

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

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

K151688

**B. Purpose for Submission:**

To obtain a substantial equivalence determination for chromID™ MRSA medium with a new intended use for the qualitative detection of methicillin resistant *Staphylococcus aureus* in skin and skin structure infections (SSSI).

**C. Measurand:**

Methicillin Resistant *Staphylococcus aureus* (MRSA)

**D. Type of Test:**

Detection of MRSA using a selective and differential chromogenic medium

**E. Applicant:**

bioMérieux, Inc.

**F. Proprietary and Established Names:**

chromID™ MRSA

**G. Regulatory Information:**

1. Regulation section:

21 CFR 866.1700

2. Classification:

Class II

3. Product code:

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

4. Panel:

**H. Intended Use:**

1. Intended use(s):

chromID™ MRSA agar is a selective and differential chromogenic medium for:

A. The qualitative detection of nasal colonization of methicillin-resistant *Staphylococcus aureus* (MRSA), to aid in the prevention and control of MRSA in healthcare settings. The test is performed on anterior nares swab specimens from patients and healthcare workers to screen for MRSA colonization. chromID™ MRSA when used to detect nasal colonization is not intended to diagnose, guide, or monitor therapy for MRSA infections, or provide results of susceptibility to methicillin.

B. The qualitative detection of MRSA from skin and skin structure infections. chromID™ MRSA is indicated for use in conjunction with other laboratory tests and clinical data available to aid in the identification and diagnosis of MRSA infections. Concomitant cultures for skin and skin structure infections are necessary to recover organisms for further microbiological susceptibility testing or epidemiological typing.

A negative result does not preclude MRSA infection. chromID™ MRSA is not intended to monitor treatment for MRSA infections, or provide results of susceptibility to methicillin.

2. Indication(s) for use:

Same as the Intended Use.

3. Special conditions for use statement(s):

Prescription use

The following compounds demonstrated an inhibitory effect on the recovery of MRSA on chromID MRSA agar and on control plates: Bacicoline, Maxidrol, Mercryl, Germ Guard, Mupiderm, Hydrocortisone, Betadine, 70% isopropyl alcohol.

4. Special instrument requirements:

Not Applicable

**I. Device Description:**

chromID MRSA is a selective medium for the detection of methicillin resistant *Staphylococcus aureus* (MRSA). The selectivity of this medium is based on the presence of antibiotics that inhibit most bacteria not belonging to the genus *Staphylococcus* and yeasts. The medium favors the growth of MRSA including hetero-resistant strains, which will

appear as green colonies on the agar medium. Colorless colonies growing on the agar are considered negative for MRSA.

**J. Substantial Equivalence Information:**

1. Predicate device name(s):

Bio-Rad MRSASelect™

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

K100589

3. Comparison with predicate:

<b>Similarities</b>		
Item	chromID MRSA (K151688)	Bio-Rad MRSASelect (K100589)
Intended Use	<p>chromID™ MRSA agar is a selective and differential chromogenic medium for :</p> <p>A. The qualitative detection of nasal colonization of methicillin-resistant <i>Staphylococcus aureus</i> (MRSA), to aid in the prevention and control of MRSA in healthcare settings. The test is performed on anterior nares swab specimens from patients and healthcare workers to screen for MRSA colonization. chromID™ MRSA when used to detect nasal colonization is not intended to diagnose, guide, or monitor therapy for MRSA infections, or provide results of susceptibility to methicillin.</p> <p>B. The qualitative detection of MRSA from skin and skin structure infections. chromID™ MRSA is indicated for use in conjunction with other laboratory tests and clinical data available to aid in the identification and diagnosis of MRSA infections. Concomitant cultures for skin and skin structure infections are necessary to recover organisms for further microbiological susceptibility testing or epidemiological typing.</p>	<p>MRSASelect™ is a selective and differential chromogenic medium for the qualitative detection of methicillin resistant <i>Staphylococcus aureus</i> (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.</p>

Similarities		
Item	chromID MRSA (K151688)	Bio-Rad MRSASelect (K100589)
	A negative result does not preclude MRSA infection. chromID™ MRSA is not intended to monitor treatment for MRSA infections, or provide results of susceptibility to methicillin.	
Reporting	MRSA	MRSA
Reading	Manual	Manual
Inoculation	Direct Specimen	Direct Specimen
Specimen Type	SSSI	SSSI
Test Methodology	selective chromogenic agar	selective chromogenic agar

Differences		
Item	chromID MRSA (K151688)	Bio-Rad MRSASelect (K100589)
Growth Detection	Green colonies after 24 hours incubation	Pink colonies after 18 to 28 hours incubation

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

Clinical and Laboratory Standards Institute (CLSI) M100-S23. Performance Standards for Antimicrobial Susceptibility Testing; Twenty-third Informational, Supplement, Vol. 33 No. 1, January 2013.

