



# Cefiderocol Retains Antibiofilm Activity in Multidrug-Resistant Gram-Negative Pathogens

## Christine A. Pybus,<sup>a</sup> Christina Felder-Scott,<sup>b</sup> Victor Obuekwe,<sup>a</sup> David E. Greenberg<sup>a,c</sup>

<sup>a</sup>Department of Internal Medicine, Infectious Diseases and Geographic Medicine, University of Texas Southwestern Medical School, Dallas, Texas, USA <sup>b</sup>School of Health Professions, University of Texas Southwestern Medical School, Dallas, Texas, USA <sup>c</sup>Department of Microbiology, University of Texas Southwestern Medical School, Dallas, Texas, USA

ABSTRACT Cefiderocol is a siderophore cephalosporin with potent antibacterial activity against a broad range of Gram-negative pathogens, including multidrug-resistant strains. Siderophore antibiotics bind ferric iron and utilize iron transporters to cross the cell membrane. In the biofilm setting, where antibiotic resistance is high but iron scavenging is important, cefiderocol may have advantageous antimicrobial properties. In this study, we compared the antimicrobial activity of cefiderocol to that of seven commonly used antibiotics in well-characterized multidrugresistant pathogens and then determined their efficacy in the biofilm setting. MIC<sub>90</sub> values for cefiderocol were consistently lower than those of other antibiotics (ceftolozane-tazobactam, ceftazidime-avibactam, ceftazidime, piperacillin-tazobactam, imipenem, and tobramycin) in all strains tested. Cefiderocol treatment displayed a reduction in the levels of *Pseudomonas aeruginosa* biofilm (93%, P < 0.0001) superior to that seen with the other antibiotics (49% to 82%). Cefiderocol was generally as effective as or superior to the other antibiotics, depending on the pathogen-antibiotic combination, in reducing biofilm in other pathogens. There was a trend toward greater biofilm reduction seen with increased antibiotic dose or with increased frequency of antibiotic treatment. We conclude that cefiderocol effectively reduces biofilm and is a potent inhibitor of planktonic growth across a range of Gram-negative medically important pathogens.

KEYWORDS cefiderocol, Gram negatives, biofilms, multidrug resistance

**G**ram-negative pathogens worldwide are increasingly developing resistance to antibiotics commonly used to treat infections, including aminoglycosides, carbapenems, cephalosporins, fluoroquinolones, and polymyxins (1–5). Multiple mechanisms exist for microorganisms to evade antibiotic selective pressure. Horizontal gene transfer plays a significant role in multidrug resistance (MDR) (6). Plasmid-encoded extended-spectrum beta-lactamases hydrolyze cephalosporins and carbapenems in the periplasmic space, whereas plasmid-based MCR-1 mediates colistin resistance by cell membrane modification (7–9). In addition, mutations in porins may result in loss of outer membrane permeability to antibiotics, and upregulation and expression of drug efflux pumps can decrease retention of antibiotics (6, 10). Finally, antibiotic resistance is likely not easily lost due to compensatory mutations and horizontal gene transfer (11, 12). Altogether, nosocomial drug resistance is a significant problem that is only becoming worse.

The ability to form biofilm further compounds this problem. Biofilms ultimately increase antibiotic resistance due to a number of factors, including loss of permeability and the presence of slow-growing persister cells (13, 14). Biofilms are clinically relevant, contributing to drug-resistant infections of wounds, prosthetic joints, catheters, the

Citation Pybus CA, Felder-Scott C, Obuekwe V, Greenberg DE. 2021. Cefiderocol retains antibiofilm activity in multidrug-resistant Gram-negative pathogens. Antimicrob Agents Chemother 65:e01194-20. https://doi.org/10 .1128/AAC.01194-20.

**Copyright** © 2021 Pybus et al. This is an openaccess article distributed under the terms of the Creative Commons Attribution 4.0 International license.

Address correspondence to David E. Greenberg, David.Greenberg@utsouthwestern.edu.

Received 12 June 2020 Returned for modification 14 July 2020 Accepted 31 October 2020

Accepted manuscript posted online 16 November 2020 Published 20 January 2021 urinary tract, and the lungs (15–18). Thus, new antibacterial agents should be evaluated for their ability to retain activity in the biofilm setting.

To overcome obstacles posed by cell permeability resistance mechanisms, researchers have investigated the use of siderophore-conjugated antibiotics (19, 20). After binding ferric iron, iron transporters (which utilize active transport by their association with outer membrane protein TonB) transfer these antibiotics into the periplasmic space. The antibiotic alters the cell wall (when conjugated to a beta-lactam) or inhibits DNA gyrase in the cytoplasm (when conjugated to ciprofloxacin) (20). Cefiderocol is a siderophore cephalosporin with potent antibacterial activity against a broad range of Gram-negative pathogens, including MDR isolates (21-25). In Pseudomonas aeruginosa, several TonB-driven iron transporters, including PiuA, have been implicated in translocating cefiderocol across the cell membrane (26, 27). Microorganisms forming biofilm may utilize bacterial siderophores to access iron (28, 29). For example, P. aeruginosa requires transport of the siderophore pyoverdine for biofilm formation (29). Consequently, siderophore antibiotics may have unique antimicrobial properties during treatment of biofilm. In this study, we compared the in vitro activities of cefiderocol and comparator antibiotics against various MDR strains. We then determined whether cefiderocol can eradicate biofilm in multiple genera and compared its potency to that of other comparator antibiotics.

## RESULTS

Cefiderocol has been previously demonstrated to effectively inhibit growth in a wide range of Gram-negative pathogens (21-25). It has weaker effects on Gram-positive or anaerobic pathogens (24); thus, we limited our study to Gram-negative genera. To assess the efficacy of cefiderocol and comparator antibiotics in inhibiting growth of the MDR strains used for this study, we first determined the MIC in both iron-depleted cation-adjusted Mueller-Hinton broth (ID-CAMHB) (Table 1) and Mueller-Hinton II broth (MHII) (Table 2). Cefiderocol MICs have typically been tested in ID-CAMHB (a CLSI requirement) because the iron-depleted conditions mimic in vivo conditions (27). However, iron has been demonstrated to be necessary for mature biofilm formation in diverse bacterial genera (Pseudomonas, Campylobacter, Vibrio, Serratia, Escherichia, Burkholderia cepacia complex [Bcc]) (30–35). In P. aeruginosa, for example, iron is essential not only for biofilm formation but also for biofilm matrix stability (36). Thus, we compared the fold differences in MIC for all antibiotics used in this study in both ID-CAMHB and MHII. The MIC<sub>90</sub> of cefiderocol ranged from 0.125  $\mu$ g/ml (*B. cepacia* complex) to 1 µg/ml (P. aeruginosa, Acinetobacter baumannii, Escherichia coli) in ID-CAMHB (Table 1). In all strains tested, MIC<sub>90</sub> values were consistently lower for cefiderocol than for the other agents (for ceftolozane-tazobactam, 16 to  $>64 \,\mu$ g/ml; for ceftazidime-avibactam, 8 to  $>64 \mu g/ml$ ; for ceftazidime, 16 to  $>64 \mu g/ml$ ; for piperacillintazobactam,  $\geq 64 \,\mu$ g/ml; for imipenem, 16 to  $> 64 \,\mu$ g/ml; for tobramycin, 8 to  $> 64 \,\mu$ g/ ml). This trend was also evident for MIC testing in MHII. The cefiderocol MIC<sub>90</sub> values in MHII were generally 2-fold higher in most cases (Table 2). These results recapitulate the previously observed potency of cefiderocol in inhibiting the planktonic growth of Gram-negative pathogens.

Next, we assessed the ability of cefiderocol and comparators to show activity in the biofilm setting. For these experiments, we used MBEC (minimum biofilm eradication concentration) plates, where biofilms previously grown on pegs on the lid of the plate were dosed every 12 h for 24 h with antibiotics and then evaluated for viability. Initially, we compared the biofilm reductions seen under conditions of treatment with antibiotics in ID-CAMHB with those seen with MHII to determine any differences in efficacy due to the limitation or presence of iron, especially for cefiderocol (Fig. 1). Unlike the impact of media on MIC, there were no differences in average biofilm reduction rates for *P. aeruginosa* or *Klebsiella pneumoniae*, whether ID-CAMHB or MHII was used in the treatment plate. At  $4 \mu q$ /ml, there was a >1-log reduction in biofilm levels in

## TABLE 1 Heat map of MIC for cefiderocol and comparator antibiotics against six MDR Gram-negative genera in MH-CAMHB<sup>a</sup>

