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Evaluation of Daptomycin Activity Tested against 34,603 Bacterial Strains from Hospitalized Patients: Summary of a Four-Year Surveillance Program for North America and Europe (2002-2005)

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ABSTRACT

Background: Daptomycin (DAP) was approved by the US-FDA for the treatment of skin and skin structure infections (SSSI) in Sep/03 and has recently been approved for the treatment of *S. aureus* (SA) bacteremia. We report the results for 4 years of the Daptomycin Surveillance Program.

Methods: Consecutive, non-duplicate bacterial isolates (prevalence format) were collected from 2002 to 2005 from patients with documented infections in 41 medical centers in North America (NA) and 31 in Europe (EU). The isolates were collected by site of infection according to the study protocol and susceptibility (S) tested against >30 antimicrobials by broth microdilution methods following CLSI guidelines. Ca^{++} content of the broth was adjusted (50 mg/L) for testing DAP.

Results: A total of 34,603 Gram-positive (GP) isolates were evaluated. They were mainly from bacteremia (22,365 strains; 65%) and SSSI (5,857; 17%). The activity of DAP against top pathogens is summarized in the table:

Organism (no. tested: NA/EU)	DAP Activity (NA/EU) MIC_{50}	MIC_{90}	Highest MIC	%S	Isolates non-S
S. aureus (SA; 10,917/7,588)	0.25/0.25	0.5/0.5	2/2	99.95/99.97	5/2
Cogulase-negative staphylococci (CoNS; 2,138/2,883)	0.25/0.25	0.5/0.5	2/4	99.81/99.97	4/1
E. faecalis (2,905/1,794)	0.5/0.5	1/1	8/4	99.97/100.00	1/0
E. faecium (1,806/697)[a]	2/2	4/4	8/8	99.39/99.71	11/2
Beta-haemolytic streptococci (ßHS; 1,237/1,099)	≤0.12/≤0.12	0.25/0.25	0.5/0.5	100.0/100.0	0/0
Viridans group streptococci (VGS; 429/535)	0.25/0.25	0.5/0.5	2/2	99.76/99.44	1/3

a. There is no FDA DAP breakpoint for *E. faecium*.

Only 30 DAP-non-S strains (0.09%) were observed, and the vast majority (29; 96.7%) had a DAP MIC one log_2 dilution above the S breakpoint. No significant year-to-year variation in DAP activity was observed. Oxacillin (OXA) R rates among SA were 45.3% in NA and 27.6% in EU, while VAN R rates among enterococci (VRE) were 30.8% in NA and 5.9% in EU. DAP was also very potent against VRE (1,736 strains; $MIC_{50/90}$, 2/4 µg/ml) with 99.4% S in both NA and EU.

Conclusions: DAP was highly active against an extensive collection of clinically important GP pathogens. Decreased S to DAP remains extremely rare after more than 2 years of clinical use in NA and non-S isolates (0.09%) usually have DAP MIC only slightly elevated (1 log_2 dilution above the S breakpoint).

INTRODUCTION

The Gram-positive cocci occupy a prominent position in the hierarchy of pathogenic microbes due to the frequency of occurrence, innate virulence of species such as *Staphylococcus aureus*, enterococci, *Streptococcus pneumoniae*, and the ß-haemolytic streptococci, and the propensity for many of these pathogens to develop multidrug-resistant (MDR) antimicrobial susceptibility profiles.

Daptomycin is a novel lipopeptide antimicrobial agent designed specifically for the treatment of drug-resistant Gram-positive bacterial infections. Daptomycin has been shown to be active against *S. aureus* resistant to methicillin (oxacillin), linezolid, and quinupristin/dalfopristin, vancomycin-resistant enterococci (VRE), and macrolide-resistant streptococci. It is important to note that the in vitro activity of daptomycin is dependent upon the calcium content of the culture medium, making accurate testing of this agent challenging for clinical microbiology laboratories.

Daptomycin was approved by the United States Food and Drug Administration (US-FDA) and by the European Medicine Agency (EMEA) for the treatment of complicated skin and skin structure infections caused by oxacillin-susceptible and –resistant *S. aureus*, and groups A and B ß-haemolytic streptococci with a daptomycin MIC breakpoint of ≤1 µg/ml, and for vancomycin-susceptible *Enterococcus faecalis* with a susceptible breakpoint of ≤4 µg/ml. Furthermore, this compound has also been recently approved by the US-FDA for the treatment of *S. aureus* bacteremia, including right-sided endocarditis.

