

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

**A. 510(k) Number:**

K041150

**B. Purpose for Submission:**

To add Cefazolin to the Gram-Negative MIC/Combo Panels on the Synergies plus™ System

**C. Analyte:**

Cefazolin at 0.5 – 32 ug/mL

**D. Type of Test:**

Quantitative growth based AST test

**E. Applicant:**

Dade Behring – Dade MicroScan, Inc.

**F. Proprietary and Established Names:**

MicroScan® Synergies plus™ Gram-Negative 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

4. Panel:

83 Microbiology

**H. Intended Use:**

1. Intended use(s):

For use with MicroScan® Synergies plus™ panels read on the WalkAway® -SI System ( including upgraded WalkAway® -40 or WalkAway® -96 to meet WalkAway® SI equivalence). 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 gram-negative bacilli. (Enterobacteriaceae, glucose non-fermenters, and non-Enterobacteriaceae glucose fermenters).

2. Indication(s) for use:

The testing of cefazolin at concentrations of 0.5-32 ug/ml to the gram negative test panel for testing Enterobacteriaceae at 4.5-18 hours or 16-20 hours for a overnight reading

3. Special condition for use statement(s):
  - Do not report results for *Klebsiella oxytoca*.
  - All *Enterobacter spp.*, *Citrobacter freundii*, *Morganella morganii*, *Proteus vulgaris*, *Providencia spp.*, *Serratia spp.* or *Yersinia enterocolitica* will not be reported in the Software or patient reports because of natural resistance.
  - Turbidity method of inoculum preparation only.
  - For prescription use only.
4. Special instrument Requirements:

#### I. Device Description:

The MicroScan® rapID/S plus™ Panel contains microdilutions of each antimicrobial in various concentrations on dehydrated and dried panels with Mueller Hinton Broth and various nutrients. Each panel contains two control wells: a no-growth control well (contains water only/no nutrients or broth), and a growth control well (contains test medium without antibiotic). The panel is rehydrated and inoculated at the same time with 0.1 ml of suspension prepared by the turbidity method (inoculum equated to a McFarland 0.5 standard, transferred to inoculum water containing pluronic-D/F-a wetting solution).

#### J. Substantial Equivalence Information:

1. Predicate device name(s):  
MicroScan® rapID/S plus Gram Negative MIC/Combo Panels – gentamicin  
MicroScan® Dried Gram-Negative MIC/Combo Panels
2. Predicate K number(s):  
K020185  
K862140
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 gram-negative bacilli. (Enterobacteriaceae, glucose non-fermenters, and non-	same

	Enterobacteriaceae glucose fermenters).	
Specimen	Isolated colonies from culture used	Isolated colonies from culture used
Inoculum	Inoculum density to 0.5 McFarland standard	Inoculum density to 0.5 McFarland standard
Incubation	<16 hours 16 – 18 hours	< 16 hours 16-18 hours
Results	Quantitative with qualitative interpretations	Quantitative with qualitative interpretations
Technology	Growth based	Growth based
<b>Differences</b>		
<b>Item</b>	<b>Device</b>	<b>Predicate</b>
Panels	Dried cefazolin at 0.5-32 ug/ml	Dried gentamicin at 0.12-32 ug/ml
Reading	Uses both a early read and overnight methods in the same system	Overnight system uses only the overnight reading methods.
Inoculum preparation	Turbidity method of inoculation only.	Inoculum prepared from isolated colonies using either the Turbidity method or Prompt® system
Instrument	WalkAway® -SI System or equivalent	autoScan® -4 or WalkAway®
Antibiotic	Cefazolin at 0.5-32 ug/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”; NCCLS M7 (M100-S14) “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, 10, 12, 16, or 18 hours (overnight instrument readings, manual readings) depending on the growth rate of the organism being tested. The initial read is subtracted from the final read to minimize variations from all components of the system. 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  $2 \times 10^7$  cells/ml are not detected. Reading considerations are built into the reading for faster growing and slower growing organisms. Organisms that do not reach a specific threshold at 4.5 hours have the minimum threshold raised at 5.5 hours. This allows for fermenters (faster grower organisms) to be read at 4.5, 5.5 or 6.5 hours and delay the reading of non-fermenters

(slow growing) to 8, 10, 12 and up to 18 hours. Less than 16 hour readings use data from one read to the next to determine when the appropriate time for reading the MIC is. MICs that are clearly susceptible or clearly resistant can be reported earlier than those with MIC closer to the interpretative breakpoints. Indicator wells are also used to detect delayed mechanisms of resistance.

