

Multicenter Evaluation of Meropenem/Vaborbactam MIC Results for *Enterobacteriaceae* Using MicroScan Dried Gram Negative MIC Panels

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ABSTRACT

Background: A multicenter study was performed to evaluate the accuracy of meropenem/vaborbactam on a MicroScan Dried Gram Negative MIC (MSDGN) Panel when compared to frozen CLSI broth microdilution reference panels.

Material/methods: For efficacy, an evaluation was conducted at three sites by comparing MICs obtained using the MSDGN panel to MICs using a CLSI broth microdilution reference panel. A total of 670 *Enterobacteriaceae* clinical isolates were tested using the turbidity and Prompt® methods of inoculation. MSDGN panels were incubated at 35 ± 2°C and read on the WalkAway System, the autoSCAN-4 instrument, and read visually. Read times for the MSDGN panels were at 16-20 hours. Frozen reference panels, prepared according to ISO/CLSI methodology, were inoculated using the turbidity inoculation method. All frozen reference panels were incubated at 35 ± 2°C and read visually. Frozen reference panels were read at 16-18 hours. CLSI breakpoints (µg/ml) used for interpretation of MIC results were: *Enterobacteriaceae* ≤4/8 S, 8/8 I and ≥ 16/8 R.

Results: When compared to frozen reference panel results, essential and categorical agreements for all clinical isolates tested are as follows:

Read Method	Essential Agreement %		Categorical Agreement %		Very Major Errors %		Major Errors %		Minor Errors %	
	T	P	T	P	T	P	T	P	T	P
Visually	98.7 (661/670)	95.8 (642/670)	99.9 (669/670)	99.9 (669/670)	0 (0/1)	0 (0/1)	0.2 (1/669)	0.2 (1/669)	0 (0/670)	0 (0/670)
WalkAway	99.0 (663/670)	98.5 (660/670)	99.9 (669/670)	99.9 (669/670)	0 (0/1)	0 (0/1)	0.2 (1/669)	0.2 (1/669)	0 (0/670)	0 (0/670)
autoSCAN-4	99.0 (663/670)	97.6 (654/670)	99.9 (669/670)	99.9 (669/670)	0 (0/1)	0 (0/1)	0.2 (1/669)	0.2 (1/669)	0 (0/670)	0 (0/670)

T = Turbidity inoculation method, P = Prompt inoculation method

Conclusions: This multicenter study showed that meropenem/vaborbactam MIC results for *Enterobacteriaceae* obtained with the MSDGN panel correlate well with MICs obtained using frozen reference panels using CLSI interpretive criteria.

INTRODUCTION

A multicenter study was performed to evaluate the performance of a MicroScan Dried Gram Negative MIC panel with meropenem/vaborbactam using *Enterobacteriaceae* isolates with CLSI interpretive breakpoints.

METHODS

Study Design: MicroScan Dried Gram Negative MIC panels were tested concurrently with a CLSI frozen broth microdilution reference panel at three sites using both the turbidity and Prompt Inoculation methods. A total of 670 *Enterobacteriaceae* clinical isolates were tested among the three sites.

Quality Control Expected Results, CLSI M100-ED29*

Escherichia coli ATCC 25922: ≤0.03/8 – 0.06/8 µg/ml
Pseudomonas aeruginosa ATCC 27853: 0.12/8 – 1/8 µg/ml
Escherichia coli ATCC 35218 : ≤0.03/8 – 0.06/8 µg/ml
Klebsiella pneumoniae ATCC 700603: ≤0.03/8 – 0.06/8 µg/ml
Klebsiella pneumoniae ATCC BAA-1705: ≤0.03/8 – 0.06/8 µg/ml

*dilutions are extrapolated to validation panel

METHODS (Continued)

Panels

•Frozen reference and MicroScan Dried Gram Negative MIC panels contained two-fold doubling dilutions of meropenem/vaborbactam 0.03/8 – 64/8 µg/ml in cation-adjusted Mueller-Hinton broth.

