

1 *In vitro* Antimicrobial Susceptibility of *Staphylococcus pseudintermedius* isolates of human
2 and animal origin

3 Romney M. Humphries^{1*}, Max T. Wu², Lars F. Westblade³, Amy E. Robertson⁴, Carey-Ann D.
4 Burnham⁵, Meghan A. Wallace⁵, Eileen M. Burd^{6,7}, Sara Lawhon⁸, and Janet A. Hindler¹

5 ¹UCLA David Geffen School of Medicine, Los Angeles, CA

6 ²Landstuhl Regional Medical Center, Landstuhl, Deutschland

7 ³Weill Cornell Medical College, New York, NY

8 ⁴New-York Presbyterian Hospital, Weill Cornell Medical Center, New York, NY

9 ⁵Washington University School of Medicine, St. Louis, MO

10 ⁶ Emory University School of Medicine, Atlanta, GA

11 ⁷ Emory Antibiotic Resistance Center, Atlanta, GA

12 ⁷Veterinary Medicine and Biomedical Sciences, Texas A&M University, TX

13

14 *Corresponding author

15 Mailing address: 10833 Le Conte Avenue. Brentwood Annex, Los Angeles, CA 90095.

16 Email: rhumphries@mednet.ucla.edu

17

18

19 ABSTRACT

20 Minimum inhibitory concentration (MIC) results for 115 *Staphylococcus*
21 *intermedius* group isolates are presented. 33% were methicillin resistant, among which
22 51.4% were susceptible to doxycycline, 29.7% to clindamycin and 21.6% to trimethoprim-
23 sulfamethoxazole. All isolates were susceptible to ceftaroline, daptomycin, linezolid,
24 nitrofurantoin, quinupristin-dalfopristin, rifampin, tigecycline, and vancomycin. 82.6%,
25 67.8% and 23.5% of all isolates were susceptible to ciprofloxacin, erythromycin, and
26 penicillin. No isolates harbored *mupA* or *qacA/B* genes, suggestive of no resistance to
27 mupirocin or chlorhexidine.

28 TEXT

29 The *Staphylococcus intermedius* group (SIG) is comprised of *Staphylococcus*
30 *intermedius*, *Staphylococcus pseudintermedius*, and *Staphylococcus delphini*. These Gram-
31 positive cocci are tube coagulase positive and slide coagulase negative (except *S.*
32 *intermedius*), and may be misidentified as *Staphylococcus aureus* by clinical laboratories that
33 test human specimens (1). A colonizer of the nares and anal mucosa of cats and dogs, the
34 presence of *S. pseudintermedius* is increasingly being recognized in human diagnostic
35 specimens (2). This may in part be due to improved diagnostic technologies, such as matrix-
36 assisted laser desorption ionization time of flight mass spectrometry (MALDI-TOF MS) now
37 being used in many clinical laboratories. *S. pseudintermedius* have been documented to
38 cause invasive infections in humans, including brain abscesses, endocarditis, and
39 bacteremia (3). Methicillin resistance among *S. pseudintermedius* isolated from dogs is
40 increasing (4), with rates of up to 47% in some regions of the world (5). This resistance is
41 predominantly due to the dissemination of the ST71 clonal lineage in Europe and ST68
42 clonal lineage in North America (4). Methicillin resistant (MR) isolates often display

