

Abstract

Background: Omadacycline is a new antibiotic, the first aminomethylcycline under development for use in skin and soft tissue and respiratory infections. Testing of this agent requires the use of fresh media (less than 12 hours old) since the compound is broken down by oxygen in the media which increases over time. Methods: This study was performed according to the Clinical and Laboratory Standards Institute (CLSI) guidelines. Broth microdilution MIC panels were prepared and distributed frozen to 8 independent laboratories for testing. Three lots of Brucella broth supplemented with hemin (5 µg/ml) and Vitamin K1 (1 µg/ml) and lysed horse blood (5%) was used to prepare omadacycline dilution. Broths were prepared on the same day that MIC panels were poured and frozen at -70 °C. Three lots of Brucella agar deeps supplemented with hemin (5 µg/ml) and Vitamin K1 (1 µg/ml) were prepared and distributed to 8 laboratories. Deepes were boiled at the test sites and laked sheep blood (5%) was added on the day of agar dilution plate preparation. Each laboratory tested 10 replicates of each ATCC quality control (QC) organism by both broth MIC and agar dilution methods. Tigecycline was tested as a control in one lot of each media type. Results: All control agent MIC results were within the approved QC ranges except for 3 replicates of B. thetaiotaomicon vs. tigecycline. The omadacycline MIC values associated with these out of control data were removed in order to establish the ranges approved.

The following QC ranges were presented the CLSI antimicrobial susceptibility subcommittee and were approved and listed in CLSI M100-S22 document in January 2012.

Table with 4 columns: Control Strain, B. fragilis ATCC 25285, B. thetaiotaomicon ATCC 29741, E. lenta ATCC 43055, C. difficile ATCC 700057. Rows show Omadacycline Broth MIC Range and Omadacycline Agar Dilution MIC Range.

Conclusions: Omadacycline MIC ranges approved were all within a 3 or 4 two-fold dilution range and each range represented 99.5 to 100% of the data results for each QC strain.

Background

Omacycline is the first aminomethylcycline to enter clinical development. OMC is being developed globally as an intravenous and oral, once daily monotherapy therapy for ABSSSI and CABP. OMC was designed to overcome tetracycline resistance mechanisms and has been shown to have potent in vitro activity and in vivo efficacy against the key pathogens of ABSSSI and CABP, including isolates resistant to standards of care. The IV and oral formulations are bioequivalent and neither shown the dose-limiting nausea and vomiting exhibited by other tetracycline derivatives.

