Experiment Number: C92013B	**Toxicokinetics Data Summary**	**Date Report Requested:** 11/09/2016
Route: Gavage, IV	**Test Compound:** 4-Methylimidazole	**Time Report Requested:** 14:00:53
Species/Strain: Rat/F344	**CAS Number:** 822-36-6	**Lab:** Battelle Columbus

Male

	Treatment Groups (mg/kg)			
	10 [a]	**50 [a]**	**100 [a]**	**10 IV [b]**
	Plasma			
$C_{0min(pred)}$ (ug/mL)				8.88 ± 0.41
C_{max} (ug/mL)	4.66 ± 0.32	11.8 ± 1.4	17.5 ± 3.6	
T_{max} (hour)	0.883 ± 0.072	0.703 ± 0.137	0.828 ± 0.362	
k_{01} (hour^-1)	1.84 ± 0.32	5.37 ± 1.63	5.03 ± 2.97	
$t_{1/2(k01)}$ (hour)	0.376 ± 0.066	0.129 ± 0.039	0.138 ± 0.081	
k_{10} (hour^-1)	0.633 ± 0.041	0.136 ± 0.034	0.0835 ± 0.0157	0.586 ± 0.019
$t_{1/2(k10)}$ (hour)	1.09 ± 0.07	5.11 ± 1.29	8.31 ± 1.56	1.18 ± 0.04
Cl (mL/hr/kg)				660 ± 24
$Cl_{1(F)}$ (mL/hr/kg)	777 ± 56	524 ± 82	444 ± 72.0	
V_1 (mL/kg)				1130 ± 50
$V_{1(F)}$ (mL/kg)	1230 ± 150	3860 ± 580	5320 ± 1230	
MRT (hour)				1.71 ± 0.06
AUC_{0-t} (ug/mL*hr)	12.7	61.1	201	14.6
AUC_{inf} (ug/mL*hr)	12.9 ± 0.9	95.4 ± 15.0	225 ± 37	15.2 ± 0.6
F (percent)	84.9	126	148	

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Female

	10 [a]	50 [a]	100 [a]	10 IV [b]
Treatment Groups (mg/kg)				
Plasma				
$C_{0min(pred)}$ (ug/mL)				9.77 ± 1.05
C_{max} (ug/mL)	6.59 ± 0.56	16.8 ± 1.5	19.3 ± 3.3	
T_{max} (hour)	0.765 ± 0.084	0.614 ± 0.098	0.579 ± 0.267	
k_{01} (hour^-1)	2.33 ± 0.51	5.95 ± 1.44	7.88 ± 4.73	
$t_{1/2(k01)}$ (hour)	0.297 ± 0.064	0.117 ± 0.028	0.0880 ± 0.0528	
k_{10} (hour^-1)	0.639 ± 0.044	0.172 ± 0.026	0.0865 ± 0.0132	0.612 ± 0.045
$t_{1/2(k10)}$ (hour)	1.08 ± 0.07	4.03 ± 0.62	8.01 ± 1.22	1.13 ± 0.08
Cl (mL/hr/kg)				626 ± 53
$Cl_{1(F)}$ (mL/hr/kg)	594 ± 54	459 ± 42	426 ± 58	
V_1 (mL/kg)				1020 ± 110
$V_{1(F)}$ (mL/kg)	930 ± 134	2670 ± 300	4920 ± 930	
MRT (hour)				1.63 ± 0.12
AUC_{0-t} (ug/mL*hr)	16.3	83.1	235	16.4
AUC_{inf} (ug/mL*hr)	16.8 ± 1.5	109 ± 10	235 ± 32	16.0 ± 1.4
F (percent)	105	136	147	

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LEGEND

Data are displayed as mean ± SEM

MODELING METHOD & BEST FIT MODEL

[a] WinNONLIN (V01.5A Core Version 19May97); Plasma concentration time profiles for the gavage males and females fit a one-compartment model with no lag phase and first order absorption and elimination.

[b] WinNONLIN (V01.5A Core Version 19May97); The rat plasma concentration time profiles for IV males and females were monophasic, one-compartment model with first order elimination

ANALYTE

4-Methylimidazole

TK PARAMETERS

$C_{0min(pred)}$ = Fitted plasma concentration at time zero (IV only)

C_{max} = Observed or Predicted Maximum plasma (or tissue) concentration

T_{max} = Time at which C_{max} predicted or observed occurs

k_{01} = Absorption rate constant, k_a

$t_{1/2(k01)}$ = Half-life of the absorption process to the central compartment

k_{10} = Elimination rate constant from the central compartment also k_e or k_{elim}

$t_{1/2(k10)}$ = Half-life for the elimination process from the central compartment

Cl = Clearance, includes total clearance

$Cl_{1(F)}$ = Apparent clearance of the central compartment, also $Cl_{(F)}$ for gavage groups in non-compartmental model

V_1 = Volume of distribution of the central compartment, includes V_d and V_{volume} of distribution, V_z apparent volume of distribution NCA, V_{app} apparent volume of distribution for intravenous studies

$V_{1(F)}$ = Apparent volume of distribution for the central compartment includes $V_{d(F)}$, $V_{(F)}$ for oral groups, and $V_{c(F)}$

MRT = Mean residence time

AUC_{0-t} = Area under the plasma concentration versus time curve, AUC, from time t_i (initial) to t_f (final), AUC_{last}

AUC_{inf} = Area under the plasma concentration versus time curve, AUC, extrapolated to time equals infinity

F = Bioavailability, absolute bioavailability

** END OF REPORT **