

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

A. 510(k) Number:

k100589

B. Purpose for Submission:

To obtain substantial equivalent determination for a premarket notification for **MRSASelect™** for direct detection of MRSA from skin and soft-tissue wound specimens

C. Measurand:

Methicillin resistant *Staphylococcus aureus* (MRSA)

D. Type of Test:

Direct detection of MRSA from skin and soft-tissue wound specimens using specific chromogenic substrates and selective antifungal/antimicrobial mixture

E. Applicant:

Bio-Rad

F. Proprietary and Established Names:

MRSASelect

G. Regulatory Information:

1. Regulation section:

CFR 866.1700

2. Classification:

II

3. Product code:

JSO: Culture media, Antimicrobial susceptibility test, excluding Mueller Hinton Agar

4. Panel:

83 Microbiology

H. Intended Use:

1. Intended use(s):

MRSASelect™ is a selective and differential chromogenic medium for the qualitative detection of methicillin resistant *Staphylococcus aureus* (MRSA) from skin and soft-tissue wound specimens. The medium is indicated for use in conjunction with other laboratory tests and clinical data available to aid in the identification and diagnosis of MRSA from patients with skin and soft-tissue infections. Concomitant cultures and susceptibility testing are necessary for all skin and soft-tissue wound specimens. **MRSASelect™** is not intended to guide, or monitor treatment for MRSA infection, or provides results of susceptibility to methicillin. Results can be interpreted after 18 to 28 hours incubation.

2. Indication(s) for use:

MRSASelect™ is a selective and differential chromogenic medium for the qualitative detection of methicillin resistant *Staphylococcus aureus* (MRSA) from skin and soft-tissue wound specimens. The medium is indicated for use in conjunction with other laboratory tests and clinical data available to aid in the identification and diagnosis of MRSA from patients with skin and soft-tissue infections. Concomitant cultures and susceptibility testing are necessary for all skin and soft-tissue wound specimens. **MRSASelect™** is not intended to guide, or monitor treatment for MRSA infection, or provides results of susceptibility to methicillin. Results can be interpreted after 18 to 28 hours incubation.

3. Special conditions for use statement(s):

Prescription use only

4. Special instrument requirements:

Not applicable

I. Device Description:

MRSASelect is a selective and differential chromogenic medium for the qualitative detection of MRSA from skin and soft-tissue wound specimens. Selective antifungal/antibiotics mixture is incorporated in the medium to inhibit the growth of yeasts, Gram negative and Gram positive bacteria except MRSA. Identification is based on the cleavage of a chromogenic substrate by a specific enzymatic activity of *Staphylococcus aureus*, leading to a strong pink coloration of the *Staphylococcus*

aureus colonies. Plates may be read within 18-28 hours incubation.

J. Substantial Equivalence Information:

1. Predicate device name(s):

MRSASelect

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

k081212

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	For detection of MRSA	For detection of MRSA
Reporting	MRSA	MRSA
Reading	Manual	Manual
Test methodology	selective chromogenic agar	selective chromogenic agar

Differences		
Item	Device	Predicate
Intended Use	In conjunction with other laboratory tests and clinical data available to aid in the identification and diagnosis of MRSA from patients with skin and soft-tissue infections.	Screen for the detection of colonization of methicillin resistant <i>Staphylococcus aureus</i> (MRSA) to aid in the prevention and control of MRSA infections in healthcare settings.
Inoculum	Direct	Direct and Indirect (saline)
Specimen sample	Skin and soft tissue	Nares

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

Clinical and Laboratory Standard Institute (CLSI) M100-S20 Performance Standards for Antimicrobial Susceptibility Testing; CLSI M29-A2 Protection of Laboratory Workers from Occupational Acquired Infections; CLSI M40-A Quality Control of Microbiological Transport Systems; Approved Standard

L. Test Principle:

MRSASelect is a selective medium for the detection and direct identification of MRSA. The selectivity of this medium is based on the presence of an antibiotic/antifungal mixture and an optimized salt concentration that inhibits the growth of yeast and the majority of Gram negative and Gram positive bacteria with the exception of methicillin-resistant *staphylococci*. Identification is based on the cleavage of a chromogenic substrate by a specific enzymatic activity of

Staphylococcus aureus, leading to a strong pink coloration of the *Staphylococcus aureus* colonies.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Reproducibility Testing was done at three sites in triplicates for three days with three lots. The study included two strains each for MRSA, MSSA and *S. epidermidis*. *S. aureus* ATCC 43300 was also tested. It was performed at concentrations of 10^6 CFU/mL for MRSA, and 10^8 CFU/mL for non-MRSA. Reproducibility was >95%.

b. *Linearity/assay reportable range:*

Not applicable

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

Negative Control

S. aureus ATCC 25923 at a concentration of $10^4 - 10^5$ CFU/plate

Positive Control

S. aureus ATCC 43300 at a concentration of $10^3 - 10^4$ CFU/plate

Test Strain	Expected Results after 24 hours at 35-37°C
<i>S. aureus</i> ATCC 25923	No Growth
<i>S. aureus</i> ATCC 43300	Growth – small pink colonies

QC was performed at each testing site on more than three lots. The testing followed the recommendations of the QC strains listed in the package insert and there were no product failures.

d. *Detection limit:*

The LoD study was performed on two well characterized MRSA strains, at six serial dilutions, per strain, per dilution, on two MRSASelect plates and by two operators. The results demonstrated the LoD of 10^3 CFU/mL.

