Paper # **D-223**

Multi-Site Evaluation of Moxifloxacin (MOX) and Gatifloxacin (GAT) on the Sensititre® Dried Susceptibility Plate Compared to NCCLS Microdilution Method

Authors: T. Kelley[1*], S. Killian[1], C.C. Knapp[1], N. Holliday[1], M.R. Jacobs[2], A. Windau[2], S. Bajaksouzian[2], E. Smith Moland[3], T. J. Lockhart[3], L. B. Olson[3], J. A. Black[3]

1. TREK Diagnostic Systems, Cleveland, OH 2. University Hospital, Cleveland, OH
3. Creighton University, Omaha, NE

TREK DIAGNOSTIC SYSTEMS
982 Keynote Circle, Suite 6
Cleveland, OH 44131
800.871.8909 • www.trekds.com

ABSTRACT

Background: A multi-site evaluation was undertaken to compare the performance of MOX (Bayer, West Haven, CT) and GAT (BMSQ, Princeton, NJ) on the Sensititre 18 – 24 hour susceptibility dried plate to the NCCLS M7-broth microdilution reference method, testing both automated and manual reading methods. The range tested for both MOX and GAT was (0.004 – 16 µg/ml).
Methods: The clinical evaluation was conducted at three sites and consisted of 306 fresh clinical gram-negative isolates and 75 CDC challenge isolates, which included both *Enterobacteriaciae* and *non-Enterobacteriaciae.* Recommended quality control organisms were tested daily and were within the NCCLS expected quality control range.
Results*: For MOX, when the automated reading method was compared to the reference method the total isolates' Essential Agreement (EA) and Categorical Agreement (CA) were 96.3% and 96.9%, respectively. When the manual reading method was compared to the reference method the EA and CA were 97.6% and 97.9%, respectively.
For GAT, when the automated reading method was compared to the reference method the total isolates' EA and CA were 97.4% and 98.4%, respectively. When the manual reading method was compared to the reference method the EA and CA were 97.6% and 99%, respectively.
For MOX, the reproducibility EA and CA were 97.3% and 92.0% for the automated method and 100% and 98.7% for the manual method. For GAT, the reproducibility EA and CA were 98.7% and 96% for the automated method and 100% and 97.3% for the manual method.
Conclusions: This multi-site evaluation indicates that the performance of MOX and GAT on the Sensititre 18-24 hour susceptibility system, using either the automated or manual reading method, was equivalent to its performance using the NCCLS M7-broth microdilution reference method.

*Abstract has been modified

PURPOSE OF THE STUDY

To evaluate the performance of Moxifloxacin and Gatifloxacin on the Sensititre 18 – 24 hour susceptibility plate compared to the NCCLS microdilution method (M7 – A6).

MATERIALS & METHODS

Organisms: The testing at 3 sites consisted of the following:
- 306 clinical gram-negative isolates
- 75 CDC challenge isolates
- 25 reproducibility isolates
- Quality Control strains

Antibiotics

Antimicrobials Tested	Range Tested	Supplied By
Moxifloxacin (MOX)	0.004 – 16	Bayer
Gatifloxacin (GAT)	0.004 – 16	BMSQ

Susceptibility Testing Methods:
- Each isolate was tested using a Sensititre 18 – 24 hour susceptibility plates. The plates were set-up and tested according to the manufacturers' instructions.
- The reference plates were tested according to the microdilution methods published by the National Committee for Clinical Laboratory Standards (NCCLS, M7-A6).
- The approved primary "Indications for Use", and clinical significance of Gatifloxacin is for: *Escherichia coli, Klebsiella pneumoniae,* and *Proteus mirabilis. In vitro* data, without clinical correlation is provided for: *Acinetobacter lwoffi, Citrobacter koseri, Citrobacter freundii, Enterobacter cloacae, Klebsiella oxytoca, Morganella morganii,* and *Proteus vulgaris.*
- The approved primary "Indications for Use", and clinical significance of Moxifloxacin is for: *Klebsiella pneumoniae. In vitro* data, without clinical correlation is provided for: *Citrobacter freundii, Enterobacter cloacae, Klebsiella oxytoca,* and *Proteus mirabilis.*

Isolates Tested

Organisms	Clinical	Challenge	Total
E. coli	60	13	73
Klebsiella species	40	10	50
Enterobacter species	38	10	48
Proteus species	30	6	36
Providencia species	11	5	16
Pseudomonas aeruginosa	52	11	63
Acinetobacter species	15	6	21
*All others tested	60	14	74
Total	**306**	**75**	**381**

* *Citrobacter spp., Morganella spp., Serratia spp., Aeromonas spp.*

RESULTS

Gatifloxacin – Automated Read Method
MIC Distribution for Clinical and Challenge Isolates vs. Gatifloxacin

Test Results \ Reference Results	0.004	0.008	0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	>16
0.004														
0.008		4	2											
0.015			44	13	1									
0.03			5	55	20									
0.06				7	19	10								
0.12				4	5	35	10							
0.25				1	2	9	20	3						
0.5							2	16	10					
1						1	1	1	13	7				
2										13	6			
4											10			
8												12	5	
16													4	1
>16													2	8
TOTALS	0	4	51	80	47	55	33	20	23	20	16	12	11	9