				/			/		/	/ /
Stirain ID	Species	Genotype		adarded ages	of the state of th	Contraction of	andres are	artugueter y	NOR TO AN	sent
			/ "	at a solit	a cataté	*/ 0	and a state	/ 1	13	/
ATCC 25922	E. col		\$0.0625	0.125	0.125	0.125	2	0.125	0.25	Index
MB1676	E. col	TEM-1	\$0.0625	≤0.0625	\$0.0625	\$0.0625	0.5	0.125	0.25	0.0525-1 µg/ml
X2290	E. col		\$0.0625	0.125	0.25	0.25	2	0.125	8	2-4 µgimi
MB130	E. col	TEM-1, ST-73	0.125	\$0.0625	0.125	0.125	4	\$0.0525	0.125	8-16 µg/ml
BCT-B-035	E. col	NDM-1	0.25	>64	64	>64	64	4	32	32-64 µg/ml
MB1283	E. col	OXA-1, CTX-M-15	0.25	0.5	0.5	8	8	0.125	16	> 64 µg/mi
M8746A	E. col	OXA-1, ST-45	0.5	1	1	32	64	1	>64	
MB1339	E. col	OXA-1, CTX-M-15	0.5	4	2	64	32	0.125	16	
M82374	E. col	OXA-1, CTX-M-15	0.5	1	1	32	64	0.125	>64	
MCR1-NJ AI90 70834	E. col	MCR-1 NDM-1	1	>64	32	>64	>64 >64	16	8	
A60 /0634	E. COI	NUMP1		>64	- 54	>64	204	16	204	
MIC 90	E. coll		1	>64	32	>64	84	16	>64	
MIC 60	E. coll		0.26	1	1	32	32	0.126	18	
FA14	P. acruginosa		\$0.0625	0.25	1	1	4	0.125	0.25	
ATCC 9027	P. acruginosa		\$0.0625	0.25	1	1	4	0.5	0.25	
ATCC 27853	P. aeruginosa		0.125	0.25	1	0.5	4	1	0.25	
MB174	P. aeruginosa	ST-1225, OXA-50, PDC-5	0.125	0.5	4	2	16	8	0.5	
MB640		ST-282, OXA-50, PDC-3, NDM-1	0.125	1	4	4	16	0.25	0.5	
M8771	P. acruginosa	8T-179, OXA-50, PDC-8	0.125	1	2	2	16	8	0.5	
MB699	P. acruginosa	OXA-SO, PDC-2	0.125	1	8	16	64	4	1	
SJW-1 MB580A	P. acruginosa	CT. 1CT. OXA. CD. DOC. 3. NO.14	1	16	32	>64	>64	8	8	
		ST-357, OXA-50, PDC-3, NDM-1	1	>64	>64	64 >64	>64 >64	>64	32 64	
M8730	P. acruginosa	OXA-50, PDC-3, NDM-1	1	>64	204	264	204	204	64	
MIC 90	P. aeruginosa		1	>64	>84	>64	>84	64	32	
MIC 60	P. aeruginosa		0.126	1	4	4	18	8	0.6	
			0.120			*				
ATCC 17978	A baumanil		\$0.0625	0.5	4	2	4	\$0.0625	0.125	
BAA-1709 SDF			\$0.0625	0.5	4	2	4	0.125	\$0.0625	
ATCC 19605	A baumanil		\$0.0625	2	16	4	8	0.25	2	
Lac-1	A baumanil		0.25	8	16	>64	>64	2	32	
AE0057	A baumanii		0.25	32	64	>64	>64	16	0.5	
835081 E30	A baumanil		1	2	4	4	16	0.125	0.25	
HumC-1	A baumanil		1	64	64	>64	>64	32	>64	
BCT-B-026	A baumanil	NDM-1	1	64	>64	>64	>64	4	32	
X60546C	A baumanil		1	>64	32	>64	>64	32	0.25	
AYE	A baumanii		8	16	8	>64	32	0.5	32	
	-									
MICSO	A barmanil						204	99		
MIC 90	A baumanii		1	64	84 18	>64	>84	32	32	
MIC 80 MIC 60	A baumanii A baumanii				84 18		>84 32	32 0.6	32 0.6	
MIC 60	A. baumanil		1	64		>64	32			
MIC 60 2015ATLBI			1 0.26	64 8	16	>64 >64		0.6	0.6	
MIC 60 2015ATLBI	A baumanil K pneumoniae	ST-16, CXA-1, SHV-1 (Zb)	1 0.25 \$0.0625	04 8 ≤0.0625	18 \$0.0625	>84 >84 \$0.0625	32	0.6 \$0.0525	0.6	
MIC 60 2015ATLBI 2015ATLBo	A. baumanil K. pneumoniae K. pneumoniae		1 0.25 \$0.0625 \$0.0625	04 8 ≤0.0625 0.125	18 \$0.0625 0.125	>84 >84 \$0.0625 0.125	32 1 1	0.6 \$0.0625 0.125	0.6 0.125 ±0.0625	
MIC 60 2015ATLBI 2015ATLBO MB471 MB928 BAA-1705	A baumanil K pneumoniae K pneumoniae K pneumoniae	ST-16, OXA-1, SHV-1 (2b) KPC+	1 0.26 \$0.0625 \$0.0625 \$0.0625 \$0.0625 0.125 0.125	64 8 \$0.0525 0.125 0.125 2 32	16 \$0.0625 0.125 0.125 1 4	>64 >64 \$0.0625 0.125 0.125 32 64	32 1 16 16 >64	0.6 20.0525 0.125 20.0525 20.0525 8	0.6 0.125 \$0.0625 16	
MIC 60 2015ATL81 2015ATL80 M8471 M9328 8AA-1705 M9026	A. baumanil K. pneumoniae K. pneumoniae K. pneumoniae K. pneumoniae K. pneumoniae	ST-16, OXA-1, SHV-1 (2b) KPC+	1 0.26 \$0.0625 \$0.0625 \$0.0625 0.125 0.125 0.125	64 8 \$0.0525 0.125 0.125 2	18 \$0.0625 0.125 0.125 1 4 4	>64 >64 \$0.0625 0.125 0.125 32 64 64 64	32 1 16 16 564 >64	0.6 \$0.0525 0.125 \$0.0525 \$0.0525 8 32	0.6 0.125 \$0.0625 16 4 16 1 1	
MIC 60 2015ATLBI 2015ATLBo M6471 M8928 8AA-1705 M8026 M8254	A. baumanil K. pneumaniae K. pneumaniae K. pneumaniae K. pneumaniae K. pneumaniae K. pneumaniae	ST-16, OXA-1, SHV-1 (2b) KPC+	1 0.25 \$0.0625 \$0.0625 \$0.0625 0.125 0.125 0.125 0.125 0.125 0.25	64 8 0.125 0.125 0.125 2 32 32 32 1	18 \$0.0625 0.125 0.125 1 4 4 4 0.5	>84 >84 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.125	32 1 16 16 >64 >64 8	0.6 \$0.0525 0.125 \$0.0525 \$0.0525 8 32 0.125	0.6 0.125 \$0.0625 16 4 16 1 1 4	
MIC 60 2015ATLBI 2015ATLBo M6471 M9328 8AA-1705 M6325 M83254 M8254	A. baumanil K. pneumaniae K. pneumaniae K. pneumaniae K. pneumaniae K. pneumaniae K. pneumaniae K. pneumaniae	ST-16, CXA-1, SHV-1 (2b) KPC+ ST-307, SHV-28 (2b), KPC2	1 0.25 \$0.0625 \$0.0625 0.125 0.125 0.125 0.125 0.25 0.25	04 8 \$0.0525 0.125 0.125 2 32 32 32 1 1 2	18 \$0.0625 0.125 0.125 1 4 4 0.5 1	>84 >84 \$0.0625 0.125 0.125 32 64 64 64 16 64	32 1 16 16 >64 >64 8 32	0.6 20.0525 0.125 20.0525 8 32 0.125 0.125	0.6 0.125 \$0.0625 16 4 16 1 1 4 8	
MIC 60 2015ATLBI 2015ATLBI MIG471 MIG28 BAA-1705 MIG26 MIG26 MIG26 MIG26 BAA-2145	A. baumanil K. pneumaniae K. pneumaniae K. pneumaniae K. pneumaniae K. pneumaniae K. pneumaniae K. pneumaniae	ST-16, OXA-1, SHV-1 (2b) KPC+	1 0.25 \$0.0625 \$0.0625 0.125 0.125 0.125 0.25 0.25 0.5	04 8 \$0.0625 0.125 0.125 2 32 32 32 1 2 >64	18 \$0.0625 0.125 1 4 4 4 0.5 1 32	>64 >64 20.0625 0.125 0.	32 1 16 16 >64 8 22 >64	0.6 20.0625 0.125 20.0625 8 32 0.125 0.125 16	0.6 0.125 \$0.0625 16 4 16 1 4 8 >64	
MIC 60 2015ATLBI 2015ATLBo M6471 M9328 8AA-1705 M6325 M83254 M8254	A. baumanil K. pneumaniae K. pneumaniae K. pneumaniae K. pneumaniae K. pneumaniae K. pneumaniae K. pneumaniae	ST-16, CXA-1, SHV-1 (2b) KPC+ ST-307, SHV-28 (2b), KPC2	1 0.25 \$0.0625 \$0.0625 0.125 0.125 0.125 0.125 0.25 0.25	04 8 \$0.0525 0.125 0.125 2 32 32 32 1 1 2	18 \$0.0625 0.125 0.125 1 4 4 0.5 1	>84 >84 \$0.0625 0.125 0.125 32 64 64 64 16 64	32 1 16 16 >64 >64 8 32	0.6 20.0525 0.125 20.0525 8 32 0.125 0.125	0.6 0.125 \$0.0625 16 4 16 1 1 4 8	
MIC 60 2015ATLB 2015ATLB0 MB471 MB328 8AA-1705 MB326 MB254 MB776A 8AA-2146 K0 NIH1	A baumanil K pneumoniae K pneumoniae K pneumoniae K pneumoniae K pneumoniae K pneumoniae K pneumoniae K pneumoniae	ST-16, CXA-1, SHV-1 (2b) KPC+ ST-307, SHV-28 (2b), KPC2 NDM-1	1 0.26 \$0.0625 \$0.0625 \$0.0625 \$0.0625 0.125 0.125 0.125 0.25 0.25 0.25 0.5 1	64 8 \$0.0625 0.125 0.125 2 32 32 1 2 2 >64 >64 >64	18 \$0.0625 0.125 0.125 1 4 4 0.5 1 32 16	>64 >64 \$0.0625 0.125 0.125 32 64 64 64 16 64 264 >64 >64 >64	32 1 1 16 16 >64 >64 8 32 >64 >64 >64 >64	0.6 20.0625 0.125 20.0625 8 32 0.125 0.125 0.125 16 64	0.5 0.125 \$20.0525 16 4 15 1 4 8 >64 8	
MIC 60 2015ATLB 2015ATLB M9471 M9528 BAA-1705 M9526 M9254 M9776A BAA-2146 K0 NIH-1 MIC 80	A baumanil K preumoniae K preumoniae K preumoniae K preumoniae K preumoniae K preumoniae K preumoniae K preumoniae K preumoniae	ST-16, CXA-1, SHV-1 (2b) KPC+ ST-307, SHV-28 (2b), KPC2 NDM-1	1 0.26 \$0.0625 \$0.0625 \$0.0625 0.125 0.125 0.125 0.125 0.25 0.25 0.5 1 1	64 8 ≤0.0525 0.125 0.125 2 32 32 32 1 2 2 >54 >64 >64	18 \$0.0625 0.125 1 4 4 0.5 1 32 16 18	>64 >84 \$0.0625 0.125 0.125 32 64 64 64 64 16 64 >64 >64 >64 >64 >64	32 1 1 16 16 364 364 32 32 364 32 364 32 364 32 32 364 32 32 364 32 32 364 32 32 32 364 365 365 365 365 365 365 365 365	0.6 20.0625 0.125 20.0625 8 32 0.125 0.125 16 64 32	0.5 0.125 \$0.0525 16 4 16 1 4 8 >64 8 18	
MIC 60 2015ATLB 2015ATLB MB471 MB528 BAA-1705 MB328 BAA-1705 MB3254 MB775A BAA-2146 K0 NH+1 MIC 80	A baumanil K pneumoniae K pneumoniae K pneumoniae K pneumoniae K pneumoniae K pneumoniae K pneumoniae K pneumoniae	ST-16, CXA-1, SHV-1 (2b) KPC+ ST-307, SHV-28 (2b), KPC2 NDM-1	1 0.26 \$0.0625 \$0.0625 \$0.0625 \$0.0625 0.125 0.125 0.125 0.25 0.25 0.25 0.5 1	64 8 \$0.0625 0.125 0.125 2 32 32 1 2 2 >64 >64 >64	18 \$0.0625 0.125 0.125 1 4 4 0.5 1 32 16	>64 >64 \$0.0625 0.125 0.125 32 64 64 64 16 64 264 >64 >64 >64	32 1 1 16 16 >64 >64 8 32 >64 >64 >64 >64	0.6 20.0625 0.125 20.0625 8 32 0.125 0.125 0.125 16 64	0.5 0.125 \$20.0525 16 4 15 1 4 8 >64 8	
MIC 60 2015ATLBI 2015ATLBI MB271 MB205 BAA-1705 MB205 MB205 MB205 MB205 MB205 K0 NH-1 MIC 60 MIC 60	A baumanil K preumoniae K preumoniae K preumoniae K preumoniae K preumoniae K preumoniae K preumoniae K preumoniae K preumoniae	ST-16, CXA-1, SHV-1 (2b) KPC+ ST-307, SHV-28 (2b), KPC2 NDM-1	1 0.25 \$2.0625 \$2.0625 \$2.0625 0.125 0.125 0.125 0.125 0.25 0.25 0.25 0.5 1 0.5 1	64 8 ≤0.0525 0.125 0.125 2 32 32 32 32 32 32 32 32 32	18 \$0.0625 0.125 0.125 1 4 4 0.5 1 22 16 18 1 1 1 1 1 1 1 1 1 1 1 1 1	>64 >64 20.0625 0.125 0.125 32 64 64 64 64 64 564 >64 >64 >64 >64 >64 32	32 1 1 16 16 >64 >64 8 22 >64 >64 >64 >64 >64 >64 >64 >64	0.6 20.0625 0.125 20.0625 8 32 0.125 0.125 16 64 32 0.125	0.5 0.125 \$0.0625 16 4 15 1 4 8 >64 8 18 18 18 18 14 4 16 4 15 1 4 15 1 4 15 15 15 16 4 15 16 16 15 16 16 16 16 16 16 16 16 16 16	
MIC 60 2015ATLB 2015ATLB 2015ATLB 2015ATLB MB471 MB228 BAA-1705 MB228 BAA-1705 MB224 MB776A BAA-2146 K0 NIH-1 MIC 80 MIC 60 AU0212	A baumanil K preumoniae K preumoniae	ST-16, CXA-1, SHV-1 (2b) KPC+ ST-307, SHV-28 (2b), KPC2 NDM-1	1 0.26 \$0.0625 \$0.0625 0.125 0.125 0.125 0.25 0.25 0.5 1 1 0.6 0.126 \$0.0625	64 8 20.0525 0.125 0.125 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	18 \$0.0625 0.125 0.125 1 4 4 4 0.5 1 32 16 18 18 10 0.5	>64 >64 >64 20.0625 0.125 0.125 0.125 64 64 64 64 564 >64 >64 >64 >64 32 0.5	32 1 1 16 364 364 32 32 364 364 364 364 364 364 364 364	0.6 \$2.0625	0.5 0.125 \$0.0625 16 4 16 1 4 8 >64 8 18 18 4 2	
MIC 60 2015ATLB 2015ATLB 2015ATLB 2015ATLB MB471 MB228 BAA-1705 MB228 BAA-1705 MB224 MB776A BAA-2146 K0 NIH-1 MIC 80 MIC 60 AU0212	A baumanil K preumoniae K preumoniae K preumoniae K preumoniae K preumoniae K preumoniae K preumoniae K preumoniae K preumoniae	ST-16, CXA-1, SHV-1 (2D) KPC+ ST-307, SHV-28 (2D), KPC2 NDM-1	1 0.25 \$2.0625 \$2.0625 \$2.0625 0.125 0.125 0.125 0.125 0.25 0.25 0.25 0.5 1 0.5 1	64 8 ≤0.0525 0.125 0.125 2 32 32 32 32 32 32 32 32 32	18 \$0.0625 0.125 0.125 1 4 4 0.5 1 22 16 18 1 1 1 1 1 1 1 1 1 1 1 1 1	>64 >64 20.0625 0.125 0.125 32 64 64 64 64 64 564 >64 >64 >64 >64 >64 32	32 1 1 16 16 >64 >64 8 22 >64 >64 >64 >64 >64 >64 >64 >64	0.6 20.0625 0.125 20.0625 8 32 0.125 0.125 16 64 32 0.125	0.5 0.125 \$0.0625 16 4 15 1 4 8 >64 8 18 18 18 18 14 4 16 4 15 1 4 15 1 4 15 15 15 16 4 15 16 16 15 16 16 16 16 16 16 16 16 16 16	
MIC 60 2015ATLBI 2015ATLBI MB320 BAA-1705 MB226 MB226 MB226 MB776A BAA-2146 K0 NH+1 MIC 80 MIC 80 AL0212 BAA-248	A baumanil K preumoniae K preumoniae B ambitra B. wethamienzia	ST-16, CXA-1, SHV-1 (2b) KPC+ ST-307, SHV-28 (2b), KPC2 NDM-1	1 0.26 \$0.0625 \$0.0625 \$0.0625 0.125 0.125 0.125 0.25 0.25 0.5 1 1 0.6 0.126 \$0.0625 \$0.0625 \$0.0625	64 8 \$0.0525 0.125 0.125 2 32 32 1 1 2 32 32 1 2 32 32 1 2 564 >64 2 0.25 0.5	18 20.0625 0.125 0.125 1 4 4 4 0.5 1 16 18 1 0.5 0.5 0.5	>64 >64 20.0625 0.125 0.125 32 64 64 64 16 64 16 64 >64 >64 >64 >64 >64 >64 >64 32 0.5 0.25	32 1 1 16 16 >64 8 22 >64 >64 >64 >64 18 0.5 0.25	0.6 20.0625 0.125 20.0625 8 32 0.125 0.125 16 64 32 0.125 0.125 0.125	0.5 0.125 \$0.0625 16 4 16 1 4 8 >64 8 18 18 4 2 2	
MIC 60 2015ATLBI 2015ATLBI MB323 8AA-1705 MB325 MB325 MB325 MB325 MB325 MB376A 8AA-2146 K0 NH-1 MIC 60 MIC 60 AL0212 BAA-248 COD-1	A baumanil K preumorise K preumorise B ambitra B. vetnamienta	ST-16, CXA-1, SHV-1 (2b) KPC+ ST-307, SHV-28 (2b), KPC2 NDM-1	1 0.26 \$0.0625 \$0.0625 0.125 0.125 0.125 0.25 0.25 0.25 0.5 1 1 0.6 0.126 \$0.0625 \$0.0625	64 8 ≤0.0525 0.125 0.125 0.125 2 32 32 32 32 32 32 32 32 32	18 \$0.0625 0.125 0.125 0.125 1 4 4 4 0.5 1 32 16 16 1 0.5 0.5 0.5 0.5	>64 >64 >64 20.0625 0.125 0.125 0.125 0.125 64 64 64 64 964 >64 >64 >64 >64 >64 32 0.5 0.5 0.5	32 1 1 16 >64 >64 >64 >64 >64 >64 >64 >6	0.6 20.0625 0.125 20.0625 8 32 0.125 0.125 16 64 32 0.125 64 32 0.125 8 8 20.0625 8	0.6 0.125 \$0.0625 16 4 15 1 4 8 8 8 18 8 8 18 4 2 2 16 16 15 15 15 16 16 15 16 16 16 16 16 16 16 16 16 16	
MIC 60 2015ATLB 2015A	A baumanil K preumoniae K preumoniae B ambitrara B. weltvorans	ST-16, CXA-1, SHV-1 (2D) KPC+ ST-307, SHV-28 (2D), KPC2 NDM-1	1 0.26 \$0.0625 \$0.0625 0.125 0.125 0.125 0.25 0.5 1 1 0.6 0.126 \$0.0625 \$0.0625 \$0.0625 \$0.0625	64 8 20.0525 0.125 0.125 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	18 \$0.0625 0.125 0.125 1 4 4 4 0.5 1 16 18 18 1 0.5 0.5 0.5 1 1	>64 >64 >60 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.4 64 64 64 >64 >64 >64 >64 >64 >64 32 0.5 0.5 0.5	32 1 1 16 16 16 16 16 16 16 16	0.6 20.0625 0.125 20.0625 20.0625 8 32 0.125 0.125 15 64 32 0.125 15 64 32 0.125 8 8 8 8 8	0.5 0.125 50.0625 16 4 16 1 4 8 >64 8 18 4 2 2 16 16 16 18 4 18 18 16 18 18 18 18 18 18 18 18 18 19 19 19 19 19 19 19 19 19 19	
MIC 60 2015ATLBI 2015ATLBI MB323 BAA-1705 MB226 MB254 MB776A BAA-2145 K0 NH-1 MIC 80 MIC 80 MIC 60 AU0212 BAA-247 BAA-247 1840-1	A baumanil K preumoniae K preumoniae B ambitran B. definamienaia B. multivorans B. cepacia	ST-16, CXA-1, SHV-1 (2D) KPC+ ST-307, SHV-28 (2D), KPC2 NDM-1	1 0.26 \$0.0625 \$0.0625 0.125 0.125 0.125 0.25 0.25 0.25 0.5 1 1 0.6 0.126 \$0.0625 \$0.0625 \$0.0625 \$0.0625 \$0.0625	64 8 \$0.0525 0.125 0.125 2 32 32 1 2 32 32 1 2 32 32 1 2 32 32 1 2 32 32 1 2 32 32 1 2 32 32 32 1 5 6 4 5 6 5 5 5 5 5 5 5 5 5 5 5 5 5	18 20.0625 0.125 0.125 0.125 1 4 4 4 4 0.5 1 1 0.5 1 1 0.5 0.5 0.5 0.5 1 1 1	>64 >64 >200625 0.125 0.125 32 64 64 64 16 64 16 64 >64 >64 >64 >64 >64 >64 32 0.5 0.25 0.5 0.5 1	32 1 1 16 16 >64 8 22 >64 >64 >64 >64 >64 >64 22 >64 18 0.5 0.25 1 16 16 16 16 16 16 16 16 16	0.6 20.0525 0.125 20.0525 20.0525 8 32 0.125 15 54 32 0.125 64 32 0.125 8 20.0525 8 20.0525 8 8 8 1	0.6 0.125 \$0.0625 16 4 16 1 4 8 8 8 8 18 18 18 18 18 18 18	