43 resistance to other classes of antimicrobials used in veterinary medicine, including
44 aminoglycosides, fluoroquinolones, lincosamides, macrolides, tetracyclines and also to
45 chloramphenicol and trimethoprim-sulfamethoxazole (SXT) (6). However, there are limited
46 susceptibility data available for *S. pseudintermedius* with antimicrobials used for humans.
47 We recently conducted a study to evaluate oxacillin and cefoxitin disk and minimum
48 inhibitory concentration (MIC) results as predictors of methicillin resistance (encoded by
49 *mecA*) in a collection of 115 SIG isolated from human and veterinary specimens associated
50 with clinical infections. This study documented that cefoxitin testing, which is
51 recommended by the Clinical and Laboratories Standards Institute (CLSI) to predict
52 methicillin resistance for other species of staphylococci, is a poor predictor of *mecA* in SIG,
53 whereas both oxacillin disk and MIC tests accurately detect *mecA*-mediated oxacillin
54 resistance in these isolates (7). As a result of our study, CLSI published *S. pseudintermedius*-
55 specific oxacillin breakpoints in the 26th edition of the M100S standard (8). The present
56 study documents the results of antimicrobial susceptibility testing (AST) for this collection
57 of 115 SIG isolates, including 111 isolates of *S. pseudintermedius* (45 from human, 56 from
58 canine, 7 from feline, 2 from avian and 1 from porcine sources) and 4 isolates of *S. delphini*
59 (3 from equine and 1 from avian sources).

60 Bacterial isolates were described in our previous article (7). AST was performed
61 according to the CLSI reference broth microdilution MIC method (8), using panels prepared
62 in-house with cation-adjusted Mueller Hinton Broth (MHB). MHB was supplemented with
63 50 mg/L CaCl₂ for daptomycin testing and 2% NaCl for oxacillin testing (9). Fifteen
64 antimicrobial agents were tested (Table 1). BMD tests were read following 16-20 hours
65 incubation at 35°C in ambient air for all antimicrobials except oxacillin and vancomycin,
66 where the final reading was done following 24 hours' incubation. MIC results were
67 interpreted according to *Staphylococcus* spp. breakpoints listed in CLSI M100S 26th edition,

68 including use of the new oxacillin *S. pseudintermedius* breakpoints and ceftaroline and
69 vancomycin breakpoints for *S. aureus* (8). Because there are no CLSI tigecycline
70 breakpoints, the Food and Drug Administration (FDA) breakpoint for *S. aureus* was used. All
71 isolates with penicillin-susceptible MICs (≤ 0.12 $\mu\text{g}/\text{ml}$) were also tested by penicillin disk
72 diffusion using the standard CLSI method and examined for beta-lactamase production
73 using a BBL Cefinase™ disk (BD, Sparks MD). In addition to taking zone measurements, the
74 zone edges were evaluated for sharp versus fuzzy borders around the penicillin disks. Beta-
75 lactamase testing was performed using growth taken from the zone margin surrounding a
76 penicillin disk test on BBL Mueller Hinton agar (MHA, BD) after 16-18 hours' incubation.
77 *mecA* PCR and SCC*mec* typing was performed as described in our previous article (7).
78 Mupirocin resistance was determined by PCR for the *mupA* gene and chlorhexidine
79 resistance by PCR for the *qacA/B* gene, as described elsewhere (10).

80 MIC results obtained for the 115 isolates are shown in Table 1. Thirty-seven isolates
81 (32.2%) harbored the *mecA* gene, including 4 of human origin and 33 of veterinary origin.
82 Using the CLSI M100S 26th edition *Staphylococcus* spp. interpretive criteria, 33 of the 78
83 (42.3%) *mecA*-negative isolates had penicillin susceptible MICs of ≤ 0.12 $\mu\text{g}/\text{mL}$ (Table 1).
84 For 27/33 isolates, MICs were ≤ 0.06 $\mu\text{g}/\text{ml}$, penicillin zone measurements were susceptible
85 at ≥ 29 mm and induced nitrocefin tests were negative. 6/33 (18.2%) yielded a positive
86 induced nitrocefin test, indicating the presence of a beta-lactamase, including 5 human
87 isolates and 1 animal isolate. Six isolates demonstrated penicillin zones ≤ 28 mm (resistant)
88 and all had "sharp" zone edges. Five of these isolates had penicillin MICs of 0.12 $\mu\text{g}/\text{mL}$ and
89 1 isolate had a penicillin MIC of ≤ 0.03 $\mu\text{g}/\text{mL}$. Repeat testing in two laboratories confirmed
90 results. When the nitrocefin tests were performed using un-induced colonies (i.e. not from a
91 penicillin zone margin), variable results were obtained, with 0-4 of the 6 isolates yielding a
92 positive result in different laboratories, on different days when testing colonies grown on

