

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

A. 510(k) Number:

K091264

B. Purpose for Submission:

Device Modification – re-evaluation K051202 performance data using the new FDA approved breakpoint interpretive criteria for Vancomycin ($S \leq 2$, $I = 4 - 8$, $R \geq 16$) used in conjunction with *S.aureus*.

C. Measurand:

Vancomycin 0.25 -128 µg/ml

D. Type of Test:

Qualitative and quantitative growth based detection algorithm using optics light detection.

E. Applicant:

Siemens Healthcare Diagnostics

F. Proprietary and Established Names:

MicroScan® Dried Gram-Positive MIC/Combo Panels with Vancomycin (0.25 – 128 µg/ml)

G. Regulatory Information:

1. Regulation section:

21 CFR 866.1640 Antimicrobial Susceptibility Test Powder

2. Classification: II

3. Product codes:

JWY – Manual Antimicrobial Susceptibility Test Systems

LRG – Instrument for Auto Reader and Interpretation of Overnight Susceptibility Systems.

LTW – Susceptibility Test Cards, Antimicrobial

LTT – Panels, Test, Susceptibility 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 facultative gram-positive cocci and *Listeria monocytogenes*. Refer to *Limitations of Procedures* section of the package insert 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. After inoculation, panels are incubated for 16-24 hours at 35°C +/- 1°C in a non-CO2 incubator, and read either visually or with MicroScan instrumentation, according to the package insert.

This particular submission is for the evaluation of antimicrobial agent Vancomycin on the MicroScan Dried Gram-Positive MIC/Combo Panels utilizing the updated *Staphylococcus aureus* interpretative criteria ($S \leq 2$, $I = 4-8$, $R \geq 16$).

The gram positive organisms which may be used for Vancomycin susceptibility testing in this panel are:

Enterococcus spp. (e.g., *Enterococcus faecalis*)
Staphylococcus spp. (including *Staphylococcus aureus*)
Staphylococcus epidermidis (including methicillin-resistant strains)
Streptococcus agalactiae
Streptococcus bovis

3. Special conditions for use statement(s):

For prescription use only.

The Prompt™ method of inoculation is an alternate method of inoculum 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 system. For best detection of VRSA, vancomycin results with staphylococci should be read/interpreted after 18 hours, especially when using the autoSCAN® 4 instrument to 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 (i.e., inoculum prepared in water, then 0.1ml transferred to 25 ml 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 environment, for 16-24 hours. The panels are then read by visual observation of growth. Panels may also be read automatically with the autoSCAN® or the WalkAway® instruments.

J. Substantial Equivalence Information:

1. Predicate device name(s):

MicroScan® Dried Gram-Positive MIC/Combo Panels – Vancomycin

2. Predicate K number(s):

K051202

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
1. Product Name	MicroScan® Dried Gram-Positive MIC/Combo Panels – Vancomycin	MicroScan® Dried Gram-Positive MIC/Combo Panels – Vancomycin (K051202)
1. Intended Use	See Item H.1	Same
2. Technology	Microdilution MIC Susceptibility test; growth based result interpretation after 16 hours of incubation	Same
3. Result Reported	Report results as minimum inhibitory concentration (MIC) and categorical interpretation (SIR)	Same
4. Antibiotic	Vancomycin 0.25-128 µg/ml	Same
5. Read Methods	Manual and Automated	Same
6. Inoculation Methods	Turbidity and Prompt™	Same
7. Instruments	autoSCAN® 4 or WalkAway®	Same

Differences		
Item	Device	Predicate
1. MIC Interpretive Breakpoints	$S \leq 2$, $I = 4-8$, $R \geq 16$	$S \leq 4$, $I = 8-16$, $R \geq 32$

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

Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test Systems; Guidance for Industry and FDA;

CLSI M7 (M100-S19) Performance Standards for Antimicrobial Susceptibility Testing; Nineteenth Informational Supplement

L. Test Principle:

After incubation in a non-CO₂ incubator for 16-24 hours, the minimum inhibitory concentration (MIC) for the test organism is read by determining the lowest antimicrobial concentration showing inhibition of growth. The panels are read either manually using a touchSCAN® SR, or using either the WalkAway® or autoSCAN® instruments. The WalkAway® and autoSCAN® instruments both use an optics system in conjunction with growth algorithms to directly measure organism growth.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

The scope of this particular submission is the evaluation of the antimicrobial agent vancomycin on the MicroScan Dried Gram-Positive MIC/Combo Panels utilizing the new, FDA approved, vancomycin breakpoint interpretative criteria ($S \leq 2$, $I = 4-8$, $R \geq 16$) for *Staphylococcus aureus*. Efficacy studies of both clinical and challenge isolates from the original 510(k), K051202, were re-evaluated using the new breakpoint interpretative criteria in order to assess device performance. No new clinical or analytical studies were conducted in support of this submission.

