

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

A. 510(k) Number:

K150039

B. Purpose for Submission:

To obtain a substantial equivalence determination for the addition of the reformulated vancomycin to the MicroScan Dried Gram-Positive MIC/Combo Panel at concentrations 0.25 to 64 µg/ml for testing Enterococci (e.g., *Enterococcus faecalis*), Staphylococci, including *Staphylococcus aureus* and *Staphylococcus epidermidis*

C. Measurand:

Vancomycin in the dilution range of 0.25 -64 µg/ml

D. Type of Test:

Quantitative Antimicrobial Susceptibility Test (AST), growth based fluorescence.

E. Applicant:

Beckman Coulter

F. Proprietary and Established Names:

MicroScan® Dried Gram-Positive MIC/Combo Panels with Vancomycin (0.25 – 64 µg/ml)

G. Regulatory Information:

1. Regulation section:

21 CFR 866.1640 Antimicrobial Susceptibility Test Powder

2. Classification:

Class II

3. Product code(s):

JWY – Manual Antimicrobial Susceptibility Test Systems

LRG – Instrument for Auto Reader & Interpretation of overnight susceptible 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 or 3 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, some fastidious aerobic gram-positive cocci and *Listeria monocytogenes*. Refer to Limitations 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 bacteria. 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 addition of the reformulated antimicrobial Vancomycin at concentration of 0.25 to 64 µg/ml to the test panel. The gram positive organisms which may be used for Vancomycin susceptibility testing in this panel are:

Enterococcus spp (e.g., *Enterococcus faecalis*)

Staphylococci, including *Staphylococcus aureus* and *Staphylococcus epidermidis* (including heterogeneous methicillin-resistant strains)

3. Special conditions for use statement(s):

For prescription use only

“The ability of the MicroScan Dried Gram Positive Panels to detect vancomycin resistant S. aureus strains is unknown due to the limited number of resistant strains tested. None of the isolates tested had an MIC of 16µg/mL.”

“The ability of the MicroScan Dried Gram Positive Panels to detect vancomycin intermediate or resistant coagulase negative Staphylococcus is unknown because intermediate or resistance strains were not encountered at the time of comparative clinical testing. Any coagulase negative Staphylococcus isolate for which the vancomycin MIC value is $\geq 8 \mu\text{g/mL}$ should be sent to a reference laboratory.”

4. Special instrument requirements:

MicroScan panels can be read either manually or automatically on the autoScan-4 or the WalkAway instrument systems.

I. Device Description:

The MicroScan Dried Gram Positive MIC/Combo Panel with vancomycin is used to determine the quantitative and/or qualitative antimicrobial agent susceptibility of colonies grown on solid media of rapidly growing aerobic and facultative gram-positive cocci. After inoculation panels are incubated for 16-20 hours at $35^{\circ}\text{C} \pm 1^{\circ}\text{C}$ in a non-CO₂ incubator and read either visually or with MicroScan instrumentation, according to the package insert “Accurate detection of resistance requires an incubation time of 24 hours for Enterococci isolates with vancomycin.

Primary inoculation Method: Turbidity, Alternate Inoculation Method: Prompt™

Primary Read Method: Manual, Alternate Read Methods: MicroScan WalkAway System and MicroScan autoSCAN4

J. Substantial Equivalence Information:

1. Predicate device name(s):

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

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

K123933

3. Comparison with predicate:

Table 1. Comparison with the Predicate Device

Similarities		
Item	Device	Predicate
Product Name	MicroScan® Dried Gram-Positive MIC/Combo Panels – Vancomycin	MicroScan® Dried Gram-Positive MIC/Combo Panels – Ceftaroline (K123933)
Technology	Overnight Microdilution MIC Susceptibility	Same
Result Reported	Report results as minimum inhibitory concentration (MIC) and categorical interpretation (SIR)	Same
Read Methods	Manual and Automated	Same
Inoculation Methods	Turbidity and Prompt™	Same
Instruments	autoSCAN® 4 or WalkAway®	Same