**L. Test Principle:**

chromID MRSA 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 mixture that inhibits most bacteria not belonging to the genus *Staphylococcus*, as well as yeasts. Identification is based on the cleavage of a chromogenic substrate in the medium by *Staphylococcus aureus*, leading to a green coloration of the growing *Staphylococcus aureus* colonies. Skin and skin structure infection specimens are inoculated directly onto the chromID MRSA agar plates and incubated aerobically at 35°-37°C for 24 hours. The cultures are examined after 24 hours incubation for the presence of green colonies, in which the presence of at least one green colony gives the sample a positive MRSA status. Any color of green should be interpreted as a positive result. No growth or colonies presenting as other than green in appearance should be interpreted as a negative result.

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

1. Analytical performance:

a. *Precision/Reproducibility:*

Reproducibility was demonstrated at three sites using a blinded panel of ten well-characterized *Staphylococcus aureus* isolates, including both *mecA* positive and *mecA* negative isolates. At each site, panel members were tested in triplicate at  $1 \times 10^3$  CFU/ml with multiple lots of chromID MRSA each day for five days. chromID MRSA plates were observed for the growth of green colonies at 24 hours. All strains produced the expected results with the chromID MRSA at 24 hours (450/450). Isolates were also plated to BAP to ensure viability and purity of cultures.

b. *Linearity/assay reportable range:*

Not Applicable

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

Quality control (QC) testing was performed at each testing site for growth/color development on chromID MRSA. Two quality control organisms (*Staphylococcus aureus* ATCC 29213 and *Staphylococcus aureus* ATCC 43300) were tested at each study site on chromID MRSA for each day of testing. The strains were also subcultured to Trypticase Soy Agar w/ 5% sheep blood to ensure viability of the organism. A single colony was touched with a sterile loop and then inoculated onto chromID MRSA agar according to the package insert instructions. QC testing results provided expected reactions at each of the four testing sites on each day tested, except on two days (Table 1). Two days *Staphylococcus aureus* ATCC 29213 grew, but colonies were not green. The submitted QC data are acceptable.

**Table 1. QC Data Summary**

QC Strain	<i>mecA</i> PCR	Expected Results after 24 hrs at 35-37°C	QC Results (all sites)
<i>Staphylococcus aureus</i> ATCC 29213	NEG	No growth	265/267
<i>Staphylococcus aureus</i> ATCC 43300	POS	Growth-green colonies	267/267

d. *Detection limit:*

Recovery Study

A Recovery Study was performed with two well-characterized MRSA strains at six serial dilutions per strain on five chromID MRSA plates. The minimum concentration of MRSA reliably detected by chromID MRSA at 24 hours was  $10^5$  CFU/ml for CDC Mu3-8R and  $10^3$  CFU/ml for ATCC 43300.

Analytical Reactivity

A study was conducted to demonstrate the sensitivity of chromID MRSA agar to detect various MRSA strains at a concentration of  $10^3$  CFU/ml. The study included 80 well-characterized MRSA *mecA* strains and 5 *mecC* strains from bioMérieux stock,

ATCC, and other commercial sources.

Results demonstrated that 58 of 80 *mecA* MRSA strains and 4/5 *mecC* MRSA strains were detected on chromID MRSA plates at 24 hours. Two MRSA strains, bioMérieux strain #9204050 and ATCC strain 43866, did not grow on chromID MRSA plates. Table 2 below shows results from the Analytical Reactivity Study.

**Table 2.** Analytical Reactivity Study Results at 24 and 48 hrs.

Strains	Number	24 hr Results		48 hr Results	
		Growth with Green Color	% Detected	Growth with Green Color	% Detected
MRSA ( <i>mecA</i> )	80	58/80	72.5%	78/80	97.5%
MRSA ( <i>mecC</i> )	5	4/5	80.0%	5/5	100%

Expression of Resistance

An Expression of Resistance Study was conducted to demonstrate chromID MRSA performance with 28 well-characterized strains [10 low level methicillin-resistant *Staphylococcus aureus*, 10 high level methicillin-resistant *Staphylococcus aureus*, 5 border-line oxacillin-resistant *Staphylococcus aureus* (BORSA), and 3 methicillin-susceptible *Staphylococcus aureus* (MSSA)] at multiple organism concentrations. Eight non-MRSA strains (5 BORSA and 3 MSSA) did not grow on chromID MRSA at the four tested concentrations. No false positives were observed. At 24 hours, all MRSA strains were detected at 10<sup>5</sup> CFU/ml. Table 3 lists results of the Expression of Resistance Study for MRSA strains at 24 hours and 48 hours.

