

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

A. 510(k) Number:

K070860

B. Purpose for Submission:

To add Clindamycin at 0.03 – 8 µg/mL (Long Dilution Sequence) and 0.12 – 2 µg/mL (5-Dilution Breakpoint [BP] Sequence) to the MicroScan® Synergies plus™ Gram-Positive MIC/Combo Panels

C. Measurand:

Clindamycin at 0.03 – 8 µg/mL (Long Dilution Sequence) and 0.12 – 2 µg/mL (5-Dilution Breakpoint [BP] Sequence)

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):

The MicroScan® Synergies plus™ 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 enterococci and staphylococci. After inoculation, panels are incubated for 4.5 – 18 hours at 35°C ± 1°C, in a WalkAway® SI, or equivalent, and read by the MicroScan® Instrumentation. Additionally, the panels may be incubated in a non-CO₂ incubator and the Antimicrobial Susceptibility Testing (AST) portions can be read visually, according to the Package Insert.

2. Indication(s) for use:

The testing of Clindamycin at concentrations of 0.03 – 8 µg/mL (Long Dilution Sequence) and 0.12 – 2 µg/mL (5-Dilution Breakpoint [BP] Sequence) to the Gram-Positive MIC/Combo test panel is indicated for testing *Staphylococcus aureus* (penicillinase and non-penicillinase producing strains) and *Staphylococcus epidermidis* (penicillinase and non-penicillinase producing strains) at 4.5-16 hours or 16-20 hours for an overnight reading.

3. Special conditions for use statement(s):

- 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 which 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® (a wetting agent), then 0.1ml transferred to 25 ml of inoculum Synergies plus Pos Broth with Pluronic®) for a

final inoculum concentration of $3-7 \times 10^5$ 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-CO₂ 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

1. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended use	MicroScan® panels are designed for use in determining quantitative and/or qualitative antimicrobial agent susceptibility and/or identification to the species level 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 – 24 hours	Same
Results	Quantitative with qualitative interpretations	Same
Technology	Growth based	Same

Item	Device	Predicate
Panels	Dried Clindamycin in water	Dried clindamycin or gentamycin in broth
Reading	Uses both a ≤ 16 hour read and overnight read method in the same system	Overnight system uses only the overnight reading method and <16 hour instruments use only the <16 hour read method.
Inoculum preparation	Turbidity method of inoculation only.	Inoculum prepared using either the Turbidity method or Prompt® system
Instrument	WalkAway® -SI System or equivalent	AutoScan® -4 or WalkAway®
Antibiotic	Clindamycin at 0.03 – 8 $\mu\text{g/mL}$ (Long Dilution Sequence) and at 0.12 – 2 $\mu\text{g/mL}$ (5-Dilution Breakpoint [BP] Sequence)	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-S17) “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, 16/18 hours (overnight instrument readings, manual readings), or 24 hours depending on the growth rate of the organism being tested. No reading below 16 hours of incubation is reported. The time of final read is dependent on the user preference, the growth rate of the organism, and the sensitivity of the automatic reader since cell densities below 2×10^7 cells/ml are not detected.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

Reproducibility was demonstrated using 360 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® 16-18 hour readings and manual readings at 16-20 hours incubation. The Reproducibility total for the Rapid read method equaled 330 isolates. The WalkAway® SI had 30 results that were not readable at <16 hours. All results were >95% reproducible for the Long Dilution and the 5-Dilution Breakpoint Sequence for all read methods. Performance claims are based on the Rapid read method.

There was a trend for the Rapid read method to produce slightly more susceptible results.

b. Linearity/assay reportable range:

Not Applicable

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

The recommended QC isolates were tested a sufficient number of times with acceptable results on all testing days with the reference method. Quality control results demonstrated the ability of the different reading parameters (manual and instrument) to produce acceptable results >95% of the time. The following tables provide the frequency of the results in each concentration with the expected range stated.

Results					
Organism	Conc. in µg/mL	# reference	MicroScan®		
Clindamycin Long Dilution			Manual overnight	Instrument overnight	<16 h instrument
<i>E. faecalis</i> ATCC 29212 Range 4 - >8 µg/mL	0.5				
	1				
	2				
	4				12
	8	52	46	54	72
	>8	36	44	36	6
Results					
Organism	Conc. in µg/mL	# reference	MicroScan®		
Clindamycin Long Dilution			Manual overnight	Instrument overnight	<16 h instrument
<i>S. aureus</i> ATCC Range 0.06 – 0.25 µg/mL	≤0.03				2
	0.06		4	8	14
	0.12	87	81	84	77
	0.25	8	9	1	3
	0.5		1	1	
	≥1		2	3	1

Results					
Organism	Conc. in µg/mL	# reference	MicroScan®		
Clindamycin 5 BP Dilution			Manual overnight	Instrument overnight	<16 h instrument
<i>E. faecalis</i> ATCC 29212 Range > 2 µg/mL	≤0.12				
	0.25				
	0.5				
	1				
	2				
	> 2	21	21	21	21
Results					
Organism	Conc. in µg/mL	# reference	MicroScan®		
Clindamycin 5 BP Dilution			Manual overnight	Instrument overnight	< 16 h instrument
<i>S. aureus</i> ATCC 29213 Range ≤0.12 – 0.25 µg/mL	≤0.12	18	17	18	18
	0.25	3	3	1	3
	0.5		1	1	
	1				
	2			1	
	> 2				

There is a slight trend for the <16 hour Long Dilution Sequence Rapid read method to produce QC results that were more susceptible than the reference result, if only by one dilution, for both the *S. aureus* ATCC 29213 and the *E. faecalis* ATCC 29212. This trend was not observed for the five Breakpoint Dilution Sequence QC results.

