TABLE S1 Cumulative MIC distributions for colistin tested against the main species and organism groups

Species/organism group (no. of isolates)	No. and cumulative % of isolates inhibited at MIC (mg/L) of:												MIC_{50}	MIC_{90}
	≤0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	> [a]		
Enterobacterales (787)														
Enterobacterales not intrinsically resistant to colistin (685) [b]	0 0.0	2 0.3	373 54.7	246 90.7	46 97.4	1 97.5	0 97.5	2 97.8	3 98.2	2 98.5	0 98.5	10 100.0	0.12	0.25
Citrobacter spp. (47)		0 0.0	26 55.3	18 93.6	3 100.0								0.12	0.25
Enterobacter cloacae species complex (52)	0 0.0	1 1.9	28 55.8	11 76.9	2 80.8	0 80.8	0 80.8	0 80.8	1 82.7	1 84.6	0 84.6	8 100.0	0.12	>32
Escherichia coli (261)	0 0.0	1 0.4	109 42.1	129 91.6	20 99.2	0 99.2	0 99.2	1 99.6	1 100.0				0.25	0.25
Klebsiella aerogenes (23)		0 0.0	17 73.9	5 95.7	0 95.7	1 100.0							0.12	0.25
Klebsiella oxytoca (37)		0 0.0	32 86.5	2 91.9	3 100.0								0.12	0.25
Klebsiella pneumoniae (265)		0 0.0	161 60.8	81 91.3	18 98.1	0 98.1	0 98.1	1 98.5	1 98.9	1 99.2	0 99.2	2 100.0	0.12	0.25
Colistin-resistant (17)							0 0.0	2 11.8	3 29.4	2 41.2	0 41.2	10 100.0	>32	>32
Meropenem-resistant (10)		0 0.0	5 50.0	2 70.0	0 70.0	0 70.0	0 70.0	1 80.0	0 80.0	0 80.0	0 80.0	2 100.0	0.12	>32
Multidrug-resistant (54)		0 0.0	27 50.0	20 87.0	4 94.4	0 94.4	0 94.4	1 96.3	0 96.3	0 96.3	0 96.3	2 100.0	0.12	0.5
Enterobacterales intrinsically resistant to colistin (102) [c]											0 0.0	102 100.0	>32	>32
Acinetobacter baumannii (264)	0 0.0	1 0.4	23 9.1	112 51.5	94 87.1	27 97.3	1 97.7	1 98.1	0 98.1	2 98.9	2 99.6	1 100.0	0.25	1
Meropenem-resistant (74)		0 0.0	6 8.1	36 56.8	26 91.9	3 95.9	0 95.9	0 95.9	0 95.9	1 97.3	1 98.6	1 100.0	0.25	0.5
Colistin-non-resistant (258)	0 0.0	1 0.4	23 9.3	112 52.7	94 89.1	27 99.6	1 100.0						0.25	1
Colistin-resistant (6)							0 0.0	1 16.7	0 16.7	2 50.0	2 83.3	1 100.0	16	
Multidrug-resistant (104)		0 0.0	8 7.7	46 51.9	38 88.5	9 97.1	0 97.7	0 97.7	0 97.7	1 98.1	1 99.0	1 100.0	0.25	1
Pseudomonas aeruginosa (263)		0 0.0	10 3.8	23 12.5	123 59.3	102 98.1	5 100.0						0.5	1

Species/organism group (no. of isolates)	No. and cumulative % of isolates inhibited at MIC (mg/L) of:												MIC_{50}	MIC_{90}
	≤0.03	0.06	0.12	0.25	0.5	1	2	4	8	16	32	> [a]		
Meropenem-resistant (31)		0 0.0	2 6.5	5 22.6	15 71.0	9 100.0							0.5	1
Multidrug-resistant (46)		0 0.0	4 8.7	7 23.9	17 60.9	16 95.7	2 100.0						0.5	1

Abbreviations: MIC, minimal inhibitory concentration.

[a] Greater than the highest concentration tested.

