Figure S1. Individual goodness-of-fit plot for final model

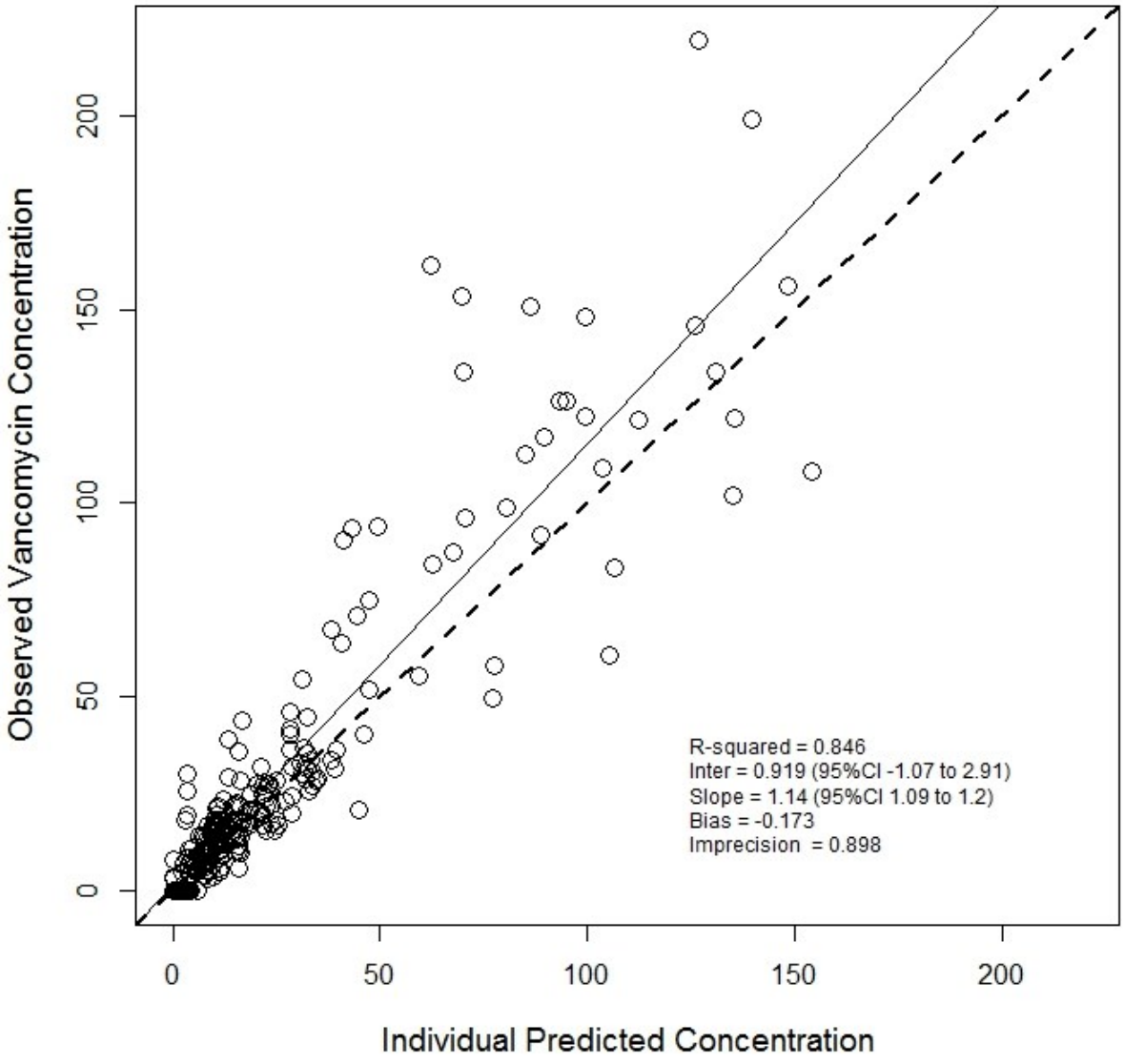
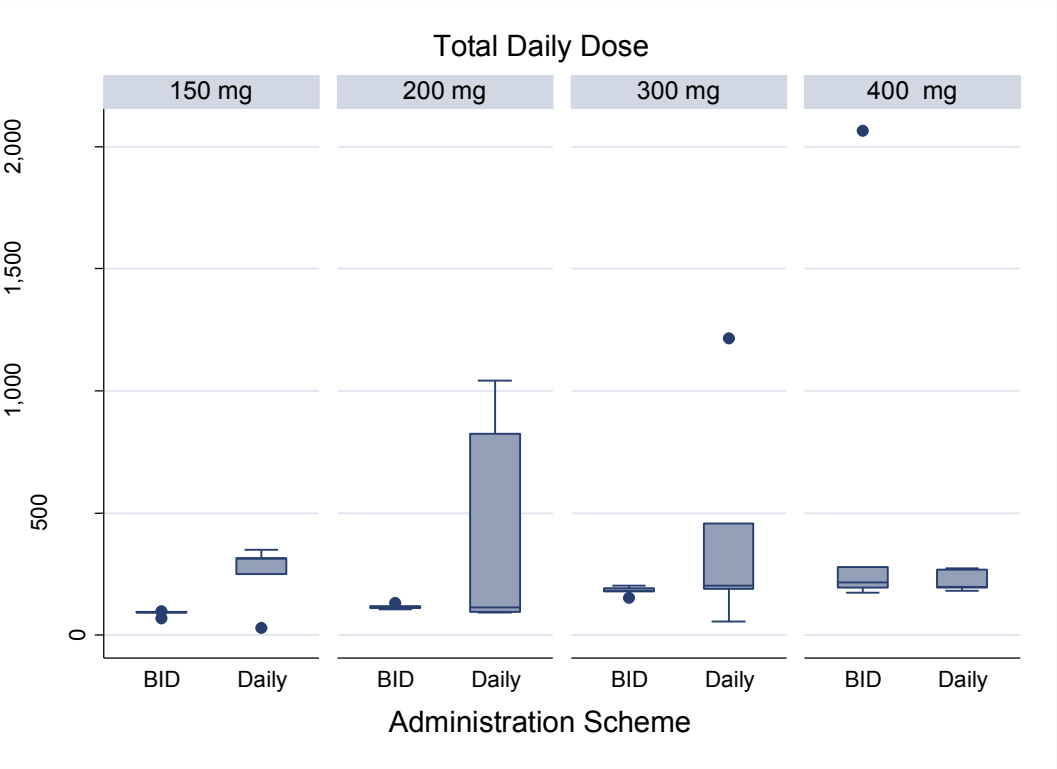


