Supplementary Information

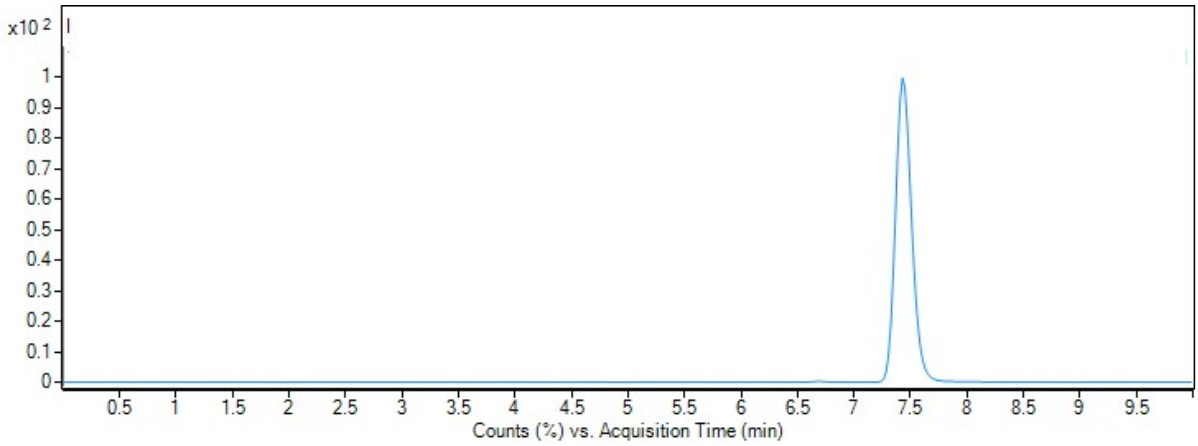

Figure S1: LC-MS chromatogram of piperacillin analytical standard showing a single, sharp peak at a retention time (RT) of 7.4 min.

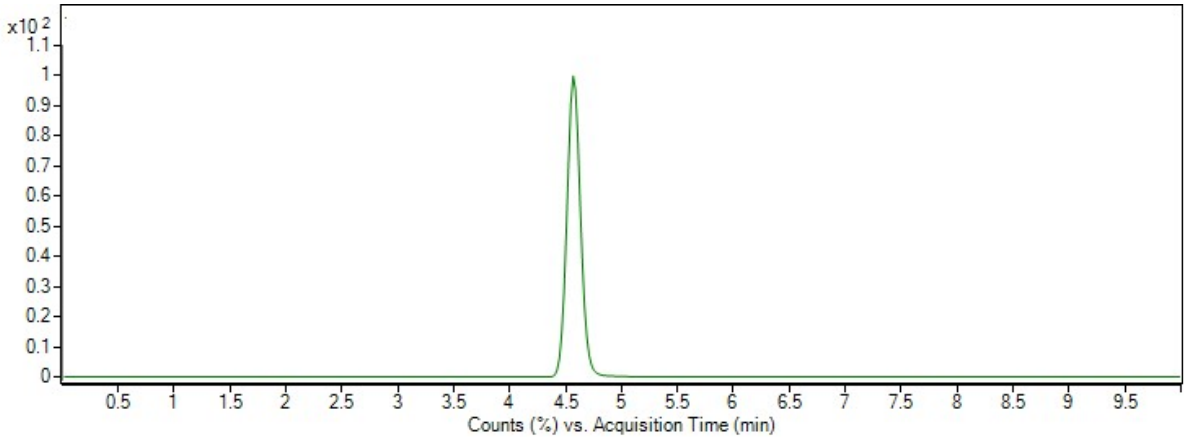

Figure S2: LC-MS chromatogram of tazobactam analytical standard showing a single, sharp peak at a retention time (RT) of 4.6 min.

