Experiment Number: S0613
Route: Gavage, IV
Species/Strain: Mouse/B6C3F1

Toxicokinetics Data Summary
Test Compound: Formamide
CAS Number: 75-12-7

Date Report Requested: 12/27/2016
Time Report Requested: 11:23:27
Lab: Midwest Research Institute

Male

	Treatment Groups (mg/kg)					
	120 [a]	**1000 [a]**	**2000 [a]**	**20 IV [b]**	**60 IV [c]**	**180 IV [c]**
	Plasma					
C_{max} (ug/mL)	152	1436	2443	49.6	96.6	239
T_{max} (hour)	0.70	0.74	0.60			
Alpha (hour^-1)				0.13		
$t_{1/2(Alpha)}$ (hour)				5.2		
Beta (hour^-1)				0.0070		
$t_{1/2(Beta)}$ (hour)				99		
k_{01} (hour^-1)	4.60	5.49	8.6			
$t_{1/2(k01)}$ (hour)	0.15	0.13	0.081			
k_{10} (hour^-1)	0.21	0.10	0.053	0.065	0.18	0.12
$t_{1/2(k10)}$ (hour)	3.2	6.8	13.0	10.7	3.9	5.6
Cl (mL/hr*kg)	52	52	50	26	110	94
V_1 (mL/kg)				403	621	753
V_{ss} (mL/kg)				2390		
$V_{1(F)}$ (mL/kg)	680	646	793			
MRT (hour)	5.5	9.3	19.8	93	5.9	6.7
AUC_{inf} (ug*hr/mL)	1170	16593	48536	781	605	1747
F (fraction)	0.51	0.87	1.22			

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	Female					
	Treatment Groups (mg/kg)					
	120 [a]	1000 [a]	2000 [a]	20 IV [d]	60 IV [c]	180 IV [c]
	Plasma					
C_{max} (ug/mL)	159	1366	2690	44.7	85.6	257
T_{max} (hour)	0.81	1.9	1.1			
k_{01} (hour^-1)	3.70	1.33	3.5			
$t_{1/2(k01)}$ (hour)	0.19	0.52	0.20			
k_{10} (hour^-1)	0.22	0.13	0.86		0.19	0.19
$t_{1/2(k10)}$ (hour)	3.2	5.2	8.0		3.6	3.7
Cl (mL/hr*kg)	73	71	72		133	131
V_1 (mL/kg)					701	701
V_{ss} (mL/kg)				1900		
$V_{1(F)}$ (mL/kg)	630	567	677			
MRT (hour)	5.6	8.0	14.4	38	5.3	5.9
AUC_{inf} (ug*hr/mL)	1190	15297	39793	404	644	1962
F (fraction)	0.72	1.08	1.44			

LEGEND

Data are displayed as mean values

MODELING METHOD & BEST FIT MODEL

[a] WinNonlin (Version 1, SCI, Cary, North Carolina) estimated Cmax, Tmax, and elimination and absorbtion half-lives. Model independent methods (CHANKIN) were used to estimate mean residence time (MRToral) and area under the plasma concentration-time curve ($AUC_{o\text{-}inf}$); One-compartment model with first-order absorption and elimination.

[b] WinNonlin (Version 1, SCI, Cary, North Carolina) estimated distribution (alpha half-life) and elimination half-lives, volumes of distribution (V_c shown as V_1, V_{ss}) and clearance Cl. Model independent methods (CHANKIN) were used to estimate mean residence time (MRTiv) and area under the plasma concentration-time curve ($AUC_{o\text{-}inf}$); Two compartment model with first order elimination.

[c] WinNonlin (Version 1, SCI, Cary, North Carolina) estimated distribution (alpha half-life) and elimination half-lives, volumes of distribution (V shown as V_1) and clearance Cl. Model independent methods (CHANKIN) were used to estimate mean residence time (MRTiv) and area under the plasma concentration-time curve ($AUC_{o\text{-}inf}$); One compartment model with first order elimination.

[d] WinNonlin (Version 1, SCI, Cary, North Carolina) unable to estimate distribution (alpha half-life) and elimination half-lives, volumes of distribution (V_c, V_{ss}) and clearance Cl. Model independent methods (CHANKIN) were used to estimate mean residence time (MRTiv) and area under the plasma concentration-time curve ($AUC_{o\text{-}inf}$); Data from female mice could not be modeled due to the erratic nature of the plasma concentration-time profile.

ANALYTE

Formamide

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

$t_{½(alpha)}$ = Half-life for the alpha phase

Beta = Hybrid rate constant of the beta phase

$t_{½(beta)}$ = 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

Cl = Clearance, includes total clearance

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

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

LEGEND

TK PARAMETERS

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 **