

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

**A. 510(k) Number:**

K092767

**B. Purpose for Submission:**

To obtain a substantial equivalent determination for a Premarket notification for a formulary modification to the cleared BBL™ CHROMagar™ MRSA (CMRSA) product.

**C. Measurand:**

Methicillin Resistant *Staphylococcus aureus* (MRSA)

**D. Type of Test:**

Detection of MRSA using a selective and differential chromogenic media

**E. Applicant:**

Becton Dickinson and Company

**F. Proprietary and Established Names:**

BBL™ CHROMagar™ MRSA II

**G. Regulatory Information:**

1. Regulation section:

21 CFR 866.1700

2. Classification:

Class II

3. Product code:

JSO

4. Panel:

Microbiology

**H. Intended Use:**

1. Intended use(s):

BBL™ CHROMagar™ MRSA II is a selective and differential chromogenic medium for the qualitative direct detection of methicillin-resistant *Staphylococcus aureus* (MRSA) to aid in the prevention and control of MRSA infections in healthcare settings. The test is performed on anterior nares swab specimens from patients to screen for MRSA colonization.

BBL™ CHROMagar™ MRSA II is not intended to diagnose MRSA infection, guide or monitor treatment for MRSA infections. A negative result does not preclude MRSA nasal colonization. Concomitant cultures are necessary to recover organism for organism identification, susceptibility testing or epidemiological typing.

2. Indication(s) for use:

BBL™ CHROMagar™ MRSA II is a selective and differential chromogenic medium for the qualitative direct detection of methicillin-resistant *Staphylococcus aureus* (MRSA) to aid in the prevention and control of MRSA infections in healthcare settings. The test is performed on anterior nares swab specimens from patients to screen for MRSA colonization.

BBL™ CHROMagar™ MRSA II is not intended to diagnose MRSA infection, guide or monitor treatment for MRSA infections. A negative result does not preclude MRSA nasal colonization. Concomitant cultures are necessary to recover organism for organism identification, susceptibility testing or epidemiological typing.

3. Special conditions for use statement(s):

Prescription use only

4. Special instrument requirements:

Not applicable

**I. Device Description:**

BBL™ CHROMagar™ MRSA II medium permits the direct detection and identification of MRSA through the incorporation of specific chromogenic substrates and the antibiotic cefoxitin. MRSA strains will grow in the presence of cefoxitin and produce mauve-colored colonies resulting from hydrolysis of the chromogenic

substrate. Selective agents are incorporated for the suppression of gram-negative organisms, yeast and enterococci and some other gram-positive cocci. Bacteria other than MRSA may utilize other chromogenic substrates in the medium resulting in the growth of colonies that are not mauve.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):

BBL CHROMagar MRSA

BBL Oxacillin Screen Agar

2. Predicate K number(s):

K042812

K863821

3. Comparison with predicate:

Item	Device	Predicate 1- BBL CHROMagar MRSA	Predicate 2- BBL Oxacillin Screen Agar (OSA)
Intended Use	Selective and differential culture media	BBL™ CHROMagar™ MRSA is a selective and differential medium for the qualitative direct detection of nasal colonization by methicillin-resistant	Oxacillin Screen Agar (OSA) is an antimicrobial susceptibility test medium to determine resistance of <i>Staphylococcus aureus</i> to oxacillin, methicillin and nafcillin.
Specimen Type	Anterior nares	Same	Pure culture isolates identified as <i>S. aureus</i>
Inoculation	Direct from specimen collection devices	Same	Dilution of pure culture from TSA
Sample Volume	Inoculate the specimen onto a BBL™ CHROMagar™ MRSA II plate and streak for isolation	Same	Suspend several well-isolated colonies of the test organism from an 18 – 24h plate culture into a tube of Trypticase Soy Broth and adjust the turbidity to a 0.5 McFarland turbidity

