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

A. 510(k) Number:

K162076

B. Purpose for Submission:

To obtain a substantial equivalence determination for chromID™ MRSA agar with a new intended use for the qualitative detection of methicillin resistant *Staphylococcus aureus* from positive blood cultures demonstrating Gram-positive cocci on Gram stain.

C. Measurand:

Methicillin Resistant *Staphylococcus aureus* (MRSA)

D. Type of Test:

Detection of MRSA using a selective and differential chromogenic media

E. Applicant:

bioMérieux, Inc.

F. Proprietary and Established Names:

chromID™ MRSA Agar

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:

   Microbiology (83)

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.
   c. The qualitative detection of MRSA from positive blood cultures demonstrating Gram-positive cocci on Gram stain. 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. Sub-culturing for positive blood cultures 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:

   See Intended Use.

3. Special conditions for use statement(s):

   Prescription Use

4. Special instrument requirements:

   The performance of chromID MRSA has not been established for blood culture bottle types other than those shown in Table 3 below.

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):

   Remel Spectra™ MRSA

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

   K092407

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	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	Remel Spectra™ MRSA is a selective and differential chromogenic medium recommended for use in 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 with anterior nares swab specimens from patients and healthcare workers to screen for MRSA colonization. Spectra™ MRSA is not intended to diagnose MRSA infection or to guide or monitor treatment for infections. Spectra™ MRSA is also intended for use in the qualitative detection of MRSA from positive blood cultures demonstrating Gram-positive cocci on Gram stain. Spectra™ MRSA is indicated for use in conjunction with other laboratory tests and clinical data available to the clinician as an aid in the detection of MRSA from patient positive blood cultures.

Similarities		
Item	Device	Predicate
	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. c. The qualitative detection of MRSA from positive blood cultures demonstrating Gram-positive cocci on Gram stain. 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. Sub-culturing for positive blood cultures 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.	Spectra™ MRSA is not intended to monitor treatment for MRSA infections, or provide results of susceptibility to methicillin. All positive blood bottles should be sub-cultured for further microbiological/ susceptibility testing.
Reporting	MRSA	MRSA
Reading	Manual	Manual
Specimen Type	Anterior nares swab specimens and Positive blood cultures	Anterior nares swab specimens and Positive blood cultures
Test Methodology	Selective and differential chromogenic agar	Selective and differential chromogenic agar

Differences		
Item	Device	Predicate
Specimen Type	Specimens from skin and skin structure infection	Device not indicated for this specimen type
Growth Detection	Green colonies after 24 hours incubation	Small to medium denim-blue colonies after 24 hours

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 the *Staphylococcus aureus* present, leading to a green coloration of the growing *Staphylococcus aureus* colonies. An aliquot from a positive blood culture bottle (exhibiting Gram-positive cocci) is 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 is interpreted as a negative result.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

To support the addition of a new specimen type (positive blood culture), a Reproducibility Study was conducted at three sites using a blinded panel of ten well-characterized *Staphylococcus aureus* strains, including both *mecA* positive and *mecA* negative isolates. At each site, panel members were tested in triplicate at $1x10^3$ CFU/ml each day for five days with multiple operators. To simulate positive blood cultures, all ten strains were tested using broth from blood culture bottles as the diluent. chromID MRSA plates were observed for the growth of green colonies at 24 hours. All strains produced the expected results with chromID MRSA (450/450). Isolates were also plated on BAP to ensure viability and purity of cultures. Broths from the following blood culture bottles were used during testing: BacT/Alert FA Plus (Aerobic) and BACTEC Plus Aerobic/F Medium.

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 ensure viability of the organism. QC testing results provided expected reactions at the four testing sites on each day tested (Table 1). The submitted QC data are acceptable.

