Experiment Number: C99037B
Route: Gavage, IV
Species/Strain: Mouse/B6C3F1

Toxicokinetics Data Summary
Test Compound: alpha-Thujone
CAS Number: 546-80-5

Date Report Requested: 01/09/2017
Time Report Requested: 11:25:15
Lab: Battelle Columbus

Male

	Treatment Groups (mg/kg)			
	40 [a]	**80 [a]**	**3.2 IV [a]**	**40 [c]**
	Brain			**Plasma**
$C_{0min(pred)}$ (ng/mL)				
$C_{max(pred)}$ (ng/mL)				228 ± 86
$T_{max(pred)}$ (minute)				5.26 ± 5.76
$C_{max(obs)}$ (ng/g) *	1580 ± 1500	5690 ± 865	1610 ± 2180	
$T_{max(obs)}$ (minute)	10.7	11.3	5.67	
$t_{1/2}$ (minute)	29.0	104	6.07	
k_{01} (minute^-1)				0.574 ± 0.923
$t_{1/2(k01)}$ (minute)				1.21 ± 1.94
k_{10} (minute^-1)				0.0334 ± 0.0112
$t_{1/2(k10)}$ (minute)				20.8 ± 7.0
Cl (mL/min/kg)				
$Cl_{1(F)}$ (mL/min/kg)				4920 ± 1650
V_1 (mL/kg)				
$V_{1(F)}$ (mL/kg)				147000 ± 71000
MRT (minute)				
AUC_{0-t} (ng/g*min)	15400	75500	34800	8760
AUC_{inf} (ng/g*min)	16700	77500	34900	8140 ± 2730

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	Treatment Groups (mg/kg)	
	80 [d]	**3.2 IV [b]**
	Plasma	
$C_{0min(pred)}$ (ng/mL)		676 ± 92
$C_{max(pred)}$ (ng/mL)	544 ± 197	
$T_{max(pred)}$ (minute)	6.59 ± 2.58	
$C_{max(obs)}$ (ng/g) *		
$T_{max(obs)}$ (minute)		
$t_{1/2}$ (minute)		
k_{01} (minute^-1)	0.167 ± 1.92	
$t_{1/2(k01)}$ (minute)	4.15 ± 47.6	
k_{10} (minute^-1)	0.0556 ± 0.677	0.113 ± 0.006
$t_{1/2(k10)}$ (minute)	12.5 ± 151	6.13 ± 0.35
Cl (mL/min/kg)		535 ± 53
$Cl_{1(F)}$ (mL/min/kg)	3290 ± 8300	
V_1 (mL/kg)		4730 ± 640
$V_{1(F)}$ (mL/kg)	59100 ± 650000	
MRT (minute)		8.85 ± 0.50
AUC_{0-t} (ng/g*min)	35300	
AUC_{inf} (ng/g*min)	24300 ± 61000	5990 ± 590

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	Treatment Groups (mg/kg)			
	40 [a]	**80 [a]**	**3.2 IV [a]**	**40 [c]**
	Brain			**Plasma**
$C_{0min(pred)}$ (ng/mL)				
$C_{max(pred)}$ (ng/mL)				356 ± 263
$T_{max(pred)}$ (minute)				7.44 ± 11.6
$C_{max(obs)}$ (ng/g) *	2280 ± 1250	5580 ± 4160	2070 ± 1720	
$T_{max(obs)}$ (minute)	9.33	10.0	6.00	
$t_{1/2}$ (minute)	50.4	37.0	4.19	
k_{01} (minute^-1)				0.499 ± 1.49
$t_{1/2(k01)}$ (minute)				1.39 ± 4.15
k_{10} (minute^-1)				0.0135 ± 0.132
$t_{1/2(k10)}$ (minute)				51.5 ± 506
Cl (mL/min/kg)				
$Cl_{1(F)}$ (mL/min/kg)				1370 ± 11700
V_1 (mL/kg)				
$V_{1(F)}$ (mL/kg)				102000 ± 155000
MRT (minute)				
AUC_{0-t} (ng/g*min)	12100	48500	43000	1460
AUC_{inf} (ng/g*min)	13300	48900	43100	29200 ± 248000

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	Treatment Groups (mg/kg)	
	80 [d]	**3.2 IV [b]**
	Plasma	
$C_{0min(pred)}$ (ng/mL)		498 ± 75
$C_{max(pred)}$ (ng/mL)	181 ± 221	
$T_{max(pred)}$ (minute)	4.44 ± 11.2	
$C_{max(obs)}$ (ng/g) *		
$T_{max(obs)}$ (minute)		
$t_{1/2}$ (minute)		
k_{01} (minute^-1)	0.257 ± 76.6	
$t_{1/2(k01)}$ (minute)	2.69 ± 802	
k_{10} (minute^-1)	0.041 ± 12.2	0.151 ± 0.012
$t_{1/2(k10)}$ (minute)	16.9 ± 4900	4.60 ± 0.36
Cl (mL/min/kg)		969 ± 95
$Cl_{1(F)}$ (mL/min/kg)	7380 ± 30400	
V_1 (mL/kg)		6430 ± 970
$V_{1(F)}$ (mL/kg)	180000 ± ND	
MRT (minute)		6.64 ± 0.52
AUC_{0-t} (ng/g*min)	21300	
AUC_{inf} (ng/g*min)	10800 ± 42400	3300 ± 320

LEGEND

Data are displayed as mean ± SEM

*Data are displayed as mean ± SD

MODELING METHOD & BEST FIT MODEL

[a] WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA; Noncompartmental Analysis (NCA).

[b] WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA; One compartment with bolus input and first order elimination with 1/Yhat2 weighting (Model No.1).

[c] WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA; One-compartment with first order absorption and elimination with 1/Yhat2 weighting (Model No. 3).

[d] WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA; Two compartment with first order absorption and elimination with 1/Y weighting (Model No. 13).

ANALYTE

alpha-Thujone

TK PARAMETERS

$C_{0min(pred)}$ = Fitted plasma concentration at time zero (IV only)

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

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

$Cl_{1(F)}$ = 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

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

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 **