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

M. A. Pfaller, H. S. Sader, P. R. Rhomberg, R. K. Flamm
JMI Laboratories, North Liberty, Iowa, USA; University of Iowa, Iowa City, Iowa, USA

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 (Gram-positive 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

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 aeruginosa, 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 delafloxa-
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 Gram-negative 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 against *Klebsiella pneumoniae* and *Providencia*, 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 ±1 log₂ dilution step for each organism group except methicillin-susceptible *S. aureus* (MSSA) (MIC₉₀, 0.03 and ≤0.004 µg/ml for U.S. and European isolates, respectively) and methicillin-susceptible coagulase-negative staphylococci (MS-CoNS; MIC₉₀, 0.12 and 0.008 µg/ml for U.S. and European isolates, respectively) (data not shown).

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 ≤0.5 µg/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 ≤0.5 µg/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 ≤0.5 µg/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 (MIC₉₀ and MIC₉₀, 0.008 and 0.015 µg/ml, respectively, for each group of organisms) and viridans group streptococci (MIC₉₀ and MIC₉₀, 0.015 and 0.03 µg/ml, respectively). All FQr strains of *S. pneumoniae* (S/S) were inhibited by ≤0.25 µg/ml of delafloxacin. The MIC₉₀ and MIC₉₀ 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. (MIC₉₀, 0.5 µg/ml for U.S. isolates and 2 µg/ml for European isolates), *Providencia* spp. (MIC₉₀, >4 µg/ml for U.S. isolates and 1 µg/ml for European isolates), other *Enterobacteriaceae* (MIC₉₀, 0.5 µg/ml for U.S. isolates and 0.12 µg/ml for European isolates), and *Acinetobacter baumannii*-A. *calcoaceticus* (MIC₉₀, 0.5 µg/ml for U.S. isolates and 4 µg/ml for European isolates). Delafloxacin was most active against *Klebsiella oxytoca* (MIC₉₀ and MIC₉₀, 0.06 and 0.12 µg/ml, respectively), *Enterobacter aerogenes* (MIC₉₀ and MIC₉₀, 0.12 and 0.25 µg/ml, respectively), *Citrobacter koseri* (MIC₉₀ and MIC₉₀, 0.015 and 0.06 µg/ml, respectively), and other *Enterobacteriaceae* (MIC₉₀ and MIC₉₀, 0.06 and 0.25 µg/ml, respectively) and was the least active against *Klebsiella pneumoniae*, *Providencia* spp., *P. aeruginosa*, and *Acinetobacter baumannii*-A.
### TABLE 1
Cumulative frequency distribution of delafloxacin in MIC results for Europe and the United States

| Organism or organism group | No. (%) of isolates for which MIC (µg/ml) was: | MIC<sub>50</sub> (µg/ml) | MIC<sub>90</sub> (µg/ml) | Total |
|----------------------------|---------------------------------------------|-----------------------------|---------------------------|-------|
| **Staphylococcus aureus**  |                                             |                             |                           |       |
| US                         | 1,100                                       | 666 (60.5)                  | 68 (62.0)                 |       |
| EU                         | 250                                         | 193 (77.2)                  | 12 (84.8)                 |       |
| **MSSA**                   |                                             |                             |                           |       |
| US                         | 591                                         | 515 (87.1)                  | 2 (58.0)                  |       |
| EU                         | 186                                         | 176 (94.6)                  | 2 (58.0)                  |       |
| **MRSA**                   |                                             |                             |                           |       |
| US                         | 509                                         | 151 (29.7)                  | 2 (29.9)                  |       |
| EU                         | 64                                          | 17 (26.6)                   | 2 (29.9)                  |       |
| **Coagulase-negative staphylococci** |                       |                             |                           |       |
| US                         | 100                                         | 51 (51.0)                   | 2 (60.4)                  |       |
| EU                         | 100                                         | 43 (43.0)                   | 8 (58.0)                  |       |
| **Enterococcus faecalis**  |                                             |                             |                           |       |
| US                         | 300                                         | 0 (0.0)                     | 2 (0.7)                   |       |
| EU                         | 150                                         | 2 (1.3)                     | 0 (0.7)                   |       |
| **Enterococcus faecium**   |                                             |                             |                           |       |
| US                         | 195                                         | 0 (0.0)                     | 1 (0.5)                   |       |
| EU                         | 100                                         | 0 (0.0)                     | 1 (0.5)                   |       |
| **Streptococcus pneumoniae** |                                          |                             |                           |       |
| US                         | 300                                         | 34 (11.3)                   | 9 (30.0)                  |       |
| EU                         | 150                                         | 16 (10.7)                   | 40 (93.3)                 |       |
| **Viridans group streptococci** |                                        |                             |                           |       |
| US                         | 196                                         | 34 (17.3)                   | 30 (96.0)                 |       |
| EU                         | 98                                          | 19 (19.4)                   | 30 (96.0)                 |       |
| **Streptococcus pyogenes** |                                             |                             |                           |       |
| US                         | 283                                         | 67 (23.7)                   | 46 (100.0)                |       |
| EU                         | 150                                         | 33 (22.0)                   | 94 (64.7)                 |       |
| **Streptococcus agalactiae** |                                          |                             |                           |       |
| US                         | 150                                         | 18 (12.0)                   | 70 (58.7)                 |       |
| EU                         | 75                                          | 5 (6.7)                     | 30 (96.0)                 |       |
| **Streptococcus dysgalactiae** |                                         |                             |                           |       |
| US                         | 82                                          | 19 (23.2)                   | 11 (98.8)                 |       |
| EU                         | 50                                          | 18 (36.0)                   | 1 (98.0)                  |       |
| **Enterobacteriaceae**     |                                             |                             |                           |       |
| US                         | 1,500                                       | 3 (0.2)                     | 8 (62.0)                  |       |
| EU                         | 750                                         | 1 (0.1)                     | 8 (62.0)                  |       |
| **Escherichia coli**       |                                             |                             |                           |       |
| US                         | 300                                         | 2 (0.7)                     | 37 (50.0)                 |       |
| EU                         | 200                                         | 1 (0.5)                     | 37 (50.0)                 |       |

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TABLE 1 (Continued)

| Organism or organism group | No. (%) of isolates for which MIC (µg/ml) was: | 0.004 | 0.008 | 0.015 | 0.03 | 0.06 | 0.12 | 0.25 | 0.5 | 1 | 2 | 4 | > 4 |
|---------------------------|-----------------------------------------------|-------|-------|-------|------|------|------|------|-----|----|----|----|-----|
| **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) | 2 | >4 |
| EU                        | 40 0 (0.0) 3 (7.5) 4 (17.5) 0 (17.5) 1 (20.0) 2 (25.0) 0 (25.0) 2 (30.0) 11 (57.5) 11 (85.0) 6 (100.0) | 2 | >4 |
| **Klebsiella pneumoniae**  | | | | | | | | | | | | | |
| US                        | 225 0 (0.0) 2 (0.9) 30 (14.2) 108 (46.2) 25 (73.3) 11 (78.2) 11 (83.1) 6 (85.8) 4 (87.6) 11 (92.4) 17 (100.0) | 0.06 | 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 |
| **K. pneumoniae 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 (9.0) 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 | 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 | 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 (85.0) 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. calcoaceticus** | | | | | | | | | | | | | |
| US                        | 100 0 (0.0) 1 (1.0) 10 (11.0) 21 (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 | >4 |
| 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 |