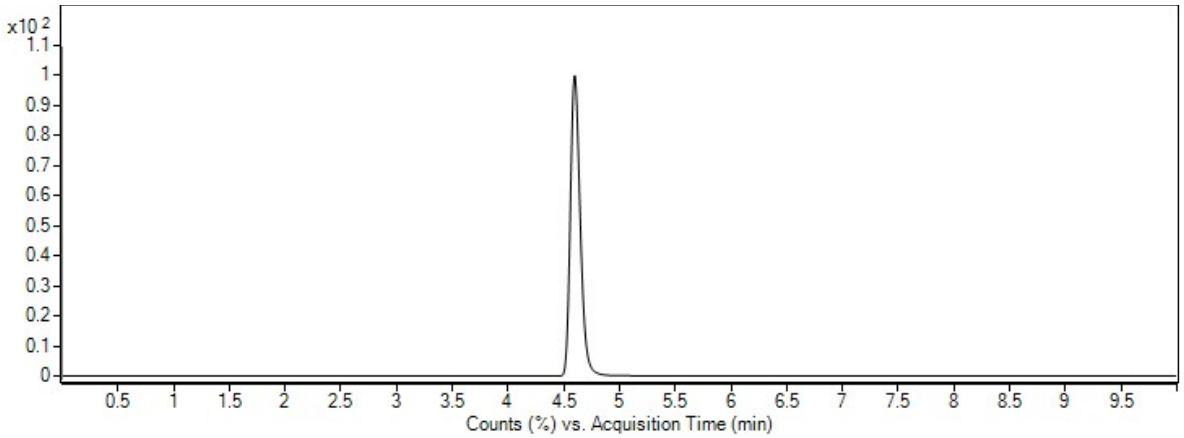

Figure S3: LC-MS chromatogram of meropenem analytical standard showing a single, sharp peak at a retention time (RT) of 4.6 min.

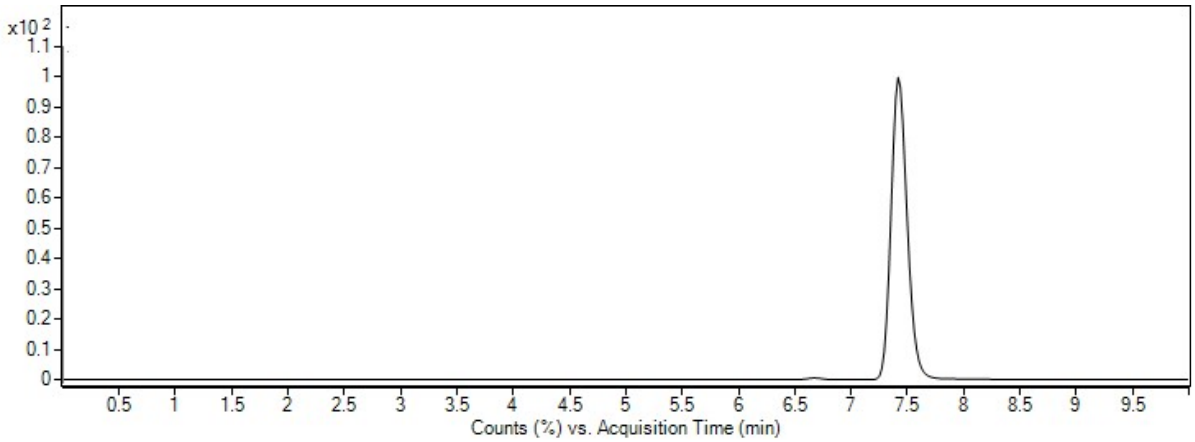

Figure S4: LC-MS chromatogram of piperacillin IS showing a single, sharp peak at a retention time (RT) of 7.4 min.

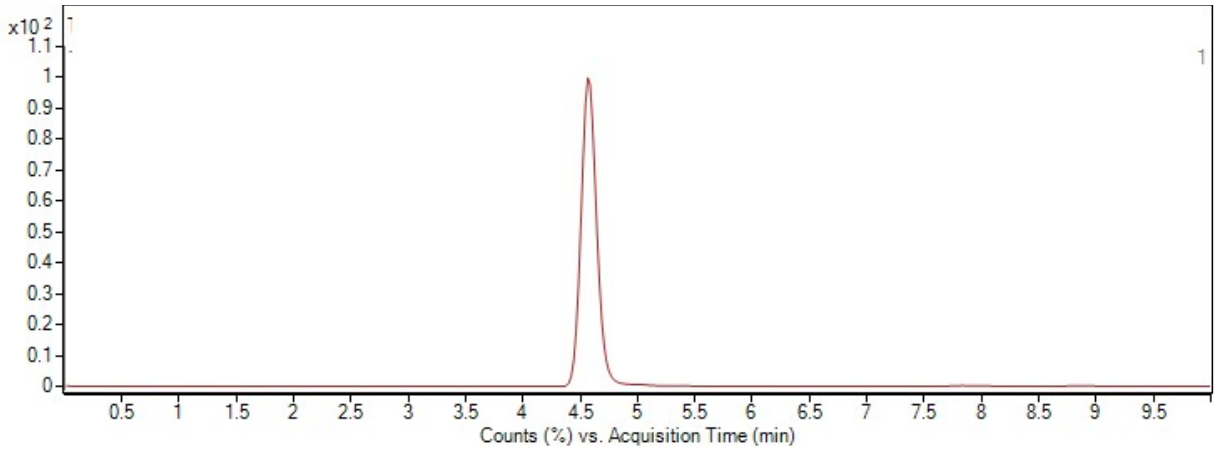

Figure S5: LC-MS chromatogram of tazobactam IS showing a single, sharp peak at a retention time (RT) of 4.6 min.