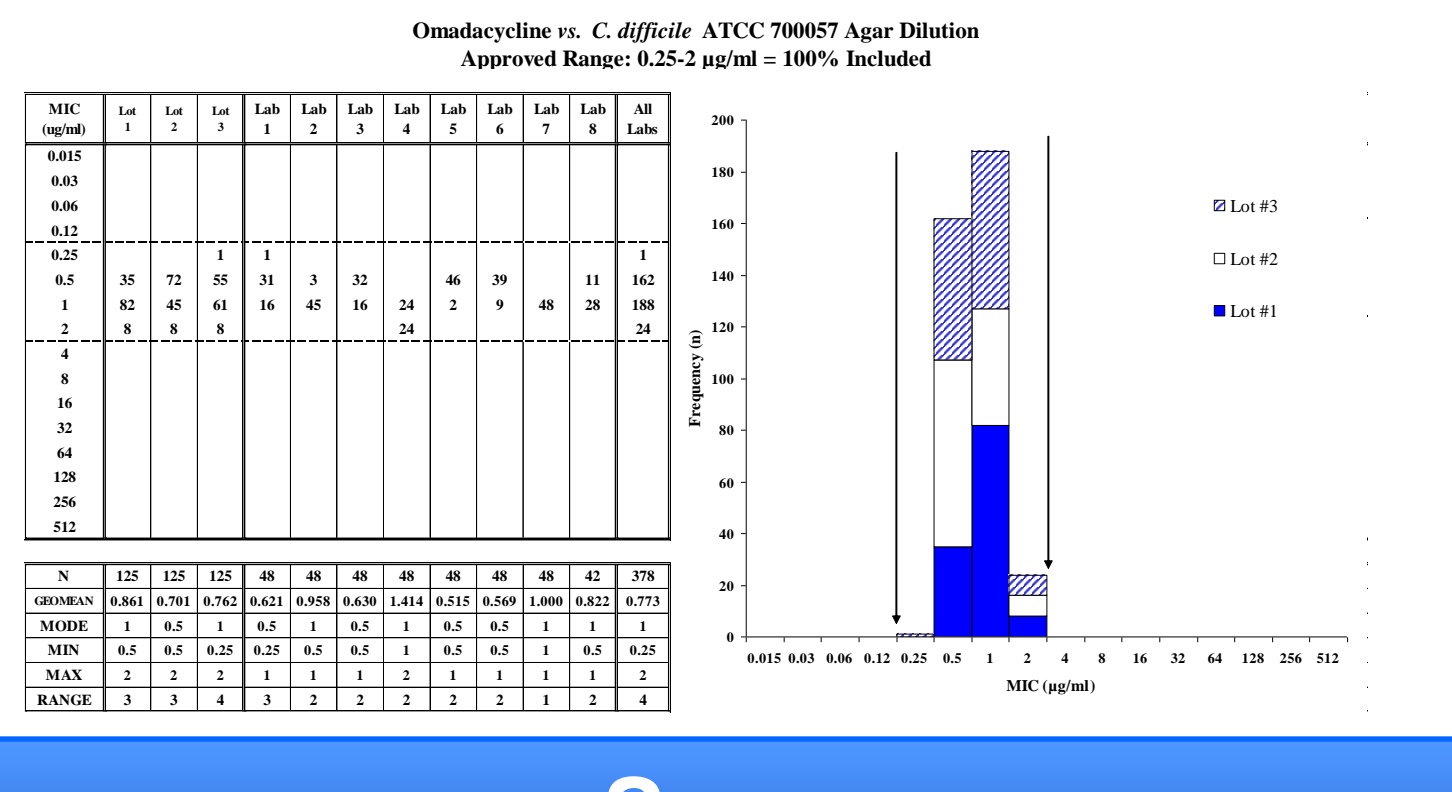
