SUSCEPTIBILITY



In Vitro Activity of Delafloxacin against Contemporary Bacterial Pathogens from the United States and Europe, 2014

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ABSTRACT The *in vitro* activities of delafloxacin and comparator antimicrobial agents against 6,485 bacterial isolates collected from medical centers in Europe and the United States in 2014 were tested. Delafloxacin was the most potent agent tested against methicillin-susceptible *Staphylococcus aureus* (MSSA), methicillin-resistant *S. aureus, Streptococcus pneumoniae*, viridans group streptococci, and beta-hemolytic streptococci and had activity similar to that of ciprofloxacin and levofloxacin against certain members of the *Enterobacteriaceae*. Overall, the broadest coverage of the tested pathogens (Grampositive cocci and Gram-negative bacilli) was observed with meropenem and tigecycline in both Europe and the United States. Delafloxacin was shown to be active against organisms that may be encountered in acute bacterial skin and skin structure infections, respiratory infections, and urinary tract infections.

KEYWORDS MRSA, delafloxacin

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The fluoroquinolone class of antibiotics is currently used as standard empirical therapy in health care-associated infections and community-acquired infections; specifically, antibiotics of this class are indicated for the treatment of urinary tract infections (UTI), respiratory tract infections (RTI), acute bacterial skin and skin structure infections (ABSSSI), and intra-abdominal infections (1–6). A recent point-prevalence study of antimicrobial use in U.S. acute care hospitals found levofloxacin to be the third most common antimicrobial agent prescribed to treat both community-acquired infections and health care-acquired infections (7). In the face of such broad utilization, the emergence of fluoroquinolone resistance has been observed in both Gram-positive cocci (GPC) and Gram-negative bacilli (GNB) (1, 6, 8).

Fluoroquinolones are the only class of antibiotics in clinical use that directly target two essential bacterial enzymes in DNA replication: DNA gyrase and topoisomerase IV (1, 9). Resistance to fluoroquinolones is primarily caused by target mutations (e.g., mutations in chromosomal genes that encode the subunits of DNA gyrase and topoisomerase IV), efflux pumps, and reduced target expression (9). These mechanisms may occur in various combinations in resistant strains of staphylococci, *Pseudomonas aerugi-nosa*, and *Enterobacteriaceae* (1, 6). Efforts to combat this resistance to the fluoroquinolone class have focused on improving activity against multidrug-resistant bacteria and providing a lower potential for the development of bacterial resistance (1, 4, 5, 8).

Delafloxacin is an anionic investigational fluoroquinolone with documented efficacy in phase 2 trials for the treatment of RTI and ABSSSI and has recently completed phase 3 trials for the treatment of ABSSSI (1, 10). Unlike other quinolones, which usually have a binding affinity for either DNA gyrase or topoisomerase IV, delafloxacin is equally potent against both enzymes (1, 11–13). This dual targeting is believed to help reduce the selection of resistant mutants *in vitro* and *in vivo* (11, 12, 14). Unlike other fluoroquinolones, the mutant prevention concentration for delafloxacin is within 1- to -2-log₂ dilutions of the MIC value (13). Additionally, the anionic structure of delafloxaReceived 9 December 2016 Returned for modification 7 January 2017 Accepted 31 January 2017

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cin may enhance its potency in acidic environments, characteristic of the milieu at an infection site (1, 13, 15).

Delafloxacin is active *in vitro* against a broad range of Gram-positive and Gramnegative bacteria, including anaerobes and atypical respiratory tract pathogens (e.g., *Legionella, Chlamydia*, and *Mycoplasma*) (1, 13, 16–18). Delafloxacin exhibits very low MIC values against Gram-positive pathogens, including fluoroquinolone-resistant strains of *Staphylococcus aureus*, coagulase-negative staphylococci (CoNS), and *Streptococcus pneumoniae* (1, 12, 13, 19). It has been shown to be highly active *in vitro* against pathogens that are found in ABSSSI, including methicillin-resistant *S. aureus* (MRSA), methicillinresistant coagulase-negative staphylococci (MR-CoNS), beta-hemolytic streptococci, *Enterobacteriaceae*, *P. aeruginosa*, and anaerobes (10, 11, 13, 16, 20). Delafloxacin is also active against bacteria associated with RTIs, including *S. pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis* (19).

The aim of the present study was to examine the susceptibility profiles of delafloxacin and comparator agents when tested against contemporary clinical isolates collected from European and U.S. medical centers during surveillance year 2014.

RESULTS AND DISCUSSION

Overall activity of delafloxacin. The MIC distributions for select organisms or organism groups from U.S. and European medical centers are shown in Table 1. The MIC₉₀ values for U.S. and European isolates of GPC were within $\pm 1 \log_2$ dilution step for each organism group except methicillin-susceptible *S. aureus* (MSSA) (MIC₉₀s, 0.03 and $\leq 0.004 \ \mu$ g/ml for U.S. and European isolates, respectively) and methicillin-susceptible coagulase-negative staphylococci (MS-CoNS; MIC₉₀s, 0.12 and 0.008 μ g/ml for U.S. and European isolates, respectively).

Delafloxacin showed very low MICs against Gram-positive pathogens (Table 1). Among the *S. aureus* isolates, 99.5% of MSSA isolates from both U.S. and European study sites were inhibited at the pharmacodynamic breakpoint of $\leq 0.5 \ \mu$ g/ml (1, 13, 21). European isolates of MRSA, MS-CoNS, and MR-CoNS were slightly more susceptible to delafloxacin than U.S. isolates at an MIC of $\leq 0.5 \ \mu$ g/ml (for MRSA isolates, 95.3 and 91.2% isolates from Europe and the United States, respectively; for MS-CoNS isolates, 100.0 and 97.6% isolates from Europe and the United States, respectively; and for MR-CoNS isolates, 95.5 and 84.5% isolates from Europe and the United States, respectively) (data not shown). Notably, among fluoroquinolone-resistant (FQr) strains of *S. aureus* and CoNS, 88.3% (484/548) were inhibited by $\leq 0.5 \ \mu$ g/ml of delafloxacin (data not shown).

The potency of delafloxacin against U.S. and European isolates of enterococci and streptococci was similar (Table 1). Delafloxacin was most active against isolates of *S. pneumoniae* and beta-hemolytic streptococci (MIC_{50} and MIC_{90} , 0.008 and 0.015 µg/ml, respectively, for each group of organisms) and viridans group streptococci (MIC_{50} and MIC_{90} , 0.015 and 0.03 µg/ml, respectively). All FQr strains of *S. pneumoniae* (5/5) were inhibited by $\leq 0.25 \mu$ g/ml of delafloxacin. The MIC_{50} and MIC_{90} against U.S. and European isolates of *E. faecalis* were 0.06 and 1 µg/ml, respectively, whereas isolates of *Enterococcus faecium* were not susceptible to delafloxacin (Table 1).

Similar to the activity of delafloxacin against GPC, the activity of delafloxacin was comparable against isolates of GNB from the United States and Europe, with the exception of *Enterobacter* spp. (MIC₉₀s, 0.5 μ g/ml for U.S. isolates and 2 μ g/ml for European isolates), *Providencia* spp. (MIC₉₀s, >4 μ g/ml for U.S. isolates and 1 μ g/ml for European isolates), other *Enterobacteriaceae* (MIC₉₀s, 0.5 μ g/ml for U.S. isolates and 0.12 μ g/ml for European isolates), and *Acinetobacter baumannii-A. calcoaceticus* (MIC₅₀, 0.5 μ g/ml for U.S. isolates and 4 μ g/ml for European isolates). Delafloxacin was most active against *Klebsiella oxytoca* (MIC₅₀ and MIC₉₀, 0.06 and 0.12 μ g/ml, respectively), *Enterobacter aerogenes* (MIC₅₀ and MIC₉₀, 0.12 and 0.25 μ g/ml, respectively), *Citrobacter koseri* (MIC₅₀ and MIC₉₀, 0.06 and 0.25 μ g/ml, respectively), and other *Enterobacteriaceae* (MIC₅₀ and MIC₉₀, 0.06 and 0.25 μ g/ml, respectively) and was the least active against *Klebsiella pneumoniae*, *Providencia* spp., *P. aeruginosa*, and *Acinetobacter baumannii-A*.

IABLE I CUMULATIVE TREQUEN	alstri No (e	6) of isolates	for which M	IN MIC rest	uits for Eur	ope and th		tates							
Organism or organism group	Total	0.004	0.008	0.015	0.03	0.06	0.12	0.25	0.5	-	2	4	>4	MIC ₅₀ (ma/ml)	MIC ₉₀ (ma/ml)
Staphylococcus aureus US EU	1,100 250	666 (60.5) 193 (77.2)	8 (61.3) 2 (78.0)	8 (62.0) 1 (78.4)	38 (65.5) 4 (80.0)	183 (82.1) 12 (84.8)	62 (87.7) 13 (90.0)	63 (93.5) 18 (97.2)	24 (95.6) 3 (98.4)	34 (98.7) 3 (99.6)	- 0 (98.7) 0 (99.6)	14 (100.0) 1 (100.0)	0 (100.0) 0 (100.0)	≤0.004 ≤0.004	0.25
MSSA US EU	591 186	515 (87.1) 176 (94.6)	7 (88.3) 2 (95.7)	4 (89.0) 1 (96.2)	10 (90.7) 2 (97.3)	27 (95.3) 1 (97.8)	11 (97.1) 2 (98.9)	8 (98.5) 1 (99.5)	6 (99.5) 0 (99.5)	2 (99.8) 1 (100.0)	0 (99.8)	1 (100.0)	0 (100.0) 0 (100.0)	≤0.004 ≤0.004	0.03 ≤0.004
MRSA US EU	509 64	151 (29.7) 17 (26.6)	1 (29.9) 0 (26.6)	4 (30.6) 0 (26.6)	28 (36.1) 2 (29.7)	156 (66.8) 11 (46.9)	51 (76.8) 11 (64.1)	55 (87.6) 17 (90.6)	18 (91.2) 3 (95.3)	32 (97.4) 2 (98.4)	0 (97.4) 0 (98.4)	13 (100.0) 1 (100.0)	0 (100.0) 0 (100.0)	0.06 0.12	0.5 0.25
Coagulase-negative staphylococc US EU	i 100 100	51 (51.0) 43 (43.0)	7 (58.0) 8 (51.0)	3 (61.0) 1 (52.0)	1 (62.0) 6 (58.0)	6 (68.0) 10 (68.0)	14 (82.0) 10 (78.0)	4 (86.0) 14 (92.0)	4 (90.0) 5 (97.0)	9 (99.0) 3 (100.0)	1 (100.0)		0 (100.0) 0 (100.0)	≤0.004 0.008	0.5 0.25
Enterococcus faecalis US EU	300 150	0 (0.0) 2 (1.3)	2 (0.7) 2 (2.7)	0 (0.7) 0 (2.7)	28 (10.0) 16 (13.3)	150 (60.0) 57 (51.3)	39 (73.0) 31 (72.0)	9 (76.0) 3 (74.0)	27 (85.0) 17 (85.3)	37 (97.3) 22 (100.0)	8 (100.0)		0 (100.0) 0 (100.0)	0.06 0.06	
Enterococcus faecium US EU	195 100	(0.0) 0	0 (0.0) 1 (1.0)	1 (0.5) 1 (2.0)	0 (0.5) 0 (2.0)	8 (4.6) 0 (2.0)	0 (4.6) 0 (2.0)	1 (5.1) 2 (4.0)	6 (8.2) 1 (5.0)	8 (12.3) 2 (7.0)	3 (13.8) 1 (8.0)	16 (22.1) 7 (15.0)	152 (100.0) 85 (100.0)	<	$\begin{array}{c} \vee \\ + \\ + \end{array}$
Streptococcus pneumoniae US EU	300 150	34 (11.3) 16 (10.7)	169 (67.7) 90 (70.7)	84 (95.7) 40 (97.3)	7 (98.0) 4 (100.0)	3 (99.0)	2 (99.7)	1 (100.0)					0 (100.0) 0 (100.0)	0.008 0.008	0.015 0.015
Viridans group streptococci US EU	196 98	34 (17.3) 19 (19.4)	41 (38.3) 19 (38.8)	71 (74.5) 30 (69.4)	34 (91.8) 18 (87.8)	7 (95.4) 8 (95.9)	4 (97.4) 0 (95.9)	2 (98.5) 3 (99.0)	1 (99.0) 1 (100.0)	1 (99.5)	1 (100.0)		0 (100.0) 0 (100.0)	0.015 0.015	0.03 0.06
<i>Streptococcus pyogenes</i> US EU	283 150	67 (23.7) 33 (22.0)	170 (83.7) 94 (84.7)	46 (100.0) 20 (98.0)	3 (100.0)								0 (100.0) 0 (100.0)	0.008 0.008	0.015 0.015
Streptococcus agalactiae US EU	150 75	18 (12.0) 5 (6.7)	70 (58.7) 38 (57.3)	56 (96.0) 28 (94.7)	3 (98.0) 1 (96.0)	0 (98.0) 1 (97.3)	1 (98.7) 1 (98.7)	1 (99.3) 1 (100.0)	1 (100.0)				0 (100.0) 0 (100.0)	0.008 0.008	0.015 0.015
Streptococcus dysgalactiae US EU	82 50	19 (23.2) 18 (36.0)	51 (85.4) 30 (96.0)	11 (98.8) 1 (98.0)	1 (100.0) 1 (100.0)								0 (100.0) 0 (100.0)	0.008 0.008	0.015 0.008
Enterobacteriaceae US EU	1,500 750	3 (0.2) 1 (0.1)	16 (1.3) 11 (1.6)	132 (10.1) 81 (12.4)	261 (27.5) 118 (28.1)	389 (53.4) 196 (54.3)	163 (64.3) 76 (64.4)	74 (69.2) 25 (67.7)	94 (75.5) 30 (71.7)	102 (82.3) 49 (78.3)	116 (90.0) 64 (86.8)	70 (94.7) 44 (92.7)	80 (100.0) 55 (100.0)	0.06 0.06	6 4
Escherichia coli US EU	300 200	2 (0.7) 1 (0.5)	11 (4.3) 9 (5.0)	77 (30.0) 61 (35.5)	71 (53.7) 43 (57.0)	14 (58.3) 14 (64.0)	13 (62.7) 8 (68.0)	7 (65.0) 9 (72.5)	3 (66.0) 2 (73.5)	11 (69.7) 6 (76.5)	34 (81.0) 24 (88.5)	34 (92.3) 16 (96.5)	23 (100.0) 7 (100.0)	0.03 0.03	44
													Continue	d on follov	ving page)

