

# D-1140

## Quality Control Parameters for Omadacycline Minimum Inhibitory Concentration (MIC) Susceptibility Tests Using Fresh Media

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### Abstract

**Background:** Omadacycline is a new antibiotic, the first aminomethylcycline under development for skin and soft tissue and respiratory infections. Susceptibility 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. Each lab tested the 5 ATCC quality control (QC) organisms 10 times in MIC panels containing omadacycline diluted in three lots of cation-adjusted Mueller Hinton broth. Broth was prepared on the same day that MIC panels were prepared and frozen at -70 °C immediately after pour. Tetracycline was tested as a control. **Results:** The following omadacycline MIC results were presented to the CLSI subcommittee. Tetracycline ranges obtained were all within the CLSI approved ranges. All ranges were approved and listed in the CLSI M100-S22 document in January 2012. **Conclusions:** Omadacycline MIC ranges approved were all within a 3 or 4 two-fold dilution range and each range represented 100% of the data results for each QC strain.

Control Strain	<i>E. coli</i> ATCC 25922	<i>S. aureus</i> ATCC 29213	<i>E. faecalis</i> ATCC 29212	<i>S. pneumoniae</i> ATCC 49619	<i>H. influenzae</i> ATCC 49247
Omacycline MIC Range (µg/ml)	0.25 - 2	0.12 - 1	0.06 - 0.5	0.015 - 0.12	0.5 - 2