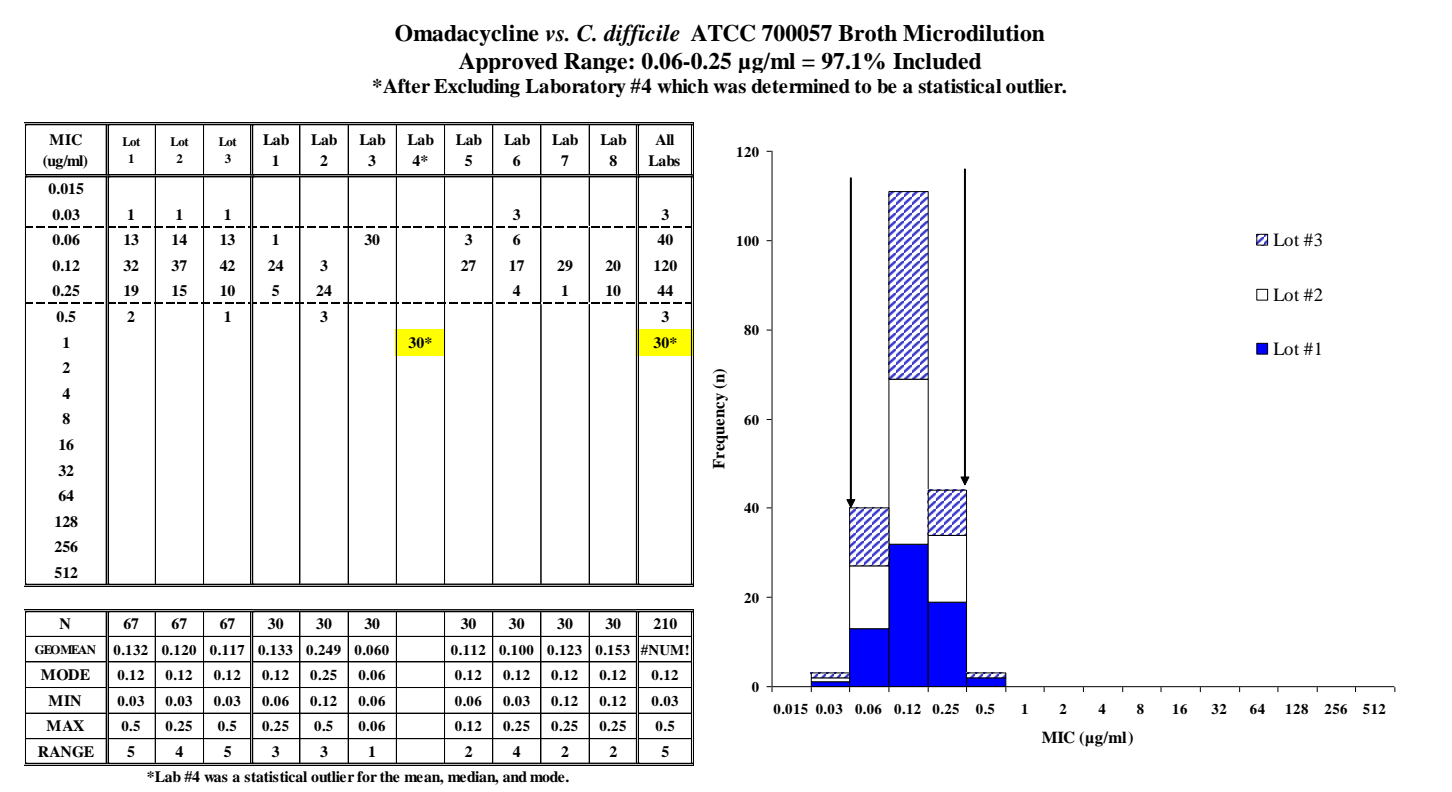
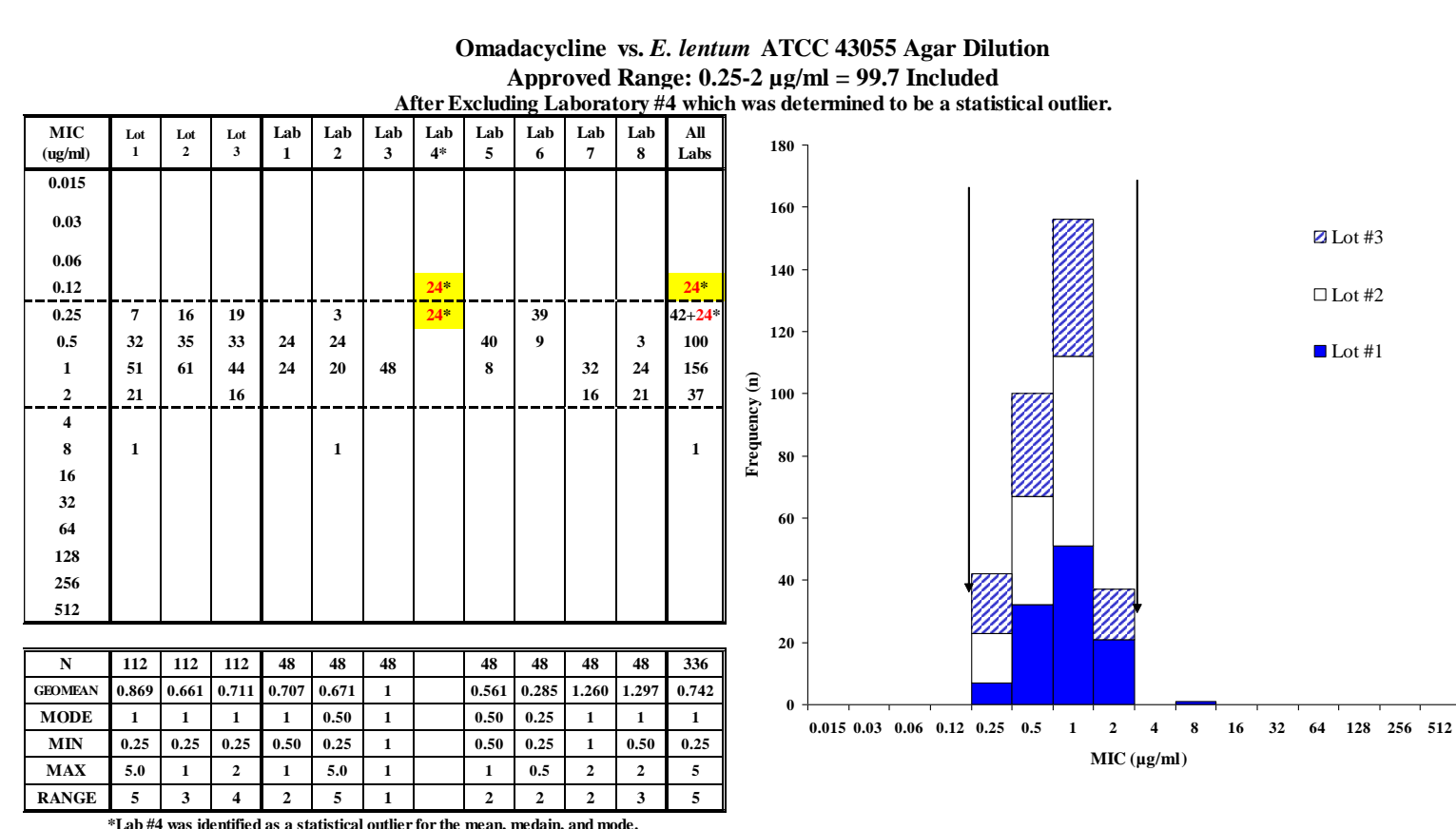