TABLE 1 (Continued)															
	No. (%) of isolate	es for which	MIC (µg/m]	was:									UIW	UIW
Organism or organism group	Total	0.004	0.008	0.015	0.03	0.06	0.12	0.25	0.5	1	2	4	>4	(mg/ml)	(lm/gµl)
E. coli isolates of the ESBL phenotype US	52	0 (0.0)	1 (1.9)	2 (5.8)	2 (9.6)	2 (13.5)	1 (15.4)	1 (17.3)	1 (19.2)	4 (26.9)	17 (59.6)	14 (86.5)	7 (100.0)	5	\ 4
EU	40		0 (0.0)	3 (7.7)	(2.71) 4	(5.71)0	1 (20.0)	2 (25.0)	0 (25.0)	2 (30.0)	(८./८) 11	11 (85.0)	6 (100.0)	7	4
Klebsiella pneumoniae US	225		0 (0.0)	2 (0.9)	30 (14.2)	108 (62.2)	25 (73.3)	11 (78.2)	11 (83.1)	6 (85.8)	4 (87.6)	11 (92.4)	17 (100.0)	90.0	4
EU	164		0 (0.0)	1 (0.6)	12 (7.9)	64 (47.0)	14 (55.5)	2 (56.7)	5 (59.8)	7 (64.0)	10 (70.1)	17 (80.5)	32 (100.0)	0.12	4
<i>K. pneumoniae</i> isolates of the ESBL phenotype															
US	35				0 (0.0)	1 (2.9)	1 (5.7)	0 (5.7)	2 (11.4)	4 (22.9)	2 (28.6)	9 (54.3)	16 (100.0)	4	>4
EU	67				0 (0.0)	4 (6.0)	2 (9.0)	0 (0.6) 0	1 (10.4)	4 (16.4)	8 (28.4)	17 (53.7)	31 (100.0)	4	4
Klebsiella oxytoca															
US	75			0 (0.0)	3 (4.0)	44 (62.7)	23 (93.3)	3 (97.3)	2 (100.0)				0 (100.0)	0.06	0.12
EU	36			0 (0.0)	4 (11.1)	18 (61.1)	11 (91.7)	1 (94.4)	1 (97.2)	1 (100.0)			0 (100.0)	0.06	0.12
Pseudomonas aeruginosa															
US	100		0 (0.0)	1 (1.0)	1 (2.0)	7 (9.0)	26 (35.0)	22 (57.0)	8 (65.0)	10 (75.0)	7 (82.0)	6 (88.0)	12 (100.0)	0.25	4
EU	100			0 (0.0)	1 (1.0)	3 (4.0)	22 (26.0)	28 (54.0)	11 (65.0)	8 (73.0)	1 (74.0)	7 (81.0)	19 (100.0)	0.25	4
Acinetobacter baumannii-															
A. curoucencus	100		000	1 (1.0)	10 (1 1 0)	01 (32.0)	11 (43.0)	4 (47.0)	7 (54.0)	5 (59.0)	8 (67.0)	8 (75.0)	25 (100.0)	0.5	~
EU	100			0 (0.0)	3 (3.0)	8 (11.0)	5 (16.0)	1 (17.0)	5 (22.0)	7 (29.0)	18 (47.0)	27 (74.0)	26 (100.0)	4	4
^a Abbreviations: EU, Europe; US, Unit	ed States;	MSSA, met	hicillin-suscep	itible S. <i>aureu</i>	s; MRSA, meth	nicillin-resistar	nt S. aureus; E	SBL, extende	ed-spectrum	β-lactamase					

calcoaceticus (MIC₉₀s, >4 µg/ml for all isolates) (Table 1). The activity of delafloxacin was considerably greater against strains of *E. coli* of the non-extended-spectrum β -lactamase [ESBL]-producing phenotype (non-ESBL phenotype) than strains of *E. coli* of the ESBL-producing phenotype (ESBL phenotype) (MIC₅₀, 0.03 µg/ml versus 2 µg/ml, respectively), non-ESBL-phenotype and ESBL-phenotype strains of *K. pneumoniae* (MIC₅₀, 0.06 µg/ml versus 4 µg/ml, respectively), and non-ESBL-phenotype and ESBL-phenotype strains of *P. mirabilis* (MIC₅₀, 0.06 µg/ml versus 2 µg/ml, respectively). Delafloxacin retained potent activity against ESBL-phenotype strains of *K. oxytoca* (MIC₅₀ and MIC₉₀, 0.06 and 0.12 µg/ml, respectively) and was more active against ceftazidime-susceptible than ceftazidime-nonsusceptible strains of *P. aeruginosa* (MIC₅₀, 0.25 µg/ml versus 4 µg/ml, respectively). More than 90% of FQr GNB showed decreased susceptibility (MIC, ≥ 2 µg/ml) to delafloxacin.

Susceptibilities of European and U.S. Gram-positive isolates to delafloxacin and comparator agents. The activities of delafloxacin and comparator agents tested against European (250 isolates) and U.S. (1,100 isolates) isolates of S. aureus are shown in Table 2. Delafloxacin was the most potent antimicrobial agent tested against isolates of MSSA (MIC₅₀ and MIC₉₀, \leq 0.004 and 0.008 μ g/ml, respectively) and on the basis of the MIC_{90} s was 8- to at least 64-fold more potent than ceftaroline and at least 64-fold more potent than levofloxacin (Table 2). Tigecycline (MIC₅₀ and MIC₅₀, 0.06 and 0.06 μ g/ml, respectively), delafloxacin (MIC₅₀ and MIC₉₀, 0.06 and 0.5 μ g/ml, respectively), and daptomycin (MIC_{50} and MIC_{90}, 0.25 and 0.5 $\mu g/ml$, respectively) were the most potent agents tested against MRSA (Table 2). Delafloxacin was at least 64-fold more potent than levofloxacin (according to the MIC₅₀s) and at least 8-fold more potent than ceftaroline against MRSA. MRSA strains exhibited high levels of resistance against levofloxacin (68.9 and 68.9% according to Clinical and Laboratory Standards Institute [CLSI] and European Committee on Antimicrobial Susceptibility Testing [EUCAST] criteria, respectively) and erythromycin (79.9 and 83.8% according to CLSI and EUCAST criteria, respectively) (Table 2). The greatest coverage of all S. aureus isolates (MSSA and MRSA isolates from both Europe and the United States) was provided by linezolid, tigecycline, and vancomycin (to which 100.0% of isolates were susceptible). Isolates from both Europe and United States also exhibited high levels of susceptibility to daptomycin (99.8% of isolates were susceptible), ceftaroline (98.0%), and trimethoprimsulfamethoxazole (98.5%) (Table 2).

The delafloxacin MIC₅₀ and MIC₉₀ values for all coagulase-negative staphylococci (CoNS) were 0.008 and 0.5 μ g/ml, respectively (Table 1). Tigecycline (MIC₅₀ and MIC₉₀, 0.03 and 0.06 μ g/ml, respectively) and delafloxacin (MIC₅₀ and MIC₉₀, \leq 0.004 and 0.06 μ g/ml, respectively) were the most potent agents tested against MS-CoNS (Table 2). When delafloxacin was tested against isolates of MS-CoNS, it was 4-fold more potent than ceftaroline, 8-fold more potent than linezolid, 32-fold more potent than vancomycin, and >64-fold more potent than levofloxacin (according to the MIC₉₀s). European isolates of MS-CoNS were more susceptible than U.S. isolates to levofloxacin (97.0% versus 81.0%, respectively), clindamycin (90.9% versus 78.6%, respectively), erythromycin (72.7% versus 66.7%, respectively), tetracycline (93.9% versus 85.7%, respectively), and trimethoprim-sulfamethoxazole (100.0% versus 85.7%, respectively) (data not shown).

The antibiogram results for MR-CoNS isolates from both Europe (67 isolates) and the United States (58 isolates) showed higher MIC values for all tested drugs except daptomycin (to which 99.2% of isolates were susceptible), linezolid (to which 100.0% of isolates were susceptible), and vancomycin (to which 100.0% of isolates were susceptible). Tigecycline (MIC₅₀ and MIC₉₀, 0.06 and 0.12 μ g/ml, respectively), delafloxacin (MIC₅₀ and MIC₉₀, 0.06 and 0.5 μ g/ml, respectively), linezolid (MIC₅₀ and MIC₉₀, 0.5 and 0.5 μ g/ml, respectively), and ceftaroline (MIC₅₀ and MIC₉₀, 0.5 and 1 μ g/ml, respectively) were the most potent antimicrobials tested against both European and U.S. strains of MR-CoNS. Levofloxacin, clindamycin, erythromycin, and trimethoprim-sulfamethoxazole all showed limited activity against MR-CoNS isolates from both regions.

TABLE 2 Activities of delafloxacin and comparator antimicrobial agents when tested against U.S. and European Gram-positive isolates

	% of isolates s	susceptible by			
Organism group (no. of isolates tested)/	the following	criteria:	MIC (μg/m	nl)	
antimicrobial agent	CLSI	EUCAST	50%	90%	Range
Staphylococcus aureus (1,350)					
Delafloxacin			≤0.004	0.25	≤0.004 to 4
Levofloxacin	64.4	64.4	0.25	>4	≤0.12 to >4
Ceftaroline	98.0	98.0	0.25	1	0.03 to 2
Ciprofloxacin	0.0	0.0	64	>128	64 to >128
Clindamycin	87.0	86.8	≤0.25	>2	≤0.25 to >2
Daptomycin	99.8	99.8	0.25	0.5	≤0.06 to 2
Erythromycin	45.9	46.3	4	>16	≤0.12 to >16
Linezolid	100.0	100.0	1	1	0.25 to 2
Oxacillin	57.6	57.6	0.5	>2	≤0.25 to >2
Tetracycline	94.3	92.5	≤0.5	≤0.5	\leq 0.5 to $>$ 8
Tigecycline	100.0 ^a	100.0	0.06	0.06	≤0.015 to 0.5
Trimethoprim-sulfamethoxazole	98.5	98.5	≤0.5	≤0.5	\leq 0.5 to $>$ 4
Vancomycin	100.0	100.0	1	1	0.25 to 2
MSSA (777)					
Delafloxacin			≤0.004	0.008	≤0.004 to 4
Levofloxacin	89.8	89.8	0.25	2	\leq 0.12 to $>$ 4
Ceftaroline	100.0	100.0	0.25	0.25	0.03 to 1
Ciprofloxacin	0.0	0.0	>128	>128	>128 to >128
Clindamycin	94.0	93.7	≤0.25	≤0.25	≤0.25 to >2
Daptomycin	100.0	100.0	0.25	0.5	≤0.06 to 1
Erythromycin	69.6	69.8	0.25	>16	≤0.12 to >16
Linezolid	100.0	100.0	1	1	0.25 to 2
Oxacillin	100.0	100.0	0.5	0.5	≤0.25 to 2
Tetracycline	95.9	94.2	≤0.5	≤0.5	≤0.5 to >8
Tigecvcline	100.0 ^a	100.0	0.06	0.06	≤0.015 to 0.5
Trimethoprim-sulfamethoxazole	99.0	99.0	≤0.5	≤0.5	≤ 0.5 to >4
Vancomycin	100.0	100.0	1	1	0.25 to 2
,					
MRSA (573)					
Delafloxacin			0.06	0.5	≤0.004 to 4
Levofloxacin	30.0	30.0	4	>4	\leq 0.12 to $>$ 4
Ceftaroline	95.3	95.3	1	1	0.25 to 2
Ciprofloxacin	0.0	0.0	>128	>128	64 to >128
Clindamycin	77.5	77.5	≤0.25	>2	≤0.25 to >2
Daptomycin	99.5	99.5	0.25	0.5	0.12 to 2
Erythromycin	13.8	14.3	>16	>16	≤0.12 to >16
Linezolid	100.0	100.0	1	1	0.25 to 2
Oxacillin	0.0	0.0	>2	>2	>2 to >2
Tetracycline	92.1	90.2	≤0.5	1	≤0.5 to >8
Tigecycline	100.0 ^a	100.0	0.06	0.06	≤0.015 to 0.5
Trimethoprim-sulfamethoxazole	97.9	97.9	≤0.5	≤0.5	≤0.5 to >4
Vancomycin	100.0	100.0	1	1	0.5 to 2
MS-CoNS (75)					
Delafloxacin			≤0.004	0.06	≤0.004 to 1
Levofloxacin	88.0	88.0	0.25	4	≤0.12 to >4
Ceftaroline			0.12	0.25	0.03 to 0.5
Clindamycin	84.0	84.0	≤0.25	>2	≤0.25 to >2
Daptomycin	100.0	100.0	0.25	0.5	≤0.06 to 1
Frythromycin	69.3	69.3	≤0.12	>16	≤0.12 to >16
Linezolid	100.0	100.0	0.5	0.5	0.25to1
Oxacillin	100.0	100.0	<0.25	1	<0.25 to 2
Tetracycline	893	86.7	<0.5	8	< 0.5 to > 8
Tigecycline	09.5	100.0	0.03	0.06	<0.015 to 0.12
Trimethonrim-sulfamethoxazole	92.0	92.0	<0.5	<0.5	≤ 0.5 to >4
Vancomycin	100.0	100.0	1	2	0.25 to 4
MP-CoNS (125)					
Delaflovacin			0.06	0.5	<0.004 +2.2
Levoflovacin	38 /	20 <i>\</i>	0.00	0.5 _/	<0.12 +0 \/
Ceftaroline	JU.7	50.4	- 0 5	- - 1	-0.12 to >4
Clindamycin	70.4	67.0	0.J <0.2E	, >	
Ciniuaniyun	70.4	07.2		~ L	≥0.25 t0 22