Differences		
Item	Device	Predicate
Intended Use	Determination of susceptibility to vancomycin with gram-positive bacteria	Determination of susceptibility to ceftaroline with gram positive bacteria
Antibiotic	Dried Vancomycin 0.25-64 µg/ml	Dried ceftaroline 0.06-16 µg/mL
MIC Interpretive Breakpoints	S. aureus : S ≤ 2, I= 4-8, R ≥ 16 Enterococci and Coagulase Negative Staphylococci: S ≤ 4, I=8-16, R ≥ 32	S ≤ 1, -, -
Labeling Limitations	<i>“The ability of the MicroScan Dried Gram Positive Panels to detect vancomycin resistance S. aureus strains is unknown due to the limited number of resistant strains tested. None of the isolates tested had an MIC of 16µg/mL.”</i> <i>“The ability of the MicroScan Dried Gram Positive Panels to detect vancomycin intermediate or resistant coagulase negative Staphylococcus is unknown because intermediate or resistance strains were not encountered at the time of comparative clinical testing. Any coagulase negative Staphylococcus isolate for which the vancomycin MIC value is ≥ 8</i>	The ability of the MicroScan Dried Gram Positive Panels to detect resistance to ceftaroline is unknown because resistant strains were not available at the time of comparative testing. Staphylococci colony counts may be elevated with the Prompt method and may be greater than the CLSI expected range. Elevated colony counts may adversely affect antibiotic results that are affected by inoculum, especially with

Differences		
Item	Device	Predicate
	<i>µg/mL should be sent to a reference laboratory.”</i>	staphylococci isolates.

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

1. Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA
<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm071462.pdf>
2. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow Aerobically, Approved Standard-9th Edition, Document M07-A9
3. Performance Standards for Antimicrobial Susceptibility Testing - 24th Informational Supplement, M100-S24 (QC parameters only)

L. Test Principle:

The antimicrobial susceptibility tests are miniaturizations of the broth dilution susceptibility test which have been dehydrated. Various antimicrobial agents are diluted in Mueller-Hinton broth supplemented with calcium and magnesium to concentrations bridging the range of clinical interest. Breakpoint Combo panels use concentrations equivalent to the categorical breakpoints of FDA and/or CLSI. After inoculation and rehydration with a standardized suspension of organism and incubation of 35°C for a minimum of 16 hours, the minimum inhibitory concentration (MIC) for the test organism is determined by observing the lowest antimicrobial concentration showing inhibition of growth.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Reproducibility data for 10 isolates including one *E. casseliflavus*, one *E. faecalis*, two *E. faecium*, three *S. aureus* (one MSSA and two MRSA), two *S. epidermidis* and one *S. haemolyticus* and one QC strain (*E. faecalis* ATCC 29212) were generated at 5 clinical trial sites. Organism selection was based on the intended use of the antimicrobial agent. Each strain was tested at each site in triplicate over three days using 2 inoculation methods (Turbidity and Prompt) and 3 reading methods (manual, WalkAway Instrument and autoSCAN-4 Instrument).

The mode of the test panel MIC results was determined for each isolate. MIC results at each site were compared to the mode value for each strain. Results were considered in agreement if the test panel MIC was equal to or within ± 1 dilution of the mode for that isolate. Agreement was calculated assuming any off-scale results were within one well from the mode (best case) and by assuming any off-scale results were greater than one well from the mode (worst case). Data were analyzed for all dilutions of Vancomycin (0.25-64 $\mu\text{g/mL}$). The agreement was calculated for each site and for the five sites combined.

For all sites combined, agreement within $1 \pm$ dilution from the mode for all inoculation and reading methods was $> 95\%$ for best case and for worst case scenarios. The reproducibility study results are acceptable. The results of the best case scenarios are shown in Table 2 below.

The results were acceptable.

Table 2. Reproducibility of Vancomycin MIC Testing with *S. aureus* (Methicillin-Susceptible and Methicillin-Resistant, *Enterococcus spp* (All Sites Combined) and Coagulase Negative Staphylococcus

Reading Method	Inoculation Method	
	Turbidity ^a	Prompt ^a
Manual	490/492 (99.6%)	491/492 (99.8%)
WalkAway	490/492 (97.6%)	488/492 (99.2%)
autoSCAN-4	490/492 (99.6%)	489/492 (99.4%)

^a Number of results within ± 1 dilution of the mode/total number of result (%)

b. *Linearity/assay reportable range:*

Not applicable

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

The organism recommended by the FDA (CDER) and the CLSI, *Enterococcus faecalis* ATCC 29212 and *S. aureus* ATCC 29213 were tested against reformulated Vancomycin. Quality control was performed at all sites using the Turbidity and the Prompt methods for inoculation, read by the manual, the WalkAway and the autoSCAN4reading methods. Tables 3 and 4 below represents the frequency of the results and all results were in acceptable range.