[b] Species included *Citrobacter amalonaticus/farmeri* (1), *Citrobacter freundii* (1), *C. freundii* species complex (26), *Citrobacter koseri* (19), *Enterobacter asburiae* (1), *Enterobacter cloacae* (14), *E. cloacae* species complex (36), *Enterobacter hormaechei* (1), *Escherichia coli* (261), *Klebsiella aerogenes* (23), *Klebsiella oxytoca* (37), and *Klebsiella pneumoniae* (265).

[c] Species included *Morganella morganii* (10), *Proteus mirabilis* (46), *Proteus penneri* (1), *Proteus vulgaris* group (5), *Providencia rettgeri* (7), *Providencia stuartii* (8), *Serratia liquefaciens* complex (3), and *Serratia marcescens* (22).

9 **TABLE S2** Cumulative MIC distributions for polymyxin B tested against the main species and organism groups

Species/organism group (no. of isolates)	No. and cumulative % of isolates inhibited at MIC (mg/L) of:											MIC_{50}	MIC_{90}
	≤0.06	0.12	0.25	0.5	1	2	4	8	16	32	> [a]		
Enterobacterales (787)													
Enterobacterales not intrinsically resistant to colistin (685) [b]	0 0.0	112 16.4	459 83.4	90 96.5	7 97.5	1 97.7	2 98.0	3 98.4	1 98.5	2 98.8	8 100.0	0.25	0.5
Citrobacter spp. (47)	0 0.0	13 27.7	30 91.5	4 100.0								0.25	0.25
Enterobacter cloacae species complex (52)	0 0.0	12 23.1	27 75.0	3 80.8	0 80.8	0 80.8	0 80.8	1 82.7	0 82.7	2 86.5	7 100.0	0.25	>32
Escherichia coli (261)	0 0.0	53 20.3	170 85.4	33 98.1	3 99.2	1 99.6	0 99.6	1 100.0				0.25	0.5
Klebsiella aerogenes (23)	0 0.0	7 30.4	14 91.3	2 100.0								0.25	0.25
Klebsiella oxytoca (37)	0 0.0	8 21.6	28 97.3	0 97.3	1 100.0							0.25	0.25
Klebsiella pneumoniae (265)	0 0.0	19 7.2	190 78.9	48 97.0	3 98.1	0 98.1	2 98.9	1 99.2	1 99.6	0 99.6	1 100.0	0.25	0.5
Colistin-resistant (17)					0 0.0	1 5.9	2 17.6	3 35.3	1 41.2	2 52.9	8 100.0	32	>32
Meropenem-resistant (10)	0 0.0	2 20.0	4 60.0	1 70.0	0 70.0	0 70.0	1 80.0	0 80.0	1 90.0	0 90.0	1 100.0	0.25	16
Multidrug-resistant (54)	0 0.0	6 11.1	37 79.6	8 94.4	0 94.4	0 94.4	1 96.3	0 96.3	1 98.1	0 98.1	1 100.0	0.25	0.5
Enterobacterales intrinsically resistant to colistin (102) [c]									0 0.0	1 1.0	101 100.0	>32	>32
Acinetobacter baumannii (264)	0 0.0	34 12.9	148 68.9	66 93.9	11 98.1	1 98.5	0 98.5	3 99.6	1 100.0			0.25	0.5
Meropenem-resistant (74)	0 0.0	12 16.2	41 71.6	17 94.6	1 95.9	1 97.3	0 97.3	1 98.6	1 100.0			0.25	0.5
Colistin-non-resistant (258)	0 0.0	34 13.2	148 70.5	66 96.1	10 100.0							0.25	0.5
Colistin-resistant (6)				0 0.0	1 16.7	1 33.3	0 33.3	3 83.3	1 100.0			8	
Multidrug-resistant (104)	0 0.0	15 14.4	59 71.2	25 95.2	2 97.1	1 98.1	0 98.1	1 99.0	1 100.0			0.25	0.5
Pseudomonas aeruginosa (263)	0 0.0	5 1.9	31 13.7	171 78.7	52 98.5	4 100.0						0.5	1

