

Experiment Number: S0594  
Route: Dosed Feed, IV  
Species/Strain: Mouse/B6C3F1

Toxicokinetics Data Summary  
Test Compound: Phenolphthalein  
CAS Number: 77-09-8

Date Report Requested: 12/06/2016  
Time Report Requested: 10:35:49  
Lab: Research Triangle Institute

Male								
Treatment Groups (ppm)								
	200 a, #	375 b, *	375 c, #	750 d, *	750 e, #	3000 f, *	3000 g, #	12000 h, *
Plasma								
C <sub>max</sub> (ug/mL)	26.7 ± 3.9	0.0445 ± 0.035	63.3 ± 3.3	0.0458 ± 0.012	102 ± 9.3	0.192 ± 0.12	244 ± 29	0.330 ± 0.020
AUC <sub>0-t</sub> (ug*hr/mL)	486.0 ± 12.0	0.226 ± 0.045	1160.0 ± 31.0	0.739 ± 0.021	1961.0 ± 49.0	2.19 ± 0.18	4502.0 ± 80.0	6.27 ± 1.7

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Male			
	Treatment Groups (ppm)		
	12000 <sup>i, #</sup>	25 IV <sup>j, *</sup>	25 IV <sup>k, #</sup>
	Plasma		
C <sub>max</sub> (ug/mL)	406 ± 35	60.1 ± 14.0	179.0 ± 23.0
AUC <sub>0-t</sub> (ug*hr/mL)	7494.0 ± 158	19.8 ± 0.27	680.0 ± 18.0

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Female								
Treatment Groups (ppm)								
	200 l, #	375 m, *	375 n, #	750 o, *	750 p, #	3000 q, *	3000 r, #	12000 s, #
Plasma								
C <sub>max</sub> (ug/mL)	49.4 ± 1.2	0.0590 ± 0.065	97.2 ± 15	0.133 ± 0.19	148 ± 2.9	0.445 ± 0.18	299 ± 17	422 ± 30
AUC <sub>0-t</sub> (ug*hr/mL)	839.0 ± 22.0	0.181 ± 0.077	1682.0 ± 38.0	0.910 ± 0.30	2589.0 ± 41.0	3.46 ± 0.23	5722.0 ± 108.0	8770.0 ± 137.0

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Female			
	Treatment Groups (ppm)		
	12000 <sup>t, *</sup>	25 IV <sup>j, *</sup>	25 IV <sup>k, #</sup>
	Plasma		
C <sub>max</sub> (ug/mL)	0.324 ± 0.37	61.1 ± 17.0	204.0 ± 20.0
AUC <sub>0-t</sub> (ug*hr/mL)	4.17 ± 0.29	18.3 ± 0.090	901.0 ± 22.0

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## LEGEND

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Data are displayed as mean  $\pm$  SD

### MODELING METHOD & BEST FIT MODEL

<sup>a</sup> Excel, Version 7 used to calculate means and standard deviation for C<sub>max</sub>, C<sub>max</sub> steady state and AUC<sub>24-hr</sub> by trapezoidal rule. To determine AUC<sub>24-hr</sub>, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 38.17 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters were not determined.

<sup>b</sup> Excel, Version 7 used to calculate means and standard deviation for C<sub>max</sub>, C<sub>max</sub> steady state and AUC<sub>24-hr</sub> by trapezoidal rule. To determine AUC<sub>24-hr</sub>, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 65.93 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters for PTH.

<sup>c</sup> Excel, Version 7 used to calculate means and standard deviation for C<sub>max</sub>, C<sub>max</sub> steady state and AUC<sub>24-hr</sub> by trapezoidal rule. To determine AUC<sub>24-hr</sub>, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 65.93 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters were not determined.

<sup>d</sup> Excel, Version 7 used to calculate means and standard deviation for C<sub>max</sub>, C<sub>max</sub> steady state and AUC<sub>24-hr</sub> by trapezoidal rule. To determine AUC<sub>24-hr</sub>, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 143.36 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters for PTH.

<sup>e</sup> Excel, Version 7 used to calculate means and standard deviation for C<sub>max</sub>, C<sub>max</sub> steady state and AUC<sub>24-hr</sub> by trapezoidal rule. To determine AUC<sub>24-hr</sub>, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 143.36 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters were not determined.

<sup>f</sup> Excel, Version 7 used to calculate means and standard deviation for C<sub>max</sub>, C<sub>max</sub> steady state and AUC<sub>24-hr</sub> by trapezoidal rule. To determine AUC<sub>24-hr</sub>, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 550.86 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters for PTH.