MIC 60 2015ATLBI 2015ATLBI MB271 MB205 BAA-1705 MB205 MB205 MB205 MB276A BAA-2146 K0 NIH-1 MIC 90 MIC 90	A baumanil K preumoniae K preumoniae K preumoniae K preumoniae K preumoniae K preumoniae K preumoniae K preumoniae K preumoniae K preumoniae B ambitra B. wethamienaia B. wethamienaia B. multivorans B. cepocia	ST-16, CXA-1, SHV-1 (2b) KPC+ ST-307, SHV-28 (2b), KPC2 NDM-1	1 0.26 \$20.0625 \$20.0625 2.0.0625 0.125 0.125 0.125 0.25 0.25 0.5 1 1 0.6 0.126 \$20.0625 \$20.0625 \$20.0625 \$20.0625 \$20.0625 \$20.0625	64 8 ≤0.0525 0.125 0.125 2 32 2 2 1 2 2 32 32 32 32 32 32 32 32	18 \$0.0625 0.125 0.125 0.125 1 4 4 4 0.5 1 32 16 16 1 1 0.5 0.5 0.5 1 1 1 1 1 1 1 1 1 1 1 1 1	>64 >64 >64 20.0625 0.125 0.125 0.125 0.125 0.125 64 64 64 >64 >64 >64 >64 >64 >64 >64 >6	32 1 1 16 364 364 364 32 32 364 364 364 364 364 364 364 364	0.6 20.0525 0.125 20.0525 20.0525 20.0525 20.0125 16 64 32 0.125 16 64 32 0.125 20.0525 20.0525 8 8 8 1 2 2	0.6 0.125 50.0625 16 4 15 1 4 8 ×64 8 ×64 8 10 4 2 2 16 16 16 16 16 16 16 16 16 16	
MIC 60 2015ATLBI 2015ATLBI MB271 MB205 BAA-1705 MB205 MB205 MB205 MB205 MB276A BAA-2146 K0 NIH-1 MIC 80 MIC 60 MIC 60 MIC 60 MIC 60 AL0212 BAA-248 COD-1 COD-1	A baumanil K preumoniae K preumoniae B ambitrara B. vietnamienaia B. multivorans B. multivorans B. cepacia	ST-16, CXA-1, SHV-1 (2D) KPC+ ST-307, SHV-28 (2D), KPC2 NDM-1	1 0.26 \$0.0625 \$0.0625 0.125 0.125 0.125 0.25 0.5 1 1 0.5 1 1 0.6 0.126 \$0.0625 \$0.0625 \$0.0625 \$0.0625 \$0.0625 \$0.0625	64 8 20.0525 0.125 0.125 2 2 2 2 2 2 2 2 2 2 2 2 2	18 \$0.0625 0.125 0.125 1 4 4 4 0.5 1 32 16 18 18 18 10 0.5 0.5 0.5 1 1 1 1 2	>64 >64 >64 200625 0.125 0.125 0.125 0.125 0.125 64 64 64 64 >64 >64 >64 >64 >64 >64 >64	32 1 1 16 364 364 322 364 322 364 322 364 322 364 322 364 322 364 322 364 322 364 322 364 322 364 322 364 322 365 322 366 366	0.6 20.0625 0.125 20.0625 20.0625 8 32 0.125 0.125 16 64 32 0.125 0.125 16 64 32 0.125 8 8 8 1 2 4	0.5 0.125 50.0625 16 4 16 1 4 8 >64 8 >64 8 18 4 2 2 16 16 1 4 18 4 16 1 1 4 16 1 1 4 16 1 16 1 16 16 16 16 16 16	
MIC 60 2015ATLBI 2015ATLBI MB323 BAA-1705 MB226 MB254 MB276A BAA-2146 ND NH-1 MIC 80 MIC 80 MIC 80 MIC 80 AU0212 BAA-243 COD-1 BAA-247 1840-1 H2424 ATCC 25416 J2315	A baumanil K preumoniae K preumoniae B ambitran B. vietnamienai B. mutivorans B. mutivorans B. ecnocepadia B. cenocepadia	ST-16, CXA-1, SHV-1 (2D) KPC+ ST-307, SHV-28 (2D), KPC2 NDM-1	1 0.26 \$2,0625 \$2,0625 0.125 0.125 0.125 0.25 0.25 0.25 0.5 1 1 0.6 0.126 \$2,0625 \$2,0625 \$2,0625 \$2,0625 \$2,0625 \$2,0625 \$2,0625	64 8 20.0525 0.125 0.125 2 32 32 1 2 32 32 1 2 32 32 1 2 32 32 32 32 1 2 32 32 32 32 32 32 32 32 32	18 \$0.0625 0.125 0.125 0.125 1 4 4 4 4 0.5 1 16 16 10 0.5 0.5 0.5 1 1 1 2 2	>64 >64 >20625 0.125 0.125 0.125 32 64 64 64 64 16 64 >64 >64 >64 >64 32 0.5 0.25 0.5 1 1 1 2 8	32 1 1 16 16 >64 8 22 >64 >64 >64 >64 >64 >64 >64 3 6 8 22 >64 >64 3 6 8 22 >64 3 6 8 22 >64 3 8 22 >64 3 8 22 >64 3 8 22 >64 3 8 22 >64 3 8 22 >64 3 8 22 >64 3 8 22 >64 3 8 22 >64 3 8 22 >64 3 8 22 >64 3 8 22 >64 3 8 3 5 6 8 3 5 6 8 3 5 6 8 3 5 6 8 3 5 6 8 3 5 6 6 8 3 5 6 6 8 5 6 6 8 5 6 6 8 5 6 6 8 5 6 8 5 6 6 8 5 6 6 8 5 6 6 6 6 6 6 6 6 6 6 6 6 6	0.6 20.0525 0.125 20.0525 20.0525 8 32 0.125 15 64 32 0.125 64 32 0.125 8 20.0525 8 8 8 8 1 1 2 4 4 16	0.6 0.125 \$0.0625 16 4 16 1 4 8 8 8 8 18 18 18 18 18 18 18	
MIC 60 2015ATLBI 2015ATLBI MB323 BAA-1705 MB226 MB254 MB776A BAA-2145 K0 NH-1 MIC 80 MIC 80 MIC 80 MIC 80 AU0212 BAA-244 COD-1 BAA-247 1840-1 H2424 ATCC 25416 J2315 BC7 AU00158	A baumanil K preumonise K preumonise B ambitra B. vietnamienais B. wietnamienais B. wietnamienais B. wietnamienais B. wietnamienais B. multvorans B. cenocepacis B. cenocepacis B. cenocepacis B. cenocepacis	ST-16, CXA-1, SHV-1 (2D) KPC+ ST-307, SHV-28 (2D), KPC2 NDM-1	1 0.26 \$0.0625 \$0.0625 0.125 0.125 0.125 0.25 0.25 0.25 0.5 1 1 0.6 0.126 \$0.0625 \$0.0	64         8           ≤0.0525         0.125           0.125         2           32         32           1         2           >64         >64           >64         >64           >0.125         0.125           0.25         0.5           0.5         0.5           0.5         0.5           0.5         0.5           0.5         16	18 \$0.0625 0.125 0.125 0.125 1 4 4 4 4 0.5 1 1 1 0.5 0.5 0.5 1 1 1 2 2 16 8	>64 >64 \$20625 0.125 0.125 32 64 64 64 16 64 >64 >64 >64 >64 >64 >64 32 0.5 0.25 0.5 0.5 1 1 1 2 8 8 >64 64 54 32	32 1 1 16 364 364 364 364 364 364 364 36	0.6 20.0525 0.125 20.0525 20.0525 8 32 0.125 0.125 15 64 32 0.125 8 20.0525 8 8 20.0525 8 1 1 2 4 4 16 64 64 64	0.5 0.125 50.0625 16 4 16 1 4 8 8 8 18 18 18 18 18 18 18 1	
MIC 60 2015ATLBI 2015ATLBI 2015ATLBI 2015ATLBI 2015ATLBI MB205 BAA-1705 MB205 MB2254 MB776A BAA-2146 K0 NIH-1 MIC 80 MIC 60 MIC 60 AU0212 BAA-248 C0D-1 BAA-	A baumanil K preumoniae K preumoniae B ambitra B. wiethamienai B. multvorans B. multvorans B. cepocia B. cepocia B. cepocia B. cenocepacia B. doiosa B. colosa	ST-16, CXA-1, SHV-1 (2D) KPC+ ST-307, SHV-28 (2D), KPC2 NDM-1	1 0.26 \$20.0625 \$20.0625 20.0625 20.0625 0.125 0.125 0.25 0.25 0.5 1 1 0.6 0.126 \$20.0625 \$20	84           8           ≤0.0525           0.125           0.125           2           32 <t< td=""><td>18 \$0.0625 0.125 0.125 0.125 1 4 4 4 0.5 1 1 32 16 1 1 0.5 0.5 0.5 0.5 1 1 1 2 16 8 8 8</td><td>&gt;64 &gt;64 &gt;64 20.0625 0.125 0.125 0.125 0.125 0.125 0.4 64 &gt;64 32 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5</td><td>32 1 1 16 &gt;64 &gt;64 &gt;64 &gt;64 &gt;64 18 0.5 0.25 1 1 16 8 8 8 5 64 &gt;64 &gt;64 &gt;64 &gt;64 &gt;64 &gt;64 &gt;64</td><td>0.6 20.0525 0.125 20.0525 20.0525 8 32 0.125 16 64 32 0.126 0.125 16 64 32 0.125 2.0525 8 8 8 1 2 4 15 64 64 64 64 64 64</td><td>0.6 0.125 50.0625 16 4 15 1 4 8 ×64 8 ×64 8 16 4 2 2 15 16 4 5 16 4 8 8 16 16 15 16 16 16 16 16 16 16 16 16 16</td><td></td></t<>	18 \$0.0625 0.125 0.125 0.125 1 4 4 4 0.5 1 1 32 16 1 1 0.5 0.5 0.5 0.5 1 1 1 2 16 8 8 8	>64 >64 >64 20.0625 0.125 0.125 0.125 0.125 0.125 0.4 64 >64 32 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5	32 1 1 16 >64 >64 >64 >64 >64 18 0.5 0.25 1 1 16 8 8 8 5 64 >64 >64 >64 >64 >64 >64 >64	0.6 20.0525 0.125 20.0525 20.0525 8 32 0.125 16 64 32 0.126 0.125 16 64 32 0.125 2.0525 8 8 8 1 2 4 15 64 64 64 64 64 64	0.6 0.125 50.0625 16 4 15 1 4 8 ×64 8 ×64 8 16 4 2 2 15 16 4 5 16 4 8 8 16 16 15 16 16 16 16 16 16 16 16 16 16	
MIC 60 2015ATLBI 2015ATLBI MB323 BAA-1705 MB226 MB254 MB776A BAA-2145 K0 NH-1 MIC 80 MIC 80 MIC 80 MIC 80 AU0212 BAA-244 COD-1 BAA-247 1840-1 H2424 ATCC 25416 J2315 BC7 AU00158	A baumanil K preumonise K preumonise B ambitra B. vietnamienais B. wietnamienais B. wietnamienais B. multvorans B. cenocepacis B. cenocepacis B. cenocepacis B. cenocepacis	ST-16, CXA-1, SHV-1 (2D) KPC+ ST-307, SHV-28 (2D), KPC2 NDM-1	1 0.26 \$0.0625 \$0.0625 0.125 0.125 0.125 0.25 0.25 0.25 0.5 1 1 0.6 0.126 \$0.0625 \$0.0	64         8           ≤0.0525         0.125           0.125         2           32         32           1         2           >64         >64           >64         >64           >0.125         0.125           0.25         0.5           0.5         0.5           0.5         0.5           0.5         0.5           0.5         16	18 \$0.0625 0.125 0.125 0.125 1 4 4 4 4 0.5 1 1 1 0.5 0.5 0.5 1 1 1 2 2 16 8	>64 >64 \$20625 0.125 0.125 32 64 64 64 16 64 >64 >64 >64 >64 >64 >64 32 0.5 0.25 0.5 0.5 1 1 1 2 8 8 >64 64 54 32	32 1 1 16 364 364 364 364 364 364 364 36	0.6 20.0525 0.125 20.0525 20.0525 8 32 0.125 0.125 15 64 32 0.125 8 20.0525 8 8 20.0525 8 1 1 2 4 4 16 64 64 64	0.5 0.125 50.0625 16 4 16 1 4 8 8 8 18 18 18 18 18 18 18 1	
MIC 60 2015ATLBI 2015ATLBI 2015ATLBI 2015ATLBI 2015ATLBI 2015ATLBI 2015ATLBI 2015ATLBI MB228 MB275A BAA-1705 MB228 MB275A BAA-2148 MB775A BAA-2148 MB775A BAA-244 C0D-1 BAA-244 C0D-1 BAA-244 C0D-1 BAA-247 1840-1 H2424 ATCC 25416 J2315 BC7 AU00158 MIC 80 M	A baumanil K preumonise K preumonise B ambitra B. vichnamiensis B. wichtamiensis B. wichtamiensis B. wichtamiensis B. cenocepacis B. cenocepacis	ST-16, CXA-1, SHV-1 (2D) KPC+ ST-307, SHV-28 (2D), KPC2 NDM-1	1 0.26 \$0.0625 \$0.0625 0.125 0.125 0.125 0.25 0.25 0.25 0.5 1 1 0.6 0.126 \$0.0625 \$0.0	64         8           ≤0.0525         0.125           0.125         2           32         1           2         32           1         2           >64         >64           >64         >64           2         0.25           0.5         0.5	18 \$0.0625 0.125 0.125 0.125 1 4 4 4 4 0.5 1 1 1 0.5 0.5 0.5 0.5 1 1 1 2 2 16 8 8 8 1	>64 >64 >20625 0.125 0.125 32 64 64 64 16 64 >64 >64 >64 >64 >64 >64 32 0.5 0.25 0.5 0.5 1 1 1 2 8 >64 64 16 16 16 16 16 16 16 16 16 16 16 16 16	32 1 1 16 364 364 364 364 364 364 364 36	0.6 20.0525 0.125 20.0525 20.0525 8 32 0.125 0.125 0.125 15 64 32 0.125 8 8 8 8 8 1 1 2 4 16 64 64 64 64 64 64 64	0.6 0.125 \$0.0625 16 4 16 1 4 8 8 8 18 18 2 16 16 16 16 16 16 16 16 16 16	
MIC 60 2015ATLBI 2015ATLBI 2015ATLBI 2015ATLBI 2015ATLBI 2015ATLBI MB225 MB225 MB225 MB225 MB276A BAA-2146 K0 NIH-1 MIC 80 MIC 8	A baumanil K preumoniae K preumoniae B ambitra B. wiethamienai B. multivorans B. cenocepacia B. cenocepacia B. cenocepacia B. cenocepacia B. cenocepacia B. doiosa Bcc Bcc	ST-16, CXA-1, SHV-1 (2D) KPC+ ST-307, SHV-28 (2D), KPC2 NDM-1	1 0.26 \$0.0625 \$0.0625 \$0.0625 0.125 0.125 0.125 0.25 0.25 0.5 1 1 0.6 0.126 \$0.0625 \$0.0625 \$0.0625 \$0.0625 \$0.0625 \$0.0625 \$0.0625 \$0.0625 \$0.0625	64         8           ≤0.0525         0.125           0.125         0.125           2         32           32         35           35 </td <td>18 \$0.0625 0.125 0.125 0.125 1 4 4 4 4 0.5 1 1 32 16 1 1 0.5 0.5 0.5 1 1 1 2 16 8 8 1 1 1 1 1 1 1 1 1 1 1 1 1</td> <td>&gt;64 &gt;64 &gt;64 20.0625 0.125 0.125 0.125 0.125 0.4 64 64 64 964 964 32 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5</td> <td>32 1 1 16 &gt;64 &gt;64 &gt;64 &gt;64 &gt;64 &gt;64 18 0.5 0.25 1 1 16 8 8 8 &gt;64 &gt;64 &gt;64 8 32 &gt;64 &gt;64 32 &gt;64 32 &gt;64 32 &gt;64 32 &gt;64 32 &gt;64 32 &gt;64 32 &gt;64 32 &gt;64 32 &gt;64 32 &gt;64 32 &gt;64 32 &gt;64 32 &gt;64 32 &gt;64 32 &gt;64 36 32 &gt;64 36 32 &gt;64 36 32 &gt;64 36 32 &gt;64 36 32 &gt;64 36 36 36 36 36 36 36 36 36 36</td> <td>0.6 20.0525 0.125 20.0525 20.0525 20.0525 20.0125 0.125 0.125 0.125 0.125 0.125 20.0525 20.55</td> <td>0.6 0.125 50.0625 16 4 16 1 4 8 ×64 8 ×64 8 16 16 16 16 16 16 16 16 16 16</td> <td></td>	18 \$0.0625 0.125 0.125 0.125 1 4 4 4 4 0.5 1 1 32 16 1 1 0.5 0.5 0.5 1 1 1 2 16 8 8 1 1 1 1 1 1 1 1 1 1 1 1 1	>64 >64 >64 20.0625 0.125 0.125 0.125 0.125 0.4 64 64 64 964 964 32 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5	32 1 1 16 >64 >64 >64 >64 >64 >64 18 0.5 0.25 1 1 16 8 8 8 >64 >64 >64 8 32 >64 >64 32 >64 32 >64 32 >64 32 >64 32 >64 32 >64 32 >64 32 >64 32 >64 32 >64 32 >64 32 >64 32 >64 32 >64 32 >64 36 32 >64 36 32 >64 36 32 >64 36 32 >64 36 32 >64 36 36 36 36 36 36 36 36 36 36	0.6 20.0525 0.125 20.0525 20.0525 20.0525 20.0125 0.125 0.125 0.125 0.125 0.125 20.0525 20.55	0.6 0.125 50.0625 16 4 16 1 4 8 ×64 8 ×64 8 16 16 16 16 16 16 16 16 16 16	
MIC 60 2015ATLB 2015ATLB 2015ATLB 2015ATLB 2015ATLB M6271 M9228 8AA-1705 M6266 M8254 M8276 8AA-2146 K0 NIH-1 MIC 60 MIC 60 AU0212 BAA-247 1840-1 BAA-240 1840-1 BAA-247 1840-1 BAA-247 1840-1 BAA-247 1840-1 BAA-247 184	A baumanil K preumonise K preumonise B ambitra B. wetharmienzis B. multivorans B. multivorans B. emocepacia B. cenocepacia B. cenocepacia	ST-16, CXA-1, SHV-1 (2D) KPC+ ST-307, SHV-28 (2D), KPC2 NDM-1	1 0.26 \$0.0625 \$0.0625 0.125 0.125 0.125 0.125 0.25 0.5 1 1 0.6 0.126 \$0.0625 \$0.0625 \$0.0625 \$0.0625 \$0.0625 \$0.0625 \$0.0625 \$0.0625 \$0.0625 \$0.0625 \$0.0625 \$0.0625 \$0.0625	64         8           \$20.0525         0.125           0.125         0.125           2         32           32         1           2         32           32         1           2         32           32         32           1         2           >64         >64           2         0.25           0.5         0.5           0.5         0.5           0.5         0.5           0.5         0.5           0.5         4           >64         16           18         0.6           0.5         4	18 \$0.0625 0.125 0.125 1 4 4 4 0.5 1 1 32 16 10 1 0.5 0.5 1 1 1 2 2 16 8 8 1 1 2 1 1 1 2 2 1 1 1 1 2 1 1 1 1 1 1 1 1 1 1 1 1 1	>64 >64 >64 20.0625 0.125 0.125 0.125 0.125 0.125 0.125 0.4 64 64 64 >64 >64 >64 >64 >64 >64 >64 >	32 1 1 16 >64 >64 >64 >64 >64 10 0.5 0.25 1 1 16 8 8 32 >64 >64 >64 >64 >64 >64 >64 >64	0.6 20.0625 0.125 20.0625 20.0625 20.0625 20.0625 20.125 16 64 32 0.125 0.125 20.0625 8 8 8 8 1 2 4 16 64 64 64 64 64 8 8 8 8 8 8 8 8 8 8 8 8 8	0.5 0.125 50.0625 16 4 16 1 4 8 ×64 8 8 ×64 8 8 ×64 8 8 8 8 8 8 8 8 8 8 8 8 8	
