Experiment Number: C20613
Route: Gavage, IV
Species/Strain: Rat/Harlan Sprague-Dawley

Toxicokinetics Data Summary
Test Compound: Perfluorohexanoic acid
CAS Number: 307-24-4

Date Report Requested: 12/29/2016
Time Report Requested: 14:35:43
Lab: Battelle Columbus

Male

	Treatment Groups (mg/kg)			
	80 [a]	**80 [a]**	**80 [a]**	**40 [b]**
	Brain	**Kidney**	**Liver**	**Plasma**
$C_{max(pred)}$ (ng/mL)				77700 ± 10200
$T_{max(pred)}$ (hour)				0.668 ± 0.154
$C_{max(obs)}$ (ng/g)	2720	125000	91600	
$T_{max(obs)}$ (hour)	1.12	0.572	0.567	
$t_{1/2}$ (hour)	2.29	1.94	2.38	
$t_{1/2(Alpha)}$ (hour)				2.35 ± 1.27
$t_{1/2(Beta)}$ (hour)				9.33 ± 20.8
k_{01} (hour^-1)				4.43 ± 1.74
$t_{1/2(k01)}$ (hour)				0.157 ± 0.062
k_{10} (hour^-1)				0.242 ± 0.058
$t_{1/2(k10)}$ (hour)				2.87 ± 0.68
k_{12} (hour^-1)				0.0367 ± 0.0424
k_{21} (hour^-1)				0.0906 ± 0.230
Cl_1 (mL/hr/kg)				
$Cl_{1(F)}$ (mL/hr/kg)				103 ± 13
V_1 (mL/kg)				
V_2 (mL/kg)				
$V_{1(F)}$ (mL/kg)				428 ± 86
$V_{2(F)}$ (mL/kg)				173 ± 284
MRT (hour)				
AUC_{0-t} (ng/mL*hr)				346000
AUC_{inf} (ng/mL*hr)				387000 ± 50000
F (percent)				131

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	Treatment Groups (mg/kg)		
	80 [b]	160 [b]	40 IV [c]
	Plasma		
$C_{max(pred)}$ (ng/mL)	145000 ± 13000	304000 ± 31000	252000 ± 42000
$T_{max(pred)}$ (hour)	0.676 ± 0.103	0.890 ± 0.134	
$C_{max(obs)}$ (ng/g)			
$T_{max(obs)}$ (hour)			
$t_{1/2}$ (hour)			
$t_{1/2(Alpha)}$ (hour)	1.78 ± 0.39	1.46 ± 0.26	0.655 ± 0.097
$t_{1/2(Beta)}$ (hour)	5.74 ± 4.59	13.7 ± 14.2	7.98 ± 2.21
k_{01} (hour^-1)	3.79 ± 1.02	2.22 ± 0.69	
$t_{1/2(k01)}$ (hour)	0.183 ± 0.049	0.312 ± 0.097	
k_{10} (hour^-1)	0.358 ± 0.041	0.424 ± 0.071	0.853 ± 0.114
$t_{1/2(k10)}$ (hour)	1.94 ± 0.22	1.63 ± 0.27	0.812 ± 0.108
k_{12} (hour^-1)	0.0212 ± 0.0245	0.0436 ± 0.0113	0.184 ± 0.054
k_{21} (hour^-1)	0.132 ± 0.120	0.0567 ± 0.0594	0.108 ± 0.032
Cl_1 (mL/hr/kg)			136 ± 13
$Cl_{1(F)}$ (mL/hr/kg)	153 ± 11	147 ± 14	
V_1 (mL/kg)			159 ± 27
V_2 (mL/kg)			271 ± 85
$V_{1(F)}$ (mL/kg)	427 ± 61	348 ± 70	
$V_{2(F)}$ (mL/kg)	68.7 ± 19.6	267 ± 297	
MRT (hour)			3.17 ± 0.62
AUC_{0-t} (ng/mL*hr)	539000	1050000	266000
AUC_{inf} (ng/mL*hr)	524000 ± 38000	1090000 ± 100000	295000 ± 28000
F (percent)	88.8	92.4	