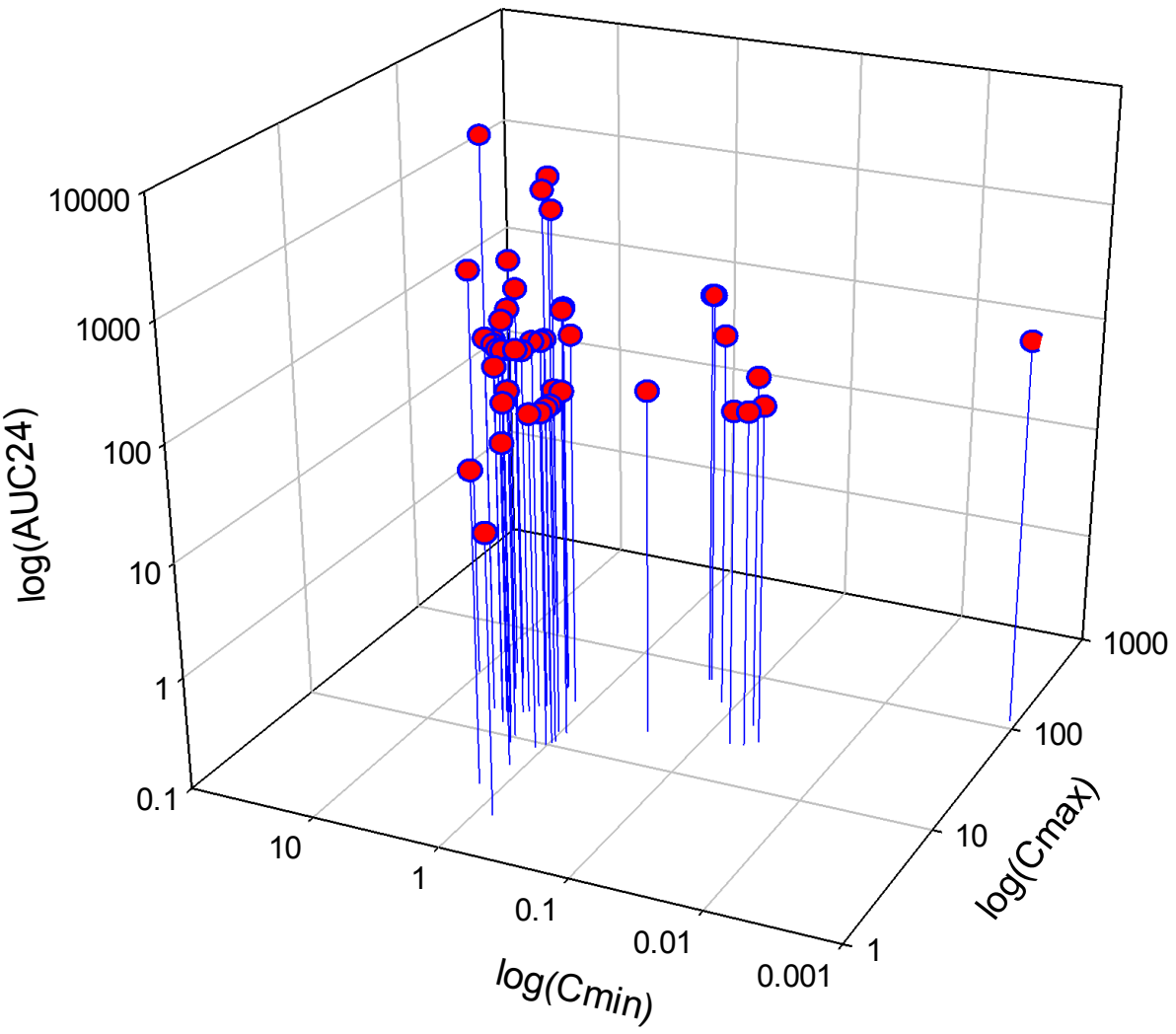
Figure S2. Box plot of exposure variability based on total daily dose and dosing scheme