**Table 3.** MRSA strains detected at various concentrations (Green Colonies).

Concentration (CFU/ml)	24 hrs	48 hrs
10 <sup>8</sup>	20/20	20/20
10 <sup>5</sup>	20/20	20/20
10 <sup>4</sup>	17/20 (85%)	20/20
10 <sup>3</sup>	14/20 (70%)	20/20

Incubation Study

An Incubation Study was performed to determine the effect of various incubation times on the performance of the chromID MRSA media when tested with three MRSA strains (ATCC 43300, *Staphylococcus aureus* 0611169, and CDC Mu3-8R) at 10<sup>3</sup> CFU/ml concentration. Two MRSA strains (ATCC 43300 and *Staphylococcus aureus* 0611169) were detected at 20 hours. Twenty-seven hours was needed for a positive identification (green colonies) for all three MRSA strains.

e. *Analytical specificity:*

Cross-Reactivity Study

In order to evaluate the performance of chromID MRSA agar against microorganisms potentially encountered in skin and skin structure infections, a Cross-Reactivity Study was performed with 71 non-MRSA strains (gram negative bacteria, gram positive bacteria, and yeast) at approximately  $10^6$  CFU/ml. Results showed that 44 organisms from the cross-reactivity panel did not grow on chromID MRSA.

Please see Table 4 below for a list of strains yielding green colonies on chromID MRSA after 24 hours.

**Table 4. Cross-Reactivity Study Results**

Incubation Time	Total Strains Tested	# Strains Growing on chromID MRSA	Strains with Green Colonies	
			# Strains	Organism Name
24 hrs	71	27/71	7	<ul style="list-style-type: none"> <li>• (3) <i>Klebsiella pneumonia</i> (KPC)</li> <li>• (1) <i>Enterobacter cloacae</i> (KPC)</li> <li>• (1) <i>Staphylococcus pseudointermedius</i> (oxacillin resistant)</li> <li>• (2) <i>Staphylococcus sciuri</i> (oxacillin resistant)</li> </ul>

#### Interference Study

Eight strains of *Staphylococcus* [4 MRSA, 2 methicillin resistant coagulase negative *Staphylococcus* species (MRCNS) and 2 methicillin susceptible *Staphylococcus aureus* (MSSA)] were used in an Interference Study. Interfering substances were evaluated at physiologically or biologically relevant concentrations and mixed with bacterial suspensions (9:1, v:v). Benzocaine (14 g/l) may delay the colony coloration or inhibit growth of MRSA on chromID MRSA. MRSA colony color and growth were not significantly affected by sodium citrate, citrate phosphate dextrose, plasma, whole blood, and buffy coat.

Swab transport media was tested, and the data was provided in K091024 for the chromID MRSA 510(k) claim for nasal specimens. Transport media tested included: Amies Gel Medium, Liquid Amies Medium, Stuart Gel Medium, Liquid Stuart Medium, and Cary-Blair Transport Media.

#### Mixed Infection Study

A Mixed Infection Study was conducted to demonstrate that high levels ( $10^4$ ,  $10^6$  or  $10^8$  CFU/ml) of non-target organism will not suppress growth of MRSA. Ten MRSA strains exhibiting different levels of methicillin-resistance were included in the study and incubated with three non-target organisms (MSSA, MRCN *Staphylococcus epidermidis*, and *Escherichia coli*). MRSA strains were tested at approximately  $10^3$  CFU/ml. At 24 hours, all five low level resistant MRSA strains were detected in the Mixed Infection Study; however, this number varied from 2/5 up to 4/5 strains for the high-level resistant MRSA strains at 24 hours. Two of the MRSA strains not producing green colonies at 24 hours also did not produce green colonies during the Analytical Reactivity Study at 24 hours. Results of the study revealed that MRSA was still detected on chromID MRSA in the presence of high levels of MSSA, *S. epidermidis*, or *E. coli* and that non-target organisms did not suppress growth of the ten MRSA strains tested on chromID MRSA. Please refer to Table 5 for results of

the 24 hour and 48 hour Mixed Infection Study.