The reproducibility studies of the original 510(k) submission for the device, for all methods, was found to be >95% reproducible.

b. *Linearity/assay reportable range:*

Not applicable

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

The FDA and CLSI recommends the testing of Quality Control (QC) isolate, *S.aureus* ATCC 29213 to monitor and ensure the accuracy, precision and integrity of the supplies, reagents and drug used in the assay system, as well as the techniques of the individuals performing the test.

The quality control results of the original 510(k), K051202, are listed in the table to follow. All results were read at 18 and 24 hours. The Prompt™ inoculation method in conjunction with the 24 hour readings for the *S. aureus* ATCC 29213, fall out-of-range on the high end, on several occasions. There was a recommendation made at that time that QC be read at 16-20 hours. This was mentioned as one reason why MicroScan® does not want to have all isolates read at 24 hours.

This 510(k) submission is for the evaluation of the antimicrobial agent vancomycin on the MicroScan Dried Gram-Positive MIC/Combo Panels using the new, FDA approved, vancomycin breakpoint interpretative criteria ($S \leq 2$, $I = 4-8$, $R \geq 16$) for *Staphylococcus aureus*. The expected range of *S. aureus* ATCC 29213 when tested in conjunction with vancomycin has not changed, therefore, a re-evaluation of the quality control data would provide no new information and is therefore not needed.

QC Table – Vancomycin (Data from original 510(k) Submission - K051202)

ORGANISM	conc. (µg/ml)	Ref. Result	Turbidity Inoculation with Read Methods						Prompt™ Inoculation with Read Methods					
			Manual		Walk Away®		auto SCAN®		Manual		Walk Away®		auto SCAN®	
			18 hr	24 hr	18 hr	24 hr	18 hr	24 hr	18 hr	24 hr	18 hr	24 hr	18 hr	24 hr
<i>S. aureus</i> ATCC 29213 Expected Range: 0.5 – 2 µg/ml	≤0.25													
	0.5	1												
	1	89	67	45	75	47	82	52	25	15	29	15	31	17
	2	7	27	49	16	45	9	40	66	71	63	73	63	26
	4						1			6		5		2
	8													

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:*

This 510(k) application was submitted for the evaluation of vancomycin on the MicroScan Dried Gram Positive MIC/Combo Panel using the new FDA approved breakpoint interpretive criteria ($S \leq 2$, $I = 4-8$, $R \geq 16$).

Performance data specific for the isolates of *S.aureus* from the original 510(k) submission, K051202, have been re-evaluated using the new interpretive criteria.

A total of 51 clinical isolates and 43 challenge isolates of *S.aureus*, representing MRSA, MSSA, and VRSA were re-evaluated. The results were compared to the reference method or expected results.

Table A below demonstrates the performance based on essential agreement and category agreement for the overall performance of the clinical and challenge isolates in combination with the turbidity method of inoculation and manual readings. Similar calculations for the different inoculation and reading methods were performed and show very little difference. These data are included in Tables B – F.

Table A. Turbidity/ Manual	Tot	EA N	%EA Total	Total Eval	EA Eval	%EA Eval	CA N	%CA	#R	min	maj	vmj
Clinical	51	51	100	51	51	100	51	100	0	0	0	0
Challenge	43	43	100	42	42	100	37	86	3	6	0	0
Combined	94	94	100	93	93	100	88	93.6	3	6	0	0

Table B. Turbidity/ autoSCAN®	Tot	EA Total	%EA Total	Total Eval	EA Eval	%EA Eval	CA Total	%CA	#R	min	maj	vmj
Clinical	51	51	100	51	51	100	51	100	0	0	0	0
Challenge	43	42	97.7	42	41	97.6	38	88.4	3	5	0	0
Combined	94	93	98.9	93	92	98.9	89	94.7	3	5	0	0

Table C. Turbidity/ WalkAway®	Tot	EA Total	%EA Total	Total Eval	EA Eval	%EA Eval	CA Total	%CA	#R	min	maj	vmj
Clinical	51	51	100	51	51	100	51	100	0	0	0	0
Challenge	43	43	100	42	42	100	37	86	3	6	0	0
Combined	94	94	100	93	93	100	88	93.6	3	6	0	0

Table D. Prompt™/ Manual	Tot	EA Total	%EA Total	Total Eval	EA Eval	%EA Eval	CA Total	%CA	#R	min	maj	vmj
Clinical	51	50	98	51	50	98	51	100	0	0	0	0
Challenge	41	39	95.1	40	38	95	33	80.5	3	8	0	0
Combined	92	89	96.7	91	88	96.7	84	91.3	3	8	0	0