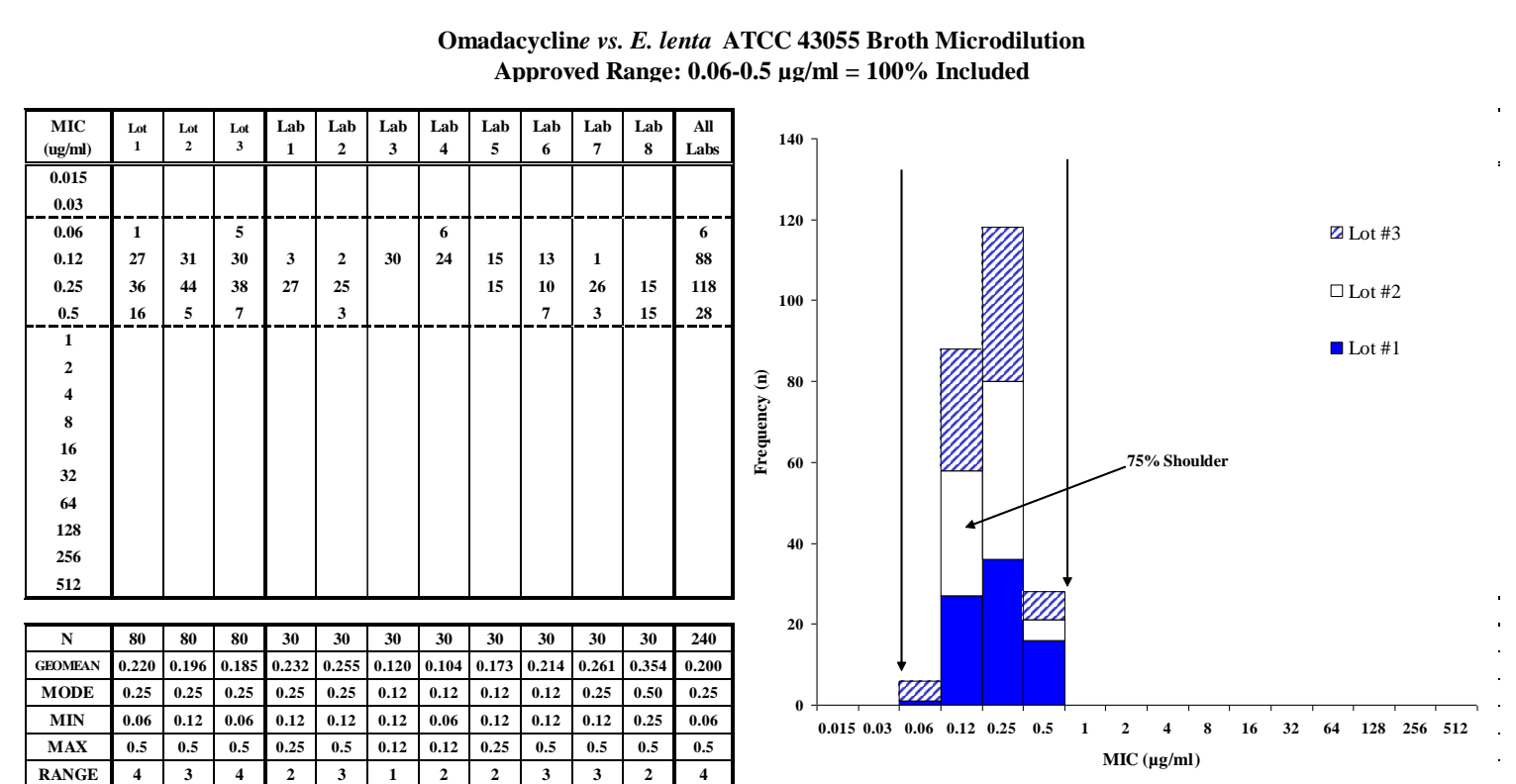
