

INTRODUCTION

The novel serine β -lactamase inhibitor ANT3310 in combination with meropenem (MEM-ANT3310) is currently in Phase I clinical development. This study was performed to establish broth microdilution (BMD) quality control (QC) ranges for MEM-ANT3310 against specific QC organisms utilized by the Clinical and Laboratory Standards Institute (CLSI). This study design met or exceeded the following CLSI M23-A3 requirements for Tier 2 QC studies: seven laboratories/independent sites; three media lots (different manufacturers); at least 10 replicates of each QC strain per laboratory (at least 70 total test points per medium lot); and at least 210 test points per QC strain/drug combination [1].

METHODS

- A multi-laboratory study to evaluate broth microdilution (BMD) QC ranges for MEM-ANT3310 was carried out according to CLSI guidelines utilizing data from eight laboratories [1].
- Four ATCC QC organisms within the spectrum of MEM-ANT3310 activity were tested: *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 27853, *Acinetobacter baumannii* NCTC 13304 (OXA-27), and *Klebsiella pneumoniae* ATCC BAA-2814 (KPC-3, SHV-11, TEM-1).
- Meropenem with ANT3310 at a fixed concentration of 8 $\mu\text{g/mL}$ was tested at concentrations of 0.004/8 - 4/8 $\mu\text{g/mL}$. Meropenem alone, ANT3310 alone, and two control agents, ceftazidime-avibactam (CZA) and sulbactam-durlobactam (SUD), were tested following CLSI guidelines for BMD [2, 3].
- Cation-adjusted Mueller Hinton Broth (CAMHB) from three manufacturers was tested on BMD panels.
- Supplies, including frozen broth microdilution panels were distributed by IHMA, Inc. (Schaumburg, IL, US) to the other seven sites.

RESULTS SUMMARY

- The MIC results were analyzed using Rangefinder MIC V.21 and the M23 method calculated as described in CLSI guidelines [1].
- The greater than 95% within range CLSI criterion was met by all data from all eight laboratories for MEM-ANT3310.
- There were no differences in MICs tested in the three different lots of broth.
- All control data (CZA and SUD) were within CLSI-approved ranges.
- The colony counts obtained were all within the acceptable range.

CONCLUSIONS

- Quality control results for MEM-ANT3310 were highly reproducible in this M23 Tier 2 study.
- QC strains *A. baumannii* NCTC 13304 and *K. pneumoniae* ATCC BAA-2814 are resistant to MEM alone (both modal MIC = 64 $\mu\text{g/mL}$) and ANT3310 alone (modal MIC = 128 and 64 $\mu\text{g/mL}$, respectively) and demonstrate no overlap of MICs with MEM-ANT3310. Both strains are recommended for routine testing of MEM-ANT3310.
- E. coli* ATCC 25922 and *P. aeruginosa* ATCC 27853 are recommended for supplemental testing of MEM-ANT3310.
- The following broth microdilution QC ranges for MEM-ANT3310 were accepted by the CLSI at the January 2024 meeting:

Antimicrobial	QC Organism	Range ($\mu\text{g/ml}$)	Size of range	% in Range (N)	
MEM-ANT3310	<i>E. coli</i> ATCC 25922	0.008/8 - 0.03/8	3	99.6%	(239/240)
	<i>P. aeruginosa</i> ATCC 27853	0.125/8 - 0.5/8	3	98.3%	(236/240)
	<i>K. pneumoniae</i> ATCC BAA-2814*	0.06/8 - 0.25/8	3	100.0%	(240/240)
	<i>A. baumannii</i> NCTC 13304*	0.125/8 - 1/8	4	100.0%	(240/240)