Table E. Prompt™/ autoSCAN®	Tot	EA Total	%EA Total	Total Eval	EA Eval	%EA Eval	CA Total	%CA	#R	min	maj	vmj
Clinical	51	50	98	51	50	98	51	100	0	0	0	0
Challenge	41	41	100	40	40	100	33	80.5	3	8	0	0
Combined	92	91	98.9	91	90	98.9	84	91.3	3	8	0	0

Table F. Prompt™/ WalkAway®	Tot	EA Total	%EA Total	Total Eval	EA Eval	%EA Eval	CA Total	%CA	#R	min	maj	vmj
Clinical	51	50	98	51	50	98	51	100	0	0	0	0
Challenge	41	39	95.1	40	38	95	33	80.5	3	8	0	0
Combined	92	89	96.7	91	88	96.7	84	91.3	3	8	0	0

EA = Essential Agreement

R = Resistant Isolates

maj = major discrepancies

CA = Category Agreement

min = minor discrepancies

vmj = very major 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 plus/minus one dilution. Essential Agreement (EA) occurs when there is agreement between the result of the reference method and that of MicroScan® within plus or minus one serial two-fold dilution of the antibiotic. Category Agreement (CA) occurs when the interpretation of the result of the reference method agrees *exactly* with the interpretation of the MicroScan® result.

Specifically related to the data of the challenge isolates tested, the percent Category Agreement (CA) falls consistently below the acceptance criteria of greater than or equal to 90%, as outlined in the *Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems Guidance*. This is due to the low number of challenge isolates tested in conjunction with the occurrence of a number of minor discrepancies, due to the change in the breakpoint interpretive criteria. In each instance (with only one exception), the minor discrepancy fell within Essential Agreement (EA) of the reference method result. In each instance, if the minor discrepancies that fall within Essential Agreement are removed, the percent Category Agreement of the challenge data would fall well within the acceptance criteria of greater than or equal to 90%.

The overall combined %EA and %CA consistently meet the acceptance criteria of greater than or equal to 90%.

The (3) tables below illustrate the clinical and challenge results that were in exact agreement with the reference method result and those that differed by one or more dilutions.

Table 1. *S. aureus* (MRSA) – Clinical (n=23) and Challenge (n=34/32) Results

Difference in the Number of Dilutions between the Reference Result and the MicroScan® Result – <i>S.aureus</i> (MRSA) with Vancomycin						
Inoculation Method	Read Method	≥ Minus 2 Dilutions	Minus 1 Dilution	Exact Agreement	Plus 1 Dilution	≥ Plus 2 Dilutions
Turbidity	Manual		2	49	6	
Turbidity	autoSCAN® 4	1	3	49	4	
Turbidity	WalkAway®		2	47	7	
Prompt	Manual			25	30	
Prompt	autoSCAN® 4		1	27	27	
Prompt	WalkAway®		1	23	31	
TOTAL		1	9	220	105	

Table 2. *S. aureus* (MSSA) – Clinical (n=28) and Challenge (n= 6) Results

Difference in the Number of Dilutions between the Reference Result and the MicroScan® Result – <i>S.aureus</i> (MSSA) with Vancomycin						
Inoculation Method	Read Method	≥ Minus 2 Dilutions	Minus 1 Dilution	Exact Agreement	Plus 1 Dilution	≥ Plus 2 Dilutions
Turbidity	Manual		2	30	2	
Turbidity	autoSCAN® 4		3	31		
Turbidity	WalkAway®		2	30	2	
Prompt	Manual		2	12	19	1
Prompt	autoSCAN® 4		2	14	17	1
Prompt	WalkAway®		2	10	21	1
TOTAL			13	127	59	3

Table 3. *S. aureus* (VRSA) Challenge (n=3) Results

Difference in the Number of Dilutions between the Reference Result and the MicroScan® Result – <i>S.aureus</i> (VRSA) with Vancomycin						
Inoculation Method	Read Method	≥ Minus 2 Dilutions	Minus 1 Dilution	Exact Agreement	Plus 1 Dilution	≥ Plus 2 Dilutions
Turbidity	Manual			1	2	
Turbidity	autoSCAN® 4		1	2		
Turbidity	WalkAway®			1	2	
Prompt	Manual			1		2
Prompt	autoSCAN® 4			2	1	
Prompt	WalkAway®			1		2
TOTAL			1	8	5	4

There is a trend of the MicroScan® towards more resistant reading in comparison to the reference method (i.e. more values in the “Plus” category). This is even more pronounced when the Prompt™ method of inoculation is used, but still an EA of greater than 95% is achieved with all read methods. The trends of more resistant reading in

general, and more resistant results for the Prompt™ method of inoculation are consistent with the findings of the original 510(k) submission (K051202).

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 aureus interpretive criteria (µg/ml):

≤2 (S), 4-8 (I), ≥16 (R)

The interpretive criteria and quality control ranges are the same as recommended in the FDA approved pharmaceutical package insert and the CLSI. These 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.