Outside setual CLSI EUCAST 50% Range Deptivingen 25.6 25.6 5.6 5.6 5.6 5.0	Organism group (no. of isolates tested)/	% of isolates suscep the following criteri	otible by a:	MIC (µg/m	nl)	
Daytomycin 992 992 0.5 0.5 :0.00 to 2 Erythromycin 25.6 25.6 >16 :0.16 :0.12 to 1 Doacilin 00.0 0.0 -2 -2 0.5 to >2 Tetracycline 80.8 77.6 1 >-8 :0.5 to >2 Trimethopimi-sufamethoxazole 65.6 65.6 :0.0 10.0 10.0 Vancomycin 100.0 100.0 10.0 1 2 :0.5 to >2 Everotoxacin forcells (450) Delafoxacin 70.7 70.7* 1 >-4 0.25 to >2 Delafoxacin 70.7 70.7* 1 >-4 0.25 to >2 Ceftaroline 2 8 0.25 to >2 :2.5 to >2 Datomycin 100.0 1 2 0.12 to >16 :0.12 to >16 Linecold 99.8 100.0 1 2 0.25 to >2 :2.5 to >3 :2.5 to >3	antimicrobial agent	CLSI	EUCAST	50%	90%	Range
Epythomycin 25.6 25.6 26.5 >16 >10 20.12 to 1 to 1 Oxacillin 0.0 0.0 >2 >2 0.5 to >2 Terracycline 80.8 77.6 1 >8 95.5 to >3 Tigerycline 100.0 0.00 1 2 0.00 to 0.2 Eventoxacin 100.0 100.0 10 2 0.50 to >4 Defrozonin 100.0 100.0 1 2 0.00 to 2 Eventoxacin 70.7 70.7 1 >4 0.025 to >4 Ampicillin 100.0 99.6 1 2 0.025 to >4 Cindamycin 100.0 99.6 1 2 0.025 to >2 Cindamycin 100.0 1 1 0.012 to >1 1 0.012 to >1 Erythomycin 100.0 1 2 0.55 to >4 0.55 to >4 Lineodid 99.8 100.0 1 1 0.012 to >16 Eretracycline 21 5.5	Daptomycin	99.2	99.2	0.5	0.5	≤0.06 to 2
Infection 100.0 100.0 0.5 <	Erythromycin	25.6	25.6	>16	>16	≤0.12 to >16
Obacillin 0.0 0.0 >2 >2 0.5 to >2 Tetarycline 0.0 0.00 10.0 0.06 0.12 \$0.015 to 0.25 Timerbopinsulfamethoxazole 0.50 0.56 \$5.6 \$0.5 >>4 \$0.05 to >2.4 Vancomycin 100.0 100.0 1 2 \$0.5 to >2.4 Exerolocar. facedis (450) 0.0 9.6 1 >2 \$0.25 to >3.2 Certaroline 100.0 99.6 1 2 \$0.25 to >3.2 Certaroline 100.0 99.6 1 2 \$0.25 to >3.2 Certaroline 2 8 \$0.25 to >3.2 \$0.25 to >3.2 \$0.12 to 4 Erythromycin 4.7 >16 >16 \$0.12 to 5 to >16 \$0.12 to 5 to >16 Certaroline 7.8 97.6 5.2 \$2.5 to >5.0 \$0.5 to >16 Certaroline 7.8 10.8 >4 >4 \$0.5 to >16 Certaroline 7.8 10.8 >4 \$0.5 to >4 \$0.5 to	Linezolid	100.0	100.0	0.5	0.5	≤0.12 to 1
Tetacycline B0.8 77.6 1 >8 =0.5 to >8 Timethopim-sulfamethoxazole 65.6 65.6 =0.5 >>4 =0.5 to >4 Vancomycin 100.0 100.0 1 2 =0.5 to >4 Delafoxacin 70.7 70.7 70.7 1 >>4 =0.004 to 2 Levofloxacin 70.7 70.7 70.7 1 >>4 =0.025 to >4 Cararoima 100.0 99.6 1 2 =0.025 to >4 Cararoima 100.0 97.6 1 >>4 =0.025 to >4 Cararoima 100.0 1 1 =0.025 to >4 =0.05 to >16	Oxacillin	0.0	0.0	>2	>2	0.5 to >2
Tigescycline 100.0 0.66 0.12 #0.015 to 0.25 Timentopinrusulfamethoxazole 65.6 65.6 40.5 >>4 65.6 to 2 Delafloxacin 100.0 100.0 1 2 0.5 to 2 Enerocccus freezols (450) 0.06 1 20.004 to 2 2 0.5 to 2 Levofloxacin 70.7 70.7 th 1 >4 0.25 to 3 2 2 2.023 to 32 0.25 to 32 Ceffarcinie 2 2 2 0.23 to 32 0.25 to 32 0.21 to 3.12 to 3.16 2 2.12 to 3.12 to 3.16 2 2.12 to 3.12 to 3.16 2 2.12 to 3.16 2.12 to 3	Tetracycline	80.8	77.6	1	>8	≤0.5 to >8
Threehoptim-sulfamethoxazole 65.6 65.6 25.5 >4 20.5 to >4 Delfloxacin 100.0 100.0 1 2 0.5 to >4 Delfloxacin 70.7 70.7* 1 >4 $=0.004$ to 2 Levelfoxacin 70.7 70.7* 1 >2 $=0.025$ to >3.4 Ampicilin 100.0 99.6 1 2 $=0.025$ to >3.4 Clindamycin 100.0 97.8 97.8 $=0.22$ $=2.2$ $=2.2$ $=2.2$ to >5.6 $=0.5$ to >3.6 $=0.5$	Tigecycline		100.0	0.06	0.12	≤0.015 to 0.25
Varicomycin 100.0 100.0 1 2 0.5 to 2 Enterecccus facedis (450)	Trimethoprim-sulfamethoxazole	65.6	65.6	≤0.5	>4	≤ 0.5 to >4
Enternacional feadils (450) 0000 to 2 00000 to 2 0000 to 2 0000 t	Vancomycin	100.0	100.0	1	2	0.5 to 2
Delafloxacin 70.7 70.7° 1 >4 0.25 to >4 AmpicIIIIn 100.0 99.6 1 2 0.25 to >32 Clindamycin 2 8 0.25 to >32 0.25 to >32 Clindamycin 100.0 91.6 >10 2 0.25 to >32 Clindamycin 100.0 1 2 0.12 to 4 50.12 to >14 Erythromycin 47 >16 >11 <0.12 to 4	Enterococcus faecalis (450)					
levefloxacin 70.7 70.7° 1 >4 0.25 to >8 AmpicIIIn 100.0 99.6 1 2 8.025 to >8.025 to >2.025 to >2.	Delafloxacin			0.06	1	≤0.004 to 2
Ampicillin 100.0 99.6 1 2 8 0.25 to 32 Ceftaraline >2 2 2 0.12 to 1 Erythromycin 100.0 >16 21.2 to 3 0.12 to 4 Erythromycin 4.7 >16 >16 50.12 to 4 Erythromycin 97.8 100.0 1 1 50.12 to 4 Trienthoprim-sulfamethoxazole 2.3.1 >8 >8 50.5 to >8 Vancomycin 97.8 97.8 1 2 0.5 to >16 Enterocccus faecium (295) - - - 4 0.008 to >4 Evedfoxacin 7.8 10.8" >4 >4 0.028 to >4 Ampicillin 10.8 10.8" >4 >4 0.120 to >16 Ceftaroline -2 2 2 0.210 to >16 >16 Cindamycin 7.8 10.8" >8 50.5 to >24 50.5 to >4 Evedfoxacin 8.9 9.0 1 1 0.5 to >1 1	Levofloxacin	70.7	70.7 ^b	1	>4	0.25 to >4
Ceffandmine 2 8 0.25 to >20 Daptomycin 10.0 1 2 0.25 to >20 Daytomycin 4.7 >16 >16 0.012 to >16 Linezolid 99.8 100.0 1 1 <0.12 to >16 Linezolid 99.8 100.0 1 1 <0.12 to >16 Tetracycline 23.1 >8 >8 <0.5 to >16 <0.5 to >16 Timethopinsulfamethoxazole 97.8 97.8 1 2 0.5 to >16 Ceffacoline 2 2.5 <0.5	Ampicillin	100.0	99.6	1	2	≤0.25 to 8
Clindamycin >2 >22 =0.25 to >22 Daptomycin 100.0 >16 >16 =0.12 to 4 Erythromycin 4.7 >16 >16 =0.12 to 4 Erythromycin 4.7 >16 >16 <0.12 to 4	Ceftaroline			2	8	0.25 to >32
Daptomycin 10.0 1 2 0.12 to 2 fo Expthromycin 4.7 >16 >16 <0.12 to 3 fo	Clindamycin			>2	>2	\leq 0.25 to $>$ 2
Eythomycin 4.7 >16 >16 ≤0.12 to >16 Linezolid 99.8 100.0 1 1 ≤0.12 to >16 Tetracycline 23.1 >8 >8 ≤0.5 to >80 Timethoprim-sulfamethoxazole =05 =05.5 ≥0.5 to >16 Delafoxacin 97.8 97.8 1 2 0.5 to >16 Delafoxacin 7.8 10.8 >4 >4 0.008 to >4 Levofloxacin 7.8 10.8 >8 >8 ≤0.25 to >8 Clindamycin 10.8 10.8 >8 >8 ≤0.25 to >8 Clindamycin 9.0 2 >2 ≥0.25 to >8 >21.2 to >32 Clindamycin 3.7 >16<>16 >16 >12.1 to >16 >16 12.1 to >16 >12.1 to >16 >12.1 to >16 >12.1 to >16 >16 >12.1 to >16 >16 >16 >16 >16 >16 >16 >16 >16 >16 >12.1 to >16 >16 >16 >16 >16 >16 <t< td=""><td>Daptomycin</td><td>100.0</td><td></td><td>1</td><td>2</td><td>0.12 to 4</td></t<>	Daptomycin	100.0		1	2	0.12 to 4
Linezolid 99.8 100.0 1 1 ≤0.12 to 4 Tetroplanin 97.8 97.6 5.2 5.2 5.2 to 5.10 > 8 Timethoptim-sulfamethoxazole 97.8 97.8 1 2 0.5 to 5.10 > 8 Delafloxacin 97.8 97.8 1 2 0.5 to 5.10 > 16 Levofloxacin 7.8 10.8" >4 >4 0.008 to 5.4 Ampicillin 10.8 10.8 >8 >8.20.25 to >36 Centamic Ceftaroline -22 >32 0.12 to 8 20.12 to 3.12 to 3.12 Cindamycin -22 >2 20.25 to >36 Erythomycin 9.90 100.0 1 10.25 to 4 20.5 to >16 21.5 v3.12 to 3.12 to 3.12 20.12 to 3.12 to 3.12 20.12 to 3.12 to 3.12 20.12 to >16 21.5 v3.12 to 3.12 20.12 to 3.12 to 3.12 20.12 to >16 20.12 to >16 21.5 v3.12 to 3.12 20.12 to >16 20.12 to >16 20.5 to >4 20.5 to >	Erythromycin	4.7		>16	>16	\leq 0.12 to $>$ 16
Tetracycline 97.8 97.6 >22 =2 =2 >2 =2 >1 2 >1 2 2 0.5 1 2 0.5 1 2 0.5 <	Linezolid	99.8	100.0	1	1	≤0.12 to 4
Tertacycline 23.1 >8 >8 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.6 <0.5 <0.5 <0.6 <0.5 <0.6 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5 <0.5	Teicoplanin	97.8	97.6	≤2	≤2	\leq 2 to $>$ 16
Trimethoprim-sulfamethoxazole S7.8 97.8 1 2 0.5 to >4 Vancomycin 97.8 97.8 1 2 0.5 to >16 Enteracoccus facelum (25) >4 >4 0.008 to >4 2 Delafloxacin 7.8 10.8° >4 >4 0.008 to >4 Ampicillin 10.8 10.8 >8 >8 <0.25 to >2 Certaroline >32 32 32 0.12 to >32 Cilndamycin 90.0 2 4 0.12 to >32 Erythromycin 3.7 >16 >16 >16 <0.25 to >16 Linezolid 90.0 100.0 1 1 0.25 to >16 Trimethoprim-sulfamethoxazole 3.2 >8 >8 <0.55 to >4 Vancomycin 43.4 43.4 >16 >16 >15 to >4 Vancomycin 98.9 98.9 1 0.5 to >4 Certaroline 98.9 98.9 1 0.5 to >4 Levofloxacin 98	Tetracycline	23.1		>8	>8	≤0.5 to >8
Vancomycin 97.8 97.8 97.8 1 2 0.5 to >16 Enteroaccus faecium (295) >4 >4 0.008 to >4 Delafloxacin 7.8 10.8° >4 >4 0.5 to >16 Ampicillin 10.8 10.8° >8 >8 <0.22 to >32 Clindamycin 22 2 <0.25 to >32 <0.12 to >32 Daptomycin 99.0 2 4 0.12 to >32 Epythromycin 3.7 >16 >16 <0.12 to >16 Inrecollanin 47.1 46.1 16 >16 <0.25 to >16 Tetracycline 3.2 >8 >8 <0.5 to >4 Vancomycin 43.4 43.4 >16 >16 >0.25 to >16 Streptococcus pneumoniae (450) <0.008	Trimethoprim-sulfamethoxazole			≤0.5	≤0.5	≤0.5 to >4
Enterococcus faccium (295) >4 >4 0.008 to >4 Delafloxacin 7.8 10.8 ^b >4 >4 0.50 to >4 Ampicillin 10.8 10.8 >8 >8 :0.25 to >32 Cindamycin >22 >2 :0.12 to >32 :0.12 to >32 Daptomycin 99.0 2 4 :0.12 to >16 Erythromycin 3.7 >16 >16 :20.12 to >16 Linezolid 99.0 100.0 1 1 0.25 to >16 Tretcoplanin 47.1 46.1 16 :20.12 to >16 :20.5 to >8 Trimethoprim-sulfamethoxazole =0.5 >4 :0.5 to >4 :0.5 to >4 Vancomycin 43.4 43.4 :16 :16 :0.25 to >16 Streptocccus pneumonize (450) :0.008 :0.015 :0.004 to 0.25 Delafloxacin 99.6' 99.3 :0.015 :0.015 to 1 Cindamycin 84.7 84.9 :0.25 :2 :0.25 to >2 Evothoxacin 99.6' 99.3 :0.012 :0.015 to 1 :0.15 to 1 <	Vancomycin	97.8	97.8	1	2	0.5 to >16
Delafloxacin > > > > > 0.008 to >4 Levofloxacin 7.8 10.8 > > > 0.50 to >4 Ceftaroline >32 >32 >32 0.12 to >32 Captomycin 90.0 $>$ 2 2 $<$ $<$ 0.02 to >32 Daptomycin 90.0 100.0 1 1 0.25 to >16 Linezolid 99.0 100.0 1 1 0.25 to >16 Fictoplanin 47.1 46.1 16 >16 >21 to >16 Trimethoprim-sulfamethoxazole $<$ $>$	Enterococcus faecium (295)					
Levofloxacin7.8 10.8^{b} >4>4 $0.5 \text{ to }>4$ Ampicillin 10.8 10.8^{b} >8>8 28 $20.25 \text{ to }>2$ Clindamycin -32 >32 $0.12 \text{ to }>32$ 22 $20.25 \text{ to }>2$ Daptomycin 99.0 2 4 $0.12 \text{ to }>32$ Erythromycin 3.7 >16 >16 $<50.12 \text{ to }>16$ Erythromycin 3.7 >16 >16 $<50.12 \text{ to }>16$ Tetracycline 33.2 >8 >8 $<50.5 \text{ to }>8$ Trimethoprim-sulfamethoxazole $= 0.5$ >4 $<50.5 \text{ to }>8$ Trimethoprim-sulfamethoxazole $= 0.05$ >4 $<50.5 \text{ to }>16$ Delafloxacin 33.4 43.4 >16 >16 $0.25 \text{ to }>16$ Streptocccus pneumoniae (450) $=$ $= 0.008$ 0.015 $<=0.004 \text{ to }0.25$ Levofloxacin 98.9 98.9 1 1 $0.5 \text{ to }>4$ Amoxicillin-clavulanic acid 91.1 $= 12$ $<=11 \text{ to }>8$ Ceftratione 99.6^{cr} 99.3 $=0.015$ 0.12 $<=0.05 \text{ to }>8$ Clindamycin 84.7 84.9 $=0.025$ $<=0.025 \text{ to }>16$ $<=0.025 \text{ to }>2$ Erythromycin 59.9 59.9 $=0.12$ >16 $<=0.12 \text{ to }>16$ Moxifloxacin 98.9 98.7 $=0.12$ $<=0.05 \text{ to }>8$ $<=0.5 \text{ to }>8$ Trimethoprim-sulfamethoxazole 68.9 7.3 $=0.05$ >8 $<=0.5 \text{ to }>8$ Ceftra	Delafloxacin			>4	>4	0.008 to >4
Ampicillin10.810.810.8 >8 >8 < 0.25 to >8 Clindamycin >32 >32 0.12 to >12 >22 >22 0.25 to >2 Daptomycin 99.0 2 4 0.12 to >16 Linezolid 99.0 100.0 1 1 0.25 to >4 Linezolid 99.0 100.0 1 1 0.25 to >4 Fetcoplanin47.1 46.1 16 >16 $>25 to >16$ Timethoprim-sulfamethoxazole $= 0.5$ >4 $= 0.5$ to >4 $= 0.5$ to >4 Vancomycin 43.4 43.4 >16 >16 0.25 to >16 Streptococcus pneumoniae (450) $= 0.088$ $= 0.015$ $= 0.004$ to 0.25 Ceftaroline 98.9 98.9 1 1 0.5 to >4 Amoxicillin-clavulanic acid 91.1 $= 11$ 2 $= 11$ to >8 Ceftaroline 99.6^{cr} 99.3 $= 0.015$ 0.12 $= 0.005$ to >16 Ceftaroline 98.9 98.7 $= 0.12$ >16 $= 0.015$ to >16 Ceftaroline 99.9 59.9 $= 0.12$ >16 $= 0.015$ to >12 Ceftaroline 98.9 98.7 $= 0.025$ >2 $= 0.025$ Ceftaroline 98.9 98.7 $= 0.12$ >16 $= 0.015$ to >12 Ceftaroline 98.9 98.7 $= 0.012$ >16 $= 0.015$ to >12 Moxifloxacin 98.9 98.7 $= 0.012$ >16 $= 0.015$ to >12 <tr< td=""><td>Levofloxacin</td><td>7.8</td><td>10.8^b</td><td>>4</td><td>>4</td><td>0.5 to >4</td></tr<>	Levofloxacin	7.8	10.8 ^b	>4	>4	0.5 to >4