Abbreviations: AUC, area under the curve; BID, twice daily dosing

Figure S3. Three-dimensional plot of relationship between vancomycin exposure metrics

S3a. Logarithmic transformations



S3b. Non-logarithmic relationship of PK exposure metrics with fitted mesh

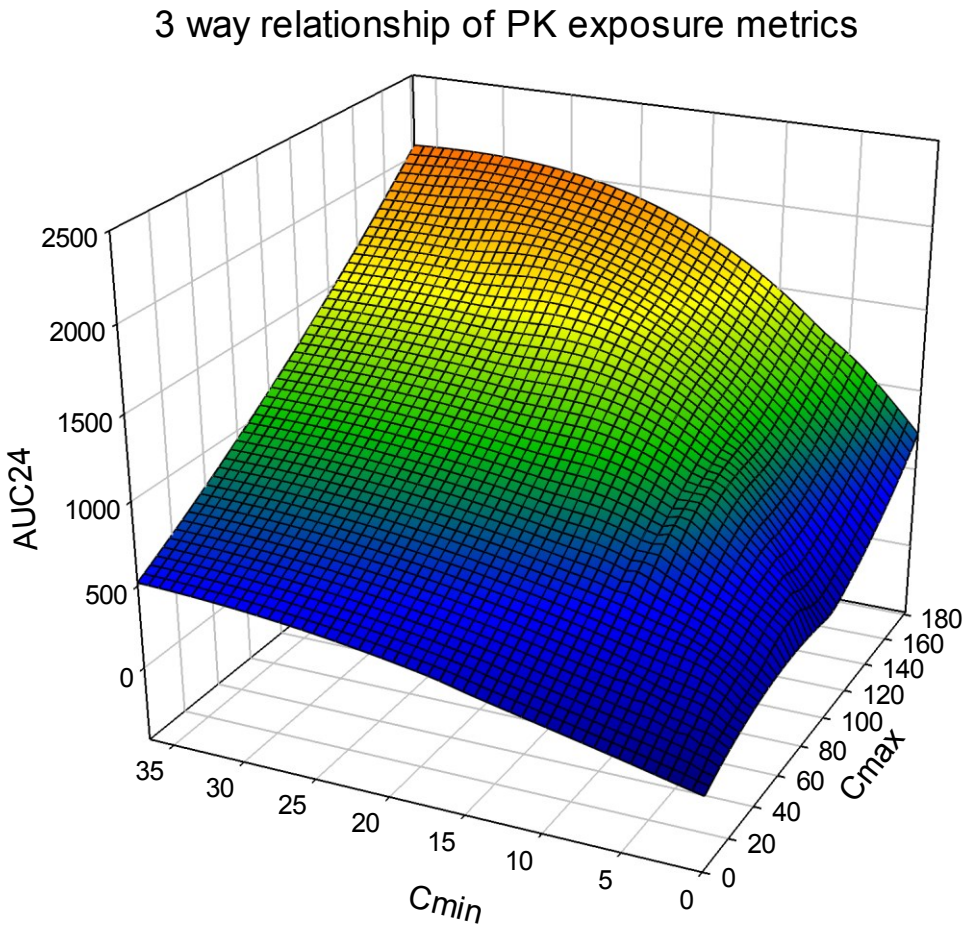


Figure S4. Exposure-Response Relationship between KIM-1 (ng/mL) and (A) $Cmax_{0\text{-}24h}$ (B) $AUC_{0\text{-}24h}$ and (C) $Cmin_{0\text{-}24h}$ in complete data (1) and with an outlier removed (2)