MIC 60           2015ATLBI           2015ATLBI           2015ATLBI           2015ATLBI           2015ATLBI           MB271           MB228           BAA-1705           MB226           MB226           MB271           MB226           MB276           MB276A           BAA-2146           NO NH-1           MIC 80           MIC 60           MIC 71           BAA-2315           BC7           AU00153           MIC 60	A baumanil K preumonise K preumonise B detabaltation B detabaltation	ST-16, CXA-1, SHV-1 (2D) KPC+ ST-307, SHV-28 (2D), KPC2 NDM-1	1 0.26 st0.625 st0.625 st0.625 d.125 0.125 0.125 0.25 0.25 0.5 1 1 0.6 0.126 st0.625 s	64         8           20.0525         0.125           0.125         2           32         1           2         32           1         2           2         32           1         2           32         0.125           0.25         0.5           0.5         0.5           0.5         0.5           0.5         0.5           0.5         0.5           0.5         0.5           0.5         4           16         0.6           0.5         4           16         16	18 \$0.0625 0.125 0.125 0.125 1 4 4 4 4 4 0.5 1 1 1 0.5 0.5 1 1 1 0.5 0.5 1 1 1 2 1 5 0.5 1 1 1 2 1 5 0.125 0.15 0.5 0.5 0.5 1 1 1 1 2 2 1 1 1 2 2 1 1 1 2 2 1 1 1 2 2 1 1 1 2 2 1 1 1 2 2 1 1 1 2 2 1 1 1 2 2 1 1 1 2 2 1 1 1 2 2 1 1 1 2 2 1 1 1 2 2 1 1 1 2 2 1 1 1 2 2 1 1 2 2 1 5 8 8 1 1 2 2 4 4 4 4 4 4	>64 >64 \$20625 0.125 0.125 32 64 64 64 16 64 >64 >64 >64 >64 32 0.5 0.5 0.5 0.5 0.5 1 1 1 2 8 >64 32 0.5 0.5 0.5 1 1 1 1 2 8 32 0.5 0.12 0.125 0.125 0.125 0.125 0.125 0.125 0.125 0.12 0.12 0.125 0.125 0.125 0.12 0.12 0.125 0.125 0.125 0.12 0.125	32 1 1 16 364 364 364 364 364 364 364 36	0.6 20.0525 0.125 20.0525 20.0525 8 32 0.125 0.125 15 64 32 0.125 8 32 0.125 8 32 0.125 8 32 0.125 8 32 0.125 8 32 0.125 9 15 64 11 64 64 64 64 64 8 8 8 8 8 8 8 8 8 8 8 8 8	0.5 0.125 \$0.0625 16 4 16 1 4 8 8 8 18 4 2 2 16 16 16 16 16 16 16 16 16 16	
MIC 60 2015ATLBI 2015ATLBI 2015ATLBI 2015ATLBI 2015ATLBI 2015ATLBI 2015ATLBI 2015ATLBI MB225 MB225 MB225 MB225 MB276 BAA-2146 K0 NIH-1 MIC 80	A baumanil K preumoniae K preumoniae B ambitra B. wiethamienai B. maitovrans B. cepacia B. cenacepatia B. cenace	ST-16, CXA-1, SHV-1 (2D) KPC+ ST-307, SHV-28 (2D), KPC2 NDM-1	1 0.26 \$2.0625 \$2.0625 \$2.0625 \$2.0625 \$2.0625 0.125 0.125 0.25 0.5 1 1 0.5 1 0.126 \$2.0625	64         8           \$20.0525         0.125           0.125         0.125           2         32           32         32           32         32           32         32           32         32           32         32           32         32           32         32           32         32           32         32           32         32           32         32           32         32           32         32	18 \$0.0625 0.125 0.125 0.125 1 4 4 4 0.5 1 1 32 16 1 1 0.5 0.5 0.5 1 1 1 2 16 8 1 1 1 2 16 8 8 1 1 1 2 4 4 32 16 8 8 1 1 1 2 16 1 1 1 1 1 1 1 1 1 1 1 1 1	>64 >64 >64 20.0625 0.125 0.125 0.125 0.125 0.125 0.4 64 64 64 64 >64 32 0.5 0.5 0.5 0.5 0.5 0.5 0.5 1 1 2 8 8 >64 64 32 0.5 0.5 0.5 1 1 1 2 8 8 >64 64 32 0.125 0	32 1 1 16 >64 >64 >64 >64 >64 >64 18 0.5 0.25 1 1 16 8 8 8 >64 >64 >64 >64 >64 >64 >64 >64	0.6 20.0525 0.125 20.0525 20.0525 20.0525 20.125 0.125 16 64 32 0.125 20.125 16 64 32 0.125 20.0525 8 8 8 1 2 4 15 64 64 64 64 64 64 64 64 64 64	0.6 0.125 50.0625 16 4 15 1 4 8 8 16 4 8 8 16 15 16 4 8 8 16 16 15 16 4 8 8 16 16 16 16 16 16 16 16 16 16	
MIC 60           2015ATLBI           2015ATLBI           2015ATLBI           2015ATLBI           2015ATLBI           2015ATLBI           2015ATLBI           MB223           BAA-1705           MB226           MB226           MB226           MB226           MB226           MB226           MB226           MB226           MB226           MB266           MIC 60           MIC 60           AU0212           BAA-248           COD-1           BAA-247           BAA-247           BAA-247           BAA-248           COD-1           BAA-247           BAA-248           COD-1           BAA-247           BAA-247           BC7           AU00158           MIC 60           MB271           L096           MB236           TIDE003	A baumanil K preumoniae K preumoniae B ambitronia B. wietnamienzia B. wietnamienzia B. multivorans B. cenocepadia B. cenocepadia	ST-16, CXA-1, SHV-1 (2D) KPC+ ST-307, SHV-28 (2D), KPC2 NDM-1	1 0.26 \$0.0625 \$0.0625 \$0.0625 \$0.0625 \$0.0625 \$0.125 0.125 0.125 0.125 0.25 0.5 1 1 0.6 <b>0.126</b> \$0.0625	64         8           \$20,0525         0,125           0,125         2           32         1           2         32           1         2           >54         >64           >64         2           0.25         0.5           0.5         0.5           0.5         0.5           0.5         0.5           0.5         4           >64         16           0.5         4           16         32           64         16	18 \$0.0625 0.125 0.125 1 4 4 4 0.5 1 1 32 16 16 1 0.5 0.5 1 1 1 2 2 5 8 1 1 2 2 5 8 1 1 1 2 2 5 6 8 1 1 1 1 1 1 1 1 1 1 1 1 1	>64 >64 >64 20.0625 0.125 0.125 0.125 0.125 0.125 0.125 0.4 *64 *64 *64 *64 *64 *64 *64 *64 *64 *6	32 1 1 16 >64 >64 >64 >64 >64 18 0.5 0.25 1 1 16 8 8 >64 >64 >64 >64 >64 >64 >64 >64	0.6 20.0625 0.125 20.0625 20.0625 20.0625 20.0625 20.125 16 64 32 0.125 0.125 20.125 8 8 8 8 8 8 1 2 4 16 64 64 64 64 64 64 8 8 8 8 8 8 8 8 8 8 8 8 8	0.6 0.125 s0.0625 16 4 16 1 4 8 ×64 8 8 ×64 8 8 ×64 8 8 ×64 8 8 ×64 8 8 8 8 8 8 8 8 8 8 8 8 8	
MIC 60 2015ATLBI 2015ATLBI 2015ATLBI 2015ATLBI 2015ATLBI 2015ATLBI 2015ATLBI 2015ATLBI MB225 MB225 MB225 MB225 MB276 BAA-2146 K0 NIH-1 MIC 80	A baumanil K preumoniae K preumoniae B ambitra B. wiethamienai B. maitovrans B. cepacia B. cenacepatia B. cenace	ST-16, CXA-1, SHV-1 (2D) KPC+ ST-307, SHV-28 (2D), KPC2 NDM-1	1 0.26 \$2.0625 \$2.0625 \$2.0625 \$2.0625 \$2.0625 0.125 0.125 0.25 0.5 1 1 0.5 1 0.126 \$2.0625	64         8           \$20.0525         0.125           0.125         0.125           2         32           32         32           32         32           32         32           32         32           32         32           32         32           32         32           32         32           32         32           32         32           32         32           32         32           32         32	18 \$0.0625 0.125 0.125 0.125 1 4 4 4 0.5 1 1 32 16 1 1 0.5 0.5 0.5 1 1 1 2 16 8 1 1 1 2 16 8 8 1 1 1 2 4 4 32 16 8 8 1 1 1 2 16 1 1 1 1 1 1 1 1 1 1 1 1 1	>64 >64 >64 20.0625 0.125 0.125 0.125 0.125 0.125 0.4 64 64 64 64 >64 32 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 1 1 2 8 8 >64 64 32 0.5 0.5 0.15 0.15 0.15 0.15 0.15 0.15 0	32 1 1 16 >64 >64 >64 >64 >64 >64 18 0.5 0.25 1 1 16 8 8 8 >64 >64 >64 >64 >64 >64 >64 >64	0.6 20.0525 0.125 20.0525 20.0525 20.0525 20.125 0.125 16 64 32 0.125 20.125 16 64 32 0.125 20.0525 8 8 8 1 2 4 15 64 64 64 64 64 64 64 64 64 64	0.6 0.125 50.0625 16 4 15 1 4 8 8 16 4 8 8 16 15 16 4 8 8 16 16 15 16 4 8 8 16 16 16 16 16 16 16 16 16 16	
MIC 60           2015ATLBI           2015ATLBI           2015ATLBI           2015ATLBI           2015ATLBI           2015ATLBI           2015ATLBI           MB225           MB225           MB225           MB226           MB275A           BAA-1705           MB276A           BAA-2145           ND NH-1           MIC 80	A baumanil K preumonise K pr	ST-16, CXA-1, SHV-1 (2D) KPC+ ST-307, SHV-28 (2D), KPC2 NDM-1	1 0.25 st0.0625 st0.0625 st0.0625 d.125 0.125 0.125 0.25 0.25 0.25 1 1 0.6 0.126 st0.0625 st0.025 st0.02	84           8           ±0.0525           0.125           0.125           0.125           1           2           33           34           35           35           35           35           35           35           35           35           35	18 \$0.0625 0.125 0.125 0.125 1 4 4 4 4 0.5 1 1 32 16 18 1 0.5 0.5 1 1 1 2 16 8 1 1 2 16 8 1 1 2 16 8 1 1 2 16 1 1 1 1 2 1 1 1 1 1 1 1 1 1 1 1 1 1	>64 >64 >64 20.0625 0.125 0.125 0.125 0.125 0.125 0.125 0.4 >64 >64 >64 >64 >64 >64 >64 32 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5	32 1 1 16 364 364 364 364 364 364 364 36	0.6 20.0525 0.125 20.0525 20.0525 8 32 0.125 0.125 16 64 32 0.125 8 32 0.125 15 64 32 0.125 8 8 8 8 1 1 2 4 16 64 8 8 8 8 8 8 8 8 8 8 8 8 8	0.6 0.125 \$0.0625 16 4 16 1 4 8 8 8 18 4 2 2 16 16 16 16 16 16 16 16 16 16	
МС 60 2015АТLBI 2015АТLBI 2015АТLBI MB271 MB225 MB225 MB225 MB225 MB276A BAA-2105 MB256 MB776A BAA-2145 Kp NIH-1 MC 80 MC 80	A baumanil K preumoniae K preumoniae B ambitra B am	ST-16, CXA-1, SHV-1 (2D) KPC+ ST-307, SHV-28 (2D), KPC2 NDM-1	1 0.26 \$2.0625 \$2.0625 \$2.0625 \$2.0625 \$2.0625 0.125 0.25 0.25 0.5 1 1 0.6 0.126 \$2.0625	84           8           \$20.0525           0.125           0.125           2           32           32           32           32           32           32           32           32           32           32           32           32           32           32           32           32           0.5           0.5           0.5           0.5           0.5           0.5           0.5           0.5           0.5           0.5           0.5           0.5           0.5           0.5           0.5           0.5           0.5           4           16           32           64           54           >64	18 \$0.0625 0.125 0.125 0.125 1 4 4 4 0.5 1 1 32 16 16 1 1 0.5 0.5 0.5 0.5 1 1 1 2 16 8 8 1 1 2 16 8 8 1 1 2 16 8 8 1 1 2 16 8 8 1 1 2 16 8 8 1 1 2 16 16 16 16 16 17 16 16 16 16 16 16 16 16 16 16	>64 >64 >64 20.0625 0.125 0.125 0.125 0.125 0.125 0.4 64 >64 64 >64 32 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 1 1 1 2 8 8 >64 64 32 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5	32 1 1 16 >64 >64 >64 >64 >64 >64 32 >64 >64 18 0.5 0.25 1 1 16 8 8 8 >64 >64 >64 >64 >64 >64 >64 >64	0.6 20.0525 0.125 20.0525 20.0525 8 32 0.125 16 64 32 0.125 0.125 16 64 32 0.125 20.0525 8 8 8 8 1 2 4 15 64 64 64 64 64 64 64 64 64 64	0.6 0.125 50.0625 16 4 15 1 4 8 ×64 8 ×64 8 16 15 16 4 4 2 2 15 16 16 8 8 16 18 8 16 18 8 16 18 18 16 10 10 10 10 10 10 10 10 10 10	
MIC 60           2015ATLBI           2015ATLBI           2015ATLBI           2015ATLBI           2015ATLBI           MB225           MB225           MB225           MB225           MB225           MB2776A           BAA-1705           MB225           MB276A           BAA-2146           K0 NIH-1           MIC 80           MIC 60           AU2212           BAA-243           COD-1           BAA-243           BC7           J2215           BC7           AUC0158           MIC 80           MB314           MB3157           MB361A           7131432           MIC 80	A baumanil K preumoniae K preumoniae B ambitra B am	ST-16, CXA-1, SHV-1 (2b) KPC+ ST-307, SHV-28 (2b), KPC2 NDM-1	1 0.26 \$20,0625 \$20,0625 20,0625 20,0625 20,0625 0,125 0,125 0,125 0,25 0,25 20,0625 \$20,0625	84           8           \$20,0525           0,125           0,125           2           32           32           32           32           32           32           32           32           32           32           32           32           32           32           32           32           0.5           0.5           0.5           0.5           0.5           0.5           0.5           0.5           0.5           0.5           0.5           0.5           0.5           0.5           0.5           0.5           0.5           4           16           32           64           54           564	18 \$0.0625 0.125 0.125 0.125 1 4 4 4 0.5 1 1 32 16 16 1 1 0.5 0.5 0.5 0.5 1 1 1 2 16 8 8 1 1 2 16 8 8 1 1 2 16 8 8 1 1 2 16 8 8 1 1 2 16 8 8 1 1 2 16 16 16 16 16 17 16 16 16 16 16 16 16 16 16 16	>64 >64 >64 20.0625 0.125 0.125 0.125 0.125 0.125 0.4 64 >64 64 >64 32 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 1 1 1 2 8 8 >64 64 32 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5	32 1 1 1 16 >64 >64 >64 >64 >64 32 >64 >64 18 0.5 0.25 1 1 1 16 8 8 8 >64 >64 >64 >64 >64 >64 >64 >64	0.6 20.0525 0.125 20.0525 20.0525 8 32 0.125 16 64 32 0.125 16 64 32 0.125 20.0525 8 8 8 1 2 4 15 64 64 64 64 64 64 64 64 64 64	0.6 0.125 50.0625 16 4 15 1 4 8 ×64 8 ×64 8 16 15 16 4 4 2 2 15 16 16 8 8 16 18 8 16 18 8 16 18 18 16 10 10 10 10 10 10 10 10 10 10	
MIC 60           2015ATLBI           20	A baumanil K preumonise K pr	ST-16, CXA-1, SHV-1 (2b) KPC+ ST-307, SHV-28 (2b), KPC2 NDM-1	1 0.25 st0.0625 st0.0625 st0.0625 d.125 0.125 0.125 0.25 0.25 0.25 1 1 0.6 0.126 st0.0625 st0.055 st0.05	84           8           ±0.0525           0.125           0.125           0.125           1           2           32      32      32	18         \$20.0625         0.125         0.125         0.125         1         4         4         0.5         1         32         16         10         0.5         0.5         0.5         0.5         1         2         16         8         1         2         16         8         1         2         64         >64         >64	>64 >64 >64 20.0625 0.125 0.125 0.125 0.125 0.125 0.125 0.4 >64 >64 >64 >64 >64 >64 32 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 1 1 1 2 8 >64 16 16 18 11 2 2 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5 0.5	32 1 1 16 364 364 364 364 364 364 364 36	0.6 20.0525 0.125 20.0525 20.0525 8 32 0.125 0.25	0.6 0.125 \$0.0625 16 4 16 1 4 8 8 8 18 18 18 2 2 16 16 16 16 16 16 16 16 16 18 8 8 18 18 18 18 18 18 18	

