Experiment Number: S0593
Route: Gavage, IV
Species/Strain: Rat/F344

Toxicokinetics Data Summary
Test Compound: 2-Hydroxy-4-methoxybenzophenone
CAS Number: 131-57-7

Date Report Requested: 11/09/2016
Time Report Requested: 14:00:07
Lab: Research Triangle Institute

Male

	Treatment Groups (mg/kg)					
	100 [a, #]	**100 [c, #]**	**100 [b, *]**	**250 [a, #]**	**250 [b, *]**	**500 [a, #]**
	Plasma					
C_{max} (mg/L)	0.220		0.149	0.367	0.454	2.43
T_{max} (minute)	30		60	90	30	60
Alpha (min^-1)		0.166 ± 0.019				
Beta (min^-1)	0.0067	0.0055 ± 0.0017		0.0034		0.0037
$t_{1/2(Beta)}$ (minute)	103			206		186
k_{01} (min^-1)		0.0152 ± 0.0048				
k_{10} (min^-1)		0.106 ± 0.015				
k_{12} (min^-1)		0.0569 ± 0.012				
k_{21} (min^-1)		0.008603 ± 0.0025				
Cl (L/min/kg)						
$Cl_{1(F)}$ (L/min/kg)	4.56			3.63		1.22
V_1 (L/kg)		0.429 ± 0.062				
$V_{1(F)}$ (L/kg)	680			1077		327
MRT (minute)	150			223		303
AUC_{0-t} (mg*min/L)			29.4		73.9	
AUC_{inf} (mg*min/L)	23.6			60.8		374
F (fraction)	0.00835			0.0105		0.0313

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	Treatment Groups (mg/kg)		
	500 [b, *]	**8 IV [a, #]**	**8 IV [b, *]**
	Plasma		
C_{max} (mg/L)	1.41	8.57	0.0840
T_{max} (minute)	60	5	5
Alpha (min^-1)			
Beta (min^-1)		0.0022	
$t_{1/2(Beta)}$ (minute)		313	
k_{01} (min^-1)			
k_{10} (min^-1)			
k_{12} (min^-1)			
k_{21} (min^-1)			
Cl (L/min/kg)		0.0381	
$Cl_{1(F)}$ (L/min/kg)			
V_1 (L/kg)		17.2	
$V_{1(F)}$ (L/kg)			
MRT (minute)		77.1	
AUC_{0-t} (mg*min/L)	246		6.86
AUC_{inf} (mg*min/L)		202	
F (fraction)			

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Female

	Treatment Groups (mg/kg)					
	100 [a, #]	**100 [d, #]**	**100 [b, *]**	**250 [a, #]**	**250 [b, *]**	**500 [a, #]**
	Plasma					
C_{max} (mg/L)	0.209		0.203	0.391	0.570	2.69
T_{max} (minute)	60		60	90	30	60
Alpha (min^-1)		0.0887 ± 0.011				
Beta (min^-1)	0.0060	0.00464 ± 0.0015		0.0062		0.0050
$t_{1/2(Beta)}$ (minute)	116			112		139
k_{01} (min^-1)		0.0126 ± 0.0035				
k_{10} (min^-1)		0.0579 ± 0.0074				
k_{12} (min^-1)		0.0283 ± 0.0071				
k_{21} (min^-1)		0.00711 ± 0.0023				
Cl (L/min/kg)						
$Cl_{1(F)}$ (L/min/kg)	6.14			4.08		1.58
V_1 (L/kg)		1.39 ± 0.15				
$V_{1(F)}$ (L/kg)	1020			660		316
MRT (minute)	175			159		172
AUC_{0-t} (mg*min/L)			41.8		105	
AUC_{inf} (mg*min/L)	17.4			53.5		286
F (fraction)	0.0127			0.0190		0.0491

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Female

	Treatment Groups (mg/kg)		
	500 [b, *]	**8 IV [a, #]**	**8 IV [b, *]**
	Plasma		
C_{max} (mg/L)	1.08	3.70	0.121
T_{max} (minute)	60	5	10
Alpha (min^-1)			
Beta (min^-1)		0.0038	
$t_{1/2(Beta)}$ (minute)		180	
k_{01} (min^-1)			
k_{10} (min^-1)			
k_{12} (min^-1)			
k_{21} (min^-1)			
Cl (L/min/kg)		0.0776	
$Cl_{1(F)}$ (L/min/kg)			
V_1 (L/kg)		20.2	
$V_{1(F)}$ (L/kg)			
MRT (minute)		95.6	
AUC_{0-t} (mg*min/L)	278		12.4
AUC_{inf} (mg*min/L)		100	
F (fraction)			

LEGEND

Data are displayed as mean ± SEM

MODELING METHOD & BEST FIT MODEL

[a] WinNonlin (Models 200 and 201), Version 1.0 (Scientific Consulting Inc., 1995); Noncompartmental modeling

[b] WinNonlin Version 1.0 (Scientific Consulting Inc., 1995); Noncompartmental modeling

[c] WinNonlin Version 1.0 (Scientific Consulting Inc., 1995); Best fit is two compartmental which simultaneously solves iv and oral data sets. Analyzed using compartmental modeling techniques with established models or models written to simultaneously solve iv (Study U) and oral data sets (Study W) using 1/YHAT weighting where YHAT is the predicted plasma HMBP concentration at a given time.

[d] WinNonlin Version 1.0 (Scientific Consulting Inc., 1995); Best fit is two compartmental which simultaneously solves iv and oral data sets. Analyzed using compartmental modeling techniques with established models or models written to simultaneously solve iv (Study V) and oral data sets (Study X) using 1/YHAT weighting where YHAT is the predicted plasma HMBP concentration at a given time.

ANALYTE

[#] 2-Hydroxy-4-methoxybenzophenone

* 2,4-Dihydroxybenzophenone

TK PARAMETERS

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

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}

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

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

Cl = Clearance, includes total clearance

$Cl_{1(F)}$ = Apparent clearance of the central compartment, also $C_{l(F)}$ 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

F = Bioavailability, absolute bioavailability

** END OF REPORT **