### 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.

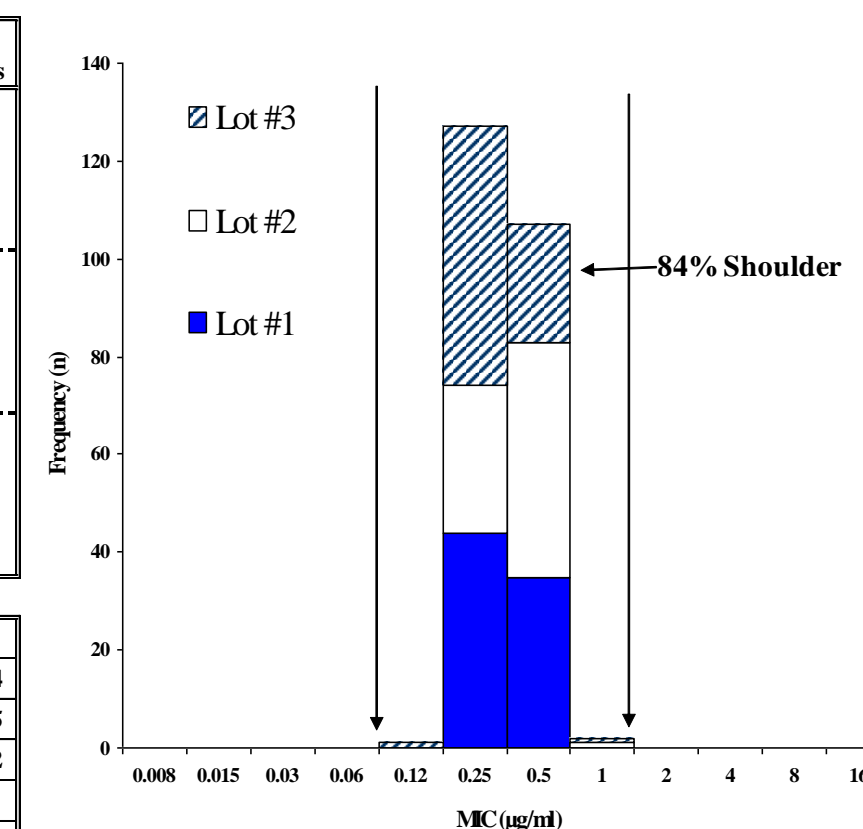
### Materials and Methods

- Eight-laboratories tested omadacycline against *S. aureus* ATCC 29213 (SA), *E. faecalis* ATCC 29212 (EF), *E. coli* ATCC 25922 (EC), *S. pneumoniae* ATCC 49619 (SP) and *H. influenzae* (HI) ATCC 49247 using the CLSI reference broth microdilution (BMD)<sup>1,2</sup>
- Three different lots of cation adjusted Mueller-Hinton broth (CAMHB) were used for all tests.
- CAMHB was used for testing SA, EF and EC, and supplemented with 3% lysed horse blood for testing SP or made up as Haemophilus test media (HTM) for testing HI.
- All laboratories tested 10 replicates of each QC strain over a period of 3 -10 days.
- All testing met or exceeded the requirements of CLSI Guideline M23-A3<sup>3</sup>
- Data was analyzed using the method described in CLSI M23-A3 and checked using method of the Turnidge, et al<sup>4</sup>.

### Results

MIC (µg/ml)	LOT 1	LOT 2	LOT 3	LAB 1	LAB 2	LAB 3	LAB 4	LAB 5	LAB 6	LAB 7	LAB 8	All Labs
0.008												
0.015												
0.03												
0.06												
0.12			1			1						1
0.25	44	30	53	16	13	23	30		19	2	24	127
0.5	35	48	24	14	17	6		28	11	28	3	107
1			1					2				2
2												
4												
8												
16												

N	79	79	79	30	30	30	30	30	30	30	27	237
GEOMEAN	0.34	0.39	0.31	0.35	0.37	0.28	0.25	0.52	0.32	0.48	0.27	0.34
MODE	0.25	0.5	0.25	0.25	0.5	0.25	0.25	0.5	0.25	0.5	0.25	0.25
MIN	0.25	0.25	0.12	0.25	0.25	0.12	0.25	0.5	0.25	0.25	0.25	0.12
MAX	0.5	1	1	0.5	0.5	0.5	0.25	1	0.5	0.5	0.5	1
RANGE	2	3	4	2	2	3	1	2	2	2	2	4

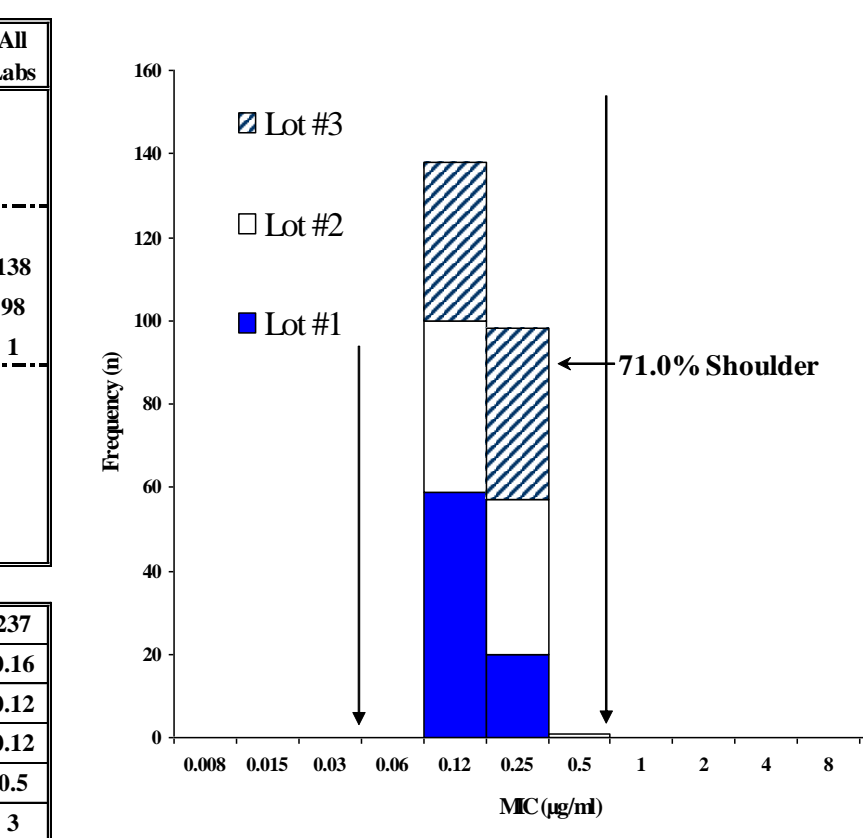


Omacycline vs. *S. aureus* ATCC 29213  
Approved Range: 0.12 - 1 µg/ml = 100% Included

