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Activity of Delafloxacin and Comparator Agents Against Bacterial Isolates from Patients with Diabetic Foot Infection in the United States and Europe (2017–2023)

Michael D Huband, Marisa L Winkler, Kelley A Fedler, Mariana Castanheira

Element Iowa City (JMI Laboratories), North Liberty, Iowa, United States

Introduction

- Delafloxacin is a fluoroquinolone antibacterial with oral and intravenous treatment options approved in 61 countries for treatment of acute bacterial skin and skin structure infection (ABSSSI) and community-acquired bacterial pneumonia (CABP) caused by specific pathogens in adults.
- Indicated organisms/organism groups for delafloxacin and ABSSSI in the United States include: staphylococci (*S. aureus* [SA] both methicillin-susceptible [MSSA] and methicillin-resistant [MRSA], *S. haemolyticus*, and *S. lugdunensis*), streptococci (*Streptococcus pyogenes*, *S. agalactiae*, and *S. anginosus* group), *Enterococcus faecalis*, Enterobacterales (*Enterobacter cloacae, Escherichia coli*, and *Klebsiella pneumoniae*), and *Pseudomonas aeruginosa*.
- In this study, the *in vitro* activity of delafloxacin, ciprofloxacin, levofloxacin, moxifloxacin, minocycline, meropenem-vaborbactam, and oritavancin were determined against bacterial isolates from patients with diabetic foot infection (DFI) in the United States (US) and Europe (2017–2023).

Materials and Methods

- ABSSSI isolates from patients with DFI were collected in the SENTRY Antimicrobial Surveillance Program (2017–2023) from medical centers located in the US and Europe.
- Broth microdilution susceptibility testing was conducted according to Clinical and Laboratory Standards Institute (CLSI) methods and CLSI, EUCAST, and FDA breakpoint interpretive criteria (2025) were applied.
- Bacterial isolate identifications were determined at participating SENTRY sites and confirmed at Element Iowa City (JMI Laboratories) using matrix-assisted laser-desorption ionization time-of-flight mass spectrometry (as needed).

Results

- The most common DFI pathogens from patients with ABSSSI in the SENTRY Antimicrobial Surveillance Program based on prevalence during 2017–2023 were *S. aureus* (38%), Enterobacterales (32%), *P. aeruginosa* (11%), enterococci (8%), streptococci (7%), other staphylococci (2%), and other non-fermenters (2%) (Figure 1).
- MRSA rates in DFI patients were 39.0% (60/154) in the US and 25.9% (42/162) in Europe.
- Overall, 87.7% (FDA) of *S. aureus* isolates from patients with DFI in the United States were susceptible to delafloxacin (Table 1), including 96.7% of MSSA and 73.3% of MRSA.
- 85.2% of *S. aureus* isolates from DFI patients in Europe were susceptible to delafloxacin (Table 1), including 96.9% of MSSA and 45.2% of MRSA.
- Comparator fluoroquinolone susceptibilities against *S. aureus* isolates from the US and Europe were 66.9% (CLSI/EUCAST/FDA) and 75.4% (CLSI/EUCAST/FDA), respectively, for levofloxacin, and 66.9% (CLSI/EUCAST/FDA) and 75.3% (CLSI/EUCAST/FDA), respectively, for moxifloxacin (Table 1).
- All *S. aureus* isolates were susceptible (100.0%; CLSI/EUCAST/FDA) to oritavancin (Table 1).
- All (100.0%) *S. haemolyticus* (n=2), *S. lugdunensis* (n=4), *S. pyogenes* (n=6), and *S. anginosus* group (n=4) isolates from patients with DFI were susceptible (ABSSSI breakpoints) to delafloxacin (data not shown).
- Susceptibility of *Streptococcus agalactiae* isolates (*n*=34) to delafloxacin was 97.1%/100.0% (EUCAST/FDA) using ABSSSI breakpoints (Table 1).
- 83.3% of *E. faecalis* isolates from DFI were susceptible to delafloxacin (FDA), levofloxacin (CLSI/EUCAST/FDA), and moxifloxacin (FDA) (Table 1).
- Overall, 60.8%/69.4% (EUCAST/FDA), 79.9% (CLSI/EUCAST/FDA), and 82.8% (CLSI/EUCAST/FDA) of all Enterobacterales isolates from patients with DFI in the US and Europe were susceptible to delafloxacin, ciprofloxacin, and levofloxacin, respectively (Table 2).
- 36.9% (116/314) of Enterobacterales isolates from patients with DFI in the US and Europe were *E. cloacae* species complex (12.4%), *E. coli* (17.8%), or *K. pneumoniae* (6.7%).
- Against indicated organism groups, 87.2% (FDA) of *E. cloacae* species complex isolates, 62.5%/71.4% (EUCAST/FDA) of *E. coli* isolates, and 57.1% (FDA) of *K. pneumoniae* isolates from patients with DFI in the US and Europe were susceptible to delafloxacin (Table 2).
- 75.0% (FDA) of *Citrobacter* spp. isolates and 76.6% (FDA) of *Proteus mirabilis* isolates from patients with DFI in the US and Europe were susceptible (ABSSSI breakpoints) to delafloxacin (Table 2).
- Overall, 66.3% (FDA), 79.3% (CLSI/EUCAST/FDA), and 68.5%/79.3%/68.5% (CLSI/EUCAST/FDA) of *P. aeruginosa* isolates from patients with DFI in the US and Europe were susceptible to delafloxacin, ciprofloxacin, and levofloxacin, respectively (Table 3).
- Susceptibility of *P. aeruginosa* isolates from patients with DFI to delafloxacin was higher in the US (74.4% [FDA]) compared to Europe (59.2% [FDA]) (Table 3).

