

**510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY**

A. 510(k) Number:

K092819

B. Purpose for Submission:

To obtain substantial equivalence for a traditional 510(k) to detect *vanA* and *vanB* genes in rectal swabs and fecal specimens from patients, to screen for VRE colonization.

C. Measurand:

vanA and *vanB* genes of vancomycin-resistant *Enterococcus* (VRE)

D. Type of Test:

Remel Spectra™ VRE is a selective and differential chromogenic medium recommended for use in the qualitative detection of gastrointestinal colonization of vancomycin-resistant *Enterococcus faecium* and *Enterococcus faecalis* (VRE)

E. Applicant:

Thermo Fisher Scientific

F. Proprietary and Established Names:

Remel Spectra™ VRE Chromogenic VRE Media

G. Regulatory Information:

Product Code	Classification	Regulation Section	Panel
JSO	II	21 CFR 866.1700	83 - Microbiology

H. Intended Use:

1. Intended use:

Remel Spectra™ VRE is a selective and differential chromogenic medium, containing 6 µg/ml of vancomycin, intended for use in the qualitative detection of gastrointestinal colonization with vancomycin-resistant *Enterococcus faecium* and *Enterococcus faecalis* (VRE) to aid in the prevention and control of VRE in healthcare settings. The test is performed with rectal swab and fecal specimens from patients to screen for VRE colonization. Spectra™ VRE is not intended to diagnose VRE infection or to guide or monitor treatment for infections. Subculture to non-selective media (e.g. Tryptic Soy Agar with 5% sheep blood) is needed for further identification, susceptibility testing, and epidemiological typing.

2. Indication for use:

Remel Spectra™ VRE is a selective and differential chromogenic medium, containing 6 µg/ml of vancomycin, intended for use in the qualitative detection of gastrointestinal colonization with vancomycin-resistant *Enterococcus faecium* and *Enterococcus faecalis* (VRE) to aid in the prevention and control of VRE in healthcare settings. The test is performed with rectal swab and fecal specimens from patients to screen for VRE colonization. Spectra™ VRE is not intended to diagnose VRE infection or to guide or monitor treatment for infections. Subculture to non-selective media (e.g. Tryptic Soy Agar with 5% sheep blood) is needed for further identification, susceptibility testing, and epidemiological typing.

3. Special conditions for use statement:

For prescription use only

4. Special instrument requirements:

Not applicable

I. Device Description:

Remel Spectra™ VRE is an opaque medium allowing differentiation of vancomycin-resistant *E. faecium* from vancomycin-resistant *E. faecalis* by incorporation of two chromogens that are targeted by phosphatase and α-galactosidase. The action of these enzymes on the chromogens results in a build-up of color within the colony. The presence of phosphatase enzymes in both *E. faecium* and *E. faecalis* results in a light

blue or navy blue colony. However, *E. faecium* also produces α -galactosidase, resulting in a mix of blue and pink chromophores within the bacterium producing navy blue, or pink-purple colonies, which are distinguished from the light blue or blue *E. faecalis* colonies. Additional antibiotics, in combination with vancomycin, are present to suppress the growth of competing flora including *E. gallinarum* and *E. casseliflavus*, both of which are intrinsically resistant to vancomycin, possessing the chromosomally encoded VanC resistance mechanism.

J. Substantial Equivalence Information:

1. Predicate Device names

Remel Bile Esculin Azide Agar with 6 µg/ml Vancomycin

2. Predicate K number:

K972359

Comparison with predicate:

Device Comparison:

Characteristic	Remel Spectra™ VRE	Remel Bile Esculin Azide with Vancomycin
Similarities		
Intended Use	Remel Spectra™ VRE is a selective and differential chromogenic medium, containing 6 µg/ml of vancomycin, recommended for use in the qualitative detection of gastrointestinal colonization of vancomycin-resistant <i>Enterococcus faecium</i> and <i>Enterococcus faecalis</i> (VRE) to aid in the prevention and control of VRE in healthcare settings. The test is performed with rectal swabs and fecal specimens from patients to screen for VRE colonization. Spectra™ VRE is not intended to diagnose VRE infection or to guide or monitor treatment for infections. Subculture to non-selective media (e.g. Tryptic Soy Agar with 5% sheep blood) is needed for further identification, susceptibility testing, and epidemiological typing.	Remel Bile Esculin Azide Agar w/ 6 µg/ml Vancomycin is a solid medium recommended for use in qualitative procedures as a screening method for primary isolation and presumptive identification of vancomycin-resistant enterococci (VRE) from surveillance cultures.
Inoculation	Direct Specimen	Direct Specimen
Sample Type	Fecal specimens Rectal swabs	Fecal Specimens Urine specimens
Interpretation	Manual, visual	Manual, visual Additional confirmation required