Abbreviations: EU, Europe; US, United States; MSSA, methicillin-susceptible S. aureus; MRSA, methicillin-resistant S. aureus; ESBL, extended-spectrum β-lactamase.
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) (MIC$_{50}$, 0.03 µg/ml versus 2 µg/ml, respectively), non-ESBL-phenotype and ESBL-phenotype strains of *K. pneumoniae* (MIC$_{50}$, 0.06 µg/ml versus 4 µg/ml, respectively), and non-ESBL-phenotype and ESBL-phenotype strains of *P. mirabilis* (MIC$_{50}$, 0.06 µg/ml versus 2 µg/ml, respectively). Delafloxacin retained potent activity against ESBL-phenotype strains of *K. oxytoca* (MIC$_{50}$ and MIC$_{90}$, 0.06 and 0.12 µg/ml, respectively) and was more active against ceftazidime-susceptible than ceftazidime-nonsusceptible strains of *P. aeruginosa* (MIC$_{50}$, 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 (MIC$_{50}$ and MIC$_{90}$, ≤0.004 and 0.008 µg/ml, respectively) and on the basis of the MIC$_{50}$ was 8- to at least 64-fold more potent than ceftaroline and at least 64-fold more potent than levofloxacin (Table 2). Tigecycline (MIC$_{50}$ and MIC$_{90}$, 0.06 and 0.06 µg/ml, respectively), delafloxacin (MIC$_{50}$ and MIC$_{90}$, 0.06 and 0.5 µg/ml, respectively), and daptomycin (MIC$_{50}$ and MIC$_{90}$, 0.25 and 0.5 µg/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 MIC$_{50}$s) 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 trimethoprim-sulfamethoxazole (98.5%) (Table 2).

The delafloxacin MIC$_{50}$ and MIC$_{90}$ values for all coagulase-negative staphylococci (CoNS) were 0.008 and 0.5 µg/ml, respectively (Table 1). Tigecycline (MIC$_{50}$ and MIC$_{90}$, 0.03 and 0.06 µg/ml, respectively) and delafloxacin (MIC$_{50}$ and MIC$_{90}$, ≤0.004 and 0.06 µg/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 MIC$_{50}$s). 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 (MIC$_{50}$ and MIC$_{90}$, 0.06 and 0.12 µg/ml, respectively), delafloxacin (MIC$_{50}$ and MIC$_{90}$, 0.06 and 0.5 µg/ml, respectively), linezolid (MIC$_{50}$ and MIC$_{90}$, 0.5 and 0.5 µg/ml, respectively), and ceftaroline (MIC$_{50}$ and MIC$_{90}$, 0.5 and 1 µg/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

| Organism group (no. of isolates tested)/antimicrobial agent | % of isolates susceptible by the following criteria: | CLSI | EUCAST | MIC (μg/ml) | 50% | 90% | Range |
|-------------------------------------------------------------|-----------------------------------------------------|------|--------|-------------|-----|-----|-------|
| Staphylococcus aureus (1,350) | | | | | | | |
| Delafloxacin | | | | | | | |
| Levofloxacin | 64.4 | 64.4 | 0.004 | 0.25 | | 0.004 to 4 |
| Cefaroline | 98.0 | 98.0 | 0.25 | 1 | | 0.12 to 2 |
| Ciprofloxacin | 0.0 | 0.0 | | 0.25 | 2 | | 0.12 to 2 |
| Clindamycin | 87.0 | 86.8 | | 0.25 | 2 | | 0.12 to 2 |
| Daptomycin | 99.8 | 99.8 | | 0.25 | 0.5 | | 0.06 to 2 |
| Erythromycin | 45.9 | 46.3 | 4 | | | | |
| Linezolid | 100.0 | 100.0 | | 1 | 1 | | 0.25 to 2 |
| Oxaclillin | 57.6 | 57.6 | 0.5 | | | | |
| Tetracycline | 94.3 | 92.5 | | 0.5 | | | |
| Tigecycline | 100.0 | 100.0 | 0.06 | | 0.06 | | 0.015 to 0.5 |
| Trimethoprim-sulfamethoxazole | 98.5 | 98.5 | 0.5 | | | 0.05 to 4 |
| Vancomycin | 100.0 | 100.0 | 1 | 1 | | 0.25 to 2 |
| MSSA (777) | | | | | | | |
| Delafloxacin | | | | | | | |
| Levofloxacin | 89.8 | 89.8 | 0.004 | 0.25 | | 0.004 to 4 |
| Cefaroline | 100.0 | 100.0 | 0.25 | | | | |
| Ciprofloxacin | 0.0 | 0.0 | | >128 | >128 | | 128 to 128 |
| Clindamycin | 94.0 | 93.7 | | 0.25 | 0.25 | | 0.12 to 2 |
| Daptomycin | 100.0 | 100.0 | | 0.25 | 0.5 | | 0.06 to 1 |
| Erythromycin | 69.6 | 69.8 | 0.25 | | | | |
| Linezolid | 100.0 | 100.0 | | 1 | 1 | | 0.25 to 2 |
| Oxaclillin | 100.0 | 100.0 | 0.5 | | | | |
| Tetracycline | 95.9 | 94.2 | | 0.5 | | | |
| Tigecycline | 100.0 | 100.0 | 0.06 | | 0.06 | | 0.015 to 0.5 |
| Trimethoprim-sulfamethoxazole | 99.0 | 99.0 | | 0.5 | | | |
| Vancomycin | 100.0 | 100.0 | 1 | 1 | | 0.25 to 2 |
| MRSA (573) | | | | | | | |
| Delafloxacin | | | | | | | |
| Levofloxacin | 30.0 | 30.0 | 4 | | | | |
| Cefaroline | 95.3 | 95.3 | | 1 | 1 | | 0.25 to 2 |
| Ciprofloxacin | 0.0 | 0.0 | | >128 | >128 | | >128 to 128 |
| Clindamycin | 77.5 | 77.5 | | 0.25 | 0.25 | | 0.12 to 2 |
| Daptomycin | 99.5 | 99.5 | | 0.25 | 0.5 | | 0.12 to 2 |
| Erythromycin | 13.8 | 14.3 | | >16 | >16 | | >12 to 16 |
| Linezolid | 100.0 | 100.0 | | 1 | 1 | | 0.25 to 2 |
| Oxaclillin | 0.0 | 0.0 | | >2 | >2 | | >2 to 2 |
| Tetracycline | 92.1 | 90.2 | | 0.5 | | | |
| Tigecycline | 100.0 | 100.0 | 0.06 | | 0.06 | | 0.015 to 0.5 |
| Trimethoprim-sulfamethoxazole | 97.9 | 97.9 | | 0.5 | | | |
| Vancomycin | 100.0 | 100.0 | 1 | 1 | | 0.5 to 2 |
| MS-CoNS (75) | | | | | | | |
| Delafloxacin | | | | | | | |
| Levofloxacin | 88.0 | 88.0 | 0.004 | 0.25 | | 0.004 to 1 |
| Cefaroline | 84.0 | 84.0 | 0.25 | | | | |
| Clindamycin | 100.0 | 100.0 | | 0.25 | 0.5 | | 0.06 to 1 |
| Daptomycin | 69.3 | 69.3 | | 0.12 | 0.16 | | 0.12 to 16 |
| Erythromycin | 100.0 | 100.0 | | 0.5 | | | |
| Linezolid | 100.0 | 100.0 | 0.03 | | 0.06 | | 0.015 to 0.12 |
| Oxaclillin | 92.0 | 92.0 | | 0.5 | | | |
| Tetracycline | 100.0 | 100.0 | | 1 | | | |
| Tigecycline | 100.0 | 100.0 | | 2 | | | |
| Trimethoprim-sulfamethoxazole | 100.0 | 100.0 | | 1 | | | |
| Vancomycin | 100.0 | 100.0 | 1 | 1 | | 0.25 to 4 |
| MR-CoNS (125) | | | | | | | |
| Delafloxacin | | | | | | | |
| Levofloxacin | 38.4 | 38.4 | 4 | | | | |
| Cefaroline | 70.4 | 67.2 | | 0.25 | 2 | | 0.25 to 2 |

