

P2770 Selection of EUCAST disk potency for WCK 5222 (cefepime-zidebactam, FEP-ZID) susceptibility testing against Enterobacterales, *Pseudomonas aeruginosa* and *Acinetobacter baumannii*

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Background: WCK 5222 (FEP-ZID) is a combination of cefepime and PBP2 binding β -lactam enhancer antibiotic, zidebactam. FEP-ZID is being developed for the treatment of MDR/XDR Enterobacterales, *Pseudomonas aeruginosa* and *Acinetobacter baumannii* infections. Based on pharmacokinetic/pharmacodynamic (PK/PD) targets, population PK model, Monte-Carlo simulations and probability of target attainment, a FEP-ZID the pharmaceutical company (Wockhardt) has proposed a FEP-ZID susceptible breakpoint of ≤ 64 mg/L for these groups of pathogens. This study was conducted to evaluate FEP-ZID 30-10, 30-20 and 30-30 μ g disk for EUCAST susceptibility testing of Enterobacterales, *Pseudomonas aeruginosa* and *Acinetobacter baumannii*

Materials/methods: Zone diameter vs FEP-ZID 1:1 broth microdilution MIC was performed following EUCAST and ISO standards, respectively, at JMI labs (318 Enterobacterales, 106 *P. aeruginosa* and 100 *A. baumannii* in duplicate) and Wockhardt Research Centre (212 Enterobacterales, 187 *P. aeruginosa* and 101 *A. baumannii*, employing isolates with a FEP-ZID MIC range of 0.008- \rightarrow 64 mg/L). The isolates were from diverse geographies, expressing ESBL, class C, AmpC, KPC, OXA-48/181, MBL, OXA-23 and other resistance mechanisms. As Enterobacterales isolates with high FEP-ZID MICs were limited, FEP-ZID and ZID selected mutants of MBL-producing *Klebsiella* with high FEP-ZID MICs were also included. The discrepancy rates were determined according to ISO standard 20776-2 employing PK/PD and theoretical breakpoints between ≤ 8 - ≤ 64 mg/L.

Results: FEP-ZID MICs and zone diameters for QC strains were within CLSI QC ranges. The FEP-ZID 30-30 disk provided better separation between organisms with different MIC values than the other disks tested. Very major discrepancy (VMD) rates were $\leq 5\%$ for breakpoints of 16, 32 or 64 mg/L for *P. aeruginosa* and *A. baumannii* and 8, 16 or 32 mg/L for Enterobacterales (Table). The FEP-ZID 30-30 μ g disk showed smaller zones for high FEP-ZID MIC mutants indicating that this disk potency is able to reliably distinguish between susceptible (S) and resistant (R) organisms.

Conclusions: The FEP-ZID 30-30 μ g disk could reliably distinguish between the S and R organisms based on potential FEP-ZID MIC breakpoints of either ≤ 16 , or ≤ 32 or ≤ 64 mg/L for *P. aeruginosa*, either ≤ 32 or ≤ 64 mg/L for *A. baumannii* and ≤ 8 mg/L for Enterobacterales. The 30-30 μ g disk was accepted by the EUCAST development laboratory for these potential breakpoints.

Table: Discrepancy rates analyses for FEP-ZID 30-30 µg disk vs. several alternative breakpoints.

Organisms	Zone Size cut-off (mm)	FEP-ZID MIC (mg/L) Cut-Off	VMD N (%)	MD N (%)
<i>P. aeruginosa</i> (N=399)	≥12	≤64	0 (0)	1 (0.25)
	≥14	≤32	3 (0.75)	2 (0.5)
	≥17	≤16	8 (2)	7 (1.8)
<i>A. baumannii</i> (N=301)	≥12	≤64	1 (0.3)	8 (2.7)
	≥14	≤32	8 (2.7)	8 (2.7)
	≥17	≤16	15 (5)	35 (11.6)
Enterobacterales (N=848)	≥13	≤64	NA	0 (0)
	≥16	≤32	3 (0.4)	6 (0.7)
	≥20	≤16	5 (0.6)	16 (1.9)
	≥21	≤8	15 (1.8)	17 (2)

VMD: Very major discrepancy; MD: Major discrepancy; NA: Not applicable

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