Omacycline vs. *E. faecalis* ATCC 29212  
Approved Range: 0.06 - 0.5 µg/ml = 100% Included

MIC (µg/ml)	LOT 1	LOT 2	LOT 3	LAB 1	LAB 2	LAB 3	LAB 4	LAB 5	LAB 6	LAB 7	LAB 8	All Labs
0.008												
0.015												
0.03												
0.06												
0.12	59	41	38	26	23	28	12		16	11	22	138
0.25	20	37	41	4	7	2	18	30	13	19	5	98
0.5		1							1			1
2												
4												
8												
16												

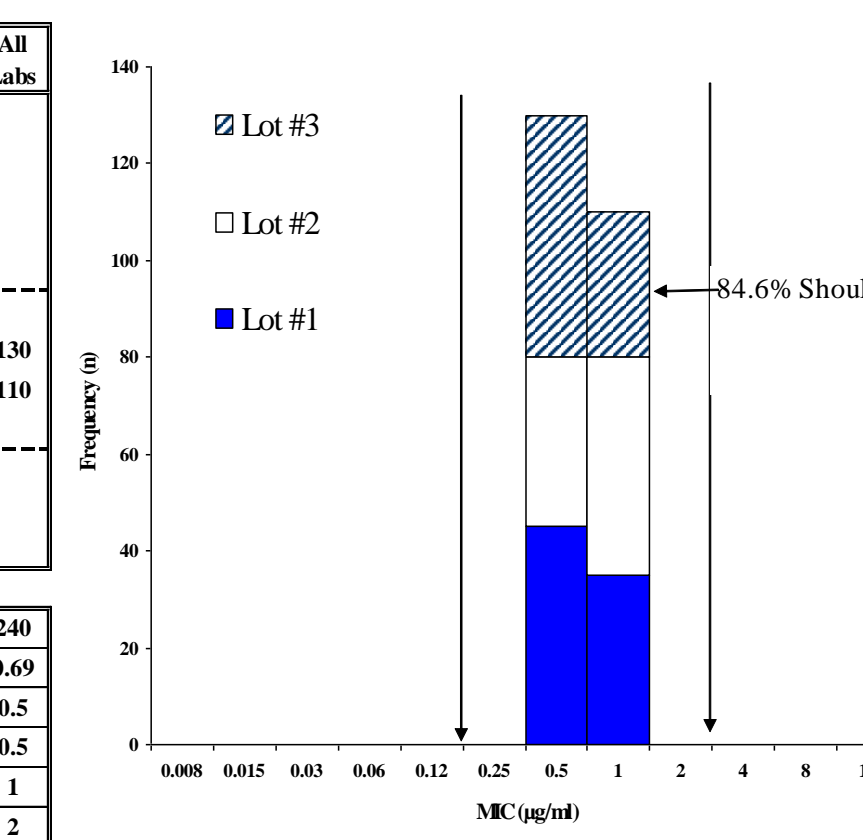
N	79	79	79	30	30	30	30	30	30	30	27	237
GEOMEAN	0.14	0.17	0.18	0.13	0.14	0.13	0.19	0.25	0.17	0.19	0.14	0.16
MODE	0.12	0.12	0.25	0.12	0.12	0.12	0.25	0.25	0.12	0.25	0.12	0.12
MIN	0.12	0.12	0.12	0.12	0.12	0.12	0.12	0.25	0.12	0.12	0.12	0.12
MAX	0.25	0.5	0.25	0.25	0.25	0.25	0.25	0.5	0.25	0.25	0.25	0.5
RANGE	2	3	2	2	2	2	2	1	3	2	2	3



Omacycline vs. *E. coli* ATCC 25922  
Proposed Range: 0.25 - 2 µg/ml = 100% Included

