Experiment Number: C20617
Route: Gavage, IV
Species/Strain: Rat/Harlan Sprague-Dawley

Toxicokinetics Data Summary
Test Compound: Perfluorooctanoic Acid
CAS Number: 335-67-1

Date Report Requested: 12/29/2016
Time Report Requested: 14:35:55
Lab: Battelle Columbus

Male

	Treatment Groups (mg/kg)			
	12 [a]	12 [a]	12 [a]	6 [b]
	Brain	Kidney	Liver	Plasma
$C_{max(pred)}$ (ng/mL)				37200 ± 2800
$T_{max(pred)}$ (hour)				4.86 ± 0.81
$C_{max(obs)}$ (ng/g)	1290	35400	62700	
$T_{max(obs)}$ (hour)	12.0	6.00	24.0	
$t_{1/2}$ (hour)	153	224	313	
$t_{1/2(Alpha)}$ (hour)				
$t_{1/2(Beta)}$ (hour)				
k_{01} (hour^-1)				1.31 ± 0.26
$t_{1/2(k01)}$ (hour)				0.531 ± 0.107
k_{10} (hour^-1)				0.00231 ± 1.4E-4
$t_{1/2(k10)}$ (hour)				300 ± 17
k_{12} (hour^-1)				
k_{21} (hour^-1)				
Cl_1 (mL/hr/kg)				
$Cl_{1(F)}$ (mL/hr/kg)				0.369 ± 0.022
V_1 (mL/kg)				
V_2 (mL/kg)				
$V_{1(F)}$ (mL/kg)				159 ± 12
MRT (hour)				
AUC_{0-t} (ng/mL*hr)				13600000
AUC_{inf} (ng/mL*hr)				16300000 ± 1000000

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	Treatment Groups (mg/kg)		
	12 [b]	**48** [b]	**6 IV** [c]
	Plasma		
$C_{max(pred)}$ (ng/mL)	76400 ± 5400	232000 ± 20000	52400 ± 2500
$T_{max(pred)}$ (hour)	6.37 ± 0.90	8.33 ± 1.28	
$C_{max(obs)}$ (ng/g)			
$T_{max(obs)}$ (hour)			
$t_{1/2}$ (hour)			
$t_{1/2(Alpha)}$ (hour)			67.3 ± 33.9
$t_{1/2(Beta)}$ (hour)			246 ± 28
k_{01} (hour^-1)	0.919 ± 0.160	0.639 ± 0.123	
$t_{1/2(k01)}$ (hour)	0.754 ± 0.131	1.09 ± 0.21	
k_{10} (hour^-1)	0.00269 ± 1.3E-4	0.00322 ± 1.5E-4	0.00453 ± 3.6E-4
$t_{1/2(k10)}$ (hour)	258 ± 12	215 ± 10	153 ± 12
k_{12} (hour^-1)			0.00219 ± 0.00179
k_{21} (hour^-1)			0.00639 ± 0.00356
Cl_1 (mL/hr/kg)			0.518 ± 0.033
$Cl_{1(F)}$ (mL/hr/kg)	0.415 ± 0.023	0.649 ± 0.044	
V_1 (mL/kg)			114 ± 5
V_2 (mL/kg)			39.2 ± 14.5
$V_{1(F)}$ (mL/kg)	154 ± 11	202 ± 18	
MRT (hour)			296 ± 12
AUC_{0-t} (ng/mL*hr)	27400000	62000000	12400000
AUC_{inf} (ng/mL*hr)	28900000 ± 1600000	73900000 ± 5000000	11600000 ± 700000

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Female

	Treatment Groups (mg/kg)			
	80 [d]	80 [a]	80 [a]	40 [e]
	Brain	Kidney	Liver	Plasma
$C_{max(pred)}$ (ng/mL)				240000 ± 25000
$T_{max(pred)}$ (hour)				3.22 ± 0.32
$C_{max(obs)}$ (ng/g)	3520	205000	162000	
$T_{max(obs)}$ (hour)	6.00	6.00	6.00	
$t_{1/2}$ (hour)		5.26	5.25	
$t_{1/2(Alpha)}$ (hour)				2.73 ± 0.62
$t_{1/2(Beta)}$ (hour)				29.4 ± 9.0
k_{01} (hour^-1)				0.375 ± 0.138
$t_{1/2(k01)}$ (hour)				1.85 ± 0.68
k_{10} (hour^-1)				0.252 ± 0.057
$t_{1/2(k10)}$ (hour)				2.75 ± 0.62
k_{12} (hour^-1)				0.00179 ± 6.7E-4
k_{21} (hour^-1)				0.0238 ± 0.0073
Cl_1 (mL/hr/kg)				
$Cl_{1(F)}$ (mL/hr/kg)				18.5 ± 1.8
V_1 (mL/kg)				
V_2 (mL/kg)				
$V_{1(F)}$ (mL/kg)				73.6 ± 20.6
$V_{2(F)}$ (mL/kg)				5.55 ± 1.62
MRT (hour)				
AUC_{0-t} (ng/mL*hr)				1750000
AUC_{inf} (ng/mL*hr)				2160000 ± 210000