Table 3. QC Table of Vancomycin *E. faecalis* (Read at 18 and 24 hours)

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>Enterococcus faecalis</i> ATCC 29212 Expected range: 1-4 µg/ml	< 0.25													
	0.5													
	1	1	1	2					1					
	2	242	247	245	241	246	248	248	249	247	247	248	251	248
	4	1	1	1	1	1	1	1				1		
	8													
	16											1		

Table 4. QC Table of Vancomycin *S. aureus* (Reading 18 hours)

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®
			<0.25					
0.5	39	3	3	2				
1	204	244	240	243	172	165	161	
2	4	2	1	4	78	85	86	
4				1	1	1	1	
8		1	1					
16								

Quality Control results for the MicroScan Dried Gram Positive MIC/Combo Panel using both inoculation methods and using either reading methods demonstrated that the system could produce the expected quality control results. The QC results were within the expected range > 95% with all reads and inoculation methods for all 5 sites combined.

The quality control results are acceptable.

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 to demonstrate that MicroScan Dried Gram-Positive MIC/Combo panels with reformulated vancomycin (Test panels) are substantially equivalent to frozen CLSI reference panels (Reference panels). Device performance was evaluated in a clinical trial that included gram-positive isolates.

A total of 128 challenge isolates were tested (40 *Enterococcus* spp, 15 MRSA, 21 MSSA, 17 CNS, 9 VRSA and 26 VISA). Of the 128 challenge isolates, the expected results for 71 strains were susceptible, and 25 strains were Resistant. The 9 VRSA strains were tested at an internal site, while the rest of the isolates were tested at external sites.

A total of 947 clinical isolates were tested (166 *Enterococcus* spp, 205 MRSA, 207 MSSA and 369 CNS). Six hundred eighty-seven (687) organisms were fresh and two hundred sixty (260) were stock isolates. The results were compared to the reference method or expected results. Of the 947 gram positive isolates tested, 882 were identified by the Reference panel to be Susceptible, and 62 isolates were identified as Resistant.

Tables 5-8 below demonstrate the performance for each group of isolates (MRSA, MSSA, CNS and *Enterococcus* species) based on essential agreement and category agreement for the overall performance of the clinical and challenge isolates. Data is shown for each inoculum preparation method (Turbidity and Prompt) and reading (Overnight Manual, Walk-Away, and autoScan4). Accurate detection of resistance requires extended incubation times of 24 hours for *Enterococci*. *Staphylococci* results were read after 16-20 hours incubation (18-20 h for autoSCAN-4 instrument reads). The results were comparable to those obtained at 24 hours with the reference method. The performance data for VRSA and VISA is shown in Tables 9 and 10, respectively. Table 11 shows the overall performance summary for all organisms.

Table 5. MicroScan Performance for testing Vancomycin against MRSA

	Total	EA	%EA	Total eval	EA of eval	%EA	CA	%CA	#R	min	maj	vmj
Overnight Manual Read												
Turbidity												
Efficacy	205	204	99.5	205	204	99.5	204	99.5	0	1	0	0
Challenge	15	15	100	15	15	100	15	100	0	0	0	0
Combined	220	219	99.5	220	219	99.5	219	99.5	0	1	0	0
Prompt												

Efficacy	205	188	91.7	205	188	91.7	204	99.5	0	1	0	0
Challenge	15	15	100	15	15	100	15	100	0	0	0	0
Combined	220	219	99.5	220	219	99.5	219	99.5	0	1	0	0
WalkAway												
Turbidity												
Efficacy	205	204	99.5	205	204	99.5	204	99.5	0	1	0	0
Challenge	15	15	100	15	15	100	15	100	0	0	0	0
Combined	220	219	99.5	220	219	99.5	219	99.5	0	1	0	0
Prompt												
Efficacy	205	185	90.2	205	185	90.2	204	99.5	0	1	0	0
Challenge	15	15	100	15	15	100	15	100	0	0	0	0
Combined	220	219	99.5	220	219	99.5	219	99.5	0	1	0	0
autoScan4												
Turbidity												
Efficacy	205	203	99.0	205	203	99.0	203	99.0	0	1	1	0
Challenge	15	15	100	15	15	100	15	100	0	0	0	0
Combined	220	219	99.5	220	219	99.5	219	99.5	0	1	0	0
Prompt												
Efficacy	205	187	91.2	205	187	91.2	204	99.5	0	1	0	0
Challenge	15	15	100	15	15	100	15	100	0	0	0	0
Combined	220	219	99.5	220	219	99.5	219	99.5	0	1	0	0