The Daptomycin Surveillance Program was implemented in 2002 with the objective of monitoring the in vitro activity of daptomycin and comparator agents. The program has been performed in two geographic regions (North America and Europe). In the present study, we evaluated the in vitro activity of daptomycin tested against recent clinical isolates collected in North American and European medical centers in the years 2002 through 2005. We also provide an analysis of the trends in daptomycin MIC values for *S. aureus* over the four-year time period.

MATERIALS AND METHODS

Bacterial strains: A total of 34,603 strains were evaluated, 19,615 strains from 40 medical centers in North America (35 in the US and 5 in Canada) and 14,988 strains from 30 medical centers in Europe (13 countries). In addition, the daptomycin MIC distribution by year was compared for 9,945 isolates of *S. aureus* from the US and 7,368 isolates from Europe. The strains were isolated mainly from bloodstream and skin and soft tissue infections from hospitalized patients. Only one bacterial strain per patient was included in the study.

Susceptibility testing: Daptomycin and comparator agents were tested in validated microdilution panels manufactured by TREK Diagnostics (Cleveland, OH) according to the Clinical and Laboratory Standards Institute guidelines. The test medium was Mueller-Hinton broth adjusted to contain physiologic levels of calcium (50 µg/ml) when testing daptomycin. US-FDA and CLSI approved daptomycin susceptible breakpoints of ≤1 µg/ml for staphylococci and streptococci and ≤4 µg/ml for enterococci were used to categorize these Gram-positive organisms as susceptible. The following quality control organisms were concurrently tested: *E. faecalis* ATCC 29212, *S. aureus* ATCC 29213 and *Streptococcus pneumoniae* ATCC 49619.

RESULTS

- Daptomycin MIC values ranged from ≤0.12 to 2 µg/ml among 18,505 *S. aureus* strains tested (MIC_{50}, 0.25 µg/ml; MIC_{90}, 0.5 µg/ml), and 99.96% of isolates tested were inhibited at ≤1 µg/ml (Tables 1 and 2). Only seven strains showed an elevated MIC value (2 µg/ml), five from North America and two from Europe.
- Among CoNS (5,019 strains tested; MIC_{50}, 0.25 µg/ml; MIC_{90}, 0.5 µg/ml), daptomycin MIC values ranged from ≤0.12 to 4 µg/ml (99.90% susceptible). Only five strains with elevated MIC values were observed, four strains with daptomycin MIC of 2 µg/ml in North America (Table 1) and one strain with a reproducible daptomycin MIC of 4 µg/ml in Europe (Table 2).
- Oxacillin-susceptible and -resistant staphylococci showed very similar daptomycin MIC distributions (Tables 1 and 2).
- Among the enterococci, 99.9% of vancomycin-susceptible (MIC_{50}, 1 µg/ml; MIC_{90}, 2 µg/ml) and 99.4% of vancomycin-resistant (MIC_{50}, 2 µg/ml; MIC_{90}, 4 µg/ml) isolates were daptomycin-susceptible at ≤4 µg/ml.
- ß-haemolytic streptococci (2,336 strains tested) showed very low daptomycin MIC values (MIC_{50}, ≤0.12 µg/ml; MIC_{90}, 0.25 µg/ml; 100.0% susceptible); while 99.6% of viridans group streptococci were inhibited at ≤1 µg/ml (Tables 1 and 2).
- Oxacillin-susceptible *S. aureus* showed susceptibility rates >90% for most antimicrobials tested, except erythromycin (71.3-85.2% susceptible), whereas oxacillin-resistant strains showed high rates of co-resistance to many antimicrobials evaluated.
- Daptomycin was highly active against *E. faecalis* (MIC_{50}, 0.5 µg/ml and MIC_{90}, 1 µg/ml; >99.9% susceptible). Ampicillin (99.2% susceptible), teicoplanin (97.8-98.1% susceptible) and linezolid (99.8-99.9% susceptible) were also highly active against *E. faecalis* (Table 3).
- Daptomycin (99.4-99.7% susceptible) and linezolid (98.8-100.0% susceptible) were the most active agents tested against *E. faecium*, followed by chloramphenicol (77.6-97.4% susceptible) and quinupristin/dalfopristin (77.0-92.0% susceptible; Table 3).
- Vancomycin resistance rates were high among *E. faecium*, especially in North America where only 22.8% of the isolates were susceptible to this compound. Daptomycin and linezolid were the only compounds remaining highly active (>98% susceptible) against both vancomycin-susceptible and -resistant enterococci (Table 3).
- The MIC distribution for US isolates of *S. aureus* was remarkably similar over time with a range of ≤0.12 to 2 µg/ml, and MIC_{50} and MIC_{90} of 0.25 and 0.5 µg/ml, respectively. The apparent one-dilution shift to a higher MIC (0.25 to 0.5 µg/ml) observed in 2004 was not observed in 2005, and the MIC distribution in 2005 was essentially the same as that in 2002 (Table 4). Likewise, there were no significant variations in the MIC results for the quality control strains tested in the four-year period.

