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Susceptibility of Cefiderocol Between US Census Regions Against Gram-Negative Organisms Collected from the SENTRY Surveillance Program: 2020–2021

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Introduction

- Gram-negative (GN) bacteria such as Enterobacterales (ENT), *Pseudomonas aeruginosa* (PsA), *Acinetobacter baumannii* complex (ABC), and *Stenotrophomonas maltophilia* (StM) can be difficult to treat and are often carbapenem resistant (CR).
- Regional variation in susceptibilities to anti-infective agents is important to understand for optimal management of infections, as well as local patterns of susceptibilities to agents.
- Cefiderocol (CFDC) is approved for the treatment of patients with complicated urinary tract infections and hospital-acquired/ventilator-associated bacterial pneumonia caused by susceptible GN pathogens.[1]
- CFDC has demonstrated a broad range of activity against GN pathogens, including ENT, PsA, ABC, and StM, particularly against CR isolates.
- The geographic differences of US regional susceptibilities for CFDC compared with other GN agents, such as the newer beta-lactam–beta-lactamase inhibitors (BL/BLIs) are not known.
- We aim to describe the *in vitro* activities of CFDC and comparator agents against isolates collected from the SENTRY program and to examine differences in susceptibility between the different US census divisions.

Methods

- GN pathogens were consecutively collected from hospitalized patients in 32 US hospitals between 2020 and 2021. All infection types were included in this study.
- Susceptibility testing was performed using the broth microdilution method; CFDC was tested in iron-depleted Mueller Hinton broth according to Clinical and Laboratory Standards Institute (CLSI) M07, 2018.
- Susceptibility was interpreted according to the current US Food and Drug Administration (FDA) and 2022 CLSI breakpoints.[2]
- Comparator agents included the BL/BLIs ceftazidime-avibactam, ceftolozane-tazobactam, imipenem-relebactam, meropenem-vaborbactam, piperacillin-tazobactam, and ampicillin-sulbactam for ENT. Additional comparators for specific pathogens include colistin for ABC; ceftazidime, levofloxacin, trimethoprim-sulfamethoxazole, and minocycline for StM.
- CR PsA and CR ABC were defined as meropenem resistant by CLSI 2022 breakpoints, while CR Enterobacterales (CRE) was defined as imipenem or meropenem resistant by CLSI 2022 breakpoints.
- Multidrug-resistant (MDR) PsA and extensively drug-resistant (XDR) PsA were classified using CLSI 2022 standards.

Results

- A total of 8328 Enterobacterales, 2241 *P. aeruginosa*, 586 *A. baumannii* complex, and 404 *S. maltophilia* isolates were collected (**Table 1**).
  - CFDC maintained the highest level of activity against all major non-CR pathogens with >92% susceptibility by CLSI breakpoints against ENT, *P. aeruginosa*, *A. baumannii* complex, and *S. maltophilia* (**Table 1**).
- Among the isolates collected, 96 were CRE, 327 were CR PsA, and 199 were CR ABC (**Table 2**). StM (N=404) is intrinsically resistant to carbapenems (**Table 1**).
- CFDC maintained high levels of activity against CR isolates with >95% susceptibility by CLSI breakpoints, except for CR ABC (i.e., CFDC susceptibility rate: 82.4% by FDA breakpoints).
- For ENT or PsA, CFDC susceptibility between the nine US census divisions remained above 92% susceptible by CLSI or FDA breakpoints in all regions (**Table 3**).
- Among the BL/BLI combinations, the majority had >90% susceptibility across regions except for piperacillin-tazobactam with 79.7% for ENT and 65.9% for PsA in the Mid-Atlantic by FDA breakpoints.
- For ABC and StM, CFDC susceptibility was >88% across all regions.
- For CR pathogens, 1.2% (n=96/8328) were CRE, 14.6% (n=327/2241) were CR PsA, and 34.0% (n=199/586) CR ABC.
  - The Mid-Atlantic had the highest number and ratio of CRE and CR PsA isolates.
  - The East North Central had the highest number and ratio of CR ABC isolates.