Ceftaroline >32 >32 0.12 to >32 Daptomycin 90.0 2 4 0.12 to >16 Erythromycin 3.7 >16 >16 ≤ 0.25 to >2 Daptomycin 99.0 100.0 1 1 ≤ 0.25 to >2 Linezolid 99.0 100.0 1 1 ~ 0.25 to >4 ≤ 0.5 to >8 Teicoplanin 47.1 46.1 16 >16 $\geq 2.0 >16$ $\geq 2.0 >16$ Trimethoprim-sulfamethoxazole ≤ 0.5 >4 ≤ 0.5 to >8 ≥ 0.5 to >4 ≥ 0.5 to >4 Streptocccus pneumoniae (450) ≤ 0.05 to >1 ≥ 0.008 $\circ 0.015$ ≤ 0.004 to 0.25 Levofloxacin 98.9 98.9 1 1 0.5 to >4 ≥ 0.015 to 1 Ceftaroline 99.6 ^c 99.3 ≤ 0.015 ≥ 0.012 to 16 ≥ 0.015 to 1 Ceftaroline 99.6 ^c 99.3 ≤ 0.015 ≥ 0.025 to 2 ≥ 2.025 to 2	Ampicillin	10.8	10.8	>8	>8	≤0.25 to >8
$\begin{array}{c c c c c c c c c c c c c c c c c c c $	Ceftaroline			>32	>32	0.12 to >32
Deptomycin99,0240.12 to 8Erythromycin3.7>16>16 <0.12 to >16Linezolid99,0100,0110.25 to 4Teicoplanin47.146.116>16 <2 to >16Tetracycline32.2>8>8 <0.5 to >8Trimethoprim-sulfamethoxazole <0.5 >4 <0.5 to >16Streptocccus pneumoniae (450) <0.08 <0.015 <0.004 to 0.25Streptocccus neumoniae (450) <0.008 0.015 <0.004 to 0.25Levofloxacin98.998.911 <0.5 to >16Armoxicillin-clavulanic acid91.1 <1 <0.068 <0.12 <0.015 to 1Ceftaroline99.6'99.3 <0.015 <0.12 <0.015 to 1Ceftaroline99.6'99.3 <0.015 <0.25 <0.25 to >2 <0.25 to >2Cifindamycin81.6', 94.2'83.6 <0.06 1 <0.06 to 8 <0.12 to >16Meropenem84.484.4'10.00' <0.015 <0.5 to >16 <0.12 to >16 <0.12 to >16 <0.12 to >16Moxifloxacin98.998.7 <0.12 <0.66 to <0.2 <0.06 to >8 <0.12 to >16 <0.12 to >16Moxifloxacin98.998.7 <0.12 <0.66 to >8 <0.12 to >16 <0.12 to >16Moxifloxacin98.998.7 <0.12 <0.66 to >8 <0.12 to >16 <0.12 to >16Moxifloxacin98.998.7 $<$	Clindamycin			>2	>2	≤0.25 to >2
Erythromycin 3.7 >16 >16 ≤0.12 to >16 Linezolid 99.0 100.0 1 1 0.25 to 4 Teicoplanin 47.1 46.1 16 >16 ≤2 to >16 Tetracycline 33.2 >8 >8 ≤0.5 to >4 Vancomycin 43.4 43.4 >16 >16 0.25 to >16 Streptococcus pneumoniae (450) 0.008 0.015 <0.004 to 0.25	Daptomycin	99.0		2	4	0.12 to 8
Linecolid99.0100.0110.25 to 4Teicoplanin47.146.116>16 ≤ 2 to >16Tetracycline33.2>8>8 ≤ 0.5 to >8Trimethoprim-sulfamethoxazole ≤ 0.5 >4 ≤ 0.5 to >4Vancomycin43.443.4>16>16 ~ 0.5 to >8Streptocccus pneumoniae (450)Delafloxacin 0.008 0.015 ≤ 0.004 to 0.25Levofloxacin98.998.911 0.008 0.015 ≤ 0.004 to 0.25Ceftaroline99.6 ^c 99.3 ≤ 0.015 0.12 ≤ 0.015 to 1 ≤ 0.004 to 0.25Ceftaroline99.6 ^c 99.3 ≤ 0.015 0.12 ≤ 0.015 to 1Ceftaroline99.6 ^c 99.3 ≤ 0.015 0.12 ≤ 0.025 to >2Ceftaroline99.6 ^c 99.9 ≤ 0.05 1 ≤ 0.006 to 8Cindamycin59.9 ≤ 0.05 2 ≤ 0.25 to >2 ≤ 0.25 to >2Enythomycin59.9 ≤ 0.12 0.15 < 0.015 to 2 Moxifloxacin88.998.7 ≤ 0.66 2 < 0.06 to 8Tetracycline78.478.4 ≤ 0.5 >8 < 0.05 to >4Viridans group streptococci (294) 2 ≤ 0.15 to >4 < 0.12 to >16 < 0.12 to >16 Delafloxacin90.986.4 0.25 1 < 0.06 to >8 Ceftaroline 2 1 2 < 0.15 to >4 < 0.5 to >4 <	Erythromycin	3.7		>16	>16	≤0.12 to >16
Tetcoplanin47.146.116>16 ≤ 2 to >16Tetracycline33.2>8>8 ≤ 0.5 to >4 ≤ 0.5 to >8Trimethoprim-sulfamethoxazole43.4 >16 >16 0.25 to >16Vancomycin43.4 43.4 >16>16 0.25 to >16Streptococcus pneumoniae (450)Delafloxacin 0.008 0.015 ≤ 0.004 to 0.25 Levofloxacin98.998.911 0.5 to >4Amoxicillin-clavulanic acid91.1 ≤ 1 2 ≤ 1 to >8Ceftratone83.6/ 94.2c83.6 ≈ 0.06 1 < 0.06 to 1Ceftratone84.784.9 ≤ 0.015 < 0.015 to >2 < 0.25 to >2Erythromycin59.959.9 < 0.12 > 16 < 0.12 to >16 Moxifloxacin98.998.7 < 0.015 0.5 < 0.015 to 2 Penicillin 63.8^{e} 63.8 ⁴ 94.4 ^a 63.8^{d} 63.8 ^a < 0.06 2 < 0.06 to 8Ceftraxone68.975.3 < 0.5 >8 < 0.04 to 2 Moxifloxacin94.112 < 0.12 to >16 Moxifloxacin94.112 < 0.12 to >4 Viridans group streptococci (294) < 79.7 ≤ 1 2 < 0.02 to >4 Delafoxacin90.986.4 0.25 < 2 < 0.02 to >4 Ceftraxone90.986.4 0.25 < 2 < 0.05 to >4 Ceftraxone90.986.4 0.25 < 0.02	Linezolid	99.0	100.0	1	1	0.25 to 4
Tetracycline 33.2 >8 >8 <0.5 >4 Trimethoprim-sulfamethoxazole 43.4 43.4 >16 >16 0.25 to >16 Streptococcus pneumoniae (450) 0.008 0.015 <0.004 to 0.25	Teicoplanin	47.1	46.1	16	>16	\leq 2 to $>$ 16
Trimethoprim-sulfamethoxazole ≤ 0.5 >4 ≤ 0.5 to >4 Vancomycin43.443.4 >16 >16 0.25 to >16 Delaftoxacin98.9 0.008 0.015 ≤ 0.004 to 0.25 Delaftoxacin98.998.911 0.5 to >4 Amoxicillin-clavulanic acid91.1 ≤ 1 2 ≤ 1 to >8 Ceftraoline99.6'99.3 ≤ 0.015 0.12 ≤ 0.015 to 1 Ceftraoline83.6' 94.2'83.6 $= 0.06$ 1 $= 0.008$ to 8 Cindamycin84.784.9 ≤ 0.25 >2 ≤ 0.25 to >2 Erythromycin59.959.9 ≤ 0.12 >16 ≤ 0.12 to >16 Meropenem84.484.4' 100.0' ≤ 0.015 0.5 ≤ 0.015 to 2 Penicillin $63.8' 63.8' 94.49'$ $63.8' 63.89'$ ≤ 0.06 2 ≤ 0.06 to 8 Trimethoprim-sulfamethoxazole 68.9 75.3 ≤ 0.5 >4 ≤ 0.5 to >4 Viridans group streptococci (294) $=$ $R4$ 79.7 ≤ 1 2 ≤ 0.015 to >4 Ceftraixone9.9 86.4 0.25 1 < 0.004 to 2 ≤ 0.015 to >4 Ceftraixone9.9 86.4 0.25 1 < 0.025 < 0.025 < 0.025 Ceftraixone9.9 86.4 0.25 1 < 0.05 to >4 < 0.05 to >2 Ceftraixone9.9 < 0.25 < 2.2 < 0.05 to >2 < 0.05 to >2 < 0.05 to >2 < 0.0	Tetracycline	33.2		>8	>8	\leq 0.5 to $>$ 8
Vancomycin 43.4 43.4 >16 >16 0.25 to >16 Streptococcus pneumoniae (450) Delafloxacin 0.008 0.015 ≤0.004 to 0.25 Levofloxacin 98.9 1 1 0.5 to >4 Amoxicillin-clavulanic acid 91.1 2 ≤1 to >8 Ceftaroline 99.6 ^o 99.3 ≤0.015 0.12 ≤0.015 to 1 Ceftaroline 99.6 ^o 99.3 ≤0.015 0.12 ≤0.015 to 1 Ceftarone 83.6 ^d 94.2 ^c 83.6 ≤0.06 1 ≤0.025 to >2 Erythromycin 59.9 ≤0.12 >16 ≤0.12 to >16 Meropenem 84.4 84.4 ^d (100.0 ^c ≤0.015 0.5 ≤0.015 to 2 Moxifloxacin 98.9 98.7 ≤0.12 0.25 ≤0.12 to 2 Penicillin 63.8 ^d 63.8 ^d 94.4 ^g 78.4 <0.5	Trimethoprim-sulfamethoxazole			≤0.5	>4	\leq 0.5 to $>$ 4
Streptococcus pneumoniae (450) 0.008 0.015 0.0004 to 0.25 Levofloxacin 98.9 1 1 0.5 to >4 Amoxicillin-clavulanic acid 91.1 ≤1 2 ≤1 to >8 Ceftaroline 99.6 ^c 99.3 ≤0.015 0.12 ≤0.015 to 1 Ceftaroline 83.6 ^d 94.2 ^c 83.6 ≤0.06 1 ≤0.025 to >2 Citridamycin 84.7 84.9 ≤0.25 >2 ≤0.25 to >2 Erythromycin 59.9 59.9 ≤0.12 >16 ≤0.12 to >16 Moxifloxacin 98.9 98.7 ≤0.12 0.25 <0.21 to 2	Vancomycin	43.4	43.4	>16	>16	0.25 to >16
Delatioxacin0.0080.015 ≤ 0.004 to 0.25Levofloxacin98.998.9110.5 to >4Amoxicillin-clavulanic acid91.1 ≤ 1 2 ≤ 1 to >8Ceftraixone83.6, ^d 94.2c83.6 ≤ 0.015 0.12 ≤ 0.015 to 1Ceftriaxone84.784.9 ≤ 0.25 >2 ≤ 0.25 to >2Erythromycin59.959.9 ≤ 0.12 >16 ≤ 0.12 to >16Moxifloxacin98.998.7 ≤ 0.12 < 0.015 0.5 < 0.12 to 2Penicillin $63.8,^e 63.8,^f 94.4^g$ $63.8,^d 63.8^g$ ≤ 0.06 2 < 0.06 to 8Tetracycline78.478.4 < 50.5 >8 < 0.5 to >4Viridans group streptococci (294) $= 1$ 12 < 0.015 to 1Delafloxacin94.179.7 < 1 2 < 0.025 to >2Levofloxacin94.112 < 0.012 to >4Amoxicillin-clavulanic acid79.7 < 1 2 < 0.015 to 1Ceftraixone90.9 86.4 0.251 < 0.05 to >8Ceftraixone90.9 86.4 0.251 < 0.05 to >8Ceftraixone93.799.0 0.06 < 2.5 < 0.25 to >2Erythromycin 33.0 $= 0.12$ < 0.25 < 0.25 to >2Ceftraixone93.799.0 0.06 < 0.25 < 0.015 to 4Moxifloxacin $= 0.12$ < 0.25 < 0.25 < 0.25 to >2Ceftraixone<	Streptococcus pneumoniae (450)					
Levofloxacin98.998.9110.5 to >4Amoxicillin-clavulanic acid91.1 ≤ 1 2 ≤ 1 to >8Ceftaroline99.6'99.3 ≤ 0.015 0.12 ≤ 0.015 to 1Ceftriaxone83.6, d' 94.2c'83.6 ≤ 0.06 1 ≤ 0.025 to >2Erythromycin84.784.9 ≤ 0.25 >2 ≤ 0.25 to >2Maxifloxacin98.998.7 ≤ 0.12 >16 ≤ 0.12 to >16Meropenem84.484.4, d' 100.0c' ≤ 0.015 0.5 ≤ 0.015 to 2Ponicillin 38.6^{e} 63.8, f 94.4g' $63.8, d^{e}$ 63.8g' ≤ 0.06 2 ≤ 0.025 to >2Penicillin 63.8^{e} 63.8, f 94.4g' $63.8, d^{e}$ 63.8g' ≤ 0.06 2 ≤ 0.05 to >8Trimethoprim-sulfamethoxazole68.9 75.3 ≤ 0.5 >4 ≤ 0.5 to >4Viridans group streptococci (294) $Y7.7$ ≤ 1 2 ≤ 0.12 to >4Amoxicillin-clavulanic acid $Y9.7$ ≤ 1 2 ≤ 0.12 to >4Ceftaroline 0.03 0.12 ≤ 0.015 to 1 ≤ 0.06 to >8Ceftaroline 0.03 0.12 ≤ 0.025 to >2 ≤ 0.25 to >2Erythromycin 89.5 89.9 ≤ 0.25 >2 ≤ 0.25 to >2Ceftraixone 90.9 86.4 0.25 1 ≤ 0.06 to >8Clindamycin 89.5 89.9 ≤ 0.25 >2 ≤ 0.25 to >2Erythromycin 53.0 ≤ 0.12 ≤ 0.12 to >16 ≤ 0.12 to >16<	Delafloxacin			0.008	0.015	≤0.004 to 0.25
Amoxicillin-clavulanic acid91.1 ≤ 1 2 ≤ 1 to >8Ceftaroline90.6'c99.3 ≤ 0.015 0.12 ≤ 0.015 to 1Ceftriaxone83.6,d '94.2c'83.6 ≤ 0.06 1 ≤ 0.06 to 8Clindamycin84.784.9 ≤ 0.25 >2 ≤ 0.25 to >2Erythromycin59.959.9 ≤ 0.12 >16 ≤ 0.015 to 2Moxifloxacin98.998.7 ≤ 0.12 ~ 16 ≤ 0.015 to 2Penicillin $63.8,e' 63.8,e' 94.4g'$ $63.8,e' 63.8g' = 0.06$ 2 ≤ 0.06 to 8Tetracycline78.478.4 ≤ 0.5 >8 ≤ 0.5 to >8Tirmethoprim-sulfamethoxazole68.975.3 ≤ 0.5 >4 < 0.5 to >4Viridans group streptococci (294)12 ≤ 1.2 to >8 < 0.012 to >8Ceftravoline94.112 < 1.2 to >8 < 0.012 to >8Ceftravoline99.986.40.251 < 0.05 to >8Ceftravoline90.986.40.251 < 0.05 to >2Ceftravoline91.7 ≤ 1.0 2 < 0.25 to >2 < 0.25 to >2Ceftravoline93.7 99.0 0.06 0.25 < 0.015 to 1Meropenem93.799.0 0.06 0.25 < 0.015 to 4Moxifloxacin < 0.12 < 0.05 to >8 < 0.012 to >16Meropenem 93.7 99.0 0.06 0.25 < 0.015 to 4Moxifloxacin < 0.12 < 0.05 to >8	Levofloxacin	98.9	98.9	1	1	0.5 to >4
$\begin{array}{cccc} Ceftaroline & 99.6^c & 99.3 & < 0.015 & 0.12 & < 0.015 to 1 \\ Ceftriaxone & 83.6, '94.2^c & 84.9 & < 0.25 & >2 & < 0.25 to >2 \\ Erythomycin & 59.9 & 59.9 & < 0.12 & >16 & < 0.12 to >16 \\ Meropenem & 84.4 & 84.4, '100.0^c & < 0.015 & 0.5 & < 0.015 to 2 \\ Moxifloxacin & 98.9 & 98.7 & < 0.12 & 0.25 & < 0.12 to 2 \\ Penicillin & 63.8, '63.8, '94.4^9 & 63.8, '63.8^9 & < 0.06 & 2 & < 0.06 to 8 \\ Tetracycline & 78.4 & 78.4 & < 0.5 & >8 & < 0.5 to >8 \\ Trimethoprim-sulfamethoxazole & 68.9 & 75.3 & < 0.5 & >4 & < 0.5 to >4 \\ \hline Viridans group streptococci (294) & & & & & & & \\ Delafloxacin & 94.1 & T & 1 & 2 & < 0.12 to 2 \\ Levofloxacin & 94.1 & T & 1 & 2 & < 0.12 to >4 \\ Ceftriaxone & 0.09 & 86.4 & 0.25 & 1 & < 0.004 to 2 \\ Levofloxacin & 94.1 & T & 2 & < 0.12 to >4 \\ Ceftraioline & 79.7 & < 1 & 2 & < 0.12 to >4 \\ Ceftriaxone & 90.9 & 86.4 & 0.25 & 1 & < 0.005 to 1 \\ Ceftriaxone & 90.9 & 86.4 & 0.25 & 1 & < 0.05 to >8 \\ Clindamycin & 89.5 & 89.9 & < 0.25 & >2 & < 0.25 to >2 \\ Ceftraioline & 0.03 & 0.12 & < 0.015 to 1 \\ Ceftriaxone & 90.9 & 86.4 & 0.25 & 1 & < 0.06 to >8 \\ Clindamycin & 89.5 & 89.9 & < 0.25 & >2 & < 0.25 to >2 \\ Ceftraixone & 93.7 & 99.0 & 0.06 & 0.25 & < 0.015 to 1 \\ Meropenem & 93.7 & 99.0 & 0.06 & 1 & < 0.05 to >4 \\ Moxifloxacin & & & & & \\ Meropenem & 93.7 & 99.0 & 0.06 & 1 & < 0.05 to >4 \\ Moxifloxacin & & & & & & & \\ Penicillin & 73.1 & 79.7 & < 0.06 & 1 & < 0.05 to >8 \\ Trimethoprim-sulfamethoxazole & & & & & & & & \\ Penicillin & 73.1 & 79.7 & < 0.06 & 1 & < 0.05 to >8 \\ Tetracycline & 64.3 & & & & & & & & & & & \\ Frithoprim-sulfamethoxazole & & & & & & & & & & & & \\ Sot for >8 & & & & & & & & & & & & & & & & & \\ Sot for >8 & & & & & & & & & & & & & & & & & & $	Amoxicillin-clavulanic acid	91.1		≤1	2	≤ 1 to > 8