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TABLE 2 (Continued)

| Organism group (no. of isolates tested)/ antimicrobial agent | % of isolates susceptible by the following criteria: | MIC (µg/ml) |
|--------------------------------------------------------------|---------------------------------------------------|-------------|
|                                                             | CLSI | EUCAST | 50% | 90% | Range |
| Daptomycin                                                   | 99.2 | 99.2   | 0.5 | 0.5 | ≤0.06 to 2 |
| Erythromycin                                                | 25.6 | 25.6   | >16 | >16 | ≤0.12 to >16 |
| Linezolid                                                    | 100.0| 100.0  | 0.5 | 0.5 | ≤0.12 to 1 |
| Oxacillin                                                    | 0.0  | 0.0    | ≥2  | ≥2  | 0.5 to >2 |
| Tetracycline                                                | 80.8 | 77.6   | 1   | >8  | ≤0.5 to >8 |
| Tigecycline                                                  | 100.0| 100.0  | 0.06| 0.12| ≤0.015 to 0.25 |
| Vancomycin                                                   | 100.0| 100.0  | 1   | 2   | 0.5 to >2 |

**Enterococcus faecalis (450)**

| Delafloxacin | 0.06 | 1 | ≤0.004 to 2 |
| Levofloxacin  | 70.7 | 70.7 | 1 | >4 | 0.25 to >4 |
| Ampicillin    | 100.0| 99.6 | 1 | 2 | ≤0.25 to 8 |
| Ceftriaxone   | 83.6 | 94.2 | 0.015 | 0.12 | ≤0.015 to 1 |
| Clindamycin   | 84.7 | 84.9 | 0.06 | 1 | ≤0.06 to 8 |
| Erythromycin  | 59.9 | 59.9 | 0.12 | >2 | ≤0.12 to >2 |
| Daptomycin    | 99.0 | 99.0 | 1 | 1 | 0.25 to 4 |
| Enterococcus faecium (295)

| Delafloxacin | >4 | >4 | 0.008 to >4 |
| Levofloxacin  | 7.8 | 10.8 | >4 | >4 | 0.5 to >4 |
| Ampicillin    | 10.8 | 10.8 | >8 | >8 | ≤0.25 to >8 |
| Enterococcus faecalis (450)

| Delafloxacin | 0.004 | 0.015 | ≤0.004 to 0.25 |
| Levofloxacin  | 98.9 | 98.9 | 1 | 1 | 0.5 to >4 |
| Amoxicillin-clavulanic acid | 91.1 | 1 | 2 | 1 to >8 |
| Ceftriaxone   | 99.6 | 99.3 | ≤0.015 | 0.12 | ≤0.015 to 1 |
| Ceftriaxone   | 83.6 | 83.6 | 0.06 | 1 | ≤0.06 to 8 |
| Clindamycin   | 84.7 | 84.9 | 0.25 | >2 | ≤0.25 to >2 |
| Erythromycin  | 59.9 | 59.9 | 0.12 | ≥16 | ≤0.12 to >16 |
| Meropenem     | 84.4 | 84.4 | 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 | 0.06 | 2 | ≤0.06 to 8 |
| Tetracycline  | 78.4 | 78.4 | 0.5 | >8 | ≤0.5 to >8 |
| Trimepram-sulfamethoxazole | 68.9 | 75.3 | 0.5 | >4 | ≤0.5 to >4 |

**Viridans group streptococci (294)**

| Delafloxacin | 0.015 | 0.03 | ≤0.004 to 2 |
| Levofloxacin  | 94.1 | 79.7 | 1 | 2 | ≤0.12 to >4 |
| Amoxicillin-clavulanic acid | 91.1 | 1 | 2 | 1 to >8 |
| 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 | 86.4 | 0.12 | 8 | ≤0.12 to >16 |
| Meropenem     | 93.7 | 99.0 | 0.06 | 0.25 | ≤0.015 to 4 |
| Moxifloxacin  | 73.1 | 73.1 | 0.12 | 0.25 | ≤0.12 to >4 |
| Penicillin    | 64.3 | 64.3 | 0.06 | 1 | ≤0.06 to 8 |
| Tetracycline  | 64.3 | 64.3 | 0.5 | >8 | ≤0.5 to >8 |
| Trimepram-sulfamethoxazole | 64.3 | 64.3 | 0.5 | >4 | ≤0.5 to >4 |

(Continued on following page)
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 (MIC<sub>50</sub> and MIC<sub>90</sub>, 0.06 and 1 μg/ml, respectively) and linezolid (MIC<sub>50</sub> and MIC<sub>90</sub>, 1 and 1 μg/ml, respectively) were the most potent antimicrobials tested (Table 2).