Table 1. Overall susceptibility of antimicrobial agents tested against Enterobacterales, *P. aeruginosa, A. baumannii complex,* and *S. maltophilia* isolates in the SENTRY program collected from US medical centers

Agent	Count	MIC_{50}	MIC_{90}	Range	CLSI[a] %S	CLSI[a] %I	CLSI[a] %R	US FDA[a] %S	US FDA[a] %I	US FDA[a] %R
Enterobacterales (n=8328)[b]										
Cefiderocol	8328	0.06	0.5	≤0.004 to >64	99.8	0.1	<0.1	99.8	0.1	<0.1
Imipenem-relebactam	8328	0.12	0.5	≤0.03 to >8	94.7	4.2	1.0[b]	94.7	4.2	1
Meropenem-vaborbactam	8322	0.03	0.06	≤0.015 to >8	99.8	0.1	0.1	99.8	0.1	0.1[c]
Ceftazidime-avibactam	8325	0.12	0.25	≤0.015 to >32	99.8		0.2	99.8		0.2[c]
Ceftolozane-tazobactam	8323	0.25	1	≤0.12 to >16	93.7	1.5	4.8	93.7	1.5	4.8[d]
Piperacillin-tazobactam	8315	2	16	≤0.06 to >128	87.1	3.8	9.1	87.1	3.8	9.1[c]
Ampicillin-sulbactam	8322	16	64	≤0.5 to >64	49	15.5	35.5	49	15.5	35.5[c]
***Pseudomonas aeruginosa* (n=2241)**										
Cefiderocol	2241	0.12	0.25	≤0.004 to 16	99.8	0.1	0.1	98.5	1	0.5
Imipenem-relebactam	2241	0.25	1	≤0.03 to >8	97.2	1.9	0.9	97.2	1.9	0.9
Ceftazidime-avibactam	2241	2	8	0.03 to >32	96.4		3.6	96.4		3.6[c]
Ceftolozane-tazobactam	2239	0.5	2	≤0.12 to >16	97.5	1.1	1.3	97.5	1.1	1.3[c]
Piperacillin-tazobactam	2238	4	128	≤0.06 to >128	79.2	10	10.8	79.2	10	10.8[c]
***Acinetobacter baumannii* complex (n=586)**										
Cefiderocol	586	0.12	1	0.008 to >64	98.1	0.7	1.2	92	4.6	3.4
Imipenem-relebactam	586	0.25	>8	0.06 to >8				66.6	0.7	32.8
Piperacillin-tazobactam	578	16	>128	≤0.06 to >128	55.2	6.4	38.4	55.2	6.4	38.4[c]
Ampicillin-sulbactam	586	4	64	≤0.5 to >64	64.2	7.5	28.3	64.2	7.5	28.3[c]
Colistin	585	0.5	1	0.12 to >8		95.6	4.4			
***Stenotrophomonas maltophilia* (n=404)**										
Cefiderocol	404	0.06	0.25	0.008 to 4	98.8					
Ceftazidime	403	>32	>32	1 to >32	19.6	10.4	70	19.6	10.4	70.0[c]
Levofloxacin	403	1	8	≤0.015 to >32	81.4	8.2	10.4			
Trimethoprim-sulfamethoxazole	404	≤0.12	0.5	≤0.12 to >4	98		2			
Minocycline	404	0.5	1	0.12 to 16	99.8	0	0.2			

[a]Criteria as published by CLSI (2022), and US FDA (2022). [b]All Enterobacterales species were included in the analysis, but CLSI excludes *Morganella*, *Proteus*, and *Providencia* species. [c]CLSI M100 standard is recognized. [d]US FDA breakpoints were applied for disks. CLSI M100 standard is recognized for MICs only.
Organisms included: *Citrobacter amalonaticus / farmeri* (14), *C. braakii* (1), C. *freundii* (11), *C. freundii* species complex (230), *C. koseri* (200), *C. sedlakii* (1), *Cronobacter sakazakii* (3), *Enterobacter asburiae* (2), *E. cancerogenus* (1), *E. cloacae* (153), *E. cloacae* species complex (493), *E. hormaechei* (3), *E. kobei* (2), *Escherichia coli* (3423), *E. hermannii* (1), Gram-negative rods in the family *Enterobacteriaceae* (2), *Hafnia alvei* (9), *Klebsiella aerogenes* (314), *K. ornithinolytica* (1), *K. oxytoca* (360), *K. planticola* (1), *K. pneumoniae* (1545), *K. variicola* (72), *Kluyvera ascorbata* (1), *Leclercia adecarboxylata* (2), *Lelliottia amnigena* (1), *Morganella morganii* (161), *Pantoea agglomerans* (10), *P. ananatis* (1), *P. anthophila* (1), *P. calida* (1), *P. dispersa* (1), *Phytobacter diazotrophicus* (1), *Pluralibacter gergoviae* (8), *Proteus hauseri* (3), *P. mirabilis* (483), *P. penneri* (14), *P. vulgaris* (40), *P. vulgaris* group (38), *Providencia rettgeri* (53), *P. stuartii* (44), *Pseudocitrobacter faecalis* (1), *Rahnella aquatilis* (1), *Raoultella ornithinolytica* (12), *R. planticola* (3), *Serratia fonticola* (1), *S. liquefaciens* (12), *S. liquefaciens* complex (5), *S. marcescens* (550), *S. odorifera* (2), *S. rubidaea* (1), unspeciated *Citrobacter* (5), unspeciated *Klebsiella* (1), unspeciated *Pantoea* (1), unspeciated *Providencia* (3), unspeciated *Raoultella* (23), *Yersinia enterocolitica* (1), *Yokenella regensburgei* (1).
CLSI, Clinical and Laboratory Standards Institute; FDA, Food and Drug Administration; I, intermediate; MIC, minimum inhibitory concentration; MIC_{50}/MIC_{90}, MIC at which ≥50%/≥90% of isolates tested are inhibited; R, resistant; S, susceptible.