Ceftriaxone 83.6^d 94.2^c 83.6 ≤ 0.06 1 ≤ 0.06 to 8 Clindamycin 84.7 84.9 ≤ 0.25 >2 ≤ 0.25 to >2 Erythromycin 59.9 ≤ 0.12 >16 ≤ 0.12 to >16 Meropenem 84.4 84.4^d 100.0^c ≤ 0.015 0.5 ≤ 0.015 to 2 Moxifloxacin 98.9 98.7 ≤ 0.12 0.25 ≤ 0.12 to 2 Penicillin 63.8^e 63.8^f 94.7 ≤ 0.06 2 ≤ 0.06 to 8 Tetracycline 78.4 78.4 ≤ 0.5 >8 ≤ 0.5 to >4 Trimethoprim-sulfamethoxazole 68.9 75.3 ≤ 0.5 >4 ≤ 0.004 to 2 Levofloxacin 94.1 1 2 ≤ 0.12 to >4 Amoxicillin-clavulanic acid 79.7 ≤ 1 2 ≤ 1.2 to >4 Ceftraroline $0.99.9$ 86.4 0.25 1 < 0.015 to 1 Ceftraroline 90.9 86.4 0.25 1 < 0.06 to >8 Ceftraroline 20.5 89.9 ≤ 0.25 >2 < 0.25 to >2 Erythromycin 53.0 $= 0.12$ 8 < 0.12 to >16 Meropenem 93.7 99.0 0.06 0.25 < 0.015 to 4 Moxifloxacin $= 0.12$ 0.25 < 0.015 to 4 Penicillin 73.1 79.7 ≤ 0.65 >8 < 0.5 to >8 Trimethoprim-sulfamethoxazole < 0.5 < 8 < 0.5 to >8 < 0.5 to	Ceftaroline	99.6 ^c	99.3	≤0.015	0.12	≤0.015 to 1
Clindamycin84.784.9 ≤ 0.25 >2 ≤ 0.25 to >2 Erythromycin59.959.9 ≤ 0.12 >16 ≤ 0.12 to >16 Meropenem84.484.4,d 100.0c ≤ 0.015 0.5 ≤ 0.015 to 2 Moxifloxacin98.998.7 ≤ 0.12 0.25 ≤ 0.12 to 2 Penicillin $63.8,^e 63.8,^f 94.4^9$ $63.8,^d 63.8^g$ ≤ 0.06 2 ≤ 0.06 to 8 Tetracycline78.478.4 ≤ 0.5 >8 ≤ 0.5 to >8 Trimethoprim-sulfamethoxazole68.975.3 ≤ 0.5 >4 ≤ 0.5 to >4 Viridans group streptococci (294) V 1 2 ≤ 0.12 to >4 Delafloxacin94.11 2 ≤ 0.12 to >4 Amoxicillin-clavulanic acid79.7 ≤ 1 2 ≤ 0.12 to >4 Ceftraoline0.030.12 <0.015 to 1 <0.06 to >8 Citriaxone90.9 86.4 0.25 1 <0.06 to >8 Clindamycin89.589.9 <0.25 >2 <0.25 to >2 Erythromycin53.0 <0.06 0.25 <0.015 to 1 Meropenem93.7 99.0 0.06 0.25 <0.015 to >4 Meropenem93.7 99.0 0.06 1 <0.06 to >8 Meropenem 73.1 79.7 <0.06 1 <0.06 to >8 Trimethoprim-sulfamethoxazole <0.3 <0.5 <8 <0.5 to >4 <0.5 to >8	Ceftriaxone	83.6, ^d 94.2 ^c	83.6	≤0.06	1	≤0.06 to 8
Erythromycin59.959.9 ≤ 0.12 >16 ≤ 0.12 to >16Meropenem84.4 84.4^d 100.0c ≤ 0.015 0.5 ≤ 0.015 to 2Moxifloxacin98.998.7 ≤ 0.12 0.25 ≤ 0.012 to 2Penicillin 63.8^e 63.8^f 94.49 63.8^d 63.8^g ≤ 0.06 2 ≤ 0.06 to 8Tetracycline78.478.4 ≤ 0.5 >8 ≤ 0.5 to >8Trimethoprim-sulfamethoxazole 68.9 75.3 ≤ 0.5 >4 ≤ 0.5 to >4Viridans group streptococci (294) $=$ 1 2 ≤ 0.024 to 2Delafloxacin94.112 ≤ 0.12 to >4Amoxicillin-clavulanic acid79.7 ≤ 1 2 ≤ 0.12 to >4Ceftraixone90.9 86.4 0.25 1 ≤ 0.06 to 8Ciftriaxone90.9 86.4 0.25 2 ≤ 0.25 to >2Erythromycin 89.5 89.9 ≤ 0.25 >2 < 0.25 to >2Meropenem 93.7 99.0 0.06 0.25 < 0.015 to 4Moxifloxacin73.179.7 < 0.06 1 < 0.06 to >8Tetracycline 64.3 $=$ < 0.5 > 8 < 0.5 to >4	Clindamycin	84.7	84.9	≤0.25	>2	≤0.25 to >2
Meropenem84.484.4,d 100.0^c ≤ 0.015 0.5 ≤ 0.015 to 2Moxifloxacin98.998.7 ≤ 0.12 0.25 ≤ 0.12 to 2Penicillin $63.8,^e 63.8,^f 94.4^g$ $63.8,^d 63.8^g$ ≤ 0.06 2 ≤ 0.06 to 8Tetracycline78.478.4 ≤ 0.5 >8 ≤ 0.5 to >8Trimethoprim-sulfamethoxacole 68.9 75.3 ≤ 0.5 >4 ≤ 0.5 to >8Viridans group streptococci (294) $=$ 0.015 0.03 ≤ 0.004 to 2Delafloxacin94.112 ≤ 0.12 to >4Amoxicillin-clavulanic acid79.7 ≤ 1 2 ≤ 1.1 to >8Ceftaroline0.030.12 ≤ 0.05 to >8 ≤ 0.05 to >8Ceftraixone90.986.40.251 ≤ 0.06 to >8Clindamycin89.589.9 ≤ 0.25 >2 ≤ 0.25 to >2Erythromycin53.0 ≤ 0.12 ≈ 0.12 to >16 ≤ 0.12 to >4Meropenem93.799.0 0.06 0.25 ≤ 0.12 to >4Moxifloxacin79.7 ≤ 0.12 ≈ 0.12 to >16 ≤ 0.12 to >16Meropenem93.799.0 0.66 0.25 ≤ 0.12 to >4Moxifloxacin79.7 ≤ 0.06 1 ≤ 0.05 to >8Trimethoprim-sulfamethoxazole ≤ 3.11 ≤ 0.5 to >8 ≤ 0.5 to >8	Erythromycin	59.9	59.9	≤0.12	>16	≤0.12 to >16
Moxifloxacin98.998.7 ≤ 0.12 0.25 ≤ 0.12 to 2Penicillin $63.8,^e 63.8,^f 94.4^g$ $63.8,^d 63.8^g$ ≤ 0.06 2 ≤ 0.06 to 8Tetracycline 78.4 78.4 ≤ 0.5 >8 ≤ 0.5 to >8Timethoprim-sulfamethoxazole 68.9 75.3 ≤ 0.5 >4 ≤ 0.5 to >4Viridans group streptococci (294) 53.6 94.1 1 2 ≤ 0.004 to 2Levofloxacin 94.1 1 2 ≤ 0.12 to >4Amoxicillin-clavulanic acid 79.7 ≤ 1 2 ≤ 0.12 to >8Ceftaroline 0.03 0.12 ≤ 0.05 to 1Ceftriaxone 90.9 86.4 0.25 1 ≤ 0.06 to >8Clindamycin 89.5 89.9 ≤ 0.25 >2 ≤ 0.25 to >2Erythromycin 53.0 ≤ 0.12 ≈ 0.06 0.25 ≤ 0.012 to >16Moxifloxacin $=$ $=$ ≤ 0.12 $<$ $<$ Penicillin 73.1 79.7 ≤ 0.06 1 $<$ $<$ Tetracycline 64.3 $=$ $<$ $<$ $<$ $<$ $<$ Tetracycline 64.3 $=$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ Penicillin $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ $<$ </td <td>Meropenem</td> <td>84.4</td> <td>84.4,^d 100.0^c</td> <td>≤0.015</td> <td>0.5</td> <td>≤0.015 to 2</td>	Meropenem	84.4	84.4, ^d 100.0 ^c	≤0.015	0.5	≤0.015 to 2
Penicillin $63.8,^e 63.8,^f 94.4^g$ $63.8,^d 63.8^g$ ≤ 0.06 2 ≤ 0.06 to 8 Tetracycline 78.4 78.4 ≤ 0.5 >8 ≤ 0.5 to >8 Trimethoprim-sulfamethoxazole 68.9 75.3 ≤ 0.5 >4 ≤ 0.5 to >4 Viridans group streptococci (294) 20.5 >4 ≤ 0.004 to 2 Delafloxacin 94.1 1 2 ≤ 0.02 to >4 Amoxicillin-clavulanic acid 94.1 79.7 ≤ 1 2 ≤ 0.12 to >4 Ceftaroline 0.03 0.12 ≤ 0.015 to 1 Ceftriaxone 90.9 86.4 0.25 1 ≤ 0.06 to >8 Clindamycin 89.5 89.9 ≤ 0.25 >2 ≤ 0.25 to >2 Erythromycin 53.0 ≤ 0.12 8 ≤ 0.12 to >16 Meropenem 93.7 99.0 0.06 0.25 ≤ 0.12 to >4 Moxifloxacin 73.1 79.7 ≤ 0.06 1 ≤ 0.05 to >8 Tetracycline 64.3 $=$ ≤ 0.5 < 4 < 0.5 to >8	Moxifloxacin	98.9	98.7	≤0.12	0.25	≤0.12 to 2
Tetracycline Trimethoprim-sulfamethoxazole78.478.4 ≤ 0.5 >8 ≤ 0.5 to >8Trimethoprim-sulfamethoxazole68.975.3 ≤ 0.5 >4 ≤ 0.5 to >4Viridans group streptococci (294) Delafloxacin Levofloxacin94.10.0150.03 ≤ 0.004 to 2Levofloxacin Amoxicillin-clavulanic acid94.112 ≤ 0.12 to >4Ceftaroline79.7 ≤ 1 2 ≤ 1 to >8Ceftaroline0.030.12 ≤ 0.015 to 1Ceftriaxone90.986.40.251 ≤ 0.06 to >8Clindamycin89.589.9 ≤ 0.25 >2 ≤ 0.25 to >2Erythromycin53.0 ≤ 0.12 8 ≤ 0.12 to >16Moxifloxacin93.799.00.060.25 ≤ 0.12 to >4Penicillin73.179.7 ≤ 0.06 1 ≤ 0.06 to >8Tetracycline64.3 ≤ 0.5 >8 ≤ 0.5 to >4 ≤ 0.5 to >4	Penicillin	63.8, ^e 63.8, ^f 94.4 ^g	63.8, ^d 63.8 ^g	≤0.06	2	≤0.06 to 8
Trimethoprim-sulfamethoxazole 68.9 75.3 ≤0.5 >4 ≤0.5 to >4 Viridans group streptococci (294) 0.015 0.03 ≤0.004 to 2 Levofloxacin 94.1 1 2 ≤0.12 to >4 Amoxicillin-clavulanic acid 79.7 ≤1 2 ≤1 to >8 Ceftaroline 0.03 0.12 ≤0.006 to >8 2 Ceftriaxone 90.9 86.4 0.25 1 ≤0.05 to >2 Clindamycin 89.5 89.9 ≤0.25 >2 ≤0.25 to >2 Erythromycin 53.0 ≤0.12 8 ≤0.12 to >4 Moxifloxacin 93.7 99.0 0.06 0.25 ≤0.12 to >4 Penicillin 73.1 79.7 ≤0.06 1 ≤0.06 to >8 Tetracycline 64.3 ≤0.5 >8 ≤0.5 to >4	Tetracycline	78.4	78.4	≤0.5	>8	≤0.5 to >8
Viridans group streptococci (294) 0.015 0.03 ≤0.004 to 2 Levofloxacin 94.1 1 2 ≤0.12 to >4 Amoxicillin-clavulanic acid 79.7 ≤1 2 ≤1 to >8 Ceftaroline 0.03 0.12 ≤0.015 to 1 Ceftriaxone 90.9 86.4 0.25 1 ≤0.06 to >8 Clindamycin 89.5 89.9 ≤0.25 >2 ≤0.25 to >2 Erythromycin 53.0 ≤0.12 8 ≤0.12 to >16 Meropenem 93.7 99.0 0.06 0.25 ≤0.12 to >4 Penicillin 73.1 79.7 ≤0.06 1 ≤0.06 to >8 Tetracycline 64.3 ≤0.5 >8 ≤0.5 <8	Trimethoprim-sulfamethoxazole	68.9	75.3	≤0.5	>4	\leq 0.5 to $>$ 4
Delafloxacin 0.015 0.03 ≤0.004 to 2 Levofloxacin 94.1 1 2 ≤0.12 to >4 Amoxicillin-clavulanic acid 79.7 ≤1 2 ≤1 to >8 Ceftaroline 0.03 0.12 ≤0.006 to 1 Ceftriaxone 90.9 86.4 0.25 1 ≤0.05 to 2 Clindamycin 89.5 89.9 ≤0.25 >2 ≤0.25 to >2 Erythromycin 53.0 ≤0.12 8 ≤0.12 to >4 Moxifloxacin 93.7 99.0 0.06 0.25 ≤0.12 to >4 Penicillin 73.1 79.7 ≤0.06 1 ≤0.06 to >8 Tetracycline 64.3 ≤0.5 >8 ≤0.5 to >4	Viridans group streptococci (294)					
Levofloxacin94.112 ≤ 0.12 to >4Amoxicillin-clavulanic acid79.7 ≤ 1 2 ≤ 1 to >8Ceftaroline0.030.12 ≤ 0.015 to 1Ceftriaxone90.986.40.251 ≤ 0.06 to >8Clindamycin89.589.9 ≤ 0.25 >2 ≤ 0.25 to >2Erythromycin53.0 ≤ 0.12 8 ≤ 0.12 to >4Moxifloxacin93.799.00.060.25 ≤ 0.015 to 4Penicillin73.179.7 ≤ 0.06 1 ≤ 0.06 to >8Tetracycline64.3 ≤ 0.5 < 4 ≤ 0.5 to >4 < 0.5 to >4	Delafloxacin			0.015	0.03	≤0.004 to 2
Amoxicillin-clavulanic acid 79.7 ≤ 1 2 ≤ 1 to >8 Ceftaroline 0.03 0.12 ≤ 0.015 to 1 Ceftriaxone 90.9 86.4 0.25 1 ≤ 0.06 to >8 Clindamycin 89.5 89.9 ≤ 0.25 >2 ≤ 0.025 to >2 Erythromycin 53.0 ≤ 0.12 8 ≤ 0.12 to >16 Meropenem 93.7 99.0 0.06 0.25 ≤ 0.12 to >4 Penicillin 73.1 79.7 ≤ 0.06 1 ≤ 0.06 to >8 Tetracycline 64.3 ≤ 0.5 >8 ≤ 0.5 to >4 ≥ 0.5 to >4	Levofloxacin	94.1		1	2	≤0.12 to >4
Ceftaroline0.030.12 ≤ 0.015 to 1Ceftriaxone90.986.40.251 ≤ 0.06 to > 8 Clindamycin89.589.9 ≤ 0.25 > 2 ≤ 0.25 to > 2 Erythromycin53.0 ≤ 0.12 8 ≤ 0.12 to >16 Meropenem93.799.00.060.25 ≤ 0.015 to 4 Moxifloxacin ≤ 0.12 ≈ 0.12 to >4 ≥ 0.12 to >4 Penicillin73.179.7 ≤ 0.06 1 ≤ 0.06 to >8 Tetracycline 64.3 ≤ 0.5 > 8 ≤ 0.5 to >4	Amoxicillin-clavulanic acid		79.7	≤1	2	≤1 to >8
Ceftriaxone90.986.40.251 ≤ 0.06 to >8 Clindamycin89.589.9 ≤ 0.25 >2 ≤ 0.25 to >2 Erythromycin53.0 ≤ 0.12 8 ≤ 0.12 to >16 Meropenem93.799.00.060.25 ≤ 0.015 to 4 Moxifloxacin ≤ 0.12 ≤ 0.12 ≤ 0.12 to >4 Penicillin73.179.7 ≤ 0.06 1 ≤ 0.06 to >8 Tetracycline 64.3 ≤ 0.5 >8 ≤ 0.5 to >8 Trimethoprim-sulfamethoxazole ≤ 0.5 4 ≤ 0.5 to >4	Ceftaroline			0.03	0.12	≤0.015 to 1
$ \begin{array}{c c c c c c c c c c c c c c c c c c c $	Ceftriaxone	90.9	86.4	0.25	1	\leq 0.06 to $>$ 8
Erythromycin53.0 ≤ 0.12 8 ≤ 0.12 to >16Meropenem93.799.00.060.25 ≤ 0.015 to 4Moxifloxacin ≤ 0.12 0.25 ≤ 0.12 to >4Penicillin73.179.7 ≤ 0.06 1 ≤ 0.06 to >8Tetracycline64.3 ≤ 0.5 >8 ≤ 0.5 to >4Trimethoprim-sulfamethoxazole ≤ 0.5 4 ≤ 0.5 to >4	Clindamycin	89.5	89.9	≤0.25	>2	\leq 0.25 to $>$ 2
Meropenem 93.7 99.0 0.06 0.25 ≤0.015 to 4 Moxifloxacin ≤0.12 0.25 ≤0.12 to >4 Penicillin 73.1 79.7 ≤0.06 1 ≤0.06 to >8 Tetracycline 64.3 ≤0.5 >8 ≤0.5 to >4 Trimethoprim-sulfamethoxazole ≤0.5 4 ≤0.5 to >4	Erythromycin	53.0		≤0.12	8	≤0.12 to >16
Moxifloxacin ≤0.12 0.25 ≤0.12 to >4 Penicillin 73.1 79.7 ≤0.06 1 ≤0.06 to >8 Tetracycline 64.3 ≤0.5 >8 ≤0.5 to >8 Trimethoprim-sulfamethoxazole ≤0.5 4 ≤0.5 to >4	Meropenem	93.7	99.0	0.06	0.25	≤0.015 to 4
Penicillin 73.1 79.7 ≤0.06 1 ≤0.06 to >8 Tetracycline 64.3 ≤0.5 >8 ≤0.5 to >8 Trimethoprim-sulfamethoxazole ≤0.5 4 ≤0.5 to >4	Moxifloxacin			≤0.12	0.25	≤0.12 to >4
Tetracycline 64.3 ≤0.5 >8 ≤0.5 to >8 Trimethoprim-sulfamethoxazole ≤0.5 4 ≤0.5 to >4	Penicillin	73.1	79.7	≤0.06	1	\leq 0.06 to $>$ 8
Trimethoprim-sulfamethoxazole ≤ 0.5 4 ≤ 0.5 to >4	Tetracycline	64.3		≤0.5	>8	\leq 0.5 to $>$ 8
	Trimethoprim-sulfamethoxazole			≤0.5	4	\leq 0.5 to $>$ 4