93 BAP or on MHA. As such, a test for beta-lactamase production should be performed for all
94 penicillin-susceptible *S. pseudintermedius* isolates, as is done for other *Staphylococcus* spp.
95 Whether a penicillin zone edge test is sufficient for this purpose, or if an induced nitrocefin-
96 based test is needed, remains to be determined. However, in our limited analysis, the
97 penicillin zone edge test was 100% concordant with nitrocefin results obtained when
98 testing induced colonies. All isolates were susceptible to ceftaroline, the cephalosporin with
99 high affinity binding to PBP2a expressed by *mecA*.

100 With regards to the non-beta-lactam agents, significant differences were noted in
101 the percentage of methicillin-resistant isolates susceptible to doxycycline, SXT, and
102 clindamycin, as compared to what has been documented with contemporary isolates of *S.*
103 *aureus* (11). This constellation of multi-drug resistance is consistent with the multi-drug
104 resistant (MDR) *S. pseudintermedius* clones, ST68 and ST71, which harbor mutations within
105 *gyrA* and *griA* (conferring resistance to fluoroquinolones), as well as a TN5404-like
106 transposon element that harbors the *dfzG* (sulfamethoxazole resistance) and *ermB*
107 (clindamycin and erythromycin resistance) genes (4). Interestingly, differences were noted
108 in our collection based on the *SCCmec* type. Isolates with *SCCmec* V were more commonly
109 resistant to erythromycin and clindamycin (10/11 isolates, 90.9%), SXT (10/11 isolates,
110 90.9%), doxycycline (8/11 isolates, 72.7%) and ciprofloxacin (9/11 isolates, 81.8%) as
111 compared to those with *SCCmec* types IV or III. For *SCCmec* type IV, 4/8 (50.0%), 8/8
112 (100%), 1/8 (12.5%), and 0/8 (0.0%) isolates were resistant to these antimicrobials,
113 respectively. For isolates with *SCCmec* type III, 4/9 (44.4%), 2/9 (22.2%), 4/9 (44.4%) and
114 0/9 (0.0%) were resistant. Isolates of the MDR North American ST68 lineage harbor
115 *SCCmec* V, similar to the more resistant isolates in our collection (4).

116 Doxycycline susceptibility was 89.7% among *mecA*-negative isolates and only 51.4%
117 among *mecA*-positive isolates (Table 1). This is in striking contrast to doxycycline
118 susceptibility rates among human isolates of methicillin-resistant *S. aureus* (MRSA), which
119 were 96% among a collection of >4,000 isolates recovered from human diagnostic
120 specimens in 2010 (12). Doxycycline susceptibility rates were similarly high among
121 methicillin-resistant CoNS, at 94.1% in one study of 1,473 isolates (13). Our data are
122 consistent with previous studies that documented 31-38% doxycycline susceptibility
123 among methicillin-resistant *S. pseudintermedius* (MRSP) isolates from canine sources (14,
124 15). No difference was noted in susceptibility to doxycycline between human (n=5, 40.0%
125 susceptible) and veterinary (n=32, 53.1% susceptible) MRSP isolates in the present study.

126 Of note, canine-specific breakpoints for doxycycline have been proposed to
127 accommodate the pharmacokinetics of doxycycline doses used for dogs. The canine
128 breakpoints are ≤ 0.125 $\mu\text{g}/\text{mL}$ (susceptible), 0.25 $\mu\text{g}/\text{mL}$ (intermediate) and ≥ 0.5 $\mu\text{g}/\text{mL}$
129 (resistant), but these have yet to be published in the CLSI VET antimicrobial susceptibility
130 testing document (16). The lowest concentration of doxycycline tested in our study was 1
131 $\mu\text{g}/\text{mL}$, and as such we cannot estimate the effect these breakpoints would have on our
132 collection of isolates. However, 35% of *mecA*-positive and 10.2% of *mecA*-negative isolates
133 had MICs of 2 – 4 $\mu\text{g}/\text{mL}$, which are resistant by the canine breakpoints but susceptible by
134 the human breakpoints. Resistance to the tetracyclines is mediated through acquisition of
135 tetracycline resistance genes (*tet* genes), four of which have been identified among *S.*
136 *pseudintermedius* isolates. These are *tet(M)* and *tet(O)*, which mediate ribosomal protection,
137 and *tet(K)* and *tet(L)*, which encode efflux pumps. The most commonly occurring of these
138 are *tet(M)* and *tet(K)* in *S. pseudintermedius* (16, 17). Isolates that harbor none of these
139 genes typically have MICs ≤ 0.125 $\mu\text{g}/\text{mL}$ to doxycycline, whereas acquisition of the *tet(M)*
140 gene can be associated with MICs that are elevated, but below the 4 $\mu\text{g}/\text{mL}$ CLSI M100S 26th

