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

A. 510(k) Number:

k092407

B. Purpose for Submission:

To obtain a substantial equivalence determination for Remel Spectra™ MRSA for use in the qualitative detection of MRSA from positive blood cultures demonstrating Gram positive cocci on Gram stain

C. Measurand:

Methicillin Resistant *Staphylococcus aureus* (MRSA)

D. Type of Test:

A selective and differential chromogenic media for detection of MRSA

E. Applicant:

Thermo Fisher Scientific

F. Proprietary and Established Names:

Remel Spectra™ MRSA

G. Regulatory Information:

1. Regulation section:

   21CFR 866.1700 Culture medium for antimicrobial susceptibility tests

2. Classification:

   II

3. Product code:

   JSO

4. Panel:

   83-Microbiology

H. Intended Use:

1. Intended use(s):

   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. 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.

2. Indication(s) for use:

   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. 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.

3. Special conditions for use statement(s):

   For prescription use only.

4. Special instrument requirements:

   Not applicable

I. Device Description:

Remel Spectra™ MRSA is an opaque medium, which uses a novel chromogen that yields a denim-blue color as a result of phosphatase activity. This enzyme is present in *Staphylococcus aureus*, including MRSA. To allow the medium to differentiate MRSA accurately, it contains a combination of antibacterial compounds designed to inhibit the growth of a wide variety of competitor organisms. Also included are compounds that encourage the production of MRSA pathogenicity marker, ensuring expression of the phosphatase enzyme and so providing enhanced sensitivity and specificity.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   Remel Spectra™ MRSA (Nasal)

2. Predicate K number(s):

   k073027

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	For MRSA detection	For MRSA detection
Reporting	MRSA	MRSA
Reading	Manual	Manual
Test Methodology	selective and differential chromogenic prepared culture medium	selective and differential chromogenic prepared culture medium
Incubation	24 hours	24 hours

Differences		
Item	Device	Predicate
Inoculum	Positive blood culture	Anterior nares swabs

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

Not applicable.

L. Test Principle:

Remel Spectra™ MRSA is an opaque medium, which uses a novel chromogen that yields a denim-blue color as a result of phosphatase activity. This enzyme is present in all *Staphylococcus aureus*, including MRSA. To allow the medium to differentiate MRSA accurately, it contains a combination of antibacterial compounds designed to inhibit the growth of a wide variety of competitor organisms. Also included are compounds that encourage the production of MRSA pathogenicity marker, ensuring expression of the phosphatase enzyme and so providing enhanced sensitivity and specificity.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. Precision/Reproducibility:

Reproducibility was demonstrated at six sites using a panel of 20 *S. aureus* strains including thirteen MRSA, six MSSA, and one borderline oxacillin-resistant *S. aureus* (BORSA) isolates. Each isolate was tested once on each of three days at each site resulting in 360 data points. All were in agreement with expected values at 24 hours. The BORSA strain included in this evaluation at four sites is considered variable and produced a positive test result for 7/12 data points at 24 hours.

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 25923 as negative control were used. The clinical trial was conducted at four independent trial sites from July 31, 2007 through February 16, 2009. Weekly QC testing was conducted each week of testing clinical specimens utilizing CLSI interpretive criteria where applicable. All QC results obtained were acceptable.

d. Detection limit:

Not applicable.

e. Analytical specificity:

Cross-reactivity

Although cross reactivity studies were conducted as part of the anterior nares culture submission (k073027), additional studies were conducted to test for cross-reactivity with organisms that may be isolated from blood cultures because of the indication for use with blood culture bottles. In total, two hundred ninety-seven isolates were tested as part of this submission and 280 were tested as part of the earlier k073027 submission) microorganisms representing gram-negative rods, yeast, streptococci, enterococci, staphylococci and related organisms were evaluated with Spectra™ MRSA at 10^5–10^6 colony-forming units per ml concentration. No cross-reactivity (denim blue colonies) was observed following 24 hours incubation.

Supplemental cross reactivity studies were added as part of this submission. This included oxacillin MIC values against 97 coagulase negative staphylococci (27 isolates were resistant to oxacillin). No cross reactivity (denim blue colonies) was seen with any of these organisms following 24 hours incubation.

