Experiment Number: S0629
Route: Dosed Feed, Gavage, IV
Species/Strain: Hamster/Syrian Golden

Toxicokinetics Data Summary
Test Compound: Wyeth-14643
CAS Number: 50892-23-4

Date Report Requested: 11/09/2016
Time Report Requested: 14:05:11
Lab: Research Triangle Institute

Male

	Treatment Groups (mg/kg)						
	1 [a]	**1 [b]**	**3 [a]**	**10 [a]**	**100 [c]**	**1000 [c]**	**3 IV [a]**
	Plasma						
$C_{max(obs)}$ (ug/mL)	0.485		2.88	6.04	0.447	4.04	
$T_{max(obs)}$	10.0 m		15.0 m	15.0 m	1000 h	1000 h	
Alpha (min^-1)		0.1494 ± 0.0115					
Beta (min^-1)		0.0244 ± 0.0021					
$t_{1/2(Beta)}$ (minute)	51.7		78.6	51.1			108.0
k_{01} (min^-1)		0.0139					
k_{10} (min^-1)		0.0852 ± 0.0034					
k_{12} (min^-1)		0.0458 ± 0.0063					
k_{21} (min^-1)		0.0428 ± 0.0052					
Cl (mL/min/kg)							3.72
$Cl_{1(F)}$ (mL/min/kg)	20.1		15.8	23.2			
V_1 (L/kg)		0.0480 ± 0.0019					
MRT (minute)	97.1		102	100.0			38.1
AUC_{inf} (ug/mL*min)	50		190.0	431.0	301.0	3390.0	806.0
F (fraction)	0.19		0.24	0.16			

LEGEND

Data are displayed as mean ± SEM

m = minutes; h = hours

MODELING METHOD & BEST FIT MODEL

[a] Models 200 and 201, PCNONLIN software, Version 4.2, SCI Software, Lexington, KY; Noncompartmental model

[b] PCNONLIN software, Version 4.2, SCI Software, Lexington, KY; Best fit is two compartmental which simultaneously solves iv and low dose oral data sets. Simultaneous solution of hamster intravenous dose (3.0 mg/kg Study T) and mid oral gavage dose (1.0 mg/kg Study U).

[c] PCNONLIN software, Version 4.2, SCI Software, Lexington, KY; Noncompartmental model

ANALYTE

Wyeth-14643

TK PARAMETERS

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

$T_{max(obs)}$ = Time at which C_{max} predicted or observed occurs

Alpha = Hybrid rate constant of 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

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

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

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 **