Delafloxacin (MIC<sub>50</sub> and MIC<sub>90</sub>, >4 and >4 μg/ml, respectively; 10.5% of isolates were susceptible to delafloxacin at ≤1 μg/ml), levofloxacin (MIC<sub>50</sub> and MIC<sub>90</sub>, >4 and >4 μg/ml, respectively; 7.8% of isolates were susceptible according to CLSI breakpoints, respectively), erythromycin (MIC<sub>50</sub> and MIC<sub>90</sub>, >16 and >16 μg/ml, respectively; 3.7% of isolates were susceptible according to the CLSI criterion), and ampicillin (MIC<sub>50</sub> and MIC<sub>90</sub>, >8 and >8 μg/ml, respectively; 10.8% of isolates were susceptible according to CLSI and EUCAST criteria, respectively) displayed

### TABLE 2 (Continued)

| Organism group (no. of isolates tested)/ antimicrobial agent | % of isolates susceptible by the following criteria: | MIC (μg/ml) |
|-----------------|---------------------------------|------------|
|                 | CLSI                             | EUCAST     | 50% | 90% | Range       |
| Streptococcus pyogenes (433) |                                 |            |     |     |             |
| Delafloxacin    | 99.8                            | 96.5       | 0.008 | 0.015 | ≤0.004 to 0.03 |
| Levofloxacin    | 100.0                           | 100.0      | 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 |
| Ceftaxone       | 100.0                           | 100.0      | ≤0.06  | ≤0.06  | ≤0.06 to 0.05 |
| 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                           | 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    | 97.8                            | 96.9       | 0.008 | 0.015 | ≤0.004 to 0.05 |
| Levofloxacin    | 100.0                           | 100.0      | 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 | ≤0.03  | ≤0.015 to ≤0.03 |
| Ceftaxone       | 100.0                           | 100.0      | ≤0.06  | 0.12  | ≤0.06 to 0.25 |
| Clindamycin     | 70.7                            | 72.4       | ≤0.25  | >2    | ≤0.25 to >2 |
| Erythromycin    | 52.4                            | 52.4       | ≤0.12  | >16   | ≤0.12 to >16 |
| Meropenem       | 100.0                           | 100.0      | 0.03   | 0.06  | ≤0.015 to 0.12 |
| Moxifloxacin    | 97.8                            | 100.0      | ≤0.12  | 0.25  | ≤0.12 to >4 |
| Penicillin      | 100.0                           | 100.0      | ≤0.06  | ≤0.06  | ≤0.06 to ≤0.06 |
| Tetracycline    | 17.4                            | 17.0       | >8     | >8    | ≤0.5 to >8  |
| Vancomycin      | 100.0                           | 100.0      | 0.5    | 0.5   | 0.25 to 1 |

| Streptococcus dysgalactiae (132) |                                 |            |     |     |             |
| Delafloxacin    | 99.2                            | 97.0       | 0.008 | 0.015 | ≤0.004 to 0.03 |
| Levofloxacin    | 100.0                           | 100.0      | 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 |
| Ceftaxone       | 100.0                           | 100.0      | ≤0.06  | ≤0.06  | ≤0.06 to 0.05 |
| 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                           | 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    | ≤0.5 to >8  |
| Vancomycin      | 100.0                           | 100.0      | 0.25   | 0.25  | ≤0.12 to 1  |

- Breakpoints from FDA package insert, revised December 2014.
- Uncomplicated UTI only.
- Using nonmeningitis breakpoints.
- Using meningitis breakpoints.
- Using oral breakpoints.
- Using parenteral, meningitis breakpoints.
- Using parenteral, nonmeningitis breakpoints.
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* (MIC$_{50}$ and MIC$_{90}$, 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$0.03 μg/ml of delafloxacin; the highest delafloxacin MIC value for U.S. isolates was 0.25 μg/ml (Table 1 and 2). Delafloxacin was 8-fold more active than ceftaroline (MIC$_{50}$ and MIC$_{90}$, $\leq$0.015 and 0.12 μg/ml, respectively), 16-fold more active than moxifloxacin (MIC$_{50}$ and MIC$_{90}$, $\leq$0.12 and 0.25 μg/ml, respectively), and 64-fold more active than levofloxacin (MIC$_{50}$ and MIC$_{90}$, 1 and 2 μg/ml, respectively) (Table 2). For other common-use antimicrobials, the rate of penicillin resistance (MIC, $\geq$2 μg/ml, oral breakpoint) was 11.3% (0.7%; MIC, $\geq$8 μg/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, $>$4 μg/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 μg/ml; Tables 1 and 2), moxifloxacin (MIC$_{50}$ and MIC$_{90}$, $\leq$0.12 and 0.25 μg/ml, respectively), and ceftaroline (MIC$_{50}$ and MIC$_{90}$, 0.03 and 0.12 μg/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 μg/ml. The highest delafloxacin MIC value for *S. agalactiae* was 0.5 μg/ml, and 97.3% of *S. agalactiae* isolates were inhibited by delafloxacin at $\leq$0.03 μg/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 MIC$_{50}$ and MIC$_{90}$ values of 0.06 and 4 μg/ml, respectively, and with 80.9% of isolates being inhibited by delafloxacin at $\leq$1 μg/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-resistant *Enterobacteriaceae* isolates showed decreased susceptibility (MIC, $>$1 μg/ml) to delafloxacin (data not shown). The rates of susceptibility to aztreonam, ceftriaxone, cefepime, and ceftazidime ranged from 80.3% to 90.8% (Table 3). Meropenem (MIC$_{50}$ and MIC$_{90}$, 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 (MIC$_{50}$ and MIC$_{90}$, 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