141 edition susceptible breakpoint. Clinically, it is unclear whether such isolates that are
142 susceptible by the CLSI M100S 26th edition breakpoint and harbor a *tet* gene are associated
143 with treatment failures, but these isolates would be considered resistant by the proposed
144 veterinary breakpoint (16). The EUCAST susceptible breakpoint for doxycycline is ≤ 1
145 $\mu\text{g}/\text{mL}$ for human isolates of *Staphylococcus* spp. (www.eucast.org) and when applying this
146 breakpoint, only 18.1% of methicillin-resistant and 79.5% of methicillin-susceptible isolates
147 in our study would be doxycycline susceptible. Regardless, the *tet* genes are carried on
148 Tn5801 and Tn916 elements (6), the same as are found in human and veterinary isolates of
149 tetracycline-resistant *S. aureus* (18). The Tn916 *tet(M)* gene was found in all isolates of the
150 clonal complex (CC) 398 of *S. aureus*, suggesting this element was integrated into the
151 genome of the clone early and disseminated vertically. This may also be the case for the
152 ST71 and ST68 clonal lineages of *S. pseudintermedius*, and may account for the common
153 occurrence of doxycycline resistance in these isolates. Doxycycline resistance may also be
154 selected for through the common use of this agent for the treatment of pyoderma in small
155 animal veterinary medicine.

156 SXT susceptibility was only 21.6% among *mecA* positive isolates. In contrast, human
157 isolates of MRSA are typically susceptible to this agent; in 2013, 98.0% of isolates in a
158 collection of over 9,000 MRSA were susceptible to SXT (19). SXT susceptibility is lower
159 among coagulase-negative staphylococci. In the same study conducted in 2013 52.7% of
160 2,268 methicillin-resistant coagulase-negative staphylococci were susceptible to SXT (19).

161 All isolates in this study that were resistant to erythromycin were also resistant to
162 clindamycin and susceptibility rates for both agents were only 29.7% among MRSP (Table
163 1). Consequently, no inducible clindamycin resistance was observed, although an inducible
164 *erm* gene has been documented previously in *S. pseudintermedius* (20).

165 We documented 51.4% ciprofloxacin susceptibility in MRSP, which is similar to
166 what has been observed for MRSA and MR coagulase-negative *Staphylococcus* (CoNS)
167 isolates (19). However, this susceptibility rate is significantly higher than has been
168 documented in some studies of veterinary SIG isolates, where susceptibility rates as low as
169 2.7% have been reported using the same susceptible breakpoint of 1 µg/mL (21). A single
170 point mutation in topoisomerase II or IV genes confers fluoroquinolone resistance in *S.*
171 *pseudintermedius* (22).

