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P2769 Selection of EUCAST disk potency for WCK 4282 (cefepime-tazobactam, FEP-TAZ) susceptibility testing against *Enterobacterales* and *Pseudomonas aeruginosa*

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Background: WCK 4282 (FEP-TAZ) is a high dose and extended infusion combination of cefepime and tazobactam. This combination is being developed as a potential carbapenem sparing therapy. FEP-TAZ shows activity against cefepime and piperacillin-tazobactam resistant Enterobacterales. Based on identified in vivo pharmacokinetic/pharmacodynamic (PK/PD) targets, population PK model, Monte-Carlo simulations and probability of target attainment, the company (Wockhardt) has proposed breakpoints for Enterobacterales and *Pseudomonas aeruginosa*; S≤16 and R>32 mg/L and S,≤16 and R>16 mg/L, respectively. This study was performed to assess the appropriateness of different inhibitor concentrations to combine with cefepime 30 µg for EUCAST susceptibility testing of Enterobacterales and *P. aeruginosa*.

Materials/methods: Zone diameter *vs* FEP-TAZ (fixed TAZ 8 mg/L) broth microdilution MIC was performed following EUCAST and ISO standards, respectively, at Wockhardt Research Centre (372 ENT and 128 PA) employing isolates with FEP-TAZ MICs ranging from 0.016 to >128 mg/L. The isolates were from diverse geographies, expressing ESBL, class C, AmpC, KPC, OXA-48/181, MBL and other resistance mechanisms. The discrepancy rates were determined according to ISO standard 20776-2 employing the breakpoints proposed by the company for FEP-TAZ and the current EUCAST cefepime breakpoints. Disks containing cefepime 30 µg combined with tazobactam 5, 10 and 20 µg were assessed.

Results: FEP-TAZ MICs and zone diameters for QC strains were within CLSI QC ranges. The FEP-TAZ 30-20 provided better separation between organisms with different MIC values than the other disk concentrations tested. FEP-TAZ 30-20 µg disks showed acceptable level of discrepancies, with very major discrepancy (VMD) rates of ≤0.5 % in separating susceptible, intermediate and resistant population of Enterobacterales based on FEP-TAZ PK/PD MIC breakpoints and EUCAST cefepime MIC breakpoints (Figure 1A). For *P. aeruginosa*, the VMD rates were ≤ 4% for both FEP-TAZ PK/PD MIC breakpoints and EUCAST cefepime MIC breakpoints (Figure 1B).

Conclusions: FEP-TAZ 30-20 µg disk potency was able to reliably distinguish susceptible and resistant organisms of Enterobacterales and *P. aeruginosa* for the theoretical susceptible breakpoints of ≤1, ≤8 or ≤16 mg/L. The FEP-TAZ 30-20 µg disk was accepted by the EUCAST development laboratory for both Enterobacterales and *P. aeruginosa* for these theoretical breakpoints.

Figure 1A: Enterobacterales MIC vs zone diameter of FEP-TAZ 30-20 µg disk

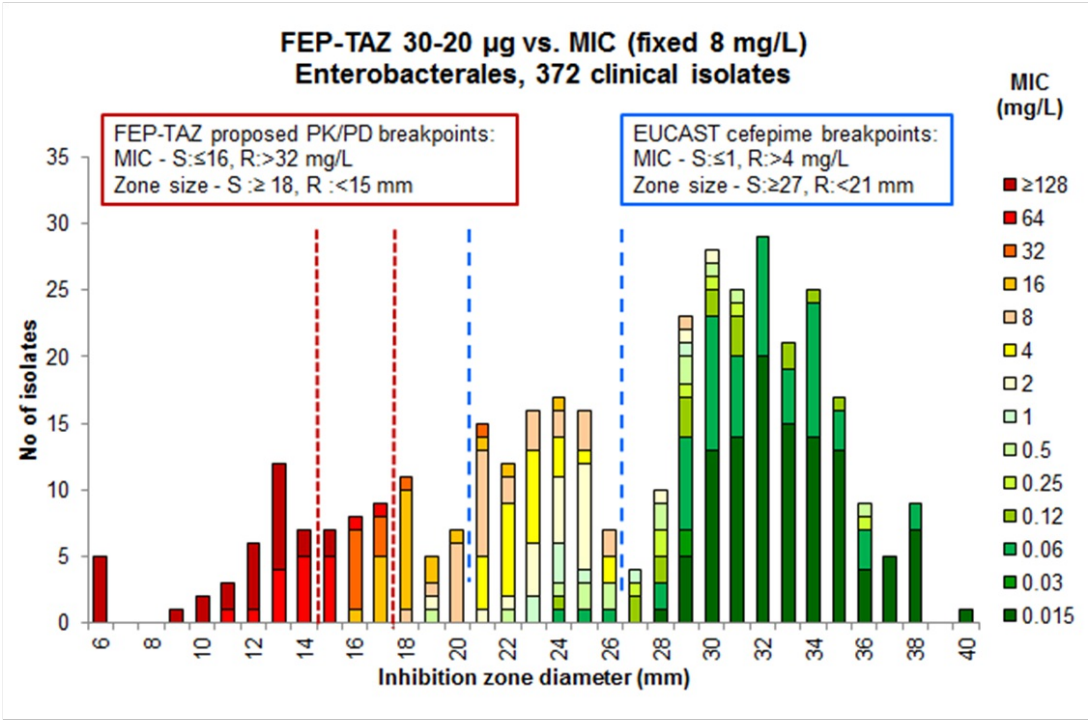

Figure 1B: *P. aeruginosa* MIC vs zone diameter of FEP-TAZ 30-20 µg disk