Table 2. Overall susceptibility of antimicrobial agents tested against CRE, CR PsA, and CR ABC isolates in the SENTRY program collected from US medical centers

Agent	Count	MIC_{50}	MIC_{90}	Range	CLSI[a] %S	CLSI[a] %I	CLSI[a] %R	US FDA[a] %S	US FDA[a] %I	US FDA[a] %R
CRE (n=96)										
Cefiderocol	96	0.5	4	0.008 to >64	97.9	1.0	1.0	97.9	1.0	1.0
Imipenem-relebactam	96	0.12	8	0.06 to >8	79.2	3.1	17.7[b]	79.2	3.1	17.7
Meropenem-vaborbactam	96	0.06	>8	≤0.015 to >8	82.3	5.2	12.5	82.3	5.2	12.5[c]
Ceftazidime-avibactam	96	1	>32	≤0.015 to >32	88.5	-	11.5	88.5	-	11.5[c]
Ceftolozane-tazobactam	96	>16	>16	0.5 to >16	4.2	3.1	92.7	4.2	3.1	92.7[d]
Piperacillin-tazobactam	96	>128	>128	2 to >128	1.0	1.0	97.9	1.0	1.0	97.9[c]
Ampicillin-sulbactam	96	>64	>64	64 to >64	0.0	0.0	100	0.0	0.0	100[c]
CR *P. aeruginosa* (n=327)										
Cefiderocol	327	0.12	0.5	≤0.004 to 16	99.1	0.3	0.6	96.3	2.1	1.5
Imipenem-relebactam	327	2	4	0.25 to >8	81.3	12.5	6.1	81.3	12.5	6.1
Ceftazidime-avibactam	327	8	16	1 to >32	80.7	-	19.3	80.7	-	19.3[c]
Ceftolozane-tazobactam	327	2	8	0.25 to >16	87.5	5.5	7	87.5	5.5	7.0[c]
Piperacillin-tazobactam	327	64	>128	4 to >128	30.3	28.4	41.3	30.3	28.4	41.3[c]
CR *A. baumannii* complex (n=199)										
Cefiderocol	199	0.5	2	0.015 to >64	95.5	1.5	3	82.4	9	8.5
Imipenem-relebactam	199	>8	>8	0.25 to >8	-	-	-	1.5	2	96.5
Piperacillin-tazobactam	199	>128	>128	8 to >128	1	5.5	93.5	1	5.5	93.5[c]
Ampicillin-sulbactam	199	32	>64	4 to >64	9	14.1	76.9	9	14.1	76.9[c]
Colistin	198	0.5	2	0.12 to >8	-	92.9	7.1	-	-	-

[a]Criteria as published by CLSI (2022) and US FDA (2022). [b]All Enterobacterales species were included in the analysis, but CLSI excludes Morganella, Proteus, and Providencia species and EUCAST excludes Morganellaceae. [c]CLSI M100 standard is recognized. [d]US FDA breakpoints were applied for disks. CLSI M100 standard is recognized for MICs only.
Organisms included: *Citrobacter freundii* species complex (3), *Enterobacter cloacae* species complex (10), *Escherichia coli* (6), *Hafnia alvei* (1), *Klebsiella aerogenes* (7), *K. oxytoca* (6), *K. pneumoniae* (51), *Providencia rettgeri* (2), *Serratia marcescens* (7), unspeciated *Raoultella* (3).
ABC, *Acinetobacter baumannii* complex; CLSI, Clinical and Laboratory Standards Institute; CR, carbapenem-resistant; CRE, carbapenem-resistant Enterobacteriaceae; EUCAST, European Committee on Antimicrobial Susceptibility Testing; FDA, Food and Drug Administration; I, intermediate; MIC, minimum inhibitory concentration; MIC_{50}/MIC_{90}, MIC at which ≥50%/≥90% of isolates tested are inhibited; PsA, *Pseudomonas aeruginosa*; R, resistant; S, susceptible.