| Organism group (no. of isolates tested)/ antimicrobial agent | % of isolates susceptible by the following criteria: | MIC (µg/ml) | 50% | 90% | Range |
|-------------------------------------------------------------|----------------------------------------------------|------------|-----|-----|-------|
| **Enterobacteriaceae (2,250)**                              |                                                    |            |     |     |       |
| Delafloxacin                                                | 83.8                                               | 0.06       | 4   |     | ≤0.004 to >4 |
| Levofloxacin                                                | 81.9                                               | ≤0.12      | >4  | ≤0.12 to >4 |
| Ampicillin-sulbactam                                        | 47.4                                               | 16         | >32 | 0.5 to >32 |
| Aztreonam                                                   | 86.3                                               | ≤0.12      | >16 | ≤0.12 to >16 |
| Cefepime                                                    | 90.8                                               | ≤0.5       | 2   | ≤0.5 to >16 |
| Ceftazidime                                                 | 86.3                                               | 0.25       | 16  | 0.03 to >32 |
| Ceftriaxone                                                 | 80.3                                               | 0.12       | >8  | ≤0.06 to >8 |
| Ciprofloxacin                                               | 81.6                                               | ≤0.03      | >4  | ≤0.03 to >4 |
| Gentamicin                                                  | 90.7                                               | ≤1         | 4   | 0.03 to >8 |
| Meropenem                                                   | 97.5                                               | 0.03       | 0.06| ≤0.015 to >32 |
| Piperacillin-tazobactam                                     | 89.3                                               | 2          | 32  | ≤0.5 to >64 |
| Tigecycline                                                 | 99.2b                                              | 0.25       | 1   | 0.03 to 4 |
| **Escherichia coli (500)**                                  |                                                    |            |     |     |       |
| Delafloxacin                                                | 69.6                                               | ≤0.12      | >4  | ≤0.12 to >4 |
| Levofloxacin                                                | 69.6                                               | 16         | >32 | 0.5 to >32 |
| Ampicillin-sulbactam                                        | 49.6                                               | ≤0.12      | 16  | ≤0.12 to >16 |
| Aztreonam                                                   | 86.4                                               | ≤0.5       | 8   | ≤0.5 to >16 |
| Cefepime                                                    | 87.0                                               | 0.12       | 8   | 0.03 to >32 |
| Ceftazidime                                                 | 89.2                                               | ≤0.06      | >8  | ≤0.06 to >8 |
| Ceftriaxone                                                 | 84.0                                               | ≤0.03      | >4  | ≤0.03 to >4 |
| Ciprofloxacin                                               | 69.4                                               | ≤1         | >8  | ≤1 to >8 |
| Gentamicin                                                  | 86.4                                               | ≤0.15      | 0.03| ≤0.015 to 4 |
| Meropenem                                                   | 99.6                                               | ≤0.15      | 0.03| ≤0.015 to >64 |
| Piperacillin-tazobactam                                     | 94.2                                               | 2          | 8   | ≤0.5 to >64 |
| Tigecycline                                                 | 100.0b                                             | 0.06       | 0.12| 0.03 to 1 |
| **E. coli isolates of the ESBL phenotype (92)**              |                                                    |            |     |     |       |
| Delafloxacin                                                | 21.7                                               | >4         | >4  | ≤0.12 to >4 |
| Levofloxacin                                                | 21.7                                               | 32         | >32 | 2 to >32 |
| Ampicillin-sulbactam                                        | 16.3                                               | ≤0.12      | 16  | ≤0.12 to >16 |
| Aztreonam                                                   | 26.1                                               | 16         | >16 | ≤0.5 to >16 |
| Cefepime                                                    | 31.5                                               | 16         | >16 | ≤0.5 to >16 |
| Ceftazidime                                                 | 41.3                                               | 8          | 32  | 0.06 to >32 |
| Ceftriaxone                                                 | 13.0                                               | 8          | >8  | 0.25 to >8 |
| Ciprofloxacin                                               | 20.7                                               | >4         | 8   | ≤0.03 to >4 |
| Gentamicin                                                  | 63.0                                               | ≤1         | >8  | ≤1 to >8 |
| Meropenem                                                   | 97.8                                               | ≤0.15      | 0.03| ≤0.015 to >64 |
| Piperacillin-tazobactam                                     | 81.5                                               | 8          | >64 | 1 to >64 |
| Tigecycline                                                 | 100.0b                                             | 0.12       | 0.12| 0.06 to 0.5 |
| **Klebsiella pneumoniae (389)**                             |                                                    |            |     |     |       |
| Delafloxacin                                                | 81.5                                               | ≤0.12      | >4  | ≤0.12 to >4 |
| Levofloxacin                                                | 80.2                                               | 8          | >32 | 1 to >32 |
| Ampicillin-sulbactam                                        | 63.2                                               | 8          | >32 | ≤0.12 to >4 |
| Aztreonam                                                   | 77.1                                               | ≤0.12      | >16 | ≤0.12 to >16 |
| Cefepime                                                    | 77.9b                                              | ≤0.5       | >16 | ≤0.015 to >16 |
| Ceftazidime                                                 | 76.9                                               | 0.12       | >32 | 0.03 to >32 |
| Ceftriaxone                                                 | 75.3                                               | ≤0.06      | >8  | ≤0.06 to >8 |
| Ciprofloxacin                                               | 77.4                                               | ≤0.03      | >4  | ≤0.03 to >4 |
| Gentamicin                                                  | 86.4                                               | ≤1         | >8  | ≤1 to >8 |
| Meropenem                                                   | 90.2                                               | 1          | ≤1  | ≤0.015 to >32 |
| Piperacillin-tazobactam                                     | 81.2                                               | 4          | >64 | ≤0.5 to >64 |
| Tigecycline                                                 | 99.7b                                              | 0.25       | 0.5 | 0.06 to 4 |
| **K. pneumoniae isolates of the ESBL phenotype (102)**       |                                                    |            |     |     |       |
| Delafloxacin                                                | 34.3                                               | >4         | >4  | ≤0.12 to >4 |
| Levofloxacin                                                | 32.4                                               | >32        | >32 | 4 to >32 |
| Ampicillin-sulbactam                                        | 1.0                                                | >16        | >16 | ≤0.12 to >16 |
| Aztreonam                                                   | 12.7                                               | >16        | >16 | ≤0.05 to >16 |
| Cefepime                                                    | 15.7                                               | >16        | >16 | ≤0.05 to >16 |
| Ceftazidime                                                 | 11.8                                               | >32        | >32 | 0.25 to >32 |

(Continued on following page)
TABLE 3 (Continued)

| Organism group (no. of isolates tested)/antimicrobial agent | % of isolates susceptible by the following criteria: | MIC (µg/ml) |
|-------------------------------------------------------------|-----------------------------------------------|-------------|
|                                                             | 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 | ≤0.015 to >32 |
| Piperacillin-tazobactam                                     | 31.4 | 23.5   | >64 | >64 | 2 to >64  |
| Tigecycline                                                 | 99.0 | 96.1   | 0.25| 0.5 | 0.12 to 4  |

Klebsiella oxytoca (111)

| Delafloxacin                                                | 100.0| 100.0 | ≤0.12| ≤0.12| 0.03 to 1  |
| 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 | 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| ≤0.06 to >8 |
| Ciprofloxacin                                               | 71.6 | 67.8  | ≤0.03| >4   | ≤0.03 to >4 |
| Gentamicin                                                  | 88.6 | 85.3  | ≤1   | 8    | ≤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 | 64.5  | 0.25 | 0.25 | 0.12 to 4  |

Proteus mirabilis (211)

| Delafloxacin                                                | 0.06 | 2     | ≤0.004| >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                                                   | 76.6 | 73.7  | ≤0.12 | >16 | ≤0.12 to >16 |
| Cefepime                                                    | 93.7 | 85.6  | ≤0.5  | 2   | ≤0.5 to >16 |
| Ceftazidime                                                 | 75.7 | 73.0  | 0.25  | >32 | 0.03 to >32 |
| Ceftriaxone                                                 | 70.6 | 70.6  | 0.25  | >8   | ≤0.06 to >8 |
| Ciprofloxacin                                               | 95.5 | 94.5  | ≤0.03 | 0.25| ≤0.03 to >4 |
| Gentamicin                                                  | 96.9 | 96.9  | ≤1   | ≤1  | ≤1 to >8   |
| Meropenem                                                   | 97.9 | 99.0  | 0.06  | 0.06| ≤0.015 to >32 |
| Piperacillin-tazobactam                                     | 81.2 | 77.2  | 2     | 64  | ≤0.5 to >64 |
| Tigecycline                                                 | 100.0| 97.6  | 0.25  | 0.25| 0.03 to 2  |

