Experiment Number: S0555
Route: Dermal, IV
Species/Strain: Rat/F344

Toxicokinetics Data Summary
Test Compound: DL-Camphor
CAS Number: 21368-68-3

Date Report Requested: 11/09/2016
Time Report Requested: 14:02:45
Lab: Research Triangle Institute

Male

	Treatment Groups (mg/kg)								
	50 [a, 2]	**200** [b, 3]	**200** [c, 4]	**200** [d, 2]	**200** [a, 4]	**200** [a, 2]	**200** [a, 3]	**400** [a, 2]	**6 IV** [a, 1]
	Plasma								
Beta (min^-1)	0.0041				0.0030	0.0043	0.0030	0.0023	0.0038
$t_{1/2(Beta)}$ (minute)	168				230	161	230	303	185
k_{01} (min^-1)		0.102 ± 0.12	0.0950 ± 0.11	0.100 ± 0.13					
k_{10} (min^-1)		0.0108 ± 0.0036	0.0105 ± 0.0033	0.0110 ± 0.0035					
Cl (L/min/kg)									0.0430
$Cl_{1(F)}$ (L/min/kg)	1.93				1.83	2.60	2.61	2.01	
V_1 (L/kg)	470	2.74 ± 0.68	2.53 ± 0.60	2.90 ± 0.68	607	602	867	880	11.5
MRT (minute)	209				236	237	244	542	165
AUC_{inf} (ug*min/L)	20789				92827	63848	76657	172514	156914
F (fraction)	0.0222				0.0235	0.0165	0.0165	0.0214	

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Female

	Treatment Groups (mg/kg)								
	50 [a, 2]	**200** [e, 3]	**200** [f, 4]	**200** [g, 2]	**200** [a, 4]	**200** [a, 2]	**200** [a, 3]	**400** [a, 2]	**6 IV** [a, 1]
	Plasma								
Beta (min^-1)	0.0028				0.0042	0.0061	0.0051	0.0073	0.0059
$t_{1/2(Beta)}$ (minute)	246				164	113	136	94.4	118
k_{01} (min^-1)		0.119 ± 0.14	0.107 ± 0.11	0.0957 ± 0.16					
k_{10} (min^-1)		0.0103 ± 0.0030	0.0107 ± 0.0030	0.0110 ± 0.0033					
Cl (L/min/kg)									0.0544
$Cl_{1(F)}$ (L/min/kg)	4.81				2.30	7.96	2.44	6.48	
V_1 (L/kg)	1710	4.24 ± 0.90	3.84 ± 0.79	3.76 ± 0.82	543	1295	479	883	9.25
MRT (minute)	327				182	178	176	120	128
AUC_{inf} (ug*min/L)	8480				72767	21100	82045	53694	123068
F (fraction)	0.0113				0.0237	0.00683	0.0223	0.00839	

LEGEND

Data are displayed as mean ± SEM

MODELING METHOD & BEST FIT MODEL

[a] WinNonlin, Version 1 .0 (Scientific Consulting Inc ., 1995); non-compartmental analysis (WinNonlin Models 200 or 201).

[b] WinNonlin, Version 1 .0 (Scientific Consulting Inc ., 1995); Compartmental models were written to simultaneously solve iv and dermal data sets (WinNonlin) with 1/YHAT weighting, where YHAT is the predicted plasma d,l-camphor concentration at a given time. O and AD simultaneously solved iv and single administration mid dose dermal unprotected, male rats.

[c] WinNonlin, Version 1 .0 (Scientific Consulting Inc ., 1995); Compartmental models were written to simultaneously solve iv and dermal data sets (WinNonlin) with 1/YHAT weighting, where YHAT is the predicted plasma d,l-camphor concentration at a given time. O and AG simultaneously solved iv and repeated administraiton mid dose dermal unprotected, male rats.

[d] WinNonlin, Version 1 .0 (Scientific Consulting Inc ., 1995); Compartmental models were written to simultaneously solve iv and dermal data sets (WinNonlin) with 1/YHAT weighting, where YHAT is the predicted plasma d,l-camphor concentration at a given time. O and Y simultaneously solved iv and single administration mid dose dermal protected, male rats.

[e] WinNonlin, Version 1 .0 (Scientific Consulting Inc ., 1995); Compartmental models were written to simultaneously solve iv and dermal data sets (WinNonlin with 1/YHAT weighting, where YHAT is the predicted plasma d,l-camphor concentration at a given time). P and AE simultaneously solved iv and single administration mid dose dermal unprotected, female rats.

[f] WinNonlin, Version 1 .0 (Scientific Consulting Inc ., 1995); Compartmental models were written to simultaneously solve iv and dermal data sets (WinNonlin) with 1/YHAT weighting, where YHAT is the predicted plasma d,l-camphor concentration at a given time. P and AH simultaneously solved iv and repeated administration mid dose dermal unprotected, female rats.

[g] WinNonlin, Version 1 .0 (Scientific Consulting Inc ., 1995); Compartmental models were written to simultaneously solve iv and dermal data sets (WinNonlin) with 1/YHAT weighting, where YHAT is the predicted plasma d,l-camphor concentration at a given time. P and Z simultaneously solved iv and single administration mid dose dermal protected, female rats.

ANALYTE

DL-Camphor

ROUTE & DOSE FREQUENCY

[1] Intravenous, 1 per study

[2] Dermal Protected, 1 per study

[3] Dermal Unprotected, 1 per study

[4] Dermal Unprotected, Repeated dose, 7 per study

TK PARAMETERS

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}

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

LEGEND

TK PARAMETERS

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 **