

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

A. 510(k) Number:

k031602

B. Analyte:

Nitrofurantoin 1-256 ug/ml AST

C. Type of Test:

Quantitative <16 hour growth based with Colorimetric Optics System

D. Applicant:

Dade Behring Inc.

E. Proprietary and Established Names:

MicroScan® rapID/S plus™ Gram-Negative MIC/Combo Panels

F. Regulatory Information:

1. Regulation section:
866.1645 Short-Term Antimicrobial Susceptibility Test System
866.1640 Antimicrobial Susceptibility Test Powder
2. Classification:
II
3. Product Code:
LON System, Test, Automated, Antimicrobial Susceptibility, Short Incubation
JWY Manual Antimicrobial Susceptibility Test Systems
LRG Instrument for auto reader & Interpretation of Overnight Susceptibility System
4. Panel:
83 Microbiology

G. Intended Use:

1. Intended use(s):
For use with MicroScan rapID/S *plus*™ panels read on the WalkAway® -SI System or equivalent (upgraded WalkAway® -40 or WalkAway® -96). 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 MicroScan® rapID/S *plus*™ 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. After inoculation, panels are incubated for 4.5-18 hours at 35° C +/- 1° C, in a WalkAway SI or equivalent, and read by MicroScan® Instrumentation. Additionally panels may be incubated in a non-CO² incubator and the AST portions can be read visually according to the Package Insert. Nitrofurantoin at concentrations of 1-256 ug/ml will be added

to the gram negative test panel for testing Enterobacteriaceae at less than (<)16 hours or greater than (>)16 hours for an overnight reading.

3. Special condition for use statement(s):

A comment will follow for all appropriate organism that states “ Due to expected natural resistance to Nitrofurantoin, Rapid and Overnight MIC and interpretive results with *Morganella morganii*, *Proteus spp.*, *Providencia spp.* or *Serratia spp.* will not be reported in the Software or patient reports”.

4. Special instrument Requirements:

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).

I. Substantial Equivalence Information:

1. Predicate device name(s):

MicroScan® rapID/S plus™ Gram Negative MIC/Combo Panels -gentamicin

2. Predicate K number(s):

K020185

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
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 instrument read ≥ 16 hours instrument read or manual read	< 16 hours instrument read ≥ 16 hours instrument read or manual read
results	Quantitative with qualitative interpretations	Quantitative with qualitative interpretations
Differences		
Item	Device	Predicate
panels	Dried nitrofurantoin at 1-256 ug/ml	Dried gentamicin at 0.12-32 ug/ml

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:

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 2×10^7 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 growing 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 16 hours. If there is insufficient amount of growth at 16 hours the panels will be held an additional amount of time to determine an overnight reading.

L. Performance Characteristics (if/when applicable):

1. Analytical performance:

a. *Precision/Reproducibility:*

A study was conducted on twenty five on-scale organisms tested one time at three different sites. These were read on the MicroScan® rapID/S *plus*™ Gram-Negative MIC panels at <16 hours, overnight (>16 hours) read manually or on the WalkAway SI system. All results were >95% reproducible with the mode of the test result.

b. *Linearity/assay reportable range:*

Not applicable

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

The recommended QC isolate was tested with acceptable results on all testing days with the reference method. The percent of *E. coli* ATCC 25922 that did not grow in time for the <16 hour reading was 2.7%. The results for the manual readings (Man) and the overnight instrument (≥ 16) readings were all acceptable.

ORGANISM		RESULTS			
	Conc in ug/ml	# reference	MicroScan		
			Man	≥ 16 h	<16h
E. coli ATCC 25922 Range 4-16	2				
	4				4
	8	108	109	110	105
	16	1	3	2	
	32				

Inoculum Density checks were controlled using turbidity meter. Colony counts were also performed weekly.

- 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:*

Broth dilution reference panels prepared according to the recommendations of the NCCLS M7. Clinical testing was performed at three sites on 531 isolates using the turbidity inoculum method for testing. This group had a “no growth” rate of 1.5% at <16 hour read time but were available at a later read time. The table below presents the results of the remaining *Enterobacteriaceae* after excluding the organisms listed in the limitation statement that MicroScan does not claim for testing with nitrofurantoin. The < 16 hour results demonstrated trending with more values one well more susceptible when compared to the reference method. A set of sixty challenge organisms were tested at one site. The performance of those that read at <16 hours is included in the table below. There were a large number of minor errors which is reflected by the large number of results that are near the interpretive cutoffs (evaluable results). These have very good essential agreement (plus or minus one well of the reference method) but most of the minor errors had a MIC on the MicroScan® rapID/S *plus*™ more susceptible than the reference by one serial dilution of nitrofurantoin.

The summary chart of <16 hour readings of *Enterobacteriaceae*

	total	EA	%EA	Total evaluable	EA of evaluable	%EA	CA	%CA	#R	min	maj	vmj
Clinical	523	519	99.2	514	512	99.6	457	87.4	64	66	0	0
Challenge	60	58	96.7	60	58	96.7	51	85	6	9	0	0
Combined	583	577	99	574	570	99.3	508	87.1	70	75	0	0

EA-Essential Agreement

CA-Category Agreement

R-resistant isolates

maj-major discrepancies

vmj-very major discrepancies

min- minor discrepancies

The challenge set of organisms were also evaluated with the ≥ 16 hour readings performed on the WalkAway and also manual readings. This performance was at least as good as the <16 hour readings with no major or very major errors. The comparison to the expected result demonstrated that although there was very good essential agreement for all reading methods the <16 hour readings were read as more susceptible as compared to the expected result than any other method. The chart below demonstrates that when the same isolates are tested on all three reading methods the rapid results more frequently produce a more susceptible result while still performing in essential agreement to the expected reference method result. The table below demonstrates that the ≥ 16 hour

instrument readings and the ≥ 16 hour manual readings were in exact agreement with the expected about 80% and 87% of the time respectively while the <16 hour readings were in exact agreement about 63% of the time with the rest of the result falling in the more susceptible range.

	Two dilution more susceptible	One dilution more susceptible	Exact agreement with reference method	One dilution more resistant
<16 hour	2	20	38	
≥ 16 hour		5	48	7
\geq manual		6	52	2

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):

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

≤ 32 (S); 64 (I); ≥ 128 (R)

These interpretive criteria, the quality control organisms and their expected value range are the same as that recommended in the NCCLS M7 and will be included in the package insert.

M. Conclusion:

This demonstrates that the MicroScan® rapID/S *plus*TM gram negative panels with nitrofurantoin at 1-256 ug/ml are substantially equivalent to the predicate when compared to the reference method as recommended in the “Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test (AST) Systems; Guidance for Industry and FDA”