Table 1. Daptomycin MIC population distributions for Gram-positive organisms isolated in North America, 2002-2005.

Organism (no. tested)	Occurrences at MIC in µg/ml (cumulative %): ≤0.12	0.25	0.5	1	2	4	8
S. aureus							
Oxacillin-susceptible (5,970)	314 (5.3)	4,185 (75.4)	1,447 (99.6)	21 (99.9)	3 (100.0)		
Oxacillin-resistant (4,947)	71 (1.4)	2,869 (59.4)	1,961 (99.1)	44 (99.9)	2 (100.0)		
CoNS							
Oxacillin-susceptible (448)	44 (9.8)	223 (59.6)	160 (95.3)	20 (99.8)	1 (100.0)		
Oxacillin-resistant (1,688)	125 (7.4)	831 (56.6)	669 (96.3)	60 (99.8)	3 (100.0)		
Enterococci							
Vancomycin-susceptible (3,336)	56 (1.7)	187 (7.3)	1,341 (47.5)	1,265 (85.4)	350 (95.9)	132 (99.9)	5 (100.0)
Vancomycin-resistant (1,560)	6 (0.4)	22 (1.8)	122 (9.6)	283 (27.8)	800 (79.0)	317 (99.4)	10 (100.0)
E. faecalis (2,905)	39 (1.3)	190 (7.9)	1,352 (54.4)	1,183 (95.1)	128 (99.6)	12 (99.9)	1 (100.0)
E. faecium (1,806)	11 (0.6)	8 (1.1)	69 (4.9)	301 (21.5)	989 (76.3)	417 (99.4)	11 (100.0)
ß-haemolytic streptococci (1,237)	908 (73.4)	296 (97.3)	33 (100.0)				
Viridans group streptococci (429)	144 (33.8)	132 (64.6)	114 (91.1)	37 (99.8)	1 (100.0)		

Table 2. Daptomycin MIC population distributions for Gram-positive organisms isolated in Europe, 2002-2005.

Organism (no. tested)	Occurrences at MIC in µg/ml (cumulative %): ≤0.12	0.25	0.5	1	2	4	8
S. aureus							
Oxacillin-susceptible (5,496)	235 (4.3)	3,896 (75.2)	1,337 (99.5)	27 (>99.9)	1 (100.0)		
Oxacillin-resistant (2,092)	44 (2.1)	1,130 (56.1)	873 (97.8)	44 (>99.9)	1 (100.0)		
CoNS							
Oxacillin-susceptible (715)	92 (12.9)	384 (66.6)	211 (96.1)	27 (99.9)	0 (99.9)	1 (100.0)	
Oxacillin-resistant (2,168)	152 (7.0)	1,115 (58.4)	829 (96.7)	72 (100.0)			
Enterococci							
Vancomycin-susceptible (2,426)	21 (0.9)	94 (4.7)	850 (39.8)	899 (76.8)	379 (92.5)	182 (>99.9)	1 (100.0)
Vancomycin-resistant (176)	0 (0.0)	4 (2.3)	27 (17.6)	39 (39.8)	78 (84.1)	27 (99.4)	1 (100.0)
E. faecalis (1,794)	12 (0.7)	90 (5.7)	827 (51.8)	787 (95.7)	72 (99.7)	6 (100.0)	
E. faecium (697)	4 (0.6)	5 (1.3)	24 (4.7)	121 (22.1)	365 (73.0)	186 (99.7)	2 (100.0)
ß-haemolytic streptococci (1,099)	903 (82.2)	179 (98.5)	17 (100.0)				
Viridans group streptococci (535)	186 (34.8)	168 (66.2)	137 (91.8)	41 (99.4)	3 (100.0)		

Table 3. Analysis of daptomycin and comparator agents against staphylococci, enterococci and streptococci from North America (NA) and Europe (EU), 2002-2005.