<sup>a</sup>Strains used in biofilm assays are highlighted in green.

No.600         E. cold         TDA1         0.125         0.025         0.125         <					7.	-	100 M	/		/	7.7
Image         East         Text         0.125         0.205         0.125         0.205         0.215         0	Strain ID	Species	Genctype	0	Alter Cold Alter	STREET SEA	See Nets C	Stations and	ANTROPACITY IN	Nosan 1	BERRE
Mitting         E. cold         TBA1         0.125         0.126         0.125         0.126	ATCC 25922	E. 004		/	0.25	0.25	0.125	2	\$0.0625		Index
Mitto         E cod         TDA1, 67:37         0.63         0.125         0.23         0.125         0.03         0.035	MB1676	E. 006	TEM-1	0.125		0.125					0.0825-1 µg/ml
LCT-64:09       E. col.       MAM-1       O.25       194       82       194       64       64       4       64       64       64       64       64       64       64       64       64       64       64       64       64       64       64       64       64       75 <th< td=""><td></td><td></td><td>TEM-1, ST-73</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td>2-4 pg/ml 8-10 µg/ml</td></th<>			TEM-1, ST-73								2-4 pg/ml 8-10 µg/ml
MB70A         E col         CVA1, EF-6         2         8         4         94         94         2         94           MB33B         E col         CVA1, EF-65         2         8         4         94         0.155         19           MB33B         E col         CVA1, EF-65         2         94         94         94         91         94           MB32B         E col         CVA1, EF-65         2         94         94         91         94           MB32B         E col         ADA1         2         946         94         91         94           MB32B         E col         ADA1         2         944         94         91         94           MB32B         E col         ADA1         2         94	BCT-B-058	E. coá	NDM-1	0.25	>64	32	>64	64	4	Č4	32-84 µg/ml
HB330         E cd         OXAL (CTAR15         2         8         2         944         94         0.015         18           MEXTAL         E cd         MAXL         2         2         1         44         51         51         53           MEXTAL         E cd         MAXL         2         2         1         44         54         50         53         53           MEXTAL         E cd         MAXL         2         2         1         44         54         52         54         55         54           MEXTAL         E cd         MAXL         2         1         4         1         0.25         1         1         4         1         0.25           Rest         E cd         MAXL         D statistic         D statistic <thd statistic<<="" td=""><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td>&gt; 64 µg/ml</td></thd>											> 64 µg/ml
MBC274         E. col.         OKA1, CZAH5         2         2         1         64         32         0.75         32           MBC14U         E. col.         NGA1         2         0.64         32         0.64         36         0           MBC 50         E. col.         NGA1         2         0.64         32         0.64         16         0.6           MBC 50         E. col.         2         2         1         44         32         0.55         16           MC 50         E. col.         2         2         1         44         32         0.55         16           MC 50         E. col.         2         2         1         44         12         1         0.55           MC 7207         P. sangtess         51-728. (MAC, PCC)         0.25         0.5         1         1         4         15         0.25           MD 71         P. sangtess         51-728. (MAC, PCC)         0.25         0.5         1         4         44         44         44           MD 71         P. sangtess         0.045. PCC 21. PCM         2         94         44         44         44           MD 70         P. sangtess <td></td>											
HSD 7054         E. od.         NGM-1         2         194         194         194         194         194         194         194           MC 00         E. col         4         544         52         344         544         52         444         544         52         61.55         61.55           MC 00         E. col         0.25         0.25         2         1         4         0.5         0.25           MC 00         E. col         0.052         0.25         1         1         4         0.5         0.25           MC 00         Stangicas         0.052         0.25         1         1         2         1         0.25           MC 00         Paragicas         0.040.000.000.000.000.000.000         0.35         1         4         4         10         8         0.5           ME00         Paragicas         0.040.000.000.000.000.000.000.000.000.0	MB2374	E. 004	OKA-1, CTX-M-15	2	2	1	64	32	0.125	32	
MC 00         E. coli         4         5-4         32         5-44         1-64         16           MC 00         E. coli         2         2         1         64         32         0.155         16           MC 00         E. coli         2         2         1         64         32         0.155         16           MC 00         E. coli         1         2         1         1         4         1         0.25           MC 10         Parangizona         51-123         0.040, (PCC 14004         0.05         0.5         2         2         8         8         0.35           MERA         Parangizona         51-023         0.05         1         9         32         7-64         8         0.35           MERA         Parangizona         Dr. Ox04, (PCC 14004         1         9         32         7-64         8         0.35           MERA         Parangizona         Dr.OC 1, NOA1         2         3-64         64         84         64         84         64         84         64         84         64         84         64         84         64         84         64         84         64         84											
MC 00         E. coli         2         2         1         64         32         0.125         14           M141         P. stroghome         0.025         0.23         2         1         4         0.05         0.23           M151         P. stroghome         0.055         0.23         0.25         2         1         4         0.05         0.25           M1511         P. stroghome         57.122.04.04.07.0C-5.00.04         0.28         0.25         1         4         1         0.25           M1517         P. stroghome         57.17.00.04.07.0C-5.00.04         0.28         0.24         48         1         168         8         0.25           M1600         P. stroghome         57.17.00.04.07.0C-3.00.04         2         1         16         4         48         164         8         19           M1500         P. stroghome         2         7.44         744         744         744         64         3.2         1         8         4         164         16         1         1         1         1         1         1         1         1         1         1         1         1         1         1         1         1	NSU 10854	E. 004	NUM-1		204	*	204	204	10	704	
ATCC 2020         P. Banglana         SO 0025         0.25         1         1         4         1         0.25           METAC 27805         P. Banglana         ST-220, COV-50, PCC-3, OLD         0.25         0.25         2         2         6         6         0.25           META         P. Banglana         ST-220, COV-50, PCC-3, OLD         0.25         1         6         4         6         1         6         6         0.25           META         P. Banglana         ST-20, COV-50, PCC-3, OLD         1         1         9         32         944         64         8         6											
ATCC 2020         P. Banglana         SO 0025         0.25         1         1         4         1         0.25           METAC 27805         P. Banglana         ST-220, COV-50, PCC-3, OLD         0.25         0.25         2         2         6         6         0.25           META         P. Banglana         ST-220, COV-50, PCC-3, OLD         0.25         1         6         4         6         1         6         6         0.25           META         P. Banglana         ST-20, COV-50, PCC-3, OLD         1         1         9         32         944         64         8         6	PA14	P annuitona		0.25	0.25	2		4	05	0.25	
MB14         P. Banglanos         ST-122. (SVA6.) PCC-10         0.25         0.25         1         6         4         1         0.51           MEOD         P. Banglanos         ST-20. (SVA6.) PCC-10.0.2         0.25         1         6         4         15         1         6         0.51           MEOD         P. Banglanos         ST-20. (SVA6.) PCC-1.0.2.         0.25         1         6         4         15         6         0.55           MEOD         P. Banglanos         ST-37. (SVA6.) PCC-1.0.2.         0.25         1         6         4         15         6         6         6         16         6         6         16         6<											
MBBOD         P surgicas         67:22         CMAD (PC2, AUA)1         60:05         1         8         4         16         0         0           MBOD         P surgicas         CVAAD (PC2, CO, CO, CO, CO, CO, CO, CO, CO, CO, CO											
MEXPT         P. surgicas         ST-ND CASE, PCC-8         0.25         1         4         4         4         10         8         0.5           MED0         P. surgicas         ST-ND CASE, PCC-3         1         19         32         3+84         64         8         0.5           MED0A         P. surgicas         ST-ND CASE, PCC-3         1         19         32         3+84         64         8         0.6           MED0A         P. surgicas         ST-ND CASE, PCC-3         1         19         32         3+84         64         64         64         64           MED0A         P. surgicas         0.253         1.4         4         4         0.253         0.5         4         2         8         0.755         0.5           ACC 17978         A Surmati         0.125         0.5         4         2         8         10         3         2         3         10         3											
S/M1         D. Burginges         T. S. OLAG, PICG, NOLAT         1         19         32         3-64         64         64         64           MBSDA         P. Burginges         CUAS, PICG, NOLAT         2         3-64	MB771		ST-179, OXA-50, PDC-8	0.25	1	4	4	16		0.5	
MBSSA         P surgices         0737, 0XA6, PCC3, NDM1         2         1+84 <th< td=""><td></td><td></td><td>OXA-50, PDC-2</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></th<>			OXA-50, PDC-2								
ME730         P. seruginosa         OXA-00, PDC-3, NDM-1         2         P44         P			ST-357 OXA-50 POC-3 NDM-1								
MCC 90         P. aeroginosa         9.25         1         8         4         16         9         0.6           AVCC 17978         A. Baumeni         0.175         0.5         4         2         8         0.175         0.5           AVCC 1978         A. Baumeni         0.0255         1         4         4         4         0.025         1.0           AVCC 1963         A. Baumeni         0.5         64         2.8         4         8         0.25         1.0 <t< td=""><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></t<>											
ATCC 1707         A. Baumani         0.125         0.5         4         2         8         0.125         0.5           BAA.1703 GDF         A. Baumani         40.0255         1         4         4         4         0.255         2           Lec.1         A. Baumani         10.055         1         4         4         4         0.255         2           Lec.1         A. Baumani         10.5         64         324         464         1         32           Lec.1         A. Baumani         1         2         8         8         16         0.125         0.25           Lec.1         A. Baumani         1         2         8         8         16         0.125         0.25           Lot 2005000         A. Baumani         1         64         944         19         464           Lot 200500         A. Baumani         1         8         19         944         32         0.25         1         0.0025         1         0.0025         1         0.0025         1         0.0025         1         0.0025         1         0.0025         1         0.0025         1         0.0025         1         0.025         0.25											
DAA TOS GOP         A baumani         DOCSS         1         4         4         4         4         0.0055           Loc-1         A baumani         DOCSS         1         4         4         4         0.025         2           Loc-1         A baumani         D1         8         16         0.025         2         8         4         8         0.025         2           Loc-1         A baumani         D1         2         8         8         10         0.025         0.025           Loc-1         A baumani         D1         2         8         8         10         0.025         0.025           Loc-1         A baumani         D1         2         64         64         24         4         64         22         0.025           Loc-2         A baumani         1         64         24         24         64         232         0.025         64           LOC 50         A baumani         1         8         16         16.0255         1         0.0255         0.25           Loc 20150/LB         K pneuronias         ST-16,0XA-1,9M-120         0.0255         0.25         10         0.0255         10         <	MIC 50	P. aeruginosa		0.25	1	8	4	16	8	0.5	
ATCC 19000       A summeri       St D025       2       8       4       8       0025       2         AB0577       A summeri       0.5       644       322       1464       644       1       32         S0505 105.0       A summeri       0.5       644       324       164       16       1         S0505 105.0       A summeri       2       644       644       344       464       464         S0505 105.0       A summeri       1       1646       322       0.55       64       344       464       464         S0505 105.0       A summeri       1       646       324       344       344       322       0.55         MC 30       A summeri       8       8       10       944       322       0.55       64         MC 30       A summeri       8       8       10       944       322       0.55       15       9205       9205       1       95005       9205       1       9205       9205       1       9205       9205       9205       1       9205       9205       1       9205       9205       1       9205       9205       1       9205       9205       920	ATCC 17978	A beumani		0.125	0.5	4	2	8	0.125	0.5	
Le-1         A summi         1         8         90         964         964         964         1         322           AB0057         A summi         1         2         8         8         10         0.755         0.25           Harc-1         A summi         1         2         84         64         944         76         15         764           Barc-1         A summi         NDM-1         1         944         64         944         64         4         64           205407         A summi         1         846         944         64         4         64           205407         A summi         1         8         8         10         944         32         0.5         64           MC 50         A burnami         1         8         16         16         715         0.125         1         0.125         0.25         0.25         0.25         0.25         0.25         1         0.025         0.25         10         0.125         0.25         10         0.125         0.25         10         0.125         0.25         10         0.125         0.25         10         0.125         0.25											
Absor?         A summi         0.5         64         92         964         96											
Hunch         A beament         C         2         64         64         964         164         16         964           2076-02         A beament         1         64         52         964         964         32         0.55           AFE         A beament         1         64         52         964         964         32         0.55           MC 90         A beament         2         64         64         >64         32         0.5         64           MC 90         A beament         1         8         8         19         >84         32         0.5         64           MC 90         A beament         1         8         16         >64         >64         >64         >64         64 <td< td=""><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></td<>											
BC7-BC20         A baumeni         NOM-1         1         0-64         0-44					2						
200540C         A. baumeni         1         0.6         32         0.44         344         32         0.25           MC 20         A. baumani         2         0.6         44         32         0.5         64           MC 30         A. baumani         2         0.6         44         >24         16         64           MC 30         A. baumani         1         8         16         >24         >24         16         64           20150110         K. pneuroniae         30.0655         0.125         0.0265         1         s0.0655         0.25           20150110         K. pneuroniae         ST-16, 0XA-1, SH/-1 (2)         s0.0655         0.25         0.25         0.25         10         0.155         10         155         16           MB770         K. pneuroniae         KPC+         0.155         2         0.5         82         0.155         16           ME324         K. pneuroniae         KPC+         0.155         2         0.5         82         0.155         16           ME324         K. pneuroniae         KPC+         0.155         2         0.5         84         44         84         32         0.155         1 <td></td> <td></td> <td>NDM-1</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>			NDM-1								
MC 89         A. baumani         1         8         16         >244         32         0.5         1           201507LB         K. pnauronias         s0.0625         0.125         0.0625         1         0.025         0.25           201507LB         K. pnauronias         ST-16, OXA-1, SPV-1 (2b)         0.0025         0.125         0.125         1         0.125         0.255         0.25         0.25         0.25         1         0.0025         16         0.0125         1         16         16         16         16         17         16         16         17         16         17         16         17         16         17         16         16	X80546C	A beumani		1	64	32	>64	>64	32	0.25	
MC 80         A. baumani         1         8         16         > 244         32         0.5         1           20150TLB         K. pneuroniae         80.0025         0.125         0.0025         1         0.0025         0.25           20150TLB         K. pneuroniae         ST-16, 0XA-1, SPL-1 (2b)         0.025         0.125         0.125         0.025         1         0.0025         1         0.0025         16         0.0025         16         0.0025         16         0.0025         16         0.0025         16         0.0025         16         0.0025         16         0.0025         16         0.0025         16         0.0025         16         0.0025         16         0.0025         16         0.0025         16         0.0025         16         0.0025         16         0.0025         16         0.0025         16         0.0125         1         16         0.0125         1         0.0125         1         16         0.0125         1         0.0125         1         16         0.0125         1         1         16         0.0125         1         1         16         0.0125         1         1         1         16         0.0125         1         1	MIC 90	A. baumanii		2	64	64	>64	>64	16	64	
2015/00/160         K. presumonise         ST.46, CXA-1, SHV-1(2b)         40.0255         0.125         0.125         1         0.125         0.25           MB771         K. presumonise         ST.46, CXA-1, SHV-1(2b)         40.0255         4.2         1-84         32         0.0255         16         40.025         16         40.42         40.42         16         40.42         16         40.42         16         40.42         40.42         16         40.42         40.42         16         40.42         40.42         16.12         16         32.2         10.12         16         32.2         10.12         16         32.2         10.12         16.02         16.025											