Conclusions

- The most prevalent pathogen in patients with DFI was *S. aureus* (38%) of which delafloxacin was the most active fluoroquinolone (86.3% susceptible [EUCAST/FDA]) tested.
 - Against MRSA, delafloxacin was active against 73.3% of isolates from patients with DFI in the United States and 45.2% of isolates from Europe.
- Delafloxacin was active against other Gram-positive DFI pathogens including *S. haemolyticus*, *S. lugdunensis*, *S. pyogenes*, and *S. anginosus* group isolates (100.0% susceptible [FDA]), *S. agalactiae* (97.1%/100.0% susceptible [EUCAST/FDA]), and *E. faecalis* (83.3% susceptible [FDA]).
- Overall, 87.2% (FDA) of *E. cloacae* species complex, 62.5%/71.4% (EUCAST/FDA) of *E. coli*, 57.1% (FDA) of *K. pneumoniae*, and 66.3% (FDA) of *P. aeruginosa* isolates from patients with DFI were susceptible to delafloxacin.
- Delafloxacin may serve as a useful treatment option (either alone or in combination) in patients with DFI including those where a broad-spectrum agent is desired. Additional clinical studies in patients with DFI are needed.

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Table 1. Activity of delafloxacin and comparators against Gram-positive isolates from patients with diabetic foot infection in the United States and Europe (2017–2023)