Table 6. Microscan Performance for testing Vancomycin against MSSA

	Total	EA	%EA	Total eval	EA of eval	%EA	CA	%CA	#R	min	maj	vmj
Overnight Manual Read												
Turbidity												
Efficacy	207	206	99.5	206	205	99.5	207	100	0	0	0	0
Challenge	21	21	100	21	21	100	21	100	0	0	0	0
Combined	228	227	99.6	227	226	99.6	228	100	0	0	0	0
Prompt												
Efficacy	207	192	92.8	206	191	92.7	206	99.5	0	1	0	0
Challenge	21	21	100	21	21	100	20	95.2	0	1	0	0
Combined	228	213	93.4	227	212	93.4	226	99.1	0	2	0	0
WalkAway												
Turbidity												
Efficacy	207	206	99.5	206	205	99.5	207	100	0	0	0	0
Challenge	21	21	100	21	21	100	21	100	0	0	0	0
Combined	228	227	99.6	227	226	99.6	228	100	0	0	0	0
Prompt												
Efficacy	207	193	93.2	206	192	93.2	206	99.5	0	1	0	0
Challenge	21	21	100	21	21	100	21	100	0	0	0	0
Combined	228	214	93.9	227	213	93.8	227	99.6	0	1	0	0
autoScan4												
Turbidity												
Efficacy	207	205	99.0	206	204	99.0	207	100	0	0	0	0
Challenge	21	21	100	21	21	100	20	95.2	0	1	0	0
Combined	228	226	99.1	227	225	99.1	227	99.6	0	1	0	0
Prompt												
Efficacy	207	193	93.2	206	192	93.2	207	100	0	0	0	0
Challenge	21	21	100	21	21	100	20	95.2	0	1	0	0
Combined	228	214	93.9	227	213	93.8	227	99.6	0	1	0	0

Table 7. Microscan Performance for testing Vancomycin against CNS

	Total	EA	%EA	Total eval	EA of eval	%EA	CA	%CA	#R	min	maj	vmj
Overnight Manual Read												
Turbidity												
Efficacy	369	368	99.7	357	356	99.7	369	369	0	0	0	0
Challenge	17	17	100	17	17	100	17	100	0	0	0	0
Combined	386	385	99.7	374	373	99.7	386	100	0	0	0	0
Prompt												
Efficacy	369	369	100	359	359	100	369	100	0	0	0	0
Challenge	17	17	100	17	17	100	17	100	0	0	0	0
Combined	386	386	100	376	376	100	386	100	0	0	0	0
WalkAway												
Turbidity												
Efficacy	369	368	99.7	357	356	99.7	369	100	0	0	0	0
Challenge	17	17	100	17	17	100	17	100	0	0	0	0
Combined	386	385	99.7	374	373	99.7	386	100	0	0	0	0
Prompt												
Efficacy	369	368	99.7	359	359	100	369	100	0	0	0	0
Challenge	17	17	100	17	17	100	17	100	0	0	0	0
Combined	386	385	99.7	376	376	100	386	100	0	0	0	0
autoScan4												
Turbidity												
Efficacy	369	367	99.5	352	350	99.4	369	100	0	0	0	0
Challenge	17	17	100	17	17	100	17	100	0	0	0	0
Combined	386	384	99.5	369	367	99.5	386	100	0	0	0	0
Prompt												
Efficacy	369	369	100	357	357	100	369	100	0	0	0	0
Challenge	17	17	100	17	17	100	17	100	0	0	0	0
Combined	386	386	100	374	374	100	386	100	0	0	0	0

Table 8. MicroScan Performance for testing Vancomycin against *Enterococcus* spp.

