Comparisons between methods were analyzed using all data (525 data points). Automated endpoints did not affect organism classification. Target essential agreement (EA) was ± one doubling dilution (ST only; MIC range, 0.015/4-32/4 µg/ml). The in-vitro activity of carbapenem antibiotics includes Enterobacteriaceae, P. aeruginosa, avibactam (MIC range, 0.4-16/1 µg/ml), and non-metallo-carbapenemases (KPC and some OXA enzymes). Carbapenem antibiotics have also been shown to be resistant to avibactam alone at a concentration of 1 µg/ml (46.9%) but not susceptible to carbapenem-resistant strains resistant to avibactam due to efflux pump mechanism.

To become an effective therapeutic agent against emerging resistant/multi-resistant (MDR) pathogens such as the ESKAPE organisms, laboratories must strive to accurately test the combination to guide treatments. In this report, we describe the results from a commercial method (Sensititre®; ThermoFisher Scientific) and a clinical method (CLSI broth microdilution) for ceftazidime-avibactam susceptibility testing when compared to the reference CLSI broth microdilution method.

### Methods

A systematic method development and validation study was designed to compare the Sensititre dry-form broth microdilution panel results monitoring carbapenem-avibactam MIC ranges (0.03/0.1-256/16 µg/ml) to results obtained from four reference CLSI broth microdilution panels. Endpoints were read manually and by automated commercial devices were also compared. All tests were performed in standardized cation-adjusted Mueller-Hinton broth with appropriate supplements (2% d-glucose) used for both screening and validation studies. Study design followed guidelines found in CLSI M23-A3 (2008), FDA guidelines, and previously used by these investigators.

The MIC values were determined (Table 1) and compared for the reference method (Sensititre®) and reference broth microdilution method (CLSI) using the following criteria:

- **Table 1** is reproduced from a recent publication by our laboratories comparing the MIC results for cefepime alone and in combination with avibactam at 6.4 and 12.8 µg/ml against 506 Enterobacteriaceae and 259 P. aeruginosa (USA strains, 2012). The results will be published in the reference from the broth microdilution method (CLSI) when testing 525 organisms in the study. The MIC result range, for clinical reporting, for cefepime-avibactam combination included 6.4–12.8 µg/ml. The concordance of MIC results was determined. The results from a commercial method (Sensititre®; ThermoFisher Scientific) and a clinical method (CLSI broth microdilution) for ceftazidime-avibactam susceptibility testing when compared to the reference CLSI broth microdilution method.

### Results

- **Table 1** is reproduced from a recent publication by our laboratories comparing the MIC results for cefepime alone and in combination with avibactam at 6.4 and 12.8 µg/ml against 506 Enterobacteriaceae and 259 P. aeruginosa (USA strains, 2012). The results will be published in the reference from the broth microdilution method (CLSI) when testing 525 organisms in the study. The MIC result range, for clinical reporting, for cefepime-avibactam combination included 6.4–12.8 µg/ml. The concordance of MIC results was determined. The results from a commercial method (Sensititre®; ThermoFisher Scientific) and a clinical method (CLSI broth microdilution) for ceftazidime-avibactam susceptibility testing when compared to the reference CLSI broth microdilution method.

- **Table 2** compares the results of the commercial broth microdilution method (Sensititre®) and CLSI method for ceftazidime-avibactam for various resistance profiles.

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### References