Species/organism group (no. of isolates)	No. and cumulative % of isolates inhibited at MIC (mg/L) of:											MIC_{50}	MIC_{90}
	≤0.06	0.12	0.25	0.5	1	2	4	8	16	32	> [a]		
Meropenem-resistant (31)	0 0.0	2 6.5	6 25.8	21 93.5	2 100.0							0.5	0.5
Multidrug-resistant (46)	0 0.0	3 6.5	8 23.9	26 80.4	8 97.8	1 100.0						0.5	1

Abbreviations: MIC, minimal inhibitory concentration.

[a] Greater than the highest concentration tested.

[b] Species included *Citrobacter amalonaticus/farmeri* (1), *Citrobacter freundii* (1), *C. freundii* species complex (26), *Citrobacter koseri* (19), *Enterobacter asburiae* (1), *Enterobacter cloacae* (14), *E. cloacae* species complex (36), *Enterobacter hormaechei* (1), *Escherichia coli* (261), *Klebsiella aerogenes* (23), *Klebsiella oxytoca* (37), and *Klebsiella pneumoniae* (265).

[c] Species included *Morganella morganii* (10), *Proteus mirabilis* (46), *Proteus penneri* (1), *Proteus vulgaris* group (5), *Providencia rettgeri* (7), *Providencia stuartii* (8), *Serratia liquefaciens* complex (3), and *Serratia marcescens* (22).

TABLE S3 Antimicrobial activity of MRX-8 and comparator agents tested against 47 *Citrobacter* spp. isolates

Antimicrobial agent	No. of isolates	mg/L			CLSI [a]			EUCAST [a]		
		MIC_{50}	MIC_{90}	MIC range	%S	%I	%R	%S	%I	%R
MRX-8	47	0.12	0.25	0.06 to 0.5						
Colistin	47	0.12	0.25	0.12 to 0.5		100.0	0.0	100.0		0.0
Polymyxin B	47	0.25	0.25	0.12 to 0.5		100.0	0.0			
Amikacin	47	2	4	0.5 to 16	100.0	0.0	0.0	97.9 [b]		2.1
Ceftazidime	47	0.25	>32	0.06 to >32	85.1	0.0	14.9	83.0	2.1	14.9
Ceftazidime-avibactam (fixed 4 mg/L)	13	0.12	0.5	≤0.015 to 0.5	100.0		0.0	100.0		0.0
Ceftriaxone	47	0.12	>8	≤0.06 to >8	83.0	2.1	14.9	83.0 [c]		17.0
								83.0 [d]	2.1	14.9
Gentamicin	47	0.5	8	≤0.12 to >16	89.4	2.1	8.5	87.2 [b]		12.8
Levofloxacin	47	≤0.03	2	≤0.03 to >32	85.1	4.3	10.6	85.1	4.3	10.6
Meropenem	47	0.03	0.06	0.015 to 16	95.7	0.0	4.3	95.7 [c]		4.3
								95.7 [d]	2.1	2.1
Piperacillin-tazobactam (fixed 4 mg/L)	47	2	128	0.25 to >128	87.2	2.1	10.6	85.1		14.9
Tigecycline	47	0.25	0.5	≤0.06 to 1	100.0 [e]	0.0	0.0			

Abbreviations: CLSI, Clinical and Laboratory Standards Institute; EUCAST, European Committee on Antimicrobial Susceptibility Testing; I, intermediate; MIC, minimal inhibitory concentration; R, resistant; S, susceptible.

[a] Criteria as published by CLSI (2021) and EUCAST (2021).

[b] For infections originating from the urinary tract. For systemic infections, aminoglycosides must be used in combination with other active therapy.

[c] Using meningitis breakpoints.

[d] Using non-meningitis breakpoints.

[e] Using FDA breakpoints.