TABLE 2 (Continued)

Organism group (no. of isolates tested)/	% of isolates the following	susceptible by criteria:	MIC (µg/n	nl)	
antimicrobial agent	CLSI	EUCAST	50%	90%	Range
Streptococcus pyogenes (433)					
Delafloxacin			0.008	0.015	\leq 0.004 to 0.03
Levofloxacin	99.8	96.5	0.5	1	0.25 to >4
Amoxicillin-clavulanic acid	100.0	100.0	≤1	≤1	≤1 to ≤1
Ceftaroline	100.0	100.0	≤0.015	≤0.015	≤0.015 to 0.03
Ceftriaxone	100.0	100.0	≤0.06	≤0.06	≤0.06 to 0.5
Clindamycin	91.5	91.9	≤0.25	≤0.25	≤0.25 to >2
Erythromycin	85.2	85.2	≤0.12	>16	≤0.12 to >16
Meropenem	100.0	100.0	≤0.015	≤0.015	≤0.015 to 0.12
Moxifloxacin		100.0	≤0.12	0.25	≤0.12 to 0.5
Penicillin	100.0	100.0	≤0.06	≤0.06	≤0.06 to 0.12
Tetracycline	80.2	78.6	≤0.5	>8	≤0.5 to >8
Vancomycin	100.0	100.0	0.25	0.5	≤0.12 to 0.5
Streptococcus agalactiae (225)					
Delafloxacin			0.008	0.015	≤0.004 to 0.5
Levofloxacin	97.8	96.9	0.5	1	0.25 to >4
Amoxicillin-clavulanic acid	100.0	100.0	≤1	≤1	≤1 to ≤1
Ceftaroline	100.0	100.0	≤0.015	0.03	≤0.015 to 0.03
Ceftriaxone	100.0	100.0	≤0.06	0.12	≤0.06 to 0.25
Clindamycin	70.7	72.4	≤0.25	>2	\leq 0.25 to $>$ 2
Erythromycin	52.4	52.4	≤0.12	>16	\leq 0.12 to $>$ 16
Meropenem	100.0	100.0	0.03	0.06	≤0.015 to 0.12
Moxifloxacin		97.8	≤0.12	0.25	≤0.12 to >4
Penicillin	100.0	100.0	≤0.06	≤0.06	\leq 0.06 to \leq 0.06
Tetracycline	17.4	17.0	>8	>8	\leq 0.5 to $>$ 8
Vancomycin	100.0	100.0	0.5	0.5	0.25 to 1
Streptococcus dysgalactiae (132)					
Delafloxacin			0.008	0.015	≤0.004 to 0.03
Levofloxacin	99.2	97.0	0.5	1	0.25 to >4
Amoxicillin-clavulanic acid	100.0	100.0	≤1	≤1	≤1 to ≤1
Ceftaroline	100.0	100.0	≤0.015	≤0.015	≤0.015 to ≤0.015
Ceftriaxone	100.0	100.0	≤0.06	≤0.06	≤0.06 to 0.5
Clindamycin	88.6	90.2	≤0.25	0.5	≤0.25 to >2
Erythromycin	68.9	68.9	≤0.12	>16	≤0.12 to >16
Meropenem	100.0	100.0	≤0.015	≤0.015	≤0.015 to 0.06
Moxifloxacin		100.0	≤0.12	0.25	≤0.12 to 0.25
Penicillin	100.0	100.0	≤0.06	≤0.06	≤0.06 to ≤0.06
Tetracycline	61.8	59.5	≤0.5	>8	\leq 0.5 to $>$ 8
Vancomycin	100.0	100.0	0.25	0.25	≤0.12 to 1