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Female

	Treatment Groups (mg/kg)			
	80 [f]	80 [g]	320 [e]	40 IV [c]
	Plasma			
$C_{max(pred)}$ (ng/mL)	398000 ± 49000	426000 ± 69000	855000 ± 252000	370000 ± 81000
$T_{max(pred)}$ (hour)	2.33 ± 0.38	2.58 ± 0.50	3.01 ± 2.54	
$C_{max(obs)}$ (ng/g)				
$T_{max(obs)}$ (hour)				
$t_{1/2}$ (hour)				
$t_{1/2(Alpha)}$ (hour)	3.72 ± 0.41	3.38 ± 0.51	1.35 ± 26.17	0.683 ± 0.478
$t_{1/2(Beta)}$ (hour)	43.7 ± 27.2	1010 ± 5150	17.9 ± 2.7	5.17 ± 0.32
k_{01} (hour^-1)	0.826 ± 0.251	0.658 ± 0.258	0.838 ± 6.36	
$t_{1/2(k01)}$ (hour)	0.839 ± 0.255	1.05 ± 0.41	0.827 ± 6.272	
k_{10} (hour^-1)	0.184 ± 0.020	0.149 ± 0.198	0.0499 ± 0.3619	0.310 ± 0.075
$t_{1/2(k10)}$ (hour)	3.77 ± 0.41	4.65 ± 6.16	13.9 ± 100.9	2.23 ± 0.54
k_{12} (hour^-1)	0.00246 ± 7.1E-4	0.0556 ± 0.1911	0.103 ± 4.696	0.400 ± 0.420
k_{21} (hour^-1)	0.0161 ± 0.0100	9.45E-4 ± 0.003619	0.400 ± 4.980	0.438 ± 0.255
Cl_1 (mL/hr/kg)				33.6 ± 3.6
$Cl_{1(F)}$ (mL/hr/kg)	24.0 ± 2.6	16.5 ± 21.4	13.6 ± 1.9	
V_1 (mL/kg)				108 ± 24
V_2 (mL/kg)				98.7 ± 39.8
$V_{1(F)}$ (mL/kg)	130 ± 24	111 ± 28	272 ± 1990	
$V_{2(F)}$ (mL/kg)	19.9 ± 12.9	6520 ± 47500	69.9 ± 1849.1	
MRT (hour)				6.16 ± 0.51
AUC_{0-t} (ng/mL*hr)	2740000	2830000	20100000	1250000
AUC_{inf} (ng/mL*hr)	3340000 ± 360000	4840000 ± 6240000	23600000 ± 3300000	1190000 ± 130000

LEGEND

Data are displayed as mean ± SEM

MODELING METHOD & BEST FIT MODEL

[a] WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA; Non-compartmental model with first order input, first order output, and uniform weighting. Parameter estimates are reported to three significant figures. Non-compartmental analysis does not calculate a standard error.

[b] WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA; One-compartment model with first order input, first order output and 1/Yhat2 weighting. Yhat2 is a weighting scheme designation for Y predicted. Parameter estimates are reported to three significant figures.

[c] WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA; Two-compartment model with bolus input, first order output and 1/Yhat2 weighting. Yhat2 is a weighting scheme designation for Y predicted. Parameter estimates are reported to three significant figures.

[d] WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA; Non-compartmental model with first order input, first order output, and uniform weighting. Elimination half-life is ND because unable to determine lambda z. Parameter estimates are reported to three significant figures. Non-compartmental analysis does not calculate a standard error.

[e] WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA; Two-compartment model with first order input, first order output and 1/Yhat2 weighting. Yhat2 is a weighting scheme designation for Y predicted. Parameter estimates are reported to three significant figures.

[f] WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA; Two-compartment model with first order input, first order output and 1/Yhat2 weighting. Parameters estimated without 192 hour time point. Yhat2 is a weighting scheme designation for Y predicted. Parameter estimates are reported to three significant figures.

[g] WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA; Two-compartment model with first order input, first order output and 1/Yhat2 weighting. Parameters estimated using all time points. Yhat2 is a weighting scheme designation for Y predicted. Parameter estimates are reported to three significant figures.

ANALYTE

Perfluorooctanoic 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

LEGEND

TK PARAMETERS

$Cl_{1(F)}$ = 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

** END OF REPORT **