- CFDC had >87.5% susceptibility in all divisions for CRE and CR PsA.
- For CR ABC, four US divisions had rates <87.5% by FDA breakpoints and the lowest rate was 63.6% for 11 isolates in the Mountain division (**Table 4**).
- For CR ABC, every BL/BLI had susceptibility ≤27.3% in every division.
  - Ampicillin-sulbactam had 27.3% susceptibility in the Mountain division.
- A total of 381 MDR and 212 XDR PsA were isolated in the SENTRY program from 2020 to 2021.
  - MDR and XDR PsA were isolated most often in the Mid-Atlantic census (i.e., 35% [132/381]; 39% [82/212], respectively) (**Figure 1**).

Table 3. US census division variability of susceptibility of antimicrobial agents tested against Enterobacterales, *P. aeruginosa*, *A. baumannii* complex, and *S. maltophilia* isolates in the SENTRY program collected from US medical centers

Agent	New England Count	New England CLSI[a] %S	New England US FDA[a] %S	Mid-Atlantic Count	Mid-Atlantic CLSI[a] %S	Mid-Atlantic US FDA[a] %S	East North Central Count	East North Central CLSI[a] %S	East North Central US FDA[a] %S	West North Central Count	West North Central CLSI[a] %S	West North Central US FDA[a] %S	South Atlantic Count	South Atlantic CLSI[a] %S	South Atlantic US FDA[a] %S	East South Central Count	East South Central CLSI[a] %S	East South Central US FDA[a] %S	West South Central Count	West South Central CLSI[a] %S	West South Central US FDA[a] %S	Mountain Count	Mountain CLSI[a] %S	Mountain US FDA[a] %S	Pacific Count	Pacific CLSI[a] %S	Pacific US FDA[a] %S
Enterobacterales[b] (N=8328)																											
Cefiderocol	705	100	100	1423	99.6	99.6	1223	99.9	99.9	763	100	100	1304	100	100	596	99.7	99.7	1185	99.8	99.8	660	99.7	99.7	469	99.8	99.8
Imipenem-relebactam	705	95.2	95.2	1423	92.8	92.8	1223	94.5	94.5	763	95.5	95.5	1304	96.5	96.5	596	92.8	92.8	1185	92.8	92.8	660	97.4	97.4	469	97.9	97.9
Meropenem-vaborbactam	705	100	100	1423	99.3	99.3	1221	100	100	762	100	100	1302	99.9	99.9	596	100	100	1184	99.6	99.6	660	99.8	99.8	469	100	100
Ceftazidime-avibactam	705	100	100	1423	99.4	99.4	1222	100	100	763	100	100	1304	99.9	99.9	596	99.8	99.8	1183	99.9	99.9	660	99.5	99.5	469	100	100
Ceftolozane-tazobactam	704	97.2	97.2	1421	89.6	89.6	1222	94.7	94.7	762	96.6	96.6	1304	94.8	94.8	596	94.0	94.0	1185	94.1	94.1	660	90.3	90.3	469	94.7	94.7
Piperacillin-tazobactam	704	92.9	92.9	1417	79.7	79.7	1220	90.2	90.2	763	91.5	91.5	1302	88.0	88.0	596	87.4	87.4	1184	86.2	86.2	660	83.9	83.9	469	90.2	90.2
Ampicillin-sulbactam	704	58.9	58.9	1422	40.1	40.1	1223	54.2	54.2	761	54.3	54.3	1304	48.0	48.0	596	49.0	49.0	1185	47.2	47.2	658	46.2	46.2	469	49.9	49.9
***Pseudomonas aeruginosa* (N=2241)**																											
Cefiderocol	135	100	98.5	462	99.6	97.0	252	100	98.8	197	100	98.5	417	100	99.8	125	100	100	389	100	98.5	165	99.4	98.2	99	98.0	98.0
Imipenem-relebactam	135	99.3	99.3	462	95.9	95.9	252	98.0	98.0	197	99.5	99.5	417	97.8	97.8	125	96.0	96.0	389	95.6	95.6	165	98.2	98.2	99	97.0	97.0
Ceftazidime-avibactam	135	98.5	98.5	462	92.9	92.9	252	99.2	99.2	197	99.5	99.5	417	97.8	97.8	125	95.2	95.2	389	95.6	95.6	165	95.2	95.2	99	97.0	97.0
Ceftolozane-tazobactam	134	99.3	99.3	462	96.1	96.1	252	98.0	98.0	197	99.0	99.0	417	98.6	98.6	125	96.8	96.8	389	97.4	97.4	165	97.6	97.6	98	94.9	94.9
Piperacillin-tazobactam	135	77.0	77.0	461	65.9	65.9	251	82.5	82.5	197	87.3	87.3	417	85.4	85.4	125	81.6	81.6	389	83.8	83.8	165	77.0	77.0	98	75.5	75.5
***Acinetobacter baumannii* complex (N=586)**																											
Cefiderocol	24	100	87.5	94	97.9	95.7	129	96.9	88.4	36	97.2	91.7	86	98.8	88.4	20	95.0	95.0	106	99.1	93.4	48	97.9	91.7	43	100	100
Imipenem-relebactam	24		95.8	94		57.4	129		65.1	36		88.9	86		74.4	20		60.0	106		42.5	48		77.1	43		90.7
Piperacillin-tazobactam	24	83.3	83.3	91	52.7	52.7	128	45.3	45.3	36	77.8	77.8	84	65.5	65.5	20	55.0	55.0	105	32.4	32.4	48	68.8	68.8	42	76.2	76.2
Ampicillin-sulbactam	24	83.3	83.3	94	58.5	58.5	129	56.6	56.6	36	80.6	80.6	86	75.6	75.6	20	55.0	55.0	106	44.3	44.3	48	79.2	79.2	43	88.4	88.4
Colistin	24			94			129			36			86			20			105			48			43		
***Stenotrophomonas maltophilia* (N=404)**																											
Cefiderocol	23	95.7		67	100		71	100		35	100		90	100		20	100		52	98.1		25	92.0		21	95.2	
Ceftazidime	23	8.7	8.7	67	22.4	22.4	71	14.1	14.1	35	20.0	20.0	89	20.2	20.2	20	20.0	20.0	52	21.2	21.2	25	36.0	36.0	21	14.3	14.3
Levofloxacin	23	82.6		67	75.8		71	88.7		35	94.3		90	80.0		20	75.0		52	76.9		25	80.0		21	76.2	
Trimethoprim-sulfamethoxazole	23	100		67	98.5		71	100		35	97.1		90	97.8		20	100		52	94.2		25	96.0		21	100	
Minocycline	23	100		67	100		71	100		35	100		90	100		20	100		52	98.1		25	100		21	100	