Antimicrobial Agent (Region; no. tested)	MIC (mg/L)			CLSI[a]		EUCAST[a]		US FDA[a]	
	MIC_{50}	MIC_{90}	MIC range	%S	%R	%S	%R	%S	%R
***Staphylococcus aureus* (United States; *n*=154)**									
Delafloxacin	0.008	0.5	0.001 to 4			87.7 [b]	12.3	87.7 [b]	7.8
Levofloxacin	0.25	>4	0.06 to >4	66.9	33.1	66.9 [c]	33.1	66.9 [d]	22.7
Moxifloxacin	≤0.06	4	≤0.06 to >4	66.9	29.9	66.9	33.1	66.9 [e]	29.9
Minocycline	0.06	0.12	≤0.03 to >8	98.7	1.3	98.1	1.9	98.7 [e]	1.3
Oritavancin	0.03	0.03	≤0.008 to 0.12	100.0		100.0	0.0	100.0 [e]	
Methicillin-resistant *Staphylococcus aureus* (United States; *n*=60)									
Delafloxacin	0.25	1	0.002 to 4			73.3 [b]	26.7	73.3 [b]	18.3
Levofloxacin	4	>4	0.12 to >4	35.0	65.0	35.0 [c]	65.0	35.0 [d]	46.7
Moxifloxacin	2	>4	≤0.06 to >4	35.0	60.0	35.0	65.0	35.0 [e]	60.0
Minocycline	0.06	0.5	≤0.03 to >8	98.3	1.7	96.7	3.3	98.3 [e]	1.7
Oritavancin	0.03	0.03	≤0.008 to 0.12	100.0		100.0	0.0	100.0 [e]	
***Staphylococcus aureus* (Europe; *n*=182)**									
Delafloxacin	0.008	0.5	≤0.0005 to 8			85.2 [b]	14.8	85.2 [b]	6.6
Levofloxacin	0.25	>4	0.06 to >4	75.4	24.6	75.4 [c]	24.6	75.4 [d]	22.0
Moxifloxacin	≤0.06	4	≤0.06 to >4	75.3	22.5	75.3	24.7	75.3 [e]	23.5
Minocycline	0.06	0.12	≤0.03 to 8	98.9	0.0	97.9	2.2	98.9 [e]	0.0
Oritavancin	0.03	0.06	≤0.008 to 0.12	100.0		100.0	0.0	100.0 [e]	
Methicillin-resistant *Staphylococcus aureus* (Europe; *n*=42)									
Delafloxacin	0.5	2	0.004 to 8			45.2 [b]	54.8	45.2 [b]	23.8
Levofloxacin	>4	>4	0.12 to >4	19.0	81.0	19.0 [c]	81.0	19.0 [d]	73.8
Moxifloxacin	4	>4	≤0.06 to >4	19.0	76.2	19.0	81.0	19.0 [e]	76.2
Minocycline	0.06	0.25	0.06 to 8	95.2	0.0	92.9	7.1	95.2 [e]	0.0
Oritavancin	0.015	0.06	≤0.008 to 0.12	100.0		100.0	0.0	100.0 [e]	
***Staphylococcus aureus* (United States and Europe; *n*=336)**									
Delafloxacin	0.008	0.5	≤0.0005 to 8			86.3 [b]	13.7	86.3 [b]	7.1
Levofloxacin	0.25	>4	0.06 to >4	75.3	28.6	75.3 [c]	28.6	75.3 [d]	22.3
Moxifloxacin	≤0.06	4	≤0.06 to >4	71.4	25.9	71.4	28.6	71.4 [e]	25.9
Minocycline	0.06	0.12	≤0.03 to >8	98.8	0.6	97.9	2.1	98.8 [e]	0.6
Oritavancin	0.03	0.06	≤0.008 to 0.12	100.0		100.0	0.0	100.0 [e]	
***Streptococcus agalactiae* (United States and Europe; *n*=34)**									
Delafloxacin	0.015	0.03	0.008 to 0.06			97.1 [b]	2.9	100.0 [b]	
Levofloxacin	1	1	0.5 to 2	100.0	0.0	100.0 [c]	0.0	100.0	0.0
Moxifloxacin	0.12	0.25	0.06 to 0.25			100.0	0.0		
Erythromycin	4	>16	0.03 to >16	33.3	66.7	33.3	66.7	33.3	66.7 [e]
Oritavancin	0.06	0.06	0.03 to 0.25	100.0		100.0	0.0	100.0 [e]	
***Enterococcus faecalis* (United States and Europe; *n*=24)**									
Delafloxacin	0.12	0.5	0.03 to 1			IE [f]	IE	83.3	12.5
Levofloxacin	1	>4	0.5 to >4	83.3	16.7	83.3 [g]	16.7	83.3	16.7 [e]
Moxifloxacin	0.25	>4	0.06 to >4					83.3	16.7
Oritavancin	0.015	0.03	0.004 to 0.03	100.0 [h]				100.0 [e,h]	
Vancomycin	1	2	0.5 to 2	100.0	0.0	100.0	0.0	100.0 [e]	0.0

[a] Criteria as published by CLSI (2025), EUCAST (2025), and US FDA (2025).
[b] Using ABSSSI breakpoints.
[c] An arbitrary susceptible breakpoint of ≤0.001 mg/L and/or >50 mm has been published by EUCAST indicating that susceptible should not be reported for this organism-agent combination and intermediate should be interpreted as susceptible, increased exposure.
[d] US FDA breakpoints were applied to all *Staphylococcus aureus*, but they are only approved for MSSA (methicillin-susceptible *S. aureus*) isolates.
[e] CLSI M100 standard is recognized.
[f] IE = Insufficient evidence that the organism or group is a good target for therapy with the agent.
[g] Uncomplicated urinary tract infection only.
[h] Vancomycin-susceptible isolates only.