	Total	EA	%EA	Total eval	EA of eval	%EA	CA	%CA	#R	min	maj	vmj
Overnight Manual Read												
Turbidity												
Efficacy	166	164	98.8	100	99	99.0	163	98.2	62	3	0	0
Challenge	40	40	100	28	28	100	37	92.5	16	3	0	0
Combined	206	204	99.0	128	127	99.2	200	97.1	78	6	0	0
Prompt												
Efficacy	166	161	97.0	100	96	96.0	161	97.0	62	4	1	0
Challenge	40	40	100	27	27	100	37	92.5	16	3	0	0
Combined	206	201	97.6	127	123	96.9	198	96.1	78	7	1	0
WalkAway												
Turbidity												
Efficacy	166	164	98.8	99	98	99.0	163	98.2	62	3	0	0
Challenge	40	40	100	28	28	100	37	92.5	16	3	0	0
Combined	206	204	99.0	127	126	99.2	200	97.1	78	6	0	0
Prompt												
Efficacy	166	161	97.0	99	95	96.0	160	96.4	62	6	0	0
Challenge	40	40	100	27	27	100	37	92.5	16	3	0	0

Combined	206	201	97.6	126	122	96.8	197	95.6	78	9	0	0
autoScan4												
Turbidity												
Efficacy	166	163	98.2	99	97	98.0	162	97.6	62	4	0	0
Challenge	40	40	100	28	28	100	37	92.5	16	3	0	0
Combined	206	203	98.5	127	125	98.4	199	96.6	78	7	0	0
Prompt												
Efficacy	166	161	97.0	99	95	96.0	161	97.0	62	5	0	0
Challenge	40	40	100	28	28	100	38	95.0	16	2	0	0
Combined	206	201	97.6	127	123	96.9	199	96.6	78	7	0	0

Table 9. Microscan Performance for testing Vancomycin against VRSA Challenge

	Total	EA	%EA	Total eval	EA of eval	%EA	CA	%CA	#R	min	maj	vmj
Overnight Manual Read												
Turbidity	9	8	88.9	1	1	100	9	100	9	0	0	0
Prompt	9	8	88.9	1	1	100	9	100	9	0	0	0
WalkAway												
Turbidity	9	8	88.9	1	1	100	9	100	9	0	0	0
Prompt	9	8	88.9	1	1	100	9	100	9	0	0	0
autoScan4												
Turbidity	9	8	88.9	1	1	100	9	100	9	0	0	0
Prompt	9	8	88.9	1	1	100	9	100	9	0	0	0

Table 10. Microscan Performance of Vancomycin against VISA Challenge

	Total	EA	%EA	Total eval	EA of eval	%EA	CA	%CA	#R	min	maj	vmj
Overnight Manual Read												
Turbidity	26	26	100	26	26	100	24	92.3	0	2	0	0
Prompt	26	25	96.2	26	25	96.2	24	92.3	0	2	0	0
WalkAway												
Turbidity	26	26	100	26	26	100	24	92.3	0	2	0	0
Prompt	26	26	100	26	26	100	25	96.2	0	1	0	0
autoScan4												
Turbidity	26	26	100	26	26	100	24	92.3	0	2	0	0
Prompt	26	26	100	26	26	100	25	96.2	0	1	0	0

Table 11. Overall Performance Summary Clinical and Challenge for all organisms

	Total	EA	%EA	Total eval	EA of eval	%EA	CA	%CA	#R	min	maj	vmj
Overnight Manual Read												
Turbidity												
Clinical Total	947	942	99.5	868	864	99.5	943	99.6	62	4	0	0
Challenge Total	128	127	99.2	108	108	100	123	96.1	25	5	0	0
Combined	1075	1069	99.4	976	972	99.6	1066	99.2	87	9	0	0
Prompt												
Clinical Total	947	910	96.1	870	834	95.9	940	99.3	62	6	1	0
Challenge Total	128	126	98.4	107	106	99.1	122	95.3	25	6	0	0
Combined	1075	1036	96.4	977	940	96.2	1062	98.8	87	12	1	0

EA-Essential Agreement CA-Category Agreement R-Resistant Isolates
min-minor discrepancies **maj**-major 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.

