Assessment of CEM-101 Susceptibility Testing Conditions and Optimization of Disk Diffusion Methods

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Background:

CEM-101, a novel macrolide-ketolide, potent activity has against susceptible (S) and resistant (R) respiratory tract infection pathogens. To prepare it for clinical trials, *in vitro* S testing details for MIC methods and the selection of disk diffusion (DD) CEM-101 content were established.

Methods:

CLSI broth microdilution (BMD) was used and test conditions were modified to determine effects of CEM-101 activity; anaerobic and CO_2 atmosphere; 5 x 10^3 and 5 x 10^7 inoculum; LHB and HTM; pH 5, 6 and 8; human serum protein at 5, 10 and 20%; calcium at 3.7 and 50 mg/L and use of polysorbate-80 (p-80) surfactant. Simultaneous changes in the pH and protein were also tested. CEM-101 DD tests with 2-, 5-, 10-, 15- and 30-µg versus 70 selected S and R strains.

Results:

By changing BMD test conditions only the following resulted in significantly (≥ 4-fold) elevated CEM-101 MIC results: high inoculum (5 x 10^7), P-80 at 2% (see Figure) and pH 5 or 6. pH effect was muted for pH 6 by presence of 10% human serum protein. Scattergrams with CEM-101 MIC values and zone diameters produced r values of 0.93-0.97 and the 15-µg disk (like other macrolides) provided best discriminaton of S and R strains of staphylococci, enterococci and *H. influenzae*.

Conclusions:

CEM-101 S testing by CLSI methods appears to be optimized for clinical trials using published BMD procedures without P-80. The 15-µg CEM-101 DD test accurately assesses this new agent's activity.