Categorical Interpretations: Susceptible ≤ 2, Intermediate = 4, Resistant ≥ 8

Moxifloxacin – Automated Read Method
MIC Distribution for Clinical and Challenge Isolates vs. Moxifloxacin

Test Results \ Reference Results	0.004	0.008	0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	>16
0.004														
0.008														
0.015			5	5	1									
0.03			3	42	14									
0.06			1	9	59	14								
0.12					5	16	9	1						
0.25					6	8	35	2	1					
0.5							7	26	9					
1						1		2	14	13				
2						1				13	6			
4							1				7	4		
8											1	9	11	1
16													9	
>16														10
TOTALS	0	0	9	56	85	40	52	31	24	26	14	13	20	11

Categorical Interpretations: Susceptible ≤ 2, Intermediate = 4, Resistant ≥ 8

Gatifloxacin – Manual Read Method
MIC Distribution for Clinical and Challenge Isolates vs. Gatifloxacin

Test Results \ Reference Results	0.004	0.008	0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	>16
0.004														
0.008		4	2											
0.015			43	8	1									
0.03			6	62	15									
0.06				5	27	10								
0.12				4	4	39	9							
0.25				1		5	21	3	1					
0.5							2	15	10					
1							1	2	11	9				
2						1			1	11	3			
4											12			
8												1	10	6
16													2	4
>16													1	7
TOTALS	0	4	51	80	47	55	33	20	23	20	16	12	11	9

Categorical Interpretations: Susceptible ≤ 2, Intermediate = 4, Resistant ≥ 8

Moxifloxacin – Manual Read Method
MIC Distribution for Clinical and Challenge Isolates vs. Moxifloxacin

Test Results \ Reference Results	0.004	0.008	0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	>16
0.004														
0.008														
0.015			5	4										
0.03			3	45	9									
0.06			1	7	65	10								
0.12					5	22	7							
0.25					6	7	35	2						
0.5							9	26	7					
1						1		3	16	8				
2									1	18	3			
4							1				10	3		
8											1	10	4	
16													10	4
>16													1	12
TOTALS	0	0	9	56	85	40	52	31	24	26	14	13	15	16

Categorical Interpretations: Susceptible ≤ 2, Intermediate = 4, Resistant ≥ 8

Reproducibility Isolates vs. Gatifloxacin / Moxifloxacin
Reference Agreement within ±1 Dilution of Modal MIC

Site	# Agreement Manual	# Agreement Autoread	Total Isolates Tested	Manual %	Autoread %
TREK	25/25	25/25	25/25	100/100	100/100
Creighton	25/25	25/25	25/25	100/100	100/100
UH	25/25	24/23	25/25	100/100	96.0/92.0
Combined	75/75	74/73	75/75	100/100	98.7/97.3

Gatifloxacin versus Clinical and Challenge Isolates

Read Method	Total Isolates Tested	% Essential Agreement	% Categorical Agreement	Number Resistant	Very Major Errors	Major Errors	Minor Errors
Manual	381	97.6	99.0	32	0	0	4
Automated	381	97.4	98.4	32	0	0	6

Moxifloxacin versus Clinical and Challenge Isolates

Read Method	Total Isolates Tested	% Essential Agreement	% Categorical Agreement	Number Resistant	Very Major Errors	Major Errors	Minor Errors
Manual	381	97.6	97.9	44	0	0	8
Automated	381	96.3	96.9	44	0	0	12

CONCLUSIONS

This investigation compared the 18 – 24 hour Sensititre® susceptibility plate with the NCCLS reference microdilution frozen plate (M7 – A6). The Sensititre plate demonstrated a high level of agreement and was very reproducible.

Clinical Isolates

Gatifloxacin:
- The overall essential agreement for Gatifloxacin, within a +/- one-well dilution range, was 97.1% for the manual method and 96.7% for the autoread method.
- The overall categorical agreement for Gatifloxacin was 99.0% for the manual method and 99.0% for the autoread method.

Moxifloxacin:
- The overall essential agreement for Moxifloxacin, within a +/- one-well dilution range, was 97.1% for the manual method and 95.8% for the autoread method.
- The overall categorical agreement for Moxifloxacin was 98.4% for the manual method and 97.4% for the autoread method.

CDC Challenge Organisms

Gatifloxacin:
- The overall essential agreement for Gatifloxacin, within a +/- one-well dilution range, was 100% for the manual method and 100% for the autoread method.
- The overall categorical agreement for Gatifloxacin was 98.7% for the manual method and 96.0% for the autoread method.

Moxifloxacin:
- The overall essential agreement for Moxifloxacin, within a +/- one-well dilution range, was 100% for the manual method and 98.7% for the autoread method. The overall categorical agreement for Moxifloxacin was 96.0% for the manual method and 94.7% for the autoread method.

Reproducibility

Gatifloxacin:
- For Gatifloxacin the Interlaboratory essential agreement reproducibility was 100% for the manual read method and 98.7% for the autoread method.
- The Interlaboratory categorical agreement reproducibility was 97.3% for the manual read method and 96.0% for the autoread method.

Moxifloxacin:
- For Moxifloxacin the Interlaboratory essential agreement reproducibility was 100% for the manual read method and 97.3% for the autoread method.
- The Interlaboratory categorical agreement reproducibility was 98.7% for the manual read method and 92.0% for the autoread method.