MB/21         K. preservonise         ST-16 (CXA-1, SHV-1 (2p)         s0.0025         0.25         0.25         16         s0.0025         16           MB778A         K. preservonise         KD0025         2         4         24         32         0.125         16           MB224         K. preservonise         KSC+         20.025         2         4         64         32         0.125         16           MB224         K. preservonise         ST-307, SHV-28 (2b), KPC2         0.125         32         4         64         344         32         1           MB226         K. preservonise         ST-307, SHV-28 (2b), KPC2         0.125         32         4         64         344         32         1           MB228         K. preservonise         NDM-1         1         164         32         0.125         8           MA2120         K. preservonise         NDM-1         1         164         32         0.125         8           MA2020         K. preservonise         NDM-1         1         164         32         0.125         8           MA20212         B. amb4wcams         s0.0025         0.5         1         1         1         4											
MB278A         K. presmonia         KPC+         S00005         S2         4         64         32         0.125         16           ME254         K. presmonia-         KPC+         S00005         S2         4         64         -964         8         19           ME254         K. presmonia-         ST307, SHV28 (2b), KPC2         O.125         S2         4         64         -964         32         1           ME026         K. presmonia-         ST307, SHV28 (2b), KPC2         O.125         S2         4         64         -964         32         1           ME026         K. presmonia-         0.125         S2         44         64         -964         64         32         1           ME026         K. presmonia-         1         >64         16         >64         2         >64         964         64         8           MC 90         K. presmonia-         S00025         0.5         1         0.5         1         1         4           C0D-1         B. multiverse         S00025         0.5         1         1         1         1         6         32           EA-244         B. entitresis         S00025         2			ST.18 OYA 1 SHULL (%)								
BAA-1705         K. preamoniae         KPC+         s0.0005         52         4         64         764         8         16           ME024         K. preamoniae         87:307, SHV28 (2b), KPC2         0.125         22         4         64         764         32         1           ME024         K. preamoniae         87:307, SHV28 (2b), KPC2         0.125         92         4         64         32         1           ME024         K. preamoniae         NDM-1         1         844         32         0.125         8           BAA-2140         K. preamoniae         NDM-1         1         844         32         0.125         8           ME0290         K. preamoniae         1         >644         16         >44         8           ME0201         K. preamoniae         1         >644         16         32         0.125         8           ME0201         K. preamoniae         100025         4         0.5         64         32         0.125         8           ME0201         K. preamoniae         20.0025         0.5         1         1         1         1         8         32         0.125         4         32         0.125			51-10 ( UVF1, 0HV-1 ( 20)	and the second se		Concession in case of the local division of		And in case of the local division of the loc	Concession of the local division of the loca		
MB003         K. preumoniae         ST.307, SHV.23 (2b), KPC2         0.125         92         4         64         92         1           MB023         K. pneumoniae         NDM-1         1         844         32         0.125         8           BAA_2148         K. pneumoniae         NDM-1         1         844         32         0.125         8           MB023         K. pneumoniae         NDM-1         1         844         32         0.125         8           MB026         K. pneumoniae         NDM-1         1         844         32         0.125         8           MB026         K. pneumoniae         1         x64         16         32         0.125         8           MB027         B. emblema         1         x64         16         32         0.125         8           MB028         K.pneumoniae         1         x64         16         32         0.125         8           MB029         K.pneumoniae         1         x64         16         32         0.125         8           MB021         B. emblema         1         0.0625         1         1         1         4         8         8			KPC+								
MB028         K. preumonies         NDM-1         0.5         4         1         64         32         0.125         8           BAA.2140         K. preumonies         NDM-1         1         >644         32         >644         >64 <td></td> <td></td> <td>ST.SOT SHALDS MAN KDCD</td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>			ST.SOT SHALDS MAN KDCD								
Kp NH-1         K preumoniae         2         x64         16         x64         x64         84         8           MIC 90         K, preumoniae         1         x64         16         x64         x64         64         16           MIC 90         K, preumoniae         20.0525         4         0.5         64         32         0.125         8           AU0212         B. ambhran         20.0525         0.5         1         0.5         1         1         4           C0D-1         B. muthvorans         40.0525         0.5         1         0.5         1         1         4           C0D-1         B. muthvorans         40.055         0.5         1         1         1         64         32           BAA-248         B. vintamienskis         40.055         2         2         2         64         4         32           HCA24         B. cenocepacia         40.055         2         2         2         64         4         32           ATCC 25416         B. cenocepacia         40.055         2         2         2         64         364         364           BC7         B. cenocepacia         40.055			01-007, 0111-00 (20), 10-02								
MIC 90         K. pneumoniae         1         >64         16         >64         32         0.125         8           AU0212         B. ambhua         s0.0625         0.5         1         0.5         1         1         4           COD-1         B. muthonan         s0.0625         0.5         1         1         1         4           COD-1         B. muthonan         s0.0625         0.5         1         1         1         4           COD-1         B. muthonan         s0.0625         0.5         1         1         1         4           COD-1         B. muthonan         s0.0625         0.5         1         1         1         4           BAA-348         B. vistominaniais         s0.0625         2         1         2         16         32           BAA-348         B. vistominaniais         s0.0625         2         2         2         64         4         32           BAA-348         B. vistominaniais         s0.0625         2         2         2         64         4         32           S2215         B. cencospecia         s0.0625         32         8         32         >64         >64 <td< td=""><td></td><td></td><td>NDM-1</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></td<>			NDM-1								
MIC 90         K. pneumoniae         \$20,0525         4         0.5         64         32         0.125         8           AU0212         B. ambiena         \$0,0025         0.5         1         0.5         1         1         4           C0D-1         B. mubiorana         \$0,0025         0.5         1         1         1         4           C0D-1         B. mubiorana         \$0,0025         0.5         2         1         2         16         \$22           BAA.348         B. vietnaminenia         \$0,0025         2         2         1         2         16         \$22           BAA.348         B. vietnaminenia         \$0,0025         2         2         2         64         4         32           BAA.348         B. vietnaminenia         \$0,0025         2         2         2         64         4         32           ATCC 25416         B. cepacia         \$0,0025         32         8         32         >64         64         8         8           J2315         B. cepacia         \$0,0025         32         8         32         >64         >64         >64         >64           AU00155         B. dotaa											
COD-1         B. multivorans         StO005         0.5         1         1         1         16         32           BAA-247         B. multivorans         StO0055         0.5         2         1         2         16         52           BAA-348         B. visionaministis         StO0055         0.5         2         1         2         16         52           BAA-348         B. visionaministis         StO0055         2         2         2         64         4         3           H12424         B. cenocospecia         StO0055         2         2         2         64         4         32           ATCC 25416         B. cenocospecia         StO0055         32         8         32         >64         8         8           J2315         B. etenocospecia         0.255         32         8         32         >64         >64         >64           ALUO155         B. doteaa         32         32         32         8         32         >64         >64         >64           MIC 90         Boc         0.25         32         8         32         >64         >64         >64           MIC 90         Boc <t< td=""><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></t<>											
BAA-247         B. mulborans         s0.0025         0.5         2         1         2         18         32           BAA-248         B. vistramientais         s0.0025         1         1         1         0.5         0.125         4           1840-1         B. oppacia         s0.0025         2         2         2         64         4         32           HU204         B. cencepacia         s0.0025         2         2         2         64         4         32           ATOC 255116         B. cencepacia         s0.0025         2         4         4         64         8         8           J2215         B. cencepacia         s0.0025         2         8         32         >664         4         32           J2215         B. cencepacia         0.25         >44         2         8         32         >664         >64         >64           AL00158         B. dotsa         32         32         8         32         >664         >64         >64           MC 90         Boc         0.25         32         8         32         >664         >64         >64           MC 90         Boc         0.025											
BAA-348         B. vietnamiania         st0 0005         1         1         1         0.5         0.125         4           1840-1         B. cepacia         st0 0005         2         2         2         84         4         8           H12Q4         B. cepocepacia         st0 0005         2         2         2         84         4         82           ATCC 25418         B. cepocepacia         st0 0005         2         2         4         4         64         8         8           J2315         B. cepocepacia         st0 0005         32         8         32         >64         64         >64           BC.77         B. cepocepacia         0.25         >44         22         >64         >64         >64           AL0015         B. dotepacia         0.25         32         8         32         >64         >64         >64           MC 90         Boc         0.25         32         8         32         >64         >64         >64           MC 90         Boc         0.25         1         1         1         \$64         >64         1           MC 90         Boc         0.25         1											
1840-1         B. cospecia         s0.0005         2         2         2         84         4         8           H12X24         B. cemocapacia         s0.0005         2         2         2         64         4         32           ATCC 25416         B. cemocapacia         s0.0005         2         2         2         64         4         32           ATCC 25416         B. cemocapacia         s0.0005         32         8         32         >64         64         8         8           J2315         B. cemocapacia         0.25         32         8         32         >64         >64         ×64           BC7         B. cemocapacia         0.25         32         8         32         >64         >64         ×64           AU00155         B. doloaa         32         32         8         32         >64         >64         >64           MIC 90         Boc         0.25         32         8         32         >64         >64         >64         10           MIC 90         Boc         90.0025         1         1         1         94         >64         0.5           MIC 90         Boc         90.00											
H12424         B. cenocepacia         st0.0025         2         2         2         64         4         52           ATCC 25616         B. cenocepacia         st0.0025         2         4         4         64         8         8           J2215         B. cenocepacia         st0.0025         52         8         52         >664         64         ×64           BC7         B. cenocepacia         0.25         32         8         32         >664         ×64         ×64           AL00155         B. dotxaa         32         32         8         32         ×64         ×64         ×64           AL00155         B. dotxaa         32         32         8         32         ×64         ×64         ×64           MIC 90         Boc         0.25         32         8         32         ×64         ×64         16           MIC 90         Boc         20.0625         1         1         1         ×64         ×64         16           MIC 90         Boc         20.0625         1         1         1         1         ×64         ×64         16           MIC 90         Boc         2         4	1840-1	B. cepacia		\$0.0825	2	2	2	64	the second design of the secon	8	
J2315         B. cenocepacia         s0.0025         92         8         32         >64         64         >64           BC7         B. cenocepacia         0.25         >64         92         8         32         >64         0.5         1         1         1         1         8.0         8.0         1         1         0.0         5         1 </td <td></td> <td></td> <td></td> <td></td> <td></td> <td>2</td> <td>2</td> <td></td> <td></td> <td></td> <td></td>						2	2				
BC7         B. cenocepada         0.25         >64         32         >64         >64         >64         >64           ALOD155         B. dobaa         32         32         8         32         >64         1         50         \$5         \$6         4         2         4         >64         >64         >64         1         \$6         \$6         \$6         \$6         \$6         \$6         \$6         \$6         \$6         \$6         \$6         \$6         \$6											
MIC 90         Boc         0.25         32         8         32         >64         >44         >64           MIC 90         Boc         50.0425         2         2         2         64         8         16           MID 90         S.matophila         50.0425         2         2         2         64         8         16           MID 91         S.matophila         50.0425         1         1         1         >64         >64         0.5           MID 971         S.matophila         50.0425         1         1         1         >64         >64         0.5           MID 971         S.matophila         50.0425         16         4         >64         >64         1           X0065         16         4         >64         >64         >64         3           MIS 1317         S. matophila         50.0425         64         >64         >64         >64         3           MIS 1317         S. matophila         50.0425         64         >64         >64         >64         3           TIC 600:6         S. matophila         50.0425         64         >64         >64         >64         >64         >64	BC7										
MIC 50         Boc         \$20,0525         2         2         2         64         8         16           MB194         S. metophila         \$20,0525         1         1         1         >64         >64         0.5           MB071         S. metophila         \$20,0525         4         2         4         >64         >64         1           IO06         S. metophila         \$20,0525         16         4         >64         >64         1           IO06         S. metophila         \$20,0525         16         4         >64         >64         8           MB1317         S. metophila         \$20,0525         64         64         >64         >64         3           TIC600/6         S. metophila         \$20,0525         64         64         64         >64         >64         3           TIC600/6         S. metophila         \$20,0525         >64         64         >64         >64         3         3           TIC600/6         S. metophila         \$20,0525         >64         >64         >64         >64         3         4           MB393         S. metophila         \$0,0525         >64         >64         >6											
MB194         S. metophila         s0.0025         1         1         1         >04         >04         0.5           MB071         S. metophila         s0.0025         4         2         4         >04         >04         1           IO08         S. metophila         s0.0025         10         4         >04         >04         1           IO08         S. metophila         s0.0025         10         4         >04         >04         3           MB1317         S. metophila         s0.0025         64         44         >04         >04         3           TD6006         S. metophila         s0.0025         64         64         >04         >04         3           TD6006         S. metophila         s0.0025         64         64         >04         >04         3           T06008         S. metophila         s0.0025         84         >84         >64         >64         3         3           T1122         S. metophila         0.0255         84         >84         >64         >64         3         4         3         3         3         3         3         3         3         3         3         3											
MB071         S. metophila         s0.0005         4         2         4         >64         >64         1           IO06         S. metophila         s0.0005         16         4         >64         >64         8           MB1317         S. metophila         s0.0005         64         >64         >64         >64         8           MB1317         S. metophila         s0.0005         64         >64         >64         >64         10           TDE0006         S. metophila         s0.0005         64         >64         >64         >64         0.25           7131432         S. metophila         s0.0005         >64         >64         >64         >64         >64          >64         >64   <											1
IO08         S. matophila         s0.0005         16         4         >64         >64         8           M61317         S. matophila         s0.0005         64         >64         >64         >64         10           TIC6006         S. matophila         s0.0005         64         64         >64         >64         010           TIC6006         S. matophila         s0.0005         64         64         >64         >64         010           TIC6006         S. matophila         s0.0005         >84         >84         >64         >64         >64         >64          >64         >64          >64         >64	MB071	S. metophile			4		4	>84	>64		
TIC6008         S. metophila         s0.0605         64         64         >64         >64         0.25           7131452         S. metophila         s0.0605         >64         <	1098	S. metophila		\$0.0825	18	4	>64	>84	>64	8	
7131432         S. mattophila         s00005         >64         4           MB005         S. mattophila         0.125         32         32         64         >64         >64         4           MB0051A         S. mattophila         1         64         >64         >64         >64         16											
MB033         8. meltophila         0.125         32         32         64         >64         >64         4           MB061A         8. meltophila         1         64         >64         >64         >64         10											
	MBØ36					32	64			4	
	MB981A	S. metophile		1	64	>64	>64	>64	>64	16	
MC 90 S. matophila 0.25 64 >64 >64 >64 >64 16	MIC 90	S. metophile		0.25	64	>64	>64	>64	>64	16	1
MIC 50 S. metophila 20.0525 32 32 64 >64 >64 4											

