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Abstract (poster session)

**Biapenem and biapenem/RPX7009 MIC quality control ranges using CLSI multi-laboratory M23-A3 study design**

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**Objectives:** To conduct a study to establish MIC quality control (QC) ranges for biapenem (BPM) and BPM in combination with RPX7009, a beta-lactamase inhibitor, using the broth microdilution (BMD) method. This broad-spectrum combination has activity against key Gram-negative pathogens including *E. coli*, *P. aeruginosa*, *Acinetobacter* spp., *Klebsiella* spp. and those organisms that produce serine beta-lactamases like KPC. **Methods:** An eight laboratory study design was compliant with CLSI M23-A3 guidelines. Six QC strains were tested (*S. aureus* ATCC 29213 [SA], *E. coli* ATCC 25922 [EC1], *E. coli* ATCC 35218 [EC2], *K. pneumoniae* ATCC 700603 [KP1], *K. pneumoniae* BAA 1705 [KP2], and *P. aeruginosa* ATCC 27853 [PA]) using three media lots (three manufacturers) of cation-adjusted Mueller-Hinton broth (MHB). Ten replicate tests were performed for each QC organism generating 720 BMD values/strain (4,320 total). Meropenem, piperacillin/tazobactam, and amoxicillin/clavulanic acid were used as controls. **Results:** The table lists the proposed MIC QC ranges for BPM and BPM/RPX7009. An alternative range suggested by the Range Finder statistical program was a four log<sub>2</sub> dilution range for KP1 (0.03 – 0.25 mg/L). A four log<sub>2</sub> dilution range was required for KP2 (KPC-producing strain) with BPM/RPX7009 at both a fixed 4 and 8 mg/L concentration due to a “shoulder” MIC at 0.03 mg/L, which had 68.2% and 85.8%, respectively, of the MIC values compared to the modal occurrences at 0.06 mg/L. A range was established for BPM alone with KP2 at >1 mg/L to be added to the appropriate CLSI table footnote and compared to the significantly lower MIC results for the combination. There were no differences in proposed QC ranges between RPX7009 fixed 4 mg/L concentration or RPX7009 fixed 8 mg/L for all six QC organisms. No significant differences were noted among MHB media lots for BPM or BPM/RPX7009. Nearly all (714/720; 99.3%) control agent MIC results were within CLSI published ranges. Meropenem MIC results for the KP2 strain were all greater than 0.5 mg/L. **Conclusions:** Proposed MIC QC ranges for BPM and BPM/RPX7009 should guide clinical or reference laboratories participating in the testing of clinical trial isolates and facilitate the regulatory review process for this investigational antimicrobial combination.

QC organism (ATCC no.)	Proposed QC ranges for BMD tests (MIC in mg/L; % in proposed range)		
	Biapenem	Biapenem/RPX7009 fixed 4 mg/L	Biapenem/RPX7009 fixed 8 mg/L
<i>S. aureus</i> ATCC 29213	0.3 – 0.12 (100.0)	0.03 – 0.12 (100.0)	0.03 – 0.12 (100.0)
<i>E. coli</i> ATCC 25922	0.03 – 0.12 (100.0)	0.03 – 0.12 (100.0)	0.03 – 0.12 (99.6)
<i>E. coli</i> ATCC 35218	0.03 – 0.12 (100.0)	0.03 – 0.12 (100.0)	0.03 – 0.12 (100.0)
<i>K. pneumoniae</i> ATCC 700603	0.03 – 0.12 (95.0)	0.03 – 0.12 (97.5)	0.03 – 0.12 (99.2)
<i>K. pneumoniae</i> ATCC BAA1705	>1 (100.0)	0.015 – 0.12 (97.5)	0.015 – 0.12 (99.2)
<i>P. aeruginosa</i> ATCC 27853	0.5 – 2 (100.0)	0.5 – 2 (100.0)	0.5 – 2 (99.6)