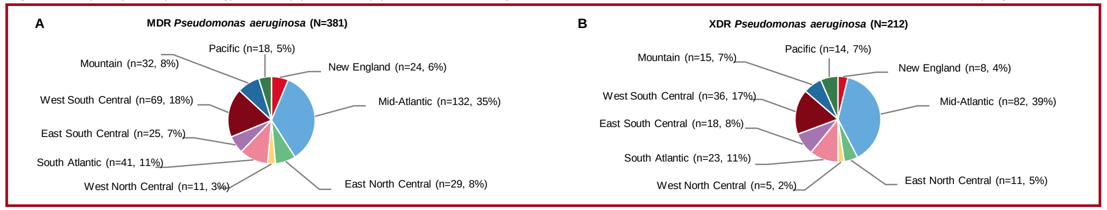
[a]Criteria as published by CLSI (2022) and US FDA (2022). [b]All Enterobacterales species were included in the analysis, but CLSI excludes *Morganella*, *Proteus*, and *Providencia* species.
Organisms included: *Citrobacter amalonaticus / farmeri* (14), *C. braakii* (1), *C. freundii* (11), *C. freundii* species complex (230), *C. koseri* (200), *C. sedlakii* (1), *Cronobacter sakazakii* (3), *Enterobacter asburiae* (2), *E. cancerogenus* (1), *E. cloacae* (153), *E. cloacae* species complex (493), *E. hormaechei* (3), *E. kobei* (2), *Escherichia coli* (3423), *E. hermannii* (1), Gram-negative rods in the family *Enterobacteriaceae* (2), *Hafnia alvei* (9), *Klebsiella aerogenes* (314), *K. ornithinolytica* (1), *K. oxytoca* (360), *K. planticola* (1), *K. pneumoniae* (1545), *K. variicola* (72), *Kluyvera ascorbata* (1), *Leclercia adecarboxylata* (2), *Lelliottia amnigena* (1), *Morganella morganii* (161), *Pantoea agglomerans* (10), *P. ananatis* (1), *P. anthophila* (1), *P. calida* (1), *P. dispersa* (1), *Phytobacter diazotrophicus* (1), *Pluralibacter gergoviae* (8), *Proteus hauseri* (3), *P. mirabilis* (483), *P. penneri* (14), *P. vulgaris* (40), *P. vulgaris* group (38), *Providencia rettgeri* (53), *P. stuartii* (44), *Pseudocitrobacter faecalis* (1), *Rahnella aquatilis* (1), *Raoultella ornithinolytica* (12), *R. planticola* (3), *Serratia fonticola* (1), *S. liquefaciens* (12), *S. liquefaciens* complex (5), *S. marcescens* (550), *S. odorifera* (2), *S. rubidaea* (1), unspeciated *Citrobacter* (5), unspeciated *Klebsiella* (1), unspeciated *Pantoea* (1), unspeciated *Providencia* (3), unspeciated *Raoultella* (23), *Yersinia enterocolitica* (1), *Yokenella regensburgei* (1).
CLSI, Clinical and Laboratory Standards Institute; FDA, Food and Drug Administration; S, susceptible.

Table 4. US regional susceptibility of antimicrobial agents tested against CRE, CR *P. aeruginosa*, and CR *A. baumannii* complex isolates in the SENTRY program collected from US medical centers

Agent	New England Count	New England CLSI[a] %S	New England FDA[a] %S	Mid-Atlantic Count	Mid-Atlantic CLSI[a] %S	Mid-Atlantic FDA[a] %S	East North Central Count	East North Central CLSI[a] %S	East North Central FDA[a] %S	West North Central Count	West North Central CLSI[a] %S	West North Central FDA[a] %S	South Atlantic Count	South Atlantic CLSI[a] %S	South Atlantic FDA[a] %S	East South Central Count	East South Central CLSI[a] %S	East South Central FDA[a] %S	West South Central Count	West South Central CLSI[a] %S	West South Central FDA[a] %S	Mountain Count	Mountain CLSI[a] %S	Mountain FDA[a] %S	Pacific Count	Pacific CLSI[a] %S	Pacific FDA[a] %S