Table 1. QC Data Summary

QC Strain	Methicillin Resistant	*mecA* PCR	Expected Results after 24 hrs at 35-37°C	Correct QC Results (all sites)
Staphylococcus aureus ATCC 29213	No	NEG	No growth	297/297
Staphylococcus aureus ATCC 43300	Yes	POS	Growth-green colonies	297/297

d. Detection limit:

Recovery Study

Since the current submission was for the addition of a new specimen type to the intended use of chromID MRSA agar, a repeat of the Recovery Study was not needed to support device performance. A short description of results from the Recovery Study in K151688 is provided below.

According to K151688, the lowest concentration of MRSA organisms demonstrating growth with a positive result was 10^3 CFU/ml for one MRSA strain (ATCC 43300) and 10^5 CFU/ml for the second MRSA strain (CDC Mu3-8R) at 24 hours.

Analytical Reactivity and Expression of Resistance

Both Analytical Reactivity and Expression of Resistance Studies were conducted as part of K151688; therefore, a repeat of these studies was not needed to support device performance. A short summary of the results for these studies is provided below.

In K151688, a challenge set composed of 80 *mecA* MRSA strains and 5 *mecC* MRSA strains was inoculated onto chromID MRSA agar plates at 10^3 CFU/ml. After 24 hours of incubation, 58/80 *mecA* MRSA strains and 4/5 *mecC* MRSA strains were detected on the chromID MRSA agar. In addition, 28 well-characterized *Staphylococcus aureus* strains (10 low level methicillin-resistant, 10 high level methicillin-resistant, 5 borderline oxacillin-resistant, and 3 methicillin-susceptible) were evaluated with chromID MRSA. All low level and high level methicillin-resistant strains were detected at $\geq 10^5$ CFU/ml.

e. Analytical specificity:

Cross-Reactivity

Cross-Reactivity Studies were conducted as part of the anterior nares swab specimen (K091024) and SSSI (K151688) submissions; therefore, an additional Cross-

Reactivity Study was not needed to support device performance. A short summary of the results of the Cross-Reactivity Study is provided below.

In K091024, 110 isolates were evaluated. Certain ESBL producers with heavy inoculum gave characteristic green color at the point of inoculation after 24 hours of incubation. For K151688, 71 non-MRSA strains representing various bacterial and fungal species were evaluated at 10^6 CFU/ml. After 24 hours of incubation, green colonies (cross-reactivity) was observed for three *Klebsiella pneumoniae* (KPC) strains, two *Staphylococcus sciuri* (oxacillin resistant) strains, one *Enterobacter cloacae* (KPC) strain, and one *Staphylococcus pseudintermedius* (oxacillin resistant) strain. The Cross-Reactivity Studies were acceptable. A limitation is included in the labeling regarding false positive results with non-MRSA strains.

Interfering Substances

Although Interference Studies were conducted as part of the anterior nares swab specimen (K091024) and SSSI (K151688) submissions, additional studies were performed to evaluate potential interference from 6 common medical substances in the detection of MRSA with chromID MRSA. Results demonstrated that MRSA strains were recovered in the presence of hemoglobin, triglyceride sera, conjugated and unconjugated bilirubin, γ globulin, and sodium polyanetholsulfonate. A separate blood culture bottle study indicated that MRSA could be recovered from the following blood culture bottles:

- BacT/ALERT—FA (Aerobic), FA Plus (Aerobic), FN (Anaerobic), FN Plus (Anaerobic), SA (Standard Aerobic), SN (Standard Anaerobic)
- BacTEC—Standard Aerobic, Standard Anaerobic, PLUS Aerobic, PLUS Anaerobic, Lytic Anaerobic, Peds PLUS Aerobic
- VersaTREK—REDOX1 (Aerobic) and REDOX2 (Anaerobic)

These study results are acceptable. Substances interfering with MRSA detection on chromID MRSA (from K091024 and K151688) are listed as limitations in the labeling.

Mixed Infection Study

For results of the Mixed Infection Study, please refer to K151688.