*Recommended routine QC strain

REFERENCES

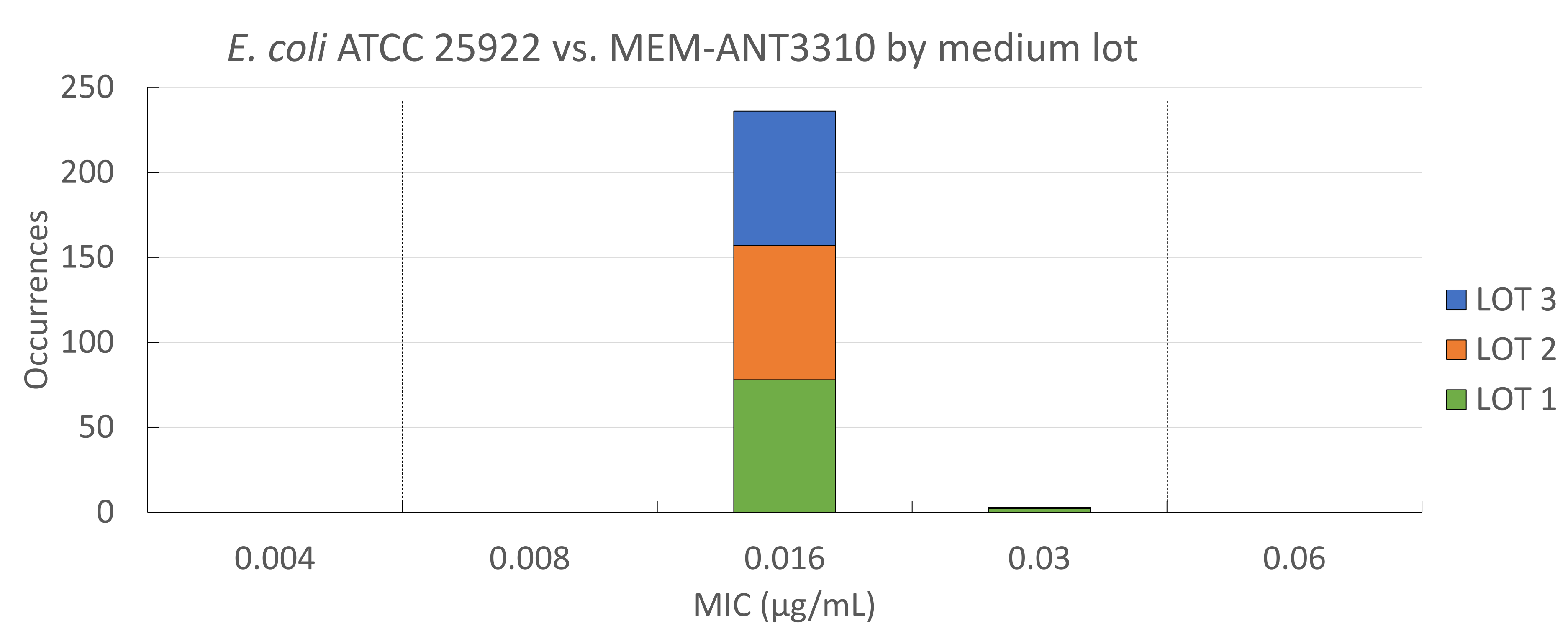
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DISCLOSURES

Part of this work was supported by a Grant to Antabio from the European Innovation Council (EIC; project sbli-ant3310, contract 190159682)