# TABLE 2 Heat map of MIC for cefiderocol and comparator antibiotics against six MDR Gram-negative genera in MHII<sup>a</sup>

<sup>a</sup>Strains used in biofilm assays are highlighted in green.



**FIG 1** Cefiderocol can reduce existing biofilm in both MHII and ID-CAMHB. Data represent averages of results determined for 4 *P. aeruginosa* (A) and *K. pneumoniae* (B) strains in three independent experiments per strain (\*\*, P < 0.001; \*\*\*, P < 0.0001). Error bars represent standard deviations from the means.

both strains compared to untreated controls (P < 0.001). Subsequently, further biofilm eradication assays were performed in MHII.

Four to five strains from each genus tested in the MIC study (with a range of antibiotic sensitivities, highlighted in Table 1) were included for biofilm eradication testing. We first examined dose responses in *P. aeruginosa* using antibiotic concentrations ranging from 32 to  $0.5 \,\mu$ g/ml and a crystal violet assay to measure biofilm biomass (Fig. 2). As measured by total biomass, there was a trend demonstrating dose responses. For cefiderocol, biomass reduction ranged from 20% at an antibiotic concentration of  $0.5 \,\mu$ g/ml to 34% at 32 $\,\mu$ g/ml. For viability experiments, we utilized a fixed antibiotic concentration of 4 $\,\mu$ g/ml.

Based on CFU measurements, cefiderocol treatment displayed a reduction of *P. aer-uginosa* biofilm (>90% reduction compared to the untreated control, or greater than 1 log CFU/ml) that was superior to that seen with the comparator antibiotics. In contrast, imipenem was the least effective (49% reduction) (Fig. 3; see also Table 3). Cefiderocol also reduced biofilm in *K. pneumoniae, Stenotrophomonas maltophilia*, and *B. cepacia* complex, by 83% to 91% (Fig. 4; see also Table 3). Cefiderocol was generally as effective at eradication as imipenem in *K. pneumoniae* or as ceftolozane-tazobactam in *B. cepa*-



**FIG 2** Cefiderocol reduces biofilm biomass in a dose-dependent fashion in *P. aeruginosa*. Data represent normalized crystal violet assay results for an average of 5 strains with three independent experiments per strain. Concentrations of antibiotics used in eradication assays are indicated with a clear bar.



**FIG 3** Cefiderocol reduces *P. aeruginosa* biofilm burden to a greater extent than comparator antibiotics. Data represent viability assay results for an average of 5 strains with three independent experiments per strain. The reduction in biofilm burden associated with each antibiotic was compared to that seen with an untreated control by 2-way ANOVA with Tukey's multiple-comparison test (\*\*, P < 0.001; \*\*\*, P < 0.0001). Error bars represent standard deviations from the means.

*cia* complex. For *S. maltophilia*, tobramycin (99% reduction) and cefiderocol (97% reduction) were superior to the other antibiotics (71% to 87% reduction). In contrast, the most potent antibiotic for *A. baumannii* and *E. coli* biofilm reduction was imipenem (>90% reduction versus 67% to 80% reduction reduction with cefiderocol) (Fig. 4; see also Table 3); however, the difference was not statistically significant by two-way analysis of variance (ANOVA) with Tukey's multiple-comparison test. Taking the results together, cefiderocol reduced biofilm to a degree equivalent to or higher than seen with comparator antibiotics at a dose of 4 µg/ml.

To gain some insight into the potency of cefiderocol and other antibiotics in the biofilm setting, we can compare the drug MIC value determined for each bacterial strain, including both drug-sensitive strains and MDR strains, with the percentage of biofilm reduction at a fixed antibiotic concentration (see Table S1 in the supplemental material). In general, for all genera examined, higher levels of biofilm reduction were observed in sensitive strains with lower planktonic MICs. This was consistently observed for cefiderocol treatment in *S. maltophilia* and *B. cepacia* complex strains, where MICs were low (1 to  $\leq 0.0625 \,\mu$ g/ml) and biofilm was reduced by 75% to 99%. There were some notable exceptions. For example, although the MIC of cefiderocol in *A. baumannii* AYE (MDR) was 8  $\mu$ g/ml, at 4  $\mu$ g/ml it reduced biofilm better than cephalosporins and better than piperacillin-tazobactam. Further, differences in potency were observed for NDM-1-expressing strains: In *E. coli* BCT-B-036, no biofilm reduction occurred with 4  $\mu$ g/ml cefiderocol treatment, although the MIC was 0.25  $\mu$ g/ml.

<b>TABLE 3</b> Summary of percent reduction for 24-h assays with 12-h challenge <sup>a</sup>
--

	% reduction									
Species	Cefiderocol	Ceftolozane- Ceftazidime- col tazobactam avibactam Ceftazidime		Ceftazidime	Pipericillin- tazobactam Imipenem Tobramycin					
P. aeruginosa	93.6	81.2	80	74.8	60.7	49.3	82.6			
K. pneumoniae	83.7	76.6	88.8	46.9	46.5	82.6	42.7			
A. baumannii	80.9	86.9	72.9	79.7	51.5	92.9	48.9			
S. maltophilia	97.2	86	87.9	81.9	75.6	71.4	99.1			
<i>B. cepacia</i> complex	83.0	83.6	74.6	62.6	43.4	21.3	70.0			
E. coli	67.6	68.9	92.2	64.1	61.2	95.9	66.3			

<sup>a</sup>Data represent reduction for biofilms challenged every 12 h for 24 h with cefiderocol and comparator antibiotics in MHII.



**FIG 4** Cefiderocol reduces biofilm in other MDR Gram-negative pathogens. (A) *K. pneumoniae*. (B) *S. maltophilia*. (C) *B. cepacia* complex. (D) *A. baumannii*. (E) *E. coli*. Data represent viability assay results for an average of 4 or 5 strains with three independent experiments per strain. The reduction in biofilm burden associated with each antibiotic was compared to that seen with an untreated control by 2-way ANOVA with Tukey's multiple-comparison test (\*, P < 0.05; \*\*, P < 0.001; \*\*\*, P < 0.0001). Error bars represent standard deviations from the means.

biofilm (46%), despite a MIC of 1  $\mu$ g/ml. On the other hand, for *P. aeruginosa* (MB640 and MB730) and *A. baumannii* (BCT-B-026) NDM-1 strains, low cefiderocol MICs ( $\leq$ 0.0625 to 2  $\mu$ g/ml) were associated with greater (>1 log) biofilm reduction. This study focused on MDR strains, and due to their inherent resistance, a minimum biofilm eradication concentration (MBEC) was difficult to calculate for all comparator antibiotics. MBEC is defined as the lowest concentration of antibiotic required to eradicate the biofilm (37, 38).

We tested whether there was a dose-dependent effect on CFU reduction in biofilm. Increasing doses of cefiderocol, imipenem, tobramycin, or ceftolozane-tazobactam (8, 16, or  $32 \mu$ g/ml) were administered every 12 h for 24 h in *P. aeruginosa*, and CFU was determined (Fig. 5). Regardless of the antibiotic used, the efficacy in reducing viable biofilm bacteria plateaued at  $16 \mu$ g/ml, with no additional CFU decrease seen with higher dosing. To address a potential issue with membrane permeability, we compared the abilities of  $8 \mu$ g/ml cefiderocol, tobramycin, and ceftolozane-tazobactam to reduce *P. aeruginosa* strain MB580A biofilm in the presence and absence of  $2 \mu$ g/ml polymyxin B nonapeptide (PMBN). However, no change in biofilm viability was detected with the addition of PMBN (data not shown).

We next tested whether dosing frequency altered biofilm breakdown. We compared breakdown levels in two MDR strains of *P. aeruginosa* (MB580A and MB730) and of *K. pneumoniae* (BAA-2146 and MB9228) using a schedule of dosing either every 12 h for 24 h or every 8 h for 24 h. Additionally, we examined the impact of increases in dosing frequency with increasing dosage amount using 4, 8, and  $16 \mu g/ml$  cefiderocol. The results of these assays are illustrated in Fig. 6. Biofilm reductions were compared



**FIG 5** *P. aeruginosa* biofilm eradication analyzed by viability count does not demonstrate dose dependence. Data represent viability assay results for an average of 5 strains with three independent experiments. The reduction in biofilm burden associated with each antibiotic was compared to that seen with an untreated control by 2-way ANOVA with Tukey's multiple-comparison test (\*, P < 0.05; \*\*\*, P < 0.0001). Error bars represent standard deviations from the means.

for each dosing regimen at each concentration of cefiderocol using 2-way ANOVA with Sidak's multiple-comparison test. Although no significant difference was found, there was a trend to further biofilm reduction with dosing every 8 h (q8) versus dosing every 12 h (q12) (Table S2). As a negative control, we examined cefiderocol's ability to reduce Gram-positive biofilm grown and treated every 8 h for 24 h (24q8) in iron-limited media (ID-CAMHB). We observed no differences between treated and untreated *Staphylococcus aureus* biofilm (see Fig. S1 in the supplemental material).

Given that we were interested in determining cefiderocol activity in MDR isolates, the doses used for the biofilm reduction assays were frequently below the MICs for comparator antibiotics in these strains. We therefore examined biofilm reduction potency in sensitive strains that had similar planktonic MICs of both cefiderocol and comparator antibiotics. For these experiments, we utilized 24q8 dosing and CFU determinations. Biofilms were grown in either MHII or ID-CAMHB and then treated in the same respective media (Fig. S2). For the individual isolates tested, the potency of cefiderocol in CFU reduction was no different from or was less than that seen with the two comparator antibiotics, imipenem and tobramycin.

## DISCUSSION

This study demonstrated that cefiderocol reduces biofilm in MDR Gram-negative bacteria. At a fixed dose, it was superior to comparator antibiotics in *Pseudomonas* and superior to most comparators in the other tested MDR pathogens. In the planktonic setting, cefiderocol was superior to comparator antibiotics in inhibiting bacterial growth, in both antibiotic-sensitive and MDR strains, as has been previously reported (21–25).

In addition, there were trends that demonstrated both concentration-dependent and time-dependent eradication of biofilm with cefiderocol. First, we observed that increased cefiderocol doses further reduced biofilm but that the results plateaued at a dose of  $16 \mu$ g/ml. Comparator antibiotics imipenem, tobramycin, and ceftolozanetazobactam showed similar results. The antibiotics assayed have two different



**FIG 6** Increasing dosage frequency does not significantly increase biofilm eradication in *P. aeruginosa* (bottom panel) and *K. pneumoniae* (top panel). The levels of eradication seen with two MDR isolates for each species were compared by challenging biofilms either every 12 h for 24 h (24q12) or every 8 h for 24 h (24q8). Data represent an average of 3 viability assays. The reductions in biofilm burden seen with the different dosing schedules were compared by 2-way ANOVA with Sidak's multiple-comparison test, but no significance was found. Error bars represent standard deviations from the means.

mechanisms of action; tobramycin prevents protein synthesis, whereas imipenem, ceftolozane-tazobactam, and cefiderocol interfere with cell wall synthesis. Furthermore, their mechanisms of cell entry are likely different; tobramycin may enter the cell through the OprB porin or by means of other active transporters (39), while cefiderocol appears to utilize TonB-dependent iron transporters (26, 27). Consequently, the mechanism responsible for the plateauing of the antibiotic doses used does not appear to correspond to an interrupted transporter or mutation of the target site. It is possible that exopolymeric substances inhibit a certain amount of antibiotic diffusion through the biofilm to the cell membrane or that the effective dosage of antibiotic is reduced when it encounters the nonviable cells that constitute part of the biofilm matrix or that antibiotics are effluxed. Second, while not statistically significant, the results seen after increasing the treatment time and dosage in two MDR strains (P. aeruginosa MB730 and K. pneumoniae MB928) showed a trend toward greater biofilm reduction. Factors affecting these results may include biofilm penetration, for reasons discussed above. Pharmacokinetic/pharmacodynamic studies showed a favorable outcome when cefiderocol was administered on a q8h dosing schedule in animal models and in renally unimpaired patients (40-42). Future work will include a larger array of isolates to test what the optimal dosing and concentration parameters should be to target biofilm in MDR or sensitive strains.

The study was designed to assess whether cefiderocol was active in the biofilm setting in MDR strains. Because of this, the concentration used for the biofilm reduction studies was frequently below the MIC for the comparator antibiotics. This is a limitation of the study in terms of addressing the issue of whether cefiderocol activity is related to its planktonic potency or whether its mechanism of entry into the cell provides an added advantage in the biofilm state. Early testing seems to support the former hypothesis as cefiderocol was not superior to imipenem or tobramycin when tested in strains that were more sensitive to these comparators. In addition, whether the biofilm was grown under iron-limited or iron-replete conditions did not make a significant difference for most strain-antibiotic combinations. A broader look at activity in multiple sensitive strains and under different biofilm conditions is ongoing. Since biofilm formation promotes siderophore production (43), we speculate that siderophore transporters may be upregulated in the biofilm setting. Future transcriptional profiling and colocalization studies could elucidate whether cefiderocol shows improved uptake through the siderophore pathway in the biofilm setting and whether it is retained in the bacterial cell. In addition, the ability of cefiderocol to have antibiofilm activity in *in vivo* infection models is yet to be determined. In summary, cefiderocol retains activity in the biofilm setting, including in isolates that are otherwise resistant to comparator antibiotics.

#### **MATERIALS AND METHODS**

**Bacterial strains and growth conditions.** Clinical isolates of MDR *Escherichia coli, Pseudomonas aeruginosa, Acinetobacter baumannii, Klebsiella pneumoniae, Burkholderia cepacia* complex (Bcc), and *Stenotrophomonas maltophilia* were included for study. Isolates were obtained from the American Type Culture Collection or were clinical isolates obtained from Samuel Shelburne (MD Anderson), John LiPuma (University of Michigan), and Joanna Goldberg (Emory). Isolates came from a variety of sources (blood, urine, sputum) and hosts (e.g., malignancy, cystic fibrosis). Strains were maintained as cryofrozen stocks and incubated on Remel tryptic soy sheep blood agar (Thermo Fisher Scientific) at 37°C in 5% CO<sub>2</sub> for 18 to 24 h before testing in MIC assays. For biofilm assays, a single colony from a blood agar plate was inoculated into cation-adjusted Mueller-Hinton III (MHII) broth and incubated with shaking overnight. The following morning, the culture was diluted into Dulbecco's phosphate-buffered saline (PBS) and measured by the use of a spectrophotometer (optical density at 600 nm [OD<sub>600</sub>], 0.07 to 0.08) to achieve a cell density of  $1 \times 10^8$  CFU/ml.