172 All isolates were susceptible to ceftaroline, daptomycin, linezolid, nitrofurantoin,
173 quinupristin-dalfopristin, rifampin, tigecycline, and vancomycin. There are currently no
174 vancomycin breakpoints for the SIG, as the CLSI only publishes *S. aureus* and CoNS
175 breakpoints for this antimicrobial agent. However, unlike the CoNS, where the modal MIC
176 for vancomycin is 2.0 µg/mL, we found vancomycin MIC mode to be 1.0 µg/mL, similar to
177 what is documented for *S. aureus*. As such, it may be reasonable for clinical laboratories to
178 interpret vancomycin MICs using the more conservative *S. aureus* susceptible breakpoints
179 of ≤2.0 µg/mL when SIG is encountered, as compared to the ≤4 µg/mL breakpoint for CoNS
180 in the M100S or for *Staphylococcus* spp. in the VET01, CLSI standards. Similar to what has
181 been seen in other studies of SIG (23) we did not document any cases of high-level
182 mupirocin resistance among the isolates in this collection, nor did we detect the presence of
183 the *qacA/B* gene in any isolates, suggestive of the absence of chlorhexidine resistance in this
184 collection of isolates.

185 In summary, we present *in vitro* susceptibility results for a large collection of SIG
186 clinical isolates tested by the CLSI reference BMD MIC method. Laboratories should
187 carefully review susceptibility results for all coagulase-positive staphylococci and consider
188 using additional identification procedures, such as MALDI-TOF MS or an automated

189 instrument, for isolates that are doxycycline and/or SXT resistant, a phenotype common to
190 *S. pseudintermedius*, but unusual for *S. aureus*. This is important, as correct identification of
191 these isolates is critical to accurate testing of SIG with oxacillin to detect methicillin
192 resistance. Clinicians should be cognizant of the dramatic difference in SXT, clindamycin,
193 and doxycycline susceptibility between SIG and *S. aureus*, as these agents are commonly
194 prescribed as empiric therapy for MRSA in wound and skin structure infections. While
195 overall, susceptibility to these antimicrobials was higher in human than in animal isolates
196 (Table 1), this is likely due to the significantly higher proportion of *mecA*- positive isolates
197 in the veterinary collection, a bias of our data set. A second limitation of the present study is
198 the inclusion of only 4 *S. delphini* and 0 *S. intermedius* isolates; further data will determine if
199 susceptibility rates differ significantly for these isolates as compared to *S. pseudintermedius*.
200 It is worth noting, however, that *S. intermedius* is very infrequently isolated in veterinary or
201 human clinical laboratories, but rather is a constituent of the normal nares flora of the wild
202 pigeon (24).

203 **References**

- 204 1. **Borjesson S, Gomez-Sanz E, Ekstrom K, Torres C, Gronlund U.** 2015. *Staphylococcus*
205 *pseudintermedius* can be misdiagnosed as *Staphylococcus aureus* in humans with dog bite
206 wounds. *Eur J Clin Microbiol Infect Dis* **34**: 839-844.
- 207 2. **Lee J, Murray A, Bendall R, Gaze W, Zhang L, Vos M.** 2015. Improved detection of
208 *Staphylococcus intermedius* group in a routine diagnostic laboratory. *J Clin Microbiol* **53**:
209 961-963.
- 210 3. **Kelesidis T, Tsiodras S.** 2010. *Staphylococcus intermedius* is not only a zoonotic
211 pathogen, but may also cause skin abscesses in humans after exposure to saliva. *Int J Infect*
212 *Dis* **14**: e838-841.
- 213 4. **Perreten V, Kadlec K, Schwarz S, Gronlund Andersson U, Finn M, Greko C, Moodley**
214 **A, Kania SA, Frank LA, Bemis DA, Franco A, Iurescia M, Battisti A, Dulm B, Wagenaar**
215 **JA, van Duijkeren E, Weese JS, Fitzgerald JF, Rossano A, Guardabassi L.** 2010. Clonal
216 spread of methicillin-resistant *Staphylococcus pseudintermedius* in Europe and North
217 America: an international multicentre study. *J Antimicrob Chemother* **65**: 1145-1154.
- 218 5. **Feng Y, Tian W, Lin D, Luo Q, Zhou Y, Yang T, Deng Y, Liu YH, Liu JH.** 2012. Prevalence
219 and characterization of methicillin-resistant *Staphylococcus pseudintermedius* in pets from
220 South China. *Vet Microbiol* **160**: 517-524.
- 221 6. **McCarthy AJ, Harrison EM, Stanczak-Mrozek K, Leggett B, Waller A, Holmes MA,**
222 **Lloyd DH, Lindsay JA, Loeffler A.** (2015) Genomic insights into the rapid emergence and
223 evolution of MDR in *Staphylococcus pseudintermedius*. *J Antimicrob Chemother* **70**: 997-
224 1007.
- 225 7. **Wu MT, Burnham CA, Westblade LF, Dien Bard J, Lawhon SD, Wallace MA, Stanley T,**
226 **Burd E, Hindler J, Humphries RM.** 2015. Evaluation of oxacillin and cefoxitin disk and MIC