Interfering Substances

Interfering substances studies were conducted as part of the anterior nares culture submission (k073027). Nine commonly used medicinal substances, human blood, mucous, and six types of transport media were evaluated for potential interference of the chromogenic reaction on the Spectra™ MRSA medium. No interference was observed except for human blood which grew pinpoint denim blue colonies.

f. Analytical sensitivity

Recovery study

A study was conducted to evaluate the recovery of methicillin-resistant *Staphylococcus aureus* (MRSA) on Remel Spectra™ MRSA subcultured from positive blood cultures that also contain organisms that could potentially be co-present in the positive blood culture. The following organisms were evaluated: methicillin-susceptible *Staphylococcus aureus* (MSSA) and methicillin-resistant *Staphylococcus epidermidis* (MRCoNS).

Blood culture bottles were spiked with blood and various concentrations of MRSA, MSSA and MRCoNS. Post-spiking, each bottle was incubated at 35-37°C for 6 hours.

This study was designed based on the limit of detection (LoD) of 10^4 CFU/mL

determined from pilot spiking studies in various blood culture bottle types. The recovery of MRSA (at 10^4 CFU/mL) was challenged with MSSA and MRCoNS at LoD and higher concentrations of 10^6 and 10^8 CFU/mL, in order to determine the impact of interfering organism on the detection of the target.

As shown in Table 1, the results from this study indicated that Spectra™ MRSA is capable of detection of MRSA ATCC 43300 from various blood culture bottles whether MRSA was alone or mixed with a heavy inoculum of MSSA and/or MRCoNS after 6 hours of incubation. Although similar results were seen with MRSA ATCC® 43300, a heteroresistant isolate, recovery of this strain was generally low and especially on the VersaTrek REDOX 2 (anaerobic) blood culture bottle.

Overall results from this recovery study demonstrated the ability of Spectra MRSA to support growth of MRSA within the confines of a six hour incubation limit when the organism was either alone or mixed with competing Staphylococci (MSSA or MRCoNS).

Table 1: Average of MRSA recovery on Spectra MRSA plate upon subculture of each blood culture bottle incubated for 6 hours

	MRSA Strain and Agar Plate			
	ATCC 43300		ATCC 33591	
Blood Culture Medium	SPECTRA	Blood Agar	SPECTRA	Blood Agar
Bactec Plus Aerobic F	53.7	75	64.6	58
Bactec Standard/10 Aerobic/F	28	35	39.3	50
Bactec Ped Plus/F	18.3	20	79.7	80
Bactec Lytic/10 Anaerobic/F	19.6	45	12.3	19
bioMerieux BacT/ALERT FA FAN Aerobic	38	60	107.7	100
bioMerieux BacT/ALERT FN FAN Anaerobic	25	30	41.7	25
VersaTrek REDOX 1 Aerobic	14.7	18	16.7	7
VersaTrek REDOX 2 Anaerobic	3.7	10	36	47

NOTE: ATCC® 43300 inoculum control = 3 colony forming units
ATCC® 33591 inoculum control = 12 colony forming units

g. Assay cut-off:

Not applicable

2. Comparison studies:

a. Method comparison with predicate device:

The performance of Spectra™ MRSA was evaluated at four geographically diverse regions of the United States. Results from the Spectra™ MRSA at 24 hours incubation were compared to results obtained from traditional subculture on Tryptic Soy Agar with 5% Sheep Blood (Blood Agar) after 48 hours incubation. Suspect isolates of *S. aureus* were identified using a latex agglutination test or a biochemical identification system. Susceptibility testing was performed using an antibiotic gradient method for oxacillin and the Oxoid PBP2' test was used for the detection of the penicillin-binding protein 2a.

A total of six hundred twenty eight (628) positive blood cultures exhibiting gram-positive cocci on initial microscopic examination were tested. Upon evaluation of the data submitted, a total of 81 Spectra™ MRSA results obtained from subculture of the following blood culture bottles were excluded from the primary analysis for the reasons stated:

1. BACTEC Lytic/10 Anaerobic/F and Standard/10 Aerobic/F because of the inability to separate the data for each bottle type
2. BACTEC Ped Plus because none were positive for MRSA

Because of these exclusions, the total blood cultures considered for evaluation of the performance of Spectra™ MRSA at 24 hours was reduced from 628 to 547 (158 MRSA and 389 non-MRSA).