Enterobacter spp. (384)

| Delafloxacin                                                | 0.06 | 2     | ≤0.008| >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 | ≤0.5 to >16 |
| Ceftazidime                                                 | 87.6 | 86.0  | 0.25  | 16  | 0.06 to >32 |
| Ceftriaxone                                                 | 87.1 | 87.1  | 0.12  | >8  | ≤0.06 to >8 |
| Ciprofloxacin                                               | 92.1 | 91.0  | ≤0.03 | 0.5 | ≤0.03 to >4 |
| Gentamicin                                                  | 95.5 | 94.4  | ≤1   | ≤1  | ≤1 to >8   |
| Meropenem                                                   | 97.8 | 98.3  | ≤0.015| 0.03| ≤0.015 to 8 |
| Piperacillin-tazobactam                                     | 90.4 | 85.4  | 2     | 16  | ≤0.5 to >64 |
| Tigecycline                                                 | 100.0| 99.4  | 0.12  | 0.25| 0.06 to 2  |

(Continued on following page)
TABLE 3 (Continued)

| Organism group (no. of isolates tested)/antimicrobial agent | % of isolates susceptible by the following criteria: | MIC (µg/ml) |
|------------------------------------------------------------|--------------------------------------------------|-------------|
|                                                            | CLSI                                             | 50%         | 90%         | Range             |
| Indole-positive Proteus spp. (249)                          |                                                  |             |             |                   |
| Delafloxacin                                               | 75.2                                             | 0.12        | 4           | 0.008 to >4       |
| Levofoxacin                                                | 70.0                                             | ≤0.12       | >4          | ≤0.12 to >4       |
| Ampicillin-sulbactam                                       | 29.6                                             | 16          | 32          | 0.5 to >32        |
| Aztreonam                                                  | 96.0                                             | ≤0.12       | 1           | ≤0.12 to >16      |
| Cefepime                                                   | 95.2<sup>a</sup>                                 | ≤0.5        | ≤0.5        | ≤0.5 to >16       |
| Ceftazidime                                                | 87.2                                             | 0.12        | 16          | 0.03 to >32       |
| Ceftriaxone                                                | 75.6                                             | ≤0.06       | 8           | ≤0.06 to >8       |
| Ciprofloxacin                                              | 73.6                                             | ≤0.03       | >4          | ≤0.03 to >4       |
| Gentamicin                                                 | 85.8                                             | ≤1          | 8           | ≤1 to >8          |
| Meropenem                                                  | 100.0                                            | 0.06        | 0.12        | ≤0.015 to 1       |
| Piperacillin-tazobactam                                    | 95.2                                             | ≤0.5        | 4           | ≤0.5 to >64       |
| Tigecycline                                                | 98.4<sup>b</sup>                                 | 0.5         | 1           | 0.12 to 4         |
| Serratia spp. (193)                                        |                                                  |             |             |                   |
| Delafloxacin                                               | 95.9                                             | 1           | 2           | 0.03 to >4        |
| Levofoxacin                                                | 93.3                                             | ≤0.12       | 1           | ≤0.12 to >4       |
| Ampicillin-sulbactam                                       | 5.2                                              | >32         | >32         | 4 to >32          |
| Aztreonam                                                  | 94.3                                             | ≤0.12       | 1           | ≤0.12 to >16      |
| Cefepime                                                   | 96.4<sup>a</sup>                                 | ≤0.5        | ≤0.5        | ≤0.5 to >16       |
| Ceftazidime                                                | 96.4                                             | 0.25        | 1           | 0.03 to >32       |
| Ceftriaxone                                                | 84.5                                             | 0.25        | 4           | ≤0.06 to >8       |
| Ciprofloxacin                                              | 93.8                                             | 0.12        | 1           | ≤0.03 to >4       |
| Gentamicin                                                 | 96.4                                             | ≤1          | 2           | ≤1 to >8          |
| Meropenem                                                  | 97.3                                             | 0.03        | 0.06        | ≤0.015 to 8       |
| Piperacillin-tazobactam                                    | 92.7                                             | 2           | 16          | ≤0.5 to >64       |
| Tigecycline                                                | 99.0<sup>b</sup>                                 | 0.5         | 0.5         | 0.06 to 4         |
| Pseudomonas aeruginosa (200)                               |                                                  |             |             |                   |
| Delafloxacin                                               | 72.5                                             | 0.25        | >4          | 0.015 to >4       |
| Levofoxacin                                                | 62.5                                             | 0.5         | >4          | ≤0.12 to >4       |
| Amikacin                                                   | 93.5                                             | 2           | 16          | ≤0.25 to >32      |
| Aztreonam                                                  | 55.5                                             | 8           | >16         | 0.25 to >16       |
| Cefepime                                                   | 83.0                                             | 2           | 16          | ≤0.5 to >16       |
| Ceftazidime                                                | 78.5                                             | 2           | >32         | 0.25 to >32       |
| Ceftriaxone                                                | 84.5                                             | >8          | >8          | 1 to >8           |
| Ciprofloxacin                                              | 75.0                                             | 0.25        | >4          | ≤0.03 to >4       |
| Gentamicin                                                 | 98.5                                             | 2           | 2           | ≤0.5 to 4         |
| Meropenem                                                  | 97.3                                             | ≤1          | 8           | ≤0.015 to >32     |
| Piperacillin-tazobactam                                    | 74.4                                             | 0.5         | 8           | ≤0.5 to >64       |
| Acinetobacter baumannii-A. calcoaceticus (200)              |                                                  |             |             |                   |
| Delafloxacin                                               | 34.0                                             | 2           | >4          | 0.015 to >4       |
| Levofoxacin                                                | 33.0                                             | >4          | >4          | ≤0.12 to >4       |
| Amikacin                                                   | 53.5                                             | 8           | >32         | 1 to >32          |
| Ampicillin-sulbactam                                       | 40.2                                             | 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                                             | >4          | >4          | 0.06 to >4        |
| Gentamicin                                                 | 92.0                                             | 1           | 2           | ≤0.5 to >8        |
| Meropenem                                                  | 48.0                                             | 8           | >8          | ≤1 to >8          |
| Piperacillin-tazobactam                                    | 41.2                                             | 16          | >32         | 0.06 to >32       |
| Tigecycline                                                | 35.2                                             | >64         | >64         | ≤0.5 to >64       |

<sup>a</sup>Intermediate is interpreted as susceptible-dose dependent.
<sup>b</sup>Breakpoints 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. pneumoniae* (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 ≤1 μg/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 ≤1 μg/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 ≤1 μg/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 ≤1 μg/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 ≤1 μg/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. Among 40 levofloxacin-resistant isolates of *P. aeruginosa*, delafloxacin MIC values were >1 μg/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 ≤1 μg/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 (MIC₉₀ and MIC₉₀ 1 and 2 μg/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 macrolide-resistant \textit{S. pneumoniae} strains (Tables 1 and 2). Isolates of \textit{E. faecium}, ESBL-phenotype \textit{Enterobacteriaceae}, ceftazidime-nonsusceptible \textit{P. aeruginosa}, and \textit{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 \textit{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). \textit{Escherichia coli}, \textit{Klebsiella pneumoniae}, \textit{Klebsiella oxytoca}, and \textit{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 $\geq 2 \mu g/ml$) (26). Isolates of \textit{P. aeruginosa} were classified as ceftazidime susceptible (MIC, $\leq 8 \mu g/ml$) and ceftazidime nonsusceptible (MICs, $>8 \mu g/ml$). QC strains were tested concurrently and included \textit{E. coli} ATCC 25922 and ATCC 35218, \textit{S. aureus} ATCC 29213, \textit{P. aeruginosa} ATCC 27853, \textit{Enterococcus faecalis} ATCC 29212, and \textit{S. pneumoniae} ATCC 49619. All QC results were within published ranges.