- 227 breakpoints for the prediction of methicillin resistance in human and veterinary isolates of
228 *Staphylococcus intermedius* group. J Clin Microbiol. In press
- 229 8. **CLSI**. 2016. Performance Standards for Antimicrobial Susceptibility Testing M100S, 26th
230 Ed. Wayne, PA: Clinical and Laboratory Standards Institute.
- 231 9. **CLSI**. 2012. Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria that Grow
232 Aerobically; Approved Standard, Ninth Edition. Wayne, PA: Clinical and Laboratory
233 Standards Institute.
- 234 10. **Fritz SA, Hogan PG, Camins BC, Ainsworth AJ, Patrick C, Martin MS, Krauss MJ,**
235 **Rodriguez M, Burnham CA**. 2013. Mupirocin and chlorhexidine resistance in
236 *Staphylococcus aureus* in patients with community-onset skin and soft tissue infections.
237 Antimicrob Agents Chemother **57**: 559-568.
- 238 11. **Richter SS, Diekema DJ, Heilmann KP, Dohrn CL, Crispell EK, Riahi F, McDanel JS,**
239 **Satola SW, Doern GV**. 2014. Activities of vancomycin, ceftaroline, and mupirocin against
240 *Staphylococcus aureus* isolates collected in a 2011 national surveillance study in the United
241 States. Antimicrob Agents Chemother **58**: 740-745.
- 242 12. **Jones RN, Stilwell MG, Wilson ML, Mendes RE**. 2013. Contemporary tetracycline
243 susceptibility testing: doxycycline MIC methods and interpretive criteria (CLSI and EUCAST)
244 performance when testing Gram-positive pathogens. Diagn Microbiol Infect Dis **76**: 69-72.
- 245 13. **Jones RN, Farrell DJ, Sader HS, Castanheira M**. 2011. Abstr. 21st ECCMID. Abstr. 944.
- 246 14. **Weese JS, Sweetman K, Edson H, Rousseau J**. 2013. Evaluation of minocycline
247 susceptibility of methicillin-resistant *Staphylococcus pseudintermedius*. Vet Microbiol **162**:
248 968-971.
- 249 15. **Hnot ML, Cole LK, Lorch G, Papich MG, Rajala-Schultz PJ, Daniels JB**. 2015.
250 Evaluation of canine-specific minocycline and doxycycline susceptibility breakpoints for