CRE[b] (N=96)																											
Cefiderocol	0			49	98.0	98.0	8	100	100	0			5	100	100	8	87.5	87.5	17	100	100	8	100	100	1	100	100
Imipenem-relebactam	0			49	77.6	77.6	8	100	100	0			5	80.0	80.0	8	87.5	87.5	17	64.7	64.7	8	87.5	87.5	1	100	100
Meropenem-vaborbactam	0			49	79.6	79.6	8	100	100	0			5	80.0	80.0	8	100	100	17	70.6	70.6	8	87.5	87.5	1	100	100
Ceftazidime-avibactam	0			49	85.7	85.7	8	100	100	0			5	80.0	80.0	8	87.5	87.5	17	94.1	94.1	8	87.5	87.5	1	100	100
Ceftolozane-tazobactam	0			49	2.0	2.0	8	0.0	0.0	0			5	0.0	0.0	8	12.5	12.5	17	5.9	5.9	8	12.5	12.5	1	0.0	0.0
Piperacillin-tazobactam	0			49	0.0	0.0	8	0.0	0.0	0			5	0.0	0.0	8	0.0	0.0	17	5.9	5.9	8	0.0	0.0	1	0.0	0.0
Ampicillin-sulbactam	0			49	0.0	0.0	8	0.0	0.0	0			5	0.0	0.0	8	0.0	0.0	17	0.0	0.0	8	0.0	0.0	1	0.0	0.0
CR *P. aeruginosa* (N=327)																											
Cefiderocol	17	100	100	119	98.3	93.3	21	100	100	6	100	100	38	100	97.4	17	100	100	66	100	98.5	29	100	96.6	14	92.9	92.9
Imipenem-relebactam	17	94.1	94.1	119	84.0	84.0	21	76.2	76.2	6	83.3	83.3	38	76.3	76.3	17	70.6	70.6	66	75.8	75.8	29	93.1	93.1	14	78.6	78.6
Ceftazidime-avibactam	17	88.2	88.2	119	76.5	76.5	21	90.5	90.5	6	100	100	38	81.6	81.6	17	76.5	76.5	66	78.8	78.8	29	86.2	86.2	14	85.7	85.7
Ceftolozane-tazobactam	17	94.1	94.1	119	87.4	87.4	21	85.7	85.7	6	83.3	83.3	38	86.8	86.8	17	82.4	82.4	66	87.9	87.9	29	93.1	93.1	14	78.6	78.6
Piperacillin-tazobactam	17	11.8	11.8	119	17.6	17.6	21	47.6	47.6	6	83.3	83.3	38	34.2	34.2	17	35.3	35.3	66	43.9	43.9	29	34.5	34.5	14	21.4	21.4
CR *A. baumannii complex* (N=199)																											
Cefiderocol	1	100	100	40	95.0	90.0	48	93.8	75.0	4	100	75.0	22	95.5	68.2	8	87.5	87.5	61	98.4	90.2	11	90.9	63.6	4	100	100
Imipenem-relebactam	1		0.0	40		0.0	48		6.2	4		0.0	22		0.0	8		0.0	61		0.0	11		0.0	4		0.0
Piperacillin-tazobactam	1	0.0	0.0	40	0.0	0.0	48	0.0	0.0	4	0.0	0.0	22	4.5	4.5	8	0.0	0.0	61	1.6	1.6	11	0.0	0.0	4	0.0	0.0
Ampicillin-sulbactam	1	0.0	0.0	40	7.5	7.5	48	10.4	10.4	4	0.0	0.0	22	13.6	13.6	8	0.0	0.0	61	6.6	6.6	11	27.3	27.3	4	0.0	0.0
Colistin	1			40			48			4			22			8			60			11			4		

