Experiment Number: C96018
Route: Gavage, IV
Species/Strain: Rat/Fischer F344

Toxicokinetics Data Summary
Test Compound: Bromodichloromethane
CAS Number: 75-27-4

Date Report Requested: 12/02/2016
Time Report Requested: 10:41:18
Lab: Battelle Columbus

Male

	Treatment Groups (mg/kg)			
	25 [a, #]	**25 [a, *]**	**50 [a, #]**	**50 [a, *]**
	Plasma			
$C_{0min(pred)}$ (ng/mL)				
C_{max} (ng/mL)	749.2	913.2	1355	2148
T_{max} (minute)	7.0	10	7.0	7
$Lambda_z$ (min^-1)	0.00478 ± 0.0015	0.00506 ± 0.00153	0.00371 ± 0.00081	0.00498 ± 0.00036
$t_{1/2}$ (minute)	145 ± 46	137 ± 42	187 ± 41	139 ± 10
Alpha (min^-1)				
$t_{1/2(Alpha)}$ (minute)				
Beta (min^-1)				
$t_{1/2(Beta)}$ (minute)				
k_{10} (min^-1)				
$t_{1/2(k10)}$ (minute)				
k_{12} (min^-1)				
k_{21} (min^-1)				
Cl (L/min/kg)	1.42 ± 0.13	0.870 ± 0.058	0.885 ± 0.072	0.501 ± 0.031
V_{ss} (L/kg)	142 ± 26	85.8 ± 11.5	136 ± 20	57.1 ± 5.7
MRT (minute)	99.8 ± 15.9	98.6 ± 11.5	154 ± 19	114 ± 9
AUC_{inf} (ng*min/mL)	17600.0 ± 1600	28700 ± 1900	56500.0 ± 4600	99700 ± 6200

Experiment Number: C96018
Route: Gavage, IV
Species/Strain: Rat/Fischer F344

Toxicokinetics Data Summary
Test Compound: Bromodichloromethane
CAS Number: 75-27-4

Date Report Requested: 12/02/2016
Time Report Requested: 10:41:18
Lab: Battelle Columbus

Male

	Treatment Groups (mg/kg)			
	100 [a, #]	**100 [a, *]**	**10 IV [a, *]**	**10 IV [b, *]**
	Plasma			
$C_{0min(pred)}$ (ng/mL)				2890.0 ± 500
C_{max} (ng/mL)	2611.0	4370	3004.0	
T_{max} (minute)	7.0	15	2	
$Lambda_z$ (min^-1)	0.00256 ± 0.0012	0.00278 ± 0.00054	0.00622 ± 0.0013	
$t_{1/2}$ (minute)	271 ± 124	250 ± 49	111 ± 24	
Alpha (min^-1)				0.0754 ± 0.0120
$t_{1/2(Alpha)}$ (minute)				9.20 ± 1.47
Beta (min^-1)				0.00624 ± 0.00088
$t_{1/2(Beta)}$ (minute)				111 ± 16
k_{10} (min^-1)				0.0547 ± 0.0079
$t_{1/2(k10)}$ (minute)				12.7 ± 1.8
k_{12} (min^-1)				0.0183 ± 0.0049
k_{21} (min^-1)				0.00860 ± 0.00155
Cl (L/min/kg)	0.330 ± 0.038	0.281 ± 0.016	0.168 ± 0.011	0.19 ± 0.02
V_{ss} (L/kg)	53.7 ± 11.4	37.6 ± 4.0	10.3 ± 1.2	10.8 ± 1.7
MRT (minute)	163 ± 29	134 ± 12	61.3 ± 6.0	
AUC_{inf} (ng*min/mL)	303000.0 ± 35000	356000 ± 20000	59400 ± 4000	59100.0 ± 3030.0

Experiment Number: C96018
Route: Gavage, IV
Species/Strain: Rat/Fischer F344

Toxicokinetics Data Summary
Test Compound: Bromodichloromethane
CAS Number: 75-27-4

Date Report Requested: 12/02/2016
Time Report Requested: 10:41:18
Lab: Battelle Columbus