Table 2. Activity of delafloxacin and comparators against Enterobacterales isolates from patients with diabetic foot infections in the United States and Europe (2017–2023)

Antimicrobial Agent (Region; no. tested)	MIC (mg/L)			CLSI[a]		EUCAST[a]		US FDA[a]	
	MIC_{50}	MIC_{90}	MIC range	%S	%R	%S	%R	%S	%R
Enterobacterales (United States; *n*=180)									
Delafloxacin	0.12	2	0.008 to >16			62.7 [b]	37.3	72.2 [c,d]	21.7
Ciprofloxacin	≤0.03	4	≤0.03 to >4	83.3	14.4	83.3 [e]	16.7	83.3 [f]	14.4
Levofloxacin	0.06	4	≤0.03 to >16	85.0	13.3	85.0	13.3	85.0 [f]	13.3
Minocycline (*n*=115)	2	32	0.25 to >32	60.0	25.2			60.0 [f]	25.2
Meropenem-vaborbactam	0.03	0.06	≤0.015 to 0.12	100.0		100.0	0.0	100.0 [f]	
Enterobacterales (Europe; *n*=134)									
Delafloxacin	0.12	4	0.008 to >16			58.2 [b]	41.8	65.7 [c,d]	27.6
Ciprofloxacin	≤0.03	4	≤0.03 to >4	75.4	21.6	75.4 [e]	21.6	75.4 [f]	21.6
Levofloxacin	0.06	4	≤0.03 to >16	79.9	14.9	79.9	14.9	79.9 [f]	14.9
Minocycline (*n*=133)	2	16	0.25 to >32	70.7	17.3			70.7 [f]	17.3
Meropenem-vaborbactam	0.03	0.06	≤0.015 to 8	99.3	0.0	100.0	0.0	99.3 [f]	0.0
Enterobacterales (United States and Europe; *n*=314 [g])									
Delafloxacin	0.12	4	0.008 to >16			60.8 [b]	39.2	69.4 [c,d]	24.2
Ciprofloxacin	≤0.03	4	≤0.03 to >4	79.9	17.5	79.9 [e]	20.1	79.9 [f]	17.5 [f]
Levofloxacin	0.06	4	≤0.03 to >16	82.8	14.0	82.8	14.0	82.8 [f]	14.0
Minocycline (*n*=248)	2	16	0.25 to >32	65.7	21.0			65.7 [f]	21.0
Meropenem-vaborbactam	0.03	0.06	≤0.015 to 8	99.7	0.0	100.0	0.0	99.7 [f]	0.0
***Citrobacter* spp. (United States and Europe; *n*=28 [g])**									
Delafloxacin	0.06	2	0.015 to 8					75.0 [c,d]	14.3
Ciprofloxacin	≤0.03	0.12	≤0.03 to 1	96.4	3.6	96.4 [e]	3.6	96.4 [f]	3.6 [f]
Levofloxacin	0.06	1	≤0.03 to 2	89.3	3.6	89.3	3.6	89.3 [f]	3.6
Minocycline (*n*=17)	2	4	0.5 to >32	94.1	5.9			94.1 [f]	5.9
Meropenem-vaborbactam	0.015	0.03	≤0.015 to 0.03	100.0	0.0	100.0	0.0	100.0 [f]	0.0
***Enterobacter cloacae* and *E. cloacae* species complex (United States and Europe; *n*=39)**									
Delafloxacin	0.12	2	0.008 to >16					87.2 [c,d]	10.3
Ciprofloxacin	≤0.03	0.5	≤0.03 to 4	89.7	7.7	89.7 [e]	7.7	89.7 [f]	7.7 [f]
Levofloxacin	0.06	0.25	≤0.03 to 2	94.8	2.6	94.8	2.6	94.8 [f]	2.6
Minocycline (*n*=31)	2	4	0.5 to >32	93.5	3.2			93.5 [f]	3.2
Meropenem-vaborbactam	0.015	0.03	≤0.015 to 0.25	100.0	0.0	100.0	0.0	100.0 [f]	0.0
***Escherichia coli* (United States and Europe; *n*=56)**									
Delafloxacin	0.06	4	0.008 to >16			62.5	37.5	71.4 [c,d]	25.0
Ciprofloxacin	≤0.03	>4	≤0.03 to >4	71.4	23.2	71.4 [e]	23.2	71.4 [f]	23.2 [e]
Levofloxacin	0.03	16	≤0.03 to >16	76.8	23.2	76.8	23.2	76.8 [f]	23.2
Minocycline (*n*=49)	1	8	0.25 to >32	84.6	7.7			84.6 [f]	7.7
Meropenem-vaborbactam	≤0.015	0.03	≤0.015 to 0.03	100.0	0.0	100.0	0.0	100.0 [f]	0.0
***Klebsiella pneumoniae* (United States and Europe; *n*=21)**									
Delafloxacin	0.12	>16	0.03 to >16					57.1 [c,d]	42.9
Ciprofloxacin	≤0.03	>16	≤0.03 to >16	52.4	42.9	52.4 [e]	47.6	52.4 [f]	42.9 [f]
Levofloxacin	0.06	32	≤0.03 to 32	71.4	28.6	71.4	28.6	71.4 [f]	28.6
Minocycline (*n*=16)	2	16	1 to >32	87.5	12.5			87.5 [f]	12.5
Meropenem-vaborbactam	0.03	0.06	≤0.015 to 8	95.2	4.8	100.0	0.0	95.2 [f]	4.8
***Proteus mirabilis* (United States and Europe; *n*=47 [g])**									
Delafloxacin	0.06	2	0.015 to >16					76.6 [c,d]	19.1
Ciprofloxacin	0.03	4	≤0.03 to >16	74.5	25.5	74.5 [e]	25.5	74.5 [f]	25.5 [f]
Levofloxacin	0.06	4	0.03 to >32	74.5	17.0	74.5	17.0	74.5 [f]	17.0
Minocycline (*n*=41)	16	>32	2 to >32	9.8	73.2			9.8 [f]	73.2
Meropenem-vaborbactam	0.06	0.12	0.03 to 0.25	100.0	0.0	100.0	0.0	100.0 [f]	0.0

