

A Multi-Site Evaluation of Levofloxacin Comparing the Sensititre™ Dried Susceptibility Panel to the NCCLS Microdilution Method

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ABSTRACT

A multi-site evaluation was undertaken to compare the performance of Levofloxacin (LEVO) on the Sensititre 18 - 24 hour susceptibility dried panel with its performance on the NCCLS microdilution reference method, using both automated and manual reading methods. The clinical evaluation was conducted at two sites and consisted of 301 fresh clinical gram-positive isolates and 127 CDC challenge isolates. These isolates included methicillin resistant and susceptible *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus species*, *Enterococcus faecalis*, *Enterococcus faecium*, *Enterococcus* and *Streptococcus species*. Reproducibility results for the automated and manual methods were 99.4% and 98.3%, respectively. The recommended quality control organisms were tested daily and were within the NCCLS expected quality control range.

When the automated reading method was compared to the reference method the clinical isolates' Essential Agreement (EA) and Categorical Agreement (CA) was: 99.0% and 100%, respectively, while the challenge isolates' EA and CA were 100% and 100%, respectively. When the manual reading method was compared to the reference method the clinical isolates' EA and CA was: 96% and 99%, respectively; and for the challenge isolates they were 100% and 100%, respectively.

This multi-site evaluation indicates that the performance of Levofloxacin on the Sensititre 18-24 hour susceptibility system, using either the automated or manual reading method, is equivalent to the NCCLS microdilution reference method.

Purpose of the Study

To evaluate the performance of Levofloxacin on the Sensititre™ 18 – 24 hour susceptibility panel compared to the NCCLS microdilution reference method (M7 – A5).

Materials and Methods

Organisms: The testing at 2 sites consisted of the following:

- 301 Total Clinical isolates (combined sites)
- 127 Challenge isolates per site (Enterococcus and CDC Gram +)
- 10 Reproducibility isolates (run in triplicate for 3 days)
- 2 Quality Control strains (run for 24 days per site)

Antimicrobial	Range Tested	Supplied By:
Levofloxacin (LEVO)	0.008 – 16	Ortho McNeil Pharmaceuticals

Number of Isolates Tested

Organism Species	Challenge Tested	Clinical Tested
<i>Staphylococcus aureus</i>	20	89
<i>Staphylococcus epidermidis</i>	13	57
<i>Staphylococcus species</i>	7	29
<i>Streptococcus species</i>	3	42
<i>Enterococcus faecalis</i>	36	55
<i>Enterococcus faecium</i>	35	29
<i>Enterococcus species</i>	13	0
Total	127	301

Susceptibility Testing Methods:

- Each isolate was tested using a Sensititre 18 – 24 susceptibility panel. The panels were set-up and tested according to the manufacturers' instructions.
- The reference panel was tested according to the microdilution methods published by the National Committee for Clinical Laboratory Standards (NCCLS, M7-A5).
- The approved primary "Indications for Use" and clinical significance of Levofloxacin is for: *Staphylococcus aureus*, *Streptococcus pyogenes* and *Enterococcus faecalis*. In vitro data, without clinical correlation is provided for: *Staphylococcus epidermidis*, *Staphylococcus saprophyticus*, and *Streptococcus agalactiae*.

Conclusion

This investigation compared the 18 – 24 hour Sensititre™ susceptibility panel with the NCCLS reference microdilution frozen panel (M7 – A5). The Sensititre panel demonstrated a high level of agreement and was very reproducible.

- **Clinical Isolates:**
The overall essential agreement for Levofloxacin, within a +/- one-well dilution range, was 96% for the manual method and 99% for the autoread method. The overall categorical agreement for Levofloxacin was 99% for the manual method and 100% for the autoread method.
- **CDC Challenge Organisms:**
The overall essential agreement for Levofloxacin, within a +/- one-well dilution range, was 100% for the manual method and 100% for the autoread method. The overall categorical agreement for Levofloxacin, was 100% for the manual method and 100% for the autoread method.
- **Reproducibility:**

Interlaboratory reproducibility was 98% for the manual read method and 99% for the autoread method.