Organisms included *Citrobacter amalonaticus/farmeri* (1), *Citrobacter freundii* (1), *C. freundii* species complex (26), and *Citrobacter koseri* (19).

TABLE S4 Antimicrobial activity of MRX-8 and comparator agents tested against 52 *Enterobacter cloacae* species complex isolates

Antimicrobial agent	No. of isolates	mg/L			CLSI [a]			EUCAST [a]		
		MIC_{50}	MIC_{90}	MIC range	%S	%I	%R	%S	%I	%R
MRX-8	52	0.12	>32	0.06 to >32						
Colistin	52	0.12	>32	0.06 to >32		80.8	19.2	80.8		19.2
Polymyxin B	52	0.25	>32	0.12 to >32		80.8	19.2			
Amikacin	52	1	2	0.5 to 4	100.0	0.0	0.0	100.0 [b]		0.0
Ceftazidime	52	0.5	>32	0.12 to >32	69.2	1.9	28.8	63.5	5.8	30.8
Ceftazidime-avibactam (fixed 4 mg/L)	23	0.5	1	0.06 to 2	100.0		0.0	100.0		0.0
Ceftriaxone	52	0.5	>8	≤0.06 to >8	65.4	1.9	32.7	65.4 [c]		34.6
								65.4 [d]	1.9	32.7
Gentamicin	52	0.25	0.5	≤0.12 to 16	98.1	0.0	1.9	98.1 [b]		1.9
Levofloxacin	51	≤0.03	4	≤0.03 to >32	84.3	0.0	15.7	84.3	0.0	15.7
Meropenem	52	0.03	0.25	0.015 to 4	98.1	0.0	1.9	98.1 [c]		1.9
								98.1 [d]	1.9	0.0
Piperacillin-tazobactam (fixed 4 mg/L)	52	4	>128	0.5 to >128	73.1	1.9	25.0	69.2		30.8
Tigecycline	52	0.5	1	0.12 to 4	94.2 [e]	5.8	0.0			

Abbreviations: CLSI, Clinical and Laboratory Standards Institute; EUCAST, European Committee on Antimicrobial Susceptibility Testing; I, intermediate; MIC, minimal inhibitory concentration; R, resistant; S, susceptible.

[a] Criteria as published by CLSI (2021) and EUCAST (2021).

[b] For infections originating from the urinary tract. For systemic infections, aminoglycosides must be used in combination with other active therapy.

[c] Using meningitis breakpoints.

[d] Using non-meningitis breakpoints.

[e] Using FDA breakpoints.

35 Organisms included *Enterobacter asburiae* (1), *Enterobacter cloacae* (14), *E. cloacae* species complex (36), and *Enterobacter hormaechei* (1).

TABLE S5 Antimicrobial activity of MRX-8 and comparator agents tested against 23 *Klebsiella aerogenes* isolates

Antimicrobial agent	No. of isolates	mg/L			CLSI [a]			EUCAST [a]		
		MIC_{50}	MIC_{90}	MIC range	%S	%I	%R	%S	%I	%R
MRX-8	23	0.12	0.25	0.06 to 0.5						
Colistin	23	0.12	0.25	0.12 to 1		100.0	0.0	100.0		0.0
Polymyxin B	23	0.25	0.25	0.12 to 0.5		100.0	0.0			
Amikacin	23	2	2	0.5 to 4	100.0	0.0	0.0	100.0 [b]		0.0
Ceftazidime	23	0.25	>32	0.12 to >32	78.3	0.0	21.7	78.3	0.0	21.7
Ceftazidime-avibactam (fixed 4 mg/L)	10	0.12	0.25	0.06 to 0.5	100.0		0.0	100.0		0.0
Ceftriaxone	23	0.12	>8	≤0.06 to >8	78.3	0.0	21.7	78.3 [c]		21.7
								78.3 [d]	0.0	21.7
Gentamicin	23	0.25	0.5	≤0.12 to 0.5	100.0	0.0	0.0	100.0 [b]		0.0
Levofloxacin	23	0.06	0.12	≤0.03 to 0.25	100.0	0.0	0.0	100.0	0.0	0.0
Meropenem	23	0.03	0.06	0.03 to 0.12	100.0	0.0	0.0	100.0 [c]		0.0
								100.0 [d]	0.0	0.0
Piperacillin-tazobactam (fixed 4 mg/L)	23	4	32	1 to 128	78.3	17.4	4.3	78.3		21.7
Tigecycline	23	0.5	0.5	0.25 to 1	100.0 [e]	0.0	0.0			