	Female			
	Treatment Groups (mg/kg)			
	25 [a, *]	**25** [a, #]	**50** [a, #]	**50** [a, *]
	Plasma			
$C_{0min(pred)}$ (ng/mL)				
C_{max} (ng/mL)	880.7	658.0	1816.0	919.3
T_{max} (minute)	10	7.0	5.0	7
$Lambda_z$ (min^-1)	0.00493 ± 0.00361	0.00163 ± 0.00084	0.00689 ± 0.00151	0.00509 ± 0.00035
$t_{1/2}$ (minute)	141 ± 100	425 ± 220	101 ± 22	136 ± 10
Alpha (min^-1)				
$t_{1/2(Alpha)}$ (minute)				
Beta (min^-1)				
$t_{1/2(Beta)}$ (minute)				
k_{10} (min^-1)				
$t_{1/2(k10)}$ (minute)				
k_{12} (min^-1)				
k_{21} (min^-1)				
Cl (L/min/kg)	1.07 ± 0.12	1.59 ± 0.13	0.646 ± 0.079	0.807 ± 0.073
V_{ss} (L/kg)	102 ± 40	304 ± 109	51.6 ± 11.1	105 ± 15
MRT (minute)	95.3 ± 35.8	192 ± 67	79.9 ± 14.2	129 ± 14
AUC_{inf} (ng*min/mL)	23400 ± 2500	15800.0 ± 1300	77400.0 ± 9500	61900 ± 5600

Experiment Number: C96018
Route: Gavage, IV
Species/Strain: Rat/Fischer F344

Toxicokinetics Data Summary
Test Compound: Bromodichloromethane
CAS Number: 75-27-4

Date Report Requested: 12/02/2016
Time Report Requested: 10:41:18
Lab: Battelle Columbus

Female

	Treatment Groups (mg/kg)			
	100 [a, *]	**100 [a, #]**	**10 IV [a, *]**	**10 IV [c, *]**
	Plasma			
$C_{0min(pred)}$ (ng/mL)				3160.0 ± 1120.0
C_{max} (ng/mL)	1783.0	3791.0	2186.0	
T_{max} (minute)	7.0	15.0	2.0	
$Lambda_z$ (min^-1)	0.00306 ± 0.00127	0.00203 ± 0.00102	0.00835 ± 0.00162	
$t_{1/2}$ (minute)	227 ± 94	341 ± 171	83.0 ± 16.1	
Alpha (min^-1)				0.170 ± 0.037
$t_{1/2(Alpha)}$ (minute)				4.08 ± 0.88
Beta (min^-1)				0.00685 ± 0.00139
$t_{1/2(Beta)}$ (minute)				101 ± 21
k_{10} (min^-1)				0.101 ± 0.026
$t_{1/2(k10)}$ (minute)				6.85 ± 1.74
k_{12} (min^-1)				0.0640 ± 0.0172
k_{21} (min^-1)				0.0115 ± 0.0032
Cl (L/min/kg)	0.545 ± 0.058	0.359 ± 0.037	0.256 ± 0.022	0.32 ± 0.05
V_{ss} (L/kg)	79.3 ± 15.0	47.4 ± 9.0	16.1 ± 2.4	20.8 ± 6.1
MRT (minute)	146 ± 23	132 ± 21	62.7 ± 7.6	
AUC_{inf} (ng*min/mL)	183000 ± 20000	278000.0 ± 29000	39000.0 ± 3400	39000.0 ± 2700.0

LEGEND

Data are displayed as mean ± SEM

MODELING METHOD & BEST FIT MODEL

[a] PROC NLIN in SAS 8.2 (SAS Intstitute Inc., Cary, NC); Non-compartmental analysis

[b] PROC NLIN in SAS 8.2 (SAS Intstitute Inc., Cary, NC); Two-compartment model with bolus input, first-order elimination. Plasma BDCM concentrations declined in a biexponential fashion with rapid early alpha phase and a terminal beta phase that was approximately 12-fold lower.

[c] PROC NLIN in SAS 8.2 (SAS Intstitute Inc., Cary, NC); Two-compartment model with bolus input, first-order elimination. Plasma BDCM concentrations declined in a biexponential fashion with rapid early alpha phase and a terminal beta phase that was approximately 25-fold lower.

ANALYTE

Bromodichloromethane

VEHICLE

[#] Corn Oil

* Deionized water-Cremophor 9 to 1

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

$Lambda_z$ = Non-compartmental analysis (NCA) terminal elimination rate constant, NCA k_e or k_{elim}

$t_{½}$ = $Lambda_z$ half-life, $t_{1/2}$, the terminal elimination half-life based on non-compartmental analysis

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

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 = Clearance, includes total clearance

V_{ss} = Volume of distribution at steady state

MRT = Mean residence time

AUC_{inf} = Area under the plasma concentration versus time curve, AUC, extrapolated to time equals infinity

** END OF REPORT **