MIC (µg/ml)	LOT 1	LOT 2	LOT 3	LAB 1	LAB 2	LAB 3	LAB 4	LAB 5	LAB 6	LAB 7	LAB 8	All Labs
0.008												
0.015												
0.03												
0.06												
0.12												
0.25												
0.5	45	35	50	26	17	14	12	23	9	27	2	130
1	35	45	30	4	13	16	18	7	21	3	28	110
2												
4												
8												
16												

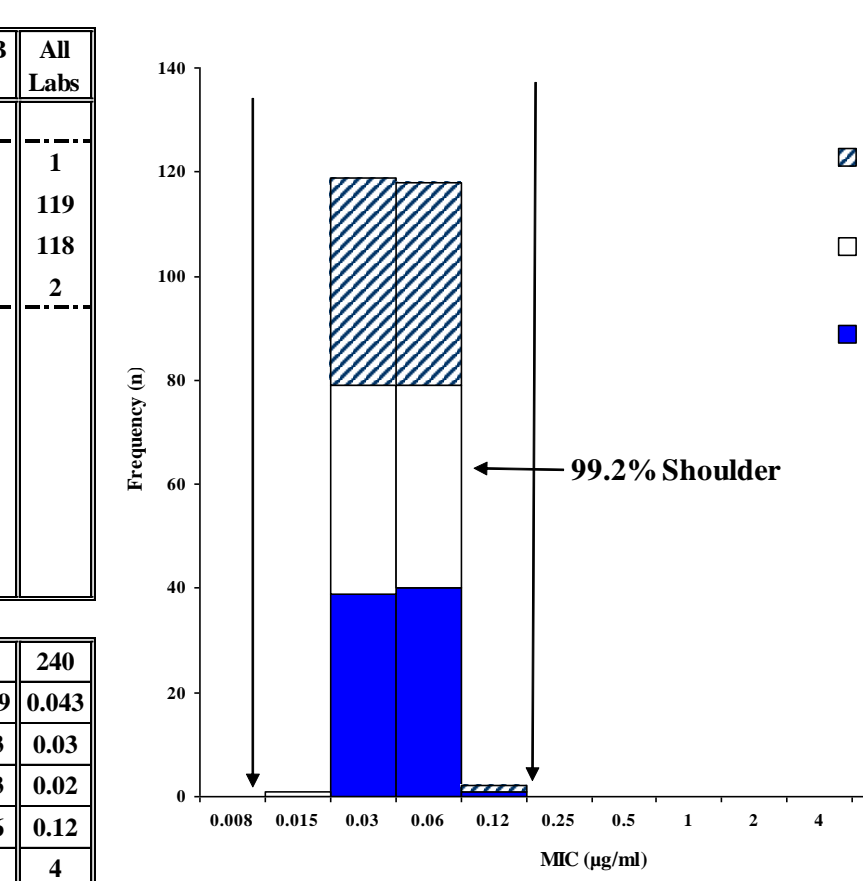
N	80	80	80	30	30	30	30	30	30	30	30	240
GEOMEAN	0.68	0.74	0.65	0.55	0.68	0.72	0.76	0.59	0.81	0.54	0.95	0.69
MODE	0.5	1	0.5	0.5	0.5	1.0	1.0	0.5	1.0	0.5	1.0	0.5
MIN	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5	0.5
MAX	1	1	1	1	1	1	1	1	1	1	1	1
RANGE	2	2	2	2	2	2	2	2	2	2	2	2



*S. pneumoniae* ATCC 49619  
Approved Range: 0.015 - 0.12 µg/ml = 100% Included

MIC (µg/ml)	LOT 1	LOT 2	LOT 3	LAB 1	LAB 2	LAB 3	LAB 4	LAB 5	LAB 6	LAB 7	LAB 8	All Labs
0.008												
0.015												
0.03	39	40	40	15	15	26	11	6	27	19	119	
0.06	40	39	39	15	28	14	4	19	24	3	111	118
0.12	1		1		2							2
0.25												
0.5												
1												
2												
4												
8												
16												