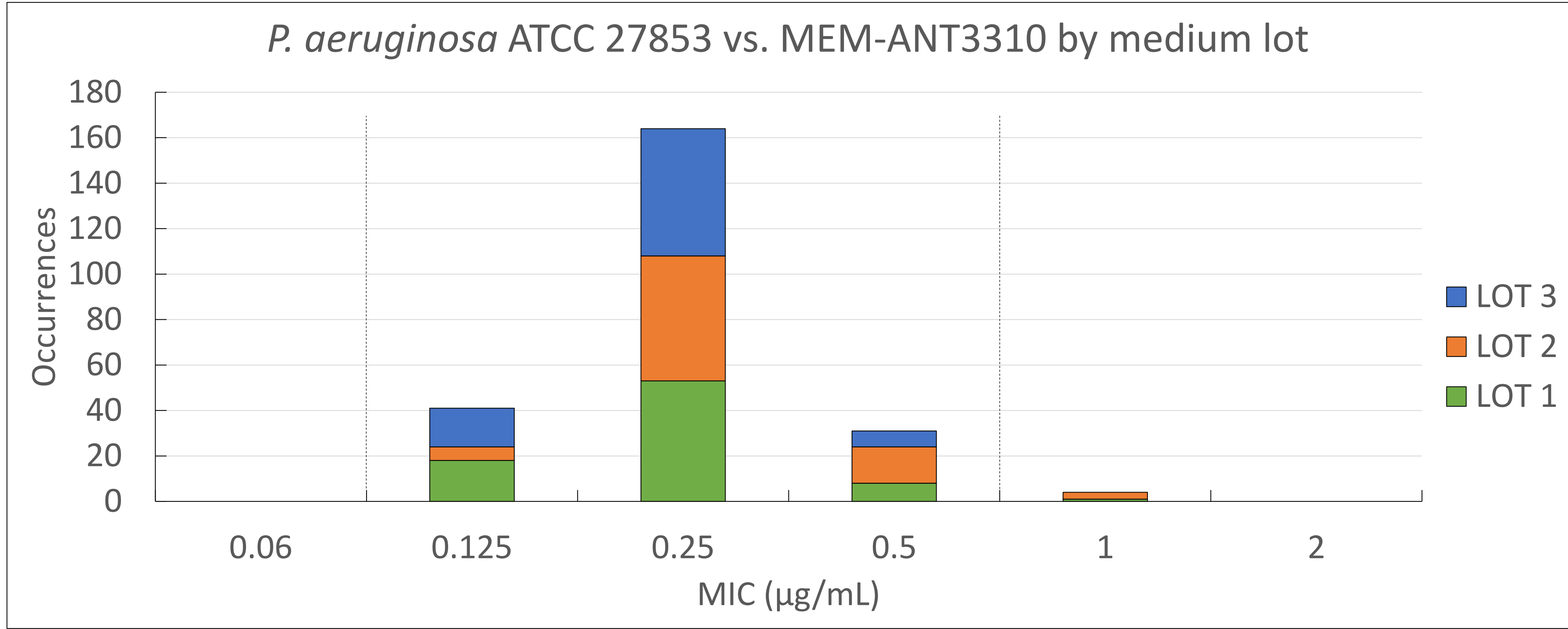
RESULTS

Figure 1. MEM-ANT3310 MIC distribution for *E. coli* ATCC 25922



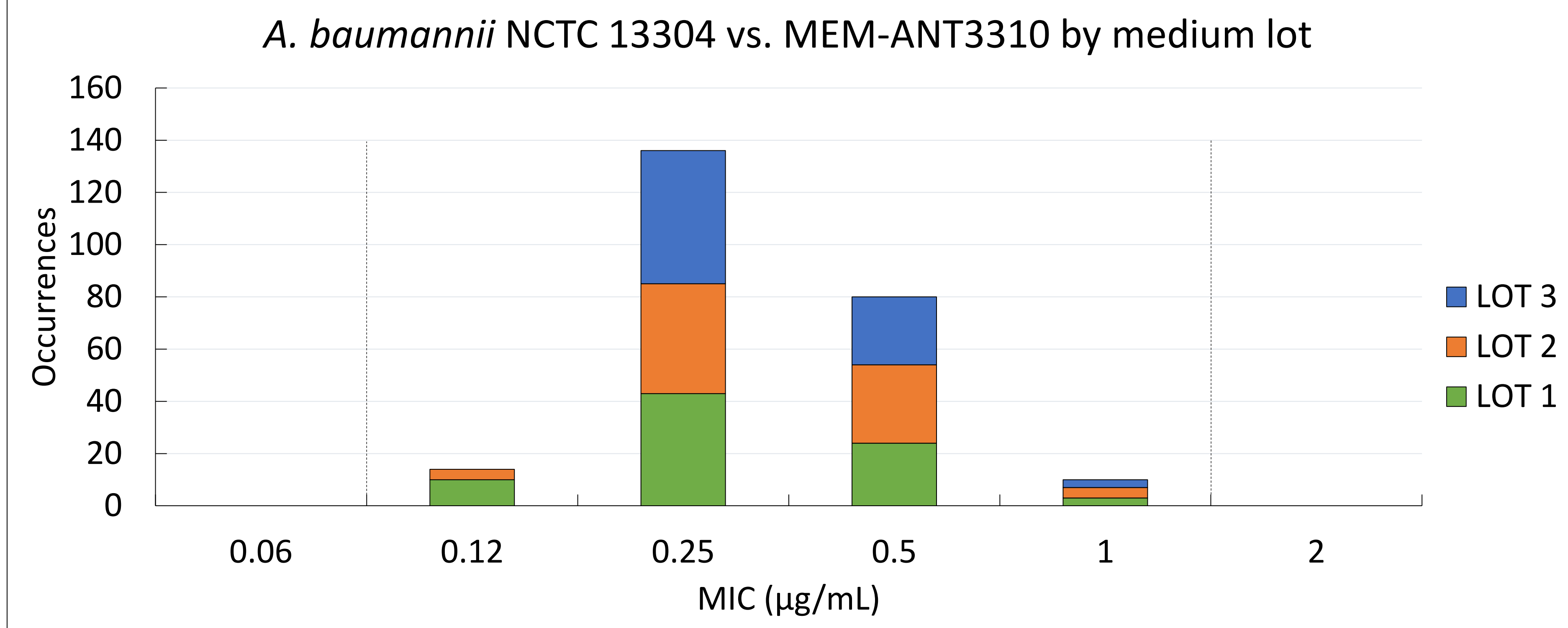
Dashed lines indicate approved CLSI QC range

