

Experiment Number: C92013B

Route: Gavage, IV

Species/Strain: Mouse/B6C3F1

Toxicokinetics Data Summary

Test Compound: 4-Methylimidazole

CAS Number: 822-36-6

Date Report Requested: 11/09/2016

Time Report Requested: 14:00:44

Lab: Battelle Columbus

Male

Treatment Groups (mg/kg)

10^a

50^a

100^a

10 IV^b

Plasma

C _{0min(pred)} (ug/mL)				5.91 ± 0.67
C _{max} (ug/mL)	3.42 ± 0.30	15.9 ± 1.8	24.3 ± 2.9	
T _{max} (hour)	0.220 ± 0.036	0.164 ± 0.082	0.213 ± 0.096	
k ₀₁ (hour ⁻¹)	8.66 ± 2.63	20.0 ± 13.9	16.8 ± 10.4	
t _{1/2(k01)} (hour)	0.0800 ± 0.0243	0.0346 ± 0.0240	0.0413 ± 0.0255	
k ₁₀ (hour ⁻¹)	1.99 ± 0.17	0.861 ± 0.048	0.523 ± 0.040	1.68 ± 0.11
t _{1/2(k10)} (hour)	0.348 ± 0.030	0.805 ± 0.045	1.33 ± 0.10	0.414 ± 0.027
Cl (mL/hr/kg)				2840 ± 210
Cl _{1(F)} (mL/hr/kg)	3760 ± 300	2350 ± 230	1920 ± 200	
V ₁ (mL/kg)				1690 ± 190
V _{1(F)} (mL/kg)	1890 ± 270	2720 ± 350	3680 ± 510	
MRT (hour)				0.597 ± 0.040
AUC _{0-t} (ug/mL*hr)	2.70	22.5	48.5	3.53
AUC _{inf} (ug/mL*hr)	2.66 ± 0.21	21.3 ± 2.0	52.1 ± 5.3	3.53 ± 0.26
F (percent)	75.4	121	148	

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Female

Treatment Groups (mg/kg)

10^a

50^a

100^a

10 IV^b

Plasma

	10 ^a	50 ^a	100 ^a	10 IV ^b
C _{0min(pred)} (ug/mL)				6.16 ± 0.51
C _{max} (ug/mL)	3.73 ± 0.29	16.8 ± 1.8	29.3 ± 2.3	
T _{max} (hour)	0.203 ± 0.037	0.262 ± 0.081	0.217 ± 0.064	
k ₀₁ (hour ⁻¹)	11.2 ± 3.4	11.9 ± 5.3	16.9 ± 6.7	
t _{1/2(k01)} (hour)	0.0620 ± 0.0191	0.0585 ± 0.0263	0.0411 ± 0.0163	
k ₁₀ (hour ⁻¹)	1.61 ± 0.13	0.623 ± 0.049	0.479 ± 0.025	1.57 ± 0.09
t _{1/2(k10)} (hour)	0.430 ± 0.036	1.11 ± 0.09	1.45 ± 0.08	0.442 ± 0.024
Cl (mL/hr/kg)				2550 ± 140
Cl _{1(F)} (mL/hr/kg)	3120 ± 210	1570 ± 150	1470 ± 100	
V ₁ (mL/kg)				1620 ± 130
V _{1(F)} (mL/kg)	1930 ± 230	2520 ± 350	3080 ± 280	
MRT (hour)				0.637 ± 0.345
AUC _{0-t} (ug/mL*hr)	3.21	32.5	70.4	3.76
AUC _{inf} (ug/mL*hr)	3.21 ± 0.22	31.9 ± 3.03	67.8 ± 4.4	3.93 ± 0.22
F (percent)	81.7	162	173	

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LEGEND

Data are displayed as mean \pm SEM

MODELING METHOD & BEST FIT MODEL

^a WinNONLIN (V01.5A Core Version 19May97); The mouse gavage plasma concentration time profiles for the 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 mouse IV plasma concentration time profiles for males and females were monophasic. The profiles fit a 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} = distribution rate constant from first to second compartment

$t_{1/2(k10)}$ = Elimination rate constant from the central compartment also k_e or k_{elim}

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 ****