Test Methodology	Enzymatic	Enzymatic
Incubation	24 hours	24–48 hours
Differences		
Target Enzyme	Phosphatase α -galactosidase	Esculin hydrolysis
Species Differentiation	<p>Positive – Vancomycin-resistant <i>E. faecium</i> colonization: Navy blue or purple-pink colonies.</p> <p>Positive – Vancomycin-resistant <i>E. faecalis</i> colonization: Light blue to blue colonies.</p> <p>Negative – No VRE colonization: No colored colonies.</p>	<p>Positive – Dark brown to black color around colonies and diffusing into the medium.</p> <p>Negative – No blackening of the media.</p>

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

Not Applicable

L. Test Principle:

Remel Spectra™ VRE is an opaque medium allowing differentiation of vancomycin-resistant *E. faecium* from vancomycin-resistant *E. faecalis* by incorporation of two chromogens that are targeted by phosphatase and α -galactosidase. The action of these enzymes on the chromogens results in a build-up of color within the colony. The presence of phosphatase enzymes in both *E. faecium* and *E. faecalis* results in a light blue or blue colony. However, *E. faecium* also produces α -galactosidase, resulting in a mix of blue and pink chromophores within the bacterium producing navy blue or pink-purple colonies, which are distinguished from the light blue or blue *E. faecalis* colonies. Additional antibiotics, in combination with vancomycin, are present to suppress the growth of competing flora including *E. gallinarum* and *E. casseliflavus*, both of which are intrinsically resistant to vancomycin, possessing the chromosomally encoded VanC resistance mechanism.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Reproducibility testing was conducted at four sites on three separate days with twenty blinded strains of vancomycin-sensitive enterococci and VRE. The strains produced the expected result with Spectra™ VRE 100% of the time at 24 hours.

Clinical Accuracy:

The performance of Spectra™ VRE was evaluated at three geographically diverse regions of the United States. A total of six hundred twenty three prospective rectal swabs, and fecal surveillance specimens (yielding 629 data points) were evaluated. Results from Spectra™ VRE at 24 hours incubation were compared to results obtained from traditional culture on Bile Esculin Azide Agar with 6 µg/ml Vancomycin (BEAV) after 48 hours incubation. Two hundred twenty VRE with minimal inhibitory concentration MICs to vancomycin of >256 µg/ml were recovered from six hundred twenty three specimens (191 vancomycin-resistant *E. faecium* and 29 vancomycin-resistant *E. faecalis*). The overall recovery of VRE on Spectra™ VRE at 24 hours was 99.1% (218/220) compared to recovery of 95.5% (210/220) on BEAV at 48 hours.

Suspect isolates of VRE were evaluated using Vitek® 2 system and biochemical tests, and an antibiotic gradient method for determination of vancomycin MIC. For detection of VRE by colored colonies isolated on Spectra™ VRE at 24 hours compared to identification and susceptibility testing as described, the overall agreement was 99.5% (626/629).

	VRE	Non-VRE
Spectra™ VRE vs. identification and susceptibility	99.1% (218/220) (95% CI = 89.2–98.4%)	99.8% (408/409) (95% CI = 98.0–99.7%)

Note : CI = Confidence Interval
Forty perianal swabs (eleven positive and twenty-eight negative) were tested which did not yield a statistically sound 95% lower bound confidence interval. The results are not included in the data.

