixer
- External positive and negative controls - The recommended controls are listed below.
 - **Control Strains for *S. aureus* isolates:**
Positive control: *Staphylococcus aureus* ATCC # BAA44
Negative control: *Staphylococcus aureus* ATCC # 25923

J. Substantial Equivalence Information:

1. Predicate device name(s):

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

- a. PBP2' Oxoid PBP2 Latex Agglutination Test (Oxoid)
- b. Remel Mueller Hinton Agar with 4% NaCl and 6 µg/mL Oxacillin

2. Predicate 510(k) number(s):

- a. K011710
- b. K850291

3. Comparison with predicate:

Similarities			
Item	Device	Predicate (K011710)	Predicate (K850291)
Intended Use	Detects methicillin resistance from <i>Staphylococcus aureus</i> isolates	Same	Same
Mode of Detection	Detects PBP2a	Detects PBP2a	Detects (resistance to penicillinase-resistant penicillin (i.e. oxacillin) – (May or may not be related to PBP2a)
Specimen Type	Identifies isolates as <i>Staphylococcus</i> species isolates	Same	Identifies isolates as <i>Staphylococcus</i> species isolates (i.e. <i>S. aureus</i>)

Differences			
Item	Device	Predicate (K011710)	Predicate (K850291)
Technology	Immuno-chromatographic membrane assay	Latex agglutination	Agar dilution
Detection mechanism	Dipstick	Sensitized latex	Agar with antibiotic (i.e. oxacillin)
Reading time	Visual read at 5 minutes after elution	Visual read within 3 minutes after extraction	Read after 24 hrs incubation

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

CLSI 2007. Performance standards for antimicrobial susceptibility testing. CLSI approved standard M100-S17. Clinical and Laboratory Standards

L. Test Principle:

The Clearview[®] Exact PBP2a Test is a qualitative, in vitro immunochromatographic assay. The procedure involves adding bacterial colonies to Reagent 1 to lyse the bacterial cell walls and expose the PBP2a protein. Subsequently, Reagent 2 is added to neutralize the sample. Once the test strips is placed in the extraction solution, the extraction solution is absorbed by the sample pad through to the conjugate pad by capillary action. The conjugate pad contains dried blue latex particles sensitized with mouse anti-PBP2a monoclonal antibody. When the sample reaches the conjugate pad, the sensitized latex is dissolved into the sample where an immune complex is formed if PBP2a protein is present in the sample. This mixture then flows into the nitrocellulose membrane. The nitrocellulose membrane is coated with two lines: one of which is mouse anti-PBP2a (the test line) and the other is anti-mouse immunoglobulin (the control line). As the sample moves over the nitrocellulose

membrane, a reaction between the immune complex and the coated anti-PBP2a antibodies creates a blue test line in positive samples. Excess conjugate is trapped on the control line. This indicates that the test results are valid.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Reproducibility study was done at three sites. Testing was done at three sites, using 18-24 hrs isolates that have been sub-cultured, by two operators in duplicates for five days. The reproducibility panel consists of six MRSA, and four MSSA; 10 x (2) duplicates x 2 operators x 5 days x 3 sites= 600

Overall reproducibility was >95%.

b. *Linearity/assay reportable range:*

Not applicable

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

Storage and Stability

Product Stability Studies were performed to generate real time and accelerated stability data to support the expiration date of each lot under stated conditions, (i.e., Clearview® Exact PBP2a Test kits should be stored at room temperature or under refrigeration (2-30 °C). Reagent 1 and Reagent 2 must be stored refrigerated (2-8 °C)).