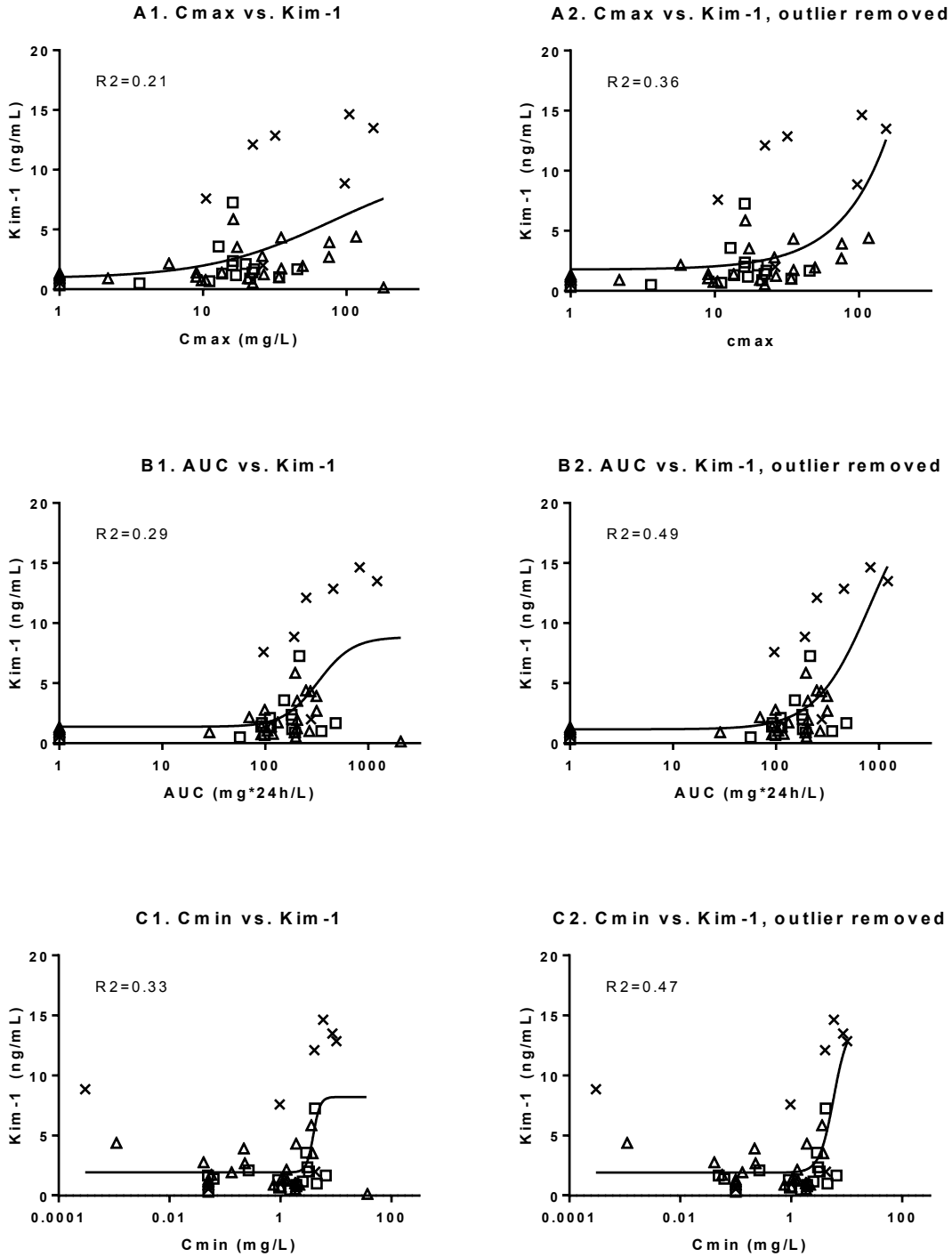


Figure Legend: Composite histopathology score: □**,** No histopathologic damage; Δ**,** Minimal histopathologic damage; **x,** mild histopathologic damage

Table S1. Covariance matrix of final pharmacokinetic model in the lower triangular form

	K_e (h^{-1})	V_0/F (L/0.28 kg)	K_a (h^{-1})	K_{12} (h^{-1})	K_{21} (h^{-1})
K_e (h^{-1})	0.022				
V_0/F (L/0.28 kg)	-0.177	4.753			
K_a (h^{-1})	-0.001	-0.432	0.948		
K_{12} (h^{-1})	-0.065	3.407	-0.082	10.215	
K_{21} (h^{-1})	0.069	-4.246	0.084	-11.862	13.976

Abbreviations: K_e, central compartment elimination constant; V_0/F, central compartment volume standardized to 0.286 kg; K_a, absorption constant from peritoneum to central compartment; K_{12} and K_{21}, intercompartmental transfer rates

Table S2. Bayesian posterior vancomycin exposure (median [IQR])

