Activity of Omadacycline and Comparators Against 876 Bacterial Clinical Isolates from Patients with Bone and Joint Infections in the United States and Europe (2015–2022)

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Introduction

- Omadacycline is a third-generation tetracycline class (aminomethylcycline) antibacterial approved for the treatment of acute bacterial skin and skin structure infection (ABSSSI) and community acquired bacterial pneumonia (CABP) caused by indicated organisms and organism groups.
- Omadacycline is active against bacterial isolates expressing common tetracycline, penicillin, fluoroquinolone, macrolide, and vancomycin resistance mechanisms.
- Omadacycline has multiple ongoing clinical trials including:
- Treatment of bone and joint infection (NCT05753215).
- Efficacy and safety of omadacycline in the treatment of diabetic foot infections and acute osteomyelitis (NCT04714411).
- This study determined the in vitro activity of omadacycline and tetracycline class comparators against 876 bacterial clinical isolates collected from patients with bone/joint infections from the omadacycline surveillance program (2015–2022).

Conclusions

- Omadacycline demonstrated potent in vitro activity against staphylococci, streptococci, enterococci, and Gram-negative bacterial isolates from patients with bone/joint infections, with activity generally greater than or equal to the other tetracycline class comparator agents.
- The greatest percentage of bone/joint infections was observed in males and in patients >55 years of age.
- Increasing rates of joint replacement surgeries will lead to the increased need for omadacycline and other antibiotics that are active against the organisms causing bone/joint infections.
- The results of this study support the continued clinical development of omadacycline for bone/joint infections and acute osteomyelitis where these bacterial pathogens are likely to be encountered.



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Materials and Methods

- 876 bacterial isolates from patients with bone/joint infections were received from 39 medical centers in the USA and 16 European countries (2015–2022).
- Organism identifications were confirmed at JMI Laboratories using standard microbiology methods and matrix-assisted laser desorption ionization-time of flight mass spectrometry (Bruker Daltonics, Bremen, Germany).
- Broth microdilution susceptibility testing of omadacycline and tetracycline class comparators was conducted according to Clinical and Laboratory Standards Institute M07 (CLSI; 2018) methodology.
- Omadacycline and comparator agent susceptibility results were interpreted using current CLSI M100 (2023) and/or FDA breakpoint interpretive criteria.

Table 1. Activity of omadacycline and comparator agents against organisms/organism groups from patients with bone and joint infections

MIC_{50/90} mg/L (% Susceptible [CLSI])

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Organism (No. of isolates)	OMC a	DOX	MIN	TET
Staphylococcus aureus (414)	0.12/0.25	≤0.06/0.25	0.06/0.12	≤0.5/≤0.5
	(98.3%)	(97.1%)	(95.9%)	(93.2%)
MRSA (143)	0.12/0.25	≤0.06/1	0.06/0.25	≤0.5/8
	(96.5%)	(95.8%)	(96.0%)	(88.8%)
MSSA (271)	0.12/0.25	≤0.06/0.25	0.06/0.12	≤0.5/≤0.5
	(99.3%)	(97.8%)	(95.9%)	(95.6%)
S. epidermidis (25)	0.25/0.5	0.5/1	0.12/—	1/>8
	(92.0%)	(100%)	(100%, <i>n</i> =4)	(80.0%)
S. lugdunensis (10)	0.06/0.06	≤0.06/≤0.06	≤0.03/—	≤0.5/≤0.5
	(90.0%)	(100%)	(100%)	(100%)
Other staphylococci (19) ^b	0.12/0.5	0.12/0.5	0.06/—	≤0.5/1
	(100%)	(100%)	(100%, <i>n</i> =6)	(94.7%)
Enterococcus faecalis (56)	0.12/0.25	4/8	8/>8	>8/>8
	(98.2%)	(64.7%)	(29.2%)	(21.4%)
Other enterococci (8) ^c	0.12/—	8/—	4/—	>8/—
	(100%)	(0.0%, <i>n</i> =2)	(50.0%, <i>n</i> =4)	(12.5%)
Streptococcus agalactiae (51)	0.12/0.12 (90.2%)	>1/>1 (—)	>1/>1 (—)	>4/>4 (17.6%)
S. dysgalactiae (22)	0.12/0.25 (72.7%)	Not tested	Not tested	0.5/>4 (57.1%)
S. pyogenes (33)	0.06/0.12	>1/— ^{d, e}	>1/ <u>e</u>	≤0.25/>4
	(100%)	(n=9)	(n=9)	(66.7%)
Other streptococci (13) ^f	0.06/0.25	0.25/—	0.12/1	0.5/4
	(84.6%)	(75.0%, <i>n</i> =4)	(—, <i>n</i> =4)	(84.6%)
Acinetobacter spp. (13) ^g	0.5/4	0.25/>8	2/—	8/>16
	(92.3%)	(76.9%)	(60.0%, <i>n</i> =5)	(46.2%)
Citrobacter spp. (13) ^h	1/2	2/4	1/—	1/8
	(92.3%)	(92.3%)	(100%, <i>n</i> =7)	(84.6%)
Enterobacter cloacae species complex (22)	2/16	2/>8	2/32	2/>16
	(81.8%)	(77.3%)	(81.2%, <i>n</i> =16)	(77.3%)
Escherichia coli (40)	0.5/2	1/8	1/2	2/>16
	(100%)	(75.0%)	(93.3%, <i>n</i> =30)	(75.0%)
Klebsiella pneumoniae (17)	2/8	8/>8	1/16	8/>16
	(88.2%)	(47.1%)	(64.3%, <i>n</i> =14)	(47.1%)
Other <i>Klebsiella</i> spp. (13) ^j	1/1	1/4	1/2	1/>16
	(100%)	(92.3%)	(90.0%, <i>n</i> =10)	(84.6%)
Serratia marcescens (14)	4/8	4/>8	2/—	16/>16
	(85.7%)	(64.3%)	(88.9%, <i>n</i> =9)	(14.3%)
Stenotrophomonas maltophilia (3)	2/—	2/—	0.12/—	8/—
	(100%)	(—)	(100%, <i>n</i> =2)	(—)
obreviations: CLSL Clinical and Laboratory Standards Institute: MRSA, methicillin-resistant Staphylococcus aureus: MSSA, methicillin-sensitive Staphylococcus aureus: OMC, omadacycline:				