[a]Criteria as published by CLSI (2022) and US FDA (2022). [b]All Enterobacterales species were included in the analysis, but CLSI excludes *Morganella*, *Proteus*, and *Providencia* species.
Organisms included: *Citrobacter amalonaticus / farmeri* (14), *C. braakii* (1), *C. freundii* (11), *C. freundii species* complex (230), *C. koseri* (200), *C. sedlakii* (1), *Cronobacter sakazakii* (3), *Enterobacter asburiae* (2), *E. cancerogenus* (1), *E. cloacae* (153), *E. cloacae species* complex (493), *E. hormaechei* (3), *E. kobei* (2), *Escherichia coli* (3423), *E. hermannii* (1), Gram-negative rods in the family *Enterobacteriaceae* (2), *Hafnia alvei* (9), *Klebsiella aerogenes* (314), *K. ornithinolytica* (1), *K. oxytoca* (360), *K. planticola* (1), *K. pneumoniae* (1545), *K. variicola* (72), *Kluyvera ascorbata* (1), *Leclercia adecarboxylata* (2), *Lelliottia amnigena* (1), *Morganella morganii* (161), *Pantoea agglomerans* (10), *P. ananatis* (1), *P. anthophila* (1), *P. calida* (1), *P. dispersa* (1), *Phytobacter diazotrophicus* (1), *Pluralibacter gergoviae* (8), *Proteus hauseri* (3), *P. mirabilis* (483), *P. penneri* (14), *P. vulgaris* (40), *P. vulgaris group* (38), *Providencia rettgeri* (53), *P. stuartii* (44), *Pseudocitrobacter faecalis* (1), *Rahnella aquatilis* (1), *Raoultella ornithinolytica* (12), *R. planticola* (3), *Serratia fonticola* (1), *S. liquefaciens* (12), *S. liquefaciens complex* (5), *S. marcescens* (550), *S. odorifera* (2), *S. rubidaea* (1), *unspeciated Citrobacter* (5), *unspeciated Klebsiella* (1), *unspeciated Pantoea* (1), *unspeciated Providencia* (3), *unspeciated Raoultella* (23), *Yersinia enterocolitica* (1), *Yokenella regensburgei* (1).
CLSI, Clinical and Laboratory Standards Institute; CR, carbapenem-resistant; CRE, carbapenem-resistant Enterobacteriaceae; FDA, Food and Drug Administration; I, intermediate; S, susceptible.

