

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

A. 510(k) Number:

K051202

B. Purpose for Submission:

Use of a revised vancomycin formulation in the Dried Gram-Positive MIC/Combo panels for the removal of a limitation on testing of *Staphylococcus aureus* by improving the detection of vancomycin-resistant *S. aureus* (VRSA)

C. Measurand:

Vancomycin at 0.25 to 128 µg/mL

D. Type of Test:

Quantitative and Qualitative growth based detection algorithm using optics light detection

E. Applicant:

Dade Behring Inc,
MicroScan®

F. Proprietary and Established Names:

MicroScan® Dried Gram-Positive MIC/Combo Panels

G. Regulatory Information:

1. Regulation section:

866.1640 Antimicrobial Susceptibility Test Powder

2. Classification:

Class II

3. Product code:

LRG-Instrument for Auto Reader & Interpretation of Overnight Antimicrobial Susceptibility Systems

JWY - Manual Antimicrobial Susceptibility Test Systems
LTT – Panels, Test, Susceptibility, Antimicrobial
LTW – Susceptibility Test Cards, Antimicrobial

4. Panel:
83 Microbiology

H. Intended Use:

1. Intended use(s):
For use with MicroScan® Dried Gram Positive MIC/Combo, Dried Gram Positive Breakpoint Combo and Dried Gram Positive ID Type 2 panels. MicroScan® Positive panels are designed for use in determining antimicrobial agent susceptibility and/or identification to the species level of rapidly growing aerobic and facultatively gram-positive cocci, some fastidious aerobic gram positive cocci and *Listeria monocytogenes*. Refer to Limitation of Procedure Section for use with fastidious streptococci.
2. Indication(s) for use:

The MicroScan® Dried Gram-Positive MIC/Combo Panel is used to determine quantitative and/or qualitative antimicrobial agent susceptibility of colonies grown on solid media of rapidly growing aerobic and facultative anaerobic gram positive cocci. This indication is for the addition of the antimicrobial vancomycin at concentrations of 0.25-128 µg/mL to the test panel.
3. Special conditions for use statement(s):
The Prompt® method of inoculation is an alternate method of inoculation preparation that is supported in the methodology along with the turbidity method. The stationary and log inoculum methods should not be used with this antibiotic.
4. Special instrument requirements:

These panels can be read at ≥ 16 hours of incubation either manually, automatically on the autoSCAN® 4, or with the WalkAway® instrument systems but for best detection of VRSA readings should be performed after 18 hours especially for the autoSCAN® 4 instrument read results.

I. Device Description:

The MicroScan® Dried Gram-Positive MIC/Combo Panel contains microdilutions of each antimicrobial agent in various concentrations with Mueller Hinton Broth and various nutrients which are dehydrated and dried in panels. Each panel contains two control wells: a no-growth control well (contains water only/no nutrients or broth), and a growth control well (contains test medium without antibiotic). The panel is rehydrated and inoculated at the same time with 0.1 ml of suspension prepared by the

turbidity method (inoculum prepared in water, then 0.1ml transferred to 25ml of inoculum water containing pluronic-D/F-a wetting solution) for a final inoculum concentration of $3-7 \times 10^5$ CFU/ml. The Prompt® method of inoculation is also recommended as an alternate means of preparing the inoculum. The panels are incubated at 35° C in a non-CO₂ for 16-24 hours and read by visual observation of growth. Panels may also be read automatically with the WalkAway® or the AutoSCAN®4.

J. Substantial Equivalence Information:

1. Predicate device name(s):

MicroScan® Dried Gram-Positive and Gram-Negative MIC/Combo Panels

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

k862140

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	See above	Same
Inoculum preparation	Inoculum prepared from isolated colonies using either the Turbidity method or Prompt® system	Same
Technology	Growth based after 16 hours incubation	Same
Results	Report results as minimum inhibitory concentration (MIC) and categorical interpretation (SIR)	Same
Instrument	autoSCAN® -4 or WalkAway®	Same
Differences		
Item	Device	Predicate
Antibiotic	Vancomycin	Different concentrations depending on the antibiotic
Test organism	Enterococcus, Staphylococcus and some Streptococcus	Varies according to the antibiotic
Limitations	Staphylococcus must read at ≥ 18 hour of incubation on the autoSCAN® 4	None

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

Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA”; Clinical and Laboratory Standards Institute (CLSI) M7 (M100-S15) “Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard”.

