

SPECIAL 510(k): Device Modification OIR Decision Summary

To: THE FILE

RE: DOCUMENT NUMBER K152346

This 510(k) submission contains information/data on modifications made to the SUBMITTER'S own Class II, Class III or Class I devices requiring 510(k). The following items are present and acceptable (delete/add items as necessary):

1. The name and 510(k) number of the SUBMITTER'S previously cleared device.
Trade Name: K150039 - MicroScan Dried Gram Positive MIC/Combo Panels - Vancomycin

2. Submitter's statement that the **INDICATION/INTENDED USE** of the modified device as described in its labeling **HAS NOT CHANGED** along with the proposed labeling which includes instructions for use, package labeling, and, if available, advertisements or promotional materials.

3. A description of the device **MODIFICATION(S)**, including clearly labeled diagrams, engineering drawings, photographs, user's and/or service manuals in sufficient detail to demonstrate that the **FUNDAMENTAL SCIENTIFIC TECHNOLOGY** of the modified device **has not changed**.

This change was for a modification to the recommended incubation time for isolates of *Enterococcus* species from 24 hours to 16 to 20 hours. The instructions in labeling of the previously cleared device indicates an incubation time of 24 hours is necessary for detection or resistance in isolates that have intermediate or susceptible MICs to vancomycin. This labeling change does not affect the intended use. There were no modifications to the device.

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4. **Comparison Information** (similarities and differences) to applicant's legally marketed predicate device including, labeling, intended use, physical characteristics, and evaluation of results obtained during the clinical study for incubation times of 16 to 20 hours for *Enterococcus* species as compared to results obtained after 24 hours of incubation.

5. A **Design Control Activities Summary** which includes:
 - a) Identification of Risk Analysis method(s) used to assess the impact of the modification on the device and its components, and the results of the analysis
 - b) Based on the Risk Analysis, an identification of the verification and/or validation activities required, including methods or tests used and acceptance criteria to be applied

The labeling for this modified subject device has been reviewed to verify that the indication/intended use for the device is unaffected by the modification. In addition, the submitter's description of the particular modification(s) and the comparative information between the modified and unmodified devices demonstrate that the fundamental scientific technology has not changed. The submitter has provided the design control information as specified in The New 510(k) Paradigm and on this basis, I recommend the device be determined substantially equivalent to the previously cleared (or their preamendment) device.

Applicant:

Beckman Coulter

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 - 20 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)

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°C ± 1°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 autoSCAN-4

Table 1. Comparison with the Predicate

Item	Similarities	
	Device MicroScan® Dried Gram-Positive MIC/Combo Panels – Vancomycin	Predicate MicroScan® Dried Gram-Positive MIC/Combo Panels – Vancomycin (K150039)
Intended Use	Determination of susceptibility to vancomycin with gram-positive bacteria	Same
Technology	Overnight Microdilution MIC Susceptibility Tests	Same

Similarities		
Item	Device MicroScan® Dried Gram-Positive MIC/Combo Panels – Vancomycin	Predicate MicroScan® Dried Gram-Positive MIC/Combo Panels – Vancomycin (K150039)
Components	Vancomycin 0.25 – 64 µg/mL	Same
Result Reported	Report results as minimum inhibitory concentration (MIC) and categorical interpretation (SIR)	Same
MIC Interpretive Breakpoints	<i>S. aureus</i> : S ≤ 2, I = 4-8, R ≥ 16 Enterococci and Coagulase Negative Staphylococci: S ≤ 4, I = 8-16, R ≥ 32	Same
Read Methods	Manual and Automated	Same
Inoculation Methods	Turbidity and Prompt™	Same
Instruments	autoSCAN® 4 or WalkAway®	Same

Differences		
Item	Device	Predicate
Incubation Times	16 – 20 hours for <i>Staphylococcus</i> species and <i>Enterococcus</i> species	16 – 20 hours for <i>Staphylococcus</i> species; 24 hours for detection of resistant <i>Enterococcus</i> species

1. **Analytical performance:**

a. *Precision/Reproducibility:*

Reproducibility data for 5 isolates of *Enterococcus* species including one isolate of *E. casseliflavus*, two isolates of *E. faecalis* and two isolates of *E. faecium* was provided. Organism selection was based on the intended use of the antimicrobial agent. Each isolate 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 were compared to the mode value for each isolate. 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 µg/mL).

For all sites combined, agreement within $1 \pm$ dilution from the mode for all inoculation and reading methods was > 95% for best case and > 94.7% for worst case scenarios. For isolates tested using the Prompt inoculation method and interpreted using the WalkAway instrument, the mode MIC of one *Enterococcus* isolate was off scale.

Reproducibility was determined using the remaining four *Enterococcus* isolates. The results of the reproducibility best and worst case scenarios are shown in Table 2 below. The reproducibility results are acceptable.

