Experiment Number: C92012B
Route: Gavage, IV
Species/Strain: Rat/Fischer 344

Toxicokinetics Data Summary
Test Compound: 2-Methylimidazole
CAS Number: 693-98-1

Date Report Requested: 11/09/2016
Time Report Requested: 14:00:27
Lab: Battelle Columbus

Male

	Treatment Groups (mg/kg)			
	25 [a]	50 [a]	100 [a]	10 IV [b]
	Plasma			
C_{max} (ug/mL)	6.29 ± 0.69	14.2 ± 1.5	28.1 ± 2.7	8.48 ± 1.31
T_{max} (hour)	0.756 ± 0.106	0.757 ± 0.100	0.757 ± 0.099	
Alpha (hour^-1)				2.96 ± 1.52
$t_{1/2(Alpha)}$ (hour)				0.234 ± 0.120
Beta (hour^-1)				0.788 ± 0.102
$t_{1/2(Beta)}$ (hour)				0.879 ± 0.114
k_{01} (hour^-1)	2.32 ± 0.69	2.28 ± 0.65	2.74 ± 0.70	
$t_{1/2(k01)}$ (hour)	0.299 ± 0.089	0.304 ± 0.086	0.253 ± 0.064	
k_{10} (hour^-1)	0.663 ± 0.083	0.679 ± 0.081	0.504 ± 0.059	1.34 ± 0.19
$t_{1/2(k10)}$ (hour)	1.04 ± 0.13	1.02 ± 0.12	1.38 ± 0.16	0.516 ± 0.074
k_{12} (hour^-1)				0.667 ± 0.587
k_{21} (hour^-1)				1.74 ± 0.90
Cl (mL/hr/kg)				1590 ± 80
$Cl_{1(F)}$ (mL/hr/kg)	1600 ± 180	1430 ± 150	1230 ± 110	
V_1 (mL/kg)				1180 ± 180
V_{ss} (mL/kg)				1630 ± 130
MRT (hour)				1.03 ± 0.06
AUC_{inf} (ug/mL*hr)	15.7 ± 1.7	35.1 ± 3.7	81.6 ± 7.0	6.31 ± 0.30
F (percent)	94.8	109.0	126.0	

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Female

	Treatment Groups (mg/kg)			
	25 [a]	50 [a]	100 [a]	10 IV [b]
	Plasma			
C_{max} (ug/mL)	6.26 ± 0.71	14.8 ± 2.0	30.4 ± 3.7	9.60 ± 1.56
T_{max} (hour)	0.519 ± 0.092	0.671 ± 0.128	0.612 ± 0.113	
Alpha (hour^-1)				5.36 ± 1.63
$t_{1/2(Alpha)}$ (hour)				0.129 ± 0.039
Beta (hour^-1)				0.803 ± 0.046
$t_{1/2(Beta)}$ (hour)				0.863 ± 0.049
k_{01} (hour^-1)	4.23 ± 1.32	3.18 ± 1.13	4.11 ± 1.31	
$t_{1/2(k01)}$ (hour)	0.164 ± 0.051	0.218 ± 0.078	0.169 ± 0.054	
k_{10} (hour^-1)	0.664 ± 0.063	0.540 ± 0.079	0.433 ± 0.061	1.81 ± 0.27
$t_{1/2(k10)}$ (hour)	1.04 ± 0.10	1.28 ± 0.19	1.60 ± 0.22	0.383 ± 0.058
k_{12} (hour^-1)				1.97 ± 0.94
k_{21} (hour^-1)				2.38 ± 0.54
Cl (mL/hr/kg)				1890 ± 70
$Cl_{1(F)}$ (mL/hr/kg)	1880 ± 210	1270 ± 160	1090 ± 110	
V_1 (mL/kg)				1040 ± 170
V_{ss} (mL/kg)				1910 ± 110
MRT (hour)				1.01 ± 0.04
AUC_{inf} (ug/mL*hr)	13.3 ± 1.5	39.5 ± 4.8	91.5 ± 9.2	5.30 ± 0.19
F (percent)	98.5	144.0	162.0	

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LEGEND

Data are displayed as mean ± SEM

MODELING METHOD & BEST FIT MODEL

[a] WinNonlin V01.5A, using Gauss-Newton (Levenberg and Hartley) method; one-compartment model with no lag phase and first order absorption and elimination. The concentration values were weighted $1/y^2$ (predicted). The six hour time point was used as the cut-off for modeling the profile and calculating the terminal linear phase.

[b] WinNonlin V01.5A, using Gauss-Newton (Levenberg and Hartley) method; two-compartmental model with first order elimination. The concentration values were weighed $1/y^2$ (predicted).

ANALYTE

2-Methylimidazole

TK PARAMETERS

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

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

Alpha = Hybrid rate constant of the alpha phase

$t_{\frac{1}{2}(alpha)}$ = Half-life for the alpha phase

Beta = Hybrid rate constant of the beta phase

$t_{\frac{1}{2}(beta)}$ = Half-life for the beta phase

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

k_{12} = Distribution rate constant from first to second compartment etc.

k_{21} = Distribution rate constant from second to first compartment etc.

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_{ss} = Volume of distribution at steady state

MRT = Mean residence time

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

F = Bioavailability, absolute bioavailability

** END OF REPORT **