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:

A clinical study was conducted with positive blood culture specimens (demonstrating Gram-positive cocci) to establish performance of chromID MRSA with the new specimen type. The performance of chromID MRSA agar was evaluated at four clinical sites, and data was collected from 1050 positive blood culture specimens (exhibiting Gram-positive cocci on Gram stain). Of these, 863 samples were included in the final performance calculations for chromID MRSA after the exclusion of 187 samples. Samples were excluded for the following reasons:

- 26 samples due to the limited number of positive pediatric blood culture bottles collected (for MRSA); all pediatric blood culture bottles were excluded from the study
- 139 samples from blood culture bottles not indicated for the BacT/ALERT or BACTEC systems were excluded according to the clinical protocol
- 22 samples due to additional protocol deviations—enrollment errors, duplicate samples, no quality control performed, cultures not saved for confirmation, no biochemical testing performed, and isolates aged greater than 5 days

Results from chromID MRSA at 24 hours incubation were compared to results obtained from traditional subculture on Tryptic Soy Agar with 5% sheep blood (BAP) at 48 hours. Suspected *Staphylococcus aureus* isolates were identified by gram stain, catalase, and latex agglutination. Susceptibility testing was performed using the 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 reference method is presented in Table 2 below. Blood culture bottles from each automated blood culture system were stratified and analyzed separately to determine the performance of chromID MRSA with each bottle type (Table 3).

Table 2. Clinical Performance Data for chromID MRSA vs Reference Method (All Sites)

ChromID MRSA (24 hrs)	**Reference Method**		
	Positive	Negative	Total
Positive	215	7[a]	222
Negative	0	641	641
Total	215	648	863
Sensitivity: 100% (215/215), 95% CI (98.3%-100%) Specificity: 98.9% (641/648), 95% CI (97.8%-99.5%)			

[a]Seven discordant specimens were observed (chromID MRSA result of MRSA positive; reference testing result of MRSA negative). Of the seven chromID MRSA positive specimens, two were confirmed as MRSA by gram stain, catalase, latex agglutination, cefoxitin screen test, *mecA* PCR, and Mass spec ID while five specimens grew green colonies on chromID MRSA that were not MRSA (two *E. faecalis*, one *S. epidermidis*, one *S. aureus*, one No ID).

Table 3. Clinical Performance for chromID MRSA Stratified by Blood Culture Bottle System

Blood Culture System	**Blood Culture Bottle Type**	**Total # Bottles**	**Sensitivity (95% CI)**	**Specificity (95% CI)**
BacT/ALERT	FA (FAN Aerobic)	46	100% (32/32) (89.3% - 100%)	100% (14/14) (78.5% - 100%)
	FA (FAN Plus Aerobic)	32	100% (22/22) (85.1% - 100%)	100% (10/10) (72.3% - 100%)
	FN (FAN Anaerobic)	36	100% (31/31) (89.0% - 100%)	100% (5/5) (56.6% - 100%)
	FN (FAN Plus Anaerobic)	27	100% (20/20) (83.9% - 100%)	100% (7/7) (64.6% - 100%)
	SA (Standard Aerobic)	187	100% (23/23) (85.7 - 100%)	98.8% (162/164) (95.7 - 99.7%)
	SN (Standard Anaerobic)	121	100% (25/25) (86.7% - 100%)	99.0% (95/96) (94.3% – 99.8%)
	SYSTEM (Combined)	449	100% (153/153) (97.6% - 100%)	99.0% (293/296) (97.1% - 99.7%)
BACTEC	Plus Aerobic/F	255	100% (30/30) (88.7% - 100%)	98.7% (222/225) (96.2% - 99.6%)
	Lytic/10 Anaerobic/F	159	100% (32/32) (89.3% - 100%)	99.2% (126/127) (95.7% - 99.9%)
	SYSTEM (Combined)	414	100% (62/62) (94.2% - 100%)	98.9% (348/352) (97.1% - 99.6%)

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:

MRSA was detected in 24.9% (215/863) of positive blood cultures exhibiting Gram-positive cocci on Gram stain and confirmed to be MRSA by the reference method. With chromID MRSA at 24 hours, MRSA was reported for 25.7% (222/863) of the samples tested.

N. Proposed Labeling:

The labeling is sufficient and it 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.