- 251 meticillin-resistant *Staphylococcus pseudintermedius* isolates from dogs. *Vet Dermatol* **26**:
252 334-e371.
- 253 16. **Maaland MG, Papich MG, Turnidge J, Guardabassi L.** 2013. Pharmacodynamics of
254 doxycycline and tetracycline against *Staphylococcus pseudintermedius*: proposal of canine-
255 specific breakpoints for doxycycline. *J Clin Microbiol* **51**: 3547-3554.
- 256 17. **Schwarz S, Roberts MC, Werckenthin C, Pang Y, Lange C.** 1998. Tetracycline
257 resistance in *Staphylococcus* spp. from domestic animals. *Vet Microbiol* **63**: 217-227.
- 258 18. **de Vries LE, Christensen H, Skov RL, Aarestrup FM, Agerso Y.** 2009. Diversity of the
259 tetracycline resistance gene tet(M) and identification of Tn916- and Tn5801-like (Tn6014)
260 transposons in *Staphylococcus aureus* from humans and animals. *J Antimicrob Chemother*
261 **64**: 490-500.
- 262 19. **Sader HS, Flamm RK, Jones RN.** 2013. Antimicrobial activity of ceftaroline tested
263 against staphylococci with reduced susceptibility to linezolid, daptomycin, or vancomycin
264 from U.S. hospitals, 2008 to 2011. *Antimicrob Agents Chemother* **57**: 3178-3181.
- 265 20. **Gold RM, Lawhon SD.** 2013. Incidence of inducible clindamycin resistance in
266 *Staphylococcus pseudintermedius* from dogs. *J Clin Microbiol* **51**: 4196-4199.
- 267 21. **Ruscher C, Lubke-Becker A, Semmler T, Wleklinski CG, Paasch A, Soba A, Stamm I,**
268 **Kopp P, Wieler LH, Walther B.** 2010. Widespread rapid emergence of a distinct
269 methicillin- and multidrug-resistant *Staphylococcus pseudintermedius* (MRSP) genetic
270 lineage in Europe. *Vet Microbiol* **144**: 340-346.
- 271 22. **Descloux S, Rossano A, Perreten V.** 2008. Characterization of new staphylococcal
272 cassette chromosome mec (SCCmec) and topoisomerase genes in fluoroquinolone- and
273 methicillin-resistant *Staphylococcus pseudintermedius*. *J Clin Microbiol* **46**: 1818-1823.
- 274 23. **Godbeer SM, Gold RM, Lawhon SD.** 2014. Prevalence of mupirocin resistance in
275 *Staphylococcus pseudintermedius*. *J Clin Microbiol* **52**: 1250-1252.

276 24. Sasaki T, Kikuchi K, Tanaka Y, Takahashi N, Kamata S, Hiramatsu K. 2007.
277 Reclassification of phenotypically identified *Staphylococcus intermediu* strains. *J Clin*
278 *Microbiol.* 45:2770-2778.
279
280

281

282 Table 1. MIC values of 15 antimicrobial agents for *Staphylococcus intermedius* group (n=115) when tested by CLSI reference broth
283 microdilution MIC method in CAMHB

Antimicrobial	Number of Isolates at MIC ($\mu\text{g/mL}$)										% susceptible				
	≤ 0.06	0.12	0.25	0.5	1	2	4	8	16	32	human	animal	<i>mecA</i> ⁻	<i>mecA</i> ⁺	All
Ceftaroline			115 ^a								100	100	100	100	100
Ciprofloxacin			94 ^a	1				20 ^b			91.1	77.1	97.4	51.4	82.6
Clindamycin			78 ^a		1				36 ^b		80.0	60.0	85.9	29.7	67.8
Daptomycin			115 ^a								100	100	100	100	100
Doxycycline					69		20	23	3 ^b		84.4	72.9	89.7	51.4	77.4
Erythromycin			78 ^a						37 ^b		80.0	60.0	85.9	29.7	67.8
Linezolid			1 ^a		63	50	1				100	100	100	100	100
Nitrofurantoin									114	1	100	100	100	100	100
Oxacillin			77 ^a		3 ^c	6	2	1	2	24 ^b	91.1	51.4	98.7	0	66.9
Penicillin	28	5	3	1	2			76 ^b			26.6 ^d	21.4 ^d	50	0	23.5 ^d
QDA					115 ^a						100	100	100	100	100
Rifampin					115 ^a						100	100	100	100	100
SXT				54 ^a	25	1	4	31 ^b			84.4	60.0	92.3	21.6	69.6
Tigecycline			115 ^a								100	100	100	100	100
Vancomycin			14 ^a		100	1					100	100	100	100	100

284

285 ^a MIC \leq value in column header; ^b value \geq value in column header; ^c includes 1 isolate that was *mecA* negative; ^d includes 5 human isolates
286 and 1 animal isolate that had penicillin susceptible MICs but were beta-lactamase positive

287 QDA, quinupristin-dalfopristin; SXT, trimethoprim-sulfamethoxazole

288 MIC values to left of vertical lines fall in the susceptible interpretive category; those to the right are in the intermediate or resistant
289 category