•Reference panels were prepared and frozen following CLSI/ISO recommendations.

Quality Control

•Quality control (QC) testing was performed daily using ATCC 25922 *E. coli*, ATCC 27853 *P. aeruginosa*, ATCC 35218 *E. coli*, ATCC 700603 *K. pneumoniae*, ATCC BAA-1705 *K. pneumoniae* using extrapolated CLSI M100-ED29 QC ranges based on the panel dilutions.

Panel Inoculation, Incubation, and Reading

•All isolates were subcultured onto trypticase soy agar (TSA) with 5% sheep blood and incubated for 18-24 hours at 34-37°C prior to testing. Isolates from frozen stocks were subcultured twice before testing.

•Inoculum suspensions for each strain were prepared with the direct standardization (turbidity standard) method for MSDGN MIC and frozen reference panels. MSDGN MIC panels were also inoculated using the Prompt Inoculation method.

•Following inoculation, MSDGN MIC panels were incubated at 35 ± 2°C in the WalkAway system for 18 ± 2 hours. All panels were read by the WalkAway, autoSCAN-4, and visually.

Data Analysis

•Essential Agreement (EA) = MSDGN panel MIC within +/- 1 dilution of the frozen reference result MIC.

•Categorical Agreement (CA) = MSDGN panel and reference categorical results (S, I, R) agree using CLSI breakpoints for *Enterobacteriaceae*. (Table 1).

Table 1. Meropenem/Vaborbactam (CLSI M100-ED29) Interpretive Breakpoints (µg/ml)

Organism Group	Susceptible	Intermediate	Resistant
<i>Enterobacteriaceae</i>	≤ 4/8	8/8	≥ 16/8

•Major Errors = Frozen reference MIC is S and MSDGN panel MIC is R; calculated for susceptible strains only.

$$\% \text{ Major Errors} = \frac{\text{No. Major Errors}}{\text{Total No. S Isolates tested}} \times 100$$

•Very Major Errors = Frozen reference is R and MSDGN panel MIC is S; calculated for resistant strains only.

$$\% \text{ Very Major Errors} = \frac{\text{No. Very Major Errors}}{\text{Total No. R Isolates tested}} \times 100$$

•Minor Errors = Frozen reference is S or R when MSDGN panel MIC is I or MSDGN panel MIC is S or R when frozen reference is I; calculated for all isolates tested.

$$\% \text{ Minor Errors} = \frac{\text{No. Minor Errors}}{\text{Total No. Isolates tested}} \times 100$$

RESULTS

Efficacy (Tables 2 and 3)

•A total of 670 *Enterobacteriaceae* clinical isolates were tested among three sites. MSDGN panels were inoculated using the turbidity inoculation method.

•Essential Agreement for *Enterobacteriaceae* between MSDGN panel and frozen reference panel was 98.7% (661/670) for manual read method, 99.0% (663/670) for WalkAway System, 99.0% (663/670) for autoSCAN-4 instrument using the turbidity inoculation method.

•Categorical Agreement for *Enterobacteriaceae* between MSDGN panel and frozen reference panel was 99.9% (669/670) for manual read method, 99.9% (669/670) for WalkAway System, 99.9% (669/670) for autoSCAN-4 instrument using the turbidity inoculation method.

Table 2. Clinical Isolates - Turbidity Inoculation Method

Read Method	Essential Agreement		Categorical Agreement		Minor Errors		Major Errors		Very Major Errors	
	No.	%	No.	%	No.	%	No.	%	No.	%
Manual	661/670	98.7	669/670	99.9	0/670	0.0	1/669	0.2	0/1	0.0
WalkAway	663/670	99.0	669/670	99.9	0/670	0.0	1/669	0.2	0/1	0.0
autoSCAN-4	663/670	99.0	669/670	99.9	0/670	0.0	1/669	0.2	0/1	0.0

•A total of 670 *Enterobacteriaceae* clinical isolates were tested among three sites MSDGN panels were inoculated using the Prompt inoculation method.

