

P2492 Cefepime-AAI101 and cefepime MIC quality-control ranges using a CLSI M23-A4 multi-laboratory study design

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Background: AAI101 is a novel extended-spectrum β -lactamase inhibitor highly active against ESBLs, the principal mechanism of β -lactam resistance amongst *Enterobacteriaceae* to oxyiminocephalosporins. Erosion of efficacy to existing β -lactam/ β -lactamase inhibitor combinations (such as piperacillin-tazobactam) due to emerging aggressive ESBLs has led to a need for new therapeutic modalities. AAI101 combined with cefepime (FEP) is entering Phase 2 clinical development. To support isolate testing in reference laboratories, broth microdilution MIC ranges for QC reference strains were obtained for FEP/AAI101 and for FEP.

Materials/methods: CLSI M23-A4 (tier 2) studies were conducted with FEP/AAI101 and FEP for 5 QC reference strains. Each study employed ≥ 7 reference laboratories, 3 lots of media from ≥ 2 manufacturers, 10 replicate tests per QC reference strain, and at least 1 comparator agent per QC reference strain.

Results: Approved broth microdilution QC ranges for FEP/AAI101 and for FEP are listed in the Table. Three-dilution QC ranges were approved for FEP/AAI101 against each QC reference strain tested, containing 99.2-100.0% of all MIC values, except FEP/AAI101 vs. *E. coli* ATCC 35218 (fixed conc. AAI101 8 mg/L) and *P. aeruginosa* ATCC 27853 (fixed conc. AAI101 4 mg/L), for which 4-dilution QC ranges are proposed.

Conclusions: Broth microdilution QC ranges for cefepime-AAI101 have been established following CLSI M23-A4 (2016) criteria. They will assist reference laboratories in MIC testing of cefepime-AAI101.

Reference strain	Approved CLSI QC ranges ($\mu\text{g/mL}$) (# of dilutions; % of values in range)		
	FEP	FEP/AAI101 (4 mg/L) ^a	FEP/AAI101 (8 mg/L) ^a
<i>E. coli</i> ATCC 25922	0.016 - 0.12 ^b (4; 100.0%)	0.03/4 - 0.12/4 (3; 100.0%)	0.03/8 - 0.12/8 (3; 100.0%)
<i>E. coli</i> ATCC 35218	0.008 - 0.06 (4; 100.0%)	0.016/4 - 0.06/4 (3; 100.0%)	0.008/8 - 0.06/8 (4; 100.0%)
<i>E. coli</i> NCTC 13353	≥ 64 (100.0%) ^c	0.06/4 - 0.25/4 (3, 99.5%) ^c	0.03/8 - 0.12/8 (3, 100.0%) ^c
<i>K. pneumoniae</i> ATCC 700603	0.5 - 2 (3; 99.8%)	0.12/4 - 0.5/4 (3; 99.2%)	0.12/8 - 0.5/8 (3, 100.0%)
<i>P. aeruginosa</i> ATCC 27853	0.5 - 4 ^b (4; 100.0%)	0.5/4 - 4/4 (4; 100.0%)	0.5/8 - 2/8 (3; 99.6%)

^a Fixed AAI101 concentration

^b Current CLSI QC range

^c Excluding data from 1 laboratory