Abbreviations: CLSI, Clinical and Laboratory Standards Institute; EUCAST, European Committee on Antimicrobial Susceptibility Testing; I, intermediate; MIC, minimal inhibitory concentration; R, resistant; S, susceptible.

[a] Criteria as published by CLSI (2021) and EUCAST (2021).

[b] For infections originating from the urinary tract. For systemic infections, aminoglycosides must be used in combination with other active therapy.

[c] Using meningitis breakpoints.

[d] Using non-meningitis breakpoints.

[e] Using FDA breakpoints.

TABLE S6 Antimicrobial activity of MRX-8 and comparator agents tested against 37 *Klebsiella oxytoca* isolates

Antimicrobial agent	No. of isolates	mg/L			CLSI [a]			EUCAST [a]		
		MIC_{50}	MIC_{90}	MIC range	%S	%I	%R	%S	%I	%R
MRX-8	37	0.12	0.12	0.06 to 0.25						
Colistin	37	0.12	0.25	0.12 to 0.5		100.0	0.0	100.0		0.0
Polymyxin B	37	0.25	0.25	0.12 to 1		100.0	0.0			
Amikacin	37	1	2	0.5 to 4	100.0	0.0	0.0	100.0 [b]		0.0
Ceftazidime	37	0.12	1	0.06 to 32	94.6	2.7	2.7	91.9	2.7	5.4
Ceftazidime-avibactam (fixed 4 mg/L)	12	0.12	0.25	0.06 to 0.5	100.0		0.0	100.0		0.0
Ceftriaxone	37	0.12	>8	≤0.06 to >8	78.4	2.7	18.9	78.4 [c]		21.6
								78.4 [d]	2.7	18.9
Gentamicin	37	0.5	1	≤0.12 to >16	91.9	0.0	8.1	91.9 [b]		8.1
Levofloxacin	37	≤0.03	0.12	≤0.03 to 0.5	100.0	0.0	0.0	100.0	0.0	0.0
Meropenem	37	0.03	0.03	0.015 to 0.06	100.0	0.0	0.0	100.0 [c]		0.0
								100.0 [d]	0.0	0.0
Piperacillin-tazobactam (fixed 4 mg/L)	37	2	>128	0.5 to >128	83.8	2.7	13.5	83.8		16.2
Tigecycline	37	0.25	0.5	0.25 to 2	100.0 [e]	0.0	0.0			

Abbreviations: CLSI, Clinical and Laboratory Standards Institute; EUCAST, European Committee on Antimicrobial Susceptibility Testing; I, intermediate; MIC, minimal inhibitory concentration; R, resistant; S, susceptible.

[a] Criteria as published by CLSI (2021) and EUCAST (2021).

[b] For infections originating from the urinary tract. For systemic infections, aminoglycosides must be used in combination with other active therapy.

[c] Using meningitis breakpoints.

[d] Using non-meningitis breakpoints.

[e] Using FDA breakpoints.