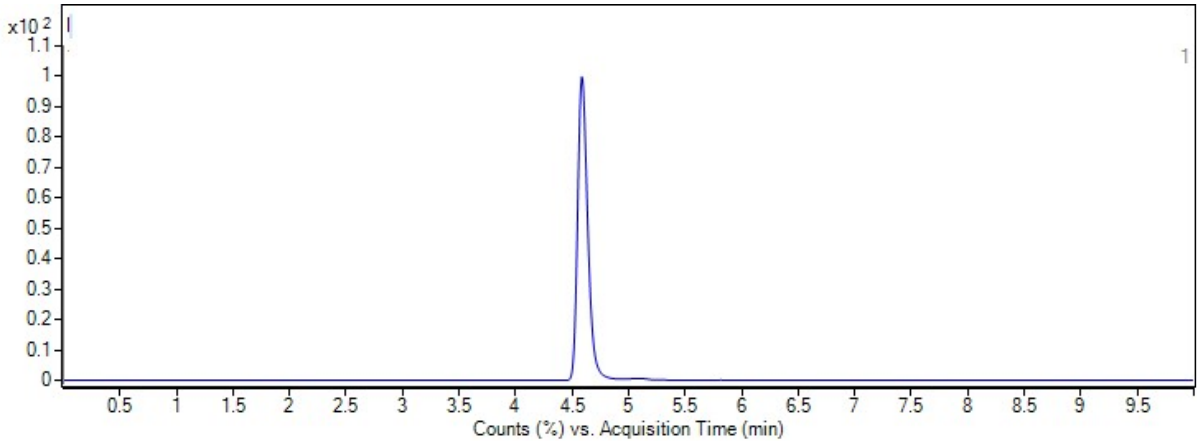

Figure S6: LC-MS chromatogram of meropenem IS showing a single, sharp peak at a retention time (RT) of 4.6 min.

Table S1. Accuracy and precision data for meropenem, piperacillin and tazobactam.

Analyte	Level	Nominal concentration	Mean measured concentration	SD	Accuracy (%Bias)	Precision (%CV)
Meropenem	L1	45000	45635	911	1.41	2.00
	L2	15000	15592	393	3.95	2.52
	L3	5000	4897	127	-2.06	2.59
	L4	1667	1576	48.6	-5.44	3.08
	L5	556	519	13.6	-6.56	2.63
	L6	185	164	5.93	-11.33	3.61
	L7	61.7	54.0	1.96	-12.60	3.63
	L8	20.6	19.1	0.37	-7.27	1.92
Piperacillin	L1	135000	138260	4223	2.41	3.05
	L2	45000	45582	1060	1.29	2.33
	L3	15000	14444	1027	-3.71	7.11
	L4	5000	4665	217	-6.69	4.65
	L5	1667	1558	42.0	-6.49	2.69
	L6	556	513	31.2	-7.73	6.09
	L7	185	172	6.00	-7.05	3.48
	L8	61.7	58.4	2.38	-5.37	4.08
	L9	20.6	22.0	0.92	6.83	4.21
Tazobactam	L1	45000	42842	1550	-4.80	3.62
	L2	15000	14466	719	-3.56	4.97
	L3	5000	4677	215	-6.46	4.60
	L4	1667	1475	82.3	-11.50	5.58
	L5	556	497	26.2	-10.46	5.27
	L6	185	161	9.69	-12.84	6.00
	L7	61.7	52.5	3.36	-14.96	6.40
	L8	20.6	19.3	2.25	-6.31	11.67

