

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

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

k033948

**B. Analyte:**

Gemifloxacin at 0.002-16 ug/mL AST

**C. Type of Test:**

Quantitative growth based detection algorithm using optics light detection

**D. Applicant:**

Dade Behring Inc.

Dade MicroScan Inc.

**E. Proprietary and Established Names:**

Dried Gram-Negative MIC/Combo panels

**F. Regulatory Information:**

1. Regulation section:  
866.1640 Antimicrobial Susceptibility Test Powder
2. Classification:  
Class II
3. Product Code:  
LRG-Instrument for Auto Reader & Interpretation of Overnight Antimicrobial Susceptibility Systems  
JWY - Manual Antimicrobial Susceptibility Test Systems  
LTT – Panels, Test, Susceptibility, Antimicrobial  
LTW – Susceptibility Test Cards, Antimicrobial
4. Panel:  
83 Microbiology

**G. Intended Use:**

1. Intended use(s):  
For use with MicroScan® Dried Gram Negative MIC/Combo Panels and Dried Gram Negative Breakpoint Combo Panels.  
MicroScan® panels are designed for use in determining antimicrobial agent susceptibility and/or identification to the species level of aerobic and facultatively anaerobic gram-negative bacilli.

The MicroScan® Dried Gram-Negative 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-negative bacilli.

2. Indication(s) for use:  
This will include the antibiotic gemifloxacin for testing the appropriate organism in the *Enterobacteriaceae* group.
3. Special condition for use statement(s):  
For Prescription use Only

The Prompt™ method of inoculation is an alternate method of inoculum preparation that is supported in the product insert along with the turbidity method. The stationary and log inoculum methods should not be used with this antibiotic.

4. Special instrument Requirements:  
These panels can be read manually, on the autoSCAN -4® or WalkAway® instrument systems.

#### **H. 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 prepared in water, then 0.1ml transferred to 25ml of inoculum water containing pluronic-D/F-a wetting solution). The panels are incubated at 35° C in a non-CO<sub>2</sub> incubator for 16-20 hours and read by visual observation for growth. Panels may also be read automatically with the WalkAway® or the AutoSCAN®4.

#### **I. Substantial Equivalence Information:**

1. Predicate device name(s):  
MicroScan® Dried Gram-Negative and Gram-Positive MIC/Combo Panels
2. Predicate K number(s):  
K862140
3. Comparison with predicate:

Similarities		
Item	Device	Predicate
Intended Use	For use with MicroScan® Dried Gram Negative MIC/Combo Panels and Dried Gram Negative Breakpoint Combo Panels. MicroScan® panels are designed for use in determining antimicrobial agent susceptibility and/or identification to the species level of aerobic and facultatively anaerobic gram-negative bacilli.	Same
Test Panel	Dried	Same
Instrument/manual	Both manual and instrument readings available.	Same
Technology	Growth based after 16 hours incubation	Same
Results	Report results as minimum inhibitory concentration (MIC) and categorical interpretation (SIR).	Same
Differences		
Item	Device	Predicate
Reading algorithm	Unique for gemifloxacin	Unique for each antibiotic
Test organism	<i>Enterobacteriaceae</i>	Gram positive and gram negative organisms
Inoculum preparation from colonies	Turbidity and Prompt™	All methods recommended in the package insert.

**J. 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-S13)  
“Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard”.

**K. Test Principle:**

After incubation in a non-CO<sub>2</sub> incubator for 16-20 hours, the minimum inhibitory concentration (MIC) for the test organisms read by determining the lowest antimicrobial concentration showing inhibition of growth. The panels are read either manually by observing growth or by instrumentation using the autoSCAN 4® or WalkAway® which uses an optics systems with growth algorithms to directly measure organism growth.

**L. Performance Characteristics (if/when applicable):**1. Analytical performance:a. *Precision/Reproducibility:*

Reproducibility was demonstrated using 10 isolates tested at 3 sites on 3 separate days in triplicate. All ten isolates had a mode that was on scale. The study included the testing of the following inoculum and reading variables; turbidity inoculum method and Prompt™ method of

inoculation with reading performed manually using a touchSCAN SR, autoSCAN 4® or the WalkAway® instrument. The following table provides the overall results for all combinations of these variables.

Difference in the number of dilutions between the mode of the MicroScan result and the actual result with each different variable for overall reproducibility							
Inoculation method	Read method	≥ Minus 2 dilutions	Minus 1 dilution	Exact	Plus 1 dilution	≥ Plus 2 dilutions	% reproducible
Turbidity	Manual(touchSCAN®)		14	212	43	1	99.6
Turbidity	WalkAway ®		16	234	16	4	98.5
Turbidity	autoSCAN® 4		14	231	21	4	98.5
Prompt™	Manual(touchSCAN®)	1	26	210	29	4	98.1
Prompt™	WalkAway ®		1	234	31	4	98.5
Prompt™	autoSCAN® 4			232	32	6	97.8

This demonstrates good reproducibility overall but the Prompt™ at one site using the autoSCAN®4 was <95%. As demonstrated in the table the Prompt™ instrument readings trend to a more resistant result but interestingly the prompt™ manual readings do not.

The reproducibility strains were also evaluated for inoculum density for the Prompt™ method with colony counts ranging from  $1 \times 10^5$  to  $99 \times 10^5$  with the same variability that was noticed in the Quality Control inoculum density studies.

*b. Linearity/assay reportable range:*

Not applicable

*c. Traceability (controls, calibrators, or method):*

Quality Control was performed daily with the turbidity method and with the Prompt™ selectively with the following results.