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Female

	Treatment Groups (mg/kg)			
	80 [a]	80 [a]	80 [a]	40 [b]
	Brain	Kidney	Liver	Plasma
$C_{max(pred)}$ (ng/mL)				94000 ± 18400
$T_{max(pred)}$ (hour)				0.529 ± 0.184
$C_{max(obs)}$ (ng/g)	1460	86900	41200	
$T_{max(obs)}$ (hour)	1.11	1.09	1.09	
$t_{1/2}$ (hour)	ND	1.44	1.51	
$t_{1/2(Alpha)}$ (hour)				1.37 ± 2.23
$t_{1/2(Beta)}$ (hour)				2.27 ± 213
k_{01} (hour^-1)				4.74 ± 3.08
$t_{1/2(k01)}$ (hour)				0.146 ± 0.095
k_{10} (hour^-1)				0.502 ± 0.167
$t_{1/2(k10)}$ (hour)				1.38 ± 0.46
k_{12} (hour^-1)				9.74E-4 ± 0.120
k_{21} (hour^-1)				0.307 ± 29.2
Cl_1 (mL/hr/kg)				
$Cl_{1(F)}$ (mL/hr/kg)				164 ± 29
V_1 (mL/kg)				
V_2 (mL/kg)				
$V_{1(F)}$ (mL/kg)				326 ± 113
$V_{2(F)}$ (mL/kg)				1.04 ± 36.4
MRT (hour)				
AUC_{0-t} (ng/mL*hr)				152000
AUC_{inf} (ng/mL*hr)				244000 ± 43000
F (percent)				200

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Female

	Treatment Groups (mg/kg)		
	80 [b]	**160 [b]**	**40 IV [c]**
	Plasma		
$C_{max(pred)}$ (ng/mL)	115000 ± 15000	236000 ± 30000	245000 ± 34000
$T_{max(pred)}$ (hour)	0.478 ± 0.119	0.695 ± 0.140	
$C_{max(obs)}$ (ng/g)			
$T_{max(obs)}$ (hour)			
$t_{1/2}$ (hour)			
$t_{1/2(Alpha)}$ (hour)	1.12 ± 0.13	1.10 ± 0.12	0.340 ± 0.020
$t_{1/2(Beta)}$ (hour)	5.46 ± 2.64	12.2 ± 23.6	7.28 ± 1.98
k_{01} (hour^-1)	5.00 ± 2.04	2.75 ± 1.03	
$t_{1/2(k01)}$ (hour)	0.139 ± 0.057	0.252 ± 0.094	
k_{10} (hour^-1)	0.607 ± 0.064	0.627 ± 0.069	2.00 ± 0.12
$t_{1/2(k10)}$ (hour)	1.14 ± 0.12	1.11 ± 0.12	0.346 ± 0.020
k_{12} (hour^-1)	0.0106 ± 0.0086	0.00472 ± 0.00203	0.0354 ± 0.0069
k_{21} (hour^-1)	0.130 ± 0.065	0.0573 ± 0.111	0.0969 ± 0.0264
Cl_1 (mL/hr/kg)			327 ± 33
$Cl_{1(F)}$ (mL/hr/kg)	314 ± 39	274 ± 37	
V_1 (mL/kg)			163 ± 22
V_2 (mL/kg)			59.6 ± 22.8
$V_{1(F)}$ (mL/kg)	518 ± 96	437 ± 94	
$V_{2(F)}$ (mL/kg)	42.4 ± 17.0	36.0 ± 64.2	
MRT (hour)			0.682 ± 0.075
AUC_{0-t} (ng/mL*hr)	249000	554000	120000
AUC_{inf} (ng/mL*hr)	255000 ± 32000	584000 ± 79000	122000 ± 12000
F (percent)	105	120	

LEGEND

Data are displayed as mean ± SEM

ND = not detected

MODELING METHOD & BEST FIT MODEL

[a] WinNonlin, Pharsight Corporation, Mountain View, CA; Non-compartment model with first order input, first order output, and uniform weighting.

[b] WinNonlin, Pharsight Corporation, Mountain View, CA; Two-compartment model with first order input, first order output, and 1/Yhat2 weighting.

[c] WinNonlin, Pharsight Corporation, Mountain View, CA; Two-compartment model with bolus input, first order output, and 1/Yhat2 weighting.

ANALYTE

Perfluorohexanoic acid

TK PARAMETERS

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

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

$t_{½}$ = Lambda$_z$ half-life, $t_{1/2}$, the terminal elimination half-life based on non-compartmental analysis

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

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

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

Cl_1 = Clearance of central compartment, Cl_{app} or apparent clearance for intravenous groups

$Cl_{1(F)}$ = 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_2 = Volume of distribution for the peripheral compartment

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

$V_{2(F)}$ = Apparent volume of distribution for the peripheral compartment

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 **