

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

A. 510(k) Number:

K071316

B. Purpose for Submission:

To add a Streptomycin Synergy Screen to the MicroScan® Synergies plus™ Gram-Positive for testing *Enterococcus* spp

C. Measurand:

Streptomycin 1000 µg/mL, 1- Dilution Breakpoint Sequence

D. Type of Test:

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):

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® Instrument System. 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:

This submission is for the addition of the antimicrobial Streptomycin Synergy Screen at a concentration of 1000 µg/mL for testing *Enterococcus spp* at 4.5-16 hours or 16-20 hours for an overnight reading.

3. Special conditions for use statement(s):

- *E. faecium* with the Rapid Read Method - hold Susceptible (<1000 µg/mL) results to overnight/manual reads (16-20 hours).
- *E. faecalis* with the Overnight Read Method - If *E. faecalis* overnight (16-20 hr) reads are critical to patient care verify with WalkAway Instrument read (footnote in the Instructions for Use Manual).
- 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® - a wetting agent, then 0.1ml transferred to 25ml 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 there is 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

3. 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	Fully automated short-term (<16 hours) Incubation Cycle Microdilution MIC Susceptibility Tests Overnight Microdilution MIC Susceptibility tests	Same
Technology	Growth based	Same
Differences		
Item	Device	Predicate
Panels	Dried streptomycin Synergy Screen	Dried clindamycin or gentamicin in broth
Reading	Uses both a ≤ 16 h 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
Results	Qualitative interpretations	Quantitative with qualitative interpretations
Instrument	WalkAway® -SI System or equivalent	autoScan® -4 or WalkAway®
Antibiotic	Streptomycin at 1000 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-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. The time of final read is dependent on the user customization, 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 ten isolates tested at three sites on three separate days in triplicate. The study included the testing on the WalkAway® SI read at less than (<) 16 hours, WalkAway® 16-18 hour readings and manual readings at 16-20 hours incubation. Acceptable reproducibility (95%) was demonstrated with only category agreement (S, R) since that is all that is detected.

b. *Linearity/assay reportable range:*

Not Applicable

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

The recommended QC *Enterococcus faecalis* ATCC 29212 and *Enterococcus faecalis* ATCC 51299 were tested a sufficient number of times with acceptable results most of the time with the reference method. Both of the QC isolates grow in the 4.5-18 hour window. Quality control results demonstrated the ability of the different reading parameters (manual and instrument) to produce acceptable results of greater than (>) 95%.

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

Quality Control Table

Organism	Conc in µg/mL	# reference	Results		
			MicroScan®		
Streptomycin Synergy Screen			Manual overnight	Instrument overnight	<16 hrs instrument
<i>E. faecalis</i> ATCC 29212 Range ≤ 1000 µg/mL	≤ 1000	62	62	62	61
	>1000				1

Organism	Conc in µg/mL	# reference	MicroScan®		
			MicroScan®		
Streptomycin Synergy Screen			Manual overnight	Instrument overnight	<16 hrs instrument
<i>E. faecalis</i> ATCC 51299 Range > 1000 µg/mL	≤ 1000			1	1
	>1000	64	64	63	63

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 *Enterococci* and the MicroScan® Synergies plus™ Gram-Positive panel with Streptomycin Synergy Screen (Test Panel) compared with a frozen reference panel. A total of 374 gram-positive isolates were tested of which 297 were fresh isolates and 68 were stock isolates. Nine isolates were reported at greater than or equal to (\geq) 16 hours and were not included as Rapid read results. Therefore, of the 374 isolates tested, 365 Rapid read isolates were analyzed. There were 83 challenge isolates selected from CDC challenge strains and stock organisms tested at one site and compared to the reference broth dilution result mode that

were determined by previous testing of each isolate multiple times in the recommended reference panel. Four challenge isolates were reported at ≥ 16 hours and were not included as Rapid read results. There were 68 isolates from the verification testing which were tested in house. These isolates were primary clinical isolates collected over time. A qualitative comparison only was performed.

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.

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 charts below demonstrates the performance of all three reading methods Rapid (WalkAway® SI, <16 hours) Overnight Instrument (> 16 hours on the WalkAway® SI, 16/18 hours) and Overnight Manual (manual/visual read, 16 - 20) with the one dilution breakpoint when compared to the reference method.

Performance Summary

	Total	CA	%CA	#R	#S	min	maj	vmj
Rapid Read Method Combined	444	438	98.6	175	269	N/A	2	4
Overnight Instrument Read Combined	457	448	98.0	179	278	N/A	6	3
Overnight Manual Read Combined	457	448	98.0	179	278	N/A	6	3

CA-Category Agreement

R-resistant isolates

CA is when the interpretation of the reference method agrees exactly with the interpretation of the MicroScan® result.

N/A - Min errors are not applicable since only S or R results are possible

maj-major discrepancies

vmj-very major discrepancies

The no growth rate was 2.9% (9/374) in the efficacy study and 5.0% (4/79) in the challenge study with the <16 hour read method.

E. faecium had a higher than expected vmj discrepancy rate of 3.3% (3/90) with the Rapid read. A limitation has been included in the package insert.

E. faecalis had a vmj discrepancy rate of 2.7% (2/75) with the overnight

manual read. A footnote has been included in the Instruction for Use Manual.

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:

Enterococcus spp. interpretive criteria: ≤ 1000 (S), >1000 (R)

N. Proposed Labeling:

The expected value range, interpretive criteria and QC are included in the package insert. The labeling is sufficient and 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.