Organism/antimicrobial agent tested (no. tested; NA/EU)	MIC in µg/ml (NA / EU): 50%	90%	Category[a] (NA / EU): % Susceptible	% Resistant
S. aureus				
Oxacillin-susceptible (5,970 / 5,496)				
Daptomycin	0.25 / 0.25	0.5 / 0.5	>99.9 / >99.9	- / -
Clindamycin	≤0.25 / ≤0.25	≤0.25 / ≤0.25	94.2 / 97.0	5.5 / 2.8
Erythromycin	0.25 / 0.25	>8 / >8	71.3 / 85.2	23.6 / 11.6
Levofloxacin	0.25 / 0.25	0.5 / 0.5	91.9 / 94.0	7.5 / 5.6
Tetracycline	≤4 / ≤4	≤4 / ≤4	96.3 / 93.5	3.1 / 6.1
Trimethoprim/sulfamethoxazole	≤0.5 / ≤0.5	≤0.5 / ≤0.5	98.3 / 99.3	1.7 / 0.7
Teicoplanin	≤2 / ≤2	≤2 / ≤2	100.0 / 100.0	0.0 / 0.0
Vancomycin	1 / 1	1 / 1	100.0 / 100.0	0.0 / 0.0
Linezolid	2 / 2	2 / 2	100.0 / 100.0	- / -
Oxacillin-resistant (4,947 / 2,092)				
Daptomycin	0.25 / 0.25	0.5 / 0.5	>99.9 / >99.9	- / -
Clindamycin	>2 / 0.5	>2 / >2	42.9 / 50.3	57. / 49.5
Erythromycin	>8 / >8	>8 / >8	4.7 / 24.6	81.0 / 63.3
Levofloxacin	>4 / >4	>4 / >4	18.4 / 8.4	79.8 / 88.4
Tetracycline	≤4 / ≤4	≤4 / >8	92.9 / 77.1	6.8 / 21.2
Trimethoprim/sulfamethoxazole	≤0.5 / ≤0.5	≤0.5 / 1	96.4 / 93.5	3.6 / 6.5
Teicoplanin	≤2 / ≤2	≤2 / ≤2	100.0 / 99.9	0.0 / 0.0
Vancomycin	1 / 1	1 / 1	100.0 / 100.0	0.0 / 0.0
Linezolid	2 / 2	2 / 2	100.0 / 100.0	- / -
CoNS				
Oxacillin-susceptible (448 / 715)				
Daptomycin	0.25 / 0.25	0.5 / 0.5	99.8 / 99.9	- / -
Clindamycin	≤0.25 / ≤0.25	0.5 / ≤0.25	90.2 / 95.2	9.4 / 4.1
Erythromycin	0.25 / 0.25	>8 / >8	59.4 / 69.5	33.7 / 21.4
Levofloxacin	0.25 / 0.25	>4 / 2	84.2 / 89.5	15.0 / 8.8
Tetracycline	≤2 / ≤2	4 / >8	90.4 / 84.7	8.7 / 14.7
Trimethoprim/sulfamethoxazole	≤0.5 / ≤0.5	>2 / 2	84.6 / 90.0	15.4 / 10.0
Teicoplanin	≤2 / ≤2	4 / 4	98.0 / 98.2	0.4 / 0.0
Vancomycin	1 / 1	2 / 2	100.0 / 100.0	0.0 / 0.0
Linezolid	1 / 1	1 / 1	100.0 / 100.0	- / -
Oxacillin-resistant (1,688 / 2,168)				
Daptomycin	0.25 / 0.25	0.5 / 0.5	99.8 / 100.0	- / -
Clindamycin	≤0.25 / ≤0.25	>8 / >8	50.1 / 64.2	49.1 / 35.3
Erythromycin	>8 / >8	>8 / >8	20.8 / 28.5	68.4 / 56.8
Levofloxacin	4 / 4	>4 / >4	34.9 / 31.0	61.0 / 69.0
Tetracycline	≤2 / ≤2	>8 / >8	86.6 / 80.8	12.6 / 18.2
Trimethoprim/sulfamethoxazole	2 / 2	>2 / >2	53.3 / 51.4	46.7 / 48.6
Teicoplanin	≤2 / ≤2	8 / 8	96.6 / 97.1	0.7 / 0.6
Vancomycin	1 / 1	2 / 2	100.0 / 100.0	0.0 / 0.0
Linezolid	1 / 1	1 / 1	99.9 / 100.0	- / -
Enterococci				
Vancomycin-susceptible (3,336 / 2,426)				
Daptomycin	1 / 1	2 / 2	99.9 / >99.9	- / -
Ampicillin	≤1 / 2	>16 / >16	88.4 / 77.9	11.6 / 22.1
Chloramphenicol	8 / 8	>16 / >16	86.5 / 74.3	12.0 / 21.8
Levofloxacin	1 / 1	>4 / >4	56.4 / 58.8	42.4 / 38.0
Quinupristin/dalfopristin	>2 / >2	>2 / >2	11.2 / 19.1	82.3 / 70.8
Gentamicin (HL)[b]	≤500 / ≤500	>1000 / >1000	73.6 / 68.5	26.4 / 31.5
Streptomycin (HL)[b]	≤1000 / ≤1000	>2000 / >2000	73.1 / 58.4	26.9 / 41.6
Teicoplanin	≤2 / ≤2	≤2 / ≤2	100.0 / 100.0	0.0 / 0.0