TABLE S7 Bacterial isolates by species and year

Species or organism group	No. of isolates			
	All years	2017	2019	2020
Enterobacterales	787	304	283	200
Enterobacterales not intrinsically resistant to colistin [a]	685	266	237	182
Citrobacter spp.	47	14	13	20
Enterobacter cloacae species complex	52	22	23	7
Escherichia coli	261	101	77	83
Klebsiella aerogenes	23	12	10	1
Klebsiella oxytoca	37	15	12	10
Klebsiella pneumoniae	265	102	102	61
Colistin-resistant	17	9	5	3
Meropenem-resistant	10	5	3	2
Multidrug-resistant	54	21	18	15
Enterobacterales intrinsically resistant to colistin [b]	102	38	46	18
Acinetobacter baumannii	264	101	91	72
Colistin-non-resistant	258	98	89	71
Colistin-resistant	6	3	2	1
Meropenem-resistant	74	29	23	22
Multidrug-resistant	104	43	32	29
Pseudomonas aeruginosa	263	101	92	70
Meropenem-resistant	31	12	8	11
Multidrug-resistant	46	19	15	12

[a] Species included *Citrobacter amalonaticus/farmeri* (1), *Citrobacter freundii* (1), *C. freundii* species complex (26), *Citrobacter koseri* (19), *Enterobacter asburiae* (1), *Enterobacter cloacae* (14), *E. cloacae* species complex (36), *Enterobacter hormaechei* (1), *Escherichia coli* (261), *Klebsiella aerogenes* (23), *Klebsiella oxytoca* (37), and *Klebsiella pneumoniae* (265).

[b] Species included *Morganella morganii* (10), *Proteus mirabilis* (46), *Proteus penneri* (1), *Proteus vulgaris* group (5), *Providencia rettgeri* (7), *Providencia stuartii* (8), *Serratia liquefaciens* complex (3), and *Serratia marcescens* (22).

TABLE S8 Bacterial isolates by infection type

Organism/organism group	Infection type						
	BSI	**PIHP**	**SSSI**	**IAI**	**UTI**	**Other**	**Total**
Enterobacterales	129	120	109	38	373	18	787
Enterobacterales not intrinsically resistant to colistin [a]	120	98	76	36	342	13	685
Citrobacter spp.	6	7	7	1	24	2	47
Enterobacter cloacae species complex	4	7	18	2	19	2	52
Escherichia coli	50	16	14	19	162	0	261
Klebsiella aerogenes	4	6	4	1	8	0	23
Klebsiella oxytoca	7	9	9	0	12	0	37
Klebsiella pneumoniae	49	53	24	13	117	9	265
Colistin-resistant	2	3	5	0	7	0	17
Meropenem-resistant	0	5	1	0	4	0	10
Multidrug-resistant	7	15	5	3	24	0	54
Enterobacterales intrinsically resistant to colistin [b]	9	22	33	2	31	5	102
Acinetobacter baumannii	30	134	66	3	21	10	264
Colistin-non-resistant	29	130	65	3	21	10	258
Colistin-resistant	1	4	1	0	0	0	6
Meropenem-resistant	4	46	19	0	3	2	74
Multidrug-resistant	8	64	24	0	6	2	104
Pseudomonas aeruginosa	20	144	49	11	33	6	263
Meropenem-resistant	1	22	3	1	4	0	31
Multidrug-resistant	2	32	4	0	8	0	46
Total	**179**	**398**	**224**	**52**	**427**	**34**	**1,314**

Abbreviations: BSI, bloodstream infection; PIHP, pneumonia in hospitalized patients; IAI, intra-abdominal infection; SSSI, skin and skin structure infection; UTI, urinary tract infection.

[a] Species included *Citrobacter amalonaticus/farmeri* (1), *Citrobacter freundii* (1), *C. freundii* species complex (26), *Citrobacter koseri* (19), *Enterobacter asburiae* (1), *Enterobacter cloacae* (14), *E. cloacae* species complex (36), *Enterobacter hormaechei* (1), *Escherichia coli* (261), *Klebsiella aerogenes* (23), *Klebsiella oxytoca* (37), and *Klebsiella pneumoniae* (265).

64 [b] Species included *Morganella morganii* (10), *Proteus mirabilis* (46), *Proteus penneri* (1), *Proteus vulgaris* group (5), *Providencia rettgeri* (7), *Providencia stuartii* (8), *Serratia*

65 *liquefaciens* complex (3), and *Serratia marcescens* (22).