

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

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

K060312

**B. Purpose for Submission:**

For addition of vancomycin on the MicroScan® Synergies plus™ Gram-Positive for testing appropriate *Staphylococcus* and *Enterococcus* spp

**C. Measurand:**

Vancomycin 0.25 – 64 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® Synergies plus™ Gram-Positive MIC/Combo Panels

**G. Regulatory Information:**

1. Regulation section:

866.1645 - Fully automated short-term incubation cycle antimicrobial susceptibility system  
866.1640 - Antimicrobial Susceptibility Test Powder

2. Classification:

Class II

3. Product code:

LON – Automated AST system short incubation  
LRG-Instrument for Auto Reader & Interpretation of Overnight Antimicrobial Susceptibility Systems  
JWY - Manual Antimicrobial Susceptibility Test Systems  
LTT – Panels, Test, Susceptibility, Antimicrobial

4. Panel:

83 Microbiology

**H. Intended Use:**

1. Intended use(s):

Vancomycin at concentrations of 0.25 to 64 µg/mL on the MicroScan® Synergies plus™ Gram-Positive MIC/Combo Panel is intended for use with MicroScan® Synergies plus™ Panels read on the WalkAway® -SI System (including upgraded WalkAway® -40 or WalkAway® -96 to meet WalkAway® SI equivalence).

MicroScan® panels are designed for use in testing colonies, grown on solid media, of rapidly growing aerobic and facultative anaerobic gram-positive cocci; the panels also provide quantitative and/or qualitative antimicrobial agent susceptibility for staphylococci and enterococci.

2. Indication(s) for use:

The addition of vancomycin at concentrations of 0.25 to 64 µg/mL to the gram-positive test panel for testing *Staphylococcus* and *Enterococcus* spp. at < 16 hours or >16 hours for an overnight reading.

3. Special conditions for use statement(s):

- *S. aureus* isolates with MICs of 8 – 16 µg/mL on MicroScan® Synergies plus™ Gram-Positive MIC/Combo Panels will be incubated for 16-18 hours for overnight instrument or visual reporting of vancomycin.
- MicroScan® Synergies plus™ Gram-Positive MIC/Combo Panel detects vancomycin resistance in the VRSA *S. aureus* strains available at the time of comparative testing. The ability of the MicroScan® Synergies plus™ Gram-Positive MIC/Combo Panel to detect resistance in other *S. aureus* strains is unknown due to the limited number of resistant strains available for comparative testing.
- Turbidity method of inoculum preparation only.
- For prescription use only.

4. Special instrument requirements:

Not Applicable

**I. Device Description:**

Each panel contains two control wells: a negative control well, and a growth control well (contains test medium without antibiotic). Antibiotics are diluted in water, buffer, or minute concentrations of broth to selected concentrations prior to dehydration of the panels. The panel is rehydrated and inoculated at the same time with 0.1 ml of suspension prepared by the turbidity method (inoculum prepared in 0.4% saline with PLURONIC®, then 0.1ml transferred to 25ml of inoculum Synergies plus Pos Broth with PLURONIC®) for a final inoculum concentration of 3-7 X 10<sup>5</sup> CFU/ml. Panels are incubated in a Walk-Away® System and read periodically starting at 4.5 hours until sufficient growth to determine the MIC. Alternately the panels may be incubated at 35° C in a non-CO<sub>2</sub> for 16-24 hours and

read by visual observation of growth.

**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  
k020185
3. Comparison with predicate:

<b>Similarities</b>		
<b>Item</b>	<b>Device</b>	<b>Predicate</b>
Intended use	MicroScan® panels are designed for use in determining quantitative and/or qualitative antimicrobial agent susceptibility of colonies, grown on solid media, of rapidly growing aerobic and facultative anaerobic organisms	Same
Specimen	Isolated colonies from culture used	Same
Inoculum	Inoculum density to 0.5 McFarland standard	Same
Incubation	<16 hours >16 hours	Same
Results	Quantitative with qualitative interpretations	Same
Technology	Growth based	Same
<b>Differences</b>		
<b>Item</b>	<b>Device</b>	<b>Predicate</b>
Panels	Dried vancomycin in water	Dried clindamycin or gentamicin in broth
Reading	Uses both an early read and overnight methods in the same system	Overnight system uses only the overnight reading methods and <16 hour instruments use only the <16 hour read methods.
Inoculum preparation	Turbidity method of inoculation only.	Inoculum prepared from isolated colonies using either the Turbidity method or Prompt® system
Instrument	WalkAway® -SI System or	autoScan® -4 or

	equivalent	WalkAway®
Antibiotic	Vancomycin 0.25 – 64 µg/mL	Different concentrations depending on the antibiotic

**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-S16) “Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard”.

**L. Test Principle:**

The WalkAway® SI uses a Colorimetric Optics System consisting of a color wheel/lamp assembly and a Photosensor. There is an initial read at 2.5 hours with a possible final read at 4.5, 5.5, 6.5, 8, 12, 16, or 18 hours (overnight instrument readings, manual readings) depending on the growth rate of the organism being tested. The time of final read is dependent on the growth rate of the organism and the sensitivity of the automatic reader since cell densities below  $2 \times 10^7$  cells/ml are not detected.