Linezolid	1 / 1	2 / 2	99.8 / >99.9	0.1 / 0.0
Vancomycin-resistant (1,560 / 176)				
Daptomycin	2 / 2	4 / 4	99.4 / 99.4	- / -
Ampicillin	>16 / >16	>16 / >16	9.9 / 28.1	90.1 / 71.9
Chloramphenicol	8 / 8	8 / 16	95.8 / 80.3	2.5 / 8.8
Levofloxacin	>4 / >4	>4 / >4	1.5 / 17.6	98.1 / 81.3
Quinupristin/dalfopristin	1 / 1	2 / 2	86.9 / 58.0	10.0 / 34.1
Gentamicin (HL)	≤500 / >1000	>1000 / >1000	58.9 / 40.9	41.1 / 59.1
Streptomycin (HL)	>2000 / >2000	>2000 / >200	32.4 / 39.2	67.6 / 60.8
Teicoplanin	>16 / >16	>16 / >16	14.8 / 26.7	73.7 / 62.5
Linezolid	1 / 1	2 / 2	98.5 / 100.0	0.9 / 0.0
E. faecalis (2,905 / 1,794)				
Daptomycin	0.5 / 0.5	1 / 1	>99.9 / 100.0	- / -
Ampicillin	≤1 / ≤1	2 / 4	99.2 / 99.2	0.8 / 0.8
Chloramphenicol	8 / 8	>16 / >16	84.1 / 73.1	14.6 / 26.4
Levofloxacin	1 / 1	>4 / >4	57.7 / 68.3	41.6 / 30.7
Quinupristin/dalfopristin	>2 / >2	>2 / >2	1.1 / 1.6	95.8 / 92.2
Gentamicin (HL)	≤500 / ≤500	>1000 / >1000	68.4 / 67.5	31.6 / 32.5
Streptomycin (HL)	≤1000 / ≤1000	>2000 / >2000	71.4 / 61.8	28.6 / 38.2
Teicoplanin	≤2 / ≤2	≤2 / ≤2	97.8 / 98.1	2.1 / 1.8
Vancomycin	1 / 1	2 / 2	95.3 / 97.8	4.2 / 2.1
Linezolid	1 / 1	2 / 2	99.8 / 99.9	0.2 / 0.0
E. faecium (1,806 / 697)				
Daptomycin	2 / 2	4 / 4	99.4 / 99.7	- / -
Ampicillin	>16 / >16	>16 / >16	5.2 / 13.1	94.8 / 86.9
Chloramphenicol	8 / 8	8 / 16	97.4 / 77.6	0.5 / 7.9
Levofloxacin	>4 / >4	>4 / >4	5.0 / 22.5	93.7 / 69.9
Quinupristin/dalfopristin	1 / 1	1 / >2	92.0 / 72.0	2.4 / 12.6
Gentamicin (HL)	≤500 / ≤500	>1000 / >1000	66.9 / 62.1	33.1 / 37.9
Streptomycin (HL)	>2000 / >2000	>2000 / >200	39.3 / 42.9	60.7 / 57.1
Teicoplanin	>16 / ≤2	>16 / >16	30.5 / 87.2	59.9 / 10.3
Vancomycin	>16 / 1	>16 / >16	22.8 / 82.2	76.2 / 15.9
Linezolid	1 / 1	2 / 2	98.8 / 100.0	0.7 / 0.0
ß-haemolytic streptococci (1,237 / 1,099)				
Daptomycin	≤0.06 / ≤0.06	0.25 / 0.25	100.0 / 100.0	- / -
Penicillin	≤0.015 / ≤0.015	0.06 / 0.06	100.0 / 100.0	- / -
Clindamycin	≤0.25 / ≤0.25	≤0.25 / ≤0.25	92.7 / 93.8	7.1 / 5.7
Erythromycin	≤0.06 / ≤0.06	4 / 8	78.4 / 81.4	21.4 / 18.2
Levofloxacin	0.5 / 0.5	1 / 1	98.8 / 99.5	0.9 / 0.4
Quinupristin/dalfopristin	≤0.25 / ≤0.25	0.5 / 0.5	100.0 / 100.0	0.0 / 0.0
Tetracycline	8 / ≤2	>8 / >8	43.4 / 53.8	50.3 / 40.8
Vancomycin	0.5 / 0.25	0.5 / 0.5	100.0 / 100.0	- / -
Linezolid	1 / 1	1 / 1	100.0 / 100.0	- / -
Viridans group streptococci (429 / 535)				
Daptomycin	0.25 / 0.25	0.5 / 0.5	99.8 / 99.4	- / -
Penicillin	0.06 / 0.06	0.5 / 2	77.6 / 75.1	2.8 / 8.0
Clindamycin	≤0.25 / ≤0.25	≤0.25 / >2	94.2 / 85.6	5.8 / 13.1
Erythromycin	≤0.25 / ≤0.25	4 / 8	57.3 / 60.2	39.9 / 35.5
Levofloxacin	1 / 1	2 / 1	94.9 / 98.1	4.7 / 1.9
Quinupristin/dalfopristin	0.5 / 0.5	1 / 1	99.1 / 98.7	0.0 / 0.0
Tetracycline	≤2 / ≤2	>8 / >8	60.4 / 58.9	28.9 / 30.3
Vancomycin	0.5 / 0.5	1 / 1	100.0 / 100.0	- / -
Linezolid	1 / 1	1 / 1	100.0 / 100.0	- / -