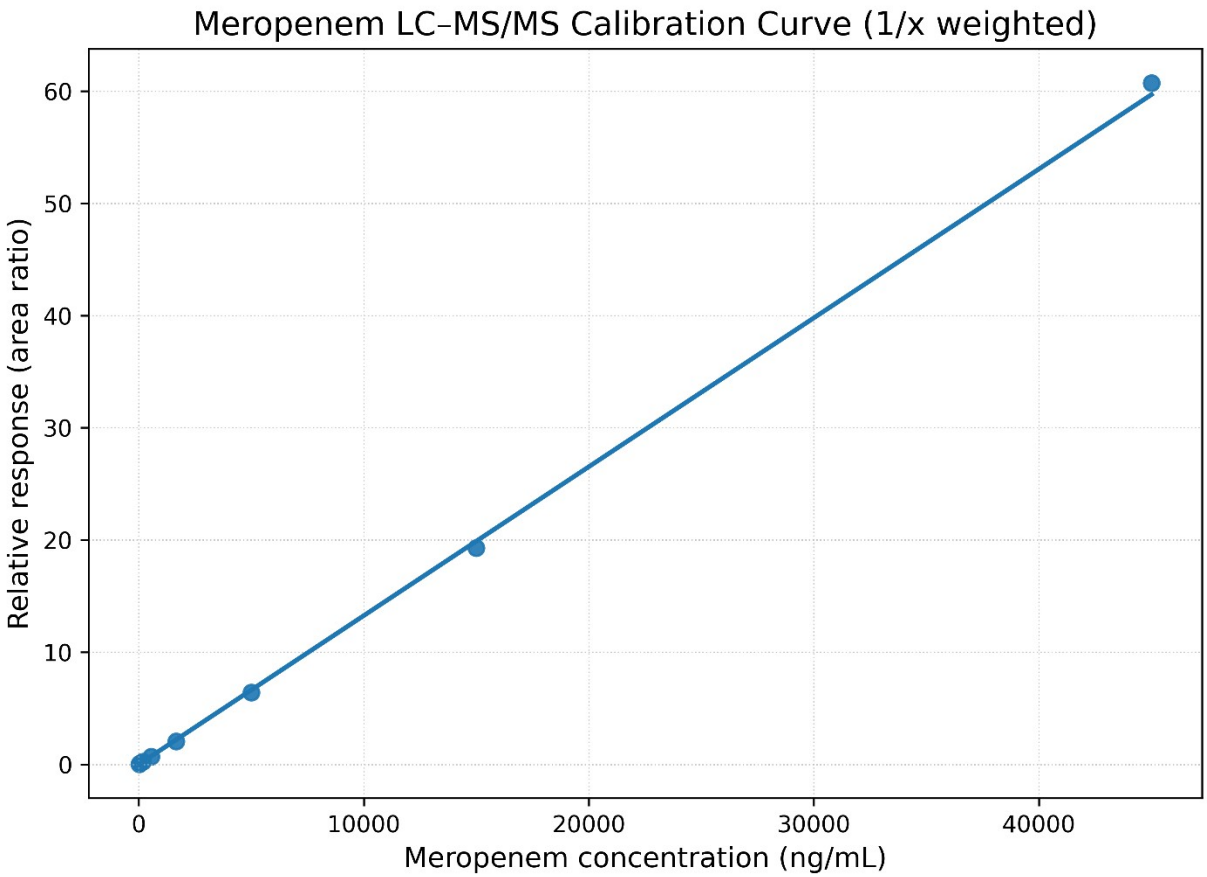

Figure S7: Meropenem calibration curve demonstrating excellent linearity across the full range (R^2 = 0.999) using a 1/x weighting model (y = 3.315815*x – 0.002110).