Item	Device	Predicate 1- BBL CHROMagar MRSA	Predicate 2- BBL Oxacillin Screen Agar (OSA)
			standard. Spot inoculate 10 µL of suspension of OSA.
Storage Condition	Refrigeration at 2 - 8°C away from light.	Same	Same
Incubation Temperature	Incubation at 35 - 37°C, aerobically.	Same	Incubation at 30 - 35°C, aerobically.
Incubation Length	Incubation for 18 – 28 hours.	Incubation for 24±4 hours. If negative, re-incubate for additional 24 ±4 hours.	Incubation for 24 hours.
Selective Agents	Cefoxitin	Same	Oxacillin
Inhibitory Agents	Contains multiple inhibitory agents	Same	None
Testing Method	Manual	Same	Manual
Growth Enhancers	Specific growth enhancers are incorporated (e.g. sodium chloride, chromopeptone)	Same	Specific growth enhancers are incorporated (e.g. sodium chloride)
Organism Differentiation	Hydrolysis of chromogenic substrates facilitates the visual differentiation of MRSA (mauve colonies) from non-MRSA (methicillin-susceptible <i>S.aureus</i> and other organisms).	Same	N/A
Shelf Life	10 Weeks	Same	N/A

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

Not applicable

**L. Test Principle:**

BBL™ CHROMagar™ MRSA II permits the direct detection and identification of MRSA through the incorporation of specific chromogenic substrates and cefoxitin. MRSA strains will grow in the presence of cefoxitin and produce mauve colonies resulting from hydrolysis of the chromogenic substrate. Additional selective agents are incorporated for the suppression of gram-negative organisms, yeast and some other gram-positive cocci. Bacteria other than MRSA may utilize other chromogenic substrates in the medium resulting in the growth of colonies that are not mauve.

## M. Performance Characteristics (if/when applicable):

### 1. Analytical performance:

#### a. *Precision/Reproducibility:*

The reproducibility study included seven MRSA (6 heterozygous and 1 homozygous MRSA isolates), three Methicillin-Susceptible *S. aureus* (MSSA), tested in triplicates, on three separate days, at three clinical sites. All results were as expected.

10 x 3 operators x 3 days x 3 sites= 270

Reproducibility was >95%.

The precision study was performed using three different lots over three days by three independent readers. There were nine MRSA, two Borderline Oxacillin Resistant *S. aureus* (BORSA), and nine non-MRSA.

All results were as expected.

#### b. *Linearity/assay reportable range:*

Not applicable

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

The recommended quality control (QC) organisms, *S. aureus* ATCC 43300 as positive control, and *S. aureus* ATCC 29213 as negative control were used. Quality control data were compiled across all three sites and all QC results were acceptable.

#### d. *Detection limit:*

Not applicable

#### e. *Analytical sensitivity:*

**Analytical reactivity (sensitivity)** study was performed on archived collection of 292 MRSA (including USA 100, 300, 400, 500, 700, 800) isolates. Each MRSA isolate was inoculated using a suspension of  $10^5$  CFU/mL on two CMRSA II plates and read by at least two readers. Three different lots were used in the analytical sensitivity study. The table below demonstrates the analytical sensitivity of CMRSA II with MRSA strains.

CHROMA<sup>®</sup>Agar II Analytical Reactivity (Sensitivity) with MRSA strains

Lot	Reader	Total N	#Correct	Sensitivity
1	1	584	537	91.95% 89.44% - 94.03%
	2	584	543	92.98% 90.6% - 94.92%
2	1	584	539	92.29% 89.83% - 94.32%
	2	584	543	92.98 90.60% - 94.92%
3	1	584	541	92.64% 90.21% - 94.62%
	2	584	546	93.49% 91.18% - 95.35%

There were 25 false negatives with lot 1. Five MRSA strains did not grow on the CMRSA II and 20 MRSA strains produced non-mauve colonies on the CMRSA II.

There were also 25 false negatives with lot 2. Five MRSA strains did not grow on the CMRSA II and 20 MRSA strains produced non-mauve colonies on the CMRSA II.