a. Criteria as published by the CLSI.
b. HL = high-level resistance.

Table 4. Geographic and temporal trends in daptomycin MIC distributions for *Staphylococcus aureus* isolates from the United States (US) and Europe (2002-2005).

Year	Country (no. tested)	% of population at each MIC (µg/ml):[a] ≤0.12	0.25	0.5	1	2
2002	US (1,829)	3.5	68.2	27.8	0.5	0.1
	Europe (177)	6.2	66.7	28.8	1.1	
2003	US (1,648)	5.7	75.0	18.9	0.4	
	Europe (2,499)	5.6	77.2	16.6	0.6	<0.1
2004	US (2,855)	1.5	50.6	47.1	1.1	0.1
	Europe (2,166)	1.8	54.5	42.0	1.6	<0.1
2005	US (3,613)	3.2	66.8	29.4	0.6	0.1
	Europe (2,526)	3.1	65.4	30.7	0.7	

a. MIC results determined by reference methods.

CONCLUSIONS

- Daptomycin was highly active against *S. aureus*. Only 7 of 18,505 (0.04%) isolates tested were found to have daptomycin MIC values greater than 1 µg/ml (all were 2 µg/ml) with no significant trend towards higher MIC results over time in either geographic region.
- The minor variation in potency detected in 2004 was essentially the same among isolates from a region where daptomycin was used clinically (North America) and among isolates from a region where the drug was largely unavailable (Europe). Such a small variation may simply be spurious or more likely attributable to:
  a) low calcium content media used for testing in 2004, or
  b) manufacture production changes in panel drying methods, or
  c) potency issues of the daptomycin dry powder lots used to produce the testing panels.

  Regardless of the underlying cause, it does not appear that either a spontaneous or selected subpopulation of *S. aureus* with reduced susceptibility to daptomycin has occurred in North America or Europe during 2004.
- The results of this survey document the continued high potency and wide spectrum of daptomycin against the targeted Gram-positive pathogens.

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