Figure 1. Frequency and epidemiology of MDR (**A**) and XDR (**B**) *Pseudomonas aeruginosa* in the US census divisions from the 2020–2021 US SENTRY surveillance program



MDR, multidrug-resistant; XDR, extensively drug-resistant.

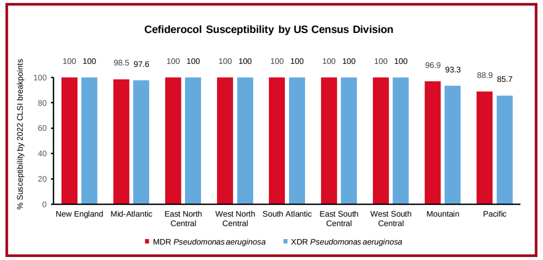
- CFDC had the highest level of activity against MDR and XDR PsA with >90% susceptibility by US FDA and CLSI standards (**Table 5**).
- High resistance rates were observed for piperacillin-tazobactam among MDR and XDR PsA.
- CFDC maintained >90% susceptibility against MDR and XDR PsA across 8/9 US census divisions and >95% susceptibility in divisions other than the Mountain or Pacific regions (**Figure 2**).
  - In the Pacific division, MDR (n=18) and XDR (n=14) PsA isolates had 88.9% and 85.7% susceptibility to CFDC, respectively.
  - In divisions with >15 isolates, CFDC had the highest rate of susceptibility compared with the other common BL/BLI combinations.

Table 5. Activity of cefiderocol and comparator antimicrobial agents tested against CLSI 2022 MDR *P. aeruginosa* isolates and CLSI 2022 XDR *P. aeruginosa* isolates in the SENTRY program, collected from US medical centers

Antimicrobial agent	mg/L MIC_{50}	mg/L MIC_{90}	MIC range	CLSI[a] %S	CLSI[a] %I	CLSI[a] %R	US FDA[a] %S	US FDA[a] %I	US FDA[a] %R
MDR[b] *Pseudomonas aeruginosa* (N=381)									
Cefiderocol	0.12	0.5	≤0.004 to 16	98.9	0.6	0.4	95.6	2.3	2.1
Imipenem-relebactam	1	4	≤0.03 to >8	84.8	10.1	5.1	84.8	10.1	5.1
Meropenem-vaborbactam	8	>8	0.03 to >8						
Ceftazidime-avibactam	8	16	0.5 to >32	79.1		20.9	79.1 [b]		20.9
Ceftolozane-tazobactam	2	8	0.5 to >16	85.9	6.3	7.8	85.9 [b]	6.3	7.8
Piperacillin-tazobactam	64	>128	0.5 to >128	17.9	34.8	47.3	17.9 [b]	34.8	47.3
XDR[b] *Pseudomonas aeruginosa* (N=212)									
Cefiderocol	0.12	1	≤0.004 to 16	97.6	1.4	0.9	92.9	3.3	3.8
Imipenem-relebactam	2	4	0.12 to >8	78.8	14.6	6.6	78.8	14.6	6.6
Meropenem-vaborbactam	>8	>8	0.06 to >8						
Ceftazidime-avibactam	8	32	0.5 to >32	71.7		28.3	71.7[c]		28.3
Ceftolozane-tazobactam	2	16	0.5 to >16	80.2	8.5	11.3	80.2[c]	8.5	11.3
Piperacillin-tazobactam	128	>128	8 to >128	6.1	36.8	57.1	6.1[c]	36.8	57.1

[a]Criteria as published by CLSI (2022) and US FDA (2022). [b]MDR *Pseudomonas aeruginosa* and XDR *Pseudomonas aeruginosa* were classified using CLSI 2022 standards. [c]CLSI M100 standard is recognized.
CLSI, Clinical and Laboratory Standards Institute; FDA, Food and Drug Administration; I, intermediate; MDR, multidrug-resistant; MIC, minimum inhibitory concentration; MIC_{50}/MIC_{90}, MIC at which ≥50%/≥90% of isolates tested are inhibited; R, resistant; S, susceptible; XDR, extensively drug-resistant.

Figure 2. MDR and XDR Pseudomonas aeruginosa susceptibility to cefiderocol by US census division



CLSI, Clinical and Laboratory Standards Institute; MDR, multidrug-resistant; XDR, extensively drug-resistant.

Conclusions

- Susceptibilities varied across US census divisions.
- GN isolates had high susceptibilities to CFDC across the US census divisions, including CR pathogens and MDR and XDR PsA.
- CFDC remains an important treatment option for GN infections in all US census divisions.

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