<sup>g</sup> Excel, Version 7 used to calculate means and standard deviation for C<sub>max</sub>, C<sub>max</sub> steady state and AUC<sub>24-hr</sub> by trapezoidal rule. To determine AUC<sub>24-hr</sub>, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 550.86 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters were not determined.

<sup>h</sup> Excel, Version 7 used to calculate means and standard deviation for C<sub>max</sub>, C<sub>max</sub> steady state and AUC<sub>24-hr</sub> by trapezoidal rule. To determine AUC<sub>24-hr</sub>, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 2134.66 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters for PTH.

<sup>i</sup> Excel, Version 7 used to calculate means and standard deviation for C<sub>max</sub>, C<sub>max</sub> steady state and AUC<sub>24-hr</sub> by trapezoidal rule. To determine AUC<sub>24-hr</sub>, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 2134.66 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters were not determined.

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### MODELING METHOD & BEST FIT MODEL

<sup>j</sup> Excel, Version 7 used to calculate means and standard deviation for C<sub>max</sub>, C<sub>max</sub> steady state and AUC<sub>24-hr</sub> by trapezoidal rule; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters for PTH.

<sup>k</sup> Excel, Version 7 used to calculate means and standard deviation for C<sub>max</sub>, C<sub>max</sub> steady state and AUC<sub>24-hr</sub> by trapezoidal rule; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters were not determined.

<sup>l</sup> Excel, Version 7 used to calculate means and standard deviation for C<sub>max</sub>, C<sub>max</sub> steady state and AUC<sub>24-hr</sub> by trapezoidal rule. To determine AUC<sub>24-hr</sub>, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 42.20 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters were not determined.

<sup>m</sup> Excel, Version 7 used to calculate means and standard deviation for C<sub>max</sub>, C<sub>max</sub> steady state and AUC<sub>24-hr</sub> by trapezoidal rule. To determine AUC<sub>24-hr</sub>, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 74.37 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters for PTH.

<sup>n</sup> Excel, Version 7 used to calculate means and standard deviation for C<sub>max</sub>, C<sub>max</sub> steady state and AUC<sub>24-hr</sub> by trapezoidal rule. To determine AUC<sub>24-hr</sub>, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 74.37 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters were not determined.

<sup>o</sup> Excel, Version 7 used to calculate means and standard deviation for C<sub>max</sub>, C<sub>max</sub> steady state and AUC<sub>24-hr</sub> by trapezoidal rule. To determine AUC<sub>24-hr</sub>, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 179.58 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters for PTH.

<sup>p</sup> Excel, Version 7 used to calculate means and standard deviation for C<sub>max</sub>, C<sub>max</sub> steady state and AUC<sub>24-hr</sub> by trapezoidal rule. To determine AUC<sub>24-hr</sub>, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 179.58 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters were not determined.

<sup>q</sup> Excel, Version 7 used to calculate means and standard deviation for C<sub>max</sub>, C<sub>max</sub> steady state and AUC<sub>24-hr</sub> by trapezoidal rule. To determine AUC<sub>24-hr</sub>, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 654.05 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters for PTH.

<sup>r</sup> Excel, Version 7 used to calculate means and standard deviation for C<sub>max</sub>, C<sub>max</sub> steady state and AUC<sub>24-hr</sub> by trapezoidal rule. To determine AUC<sub>24-hr</sub>, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 654.05 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters were not determined.

<sup>s</sup> Excel, Version 7 used to calculate means and standard deviation for C<sub>max</sub>, C<sub>max</sub> steady state and AUC<sub>24-hr</sub> by trapezoidal rule. To determine AUC<sub>24-hr</sub>, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 2540.50 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters were not determined.

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<sup>t</sup> Excel, Version 7 used to calculate means and standard deviation for C<sub>max</sub>, C<sub>max</sub> steady state and AUC<sub>24-hr</sub> by trapezoidal rule. To determine AUC<sub>24-hr</sub>, it was assumed that plasma concentrations of PTH and PTH-G in the 10 a.m. sample on day 14 were the same as those in plasma at 10 a.m. on day 15. Mean daily dose is 2540.50 mg/kg/day; Due to the extensive enterohepatic recycling of PTH, classical pharmacokinetic models are not applicable to the calculation of clearance, bioavailability, and other pharmacokinetic parameters for PTH.

### ANALYTE

- # Phenolphthalein Glucuronide
- \* Phenolphthalein

### TK PARAMETERS

C<sub>max</sub> = Observed or Predicted Maximum plasma (or tissue) concentration

AUC<sub>0-t</sub> = Area under the plasma concentration versus time curve, AUC, from time t<sub>i</sub> (initial) to t<sub>f</sub> (final), AUC<sub>last</sub>

**\*\* END OF REPORT \*\***