The overall recovery of MRSA on Spectra™ MRSA at 24 hours was 96.2% (152/158) compared to recovery of 100% (158/158) on Blood Agar at 48 hours. The positive and negative predictive values for Spectra™ MRSA compared to the Oxoid PBP2' test were 97.4% and 99.0% respectively as shown in Table 2. Overall Performance vs. Traditional Culture and/or Oxacillin MIC is shown in Table 3 and Overall Performance vs. PBP2 is shown in Table 4. Detailed performance is provided in Tables 5 and 6.

Table 2: Overall Performance Summary

	MRSA	**Non-MRSA**
Spectra™ MRSA vs. traditional culture*	96.2% (152/158) (95% CI = 91.9–98.6%)	100% (389/389) (95% CI = 99.2–100%)
Spectra™ MRSA vs. PBP2'	97.4% (148/152) (95% CI = 93.4–99.3%)	99.0% (391/395) (95% CI = 97.4–99.6%)
Spectra™ MRSA vs. Oxacillin MIC*	96.2% (152/158) (95% CI = 91.9–98.6%)	100% (389/389) (95% CI = 99.2–100%)

*Six strains included as MRSA with oxacillin MICs of 4-6 µg/ml that tested PBP 2a negative. Per the CLSI M100-S19 document, these types of strains should be reported as oxacillin resistant.
Note : CI = Confidence Interval

Table 3: Overall Performance vs. Traditional Culture and/or Oxacillin MIC

n=547		Traditional Culture / Oxacillin MIC	
		+	-
Spectra™ MRSA	+	152	0
	-	6	389
TOTAL		158	389

MRSA Agreement	96.2% (152/158) (95% CI = 91.9–98.6%)
Non-MRSA Agreement	100% (389/389) (95% CI = 99.2–100%)
Overall Agreement	98.9% (541/547) (95% CI = 97.6–99.6%)
Positive Predictive Value	100% (152/152) (95% CI = 98.1–100%)
Negative Predictive Value	98.5% (389/395) (95% CI = 96.7–99.4%)

Table 4: Overall Performance vs. PBP2

n=547		PBP2	
		+	-
Spectra™ MRSA	+	148	4
	-	4	391
TOTAL		152	395

MRSA Agreement	97.4% (148/152) (95% CI = 93.4–99.3%)
Non-MRSA Agreement	99.0% (391/395) (95% CI = 97.4–99.6%)
Overall Agreement	98.5% (539/547) (95% CI = 97.1–99.3%)
Positive Predictive Value	97.4% (148/152) (95% CI = 93.4–99.3%)
Negative Predictive Value	99.0% (391/395) (95% CI = 97.4–99.6%)

Table 5: Performance of Spectra™ MRSA vs. PBP2'by blood culture bottle type

Blood Culture Information	Blood Culture Bottle Type	#Spectra™ Pos MRSA/ #Total MRSA	MRSA Agreement (95% CI)	Non-MRSA Agreement (95% CI)	Positive Predictive Value (95% CI)	Negative Predictive Value (95% CI)
BacT/ALERT® (vs. PBP2)	FA (FAN® Aerobic)	38/39	97.4% (86.5 –99.9%)	100% (79/79) (95.4 –100%)	100% (92.4 –100%)	98.8% (93.2 –100%)
	FN (FAN® Anaerobic)	12/12	100% (73.5 –100%)	100% (41/41) (91.4 –100%)	100% (77.9 –100%)	100% (93.0 –100%)
	SYSTEM (Combined)	50/52	96.2% (86.8–99.5%)	100% (119/119) (96.9–100%)	100% (94.2–100%)	98.3% (94.2–99.8)
VersaTREK® (vs. PBP2)	REDOX 1® (aerobic)	42/43	97.7% (87.7 –99.9%)	97.8% (91/93) (92.4 –99.7%)	95.4% (85.4 –99.4%)	98.9% (94.1 –100%)
	REDOX 2® (anaerobic)	9/10	90.0% (55.5 –98.9%)	100% (7/7) (59.0 –100%)	100% (71.7 –100%)	87.5% (47.4 –99.7%)
	SYSTEM (Combined)	53/56	94.6% (85.1–98.9%)	100% (97/97) (96.3–100%)	100% (94.5–100%)	97.0% (91.5–99.4%)
BACTEC™ (vs. PBP2)	Plus Aerobic/F	29/30	96.7% (82.8–99.9%)	99.0% (101/102) (94.7–100%)	96.7% (82.8–99.9%)	99.0% (94.7–100%)
	Lytic/10 Anaerobic/F	18/18	100% (81.5–100%)	98.6% (72/73) (92.6–100%)	94.7% (74.0–99.9%)	100% (95.9–100%)
	Lytic/10 Anaerobic/F or Standard/10 Aerobic/F	19/19	100% (82.4–100%)	100% (54/54) (93.4–100%)	100% (85.4–100%)	100% (94.6–100%)
	PEDS PLUS™/F	0/0	N/A	100% (8/8) (63.1–100%)	N/A	100% (63.1–100%)
	SYSTEM (Combined)	68/69	98.6% (92.2–100%)	100% (235/235) (98.4–100%)	100% (95.7–100%)	99.6% (97.7–100)
	SYSTEM (with exclusions*)	47/48	97.9% (88.9–100%)	98.9% (173/175) (95.9–99.9%)	95.9% (86.0–99.5%)	99.4% (96.8–100%)