There were 23 false negatives with lot 3. Three MRSA strains did not grow on the CMRSA II and 20 MRSA strains produced non-mauve colonies on the CMRSA II.

There were a total of 27 discrepant results in the analytical reactivity study. These discrepant results were further evaluated on the CMRSA II using a suspension of  $10^6$  CFU/mL. Ten  $\mu$ l of this suspension was then inoculated on to CMRSA II. Twenty-five of the twenty-seven isolates evaluated produced mauve colonies on CMRSA II at 24 h at this concentration.

**Recovery Study (Limit of Detection (LoD))**

The recovery study included two well characterized and recognized MRSA strains (ATCC 33592 and ATCC 43300) and two in house strains. Analytical studies such as incubation time, analytical reactivity or sensitivity, interfering substances and reproducibility study were all performed using MRSA concentration of  $1 \times 10^5$  CFU/mL. Challenge testing was performed at a final concentration  $10^7$  to  $10^8$  CFU/mL.

f. Analytical specificity:

Analytical specificity was performed on archived collection of 275 non-MRSA (including 96 Methicillin Sensitive *Staphylococcus aureus* (MSSA), 88 Coagulase negative *Staphylococci* and 91 miscellaneous) isolates. Each isolate was inoculated on two CMRSA II plates and read by at least two readers. Three different lots were used in the analytical specificity study. The table below demonstrates the analytical specificity of CMRSA II with non-MRSA strains.

**CMRSA II Specificity**

Lot	Reader	Total N	#Correct	Specificity
1	1	550	537	97.64% (95.99% - 98.74%)
	2	550	536	97.45% 95.77% - 98.60%
2	1	550	538	97.82% 96.22% - 98.87%
	2	500	539	98% 96.45% - 99%
3	1	550	535	97.27% 95.54% - 98.47%
	2	550	536	97.45% 95.77% - 98.6%

With Lot 1, there were 11 non-MRSA strains that produced mauve colonies. Six of these strains were Methicillin Susceptible *S. aureus* (MSSA). *C. meningosepticum*, *C. jekeium*, *R. equi*, *B. cereus*, and *S. simulans* also produced mauve colonies.

With Lot 2, there were 11 non-MRSA strains that produced mauve colonies. Five of these strains were Methicillin Susceptible *S. aureus* (MSSA). *C. meningosepticum*, *C. jekeium*, *R. equi*, *E. faecalis* (VRE), *B. cereus*, and *S. simulans*.

With Lot 3, there were 12 non-MRSA strains that produced mauve colonies. Seven of these strains were Methicillin Susceptible *S. aureus* (MSSA). *C. meningosepticum*, *C. jekeium*, *R. equi*, *B. cereus*, and *S. simulans* also produced mauve colonies.

Additional specificity studies were performed to include isolates of ESBL producers, KPC producers, additional *Pseudomonas* species, *Cryptococcus neoformans* and *Bacillus sp.* which demonstrated negative results.

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### **Interference Study**

Interfering substances, such as, human blood, over-the-counter (OTC) nasal sprays, antihistamines, steroids, mucous, and menthol were evaluated for potential interference of growth of MRSA on BBL™ CHROMagar™ MRSA II (CMRSA II) medium. Nasal sprays containing azelastine hydrochloride, fluticasone propionate, oxymetazoline hydrochloride and OTC throat drops containing menthol were found to have an inhibitory effect on the growth of MRSA. These substances will be listed in the proposed package insert as potentially interfering substances.

Additionally, five transport devices were evaluated for their impact on the recovery of MRSA on the CMRSA II medium. All five transport devices were found to have no effect on MRSA recovery.

### **Incubation Time**

An Incubation Time study was performed on 50 MRSA and 50 non-MRSA to determine the performance of CMRSA II at specified incubation times. A recommendation of 24-hour read (20 – 26 hours incubation) will be included in the package insert. A limitation statement will be included that incubation shorter than 20 hours may reduce the sensitivity of CMRSA II.