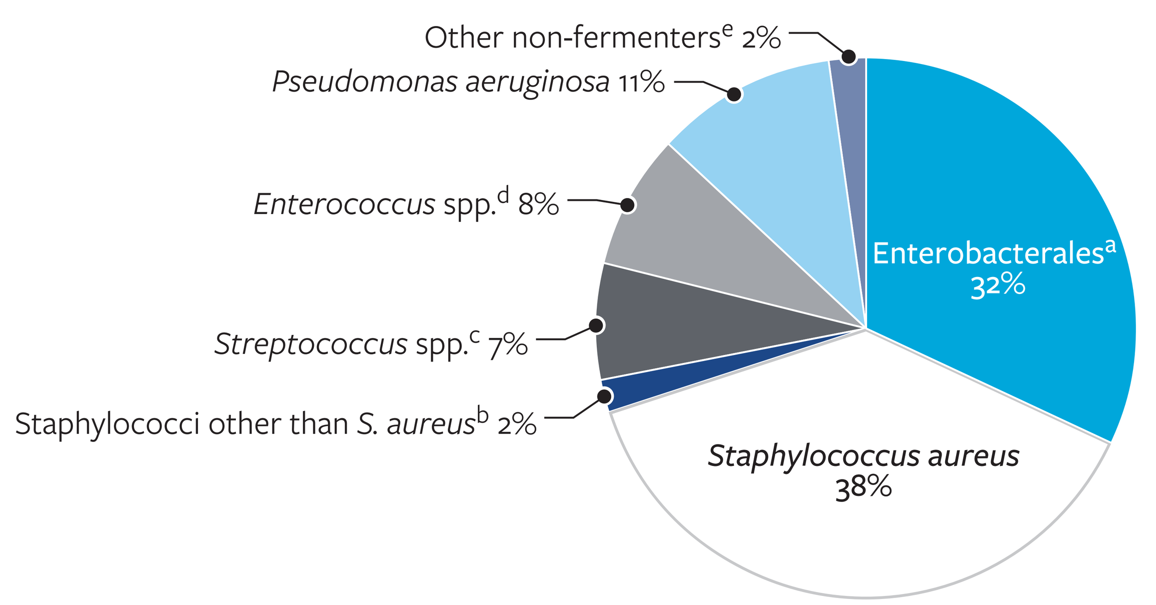
[a] Criteria as published by CLSI (2025), EUCAST (2025), and US FDA (2025).
[b] *E. coli* breakpoints applied to all Enterobacterales.
[c] Using ABSSSI breakpoints.
[d] US FDA breakpoints published for *E. coli*, *K. pneumoniae*, and *E. cloacae* were applied to all Enterobacterales isolates.
[e] Using non-meningitis breakpoints.
[f] CLSI M100 standard is recognized.
[g] Organisms include *Citrobacter freundii* species complex (15), *C. koseri* (13), *Enterobacter cloacae* (14), *E. cloacae* species complex (25), *Escherichia coli* (56), *E. hermannii* (2), *Klebsiella aerogenes* (5), *K. oxytoca* (23), *K. pneumoniae* (21), *K. variicola* (1), *Morganella morganii* (32), *Proteus hauseri* (2), *P. mirabilis* (47), *P. penneri* (2), *P. vulgaris* (9), *P. vulgaris* group (16), *Providencia rettgeri* (4), *P. stuartii* (5), *Serratia liquefaciens* (2), *S. marcescens* (17), and unspeciated *Raoultella* (2).