Table 2. Reproducibility of Vancomycin MIC Testing with *Enterococcus* spp. (All Sites Combined)

Reading Method	Inoculation Method			
	Turbidity		Prompt	
	Best Case ^a	Worst Case ^a	Best Case ^a	Worst Case ^a
Manual	98.7%	95.6%	99.6%	95.1%
WalkAway	99.1%	94.7%	99.4% ^b	98.9% ^b
autoSCAN-4	99.1%	98.2%	97.8%	96.9%

^a Percent of results within ± 1 dilution of the mode

^b Reproducibility determined using results obtained from four *Enterococcus* isolates.

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

The organism recommended in the FDA approved pharmaceutical drug label and the CLSI is *Enterococcus faecalis* ATCC 29212. This organism was tested against reformulated Vancomycin and interpreted after 16-20 hours of incubation. 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. Table 3 below represents the frequency of the QC. The QC results read at 16-20 hours are acceptable for all reading methods.

Table 3. QC of Vancomycin with *E. faecalis* (Read at 16-20 hours)

ORGANISM	Conc. $\mu\text{g/ml}$	Reference Result (read at 24 hours)	Turbidity Inoculation			Prompt Inoculation		
			Manual Read	WalkAway Read	autoSCAN-4 Read	Manual Read	WalkAway Read	autoSCAN-4 Read
<i>Enterococcus faecalis</i> ATCC 29212	≤ 0.25				1			
	0.5							
	1	1	1			1		
	2	244	249	243	250	251	249	253
	4	1	1	1	1			
	8							
	16			1				
Total in Range (%)		246/246 (100)	251/251 (100)	244/245 (99.6)	251/252 (99.6)	252/252 (100)	249/249 (100)	253/253 (100)

2. Comparison studies:

Method comparison with predicate device:

This Special 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) for the detection of resistant *Enterococcus* species after 16 – 20 hours of incubation. Device performance was evaluated using 16 – 20 hour incubation data that was also collected during the conduct of studies submitted to support the clearance of the original predicate device (K150039) which were based on 24 hour incubation for *Enterococcus* species.

Previously collected results from testing of a total of 40 *Enterococcus* spp. challenge isolates and 166 clinical isolates with the dried MicroScan panels incubated for 16 – 20 hours were evaluated. The results obtained with the dried panels were compared to the reference method or expected results.

Table 4 below demonstrates the performance for *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 method (Overnight Manual, Walk-Away, and autoScan4). The results were comparable to those obtained at 24 hours with the reference method.

Table 4. Performance of MicroScan Dried Gram-Positive Panels with Vancomycin; All Inoculation Methods and Reading Methods

	Total	EA	%EA	Total eval	EA of eval	%EA eval	CA	%CA	#R	min	maj	vmj
Overnight Manual Read												
Turbidity												
Efficacy	166	163	98.2	98	96	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	126	124	98.4	199	96.6	78	7	0	0
Prompt												
Efficacy	166	162	97.6	98	95	96.9	160	96.4	62	5	1	0
Challenge	40	40	100	27	27	100	37	92.5	16	3	0	0
Combined	206	202	98.1	125	122	97.6	197	95.6	78	8	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	98	96	98.0	162	97.6	62	4	0	0
Challenge	40	40	100	28	28	100	36	90.0	16	4	0	0
Combined	206	203	98.5	126	124	98.4	198	96.1	78	8	0	0
Prompt												
Efficacy	166	162	97.6	98	95	96.9	160	96.4	62	6	0	0
Challenge	40	40	100	28	28	100	37	92.5	16	3	0	0
Combined	206	202	98.1	126	123	97.6	197	95.6	78	9	0	0

EA-Essential Agreement
min-minor discrepancies

CA-Category Agreement
maj-major discrepancies

R-Resistant Isolates
vmj-very major discrepancies

3. Risk Assessment

The risk associated with the modification of the incubation time was assessed by the sponsor as follows:

1. Risk of a false susceptible result as interpreted using the WalkAway or autoSCAN-4 instruments – Medium Risk, mitigated by use of manual read of the panels and risk file references.

2. Risk of a false resistant result as interpreted using the WalkAway or autoSCAN-4 instruments – Low Risk, mitigated by use of manual read of the panels and risk file references.
3. Risk of a false susceptible result as interpreted using manual read, WalkAway or autoSCAN-4 instrument reads – Medium risk mitigated by design, protective measures and safety information.

4. Expected values/Reference range:

The FDA interpretative criteria were used to evaluate all performance data are shown in Table 5 below.

Table 5. FDA Interpretive Criteria for Vancomycin

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

5. Device Labeling Changes

The data included in this submission validates the sponsor's proposal to remove the following statements from the device instructions for use:

1. Removal of the following statement from the Summary and Principles section of the MicroScan Dried Gram-Positive Procedural Manual for vancomycin

*Accurate detection of resistance requires extended incubation times for the following organism/antimicrobics:
24 hours Enterococci Vancomycin*

2. Removal of the following statement from the Reading the Panels section of the MicroScan Dried Gram-Positive Procedural Manual for vancomycin:

Incubation **Organisms** **Antimicrobics**
24 hours Enterococci Vancomycin