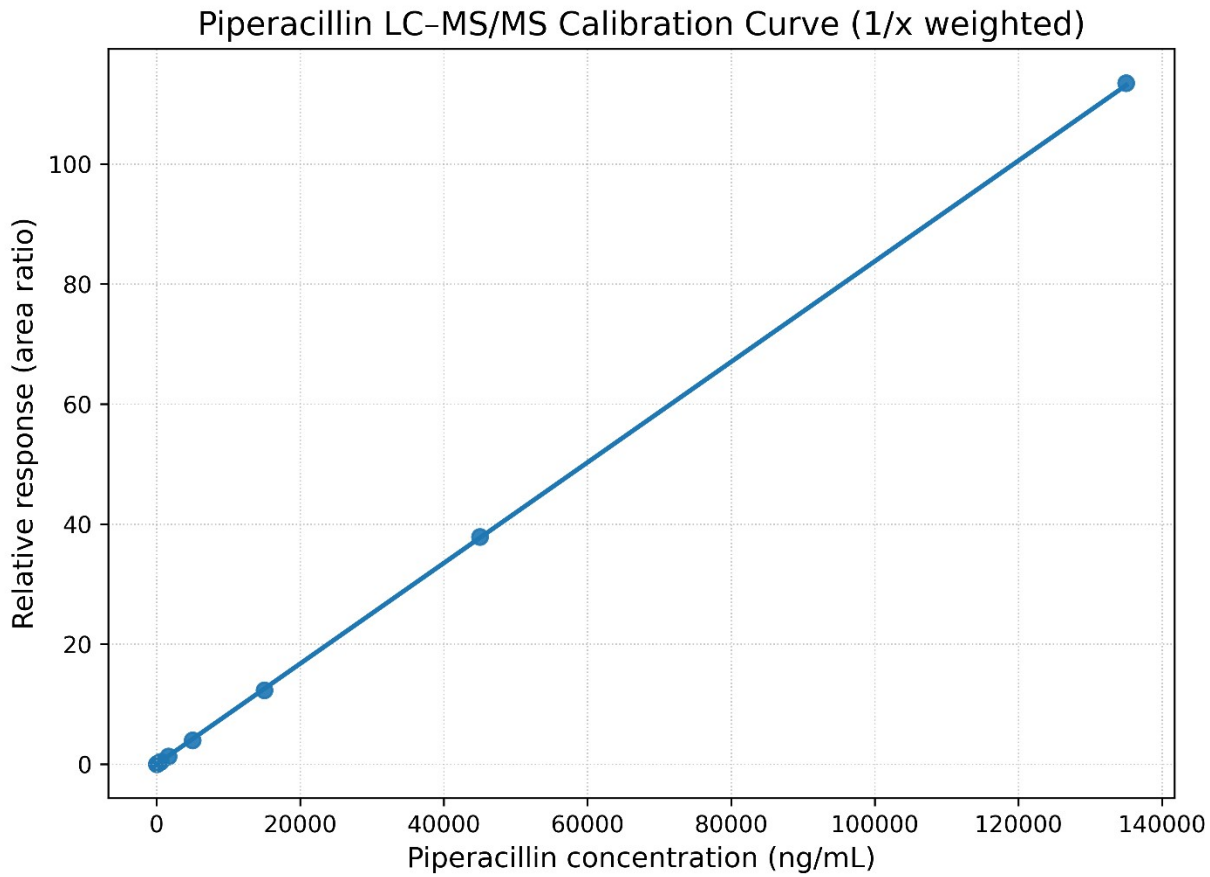

Figure S8: Piperacillin calibration curve demonstrating excellent linearity across the full range ($R^2 = 0.999$) using a 1/x weighting model ($y = 1.047313*x – 0.001015$).