Figure 2. MEM-ANT3310 MIC distribution for *P. aeruginosa* ATCC 27853



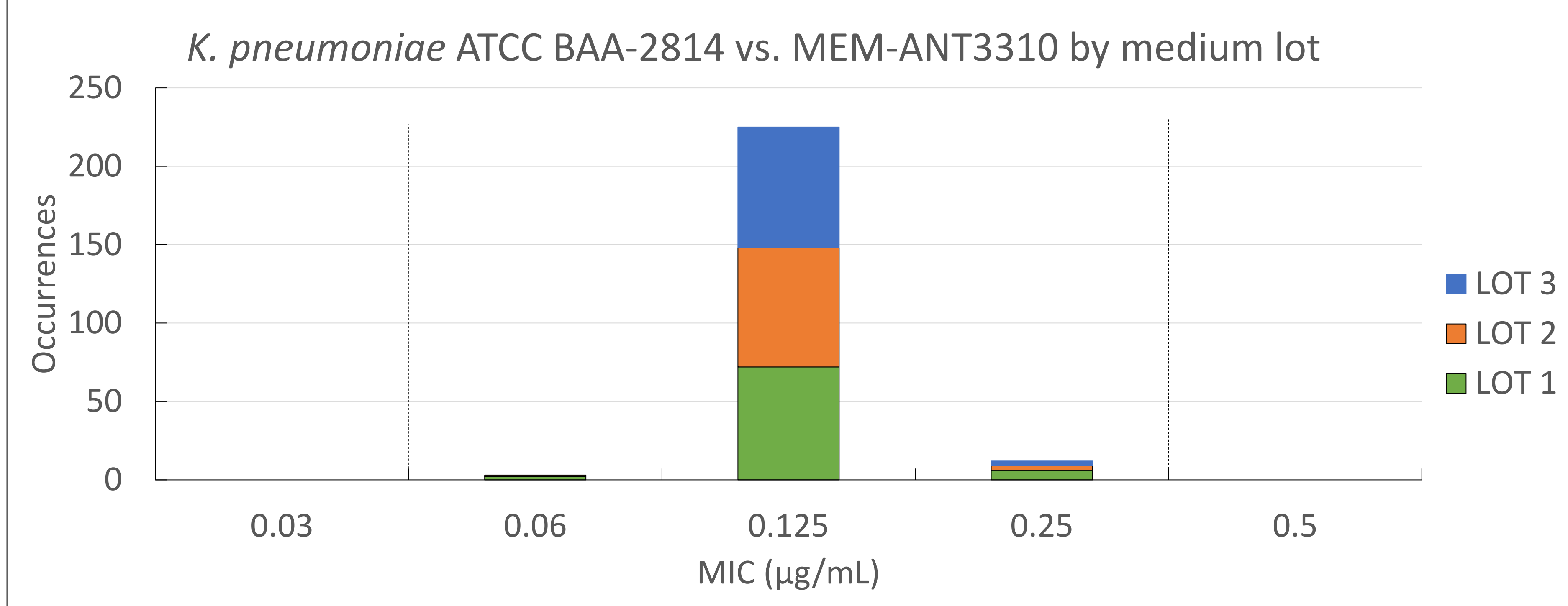
Dashed lines indicate approved CLSI QC range

Figure 3. MEM-ANT3310 MIC distribution for *A. baumannii* NCTC 13304



Dashed lines indicate approved CLSI QC range

Figure 4. MEM-ANT3310 MIC distribution for *K. pneumoniae* ATCC BAA-2814



Dashed lines indicate approved CLSI QC range