#### M. Performance Characteristics (if/when applicable):

##### 1. Analytical performance:

###### a. *Precision/Reproducibility:*

Reproducibility was demonstrated using 25 isolates tested at 3 sites on 3 separate days in triplicate. All isolates had a mode that was on scale. The study included the testing on the WalkAway® SI read at 4.5 to 18 hours if necessary, -20 hour readings and manual readings at 16-18 hours incubation. All results were >95% reproducible. An additional study was performed on readings performed at <16 hours on the WalkAway®SI with results that were >95% reproducible.

###### b. *Linearity/assay reportable range:*

Not applicable

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

The recommended QC isolate was tested >90 times with acceptable results on all testing days with the reference method. The percent that did not grow in the 4.5-16 hour window for the *E. coli* was 12.5%. Quality control results demonstrated the ability of the different reading parameters (manual and instrument) to produce acceptable results. There does appear to be a slight trend for the *E. coli* ATCC 25922 when read by the instrument in the 4.5 to 18 hour read times to be slightly more resistant.

Results						
Organism	Conc in ug/ml	# reference	MicroScan®			
			Strictly >16 hour incubation readings		Read when ready (4.5-18 hours)	
			Manual overnight	Instrument overnight	4.5-15h instrument	16-18 h instrument
E. coli ATCC 25922 Range 1-4	≤ 0.5					
	<b>1</b>	<b>45</b>	<b>96</b>	<b>100</b>	<b>12</b>	<b>4</b>
	<b>2</b>	<b>64</b>	<b>16</b>	<b>12</b>	<b>2</b>	<b>94</b>
	<b>4</b>					
	<b>8</b>					

There is a trend when reading the read when ready feature for the results of the E. coli at the 16-18 hour read time to be more resistant than the other MicroScan® readings.

Inoculum density control: A turbidity meter was used for the turbidity inoculation method. Colony counts were also performed using the turbidity method when inoculating both the dried MicroScan® panels and the frozen reference panels. The turbidity method of inoculation for test and all QC strains tested had an average inoculum that was in the range of  $2.4 \times 10^5$  to  $5.9 \times 10^5$

**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 performed at three sites using fresh isolates supplemented with stock isolates of *Enterobacteriaceae*. A comparison of the MicroScan® Dried Gram-Negative test panel results was made to the reference method conducted as recommended in the NCCLS standard M7-A6. Testing of the reference method and the MicroScan panels was performed at the same time. A challenge set was also 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. The chart below demonstrates the performance when comparing the Synergies plus™ and the reference method using the NCCLS interpretive criteria. The Synergies plus™ contains readings that were performed at times between 4.5 and 18 hours of incubation with 61% providing those results in <16 hours. 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.

	total	EA	%EA	Total evaluable	EA of evaluable	%EA	CA	%CA	#R	min	maj	vmj
<b>Clinical</b>	444	435	98%	308	301	97.7	414	93.2%	142	29	0	1
<b>Challenge</b>	75	73	97.3	68	66	97.1	68	90.7	11	5	1	1
<b>Combined</b>	519	508	97.9	376	367	97.6	482	92.9	153	31	1	2

↑ EA-Essential Agreement  
 ↑ CA-Category Agreement  
 R-resistant isolates

↑ maj-major discrepancies  
 vmj-very major discrepancies  
 min- minor discrepancies

Evaluations were also performed using the FDA approved interpretations (one well shift to less conservative) with acceptable performance also.

***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:

$\leq 8$  (S), 16 (I),  $\geq 32$  (R)

The interpretative criteria and QC are the same as recommended in NCCLS. All values will be included in the package insert.

**N. Conclusion:**

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.