*Excludes Lytic/10 Anaerobic/F or Standard/10 Aerobic/F AND PEDS PLUS™/F

Table 6: Performance of Spectra™ MRSA vs. Traditional Culture, PBP2', or Oxacillin MIC

Blood Culture System	Blood Culture Bottle Type	#Spectra™ Pos MRSA/ #Total MRSA	MRSA Agreement (95% CI)	Non-MRSA Agreement (95% CI)	Positive Predictive Value (95% CI)	Negative Predictive Value (95% CI)
All Data	vs. Traditional Culture	171/177	96.6% (92.8–98.7%)	100% (451/451) (99.2-100%)	100% (97.9–100%)	98.7% (97.2–99.5%)
	vs. PBP2'	167/171	97.7% (94.1–99.4%)	99.1% (453/457) (97.8–99.8%)	97.7% (94.1–99.4%)	99.1% (97.8–99.8%)
	vs. Oxacillin MIC	171/177	96.6% (92.8–98.7%)	100% (451/451) (99.2-100%)	100% (97.9–100%)	98.7% (97.2–99.5%)
All (with exclusions*)	vs. Traditional Culture	152/158	96.2% (91.9–98.6%)	100% (389/389) (99.1–100%)	100% (97.6–100%)	98.5% (97.4–99.7%)
	vs. PBP2'	148/152	97.4% (93.4–99.3%)	99.0% (391/395) (97.4–99.7%)	97.4% (93.4–99.3%)	99.0% (97.4–99.7%)
	vs. Oxacillin MIC	152/158	96.2% (91.9–98.6%)	100% (389/389) (99.1–100%)	100% (97.6–100%)	98.5% (97.4–99.7%)
Aerobic Blood Culture Media*	vs. Traditional Culture	112/117	95.7% (90.3–98.6)	100% (269/269) (98.6–100%)	100% (96.8–100%)	98.2% (95.8–99.4%)
	vs. PBP2'	109/112	97.3% (92.4–99.4%)	98.9% (271/274) (96.8–99.8%)	97.3% (92.4–99.4%)	98.9% (96.8–99.8%)
	vs. Oxacillin MIC	112/117	95.7% (90.3–98.6%)	100% (269/269) (98.6–100%)	100% (96.8–100%)	98.2% (95.8–99.4%)
Anaerobic Blood Culture Media*	vs. Traditional Culture	40/41	97.6% (87.1–99.9%)	100% (120/120) (97.0–100%)	100% (91.2–100%)	99.2% (95.5–100%)
	vs. PBP2'	39/40	97.5% (86.8–99.9%)	99.2% (120/121) (95.5–100%)	97.5% (86.8–99.9%)	99.2% (95.5–100%)
	vs. Oxacillin MIC	40/41	97.6% (87.1–99.9%)	100% (120/120) (97.0–100%)	100% (91.2–100%)	99.2% (95.5–100%)

*Excludes Lytic/10 Anaerobic/F or Standard/10 Aerobic/F AND PEDS PLUS™/F

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 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.