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Erratum for Pfaller et al., “In Vitro Activity of Delafloxacin against Contemporary Bacterial Pathogens from the United States and Europe, 2014”

M. A. Pfaller,a,b H. S. Sader,a P. R. Rhomberg,a R. K. Flamm,a

JMI Laboratories, North Liberty, Iowa, USAa; University of Iowa, Iowa City, iowa, USAa

Volume 61, no. 4, e02609-16, 2017, https://doi.org/10.1128/AAC.02609-16. Pages 6 to 8: In Table 2, there should be no ciprofloxacin data for any organism, as ciprofloxacin was not tested against the collection of isolates. The corrected table is shown below.
### TABLE 2 Activities of delafloxacin and comparator antimicrobial agents when tested against U.S. and European Gram-positive isolates

| Organism group (no. of isolates tested)/antimicrobial agent | % of isolates susceptible by the following criteria: MIC (µg/ml) | MIC (µg/ml) | Range |
|-------------------------------------------------------------|---------------------------------------------------------------|-------------|--------|
|                                                             | CLSI 50% | 90% | Range |
| Staphylococcus aureus (1,350)                               |          |     |        |
| Delafloxacin                                                | ≤0.004   | 0.25 | ≤0.004 to 4 |
| Levofloxacin                                                | 64.4     | 64.4 | 0.25 to >4 |
| Ceftaroline                                                 | 98.0     | 98.0 | 0.25 to 1 |
| Clindamycin                                                 | 87.0     | 86.8 | ≤0.25 to >2 |
| Daptomycin                                                  | 99.8     | 99.8 | 0.25 to 0.5 |
| Erythromycin                                                | 45.9     | 46.3 | 4 to >16 |
| Linezolid                                                   | 100.0    | 100.0| 1 to 1 |
| Oxacillin                                                   | 57.6     | 57.6 | 0.5 to >2 |
| Tetracycline                                                | 94.3     | 92.5 | ≥0.5 to ≤0.5 |
| Tigecycline                                                 | 100.0a   | 100.0| 0.06 to 0.06 |
| Trimethoprim-sulfamethoxazole                               | 98.5     | 98.5 | ≤0.5 to ≤0.5 |
| Vancomycin                                                  | 100.0    | 100.0| 1 to 1 |

| MSSA (777)                                                  |          |     |        |
| Delafloxacin                                                | ≤0.004   | 0.008 | ≤0.004 to 4 |
| Levofloxacin                                                | 89.8     | 89.8 | 0.25 to 2 |
| Ceftaroline                                                 | 100.0    | 100.0| 0.25 to 0.25 |
| Clindamycin                                                 | 94.0     | 93.7 | ≤0.25 to ≤0.25 |
| Daptomycin                                                  | 100.0    | 100.0| 0.25 to 0.5 |
| Erythromycin                                                | 69.6     | 69.8 | ≤0.25 to >16 |
| Linezolid                                                   | 100.0    | 100.0| 1 to 1 |
| Oxacillin                                                   | 100.0    | 100.0| 0.5 to 0.5 |
| Tetracycline                                                | 95.9     | 94.2 | ≥0.5 to ≤0.5 |
| Tigecycline                                                 | 100.0a   | 100.0| 0.06 to 0.06 |
| Trimethoprim-sulfamethoxazole                               | 99.0     | 99.0 | ≤0.5 to ≤0.5 |
| Vancomycin                                                  | 100.0    | 100.0| 1 to 1 |

| MRSA (573)                                                  |          |     |        |
| Delafloxacin                                                | 0.06     | 0.5 | ≤0.004 to 4 |
| Levofloxacin                                                | 30.0     | 30.0| 4 to >4 |
| Ceftaroline                                                 | 95.3     | 95.3| 1 to 1 |
| Clindamycin                                                 | 77.5     | 77.5| ≤0.25 to >2 |
| Daptomycin                                                  | 99.5     | 99.5| 0.25 to 0.5 |
| Erythromycin                                                | 13.8     | 14.3| >16 to >16 |
| Linezolid                                                   | 100.0    | 100.0| 1 to 1 |
| Oxacillin                                                   | 0.0      | 0.0 | >2 to >2 |
| Tetracycline                                                | 92.1     | 90.2| ≤0.5 to 1 |
| Tigecycline                                                 | 100.0a   | 100.0| 0.06 to 0.06 |
| Trimethoprim-sulfamethoxazole                               | 97.9     | 97.9| ≤0.5 to ≤0.5 |
| Vancomycin                                                  | 100.0    | 100.0| 1 to 1 |

| MS-CoNS (75)                                                |          |     |        |
| Delafloxacin                                                | ≤0.004   | 0.06| ≤0.004 to 1 |
| Levofloxacin                                                | 88.0     | 88.0| 0.25 to 4 |
| Ceftaroline                                                 | 84.0     | 84.0| 0.12 to 0.25 |
| Clindamycin                                                 | 100.0    | 100.0| 0.25 to 0.5 |
| Daptomycin                                                  | 69.3     | 69.3| ≤0.12 to >16 |
| Erythromycin                                                | 100.0    | 100.0| 0.5 to 0.5 |
| Linezolid                                                   | 100.0    | 100.0| 0.5 to 2 |
| Oxacillin                                                   | 100.0    | 100.0| ≤0.25 to 1 |
| Tetracycline                                                | 89.3     | 86.7| ≤0.5 to 8 |
| Tigecycline                                                 | 92.0     | 92.0| ≥0.03 to 0.06 |
| Trimethoprim-sulfamethoxazole                               | 100.0    | 100.0| 1 to 2 |
| Vancomycin                                                  | 38.4     | 38.4| 4 to >4 |
| MR-CoNS (125)                                               |          |     |        |
| Delafloxacin                                                | 38.4     | 38.4| 4 to >4 |
| Levofloxacin                                                | 70.4     | 67.2| 0.05 to 0.5 |
| Ceftaroline                                                 | 99.2     | 99.2| 0.05 to 0.5 |