Stability conditions were set up as follows:

1. *Accelerated* - Clearview® Exact PBP2a devices and Clearview® Exact PBP2a Reagent 1* at 45°C & Clearview® Exact PBP2a Reagent 2 at 22°C
2. *Real-time, room temperature*- Clearview® Exact PBP2a devices and Clearview® Exact PBP2a Reagent 1* at 30°C & Clearview® Exact PBP2a Reagent 2 at 4°C
3. *Real-time, refrigerated* - Clearview® Exact PBP2a devices and Clearview® Exact PBP2a Reagent 1 & Clearview® Exact PBP2a Reagent 2 at 4°C

Three device lots were used to test all test samples and controls using the Control Assay Procedure in the package insert. (The same lot of devices, liquid controls, and kit reagents are being used for the duration of the

stability study). All devices were interpreted at 5 minutes and negative devices were interpreted at 5 and 10 minutes. All samples were run in triplicate using the same plate. Results are outlined in the table below:

Stability Testing Summary

Product Stability (with Desiccant)			
Lot	4°C	30 °C	45°C
Device, Reagents 1 and 2 – Transfer lot 3	5 months	5 months	20 weeks
Device, Reagents 1 and 2 – Transfer lot 4	4 months	4 months	17 weeks
Product Stability (without Desiccant)			
Lot	4°C	30 °C	45°C
Device, Reagents 1 and 2 – Transfer lot 3	12 weeks	12 weeks	20 weeks

For Transfer Lot 3, the device and reagents remained stable after 20 weeks (with and without desiccant) at 45°C and 5 months (with desiccant) and 12 weeks (without desiccant) of real-time storage at 4°C and 30 °C. For Transfer Lot 4, the device and reagents remain stable after 17 weeks (with desiccant) and 10 weeks (without desiccant) at 45°C and 4 months (with desiccant) and 15 weeks (without desiccant) of real-time storage at 4°C and 30 °C. Stability continued on transfer lots 3 and 4. Stability testing of each individual component will continue until a 2-year expiration date is achieved.

d. Detection Limit:

A study was conducted using *Staphylococcus aureus* (ATCC BAA44) and the detection limit was determined to be 1.4×10^7 CFU/mL

e. Analytical specificity:

A total of 162 strains of methicillin-resistant *Staphylococcus aureus* (MRSA), 112 strains of methicillin-sensitive *Staphylococcus aureus* (MSSA), and other non-*Staphylococcal* strains were tested in the Clearview® Exact PBP2a Test with expected results

f. Assay cut-off:

Not applicable

2. Comparison studies:

A clinical study was conducted at three geographically diverse hospital laboratories (two U.S. sites and one non-U.S. site), using prospective and

retrospective isolates identified as *Staphylococcus aureus*.

A total of 516 *S. aureus* fresh and stock isolates were tested from Tryptic Soy Agar with 5% sheep blood, Columbia agar with 5% sheep blood and Mueller-Hinton Agar induced with a 1 µg oxacillin disk. Results were compared to those of 30 µg cefoxitin disk diffusion, according to Clinical and Laboratory Standards Institute (CLSI) interpretation. Of these, 30% (225/733) were stock isolates. Retrospective *S. aureus* isolates were also enrolled into the study.

Summary of Performance Characteristics:

Plate Type	Sensitivity	95% C.I.	Specificity	95% C.I.
Tryptic Soy Agar with 5% sheep blood	98.1% (206/210)	(95.2-99.3%)	98.8% (244/247)	(96.5-99.6%)
Columbia Agar with 5% sheep blood	99.0% (208/210)	(96.6-99.7%)	98.8% (244/247)	(96.5-99.6%)
Mueller Hinton with 1 µg oxacillin induction	99.5% (209/210)	(97.4-99.9%)	98.8% (244/247)	(96.5-99.6%)

a. *Method comparison with predicate device:*

Cefoxitin disk at concentration of 30 µg is a surrogate for oxacillin resistance and is used in the clinical studies. The CLSI recommendations are:

Interpretive Criteria (zone diameter in mm) for 30 µg Cefoxitin Disk Diffusion Test			
	Oxacillin Susceptible	Intermediate*	Oxacillin Resistant
<i>S. aureus</i> and <i>S. lugdunensis</i>	≥22 mm	N/A	≤21 mm

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:

In the external clinical evaluation of the Clearview[®] Exact PBP2a Test, the overall expected rate of PBP2a (MRSA) among *S. aureus* isolates was 45.9% (210/457), and among the three site populations the expected positive rate ranged from 34.6% to 49.7%.

N. Proposed Labeling:

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

O. Conclusion:

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