^aBreakpoints from FDA package insert, revised December 2014.

^bUncomplicated UTI only.

^cUsing nonmeningitis breakpoints.

^dUsing meningitis breakpoints.

^eUsing oral breakpoints.

fUsing parenteral, meningitis breakpoints.

^gUsing parenteral, nonmeningitis breakpoints.

All isolates of *E. faecalis* from Europe and the United States were susceptible to ampicillin (Table 2). A small number of *E. faecalis* strains were resistant to vancomycin (2.2%). Delafloxacin (MIC₅₀ and MIC₉₀, 0.06 and 1 μ g/ml, respectively) and linezolid (MIC₅₀ and MIC₉₀, 1 and 1 μ g/ml, respectively) were the most potent antimicrobials tested (Table 2).

Delafloxacin (MIC₅₀ and MIC₉₀, >4 and >4 μ g/ml, respectively; 10.5% of isolates were susceptible to delafloxacin at $\leq 1 \mu$ g/ml), levofloxacin (MIC₅₀ and MIC₉₀, >4 and >4 μ g/ml, respectively; 7.8 and 10.8% of isolates were susceptible according to CLSI and EUCAST criteria, respectively), erythromycin (MIC₅₀ and MIC₉₀, >16 and >16 μ g/ml, respectively; 3.7% of isolates were susceptible according to the CLSI criterion), and ampicillin (MIC₅₀ and MIC₉₀, >8 and >8 μ g/ml, respectively; 10.8 and 10.8% of isolates were susceptible according to CLSI criterion), and support (MIC₅₀ and MIC₉₀, >8 and >8 μ g/ml, respectively; 10.8 and 10.8% of isolates were susceptible according to CLSI and EUCAST criteria, respectively) displayed

limited activity against *E. faecium* strains regardless of geographic region or vancomycin susceptibility patterns (Table 2).

Delafloxacin was the most active agent tested against *S. pneumoniae* isolates from Europe and the United States (MIC₅₀ and MIC₉₀, 0.008 and 0.015 µg/ml, respectively) (Table 2). All European isolates (100.0%) and 98.0% of U.S. isolates were inhibited by $\leq 0.03 \mu$ g/ml of delafloxacin; the highest delafloxacin MIC value for U.S. isolates was 0.25 µg/ml (Table 1 and 2). Delafloxacin was 8-fold more active than ceftaroline (MIC₅₀ and MIC₉₀, ≤ 0.015 and 0.12 µg/ml, respectively), 16-fold more active than moxifloxacin (MIC₅₀ and MIC₉₀, ≤ 0.12 and 0.25 µg/ml, respectively), and 64-fold more active than levofloxacin (MIC₅₀ and MIC₉₀, 1 and 1 µg/ml, respectively) (Table 2). For other common-use antimicrobials, the rate of penicillin resistance (MIC, $\geq 2 \mu$ g/ml, oral breakpoint) was 11.3% (0.7%; MIC, $\geq 8 \mu$ g/ml, parenteral, nonmeningitis breakpoint), the rate of erythromycin resistance was 39.0%, the rate of tetracycline resistance was 21.6%, and the rate of trimethoprim-sulfamethoxazole resistance was 18.9% (Table 2). The delafloxacin MIC for the three high-level penicillin-resistant (MIC, $\geq 4 \mu$ g/ml) strains was 0.008 µg/ml (data not shown).

The most active agents tested against the viridans group streptococci were delafloxacin (MIC_{50} and MIC_{90} , 0.015 and 0.03 μ g/ml; Tables 1 and 2), moxifloxacin (MIC_{50} and MIC_{90} , ≤ 0.12 and 0.25 μ g/ml, respectively), and ceftaroline (MIC_{50} and MIC_{90} , 0.03 and 0.12 μ g/ml, respectively) (Table 2). The rate of resistance to penicillin and ceftriaxone was higher among European isolates (11.2% and 12.2%, respectively) than U.S. isolates (2.6 and 3.1%, respectively). The rates of resistance to levofloxacin and erythromycin were comparable for European isolates (5.1% and 44.9%, respectively) and U.S. isolates (5.6% and 44.6%, respectively) (Table 2). Meropenem exhibited the highest coverage against viridans group streptococci and was more active against U.S. isolates (96.4 and 100.0% of isolates were susceptible according to CLSI and EUCAST criteria, respectively) than European isolates (88.8 and 96.9% of isolates were susceptible according to CLSI and EUCAST criteria, respectively).

The activities of delafloxacin and comparator antimicrobial agents against a total of 790 isolates of beta-hemolytic streptococci (433 isolates of *Streptococcus pyogenes*, 225 of *Streptococcus agalactiae*, and 132 of *Streptococcus dysgalactiae*) were tested (Tables 1 and 2). Delafloxacin was highly potent against these organisms (Table 1). All delafloxacin MIC values for *S. pyogenes* and *S. dysgalactiae* were $\leq 0.03 \ \mu g/ml$. The highest delafloxacin MIC value for *S. agalactiae* was 0.5 $\ \mu g/ml$, and 97.3% of *S. agalactiae* isolates were inhibited by delafloxacin at $\leq 0.03 \ \mu g/ml$ (Table 1). All beta-hemolytic streptococcal isolates were susceptible to ceftaroline, ceftriaxone, meropenem, penicillin, and vancomycin (Table 2). The rates of resistance to levofloxacin were 0.2% for *S. pyogenes*, 2.2% for *S. agalactiae*, and 0.8% for *S. dysgalactiae* (Table 2). The rate of resistance to erythromycin was higher among isolates of *S. agalactiae* (46.7%) and *S. dysgalactiae* (29.5%) than among isolates of *S. pyogenes* (14.1%). The rate of resistance to clindamycin among isolates of beta-hemolytic streptococci ranged from 8.1% to 27.6% (Table 2).

Susceptibilities of European and U.S. Gram-negative isolates to delafloxacin and comparator agents. Delafloxacin was active against the majority of the *Enterobacteriaceae*, exhibiting MIC₅₀ and MIC₉₀ values of 0.06 and 4 µg/ml, respectively, and with 80.9% of isolates being inhibited by delafloxacin at $\leq 1 \mu$ g/ml (Table 1). The rates of susceptibility to fluoroquinolones, as measured by the use of ciprofloxacin and levofloxacin, for the *Enterobacteriaceae* were 81.6% and 83.8%, respectively (Table 3). More than 90% of FQ^r *Enterobacteriaceae* isolates showed decreased susceptibility (MIC, $>1 \mu$ g/ml) to delafloxacin (data not shown). The rates of susceptibility to aztreonam, ceftriaxone, cefepime, and ceftazidime ranged from 80.3% to 90.8% (Table 3). Meropenem (MIC₅₀ and MIC₉₀, 0.03 and 0.06 µg/ml, respectively; 97.5 and 97.9% of isolates were susceptible according to CLSI and EUCAST criteria, respectively) and tigecycline (MIC₅₀ and MIC₉₀, 0.25 and 1 µg/ml, respectively; 99.2 and 95.2% of isolates were susceptible according to CLSI and EUCAST criteria, respectively) were the most active agents (Table 3).

TABLE 3 Activity of delafloxacin and comparator antimicrobial agents when tested against U.S. and European Gram-negative isolates

	% of isolate	es susceptible			
	by the follo	wing criteria:	MIC (µg/ml)	
organism group (no. of isolates tested)/		FUCAST	50%	90%	Range
Enterobactoriaceae (2.250)	CLSI	LUCAJI	5070	5070	hange
Delafloxacin			0.06	4	<0.004 to >4
Levofloxacin	83.8	81.9	<0.12	>4	≤ 0.12 to >4
Ampicillin-sulbactam	47.4	47.4	16	>32	0.5 to > 32
Aztreonam	86.3	83.6	≤0.12	>16	≤ 0.12 to > 16
Cefepime	90.8	87.8	≤0.5	2	≤ 0.5 to > 16
Ceftazidime	86.3	82.8	0.25	16	0.03 to >32
Ceftriaxone	80.3	80.3	0.12	>8	≤ 0.06 to > 8
Ciprofloxacin	81.6	79.3	≤0.03	>4	≤ 0.03 to >4
Gentamicin	90.7	89.0	_0.00 ≤1	4	≤ 1 to ≥ 8
Meropenem	97.5	97.9	0.03	0.06	≤0.015 to >32
Piperacillin-tazobactam	89.3	85.7	2	32	≤ 0.5 to > 64
Tigecycline	99.2 ^b	95.2	0.25	1	0.03 to 4
Escherichia coli (500)					
Delafloxacin			0.03	4	\leq 0.004 to $>$ 4
Levofloxacin	69.6	69.6	≤0.12	>4	\leq 0.12 to $>$ 4
Ampicillin-sulbactam	49.6	49.6	16	>32	0.5 to >32
Aztreonam	86.4	82.6	≤0.12	16	\leq 0.12 to $>$ 16
Cefepime	87.0	84.2	≤0.5	8	\leq 0.5 to $>$ 16
Ceftazidime	89.2	83.4	0.12	8	0.03 to >32
Ceftriaxone	84.0	84.0	≤0.06	>8	\leq 0.06 to $>$ 8
Ciprofloxacin	69.4	68.8	≤0.03	>4	\leq 0.03 to $>$ 4
Gentamicin	86.4	86.0	≤1	>8	\leq 1 to >8
Meropenem	99.6	99.6	≤0.015	0.03	≤0.015 to 4
Piperacillin-tazobactam	94.2	90.0	2	8	\leq 0.5 to $>$ 64
Tigecycline	100.0 ^b	100.0	0.06	0.12	0.03 to 1
E. coli isolates of the ESBL phenotype (92)					
Delafloxacin			2	>4	0.008 to >4
Levofloxacin	21.7	21.7	>4	>4	≤0.12 to >4
Ampicillin-sulbactam	16.3	16.3	32	>32	2 to >32
Aztreonam	26.1	5.4	>16	>16	≤0.12 to >16
Cefepime	31.5	20.7	16	>16	\leq 0.5 to $>$ 16
Ceftazidime	41.3	9.8	8	32	0.06 to >32
Ceftriaxone	13.0	13.0	>8	>8	0.25 to >8
Ciprofloxacin	20.7	19.6	>4	>4	≤0.03 to >4
Gentamicin	63.0	62.0	≤1	>8	≤1 to >8
Meropenem	97.8	97.8	≤0.015	0.03	≤0.015 to 4
Piperacillin-tazobactam	81.5	65.2	8	>64	1 to >64
Tigecycline	100.0 ^b	100.0	0.12	0.12	0.06 to 0.5
Klebsiella pneumoniae (389)					
Delafloxacin			0.06	>4	0.015 to >4
Levofloxacin	81.5	80.2	≤0.12	>4	≤0.12 to >4
Ampicillin-sulbactam	63.2	63.2	8	>32	1 to >32
Aztreonam	//.1	/5.8	≤0.12	>16	≤ 0.12 to > 16
Cetepime	77.9 ^a	75.3	≤0.5	>16	≤0.5 to >16
Ceftazidime	/6.9	/4.8	0.12	>32	0.03 to >32
Ceftriaxone	/5.3	/5.3	≤0.06	>8	≤0.06 to >8
Ciprofloxacin	77.4	75.6	≤0.03	>4	≤0.03 to >4
Gentamicin	86.4	85.1	≤1	>8	≤ 1 to > 8
Meropenem	90.2	91.0	0.03	1	≤0.015 to >32
Piperacillin-tazobactam	81.2	75.8	4	>64	≤0.5 to >64
Tigecycline	99.7 ^b	97.7	0.25	0.5	0.06 to 4
K. pneumoniae isolates of the ESBL phenotype (102)			4	< A	
	24.2	22.4	4	>4	0.06 to >4
	34.3	32.4	>4	>4	≤ 0.12 to >4
	1.0	1.0	>32	>32	4 to >32
Aztreonam	12./	/.ð	>10	>10	≥ 0.12 to ≥ 16
Cefteridine	15./	5.9	> 10	>10	$\geq 0.5 \ 10 > 10$
Certazidime	11.8	3.9	>32	>32	0.25 to >32

TABLE 3 (Continued)

Organism group (no. of isolates tested)/	% of isolate by the follo	s susceptible wing criteria:	MIC (µg/ml)	
antimicrobial agent	CLSI	EUCAST	50%	90%	Range
Ceftriaxone	5.9	5.9	>8	>8	0.12 to >8
Ciprofloxacin	18.6	15.7	>4	>4	≤0.03 to >4
Gentamicin	48.0	43.1	>8	>8	≤1 to >8
Meropenem	62.7	65.7	0.06	>32	\leq 0.015 to $>$ 32
Piperacillin-tazobactam	31.4	23.5	>64	>64	2 to >64
Tigecycline	99.0 ^b	96.1	0.25	0.5	0.12 to 4
Klebsiella oxytoca (111)					
Delafloxacin			0.06	0.12	0.03 to 1
Levofloxacin	100.0	100.0	≤0.12	≤0.12	≤0.12 to 1
Ampicillin-sulbactam	63.1	63.1	8	>32	2 to >32
Aztreonam	83.8	81.1	0.25	>16	≤ 0.12 to > 16
Cetepime	98.2 ^a	96.4	≤0.5	1	≤ 0.5 to > 16
Ceffiziere	98.2	97.3	0.12	0.5	0.03 to > 32
Centriaxone	82.9	82.9	0.12	>8	≤ 0.06 to > 8
Cipronoxacin	98.2	98.2	≤0.03 <1	0.06	$\leq 0.03 \ 10 \ 4$
Merenonom	100.0	100.0			$\leq 1 \ 10 > 0$
Piperacillin-tazohactam	100.0 91.1	78.4	0.05	0.03	≤ 0.013 to 0.00
Tigecycline	100.0 ^b	100.0	0.12	0.25	0.06 to 1
Proteus mirabilis (211)					
Delafloxacin			0.06	2	0.015 to >4
Levofloxacin	78.7	71.1	≤0.12	>4	≤0.12 to >4
Ampicillin-sulbactam	86.7	86.7	2	16	0.5 to >32
Aztreonam	99.5	98.1	≤0.12	≤0.12	≤0.12 to 8
Cefepime	97.2 ^a	96.7	≤0.5	≤0.5	≤0.5 to >16
Ceftazidime	97.2	94.3	0.06	0.12	0.03 to 32
Ceftriaxone	93.4	93.4	≤0.06	≤0.06	\leq 0.06 to $>$ 8
Ciprofloxacin	71.6	67.8	≤0.03	>4	\leq 0.03 to $>$ 4
Gentamicin	88.6	85.3	≤1	8	\leq 1 to $>$ 8
Meropenem	100.0	100.0	0.06	0.12	≤0.015 to 1
Piperacillin-tazobactam	100.0	100.0	≤0.5	1	≤0.5 to 8
Tigecycline	94.3 ^b	64.5	1	2	0.12 to 4
Enterobacter spp. (384)					
Delafloxacin	04.4	05.0	0.06	1	≤0.004 to >4
Levofloxacin	96.6	95.8	≤0.12	0.5	≤ 0.12 to >4
Ampicillin-sulbactam	24.1	24.1	32	>32	0.5 to > 32
Aztreonam	/6.6	/3./	≤0.12	>16	≤ 0.12 to > 16
Cettepime	93.7 ^a	85.6	≤0.5 0.25	2	≤ 0.5 to > 16
Cettazidime	/5./	73.0	0.25	>32	$0.03 \ 10 > 32$
Ciproflovacin	70.0	70.6	0.25	~o 0.25	$\leq 0.00 \ 10 > 6$
Contamicin	95.5	94.5	≤0.05 <1	0.2J	$\leq 0.03 \ 10 > 4$
Meropenem	90.9	90.9			$\leq 1 \ 10 > 0$
Piperacillin-tazohactam	97.9 81.2	99.0 77 0	0.05	64	≤ 0.015 to > 64
Tigecycline	100.0 ^b	97.6	0.25	0.25	0.03 to 2
Citrobacter spp. (178)					
Delafloxacin			0.06	2	0.008 to >4
Levofloxacin	93.8	92.7	≤0.12	0.5	≤0.12 to >4
Ampicillin-sulbactam	68.5	68.5	4	>32	1 to >32
Aztreonam	89.3	87.1	≤0.12	16	≤0.12 to >16
Cefepime	97.2	94.9	≤0.5	≤0.5	\leq 0.5 to $>$ 16
Ceftazidime	87.6	86.0	0.25	16	0.06 to >32
Ceftriaxone	87.1	87.1	0.12	>8	\leq 0.06 to $>$ 8
Ciprofloxacin	92.1	91.0	≤0.03	0.5	\leq 0.03 to $>$ 4
Gentamicin	95.5	94.4	≤1	≤1	\leq 1 to >8
Meropenem	97.8	98.3	≤0.015	0.03	≤0.015 to 8
Piperacillin-tazobactam	90.4	85.4	2	16	\leq 0.5 to $>$ 64
Tigecycline	100.0 ^b	99.4	0.12	0.25	0.06 to 2

