A Multi-Site Evaluation of Sparfloxacin 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 Sparfloxacin (SPX) 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 217 fresh clinical gram-positive isolates and 43 CDC challenge isolates. These isolates included methicillin resistant and susceptible Staphylococcus aureus and Staphylococcus epidermidis, and other Staphylococcus and Streptococcus species. Reproducibility results for the automated and manual methods were 99.4% and 100%, 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) were: 87.6% and 99.5%, respectively, while the challenge isolates' EA and CA were 86.0% and 100%, respectively. When the manual reading method was compared to the reference method the clinical isolates' EA and CA were: 91.2% and 99.1%, respectively; for the challenge isolates they were 90.7% and 100%, respectively.

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

Purpose of the Study

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

Materials and Methods

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

- 217 total clinical isolates (combined sites)
- 43 CDC challenge isolates per site
- 10 reproducibility isolates (run in triplicate for 3 days)
- 2 Quality Control strains (run for 24 days per site)

Antimicrobial	Range Tested	Supplied By:
Sparfloxacin (SPX)	0.002 – 4	Rhone-Poulenc Rorer Inc.

Number of Isolates Tested

Organism Species	Challenge Tested	Clinical Tested
Staphylococcus aureus	20	89
Staphylococcus epidermidis	13	57
Staphylococcus species	7	29
Streptococcus species	3	42
Total	**43**	**217**

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 Sparfloxacin is for *Staphylococcus aureus*. In vitro data, without clinical correlation, is provided for *Streptococcus pyogenes* 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 Sparfloxacin, within a +/- one-well dilution range, was 91.2% for the manual method and 87.6% for the autoread method. The overall categorical agreement for Sparfloxacin was 99.1% for the manual method and 99.5% for the autoread method.

- **CDC Challenge Organisms:**
  The overall essential agreement for Sparfloxacin, within a +/- one-well dilution range, was 90.7% for the manual method and 86.0% for the autoread method. The overall categorical agreement for Sparfloxacin, was 100% for the manual method and 100% for the autoread method.

- **Reproducibility:**
  Interlaboratory reproducibility was 100% for the manual read method and 99.4% for the autoread method.

RESULTS

Clinical Isolates vs. Sparfloxacin

Read Method	Total Isolates Tested	% Essential Agreement	% Categorical Agreement	Number Resistant	Very Major Errors	Major Errors	Minor Errors
Manual	217	91.2	99.1	82	0	0	2
Automated	217	87.6	99.5	82	0	0	1

CDC Challenge Isolates vs. Sparfloxacin

Read Method	Total Isolates Tested	% Essential Agreement	% Categorical Agreement	Number Resistant	Very Major Errors	Major Errors	Minor Errors
Manual	43	90.7	100	3	0	0	0
Automated	43	86.0	100	3	0	0	0

Reproducibility Isolates vs. Sparfloxacin
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	90	89	90	100	98.9
Combined	180	179	180	100	99.4

Staphylococcus species - Manual Reading Method

MIC Distribution for Clinical & Challenge Isolates vs. SPX

Test Results \ Reference Results	≤0.008	0.015	0.03	0.06	0.125	0.25	0.5	1	2	4	8	> 8
≤0.008												
0.015			1	1								
0.030	1	1		3								
0.060		2	17	8	1							
0.125			9	47	8							
0.25					17	2						
0.50				1	2							
1												
2									3	1	2	
4									6	15	1	
8										12	25	6
> 8											6	17
Totals	1	3	27	60	28	2	0	0	9	28	34	23

Categorical Interpretations: Sensitive ≤ 1, Intermediate = 2, Resistant ≥ 4

Staphylococcus species - Automated Reading Method

MIC Distribution for Clinical & Challenge Isolates vs. SPX

Test Results	Reference Results											
	≤0.008	0.015	0.03	0.06	0.125	0.25	0.5	1	2	4	8	> 8
≤0.008												
0.015												
0.030	1	2		1								
0.060			12	11								
0.125		1	15	46	17							
0.25				1	9	2						
0.50				1	2							
1												
2									5	2	1	
4										14	1	
8										12	31	5
> 8											4	15
Totals	1	3	27	60	28	2	0	0	9	28	37	20

Categorical Interpretations: Sensitive ≤ 1, Intermediate = 2, Resistant ≥ 4

Streptococcus species - Manual Reading Method

MIC Distribution for Clinical & Challenge Isolates vs. SPX

Test Results	Reference Results											
	≤0.008	0.015	0.03	0.06	0.125	0.25	0.5	1	2	4	8	> 8
≤0.008												
0.015		3			1							
0.030												
0.060												
0.125					2							
0.25					6	6						
0.50	1				3	18	4					
1							1					
2												
4												
8												
> 8												
Totals	1	3	0	0	12	24	5	0	0	0	0	0

Categorical Interpretations: Sensitive ≤ 1, Intermediate = 2, Resistant ≥ 4

Streptococcus species - Automated Reading Method

MIC Distribution for Clinical & Challenge Isolates vs. SPX

Test Results	Reference Results											
	≤0.008	0.015	0.03	0.06	0.125	0.25	0.5	1	2	4	8	> 8
≤0.008												
0.015		3			1							
0.030												
0.060												
0.125					1							
0.25					4	6						
0.50					5	15	4					
1	1				1	3	1					
2												
4												
8												
> 8												
Totals	1	3	0	0	12	24	5	0	0	0	0	0

Categorical Interpretations: Sensitive ≤ 1, Intermediate = 2, Resistant ≥ 4