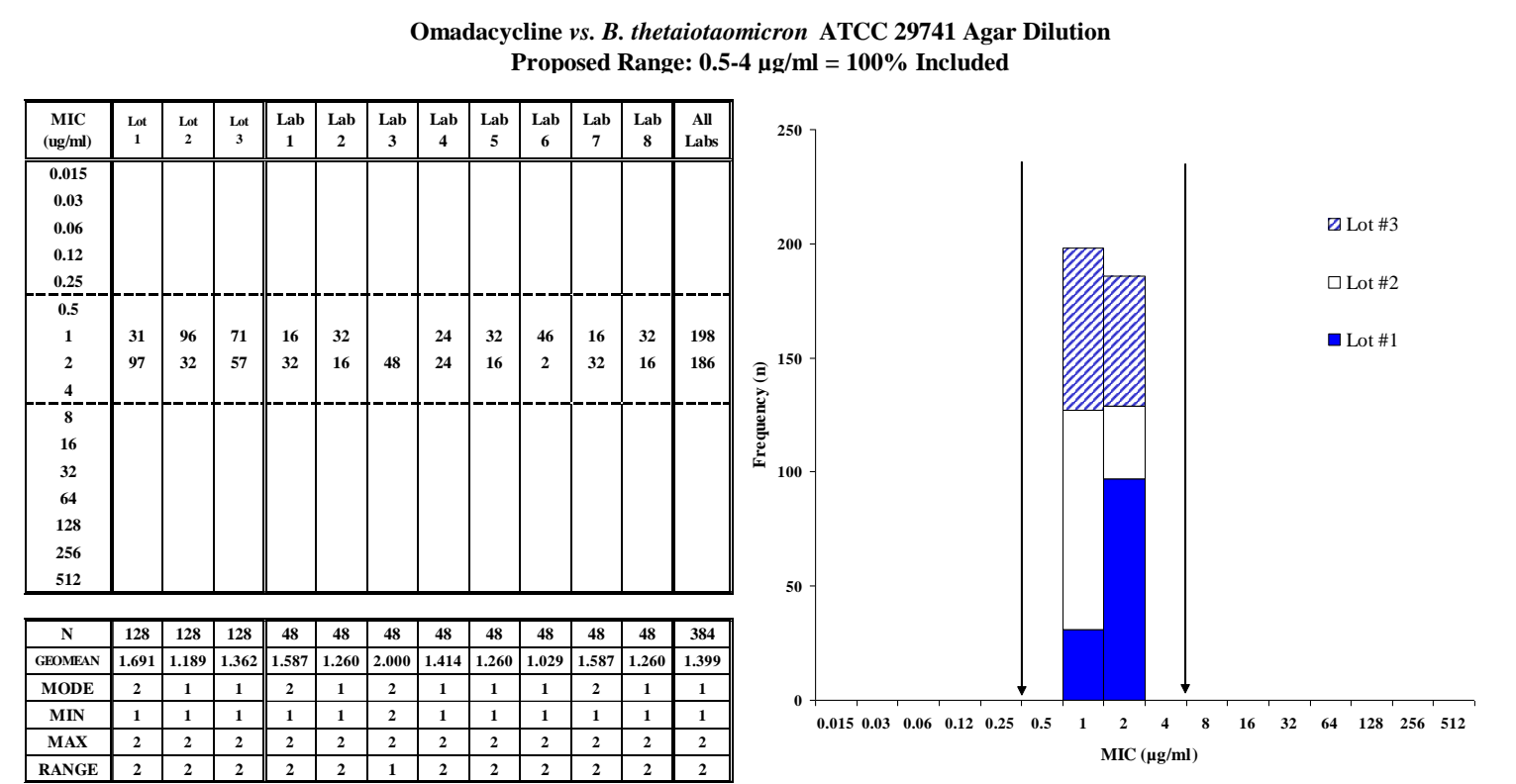
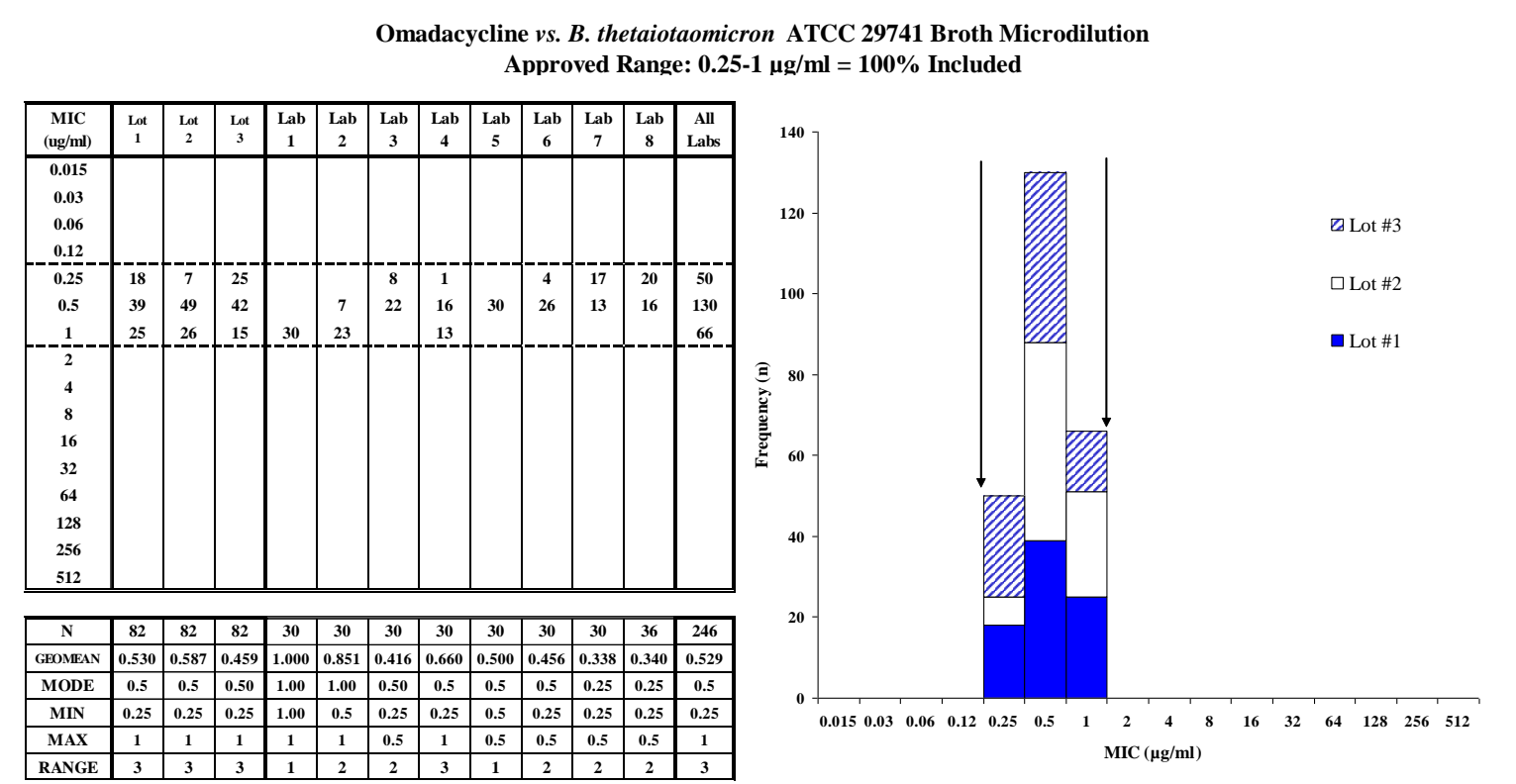