Comparator antibiotics included ceftolozane-tazobactam, ceftazidime-avibactam, ceftazidime, piperacillin-tazobactam, imipenem, and tobramycin. Cefiderocol was obtained from Shionogi & Co., Ltd., Japan. Comparator antibiotics were obtained from the University of Texas Southwestern Medical Center campus pharmacy.

**MIC.** MICs were determined for each strain in triplicate utilizing the Clinical and Laboratory Standards Institute (CLSI) broth microdilution method (CLSI 2015) for cefiderocol and seven comparator antibiotics in both iron-depleted cation-adjusted Mueller-Hinton broth (ID-CAMHB; obtained from International Health Management Associates, Inc., Schaumberg, IL, or from Thermo Fisher Scientific) and MHII. *E. coli* ATCC 25922 and *P. aeruginosa* ATCC 9027 strains were assayed regularly as controls. The acceptable range for cefiderocol in ID-CAMHB was 0.06 to 0.5  $\mu$ g/ml (44).

**Minimum biofilm eradication concentration (MBEC) assays.** Biofilm was grown in MBEC plates (Innovotech, Alberta [AB], Canada). Bacteria were inoculated with  $5 \times 10^5$  CFU/ml bacteria in MHII (or Luria-Bertani broth for *E. coli*) and incubated with shaking at  $37^{\circ}$ C for 24 h. Afterward, the lid of the plate (with pegs containing biofilm) was transferred to a fresh 96-well plate with antibiotics in MHII, LB, or ID-CAMHB and incubated as before. A second dose was administered 12 h later by moving the pegs to a new plate (stored at 4°C) with or without the antibiotic. At 48 h, the lid was washed in PBS and then either fixed and stained with crystal violet or sonicated to determine viable cell numbers. Assays comparing an 8-h dosing regimen over 24 h (24q8) to a 12-h dosing regimen over 24 h (24q12) were processed similarly, except that fresh challenge plates were not refrigerated for either test.

**Crystal violet assay.** Biofilm on the pegs was fixed with methanol and air-dried. Pegs were stained with crystal violet solution (45) (solubilized in acetic acid) for 20 min. OD<sub>570</sub> was measured in a Synergy Biotek plate reader.

**Viability assay.** Each peg was broken from the plate in a sterile fashion with pliers and added to 1 ml PBS in a 14-ml Falcon tube. The tubes were sonicated in a water bath for 15 min. After vortex mixing was performed, CFU levels were measured by drip-plating serial dilutions on sheep blood agar.

#### SUPPLEMENTAL MATERIAL

Supplemental material is available online only. **SUPPLEMENTAL FILE 1**, PDF file, 1.1 MB.

### **ACKNOWLEDGMENTS**

MIC assays and MBEC biofilm tests were funded in David E. Greenberg's laboratory by Shionogi & Co., Ltd. (grant S-649266-EF-348-R). Shionogi & Co., Ltd., did not design or conduct assays or interpret the data.

We thank Naoki Kohira for his role in supporting this project and Amila Nanayakkara for his thoughtful comments on the manuscript.

#### REFERENCES

- Ramirez MS, Nikolaidis N, Tolmasky ME. 2013. Rise and dissemination of aminoglycoside resistance: the aac(6')-lb paradigm. Front Microbiol 4:121. https://doi.org/10.3389/fmicb.2013.00121.
- 2. (CDC) Centers for Disease Control and Prevention. 2019. Antibiotic resistance threats in the United States. CDC, Atlanta, GA.
- Nordmann P, Poirel L. 2019. Epidemiology and diagnostics of carbapenem resistance in Gram-negative bacteria. Clin Infect Dis 69:S521–S528. https://doi.org/10.1093/cid/ciz824.
- Dalhoff A. 2012. Global fluoroquinolone resistance epidemiology and implictions for clinical use. Interdiscip Perspect Infect Dis 2012:976273. https://doi.org/10.1155/2012/976273.
- Jeannot K, Bolard A, Plesiat P. 2017. Resistance to polymyxins in Gramnegative organisms. Int J Antimicrob Agents 49:526–535. https://doi.org/ 10.1016/j.ijantimicag.2016.11.029.
- Blair JM, Webber MA, Baylay AJ, Ogbolu DO, Piddock LJ. 2015. Molecular mechanisms of antibiotic resistance. Nat Rev Microbiol 13:42–51. https:// doi.org/10.1038/nrmicro3380.
- Meletis G. 2016. Carbapenem resistance: overview of the problem and future perspectives. Ther Adv Infect Dis 3:15–21. https://doi.org/10.1177/ 2049936115621709.
- Ur Rahman S, Ali T, Ali I, Khan NA, Han B, Gao J. 2018. The growing genetic and functional diversity of extended spectrum beta-lactamases. Biomed Res Int 2018:9519718. https://doi.org/10.1155/2018/9519718.
- Hinchliffe P, Yang QE, Portal E, Young T, Li H, Tooke CL, Carvalho MJ, Paterson NG, Brem J, Niumsup PR, Tansawai U, Lei L, Li M, Shen Z, Wang Y, Schofield CJ, Mulholland AJ, Shen J, Fey N, Walsh TR, Spencer J. 2017. Insights into the mechanistic basis of plasmid-mediated colistin resistance from crystal structures of the catalytic domain of MCR-1. Sci Rep 7:39392. https://doi.org/10.1038/srep39392.
- Fernandez L, Hancock RE. 2012. Adaptive and mutational resistance: role of porins and efflux pumps in drug resistance. Clin Microbiol Rev 25:661–681. https://doi.org/10.1128/CMR.00043-12.
- Andersson DI, Hughes D. 2011. Persistence of antibiotic resistance in bacterial populations. FEMS Microbiol Rev 35:901–911. https://doi.org/10 .1111/j.1574-6976.2011.00289.x.
- 12. Sundqvist M. 2014. Reversibility of antibiotic resistance. Ups J Med Sci 119:142–148. https://doi.org/10.3109/03009734.2014.903323.
- Costerton JW, Stewart PS, Greenberg EP. 1999. Bacterial biofilms: a common cause of persistent infections. Science 284:1318–1322. https://doi .org/10.1126/science.284.5418.1318.
- Lewis K. 2007. Persister cells, dormancy and infectious disease. Nat Rev Microbiol 5:48–56. https://doi.org/10.1038/nrmicro1557.
- Donlan RM, Costerton JW. 2002. Biofilms: survival mechanisms of clinically relevant microorganisms. Clin Microbiol Rev 15:167–193. https://doi .org/10.1128/cmr.15.2.167-193.2002.
- McConoughey SJ, Howlin R, Granger JF, Manring MM, Calhoun JH, Shirtliff M, Kathju S, Stoodley P. 2014. Biofilms in periprosthetic orthopedic infections. Future Microbiol 9:987–1007. https://doi.org/10.2217/fmb .14.64.
- Metcalf DG, Bowler PG. 2013. Biofilm delays wound healing: a review of the evidence. Burns Trauma 1:5–12. https://doi.org/10.4103/2321-3868 .113329.
- Trautner BW, Darouiche RO. 2004. Role of biofilm in catheter-associated urinary tract infection. Am J Infect Control 32:177–183. https://doi.org/10 .1016/j.ajic.2003.08.005.
- Kong H, Cheng W, Wei H, Yuan Y, Yang Z, Zhang X. 2019. An overview of recent progress in siderophore-antibiotic conjugates. Eur J Med Chem 182:111615. https://doi.org/10.1016/j.ejmech.2019.111615.
- Negash KH, Norris JKS, Hodgkinson JT. 2019. Siderophore-antibiotic conjugate design: new drugs for bad bugs? Molecules 24:3314. https://doi .org/10.3390/molecules24183314.
- Yamano Y. 2019. In vitro activity of cefiderocol against a broad range of clinically important Gram-negative bacteria. Clin Infect Dis 69:S544–S551. https://doi.org/10.1093/cid/ciz827.
- Aoki T, Yoshizawa H, Yamawaki K, Yokoo K, Sato J, Hisakawa S, Hasegawa Y, Kusano H, Sano M, Sugimoto H, Nishitani Y, Sato T, Tsuji M, Nakamura R, Nishikawa T, Yamano Y. 2018. Cefiderocol (S-649266), a new

siderophore cephalosporin exhibiting potent activities against Pseudomonas aeruginosa and other gram-negative pathogens including multidrug resistant bacteria: structure activity relationship. Eur J Med Chem 155:847–868. https://doi.org/10.1016/j.ejmech.2018.06.014.

- 23. Hackel MA, Tsuji M, Yamano Y, Echols R, Karlowsky JA, Sahm DF. 2018. In vitro activity of the siderophore cephalosporin, cefiderocol, against carbapenem-nonsusceptible and multidrug-resistant isolates of Gram-negative bacilli collected worldwide in 2014 to 2016. Antimicrob Agents Chemother 62:e01968-17. https://doi.org/10.1128/AAC.01968-17.
- 24. Ito A, Sato T, Ota M, Takemura M, Nishikawa T, Toba S, Kohira N, Miyagawa S, Ishibashi N, Matsumoto S, Nakamura R, Tsuji M, Yamano Y. 2018. In vitro antibacterial properties of cefiderocol, a novel siderophore cephalosporin, against Gram-negative bacteria. Antimicrob Agents Chemother 62:e01454-17. https://doi.org/10.1128/AAC.01454-17.
- Dobias J, Dénervaud-Tendon V, Poirel L, Nordmann P. 2017. Activity of the novel siderophore cephalosporin cefiderocol against multidrug-resistant Gram-negative pathogens. Eur J Clin Microbiol Infect Dis 36: 2319–2327. https://doi.org/10.1007/s10096-017-3063-z.
- Luscher A, Moynié L, Auguste PS, Bumann D, Mazza L, Pletzer D, Naismith JH, Köhler T. 2018. TonB-dependent receptor repertoire of Pseudomonas aeruginosa for uptake of siderophore-drug conjugates. Antimicrob Agents Chemother 62:e00097-18. https://doi.org/10.1128/AAC.00097-18.
- Ito A, Nishikawa T, Matsumoto S, Yoshizawa H, Sato T, Nakamura R, Tsuji M, Yamano Y. 2016. Siderophore cephalosporin cefiderocol utilizes ferric iron transporter systems for antibacterial activity against Pseudomonas aeruginosa. Antimicrob Agents Chemother 60:7396–7401. https://doi .org/10.1128/AAC.01405-16.
- Wilson BR, Bogdan AR, Miyazawa M, Hashimoto K, Tsuji Y. 2016. Siderophores in iron metabolism: from mechanism to therapy potential. Trends Mol Med 22:1077–1090. https://doi.org/10.1016/j.molmed.2016.10.005.
- Harrison F, Buckling A. 2009. Siderophore production and biofilm formation as linked social traits. ISME J 3:632–634. https://doi.org/10.1038/ ismej.2009.9.
- Banin E, Vasil ML, Greenberg EP. 2005. Iron and Pseudomonas aeruginosa biofilm formation. Proc Natl Acad Sci U S A 102:11076–11081. https://doi .org/10.1073/pnas.0504266102.
- Oh E, Andrews KJ, Jeon B. 2018. enhanced biofilm formation by ferrous and ferric iron through oxidative stress in Campylobacter jejuni. Front Microbiol 9:1204. https://doi.org/10.3389/fmicb.2018.01204.
- Mey AR, Craig SA, Payne SM. 2005. Characterization of Vibrio cholerae RyhB: the RyhB regulon and role of ryhB in biofilm formation. Infect Immun 73:5706–5719. https://doi.org/10.1128/IAI.73.9.5706-5719.2005.
- Lin CS, Tsai YH, Chang CJ, Tseng SF, Wu TR, Lu CC, Wu TS, Lu JJ, Horng JT, Martel J, Ojcius DM, Lai HC, Young JD. 2016. An iron detection system determines bacterial swarming initiation and biofilm formation. Sci Rep 6:36747. https://doi.org/10.1038/srep36747.
- Butt AT, Thomas MS. 2017. Iron acquisition mechanisms and their role in the virulence of Burkholderia species. Front Cell Infect Microbiol 7:460. https://doi.org/10.3389/fcimb.2017.00460.
- Wu Y, Outten FW. 2009. lscR controls iron-dependent biofilm formation in Escherichia coli by regulating type I fimbria expression. J Bacteriol 191:1248–1257. https://doi.org/10.1128/JB.01086-08.
- 36. Greenberg PE, Banin E. 2008. Ironing out the biofilm problem: the role of iron in biofilm formation, p 141–156. *In* Balaban N (ed), Control of biofilm infections by signal manipulation, 1 ed. Springer, Berlin, Germany. https://doi.org/10.1007/7142\_2007\_014.
- Ceri H, Olson ME, Stremick C, Read RR, Morck D, Buret A. 1999. The Calgary biofilm device: new technology for rapid determination of antibiotic susceptibilities of bacterial biofilms. J Clin Microbiol 37:1771–1776. https://doi.org/10.1128/JCM.37.6.1771-1776.1999.
- Thieme L, Hartung A, Tramm K, Klinger-Strobel M, Jandt KD, Makarewicz O, Pletz MW. 2019. MBEC versus MBIC: the lack of differentiation between biofilm reducing and inhibitory effects as a current problem in biofilm methodology. Biol Proced Online 21:18. https://doi.org/10.1186/s12575 -019-0106-0.
- MacLeod DL, Velayudhan J, Kenney TF, Therrien JH, Sutherland JL, Barker LM, Baker WR. 2012. Fosfomycin enhances the active transport of

tobramycin in Pseudomonas aeruginosa. Antimicrob Agents Chemother 56:1529–1538. https://doi.org/10.1128/AAC.05958-11.

- Ghazi IM, Monogue ML, Tsuji M, Nicolau DP. 2018. Pharmacodynamics of cefiderocol, a novel siderophore cephalosporin, in a Pseudomonas aeruginosa neutropenic murine thigh model. Int J Antimicrob Agents 51:206–212. https://doi.org/10.1016/j.ijantimicag.2017.10.008.
- 41. Nakamura R, Ito-Horiyama T, Takemura M, Toba S, Matsumoto S, Ikehara T, Tsuji M, Sato T, Yamano Y. 2019. In vivo pharmacodynamic study of cefiderocol, a novel parenteral siderophore cephalosporin, in murine thigh and lung infection models. Antimicrob Agents Chemother 63: e02031-18. https://doi.org/10.1128/AAC.02031-18.
- Katsube T, Echols R, Wajima T. 2019. Pharmacokinetic and pharmacodynamic profiles of cefiderocol, a novel siderophore cephalosporin. Clin Infect Dis 69:S552–S558. https://doi.org/10.1093/cid/ciz828.
- Kang D, Kirienko NV. 2018. Interdependence between iron acquisition and biofilm formation in Pseudomonas aeruginosa. J Microbiol 56: 449–457. https://doi.org/10.1007/s12275-018-8114-3.
- Huband MD, Ito A, Tsuji M, Sader HS, Fedler KA, Flamm RK. 2017. Cefiderocol MIC quality control ranges in iron-depleted cation-adjusted Mueller-Hinton broth using a CLSI M23-A4 multi-laboratory study design. Diagn Microbiol Infect Dis 88:198–200. https://doi.org/10.1016/j.diagmicrobio .2017.03.011.
- 45. Howard JJ, Sturge CR, Moustafa DA, Daly SM, Marshall-Batty KR, Felder CF, Zamora D, Yabe-Gill M, Labandeira-Rey M, Bailey SM, Wong M, Goldberg JB, Geller BL, Greenberg DE. 2017. Inhibition of Pseudomonas aeruginosa by peptide-conjugated phosphorodiamidate morpholino oligomers. Antimicrob Agents Chemother 61:e01938-16. https://doi.org/ 10.1128/AAC.01938-16.