ORGANISM			RESULTS					
	ug/mL	ref	Turbidity inoculation			Prompt™ inoculation		
			Manual	autoSCAN®	WalkAway®	Manual	autoSCAN®	WalkAway®
<i>E. coli</i> ATCC 25922 Expected range 0.004-0.016 ug/mL	0.002							
	0.004	5	1			2		
	.008	104	108	85	85	93	79	82
	.016	6	6			20	5	3
	.03							
	.06							
	2							
<i>P aeruginosa</i> ATCC 27853 Expected	0.12							
	0.25	15	5	2		3		
	0.5	86	91	66	71	92	68	69

range 0.25-1 ug/mL	1	3	8	4	3	9	3	6
	2		1	1	1	2	2	1
	4						1	
	>16			2			2	

Quality control results demonstrated the ability of all variables of the procedure (reading and inoculation) to produce acceptable results with the organism intended for testing. There does not appear to be any tending in any of the methods since all appear to have the same mode, but the Prompt™ results were less reproducible than the turbidity method of inoculation. Also the *P. aeruginosa* with the Prompt™ method of inoculation and the autoSCAN® 4 had <95% of the results within the expected range. *P. aeruginosa* is not recommended for testing with gemifloxacin.

Inoculum density control: A turbidity meter was used for the turbidity inoculation method. The Prompt™ method of inoculation had colony counts performed periodically throughout the study to determine the average inoculum density since there is no visual check of the inoculum using this device. 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 the reference test had an average inoculum that was in the range of  $2.4 \times 10^5$  to  $4 \times 10^5$ , while the Prompt™ method of inoculation had far more variability with average inoculum ranges from  $5.4$  to  $14 \times 10^5$ . The inoculum of the Prompt™ method of inoculation generally provides a higher number of CFU with more variability than a method using a turbidity meter. The chart below shows this comparison using the average CFU at each site.

organism	Method of inoculation	Lowest CC x 10 <sup>5</sup>	Highest CC x 10 <sup>5</sup>	Average CC x 10 <sup>5</sup>
<i>E. coli</i> ATCC 25922	Prompt™	1.8	92	8.6
	Reference	1.6	4.9	3
<i>E. coli</i> ATCC 35218	Prompt™	3.2	16.3	9.6
	Reference	2.3	6.8	3.9
<i>P. aeruginosa</i> ATCC 27853	Prompt™	1.7	12.3	6.6
	Reference	2	7.2	3.7

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.

	total	EA	%EA	Total evaluable	EA of evaluable	%EA	CA	%CA	#R	min	maj	vmj
<b>Clinical</b>	302	297	98.3	293	288	98.3	291	96.4	42	11	0	0
<b>Challenge</b>	79	78	98.7	74	73	98.6	77	97.5	42	2	0	0
<b>Combined</b>	381	375	98.4	367	361	98.4	368	96.6	84	13	0	0

**EA**-Essential Agreement

**CA**-Category Agreement

**R**-resistant isolates

**maj**-major discrepancies

**vmj**-very major discrepancies

**min**- minor discrepancies

Evaluable results are those that fall within the test range of the reference method and could also be on-scale with the new device if within the plus/minus one well variability. EA is when there is agreement between the reference method and the MicroScan® within plus or minus one serial two-fold dilution of antibiotic. CA is when the interpretation of the reference method agrees exactly with the interpretation of the MicroScan® result.

The challenge set of organisms was also tested using the Prompt™ method of inoculation with all reading methods and the turbidity method of inoculation with the WalkAway® and the autoSCAN®4. This included seventy nine challenge isolates that were tested at one site. The inoculum was prepared by the turbidity or Prompt™ method and incubated in the WalkAway® instrument. All panels had additional readings performed after the WalkAway® reading was completed using the autoSCAN®-4 and then manually on the touchSCAN®-SR.

Although all methods were  $\geq 95$  % essential agreement, there is more variability with the Prompt™ method with results trending to a more resistant result. The Prompt™ method of inoculation also has the higher CFU/ml in the final inoculum.

The following table demonstrates the performance based on essential agreement and category agreement for the challenge set and the different inoculation and reading methods.

	total	EA	%EA	Total evaluable	EA of evaluable	%EA	CA	%CA	#R	min	maj	vmj
<b>Turbidity/ manual</b>	79	78	98.7	74	73	98.6	77	97.5	42	2	0	0
<b>Turbidity/ WalkAway®</b>	79	79	100	74	74	100	78	98.7	42	1	0	0
<b>Turbidity/ autoSCAN®</b>	79	78	98.7	74	73	98.6	77	97.5	42	1	1	0
<b>Prompt™/ manual</b>	79	75	94.9	74	70	94.6	76	96.2	42	3	0	0
<b>Prompt™/ WalkAway®</b>	79	77	97.4	74	72	97.3	76	96.2	42	2	0	1
<b>Prompt™/ autoSCAN®</b>	79	76	96.2	74	71	95.9	76	96.2	42	2	0	1

Although the EA and CA are all acceptable there is a reduction of EA when using the Prompt™ method and the line data shows a trend to a more resistant result for the Prompt™ results.

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:

*Enterobacteriaceae* only.  $\leq 0.25$  (S), 0.5 (I), 1 (R)

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

## M. Conclusion:

The reproducibility, quality control results and overall performance is acceptable as described in the “Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA” which was used in the design and evaluation of the study. The appropriate control organisms are included in the labeling and are the same as those recommended in the NCCLS M7-(M100-S14) document. This performance as compared to a standard method demonstrates substantial equivalency to the predicate.