(Continued on next page)
### TABLE 2 (Continued)

| Organism group/antimicrobial agent | CLSI | EUCAST | 50% | 90% | Range |
|-----------------------------------|------|--------|-----|-----|-------|
| Erythromycin                      | 25.6 | 25.6   | >16 | >16 | ≤0.12 to >16 |
| Linezolid                         | 100.0| 100.0  | 0.5 | 0.5 | ≤0.12 to 1 |
| Oxacillin                         | 0.0  | 0.0    | >2  | >2  | 0.5 to >2 |
| Tetracycline                      | 80.8 | 77.6   | 1   | >8  | ≤0.5 to >8 |
| Teigycline                        | 100.0| 100.0  | 0.06| 0.12| ≤0.015 to 0.25 |
| Trimethoprim-sulfamethoxazole     | 65.6 | 65.6   | ≤0.5| >4  | ≤0.5 to >4 |
| Vancomycin                        | 100.0| 100.0  | 1   | 2   | 0.5 to 2 |

**Enterococcus faecalis (450)**

| Delafloxacin                      | 0.06| 1       | ≤0.004 to 2 |
| Levofloxacin                      | 70.7| 70.7b   | 1   | >4  | 0.25 to >4 |
| Ampicillin                        | 100.0| 99.6   | 1   | 2   | ≤0.25 to 8 |
| Ceftaroline                       | 2   | 8       | 0.25 to >32 |
| Clindamycin                       | >2  | >2      | ≤0.25 to >2 |
| Daptomycin                        | 100.0|        | 1   | 2   | 0.12 to 4 |
| Erythromycin                      | 4.7 | >16     | ≤0.12 to >16 |
| Linezolid                         | 99.8| 100.0  | 1   | 1   | ≤0.12 to 4 |
| Teicoplanin                       | 97.8| 97.6   | ≤2  | ≤2  | ≤2 to >16 |
| Tetracycline                      | 23.1| >8      | ≤0.5 to >8 |
| Trimethoprim-sulfamethoxazole     | ≤0.5| ≤0.5   | ≤0.5 to >4 |
| Vancomycin                        | 97.8| 97.8   | 1   | 2   | 0.5 to >16 |

**Enterococcus faecium (295)**

| Delafloxacin                      | >4  | >4      | 0.008 to >4 |
| Levofloxacin                      | 7.8 | 10.8b   | >4  | >4  | 0.5 to >4 |
| Ampicillin                        | 10.8| 10.8    | >8  | >8  | ≤0.25 to >8 |
| Ceftaroline                       | >32 | >32     | 0.12 to >32 |
| Clindamycin                       | >2  | >2      | ≤0.25 to >2 |
| Daptomycin                        | 99.0|        | 2   | 4   | 0.12 to 8 |
| Erythromycin                      | 3.7 | >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      | ≤0.5 to >8 |
| Trimethoprim-sulfamethoxazole     | ≤0.5| >4      | ≤0.5 to >4 |
| 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 | 98.9  | 1   | 1   | 0.5 to >4 |
| Amoxicillin-clavulanic acid       | 91.1 | ≤1    | ≤1 to >8 |
| Ceftaroline                       | 99.6c| 99.3  | ≤0.015| 0.12 | ≤0.015 to 1 |
| Ceftriaxone                       | 83.6c, 94.2c | 83.6 | ≤0.06 | 1 | ≤0.06 to 8 |
| Clindamycin                       | 84.7 | 84.9  | ≤0.25| >2  | ≤0.25 to >2 |
| Erythromycin                      | 59.9 | 59.9  | ≤0.12| >16 | ≤0.12 to >16 |
| Meropenem                         | 84.4 | 84.4, 100.0c | ≤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, 63.8, 63.8 | 63.8, 63.8, 63.8 | 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)**

| Delafloxacin                      | 0.015| 0.03  | ≤0.004 to 2 |
| Levofloxacin                      | 94.1 |       | 1   | 2   | ≤0.12 to >4 |
| Amoxicillin-clavulanic acid       | 98.7 |       | ≤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| ≤0.015 to 4 |
| Moxifloxacin                      | ≤0.12|       | 0.25 | ≤0.12 to >4 |

(Continued on next page)
| Organism group | % of isolates susceptible by the following criteria: | MIC (µg/ml) | CLSI | EUCAST | 50% | 90% | Range |
|---------------|--------------------------------------------------|-------------|------|--------|------|------|-------|
| 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 |
| *Streptococcus pyogenes* (433) | Delafloxacin | 99.8 | 96.5 | 0.5 | 1 | 0.25 to >4 |
| | Levofloxacin | 100.0 | 100.0 | ≤1 | ≤1 | ≤1 to ≤1 |
| | Amoxicillin-clavulanic acid | 100.0 | 100.0 | ≤0.015 | ≤0.015 | 0.0015 | ≤0.015 to ≤0.015 |
| | Ceftriazone | 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 | 0.0015 | ≤0.015 to ≤0.015 |
| | Moxifloxacin | 100.0 | 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 | 97.8 | 96.9 | 0.5 | 1 | 0.25 to >4 |
| | Levofloxacin | 100.0 | 100.0 | ≤1 | ≤1 | ≤1 to ≤1 |
| | Amoxicillin-clavulanic acid | 100.0 | 100.0 | ≤0.015 | ≤0.03 | ≤0.015 | ≤0.015 to ≤0.03 |
| | Ceftriazone | 100.0 | 100.0 | ≤0.06 | 0.12 | ≤0.06 to 0.25 |
| | Clindamycin | 70.7 | 72.4 | ≤0.25 | >2 | ≤0.25 to >2 |
| | Erythromycin | 52.4 | 52.4 | ≤0.12 | >16 | ≤0.12 to >16 |
| | Meropenem | 100.0 | 100.0 | 0.03 | 0.06 | ≤0.015 to ≤0.12 |
| | Moxifloxacin | 97.8 | 97.8 | ≤0.12 | 0.25 | ≤0.12 to >4 |
| | Penicillin | 100.0 | 100.0 | ≤0.06 | ≤0.06 | ≤0.06 to ≤0.06 |
| | Tetracycline | 17.4 | 17.0 | >8 | >8 | ≤0.5 to >8 |
| | Vancomycin | 100.0 | 100.0 | 0.5 | 0.5 | 0.25 to 1 |
| *Streptococcus dysgalactiae* (132) | Delafloxacin | 99.2 | 97.0 | 0.5 | 1 | 0.25 to >4 |
| | Levofloxacin | 100.0 | 100.0 | ≤1 | ≤1 | ≤1 to ≤1 |
| | Amoxicillin-clavulanic acid | 100.0 | 100.0 | ≤0.015 | ≤0.015 | 0.0015 | ≤0.015 to ≤0.015 |
| | Ceftriazone | 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 | 0.0015 | ≤0.015 to ≤0.015 |
| | Moxifloxacin | 100.0 | 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 | ≤0.5 to >8 |
| | Vancomycin | 100.0 | 100.0 | 0.25 | 0.25 | ≤0.12 to 1 |

*Breakpoints from FDA package insert, revised December 2014.*
*Uncomplicated UTI only.*
*Using nonmeningitis breakpoints.*
*Using meningitis breakpoints.*
*Using oral breakpoints.*
*Using parenteral, meningitis breakpoints.*
*Using parenteral, nonmeningitis breakpoints.*