Inoculum density control: A turbidity meter was used for the turbidity inoculation method. Turbidity inoculum verification provided.

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 three sites using fresh isolates supplemented with stock isolates. A total of 304 gram-positive isolates were tested of which 268 were fresh isolates and 36 were stock isolates. Fourteen (14) Clinical isolates for the Long Dilution and the Breakpoint Dilution Sequences were reported at ≥ 16 hours and were not included as Rapid read results. There were 75 challenge isolates tested at one site and compared to the reference broth dilution result mode that was determined by previous testing of each isolate multiple times in the recommended reference panel. Fourteen (14) Challenge isolates for the Long Dilution and the Breakpoint Dilution Sequences were reported at ≥ 16 hours and were not included as Rapid read results.

The Synergies plus™ readings were obtained at times between 4.5 and 16 hours of incubation for > 95% of the results. An additional comparison was done with readings on the instrument after overnight incubation and also read manually when incubated 16 - 18 hours. Performance by these alternate reading methods was also acceptable with no apparent differences or trends.

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. QC was also performed. There was a slight trend for the Rapid read method to produce more susceptible QC results than the reference method results, if only by one dilution. This trend was also observed in the Reproducibility studies.

The chart below demonstrates the performance of all three reading methods (Synergies plus™ readings at <16 hours, overnight on the WalkAway® and manually read at 18 hours using the TouchScan®-SR) when compared to the reference method.

Clinical and Challenge Data – Read Method comparisons for Clindamycin

	Total	EA	%EA	Total Eval	EA of Eval	%EA of Eval	CA	%CA	#R	min	maj	vmj
<16 h												
• Long	351	344	98.0	234	228	97.4	348	99.1	115	2	1	0
• 5 Dil. BP	351	NA	NA	NA	NA	NA	348	99.1	115	2	1	0
Overnight instrument												
• Long	379	375	98.9	253	251	99.2	373	98.4	124	4	1	1
• 5 Dil. BP	379	NA	NA	NA	NA	NA	373	98.4	124	4	1	1
Overnight Manual												
• Long	379	376	98.9	253	251	99.2	373	98.4	124	4	1	1
• 5 Dil. BP	379	NA	NA	NA	NA	NA	373	98.4	124	4	1	1

EA-Essential Agreement

CA-Category Agreement

R-resistant isolates

NA – Essential Agreement result are not applicable for Breakpoint format

maj-major discrepancies

vmj-very major discrepancies

min- minor discrepancies

Essential agreement (EA) is when the MicroScan® Synergies plus panel agrees with the reference test panel results exactly or within one doubling dilution of the reference method. Category agreement (CA) is when the MicroScan® Synergies plus panel interpretation (S-I-R) agrees exactly with the reference panel interpretation. Evaluable (Eval) are results that are within the test range and on scale.

Of the 75 Challenge isolates tested, the expected results for 41 strains were Susceptible and 34 strains were Resistant. One very major error (1/7, 14.3%) occurred in the Challenge Set data. The vmj error was generated by one *S. epidermidis* (methicillin-resistant) by the Overnight Instrument and the Overnight Manual read methods in both the Long Dilution and the 5-Dilution Breakpoint Sequence data, but a vmj error was not detected by the Rapid read method, because the read time was >16 hours. Although the expected result for this isolate was resistant, the reference result on the day of testing was susceptible and was in agreement with the Overnight Instrument and the Overnight Manual read methods results. The overall combined EA and the CA for the Challenge Set Data was >95% for all read methods and dilution combinations. There was one (1) major error (6.7%, 1/15) produced by one *S. aureus* (methicillin-sensitive) generated by the Rapid read method only. The overall maj error rate of 2.9% (1/34) for the Challenge Set Data for all read methods was in the acceptable range. Therefore, the Challenge Set performance data are acceptable.

Clinical Data Read Method Comparison - Clindamycin

	Total	EA	%EA	Total Eval	EA of Eval	%EA of Eval	CA	%CA	#R	min	maj	vmj
<16 h • Long • 5 Dil BP	290	285	98.3	200	196	98.0	288	99.3	88	2	0	0
	290	NA	NA	NA	NA	NA	288	99.3	88	2	0	0
Overnight instrument • Long • 5 Dil BP	304	301	99.0	211	209	99.1	300	98.7	90	3	1	0
	304	NA	NA	NA	NA	NA	300	98.7	90	3	1	0
Overnight Manual • Long • 5 Dil BP	304	301	99.0	211	209	99.1	300	98.7	90	3	1	0
	304	NA	NA	NA	NA	NA	300	98.7	90	3	1	0

Performance claims (in bold) that will appear in the labeling and the procedural manual are based on the clinical Rapid read (<16 hour) method results only. The table above displays the Clinical data results compared by reading method.

The Clinical data Rapid read method EA of 98.3% and the CA of 99.3% are both very good. Overnight Instrument and Manual read methods EA and CA are both very similar to the Rapid read method results for the Long Dilution and the 5-Dilution Breakpoint Sequence data results.

There were no vmj errors generated by any of the read methods. There was 1 maj error (1/213, 0.5%) produced by the Overnight Instrument and the Overnight Manual read methods. This maj error was not observed in the Rapid read method results because the time-to-results was >16 hours. Because of the number of off-scale results in the Clinical data results, no real trending was observed.

The overall error rates are within acceptable limits for all reading methods. The performance data are acceptable for both the Long Dilution and for the 5-Dilution Breakpoint Sequence results using the Rapid read (<16 hour) method.

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 species Interpretive criteria: ≤ 0.5 (S), 1 – 2 (I), ≥ 4 (R)

The interpretative criteria and Quality Control Ranges 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.