Proposed MIC Quality Control Ranges for CEM-101 Using the CLSI Multi-Laboratory M23-A2 Study Design

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Background:

CEM-101 is a promising new macrolide in development for treating community-acquired (CA) macrolide-resistant and -susceptible bacteria. This study was performed to establish quality control (QC) ranges for CEM-101 for use in clinical or reference laboratories when performing Clinical and Laboratory Standards Institute (CLSI) broth microdilution MIC methods. QC strains included *S. aureus* ATCC 29213 (SA), *E. faecalis* ATCC 29212 (EF), *S. pneumoniae* ATCC 49619 (SPN) and *H. influenzae* ATCC 49247 (HI).

Methods:

CLSI broth microdilution methods were utilized in an eight laboratory study design compliant with M23-A2 specifications. Four media lots (three manufacturers) of cation-adjusted Mueller-Hinton (MH) broth (with 2-5% lysed horse blood for testing SPN) or HTM broth were evaluated. Ten replicate MIC tests were performed for each QC organism generating 320 values for each strain (1,280 total). Azithromycin and/or erythromycin and/or clarithromycin were used as internal controls.

Results:

The table lists the recommended QC MIC ranges for CEM-101. Modal MIC values (% of total) observed were: SA at 0.06 µg/ml (64.1), EF at 0.03 µg/ml (67.8), SPN at 0.008 µg/ml (85.3) and HI at 2 µg/ml (93.1). No significant differences were noted between media lots or testing site performance for either CEM-101 or the three control agents. All control agent MIC values were within CLSI published ranges.

	CEM-101 MIC (µg/ml)	
QC Organism (ATCC no.)	Proposed range (log_2 dilutions)	% in range
S. aureus ATCC 29213	0.03-0.12 (3)	96.6
E. faecalis ATCC 29212	0.015-0.06 (3)	95.6
S. pneumoniae ATCC 49619	0.004-0.015 (3)	99.3
H. influenzae ATCC 49247	1-4 (3)	99.7

Conclusions:

CEM-101 is a novel macrolide to be directed against CA respiratory tract infections and possibly other infections commonly treated with MLS_B-class agents. Proposed MIC QC ranges will help guide clinical or reference laboratories involved in the testing of clinical trial isolates and facilitate the regulatory review process.