•Essential Agreement for *Enterobacteriaceae* between MSDGN panel and frozen reference panel was 95.8% (642/670) for manual read method, 98.5% (660/670) for WalkAway System, 97.6% (654/670) for autoSCAN-4 instrument using the Prompt inoculation method.

•Categorical Agreement for *Enterobacteriaceae* between MSDGN panel and frozen reference panel was 99.9% (669/670) for manual read method, 99.9% (669/670) for WalkAway System, 99.9% (669/670) for autoSCAN-4 instrument using the Prompt inoculation method.

Table 3. Clinical Isolates – Prompt Inoculation Method

Read Method	Essential Agreement		Categorical Agreement		Minor Errors		Major Errors		Very Major Errors	
	No.	%	No.	%	No.	%	No.	%	No.	%
Manual	642/670	95.8	669/670	99.9	0/670	0.0	1/669	0.2	0/1	0.0
WalkAway	660/670	98.5	669/670	99.9	0/670	0.0	1/669	0.2	0/1	0.0
autoSCAN-4	654/670	97.6	669/670	99.9	0/670	0.0	1/669	0.2	0/1	0.0

Performance of meropenem/vaborbactam when testing *Morganella morganii* using the Prompt Inoculation system with the autoSCAN-4 or manual read methods were outside of essential agreement compared to the reference method and should be tested using the turbidity inoculation method.

Quality Control (Tables 4 and 5)

•Overall QC results for the frozen reference panel were 99.2-100% in range for ATCC 25922 *E. coli*, ATCC 27853 *P. aeruginosa*, ATCC 35218 *E. coli*, ATCC 700603 *K. pneumoniae*, ATCC BAA-1705 *K. pneumoniae*

Table 4. Quality Control - Turbidity Inoculation Method

Organism	QC Range (µg/mL)	Percent (%) in Range			
		Ref	Manual	WalkAway	autoSCAN-4
<i>E. coli</i> ATCC 25922	≤0.03/8-0.06/8	100%	120/121 99.2%	119/120 99.2%	120/121 99.2%
<i>P. aeruginosa</i> ATCC 27853	0.12/8-1/8	100%	121/121 100%	121/121 100%	121/121 100%
<i>E. coli</i> ATCC 35218	≤0.03/8-0.06/8	100%	118/118 100%	117/117 100%	118/118 100%
<i>K. pneumoniae</i> ATCC 700603	≤0.03/8-0.06/8	99.2%	112/117 95.7%	112/117 95.7%	112/117 95.7%
<i>K. pneumoniae</i> ATCC BAA-1705	≤0.03/8-0.06/8	100%	111/117 94.9%	111/117 94.9%	111/117 94.9%

Table 5. Quality Control - Prompt Inoculation Method

Organism	QC Range (µg/mL)	Percent (%) in Range			
		Ref	Manual	WalkAway	autoSCAN-4
<i>E. coli</i> ATCC 25922	≤0.03/8-0.06/8	100%	121/121 100%	121/121 100%	121/121 100%
<i>P. aeruginosa</i> ATCC 27853	0.12/8-1/8	100%	118/121 97.5%	117/120 97.5%	118/121 97.5%
<i>E. coli</i> ATCC 35218	≤0.03/8-0.06/8	100%	117/118 99.2%	116/117 99.1%	117/118 99.2%
<i>K. pneumoniae</i> ATCC 700603	≤0.03/8-0.06/8	99.2%	112/118 94.9%	112/118 94.9%	112/118 94.9%
<i>K. pneumoniae</i> ATCC BAA-1705	≤0.03/8-0.06/8	100%	116/116 100%	117/117 100%	116/117 99.1%

CONCLUSION

This multicenter study showed that meropenem/vaborbactam MIC results for *Enterobacteriaceae* obtained with the MSDGN panel correlate well with MICs obtained using frozen reference panels using CLSI interpretive criteria.

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