Spectra™ VRE vs. Conventional Methods

	Positive % Agreement	Negative % Agreement
VR- <i>E. faecium</i>	99.0% (189/191) ^a (95% CI = 96.3–99.9%)	99.8% (437/438) ^b (95% CI = 98.7–100%)
VR- <i>E. faecalis</i>	100% (29/29) (95% CI = 88.1–100%)	100% (600/600) (95% CI = 99.4–100%)

Note : CI = Confidence Interval

^a One isolate showed expected results at 28 hours and one isolate showed expected results at 48 hours ^b One isolate developed pink colonies and was identified as *Lactobacillus* sp

Challenge Studies

Spectra™ VRE was evaluated with fifty well-characterized strains of enterococci (vancomycin susceptible and resistant enterococci) from the Centers for Disease Control and Prevention. Three strains of *E. faecium* with vancomycin MICs between 128-1024 µg/ml failed to grow at 24 hours. One strain of *E. faecium* with a vancomycin MIC of 16 µg/ml grew and produced pink-purple colonies.

b. *Linearity/assay reportable range:*

Not Applicable

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

All lot numbers of Spectra™ VRE have been tested using the following quality control organisms and have been found to be acceptable. Quality control requirements must be performed in accordance with applicable local, state, and/or federal regulations or accreditation requirements and the laboratory's quality control procedures. If aberrant quality control results are noted, patient results are not to be reported.

CONTROL	INCUBATION	RESULTS
<i>Enterococcus faecalis</i> ATCC® 51299	Aerobic, 24 h @ 33-37°C	Light blue colonies
<i>Enterococcus faecium</i> ATCC® 51559	Aerobic, 24 h @ 33-37°C	Pink-purple colonies
<i>Enterococcus faecalis</i> ATCC® 29212	Aerobic, 24 h @ 33-37°C	No growth

d. *Detection limit:*

Not Applicable

e. *Analytical specificity:*

Cross Reactivity Study

Two hundred twenty-nine (229) microorganisms representing gram-negative rods, yeast, streptococci, enterococci, staphylococci, and related organisms were evaluated with Spectra™ VRE. Six of eleven KPC-producing *Klebsiella pneumoniae* developed large blue colonies on Spectra™ VRE at 24 hours. No other cross reactivity was observed following 24 hours incubation.

The study results are reflected in the Limitation and Cross Reactivity sections of the device package insert.

Interference Study

The following substances were evaluated for potential interference of the chromogenic reaction of Spectra™ VRE. These substances were tested in combination with vancomycin-resistant *E. faecalis* and *E. faecium* isolates at a concentration of 50 CFU: blood, mucous, MYLANTA® Maximum Strength, Pepto-Bismol®, Imodium® A-D, Kaopectate®, Fletcher's Castoria®, PEPCID® AC Maximum Strength, Tagamet HB 200®, Prilosec OTC®, vancomycin, metronidazole, barium sulfate, Preparation H®, petroleum jelly, glycerin, bisacodyl, witch hazel, miconazole, nonoxynol-9, KY® Jelly. Hydrocortisone acetate was not evaluated. Blood, Pepto-Bismol®, glycerin, vancomycin, miconazole, and Preparation H® may reduce the recovery of vancomycin resistant *E. faecalis* and *E. faecium* strains.

2. Comparison studies:

a. *Method comparison with predicate device:*

Spectra™ VRE was compared to culture on Bile Esculin Azide with 6 µg/ml Vancomycin, with subsequent identification and susceptibility testing. There was 82.7% (520/629) agreement with six hundred twenty-nine isolates. The Bile Esculin Azide with 6µg/ml Vancomycin demonstrated 95.5% (210/220) agreement for the recovery of VRE (acquired resistance) and 75.8% (310/409) agreement for non-VRE.

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:

Information collected by the Centers for Disease Control and Prevention during 2006 and 2007 showed that enterococci caused about 1 of every 8 infections in hospitals, with roughly 30% of isolates resistant to vancomycin (i.e. VRE). VRE are the third leading cause of hospital-acquired infection. Hospital-acquired enterococcal infections typically occur in very ill or debilitated patients who have been exposed to broad-spectrum antibiotics. They are also the third most common cause of hospital-acquired bloodstream infections in the U.S. The overall prevalence rate of VRE colonization in this study was 35%.

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.