Validation of Cefepime-Taniborbactam MIC Antimicrobial Susceptibility Test for MicroScan Dried Gram-Negative MIC Panels from a Multicenter Assessment of Enterobacterales and *Pseudomonas aeruginosa*

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ABSTRACT

Background: Cefepime-taniborbactam is an investigational agent with activity against carbapenem- and multidrug-resistant Enterobacterales and *Pseudomonas aeruginosa*.[1] Given the need for accurate antimicrobial susceptibility testing results to support patient care decisions, we conducted a multicenter study with clinical isolates of Enterobacterales and *Pseudomonas aeruginosa* on an investigational MicroScan Dried Gram-Negative MIC (MSDGN) panel with cefepime-taniborbactam.[2]

Materials/Methods: MSDGN panels were evaluated at three clinical sites by comparing MIC values obtained using the MSDGN panels to MICs utilizing a CLSI broth microdilution reference panel. The study included a total of 490/491 Enterobacterales and 65 *Pseudomonas aeruginosa* clinical isolates tested using the Prompt® and turbidity methods of inoculation during the combined phases of efficacy and challenge. MSDGN panels were incubated at 35 ± 1°C and read on the WalkAway System, the autoSCAN-4 instrument, and visually at 16-20 hours. Frozen reference panels were prepared according to CLSI/ISO methodology, incubated for 16-20 hours and read visually.

Results: Essential agreement was calculated compared to MIC results from frozen reference panels for all isolates tested in efficacy and challenge and found in the following table.

Table 1. Enterobacterales and *Pseudomonas aeruginosa* Essential Agreement

Read Method	Enterobacterales Essential Agreement %		*Pseudomonas aeruginosa* Essential Agreement %	
	Prompt	Turbidity	Prompt	Turbidity
WalkAway	90.0 (441/490)	99.2 (487/491)	100.0 (65/65)	100.0 (65/65)
autoSCAN-4	94.3 (462/490)	99.0 (486/491)	98.5 (64/65)	98.5 (64/65)
Manual	92.7 (454/490)	99.2 (487/491)	100.0 (65/65)	100.0 (65/65)

Prompt = Prompt inoculation method
Turbidity = Turbidity inoculation method

Conclusion: Cefepime-taniborbactam MIC results for Enterobacterales and *Pseudomonas aeruginosa* obtained with the MSDGN panel correlate well with MICs obtained using frozen reference panels in this multicenter study.

INTRODUCTION

Data from a multicenter study evaluated the performance of a MSDGN MIC panel with cefepime-taniborbactam using Enterobacterales and *Pseudomonas aeruginosa.* Cefepime-taniborbactam is an investigational agent with activity against carbapenem- and multidrug-resistant Enterobacterales and *Pseudomonas aeruginosa*.[1]

METHODS

Study Design: MSDGN 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 490/491 Enterobacterales and 65 *Pseudomonas aeruginosa* clinical isolates were tested among the three sites.

Quality Control Expected Results
Escherichia coli NCTC 13353
- ≤0.25/4 – 1/4 µg/ml (MSDGN panel)
- 0.12/4 – 1/4 µg/ml (CLSI M100-Ed33)
- ≥64 µg/ml (for cefepime reference panel only to confirm integrity of *E. coli* NCTC 13353)

Pseudomonas aeruginosa ATCC 27853
- 0.5/4 – 4/4 µg/ml (MSDGN panel and CLSI M100-Ed33)

Klebsiella pneumoniae ATCC BAA-1705
- ≤0.25/4 – 0.5/4 µg/ml (MSDGN panel)
- 0.12/4 – 0.5/4 µg/ml (CLSI M100-Ed33)

Panels
MSDGN MIC panels contained two-fold doubling dilutions of cefepime-taniborbactam 0.06/4 – 64/4 µg/ml in cation-adjusted Mueller-Hinton broth. Reference panels (0.06/4 – 64/4 µg/ml dilutions) were prepared and frozen according to CLSI M07-Ed11 standards. Dilutions evaluated are 0.25/4 – 64/4 µg/ml.

Quality Control
Quality control (QC) testing was performed daily using NCTC 13353 *E. coli*, ATCC 27853 *P. aeruginosa*, and ATCC BAA-1705 *K. pneumoniae* for a minimum of 20 replicates per site.