L. Test Principle:

After incubation in a non-CO₂ incubator for 16-24 hours, the minimum inhibitory concentration (MIC) for the test organisms are read by determining the lowest antimicrobial concentration showing inhibition of growth. The panels are read either manually using a touchSCAN® SR, or with the autoSCAN® 4 or the WalkAway® instrument, which uses an optics systems with growth algorithms to directly measure organism growth.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Reproducibility was demonstrated using 5 isolates tested at 2 sites and included the three VRSA and two QC strains. Three reading methods and two inoculation methods were tested at one site and the other site tested in replicates of three with each inoculation method using the manual reading method only. The QC strains were additionally tested at 5 sites using all methods. The following table provides the overall results for all combinations of these variables. This represents the reproducibility of each method based on the mode of that method and not the expected value.

Difference in the number of dilutions between the mode of the MicroScan® result and the actual result with each different variable						
Inoculation method	Read method	≥ Minus 2 dilutions	Minus 1 dilution	Exact	Plus 1 dilution	≥ Plus 2 dilutions
Turbidity	Manual(touchSCAN®)		8	160	28	2
Turbidity	WalkAway ®		11	158	17	
Turbidity	autoSCAN®4		30	150	9	1
Prompt®	Manual(touchSCAN®)	1	38	150		3
Prompt®	WalkAway ®		44	146		3
Prompt®	autoSCAN® 4		46	144		

b. *Linearity/assay reportable range:*

Not Applicable

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

Quality Control was performed daily with the turbidity method and with the Prompt® with the following results.

Organism	Conc. In µg/mL	Reference result	Turbidity inoculation with Read methods			Prompt® inoculation with Read methods		
			Manual	Walk- Away®	Auto- SCAN®	Manual	Walk- Away®	Auto- SCAN®
<i>E. faecalis</i> ATCC 29212 Expected range 1-4 µg/mL	≤ 0.25							
	0.5							
	1					1		
	2	95	8	11	30	13	15	15
	4	1	87	78	62	78	77	75
<i>S. aureus</i> ATCC 29213 Expected range 0.5-2 µg/mL	≤ 0.25							
	0.5	1						
	1	89	67	75	82	25	29	31
	2	7	27	16	9	66	63	63
	4				1			
	8							
	≥ 128			1				

Quality control results demonstrated the ability of all variables of the procedure (reading and inoculation) to produce acceptable results. There does appear to be slight trending in all of the methods for both QC strains to appear one dilution more resistant than the reference method result but still in the expected range an acceptable number of times. This is even more apparent with the Prompt® method of inoculation and the *S. aureus* QC strain.

Inoculum density control: A turbidity meter was used for the turbidity inoculation method. The Prompt® method of inoculation had colony counts performed periodically throughout the study to determine the average inoculum density since there is no visual check of the inoculum using this device. QC strains were also included in the colony count study. The inoculum with the Prompt® method of inoculation generally provides a higher number of CFU with more variability than a method using turbidity meter although the *S. aureus* did have more variability even in the turbidity method but the average was still in the acceptable range for the turbidity method but not for the Prompt®. There are limitations for the use of the Prompt® and certain antibiotics that are more sensitive to inoculum concentration and those are stated in the package insert. Vancomycin will require no such statement. The chart below shows the CFU study results.

