

**Table S1.** Experimental design for the pharmacokinetic and histopathological studies

Experiment	Drug	Dosage Regimen	Sampling Time	Sample	Number of Animals
Single dose PK study	Colistin	0.66 and 1.32 mg base/kg	<b>IV (for plasma):</b> 10, 20, and 30 min, and 1, 1.5, 2, 3, 4, 6, 12 and 24 h	Plasma	3
			<b>IV (for BALF collection):</b> 10 min, and 2, 6 and 12 h	BALF	3 per time point
			<b>DPI (Group 1):</b> 10 and 30 min, and 1, 2 and 4 h	Plasma	3
			<b>DPI (Group 2):</b> 10 and 30 min, and 1, 2, 4, 6 and 12 h	BALF	3 per time point

Histopathological examination	Colistin	0.66 and 1.32 mg base/kg	<b>DPI 0.66 mg base/kg: 0.5 and 24 h</b> <b>DPI 1.32 mg base/kg: 0.5, 2, 6 and 24 h</b> <b>Solution 1.32 mg base/kg: 24 h</b>	Lung	At least 3 per group
-------------------------------	----------	--------------------------	---	------	----------------------

---

BALF: Bronchoalveolar lavage fluid

DPI: Dry powder inhalation

IV: Intravenous

PK: Pharmacokinetics

**Table S2.** Accuracy and precision of the assay for the quantification of colistin in ELF and plasma.

	Intraday (n=9)				Interday (n=9)			
Concentration (mg/L)	0.2	1	4	8	0.2	1	4	8
<b>Epithelial lining fluid (ELF)</b>								
Accuracy (%)	-6.86	6.62	9.30	5.83	-14.2	4.05	9.30	-2.09
Precision (%)	2.06	1.39	3.64	0.54	7.56	2.53	2.17	6.14
<b>Plasma</b>								
Accuracy (%)	10.8	4.96	-5.35	-1.52	8.77	11.2	8.42	-3.27
Precision (%)	2.87	3.53	1.99	1.19	2.35	4.96	1.64	3.50

ND: Not determined

**Figure S1.** Goodness-of-fit plots of the final pharmacokinetic model. Observation versus population predicted concentration plots for **(A)** ELF and **(B)** plasma. The solid red lines represent the line of identity.

