

Comparison of Solithromycin MICs Generated by BSAC and CLSI Methods

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Background: Solithromycin is a fourth generation macrolide in development in Europe and the US that has successfully completed two global Phase 3 trials for community-acquired bacterial pneumonia. The aim of this study was to establish the comparability of solithromycin MICs generated by CLSI and BSAC methods for susceptibility testing.

Methods: 30 isolates of *S. pneumoniae*, *H. influenzae*, and *S. aureus* from the University of Rochester Medical Center were chosen to represent a range of MICs. Due to the highly susceptible nature of *M. catarrhalis* that results in a narrow range of MICs, only 15 isolates were used and an additional 15 isolates of Gram-negative enterics were included for generation of scatterplots. All isolates were evaluated following methods for agar and broth dilution recommended by BSAC and CLSI. Comparisons were made by analyzing scatterplots and by determining the doubling dilution difference (DD) in the MIC by calculating $\log_2(\text{method 1 MIC}) - \log_2(\text{method 2 MIC})$.

Results: For most comparisons, good to excellent correlations were observed in scatterplot comparisons. When doubling dilution differences were compared, a good correlation was observed for *H. influenzae* and *M. catarrhalis* BSAC agar compared to CLSI broth dilution. Although almost all isolates were within $\pm 2DD$, the overall correlation was poor for *S. aureus* and *S. pneumoniae*. Specifically, MICs were frequently lower for *S. aureus* and higher for *S. pneumoniae* with BSAC agar versus CLSI broth. For all species, excellent agreement was observed when comparing BSAC agar to CLSI agar and good agreement for BSAC broth to CLSI broth. For CLSI broth versus CLSI agar comparisons, *H. influenzae* was excellent, *S. aureus* and *S. pneumoniae* were good, and *M. catarrhalis* was poor.

	BSAC Agar vs CLSI Broth		BSAC Agar vs CLSI Agar		BSAC Broth vs CLSI Broth		CLSI Agar vs CLSI Broth	
	$\pm 1DD$	$\pm 2DD$	$\pm 1DD$	$\pm 2DD$	$\pm 1DD$	$\pm 2DD$	$\pm 1DD$	$\pm 2DD$
<i>H. influenzae</i>	87%	97%	90%	100%	87%	100%	100%	100%
<i>M. catarrhalis</i>	80%	100%	100%	100%	80%	100%	47%	93%
<i>S. aureus</i>	77%	97%	90%	100%	83%	100%	83%	100%
<i>S. pneumoniae</i>	73%	97%	100%	100%	83%	100%	87%	97%

DD: MIC doubling dilution difference

Conclusion: There is excellent agreement between BSAC agar and CLSI agar dilution methods and good agreement between methods when broth dilution is performed. When comparing MICs generated by BSAC agar dilution to those generated by CLSI broth dilution, some degree of caution is warranted, particularly for *S. aureus* and *S. pneumoniae*, where although most MICs are within 1DD, there is a tendency toward lower MICs for *S. aureus* and higher MICs for *S. pneumoniae* using the BSAC agar method.