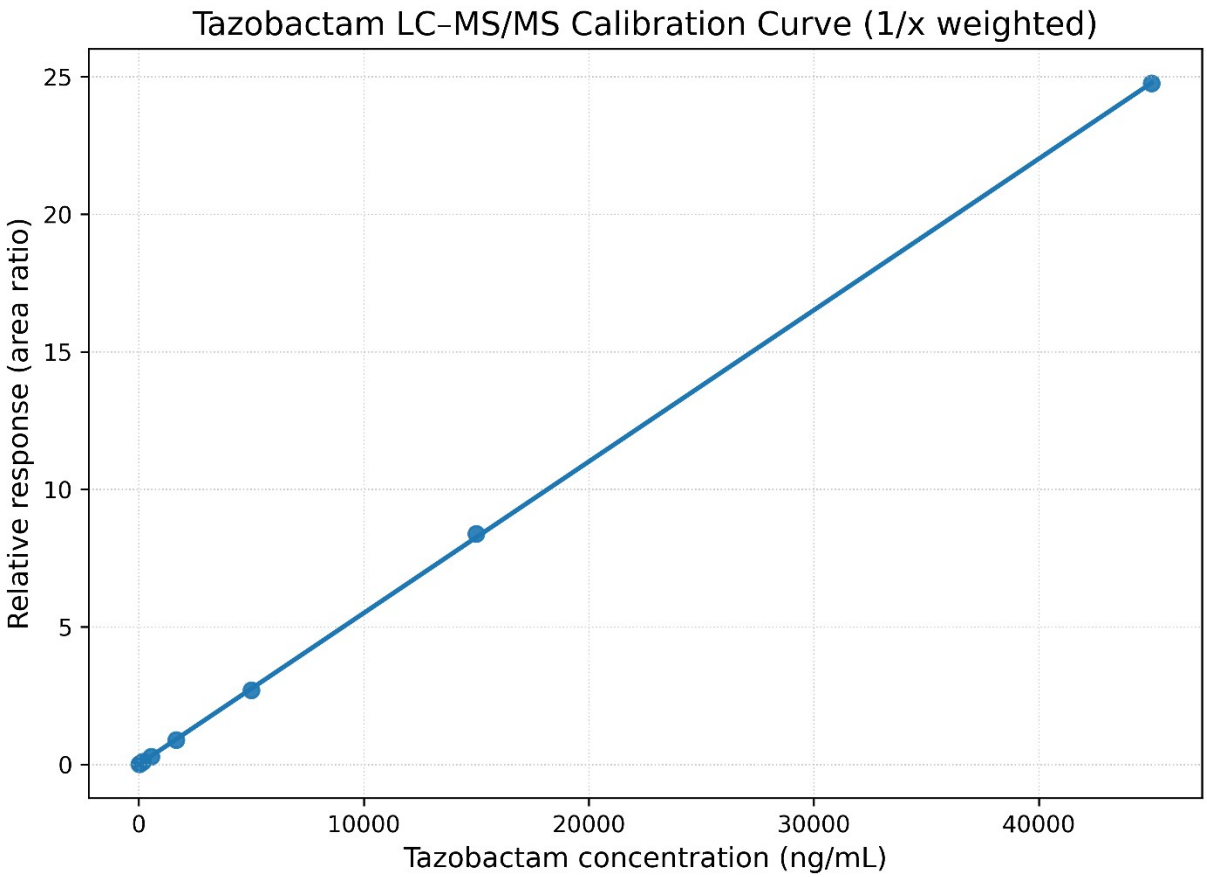

Figure S9: Tazobactam calibration curve demonstrating excellent linearity across the full range (R^2 = 0.999) using a 1/x weighting model (y = 0.688230*x – 0.001349).

Table S2. Lower limit of quantification (LLOQ) and upper limit of quantification (ULOQ) performance for analytes.

Analyte	Level	%Bias	%CV
Piperacillin	LLOQ	6.84	4.49
	ULOQ	2.41	3.05
Tazobactam	LLOQ	−1.19	7.37
	ULOQ	−4.40	3.80
Meropenem	LLOQ	−7.27	1.92
	ULOQ	1.41	2.00

Table S3. Within-run Accuracy and Precision.

Analyte	QC Level	%Bias	%CV
Piperacillin	QC1	1.62	2.78
	QC5	–6.86	2.80
	QC8	–7.92	6.00
	QC9	7.76	4.05
Tazobactam	QC1	–3.23	2.86
	QC4	–8.85	4.56
	QC7	–13.64	3.14
	QC8	–7.62	9.78
Meropenem	QC1	1.35	1.79
	QC4	–6.21	3.23
	QC7	–12.75	3.27
	QC8	–7.01	1.80

Table S4. Between-run Accuracy and Precision.

Analyte	QC Level	%Bias	%CV
Piperacillin	QC1	2.32	2.84
	QC5	–7.38	2.15
	QC8	–7.03	2.57
	QC9	5.53	2.47
Tazobactam	QC1	–3.75	1.73
	QC4	–4.54	5.33
	QC7	–9.16	3.25
	QC8	1.14	1.07
Meropenem	QC1	2.20	1.45
	QC4	–7.58	2.47
	QC7	–11.54	2.08
	QC8	–6.24	1.71

Table S5. Matrix Effect Summary for Piperacillin, Tazobactam, and Meropenem.

Analyte	QC Level	%Bias	%CV
Piperacillin	QC1	2.13	2.16
	QC5	-1.27	1.91
	QC9	3.48	4.68
Tazobactam	QC1	-1.93	1.61
	QC4	-2.53	1.69
	QC8	-2.91	5.36
Meropenem	QC1	-0.06	2.36
	QC4	-2.05	0.68
	QC8	-5.31	2.93

Table S6. Freeze–thaw stability of piperacillin, tazobactam, and meropenem over three cycles.

Analyte	QC Level	%Bias	%CV
Piperacillin	QC1	2.10	6.79
	QC5	–0.30	2.71
Tazobactam	QC1	–14.21	5.87
	QC4	–14.88	5.85
Meropenem	QC1	–2.60	3.96
	QC4	14.58	5.32