TABLE 3 (Continued)

	% of isolate	es susceptible			
Organism group (no. of isolates tested)/	by the follo	owing criteria:	MIC (μ g/ml)	
antimicrobial agent	CLSI	EUCAST	50%	90%	Range
Indole-positive Proteus spp. (249)					
Delafloxacin			0.12	4	0.008 to >4
Levofloxacin	75.2	70.0	≤0.12	>4	\leq 0.12 to $>$ 4
Ampicillin-sulbactam	29.6	29.6	16	32	0.5 to >32
Aztreonam	96.0	92.0	≤0.12	1	\leq 0.12 to $>$ 16
Cefepime	95.2 ^a	94.0	≤0.5	≤0.5	\leq 0.5 to $>$ 16
Ceftazidime	87.2	82.0	0.12	16	0.03 to >32
Ceftriaxone	75.6	75.6	≤0.06	8	\leq 0.06 to $>$ 8
Ciprofloxacin	73.6	66.8	≤0.03	>4	\leq 0.03 to $>$ 4
Gentamicin	85.8	77.6	≤1	8	≤1 to >8
Meropenem	100.0	100.0	0.06	0.12	≤0.015 to 1
Piperacillin-tazobactam	95.2	94.0	≤0.5	4	\leq 0.5 to $>$ 64
Tigecycline	98.4 ^b	95.2	0.5	1	0.12 to 4
Serratia spp. (193)					
Delafloxacin			1	2	0.03 to >4
Levofloxacin	95.9	93.3	≤0.12	1	≤0.12 to >4
Ampicillin-sulbactam	5.2	5.2	>32	>32	4 to >32
Aztreonam	94.3	90.7	≤0.12	1	≤0.12 to >16
Cefepime	96.4 ^a	94.8	≤0.5	≤0.5	≤0.5 to >16
Ceftazidime	96.4	93.3	0.25	1	0.03 to >32
Ceftriaxone	84.5	84.5	0.25	4	≤0.06 to >8
Ciprofloxacin	93.8	87.6	0.12	1	≤0.03 to >4
Gentamicin	96.4	94.3	≤1	2	≤1 to >8
Meropenem	97.3	97.9	0.03	0.06	≤0.015 to 8
Piperacillin-tazobactam	92.7	88.1	2	16	≤0.5 to >64
Tigecycline	99.0 ^b	98.4	0.5	0.5	0.06 to 4
Pseudomonas aeruginosa (200)					
Delafloxacin		<i>(</i>) =	0.25	>4	0.015 to >4
Levofloxacin	72.5	62.5	0.5	>4	≤ 0.12 to >4
Amikacin	93.5	89.5	2	16	≤ 0.25 to > 32
Aztreonam	55.5	3.5	8	>16	0.25 to > 16
Cettepime	83.0	83.0	2	16	≤ 0.5 to > 16
Certazidime	/8.5	/8.5	2	>32	0.25 to > 32
Cierce Revension	75.0	70.0	>8	>8	1 to >8
Ciprofioxacin	75.0	70.0	0.25	>4	≤ 0.03 to >4
Consun	98.5	100.0	2	2	$\leq 0.5 \ 104$
Gentamicin	85.5	85.5	≥1 0.5	>8 0	$\leq 1 \ 10 > 8$
Piperacillin-tazobactam	74.4 78.0	74.4 78.0	0.5 8	8 >64	≤ 0.015 to > 32 ≤ 0.5 to > 64
Acinetobacter baumannii-A. calcoaceticus (200)					
Delafloxacin			2	>4	0.015 to >4
Levofloxacin	34.0	33.0	>4>4		< 0.12 to > 4
Amikacin	53.5	51.0	8	>32	1 to > 32
Ampicillin-sulbactam	40.2	5110	16	>32	0.5 to > 32
Aztreonam			>16	>16	4 to > 16
Cefepime	36.0		>16	>16	≤0.5 to >16
Ceftazidime	38.5		>32	>32	0.5 to > 32
Ciprofloxacin	32.5	32.5	>4	>4	0.06 to >4
Colistin	92.0	92.0	1	2	≤0.5 to >8
Gentamicin	48.0	48.0	8	- >8	≤ 1 to >8
Meropenem	41 2	41.2	16	>32	0.06 to > 32
Piperacillin-tazobactam	35.2		>64	>64	≤0.5 to >64

^aIntermediate is interpreted as susceptible-dose dependent.

^bBreakpoints from the FDA package insert, revised December 2014.

Among ESBL-phenotype isolates of *E. coli* and *K. pneumoniae*, the potencies of all comparator agents were markedly decreased (Table 3). Meropenem (97.8 and 97.8% of isolates were susceptible according to CLSI and EUCAST criteria, respectively) retained potent activity against ESBL-phenotype strains of *E. coli*, whereas the rate of meropenem resistance was high (34.3 and 26.5% of isolates were susceptible according to

CLSI and EUCAST criteria, respectively) among isolates of ESBL-producing *K. pneu-moniae* (Table 3). ESBL-phenotype *K. pneumoniae* isolates remained susceptible to tigecycline (99.0 and 96.1% of isolates were susceptible according to CLSI and EUCAST criteria, respectively). Only 28.3% of ESBL-phenotype *E. coli* isolates and 18.6% of ESBL-phenotype *K. pneumoniae* isolates were inhibited by delafloxacin at $\leq 1 \mu$ g/ml (Table 1).

In contrast to the results observed with *K. pneumoniae*, the activity of delafloxacin was higher against *K. oxytoca* isolates (100.0% of *K. oxytoca* isolates but only 76.6% of *K. pneumoniae* isolates were inhibited by delafloxacin at $\leq 1 \mu$ g/ml; Table 1), including ESBL-phenotype strains (Table 1). The rates of susceptibility to ciprofloxacin, levofloxacin, cefepime, meropenem, gentamicin, and tigecycline for *K. oxytoca* were >96.0% (Table 3), despite the inclusion of 22 ESBL-phenotype isolates.

Delafloxacin was active against species of *Enterobacteriaceae* with high rates of ceftazidime resistance due to AmpC β -lactamase production, including *Enterobacter*, *Citrobacter*, and *Serratia* isolates (Tables 1 and 3). Delafloxacin at $\leq 1 \mu$ g/ml inhibited 91.4% of *Enterobacter* spp. (87.4 and 92.7% of isolates from Europe and the United States, respectively). Delafloxacin MIC values were $\leq 1 \mu$ g/ml for 87.6% of *Citrobacter* spp. (88.3 and 87.3% of isolates from Europe and the United States, respectively) and 76.7% of *Serratia* spp. (73.8 and 78.0% of isolates from Europe and the United States, respectively) (Table 1). The rates of susceptibility of isolates of these three genera to ciprofloxacin, levofloxacin, cefepime, meropenem, and tigecycline were >90.0% (Table 3). *Proteus mirabilis* and indole-positive *Proteae* were generally susceptible to aztreonam, cefepime, meropenem, and piperacillin-tazobactam but showed decreased susceptibility to the fluoroquinolones, including delafloxacin.

Among European and U.S. isolates of *P. aeruginosa*, only amikacin (93.5 and 89.5% of isolates were susceptible according to CLSI and EUCAST criteria, respectively) and colistin (98.5 and 100.0% of isolates were susceptible according to CLSI and EUCAST criteria, respectively) were active against >90% of isolates tested (Table 3). Delafloxacin at $\leq 1 \mu$ g/ml inhibited 74.0% of *P. aeruginosa* isolates (Table 1). The rates of susceptibility to ciprofloxacin were 75.0 and 70.0% according to CLSI and EUCAST criteria, respectively, and the rates of susceptibility to levofloxacin were 72.5 and 62.5% according to CLSI and EUCAST criteria, respectively, and EUCAST criteria, respectively. Among 40 levofloxacin-resistant isolates of *P. aeruginosa*, delafloxacin MIC values were >1 μ g/ml for 39 isolates (data not shown). The rates of resistance to ceftazidime among isolates of *P. aeruginosa* were 16.5 and 21.5% according to CLSI and EUCAST criteria, respectively (Table 3). The susceptibility of ceftazidime-resistant *P. aeruginosa* isolates to all agents except colistin was poor (data not shown).

A. baumannii-A. calcoaceticus isolates were nonsusceptible (intermediate or resistant by CLSI and EUCAST criteria) to most agents tested (Table 3). Delafloxacin at $\leq 1 \mu g/ml$ inhibited 44.0% of isolates (Table 1). The rates of susceptibility to ciprofloxacin and levofloxacin were 32.5% and 34.0%, respectively (Table 3), and ranged from 48.0% to 50.0% for U.S. isolates and from 17.0% to 18.0% for European isolates (data not shown). Only the rate of susceptibility to colistin (MIC₅₀ and MIC₉₀, 1 and 2 $\mu g/ml$, respectively; 92.0 and 92.0% of isolates were susceptible according to CLSI and EUCAST criteria, respectively) achieved a value of >90.0% (Table 3). In general, resistance to the tested agents was greater for European isolates than U.S. isolates of *Acinetobacter*.

Antibiotic resistance is a growing problem in both European and U.S. medical centers (22). Active surveillance and antimicrobial stewardship efforts are essential to combat this threat to patient safety across all health care settings (23, 24). In the present survey, we examined the *in vitro* susceptibility profiles of 6,485 isolates of GPC and GNB from European and U.S. medical centers for the year 2014. The data from the present survey document the comparable activity of delafloxacin against European and U.S. bacterial isolates. Overall, the broadest coverage of the tested pathogens was observed with meropenem and tigecycline in both Europe and the United States (Tables 2 and 3). The most active agents against staphylococci and streptococci were delafloxacin, daptomycin, and tigecycline, whereas meropenem and tigecycline were

the most active agents against GNB. Delafloxacin was active against MRSA, MR-CoNS, viridans group streptococci, beta-hemolytic streptococci, and penicillin- and macrolideresistant *S. pneumoniae* strains (Tables 1 and 2). Isolates of *E. faecium*, ESBL-phenotype *Enterobacteriaceae*, ceftazidime-nonsusceptible *P. aeruginosa*, and *Acinetobacter* were considerably less susceptible to delafloxacin than the GPC and wild-type GNB. In contrast, delafloxacin showed activity comparable to that of the other fluoroquinolones tested against AmpC-producing strains of *Enterobacteriaceae*.

These data build on reports by previous investigators (11, 12, 14, 19, 20) and indicate that delafloxacin merits further study for the treatment of ABSSSI, RTI, and urinary tract infections where an acid environment and mixed GPC and GNB infections are common.

MATERIALS AND METHODS

Organisms. A total of 6,485 nonduplicate bacterial isolates were collected prospectively from 69 medical centers located in the United States (4,410 isolates) and from 44 medical centers located in 25 European countries (2,075 isolates) in the year 2014. All organisms were isolated from hospitalized patients with bloodstream infections (1,373 isolates), RTI (1,368 isolates), ABSSSI (2,177 isolates), UTI (735 isolates), intra-abdominal infections (267 isolates), and other types of infections (565 isolates). Isolates were identified to the species level at each participating medical center, and the identity was confirmed by the monitoring laboratory (JMI Laboratories, North Liberty, IA, USA) using standard bacteriological algorithms and methodologies or matrix-assisted laser desorption ionization–time of flight mass spectrometry (Bruker, Billerica, MA, USA), when necessary.

Antimicrobial susceptibility testing. MICs were determined using the reference Clinical and Laboratory Standards Institute (CLSI) broth microdilution method (25). Quality control (QC) and interpretation of results were performed in accordance with the CLSI M100-S26 standard (26) and the European Committee on Antimicrobial Susceptibility Testing (EUCAST) 2016 guidelines (27). *Escherichia coli, Klebsiella pneumoniae, Klebsiella oxytoca,* and *Proteus mirabilis* were grouped as ESBL-phenotype strains on the basis of the CLSI screening criteria for potential ESBL production (i.e., a ceftazidime, ceftriaxone, or aztreonam MIC of $\geq 2 \mu g/mI$) (26). Isolates of *P. aeruginosa* were classified as ceftazidime susceptible (MICs, $\geq 8 \mu g/mI$) and ceftazidime nonsusceptible (MICs, $\geq 8 \mu g/mI$). QC strains were tested concurrently and included *E. coli* ATCC 25922 and ATCC 35218, *S. aureus* ATCC 29213, *P. aeruginosa* ATCC 27853, *Enterococcus faecalis* ATCC 29212, and *S. pneumoniae* ATCC 49619. All QC results were within published ranges.

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