S. aureus ATCC 43300

Inoculum* (CFU/mL)	MRSASelect							
	18 Hours				28 Hours			
	CFU	Color	CFU	Color	CFU	Color	CFU	Color
9.13×10^6	>100	Pink	>100	Pink	>100	Pink	>100	Pink
8.40×10^5	>100	Pink	>100	Pink	>100	Pink	>100	Pink
7.53×10^4	>100	Pink	>100	Pink	>100	Pink	>100	Pink
9.18×10^3	3/10	Pink	29/39	Pink	4/15	Pink	35/49	Pink
7.12×10^2	2/2	Pink	5/1	Pink	2/3	Pink	5/3	Pink
7.50×10^1	0/1	Pink	0/0	Pink	1/1	Pink	0/0	Pink

* Average CFU/mL obtained on Blood Agar Plate

S. aureus NRS660

Inoculum* (CFU/mL)	MRSASelect							
	18 Hours				28 Hours			
	CFU	Color	CFU	Color	CFU	Color	CFU	Color
1.47×10^7	>100	Pink	>100	Pink	>100	Pink	>100	Pink
1.27×10^6	>100	Pink	>100	Pink	>100	Pink	>100	Pink
1.52×10^5	>100	Pink	>100	Pink	>100	Pink	>100	Pink
1.42×10^4	50/100	Pink	50/100	Pink	103/161	Pink	102/180	Pink
1.46×10^3	10/12	Pink	11/25	Pink	10/13	Pink	11/27	Pink
1.42×10^2	0/0	Pink	1/3	Pink	0/0	Pink	3/1	Pink

* Average CFU/mL obtained on Blood Agar Plate

Analytical reactivity

The study included 102 well characterized MRSA from the Network on Antimicrobial Resistance in *Staph aureus* (NARSA) collection, tested at concentrations 10^3 - 10^4 CFU/mL. They were USA100, 200, 300, 500, 600, 700, 800, and 1000. The USA300-0114 (NRS 384) was also tested.

Results demonstrated that strains NRS722, 727, and 730 produce white colonies at 18hrs, but pink colonies at 24 hrs; NRS676, and 745 produce pink colonies at $\geq 10^5$ CFU/mL, higher than the LoD of 10^3 CFU/mL.

e. *Analytical specificity:*

Interference Study

The interference study included blood, pus and non-prescription debriding agents. The debriding agents tested were 1U/g fibrinolysin and 666U/g desoxyribonuclease, Papain+urea (1%), and Papain+urea (5%). No

interference observed.

Topical compounds commonly used in wound care were also tested. The following compounds demonstrated inhibitory effect on the recovery of MRSA:

- Bactine- Benzalkonium chloride 0.13%, Lidocaine hydrochloride 2.5%
- Betadine (liquid) - Povidone-iodine 10%
- Iodine Tincture (liquid) - Iodine 2%
- Biseptine (liquid) - Chlorhexidine Gluconate 0.25%, Benzalkonium chloride 0.025%
- Sodium hypochlorite (liquid)
- StaphAseptic (ointment) - Benzethonium Chloride 0.2%, Lidocaine HCl 2.5%
- Silver chloride (gel)
- Neosporin
- Polysporin

This information will be added to the Package Insert in Limitations section (item# i).

Cross Reactivity Study

There were 35 non-staphylococcal isolates tested at concentration of $\geq 10^6$ CFU/mL in the SSTI premarket application. No pink colonies observed.

The isolates whose performance resulted in a limitation statement for the nasal submission was also included in this submission (i.e. faint pink colonies for some *S. epidermidis*, pink coloration for some Gram negative rods, and *Acinetobacter*); pinpoint white colonies were observed for *Corynebacterium jeikeium* and *Candida tropicalis*.

Mixed infection study

A mixed infection study was performed to demonstrate the performance of the MRSASelect if mixed infection was encountered in wound or SSTI samples. *S. aureus* ATCC43300 at LoD (i.e. 10^3 CFU/mL), oxacillin resistant *S. epidermidis* and *K. pneumoniae* at increasing concentrations up to 10^6 CFU/mL each were tested. No interference was observed.

f. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

Not applicable. Compared to Standard Reference Method

b. *Matrix comparison:*

Not applicable

3. Clinical studies:

a. *Clinical Sensitivity:*

The MRSASelect™ culture media was evaluated at four clinical sites which included testing of 943 specimens. All the samples were inoculated directly onto the following media:

- Trypticase Soy Agar (TSA) with 5% Sheep Blood
- MRSASelect
- Tryptic Soy Broth (TSB) with 6.5% NaCl

MRSASelect plates, TSA, and TSB were incubated at 35- 37°C in ambient air. Positive TSBs were subcultured to a TSA, and negative TSB were incubated for a total of 48 hrs. Suspected *Staph aureus* colonies from TSA were identified by Gram stain, catalase, Pastorex Staph Plus, and *mecA* mediated oxacillin resistance by using cefoxitin (30µg) disk.

Pink colonies of any intensity on MRSASelect between 18- 28 hrs of incubation indicated the presence of MRSA. The tables below are the performance summary of the clinical studies:

Summary of read hours (incubation time)

		Incubation time (hours)				Total
		18-20	21-23	24-26	27-28	
MRSASelect Result	POS	78	74	58	3	213
	NEG	245	233	225	27	730
	Total	323	307	283	30	943

MRSASelect vs. Culture + Enrichment Broth

	Pos	Neg	Total
Pos	209	4	213
Neg	19	711	730
Total	228	715	943

Sensitivity 91.7% (87.3, 94.7)

Specificity 99.4% (98.5, 99.8)

b. *Clinical specificity:*

See above

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:

The overall prevalence of MRSA colonization by routine culture and Tryptic Soy Broth (TSB) with 6.5% NaCl was 24.2% (228/943). The prevalence detected using routine culture alone was 22.9% (216/943) and the prevalence detected by **MRSASelect™** was 22.6% (213/943).

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.