

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

A. 510(k) Number:

K071268

B. Purpose for Submission:

To add tetracycline at concentrations of 0.25-16 µg/mL 7- Dilution Sequence, 0.5-8 µg/mL 5-Dilution Breakpoint Sequence and 2- 8 µg/mL 3-Dilution Breakpoint Sequence for *Enterococci* and *Staphylococci*, to the Microscan® Synergies plus™ Gram-Positive MIC/Combo Panels.

C. Measurand:

Tetracycline 0.25- 16 µg/mL 7- Dilution Sequence

Tetracycline 0.5- 8 µg/mL 5-Dilution Breakpoint

Tetracycline 2- 8 µg/mL 3-Dilution Breakpoint

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 - Tetracycline

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 Panels - Tetracycline is intended 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 gram-positive *Enterococci* and *Staphylococci*. The MicroScan® Synergies plus™ Panels are read on the WalkAway® -SI System (including upgraded WalkAway® -40 or WalkAway® -96 to meet WalkAway® SI equivalence).

2. Indication(s) for use:

It is indicated for use for the addition of Tetracycline at concentrations 0.25- 16 µg/mL (7-Dilution MIC Sequence), 0.5-8 µg/mL (5-Dilution BP Sequence), and 2-8 µg/mL (3-Dilution BP Sequence), to the gram-positive test panel for testing of *Enterococci* spp. and *Staphylococci* spp. at 4.5- 16 hrs 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.
- Hold all susceptible (<8 µg/mL) *Enterococcus faecium* isolates to overnight reporting (16/18 hours)

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®, 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 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

MicroScan® Synergies plus™ 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	<16 hours 16 – 24 hours	Same
Results	Quantitative with qualitative interpretations	Same
Technology	Growth based	Same
Differences		
Item	Device	Predicate

Panels	Dried tetracycline in water with 5% broth	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
Instrument	WalkAway® -SI System or equivalent	autoScan® -4 or WalkAway®
Antibiotic	Tetracycline at 0.25- 16 µg/	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, or 18 hours (overnight instrument readings, manual readings) depending on the growth rate of the organism being tested. The time of final read is dependent on 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 10 isolates tested at six sites on three separate days in triplicate. The study included the testing on the Rapid (WalkAway® SI read at <16 hours), Overnight Instrument (WalkAway® 16-18 hour readings), and Overnight Manual (manual/visual read at 16-20 hours). There are three dilution sequences included in this submission using different reading algorithms namely 7-MIC Dilution sequence (i.e. 0.25 – 16 µg/mL), 5-Dilution Breakpoint Sequence (i.e. 0.5 – 8 µg/mL), and the 3-Dilution Breakpoint Sequence (i.e. 2 – 8 µg/mL). All dilution sequences were done on the same 10 isolates. The BP dilutions (5-Dilution Breakpoint Sequence, and the 3-Dilution

Breakpoint Sequence) with reproducibility reading were based only on category agreement. There were no isolates that did not grow. All results were >95% reproducible.

b. Linearity/assay reportable range:

Not Applicable

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

The recommended QC isolates, *E. faecalis* ATCC 29212 and *S. aureus* ATCC 29213 were tested a sufficient number of times with acceptable results most of the time with the reference method. Quality control results demonstrated the ability of the different reading parameters (manual and instrument) to produce acceptable results.

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

Organism	Conc in µg/mL	# reference	Results		
			MicroScan®		
Tetracycline			Manual overnight	Instrument overnight	<16 hrs instrument
<i>E. faecalis</i> ATCC 29212 Expected Range 8-32 µg/mL	<=0.06				
	0.12				
	0.25				
	0.5	1	1	1	1
	1				
	2				
	4				
	8	39	2		39
	16	84	104	116	89
	32	5	24	14	2
	>32				
<i>S. aureus</i> ATCC 29213 Expected Range CLSI: 0.12 – 1 µg/mL	<=0.06				
	0.12	5			14
	0.25	78	78	99	110
	0.5	50	55	36	6
	1	3	5		
	2	1			
	4		1		
	8			2	
	16				
	32				2
	>32			2	7

The 3 Dilution sequence, and 5 Dilution sequence breakpoint panels using separate reading algorithms also demonstrated acceptable quality control

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 six sites using fresh isolates supplemented with stock isolates. A total of 610 gram-positive *Staphylococci* and *Enterococci* were tested of which 564 were fresh isolates and 46 were stock isolates. There were 75 challenge isolates tested at two sites 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. The Rapid method 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 test device had a no growth rate of <10%.

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 with no difference apparent in the results.

The charts below demonstrates the performance of all three reading methods (Rapid instrument readings at <16 hours, overnight on the WalkAway® and manually read at 18 hours using the touchScan®-SR) with the 7-Dilution sequence when compared to the reference method.

Summary Table for the Rapid Instrument Read (7-Dilution Sequence)

	Total	EA	%EA	Total eval	EA of eval	%EA	CA	%CA	#R	min	maj	vmj
Efficacy	585	559	95.6	134	120	89.6	558	95.4	203	19	5	3
Challenge	66	58	87.9	12	9	75.0	60	90.9	29	2	4	0
Combined	651	617	94.8	146	129	88.4	618	94.9	232	21	9	3

Summary Table for the Overnight Instrument Read (7-Dilution Sequence)

	Total	EA	%EA	Total eval	EA of eval	%EA	CA	%CA	#R	min	maj	vmj
Efficacy	610	598	98.0	86	76	88.4	597	97.9	217	11	2	0
Challenge	75	75	100	14	14	100	74	98.7	30	1	0	0
Combined	685	673	98.2	100	90	90.0	671	98.0	247	12	2	0

Summary Table for the Overnight Manual Read (7-Dilution Sequence)

	Total	EA	%EA	Total eval	EA of eval	%EA	CA	%CA	#R	min	maj	vmj
Efficacy	610	604	99.0	105	99	94.3	601	98.5	217	8	1	0
Challenge	75	75	100	17	17	100	74	98.7	30	1	0	0
Combined	685	679	99.1	122	116	95.1	675	98.5	247	9	1	0

EA-Essential Agreement

CA-Category Agreement

R-resistant isolates

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 agrees exactly with the reference panel interpretation. Evaluable (Eval) are results that are within the test range and on scale.

Similar results were obtained when the algorithm for reading the 3 Dilution sequence with 2, 4 and 8 µg/mL wells and algorithm for reading the 5 Dilution sequence with 0.5, 1, 2, 4 and 8 wells were applied with no difference in CA. EA was not calculated for these readings since insufficient numbers of concentrations were available for the evaluation.

The *E. faecium* group had a higher than expected vmj error rate of 5.4% with the Rapid read method. However, no vmj errors were observed with the overnight instrument or overnight manual read methods. Therefore, a limitation statement will be included for this drug/bug combination, e.g., “Hold all susceptible (<8 µg/mL) *Enterococcus faecium* isolates to overnight reporting (16/18 hours).”

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 spp. and *Enterococcus* spp. ≤ 4 (S), 8 (I), ≥ 16 (R)

N. Proposed Labeling:

The expected value range, interpretive criteria and QC for gram positive panels 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.