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

1. Analytical performance:

a. *Precision/Reproducibility:*

Reproducibility was demonstrated using 10 isolates tested at 3 sites on 3 separate days in triplicate. The study included the testing on the WalkAway® SI read at <16 hours, WalkAway® >16 hour readings and manual readings at >16 hour incubation. All results were >95% reproducible.

b. *Linearity/assay reportable range:*

Not Applicable

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

The recommended QC isolates, *S. aureus* ATCC 29213 and *E. faecalis* ATCC 29212 were tested a sufficient number of times with acceptable results on all testing days with the reference method. The *E. faecalis* ATCC 29212 isolates grew in the range of 6.5 – 24 hours read times while all QC results of *S. aureus* ATCC 29213 grew in the 4.5-16 hour window on the Synergies Plus. Quality control results demonstrated the ability of the different reading parameters (manual and instrument) to produce acceptable results.

The following table provides the frequency of the results in each concentration with the expected range stated.

Organism	Conc in $\mu\text{g/mL}$	# reference	Results		
			MicroScan®		
			>16 Hour Manual overnight	>16 Hour Instrument overnight	<16 Hour
<i>S. aureus</i> ATCC 29213 Expected Range: 0.25 – 1 $\mu\text{g/mL}$	0.5	30			
	1	53	79	82	84
	2	1	5	2	
<i>E. faecalis</i> ATCC 29212 Expected Range: 1 – 4 $\mu\text{g/mL}$	2	84	47	60	60
	4		37	24	24

Inoculum density control: A turbidity meter was used for the turbidity inoculation method.

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:*

Clinical testing was conducted at 3 sites using fresh isolates supplemented with stock isolates. A total of 549 gram positive *Enterococci* and *Staphylococci* were tested of which 476 were fresh isolates and 73 were stock isolates. There were 78 challenge isolates tested which included the 3 VRSA (Vancomycin Resistant *S. aureus*). All challenge isolates were tested at one site with the exception of the 3 VRSA (Vancomycin Resistant *S. aureus*) which were tested at a different site. These challenge isolates were compared to the reference broth dilution result mode that was determined by previous testing of each isolate multiple times in the recommended reference panel. The Synergies plus™ readings were obtained between 4.5 and 16 hours of incubation for > 90% of the results. An additional comparison was done with

readings on the instrument after overnight incubation and also read manually when incubated >16 hours. Performance by these alternate reading methods was also acceptable. The recommended CLSI reference method was followed with the exception of the use of a small amount (0.1%) PLURONIC® in the final inoculum. A validation of the use of PLURONIC® in the frozen reference panels was conducted. Similar calculations for the different reading methods were performed with very little difference. The test device had a no growth rate of <10%.

The charts below demonstrated the performance of all three reading methods (Synergies plus™ readings at <16 hours, > 16 hours on the WalkAway® and manually read at >16 hours using the touchScan®-SR) with the long dilution sequence when compared to the reference method.

**Performance Summary of the <16 Hour Read Method**

	Total	EA	%EA	Total eval	EA of eval	%EA	CA	%CA	#R	min	maj	vmj
<b>Efficacy</b>	507	497	98.0	443	435	98.2	501	98.8	59	2	4	0
<b>Challenge</b>	72	68	94.4	59	56	94.9	68	94.4	15	3	1	0
<b>Combined</b>	579	565	97.6	502	491	97.8	569	98.3	74	5	5	0

**Performance Summary of the >16 Hour Instrument Read**

	Total	EA	%EA	Total eval	EA of eval	%EA	CA	%CA	#R	min	maj	vmj
<b>Efficacy</b>	549	540	98.4	486	478	98.4	546	99.5	61	1	2	0
<b>Challenge</b>	78	73	93.6	65	61	93.8	74	94.9	15	3	1	0
<b>Combined</b>	627	613	97.8	551	539	97.8	620	98.9	76	4	3	0

**Performance Summary of the >16 Hour Manual Read**

	Total	EA	%EA	Total eval	EA of eval	%EA	CA	%CA	#R	min	maj	vmj
<b>Efficacy</b>	549	543	98.9	486	481	99.0	547	99.6	61	1	1	0
<b>Challenge</b>	78	73	93.6	65	61	93.8	73	93.6	15	4	1	0
<b>Combined</b>	627	616	98.2	551	542	98.4	620	98.9	76	5	2	0

**EA**-Essential Agreement  
**CA**-Category Agreement  
**R**-resistant isolates

**maj**-major discrepancies  
**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 <16 Hour Read Method had 42 isolates that did not grow in 16 hours

for a no growth rate of 7.7% (48/627) but provided results at >16 hour. There appears to be a slight trend where the test device is more resistant than the reference device as reflected in the number of major errors for each read method. This observation was also noted in the QC organisms where results are at the higher end of the expected range.

- 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.* ≤4 (S), 8 – 16 (I), ≥32 (R)  
*Enterococcus spp.* ≤4 (S), 8 – 16 (I), ≥32 (R)
  - S. aureus* comment only:
    - *S. aureus* isolates with vancomycin MICs ≥4 µg/mL should alert the user that additional testing is advised and the isolate with confirmed, or potential, vancomycin resistance should be reported immediately through state and local health departments to the CDC

#### **N. Proposed Labeling:**

The interpretative criteria are the same as recommended by the FDA. All values are included in the package insert.

#### **O. Conclusion:**

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.