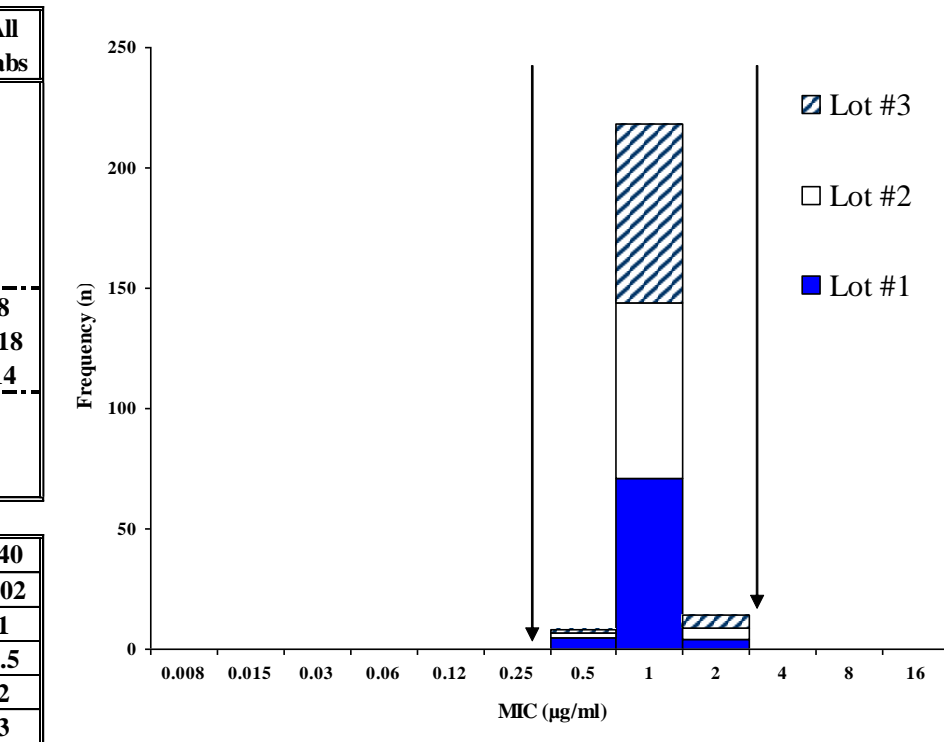
N	80	80	80	30	30	30	30	30	30	30	30	240
GEOMEAN	0.043	0.042	0.043	0.042	0.063	0.041	0.033	0.047	0.052	0.032	0.039	0.043
MODE	0.06	0.03	0.03	0.03	0.06	0.03	0.06	0.06	0.06	0.03	0.03	0.03
MIN	0.03	0.02	0.03	0.03	0.06	0.02	0.03	0.03	0.03	0.03	0.03	0.02
MAX	0.12	0.06	0.12	0.06	0.12	0.06	0.06	0.06	0.06	0.06	0.06	0.12
RANGE	3	3	3	2	2	3	2	2	2	2	2	4



Omacycline vs. *H. influenzae* ATCC 49247  
Approved Range: 0.5 - 2 µg/ml = 100% Included

MIC (µg/ml)	LOT 1	LOT 2	LOT 3	LAB 1	LAB 2	LAB 3	LAB 4	LAB 5	LAB 6	LAB 7	LAB 8	All Labs
0.008												
0.015												
0.03												
0.06												
0.12												
0.25												
0.5	5	2	1						6			8
1	71	73	74	30	30	26	30	18	24	30	30	218
2	4	5	5			2		12				14
4												
8												
16												

N	80	80	80	30	30	30	30	30	30	30	30	240
GEOMEAN	0.99	1.03	1.04	1.00	1.00	1.00	1.00	1.32	0.87	1.00	1.00	1.02
MODE	1	1	1	1	1	1	1	1	1	1	1	1
MIN	0.5	0.5	0.5	1	1	0.5	1	1	0.5	1	1	0.5
MAX	2	2	2	1	1	2	1	2	1	1	1	2
RANGE	3	3	3	1	1	3	1	2	2	1	1	3



### Summary

#### Omacycline CLSI Published MIC Quality Control Ranges

QC Organ
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