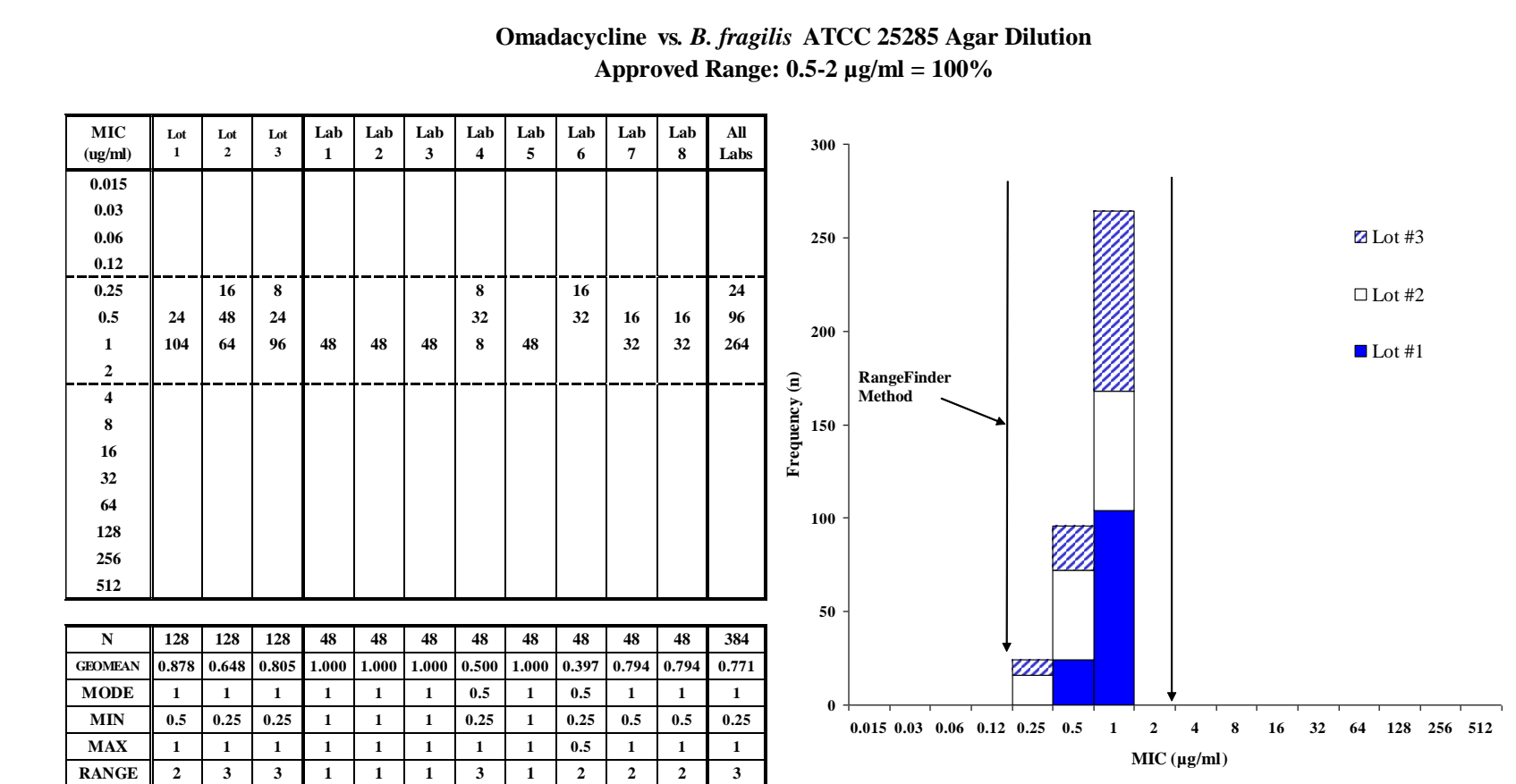