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

MIC Trend Analysis:

Using the data provided by the sponsor in the diagonal table format recommended in the AST Guidance, an analysis was conducted to check for trending in MIC values.

As summarized in Table 12 below, a lower reading trend was observed in the overall performance of *Coagulase negative Staphylococcus for the turbidity inoculation method* in the three reading methods (overnight manual, WalkAway and autoScan4) compared to the CLSI broth micro-dilution method, which raises concerns for potential very major errors.

Table 12. Trending of Results by Turbidity Method in Combined Clinical and Challenge Study

Organism	Difference in MIC as Compared to the CLSI Reference Method				
	-2	-1	0	+1	+2
Overnight Manual Read					
CoNS combined	0% (1/386)	50.5% (195/386)	47.9% (185/386)	1.3% (5/386)	0
WalkAway					
CoNS combined	0% (1/386)	49.2% (190/386)	49.2% (190/386)	1.3% (5/386)	0
AutoScan4					
CoNS combined	0.5% (2/386)	52% (201/386)	46.4% (179/386)	1% (4/386)	0

Based on our analysis, the overall performance of *S. aureus* (MRSA, MSSA) for the prompt inoculation method, demonstrates a trend towards higher reading compared to the CLSI broth micro-dilution method for all reading methods. This information is summarized in Table 13 below.

Table 13. Trending of Results by Prompt Method in Combined Clinical and Challenge Study

Organism	Difference in MIC as Compared to the CLSI Reference Method				
	-2	-1	0	+1	+2
Overnight Manual Read					
MRSA combined	0	3.6% (8/221)	46.2% (102/221)	42.5% (94/221)	7.7% (17/221)
MSSA combined	0	1.8% (4/228)	44.7% (102/228)	46.9% (107/228)	6.6% (15/228)
WalkAway					
MRSA combined	0	5.7% (14/245)	49.8% (122/245)	36.3% (89/245)	8.2% (20/245)
MSSA combined	0	1.8% (4/228)	44.7 (102/228)	47.4% (108/228)	6.1% (14/228)
AutoScan4					
MRSA combined	0 (1/221)	4% (9/221)	45% (100/221)	43% (94/221)	8% (17/221)
MSSA combined	0	1% (3/228)	45% (102/228)	48% (109/228)	6% (14/228)

This trending and the potential for occurrence of major and very major errors(s) for Vancomycin when testing *Coagulase negative S. aureus* and *MRSA* and *MSSA* was also addressed by adding the following footnotes in the in labeling:

- Footnote 1:
“MicroScan vancomycin MIC values tended to be one doubling dilution lower when testing coagulase negative *Staphylococcus* by the turbidity inoculation method using manual, WalkAway and autoScan4 reading methods compared to reference broth micro-dilution.
- Footnote 2:
“MicroScan vancomycin MIC values tended to be one doubling dilution higher when testing *S. aureus* (MR and MS) by the Prompt inoculation method using manual, WalkAway and AutoScan-4 reading methods compared to reference broth micro-dilution.

Growth Rate:

All isolates tested during the clinical (efficacy) trials grew in both the frozen reference panel and the dried MicroScan panels.

Prompt Hold Study:

An external study was performed to determine the agreement of results obtained with the Prompt inoculation method using hold times of 0 hours and 4 hours prior to inoculation of the panels. Results of 4-hour holds were compared to 0-hour hold using the same inoculum and with expected results as determined by the reference method. Testing was performed with all three read methods (WA, AS4 and manually). The results showed that there is no statistical difference in the Vancomycin dried result between 4 hours and 0 hours to all read. There is no statistical

difference in the Vancomycin dried results compared to the frozen results at 0 hour and 4 hour hold time for all read methods. The performance was acceptable for all organisms tested. No major or very major errors were noted with each method inoculated after extended hold times. Only minor errors were observed.

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:

The FDA interpretative criteria were used to evaluate all performance data are shown in Table 14 below.

Table 14. FDA Interpretive Criteria for Vancomycin

Organism	Interpretive Criteria (Vancomycin MIC in µg/mL)		
	S	I	R
<i>Enterococcus spp</i>	≤4	8-16	≥32
<i>Coag Neg Staphylococcus spp</i>	≤4	8-16	≥32
<i>S. aureus</i>	≤2	4-8	≥16

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.