

**P2778 Proposed cefepime-AAI101 (30/20 ug) and cefepime (30 ug) disk diffusion quality control ranges using a CLSI M23 (2018) multi-laboratory study design**Michael Huband\*<sup>1</sup>, Kelley Fedler<sup>1</sup>, Amy A. Watters<sup>1</sup>, Adam C Belley<sup>2</sup>, Philipp Knechtle<sup>2</sup>, Robert Flamm<sup>1</sup><sup>1</sup> JMI Laboratories, North Liberty, United States, <sup>2</sup> Allegra Therapeutics, Saint-Louis, France

**Background:** Erosion of efficacy to existing  $\beta$ -lactam/ $\beta$ -lactamase inhibitor combinations (e.g. piperacillin-tazobactam) due to the spread of more aggressive ESBLs has led to a need for new therapeutic modalities. AAI101 is a novel extended-spectrum  $\beta$ -lactamase (ESBL) inhibitor highly active against ESBLs, the principal mechanism of  $\beta$ -lactam resistance among Enterobacteriaceae. AAI101 combined with cefepime has recently entered Phase 3 clinical development. To support susceptibility testing in reference laboratories, disk diffusion quality control (QC) ranges for reference strains were established for cefepime-AAI101 (30/20  $\mu$ g) and cefepime (30  $\mu$ g) disks.

**Materials/methods:** CLSI M23-A5 tier-2 studies were conducted with cefepime-AAI101 (30/20  $\mu$ g; 2 disk lots) and cefepime (30  $\mu$ g; 2 disk lots) against 5 QC reference strains (table). Eight reference laboratories tested 3 lots of media from 3 manufacturers, 10 replicate tests per reference strain, and at least 1 comparator agent per QC reference strain.

**Results:** Proposed and approved disk diffusion QC ranges for cefepime-AAI101 (30/20  $\mu$ g) and cefepime (30  $\mu$ g) disks are listed in the table. Seven mm QC ranges are proposed for cefepime-AAI101 (30/20  $\mu$ g) disks against each of the 5 QC reference strains tested, containing 97.1-100.0% of all cefepime-AAI101 (30/20  $\mu$ g) zone diameter values. Similarly, a 7 mm QC range is proposed for cefepime (30  $\mu$ g) disks against *Escherichia coli* ATCC 35218 containing 100.0% of all zone diameter values.

**Conclusions:** Establishing the QC ranges for cefepime-AAI101 (30/20  $\mu$ g) disks will ensure that appropriate disk diffusion standards are implemented by reference and clinical laboratories. *E. coli* NCTC 13353 is recommended for routine QC testing of cefepime-AAI101 (30/20  $\mu$ g) disks as it controls for AAI101 activity against ESBL-producing organisms.

Reference strain	Proposed Disk Diffusion QC ranges (mm)	
	Cefepime-AAI101 (30/20 $\mu$ g) (mm; % in range)	Cefepime (30 $\mu$ g) (mm; % in range)
<i>E. coli</i> ATCC 25922	32 – 38 (7; 97.1%)	31 – 37 <sup>a</sup> (7; 97.1%)
<i>E. coli</i> ATCC 35218	32 – 38 (7; 100.0%)	31 – 37 (7; 100.0%)
<i>E. coli</i> NCTC 13353	27 – 33 (7; 100.0%)	6 – 15 <sup>a,b</sup> (10; 99.5%)
<i>Klebsiella pneumoniae</i> ATCC 700603	26 – 32 (7; 98.3%)	23 – 29 <sup>a</sup> (7; 99.8%)
<i>Pseudomonas aeruginosa</i> ATCC 27853	26 – 32 (7; 99.4%)	25 – 31 <sup>a</sup> (7; 99.2%)

<sup>a</sup> Current CLSI QC range<sup>b</sup> Excluding data from 1 laboratory