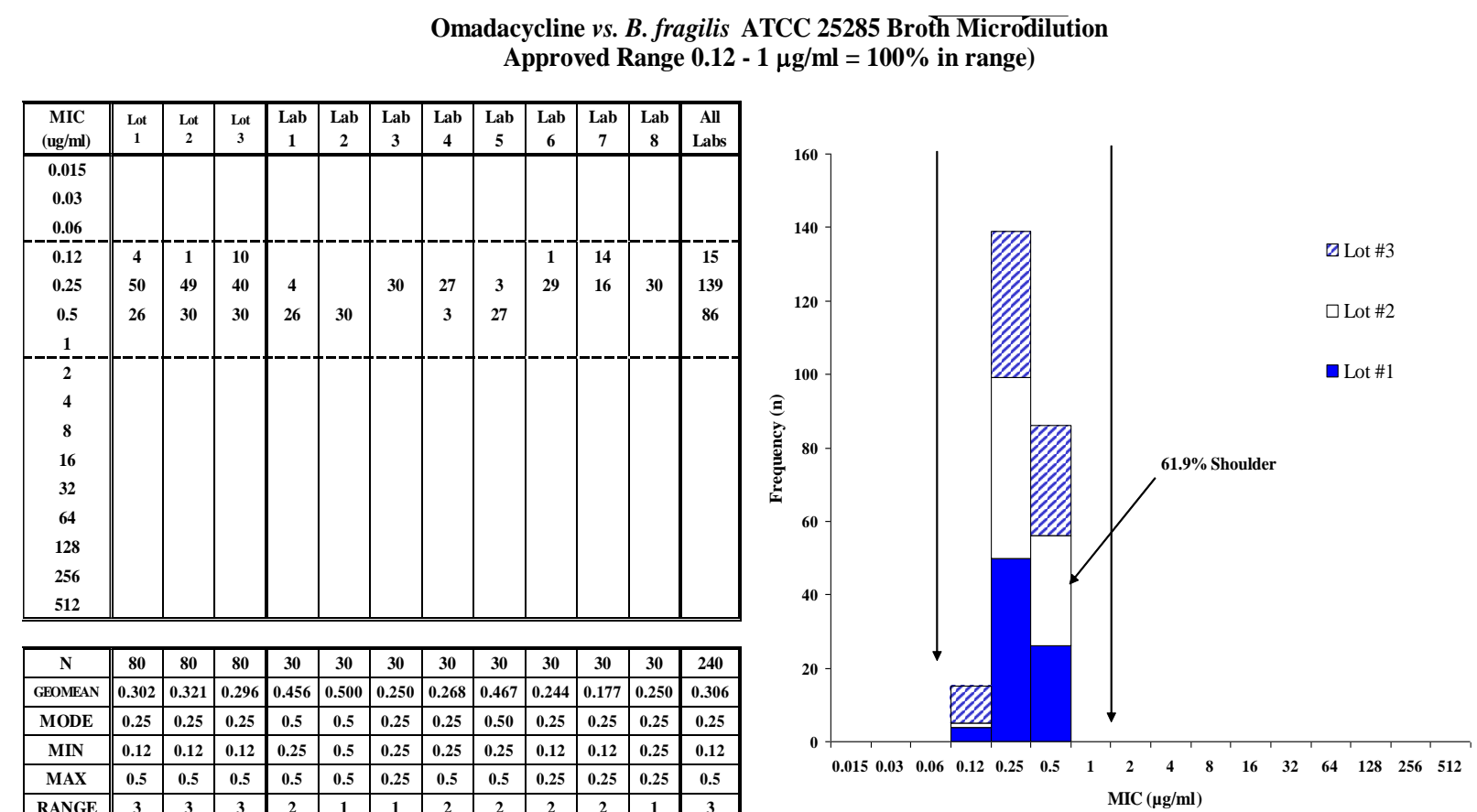
Acknowledgement