Table 3. Activity of delafloxacin and comparators against *Pseudomonas aeruginosa* isolates from patients with diabetic foot infections in the United States and Europe (2017–2023)

Antimicrobial Agent (Region; no. tested)	MIC (mg/L)			CLSI[a]		EUCAST[a]		US FDA[a]	
	MIC_{50}	MIC_{90}	MIC range	%S	%R	%S	%R	%S	%R
***Pseudomonas aeruginosa* (United States; *n*=43)**									
Delafloxacin	0.5	2	0.12 to 16			IE [b]	IE [b]	74.4 [c]	18.6
Ciprofloxacin	0.12	1	0.06 to 8	86.0	9.3	86.0 [d]	14.0	86.0 [e]	9.3
Levofloxacin	0.5	4	0.25 to 16	79.1	16.3	83.7 [d]	16.3	79.1 [e]	16.3
Meropenem-vaborbactam	0.25	2	0.06 to 8			100.0	0.0		
***Pseudomonas aeruginosa* (Europe; *n*=49)**									
Delafloxacin	0.5	16	0.015 to >16			IE [b]	IE [b]	59.2 [c]	28.6
Ciprofloxacin	0.12	>4	≤0.03 to >16	73.5	24.5	73.5 [d]	26.5	73.5 [e]	24.5
Levofloxacin	1	32	0.06 to >32	59.2	24.5	75.5 [d]	24.5	59.2 [e]	24.5
Meropenem-vaborbactam	0.5	8	0.06 to >32			91.8	8.2		
***Pseudomonas aeruginosa* (United States and Europe; *n*=92)**									
Delafloxacin	0.5	8	0.015 to >16			IE [b]	IE [b]	66.3 [c]	23.9
Ciprofloxacin	0.12	8	≤0.03 to >16	79.3	17.4	79.3 [d]	21.7	79.3 [e]	17.4
Levofloxacin	0.5	16	0.06 to >32	68.5	20.7	79.3 [d]	20.7	68.5 [e]	20.7
Meropenem-vaborbactam	0.5	2	0.06 to >32			95.7	4.3		

[a] Criteria as published by CLSI (2025), EUCAST (2025), and US FDA (2025).
[b] IE = Insufficient evidence that the organism or group is a good target for therapy with the agent.
[c] Using ABSSSI breakpoints.
[d] An arbitrary susceptible breakpoint of ≤0.001 mg/L and/or >50 mm has been published by EUCAST indicating that susceptible should not be reported for this organism-agent combination and intermediate should be interpreted as susceptible, increased exposure.
[e] CLSI M100 standard is recognized.

Figure 1. Prevalence of DFI pathogens from patients in the United States and Europe (SENTRY 2017 to 2023)


Other non-fermenters[e] 2%
Pseudomonas aeruginosa 11%
Enterococcus spp.[d] 8%
Enterobacterales[a] 32%
Streptococcus spp.[c] 7%
Staphylococci other than S. aureus[b] 2%
Staphylococcus aureus 38%

[a] Contains *Citrobacter freundii* species complex (12), *C. koseri* (6), *Enterobacter cloacae* (12), *E. cloacae* species complex (21), *Escherichia coli* (56), *E. hermannii* (2), *Klebsiella aerogenes* (4), *K. oxytoca* (19), *K. pneumoniae* (14), *K. variicola* (1), *Morganella morganii* (24), *Proteus hauseri* (2), *P. mirabilis* (40), *P. penneri* (2), *P. vulgaris* (4), *P. vulgaris* group (8), *Providencia rettgeri* (1), *P. stuartii* (3), *Serratia liquefaciens* (2), *S. marcescens* (17), and unspeciated *Raoultella* (2).
[b] Contains *Staphylococcus capitis* (2), *S. epidermidis* (4), *S. haemolyticus* (2), *S. lugdunensis* (8), *S. pseudintermedius* (1), *S. simulans* (1).
[c] Contains *Streptococcus agalactiae* (38), *S. anginosus* group (6), *S. canis* (1), *S. dysgalactiae* (10), *S. pyogenes* (4).
[d] Contains *Enterococcus avium* (2), *E. casseliflavus* (1), *E. faecalis* (44), *E. faecium* (16), *E. raffinosus* (2).
[e] Contains *Acinetobacter baumannii-calcoaceticus* species complex (8), *A. courvalinii* (1), *Stenotrophomonas maltophilia* (4).

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