: MRSA. methicillin-resistant Staphylococcus aureus: MSSA. methicillin-sensitive Staphylococcus aureus; OMC, omadacycline;

— = insufficient isolates tested to calculate an MIC₂₀ value.

f Contains Streptococcus anginosus (2), S. canis (2), S. gallolyticus (2), S. mitis group (1), and S. pneumoniae (6).

g Contains Acinetobacter baumannii calcoaceticus species complex (11), A. lwoffii (1), and A. radioresistens (1). Contains Citrobacter amalonaticus (1), C. freundii (1), C. freundii species complex (5), and C. koseri (6).

Contains Enterobacter cloacae (14) and E. cloacae species complex (8). Contains Klebsiella aerogenes (4) and K. oxytoca (9).

Results

- The most common bone/joint infection pathogen was S. aureus (47.3% of all bone/joint infection isolates) including methicillin-resistant *S. aureus* (MRSA) isolates (34.5% of all *S. aureus*) (Figure 1).
- Other common bone/joint infection pathogens included: streptococci (13.6%), enterococci (7.3%), staphylococci other than *S. aureus* (6.2%), and Enterobacterales (18.5%) isolates (Figure 1).
- Omadacycline ABSSSI breakpoint interpretive criteria were applied for the specific organisms or similar organism groups for comparison purposes:

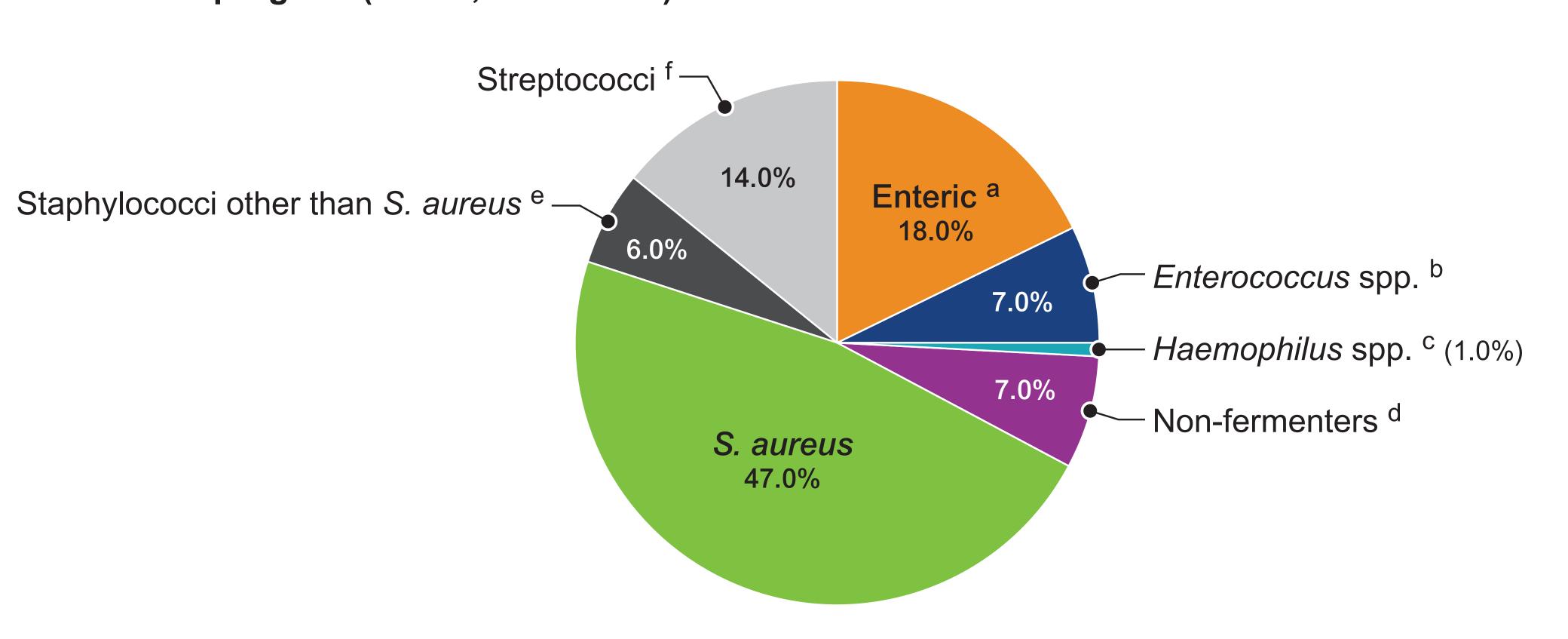
% Susceptibility of Gram-positives to omadacycline:

- 98.3% of S. aureus (MIC_{50/90}, 0.12/0.25 mg/L), 96.5% of MRSA (MIC_{50/90}, 0.12/0.25 mg/L), 92.0% of S. epidermidis (MİC_{50/90}, 0.25/0.5 mg/L), 90.0% of S. lugdunensis (MİC_{50/90}, 0.06/0.06 mg/L), and 100% of other Staphylococci (MIC_{50/90}, 0.12/0.5 mg/L) isolates (Table 1).
- In comparison to omadacycline, tetracycline susceptibility for MRSA and S. epidermidis was lower, 88.8% and 80.0% respectively.
- 98.2% of E. faecalis (MIC_{50/90}, 0.12/0.25 mg/L) isolates were susceptible to omadacycline, whereas other tetracycline class comparator agent susceptibilities ranged from 21.4% to 64.7% (Table 1)
- 90.2% of *S. agalactiae* (MIC_{50/90}, 0.12/0.12 mg/L) and 100% of *S. pyogenes* (MIC_{50/90}, 0.06/0.12 mg/L) isolates were susceptible to omadacycline, whereas tetracycline susceptibility was 17.6% and 66.7%, respectively (Table 1).

% Susceptibility of Gram-negatives to omadacycline:

- 92.3% of *Acinetobacter* spp. (MIC_{50/90}, 0.5/4 mg/L), 92.3% of *Citrobacter* spp. (MIC_{50/90}, 1/2 mg/L), 81.8% of Enterobacter cloacae species complex (MIC_{50/90}, 2/16 mg/L), 100% of Escherichia coli (MIC_{50/90}, 0.5/2 mg/L), 88.2% of *Klebsiella pneumoniae* (MIC_{50/90}, 2/8 mg/L), 85.7% of *Serratia* marcescens (MIC_{50/90}, 4/8 mg/L), and 100% of Stenotrophomonas maltophilia (MIC₅₀, 2 mg/L)
- For each of the age groups listed, the percentage of patients with bone/joint infections was 1.5 to 3.4 times higher for males than for females (Figure 2).
- Overall, patients >55 years of age had the greatest number of bone/joint infections (Figure 2).

