Experiment Number: K10265
Route: Gavage, IV
Species/Strain: Mouse/B6C3F1

Toxicokinetics Data Summary
Test Compound: Methyleugenol
CAS Number: 93-15-2

Date Report Requested: 11/09/2016
Time Report Requested: 14:03:47
Lab: Battelle Northwest Laboratory

Male

	Treatment Groups (mg/kg)			
	37 [a]	**75 [a]**	**150 [a]**	**37 IV [b]**
	Plasma			
$C_{0min(pred)}$ (ug/mL)				10.9 ± 2.8
C_{max} (ug/mL) *	0.153 ± 0.075	0.505 ± 0.207	3.74 ± 1.34	
T_{max} (minute)	20	30	30	
Alpha (min^-1)				0.112 ± 0.018
$t_{1/2(Alpha)}$ (minute)				6.21 ± 0.98
Beta (min^-1)				0.00971 ± 0.00172
$t_{1/2(Beta)}$ (minute)				71.4 ± 12.7
Cl (mL/min/kg)				271 ± 20
$Cl_{1(F)}$ (mL/min/kg)	3050 ± 360	2160 ± 240	717 ± 93	
V_1 (L/kg)				28.0 ± 5.4
AUC_{0-t} (ug/mL*min)	10.2 ± 0.8	30.2 ± 2.5	205 ± 27	111 ± 8
AUC_{inf} (ug/mL*min)				113 ± 15
F (percent)	8.9			

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	Female			
	Treatment Groups (mg/kg)			
	37 [a]	75 [a]	150 [a]	37 IV [b]
	Plasma			
$C_{0min(pred)}$ (ug/mL)				13.6 ± 2.4
C_{max} (ug/mL) *	0.132 ± 0.015	0.520 ± 0.389	3.46 ± 0.42	
T_{max} (minute)	20	20	20	
Alpha (min^-1)				0.0923 ± 0.0142
$t_{1/2(Alpha)}$ (minute)				7.51 ± 1.16
Beta (min^-1)				0.0179 ± 0.0018
$t_{1/2(Beta)}$ (minute)				38.7 ± 3.8
Cl (mL/min/kg)				182 ± 16
$Cl_{1(F)}$ (mL/min/kg)	2550 ± 160	2940 ± 370	807 ± 110	
V_1 (L/kg)				10.2 ± 1.4
AUC_{0-t} (ug/mL*min)	12.9 ± 0.9	24.9 ± 3.2	185 ± 25	176 ± 18
AUC_{inf} (ug/mL*min)				181 ± 21
F (percent)	7.2			

LEGEND

Data are displayed as mean ± SEM

* Data are displayed as mean ± SD

MODELING METHOD & BEST FIT MODEL

[a] Manual; Plasma MEG concentration-versus-time profiles for both species were characterized by an early absorption phase followed by at least one secondary peak which prevented estimation of elimination rates. No modeling was done on the oral gavage data. Model-independent toxicokinetic parameters were calculated from the gavage data using observed values.

[b] Nonlinear least-squares fitting program SAS PROC NLIN, SAS Institute, Inc., Cary, NC; TK parameters of intravenously administered MEG were determined for both species by fitting data to the equation C(t) = Aoe^-alpha*t + Boe^-beta*t where C(t) is the plasma MEG concentration at any post-administration time (t), alpha and beta are the hybrid elimination rate constants (min^-1) obtained from the fit, Ao and Bo are the intercepts on the ordinate (concentration) axis of the extrapolated initial and terminal phases, respectively, using a weighting factor of [mean plasma MEG concentration]-1 for mice.

ANALYTE

Methyleugenol

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

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

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

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 **