Organism	Number tested and method of inoculation	Average CFU X 10 ⁵	Minimum CFU X 10 ⁵	Maximum CFU X 10 ⁵
<i>S. aureus</i>	51 Prompt®	15	2.7	54
<i>S. aureus</i> ATCC 29213	36 Prompt®	15.5	0.56	50
<i>S. aureus</i> ATCC 29213	18 Prompt®	18	2.3	30
<i>S. aureus</i> ATCC 29213	31 Turbidity	3.8	0.8	54
<i>E. faecalis</i> ATCC 29212	32 Prompt®	4.8	0.5	12
<i>E. faecalis</i> ATCC 29212	14 Prompt®	4.47	3	6.8
<i>E. faecalis</i> ATCC 29212	41 Turbidity	1.85	0.37	4

d. *Detection limit:*

Not Applicable

e. *Analytical specificity:*

Not Applicable

f. *Assay cut-off:*

Not Applicable

2. Comparison studies:

a. *Method comparison with predicate device:*

The study was conducted at 5 sites. One hundred seventy two clinical isolates were tested and 106 challenge isolates. Challenge set includes the CDC Enterococci challenge set which includes 11 Van A, 19 Van B, 5 Van C1 and 5 Van C2. Also included were 53 Staphylococci from the Network on Antimicrobial Resistance in *Staphylococcus aureus* (NARSA) which have interpretations near the intermediate breakpoint. This set also included the three known VRSA strains tested at MicroScan®. The results were compared to the reference expected results. The following table demonstrates the performance based on essential agreement and category agreement for the overall performance of the clinical isolates and the challenge with the turbidity method of inoculation and manual readings. Similar calculations for the different inoculation and reading methods were performed with very little difference.

	total	EA	%EA	Total evaluable	EA of evaluable	%EA	CA	%CA	#R	min	maj	vmj
Clinical	172	172	100	161	161	100	172	100	10	0	0	0
Challenge	106	104	98.1	95	93	97.9	101	95.3	28	5	0	0
Combined	278	276	99.3	256	254	99.2	273	98.2	38	5	0	0

EA-Essential Agreement

maj-major discrepancies

CA-Category Agreement
R-resistant isolates

vmj-very major discrepancies
min- minor discrepancies

Evaluable results are those that fall within the test range of the reference method and could also be on-scale with the new device if within the plus/minus one dilution variability. EA is when there is agreement between the reference method and the MicroScan® within plus or minus one serial two-fold dilution of antibiotic. CA is when the interpretation of the reference method agrees exactly with the interpretation of the MicroScan® result.

The table below demonstrates the clinical and challenge results that were in exact agreement with the reference method result and those that differed by one or more dilutions.

Difference in the number of dilutions between the reference result and the MicroScan® Result						
Inoculation method	Read method	≤ minus 2 dilutions	minus 1 dilution	Exact	Plus 1 dilution	≥ Plus 2 dilutions
Turbidity	Manual	1	24	201	51	1
Turbidity	WalkAway ®	0	11	210	56	1
Turbidity	autoSCAN® 4	0	25	217	36	0
Prompt®	Manual	0	23	136	110	6
Prompt®	WalkAway ®	0	11	146	112	6
Prompt®	autoSCAN® 4	2	21	154	95	3

There appears to be a slight trend of the MicroScan® to be more resistant than the reference method (more values in the plus category). This is even more exaggerated using the Prompt® method of inoculation but still in EA at >95% with all read methods. This trend to slightly more resistant results for the Prompt® method of inoculation is consistent with the reproducibility data and also the higher CFU/ml in the Prompt® inoculum.

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:

Staphylococcus spp. and Enterococcus spp. interpretive criteria:

$\leq 4 \mu\text{g/mL (S)}$, $8\text{-}16 \mu\text{g/mL (I)}$, $\geq 32 \mu\text{g/mL (R)}$

Streptococcus other than *S. pneumoniae* interpretive criteria

$\leq 1 \text{ (S)}$

The interpretative criteria and Quality Control Ranges are the same as recommended in the FDA approved pharmaceutical package insert and the CLSI. All values are included in the package insert.

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.