### **Additional Tests**

One hundred and sixty five characterized isolates were evaluated to determine whether coagulase and *Staphylococcus* latex agglutination testing could be performed directly from the CMRSA II plate. Each isolate was inoculated onto a blood agar plate and then onto CMRSA II. Tube coagulase and *Staphylococcus* latex agglutination testing was then performed from each plate and compared to the expected result. Both the blood agar plate and CMRSA II plates demonstrate expected results.

*f. Assay cut-off:*

Not applicable

2. Comparison studies:

*a. Method comparison with predicate device:*

The performance of the CMRSA II was evaluated at three sites using 1187 anterior nares specimens. Specimens were evaluated by comparing the recovery of MRSA on Trypticase Soy Agar with 5% Sheep Blood (TSA II)

plates and each site's routine procedure for identification of *S. aureus*, i.e., (Traditional Culture) to CMRSA II plates. The traditional culture method included *Staphylococcal* latex agglutination testing for two sites and the third site included coagulase testing. All *S. aureus* recovered were tested for *mec-A* mediated oxacillin resistance by the cefoxitin disk diffusion test. Cefoxitin disk (30µg) diffusion test results followed CLSI methods and interpretive criteria. The CMRSA II was interpreted as positive for MRSA at 20-26 hours based on detection of mauve colonies. The performance of CMRSA II vs Cefoxitin Disk is demonstrated in the table below.

### CMRSA II Performance versus Cefoxitin Disk

	Cefoxitin Disk		
CMRSA II Result	MRSA	Not MRSA	Total
MRSA	149	1	150
Not MRSA	13	1024	1037
	162	1025	1187
Reference Method: Cefoxitin Disk Positive Percent Agreement: 92% (86.7%, 95.7%) Negative Percent Agreement: 99.9% (99.5%, 100%)			

The positive percent agreement and negative percent agreement of CMRSA II at 20-26 hours was 92% and 99.9%, respectively, using the cefoxitin disk result as reference.

With combined data from two clinical trial sites, the positive percent agreement of CMRSA II when compared to Traditional Culture was 92% at 20-26 hours and the negative percent agreement was 98.8%. Performance is shown in the table below.

### BBL CHROMagar MRSA II Performance vs. Traditional Culture at Two Clinical Trial Sites

	Traditional Culture		
CMRSA II Result	MRSA	Not MRSA	Total
MRSA	92	9*	101
Not MRSA	8	760	768
	100	769	869
Reference Method: Traditional Culture Positive Percent Agreement: 92% (84.8%, 96.5%) Negative Percent Agreement: 98.8% (97.8%, 99.5%)			

\* Nine samples that were positive on CMRSA II and negative by Traditional Culture

were confirmed as MRSA by cefoxitin disk diffusion testing.

There were 13 false negative with the CMRSA II. Twelve of these false negatives did not grow on the CMRSA II and one produced non-mauve colonies. The read time of all 13 isolates were from 21 to 26 hours.

At the third clinical trial site, the positive percent agreement of CMRSA II when compared to Traditional Culture was 90.2% at 20-26 hours and the negative percent agreement was 98.9%. Results are demonstrated in the table below.

**BBL CHROMagar MRSA II Performance vs. Traditional Culture at Third Clinical Trial Site**

	Traditional Culture		
CMRSA II Result	MRSA	Not MRSA	Total
MRSA	46	3*	49
Not MRSA	5	264	269
	51	267	318
Reference Method: Traditional Culture Positive Percent Agreement: 90.2% (78.6%, 96.7%) Negative Percent Agreement: 98.9% (96.8%, 99.8%)			

\* Two samples that were positive on BBL CHROMagar MRSA II and negative by Traditional Culture were confirmed as MRSA by cefoxitin disk diffusion testing.

Challenge testing for CMRSA II was performed on 14 MRSA and 6 MSSA. The final concentration of the isolate suspension inoculated onto the CMRSA II plates during the Challenge portion of the Clinical Study was  $10^7$  to  $10^8$  CFU/mL. All challenge isolates demonstrated expected results.

*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 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.