	150 mg/kg/day		200 mg/kg/day		300 mg/kg/day		400 mg/kg/day	
	150 mg/kg daily	75 mg/kg BID	200 mg/kg daily	100 mg/kg BID	300 mg/kg daily	150 mg/kg BID	400 mg/kg daily	200 mg/kg BID
AUC (mg*h/L)	313.7 [248.5-314.4]	91.6 [91.2-92.6]	112.8 [96.1-824.6]	113.4 [110.9-118.4]	203.4 [190.5-455.9]	181.6 [179.4-193.1]	197.3 [193.9-267.3]	214.3 [194.7-278.0]
Cmax (mg/L)	75.5 [34.0-76.2]	22.1 [9.8-22.8]	13.6 [10.5-104.6]	13.5 [10.5-19.9]	49.6 [31.9-97.4]	16.2 [16.0-20.6]	22.2 [21.3-33.9]	17.9 [16.3–26.2]
Cmin (mg/L)	0.23 [0.22-0.75]	0.06 [0.05-1.0]	1.2 [0.94-6.53]	1.0 [0.27-1.83]	1.5 [0.13-8.6]	2.9 [2.2-3.0]	1.9 [1.9-1.9]	4.1 [3.6-4.2]
Tmax (h)	0.12 [0.10-0.12]	0.15 [0.12-0.18]	0.08 [0.08-0.12]	0.20 [0.20-0.20]	0.20 [0.20-0.20]	0.20 [0.20-0.20]	0.20 [0.20-0.20]	0.20 [0.03-0.20]

Table S3. Toxicodynamic results by AUC bin

	AUC 0	AUC 1-100	AUC 101-200	AUC 201-300	AUC > 300
Animals (n)	5	10	16	9	9
KIM-1 (ng/mL), median (IQR)	0.927 [0.55-1.18]	1.4 [0.75-2.16]	1.39 [0.91-2.35]	3.53 [1.94-4.40]	3.30 [1.34-13.18]
Clusterin (ng/mL), median (IQR)	449 [409-486]	547 [304-768]	450 [272-624]	506 [412-817]	944 [482-1228]
Osteopontin (ng/mL), median (IQR)	0.062 [0.087-0.258]	0.122 [0.087-0.258]	0.116 [0.083-0.152]	0.167 [0.111-0.317]	0.340 [0.104-0.589]
Cystatin-C (ng/mL), median (IQR)	517 [434-560]	792 [370-1121]	402 [192-583]	416 [215-524]	495 [251-812]
NGAL (ng/mL), median (IQR)	634 [400-1114]	1728 [763-2619]	1247 [997-2890]	1613 [671-2246]	1252 [476-2646]
Composite Histopathology Score, median (IQR)	1 [1-1]	1 [0-1]	0.5 [0-1]	1 [1-1]	1 [1-2]
Proximal Tubular Damage Score, median (IQR)	0 [0-0]	0 [0-1]	0 [0-0]	0 [0-1]	0 [0-1]

Table S4. Toxicodynamic results by Cmax bin

	Cmax 0	Cmax 1-15	Cmax 16-30	Cmax 31-60	Cmax > 60
Animals (n)	5	12	17	7	8
KIM-1 (ng/mL), median (IQR)	0.927 [0.55-1.18]	1.17 [0.76-1.77]	2.00 [1.21-3.16]	1.72 [1.01-4.33]	4.40 [2.69-13.49]
Clusterin (ng/mL), median (IQR)	449 [409-486]	465 [383-684]	431 [383-684]	652 [382-1175]	874 [583-1015]
Osteopontin (ng/mL), median (IQR)	0.062 [0.087-0.258]	0.114 [0.085-0.123]	0.138 [0.101-0.268]	0.317 [0.094-0.625]	0.140 [0.097-0.540]
Cystatin-C (ng/mL), median (IQR)	517 [434-560]	524 [361-798]	433 [242-676]	448 [215-802]	416 [217-562]
NGAL (ng/mL), median (IQR)	634 [400-1114]	1000 [686-1943]	2497 [1649-2813]	997 [517-2918]	762 [274-1600]
Composite Histopathology Score, median (IQR)	1 [1-1]	1 [0-1]	0 [0-1]	1 [0-1]	1.5 [1-2]
Proximal Tubular Damage Score, median (IQR)	0 [0-0]	0 [0-0.5]	0 [0-0]	0 [0-1]	0.5 [0-1.5]