**Table 5.** Summary of Mixed Infection Study at 24 hrs and 48 hrs

MRSA Concentration (CFU/ml)	Non-Target Organism Concentration (CFU/ml)	Growth (24 hrs)	Characteristic Green Colonies (24 hrs)	Growth (48 hrs)	Characteristic Green Colonies (48 hrs)
5 MRSA strains (low level resistance) + MSSA ATCC 29213					
10 <sup>3</sup> CFU/ml MRSA	10 <sup>8</sup> CFU/ml MSSA	5/5	5/5	5/5	5/5
	10 <sup>6</sup> CFU/ml MSSA	5/5	5/5	5/5	5/5
	10 <sup>4</sup> CFU/ml MSSA	5/5	5/5	5/5	5/5
5 MRSA strains (low level resistance) + <i>S. epidermidis</i> 8402199					
10 <sup>3</sup> CFU/ml MRSA	10 <sup>8</sup> CFU/ml <i>S. epidermidis</i>	5/5	5/5	5/5	5/5
	10 <sup>6</sup> CFU/ml <i>S. epidermidis</i>	5/5	5/5	5/5	5/5
	10 <sup>4</sup> CFU/ml <i>S. epidermidis</i>	5/5	5/5	5/5	5/5
5 MRSA strains (low level resistance) + <i>E. coli</i> ATCC 8739					
10 <sup>3</sup> CFU/ml MRSA	10 <sup>8</sup> CFU/ml <i>E. coli</i>	5/5	5/5	5/5	5/5
	10 <sup>6</sup> CFU/ml <i>E. coli</i>	5/5	5/5	5/5	5/5
	10 <sup>4</sup> CFU/ml <i>E. coli</i>	5/5	5/5	5/5	5/5
5 MRSA strains (high level resistance) + MSSA ATCC 29213					
10 <sup>3</sup> CFU/ml MRSA	10 <sup>8</sup> CFU/ml MSSA	5/5	2/5	5/5	5/5
	10 <sup>6</sup> CFU/ml MSSA	5/5	2/5	5/5	5/5
	10 <sup>4</sup> CFU/ml MSSA	5/5	3/5	5/5	5/5
5 MRSA strains (high level resistance) + <i>S. epidermidis</i> 8402199					
10 <sup>3</sup> CFU/ml MRSA	10 <sup>8</sup> CFU/ml <i>S. epidermidis</i>	5/5	4/5	5/5	5/5
	10 <sup>6</sup> CFU/ml <i>S. epidermidis</i>	5/5	3/5	5/5	5/5
	10 <sup>4</sup> CFU/ml <i>S. epidermidis</i>	5/5	2/5	5/5	5/5
5 MRSA strains (high level resistance) + <i>E. coli</i> ATCC 8739					
10 <sup>3</sup> CFU/ml MRSA	10 <sup>8</sup> CFU/ml <i>E. coli</i>	5/5	4/5	5/5	5/5
	10 <sup>6</sup> CFU/ml <i>E. coli</i>	5/5	3/5	5/5	5/5
	10 <sup>4</sup> CFU/ml <i>E. coli</i>	5/5	4/5	5/5	5/5

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:

chromID MRSA culture media was evaluated at four clinical sites, which included

690 SSSI specimens. Three specimens were excluded because they did not meet specimen acceptance criteria. Seven specimens were removed due to protocol deviations. A total of 680 compliant SSSI specimens were included in the performance calculations for chromID MRSA.

All samples were inoculated onto the following media:

- chromID MRSA
- Tryptic Soy Broth (TSB) with 6.5% NaCl

For the enrichment culture method, specimens inoculated into TSB with 6.5% NaCl were incubated at 35°C for 24 hours in ambient air. Positive broth cultures were subcultured to Tryptic Soy Agar with 5% sheep blood, while negative broth cultures were incubated for an additional 24 hours before calling negative. Suspected *Staphylococcus aureus* colonies from plates were identified by Gram stain, catalase, latex agglutination, and cefoxitin screen test (30 µg disk).

chromID MRSA plates were incubated at 35°C for 24 hours in ambient air. Green colonies detected on chromID MRSA plates after 24 hours of incubation indicated the presence of MRSA. Performance (sensitivity and specificity) of chromID MRSA compared to the enriched culture method is presented in Table 6 below.

**Table 6.** Comparison between chromID MRSA and Enrichment Culture

chromID MRSA (24 hr result)	Enriched Culture Method		
	Positive	Negative	Total
Positive	166	13 <sup>a</sup>	179
Negative	11 <sup>b</sup>	490	501
Total	177	503	680
	Sensitivity: 93.8%, 95% CI: 89.2%-96.5%		
	Specificity: 97.4%, 95% CI: 95.6%-98.5%		

<sup>a</sup>13 discordant specimens (chromID MRSA result of MRSA positive; culture-based testing result of MRSA negative) were observed. 5 of the 13 chromID MRSA positive specimens were confirmed as MRSA by cefoxitin screen test. 8 specimens grew green colonies on chromID MRSA that were not MRSA.

<sup>b</sup>11 discordant specimens (chromID MRSA result of MRSA negative; culture-based testing result of MRSA positive) were observed. Six specimens displayed no growth on chromID MRSA. Four specimens grew non-green MRSA colonies on chromID MRSA. One specimen grew green colonies on chromID MRSA that was not identified as MRSA. Six of 10 specimens that were negative for MRSA after 24 hours of incubation on chromID™ MRSA grew colonies indicative of MRSA at 48 hours.

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 by the Enrichment Culture Method was 26.0% (177/680). The prevalence reported for chromID MRSA at 24 hours was 26.3% (179/680).

**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.