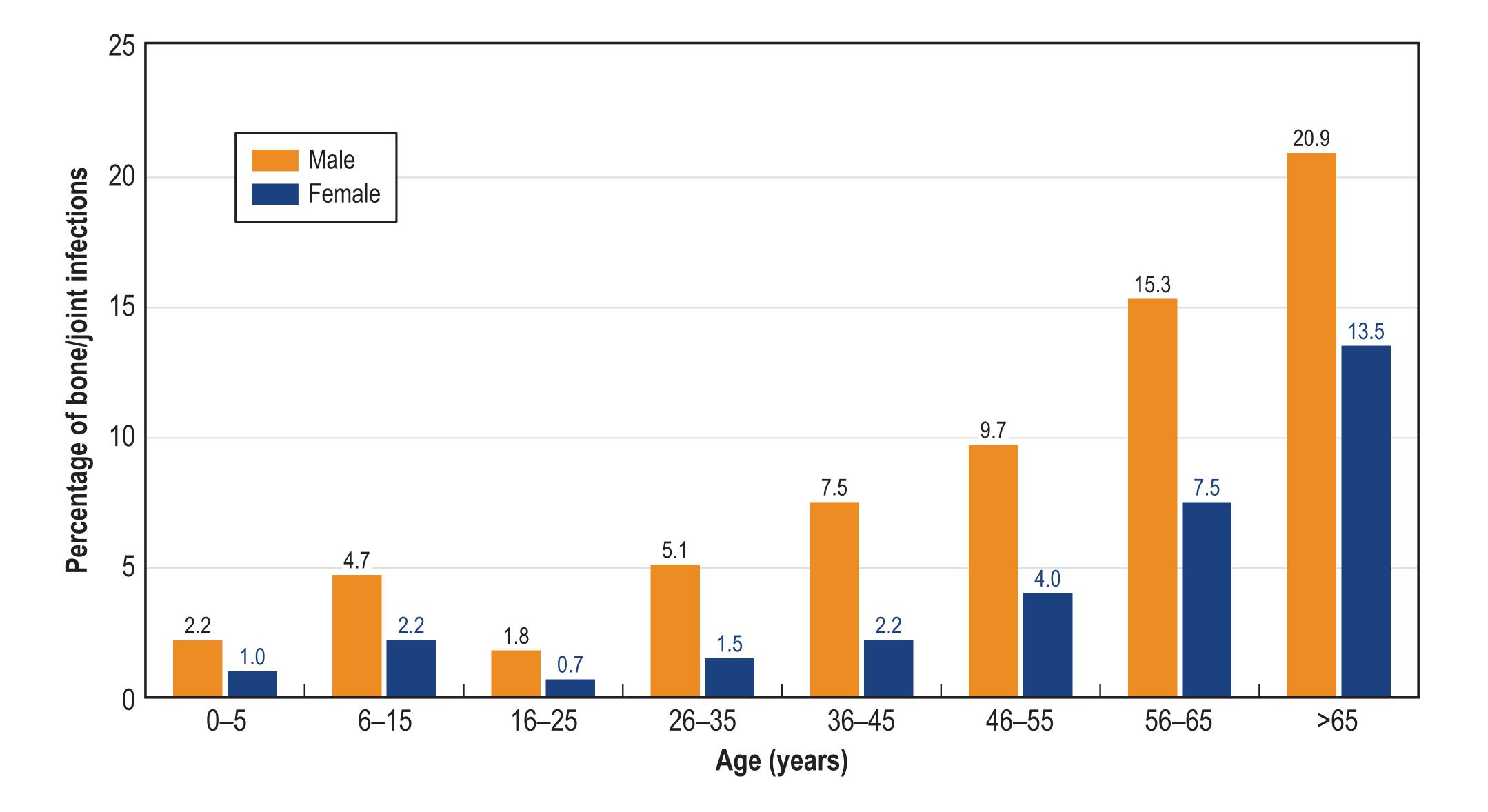
Figure 1. Occurrence of bacterial pathogens from bone/joint infections in the omadacycline surveillance program (*n*=876; 2015–2022)



K. oxytoca (9), K. pneumoniae (17), Morganella morganii (12), Proteùs mirabilis (20), P. vulgaris group (4), Providencia rettgeri (1), P. stuartii (3), Raoultella ornithinolytica (1), Serratia liquefa-° Contains *Enterococcus àvium* (1), *E. faecalis* (56), *E. fàecium* (7)

Contains Streptococcus agalactiae (51), S. anginosus (2), S. canis (2), S. dysgalactiae (22), S. gallolyticus (2), S. mitis group (1), S. pneumoniae (6), S. pyogenes (23).

Figure 2. Distribution of bone/joint infections by patient population



Acknowledgements

This study has been funded in part by federal funds from the U.S. Department of Health and Human Services, Administration for Strategic Preparedness and Response, Biomedical Advanced Research and Development Authority (BARDA), under Contract No. 75A50120C00001 and Paratek Pharmaceuticals, Inc.

This study and poster presentation were also funded, in part, by Paratek Pharmaceuticals, Inc.

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Contains Haemophilus influenzae (1), H. parainfluenzae (5) Contains Acinetobacter baumannii-calcoaceticus species complex (11), A. Iwoffii (1), A. radioresistens (1), Pseudomonas aeruginosa (41), Stenotrophomonas maltophilia (3). Contains Staphylococcus capitis (3), S. caprae (6), S. epidermidis (25), S. haemolyticus (7), S. hominis (1), S. lugdunensis (10), S. simulans (2)