RESULTS

Clinical Isolates vs. Levofloxacin

Read Method	Total Isolates Tested	% Essential Agreement	% Categorical Agreement	Number Resistant	Very Major Errors	Major Errors	Minor Errors
Manual	301	96	99	114	0	0	2
Automated	301	99	100	114	0	0	0

CDC Challenge Isolates vs. Levofloxacin

Read Method	Total Isolates Tested	% Essential Agreement	% Categorical Agreement	Number Resistant	Very Major Errors	Major Errors	Minor Errors
Manual	127	100	100	13	0	0	0
Automated	127	100	100	13	0	0	0

**Reproducibility Isolates vs. Levofloxacin
Reference Agreement Within ± 1 Dilution of Modal MIC**

Site	# Agreement Manual	# Agreement Autoread	Total Isolates Tested	Manual%	Autoread%
Trek	90	90	90	100	100
Summa	87	89	90	96.7	98.9
Combined	177	179	180	98.3	99.4

Staphylococcus species - Manual Reading Method MIC Distribution for Clinical & Challenge Isolates vs. LEVO

		Reference Results											
		≤0.008	0.015	0.03	0.06	0.125	0.25	0.5	1	2	4	8	> 8
Test Results	<0.008					1							
	0.015												
	0.030					1							
	0.060				1		2						
	0.125				2	40	11	2					
	0.25					14	35						
	0.50					1	1	8	1				
	1								1	1			
	2								2	2			
	4									1	18	5	2
	8										1	26	1
	> 8											5	30
Totals		0	0	0	3	57	49	10	4	4	19	36	33

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

Staphylococcus species - Automated Reading Method MIC Distribution for Clinical & Challenge Isolates vs. LEVO

		Reference Results											
		≤0.008	0.015	0.03	0.06	0.125	0.25	0.5	1	2	4	8	> 8
Test Results	≤0.008												
	0.015												
	0.030					1							
	0.060				1								
	0.125				2	45	15						
	0.25					9	34						
	0.50					1	1	10	1				
	1								1	1			
	2								2	2	6		
	4									1	10	13	
	8											25	6
	> 8											2	26
Totals		0	0	0	3	56	50	10	4	4	16	40	32

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

Streptococcus species - Manual Reading Method MIC Distribution for Clinical & Challenge Isolates vs. LEVO

		Reference Results											
		≤0.008	0.015	0.03	0.06	0.125	0.25	0.5	1	2	4	8	> 8
Test Results	≤0.008												
	0.015						1						
	0.030												
	0.060												
	0.125						1						
	0.25						1	1					
	0.50						3	15	1				
	1							12	9				
	2									1			
	4												
	8												
	> 8												
Totals		0	0	0	0	0	6	28	10	1	0	0	0

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

Streptococcus species - Automated Reading Method MIC Distribution for Clinical & Challenge Isolates vs. LEVO

		Reference Results											
		≤0.008	0.015	0.03	0.06	0.125	0.25	0.5	1	2	4	8	> 8
Test Results	≤0.008												
	0.015						1						
	0.030												
	0.060												
	0.125												
	0.25							1					
	0.50						5	17	3				
	1							10	7	1			
	2									1			
	4										1		
	8											1	
	> 8												1
Totals		0	0	0	0	0	6	28	10	1	0	0	0

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

Enterococcus species - Manual Reading Method MIC Distribution for Clinical & Challenge Isolates vs. LEVO

		Reference Results											
		≤0.008	0.015	0.03	0.06	0.125	0.25	0.5	1	2	4	8	> 8
Test Results	<0.008												
	0.015												
	0.030												
	0.060												
	0.125												
	0.25								1				
	0.50							7	2				
	1								7	37			
	2									20	25	1	
	4										6	3	
	8											1	1
	> 8												1
Totals		0	0	0	0	0	0	14	60	31	5	2	56

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

Enterococcus species - Automated Reading Method MIC Distribution for Clinical & Challenge Isolates vs. LEVO

		Reference Results											
		≤0.008	0.015	0.03	0.06	0.125	0.25	0.5	1	2	4	8	> 8
Test Results	≤0.008												
	0.015												
	0.030												
	0.060												
	0.125												
	0.25												
	0.50							9	6				
	1							5	45	6			
	2								9	24	4		
	4									1			
	8										1	1	
	> 8											1	56
Totals		0	0	0	0	0	0	14	60	31	5	2	56

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