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 35±2ºC 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, frozen reference panels were incubated at 35±2ºC and read visually at 16-20 hours for Enterobacterales and *P. aeruginosa*. MSDGN MIC panels were incubated at 35±1ºC in the WalkAway system for 18 hours. All MSDGN 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) was not evaluated because there are no FDA, CLSI, or EUCAST breakpoints.
Bias = For all on-scale isolates irrespective of reference/test MIC result, |(% test results above reference)–(% test results below references)|. A bias of ≤30% is considered indicative of random variation.

RESULTS

Table 2. Enterobacterales Clinical Isolates - Prompt Inoculation Method

Read Method	Essential Agreement		Bias	
	No.	%	%	Trend
WalkAway	441/490	90.0	42.6	Right Shift
autoSCAN-4	462/490	94.3	15.9	No Bias
Manual	454/490	92.7	33.7	Right Shift

Table 3. *P. aeruginosa* Clinical Isolates - Prompt Inoculation Method

Read Method	Essential Agreement		Bias	
	No.	%	%	Trend
WalkAway	65/65	100.0	1.6	No Bias
autoSCAN-4	64/65	98.5	12.7	No Bias
Manual	65/65	100.0	11.3	No Bias

Table 4. Enterobacterales Clinical Isolates - Turbidity Inoculation Method

Read Method	Essential Agreement		Bias	
	No.	%	%	Trend
WalkAway	487/491	99.2	57.7	Left Shift
autoSCAN-4	486/491	99.0	55.8	Left Shift
Manual	487/491	99.2	51.9	Left Shift

Table 5. *P. aeruginosa* Clinical Isolates - Turbidity Inoculation Method

Read Method	Essential Agreement		Bias	
	No.	%	%	Trend
WalkAway	65/65	100.0	19.4	No Bias
autoSCAN-4	64/65	98.5	27.4	No Bias
Manual	65/65	100.0	12.9	No Bias

Quality Control (Tables 6 and 7)
Overall quality control results were ≥95% within range for each read and inoculation method on the dried test panel for *E. coli* NCTC 13353, *P. aeruginosa* ATCC 27853, and *K. pneumoniae* ATCC BAA-1705. *E. coli* NCTC 13353 includes QC development data only for the autoSCAN-4 read method with Prompt inoculation method. Quality control results were >95% within range for the frozen reference panel, which were inoculated using the turbidity method and read visually. The number of replicates and percentage within QC range are indicated in Tables 6 and 7. Variations in total number tested for each read method are due to technical error elimination.

Table 6. Quality Control – Frozen Reference Results

Organism	QC Range (µg/mL)	Manual
		Turbidity
E. coli NCTC 13353	≤0.25/4 – 1/4	100.0% (79/79)
P. aeruginosa ATCC 27853	0.5/4 – 4/4	100.0% (77/77)
K. pneumoniae ATCC BAA-1705	≤0.25/4 – 0.5/4	98.7% (78/79)

Table 7. Quality Control – Dried Test Results

Organism	QC Range (µg/mL)	WalkAway		autoSCAN-4		Manual	
		Prompt	Turbidity	Prompt	Turbidity	Prompt	Turbidity
E. coli NCTC 13353	≤0.25/4 – 1/4	96.2% (76/79)	100.0% (79/79)	97.2% (210/216)	100.0% (79/79)	94.9% (75/79)	100.0% (79/79)
P. aeruginosa ATCC 27853	0.5/4 – 4/4	100.0% (77/77)	100.0% (77/77)	100.0% (77/77)	100.0% (77/77)	100.0% (77/77)	100.0% (77/77)
K. pneumoniae ATCC BAA-1705	≤0.25/4 – 0.5/4	98.7% (78/79)	97.5% (77/79)	98.7% (78/79)	97.5% (77/79)	98.7% (78/79)	97.5% (77/79)

CONCLUSION

This multicenter study showed that cefepime-taniborbactam MIC results for Enterobacterales and *Pseudomonas aeruginosa* obtained with the MSDGN panel correlate well with MICs obtained using frozen reference panels.

1. Pending approval by the United States Food and Drug Administration; not available for use in the U.S. Not for Distribution in the United States.
2. Pending submission and clearance by the United States Food and Drug Administration; not yet available for in vitro diagnostic use in the US.
For Investigational Use Only. The performance characteristics of this product have not been established.