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Materials and Methods

- Eight-laboratories tested Omadacycline against B. fragilis ATCC 25285 (BF), B. thetaiotaomicon ATCC 29741 (BT) and C. difficile ATCC 700057 (CD) and E. lenta ATCC 43055 (EL) using the CLSI reference broth microdilution (BMD) and agar dilution (AD) methods for anaerobes. Three lots each of Brucella broth and Brucella agar supplemented with 5 µg/ml hemin, 1 µg/ml vitamin K1, and 5% lysed horse blood (BMD) or 5% lysed sheep blood (AD) were used for testing all strains. Broth was prepared less than 12 hours prior to preparing and freezing MIC panels. Agar plates were poured fresh on the day of testing. Colony counts were performed at all laboratories. All testing met or exceeded the requirements of CLSI Guideline M23-A33 Data was analyzed using the method described in CLSI M23-A3 and checked using method of the Turnidge, et al4

Results



Summary

CLSI Approved Quality Control Ranges (µg/mL)

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Conclusions: Omadacycline MIC ranges approved were all within a 3 or 4 two-fold dilution range and each range represented 99.5 to 100% of the data results for each QC strain.

All control agent MIC results were within the approved QC ranges except for 3 replicates of B. thetaiotaomicon vs. tigecycline. The omadacycline MIC values associated with these out of control data were removed in order to establish the ranges approved.

References

- 1. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard-Eighth Edition, M07-A8 Vol. 29 No. 2, January 2009, Clinical Laboratory Standards Institute, Wayne PA. 2. Methods for Antimicrobial Susceptibility Testing of Anaerobic Bacteria; Approved Standard-Seventh Edition, M11-A7 Vol. 27 No. 2, January 2007, Clinical Laboratory Standards Institute, Wayne, PA. 3. Development of In Vitro Susceptibility Testing Criteria and Quality Control Parameters; Approved Guideline-Third Edition, M23-A3 Vol. 28 No. 27, October 2008. Clinical Laboratory Standards Institute, Wayne PA. 4. Turnidge H, Bordash G. Statistical methods for establishing quality control ranges for antibacterial agents in Clinical and Laboratory Standards Institute susceptibility testing. J. Antimicro Agents Chemother. 2007;51:2483-2488