

Experiment Number: C99028

Route: Dermal, IV

Species/Strain: Rat/F344

Toxicokinetics Data Summary

Test Compound: Bis 2-Chloroethoxy Methane

CAS Number: 111-91-1

Date Report Requested: 02/07/2017

Time Report Requested: 14:10:39

Lab: Battelle Columbus

Male

Treatment Groups (mg/kg)

100^{a, #}

400^{b, *}

400^{a, #}

20 IV^{c, #}

Heart

$C_{\max(\text{obs})}$	2.95 ug/g	3.35 ug/g	18.2 ug/g	12.6 ug/g
$T_{\max(\text{obs})}$ (minute)	34.0	360	34.7	14.9
$t_{1/2}$ (minute)	71.5	422	91.0	69.9

Experiment Number: C99028

Route: Dermal, IV

Species/Strain: Rat/F344

Toxicokinetics Data Summary

Test Compound: Bis 2-Chloroethoxy Methane

CAS Number: 111-91-1

Date Report Requested: 02/07/2017

Time Report Requested: 14:10:39

Lab: Battelle Columbus

Male

Treatment Groups (mg/kg)

100^{b, #}

400^{b, *}

400^{a, #}

20 IV^{c, #}

Liver

$C_{\max(\text{obs})}$	1.66 ug/g	84.4 ug/g	11.1 ug/g	3.89 ug/g
$T_{\max(\text{obs})}$ (minute)	34.0	360	64.3	43.7
$t_{1/2}$ (minute)	58.4	296	86.1	39.1

Experiment Number: C99028

Route: Dermal, IV

Species/Strain: Rat/F344

Toxicokinetics Data Summary
Test Compound: Bis 2-Chloroethoxy Methane
CAS Number: 111-91-1

Date Report Requested: 02/07/2017

Time Report Requested: 14:10:39

Lab: Battelle Columbus

Male

Treatment Groups (mg/kg)

	100 d, #			200 d, #			400 b, *			400 d, #		
--	----------	--	--	----------	--	--	----------	--	--	----------	--	--

Plasma

C _{max(pred)} (ug/mL)	5.26	±	0.68	7.92	±	0.87			12.2	±	1.7
T _{max(pred)} (minute)	14.1	±	3.8	15.0	±	3.2			31.7	±	6.9
C _{max(obs)}									5.51 ug/mL		
T _{max(obs)} (minute)									180		
t _{1/2} (minute)									322		
Alpha (minute ⁻¹)	0.0278	±	0.0062	0.0265	±	0.0027			0.0111	±	0.0012
t _{1/2(Alpha)} (minute)	24.9	±	5.6	26.1	±	2.7			62.2	±	6.8
Beta (minute ⁻¹)	0.00513	±	0.00152	0.000925	±	0.000430			0.000712	±	0.000367
t _{1/2(Beta)} (minute)	135	±	40	749	±	348			973	±	501
k ₀₁ (minute ⁻¹)	0.148	±	0.075	0.136	±	0.050			0.0686	±	0.0260
t _{1/2(k01)} (minute)	4.67	±	2.37	5.10	±	1.89			10.1	±	3.8
k ₁₀ (minute ⁻¹)	0.0240	±	0.0047	0.0237	±	0.0026			0.0104	±	0.0012
t _{1/2(k10)} (minute)	28.9	±	5.6	29.2	±	3.2			66.8	±	7.7
k ₁₂ (minute ⁻¹)	0.00303	±	0.00149	0.00270	±	0.00073			0.000722	±	0.000161
k ₂₁ (minute ⁻¹)	0.00595	±	0.00203	0.00104	±	0.00046			0.000766	±	0.000391

Experiment Number: C99028

Route: Dermal, IV

Species/Strain: Rat/F344

Toxicokinetics Data Summary

Test Compound: Bis 2-Chloroethoxy Methane

CAS Number: 111-91-1

Date Report Requested: 02/07/2017

Time Report Requested: 14:10:39

Lab: Battelle Columbus

Male

Treatment Groups (mg/kg)

100 d, #

200 d, #

400 b, *

400 d, #

Plasma

Cl _{1(F)} (mL/min/kg)	312 ± 34	403 ± 42		239 ± 33
Cl _{2(F)} (mL/min/kg)	39.5 ± 15.9	45.9 ± 14.8		16.6 ± 5.5
V _{1(F)} (mL/kg)	13000 ± 3100	17000 ± 2900		23100 ± 5000
V _{2(F)} (mL/kg)	6630 ± 1930	44300 ± 30100		21700 ± 14900
AUC _{int} (ug/mL*min)	320 ± 35	496 ± 52		1670 ± 230

Experiment Number: C99028

Route: Dermal, IV

Species/Strain: Rat/F344

Toxicokinetics Data Summary

Test Compound: Bis 2-Chloroethoxy Methane

CAS Number: 111-91-1

Date Report Requested: 02/07/2017

Time Report Requested: 14:10:39

Lab: Battelle Columbus

Male

Treatment Groups (mg/kg)

	20 IV ^e , #	100 ^a , #	400 ^b , *	400 ^a , #
	Plasma	Thymus		
C _{max} (pred) (ug/mL)	12.4 ± 2.2			
T _{max} (pred) (minute)				
C _{max} (obs)		6.07 ug/g	5.47 ug/g	28.7 ug/g
T _{max} (obs) (minute)		34.0	480	34.7
t _{1/2} (minute)		65.5	853	175
t _{1/2} (Alpha) (minute)	17.0 ± 2.3			
t _{1/2} (Beta) (minute)	83.4 ± 10.3			
k ₁₀ (minute ⁻¹)	0.0346 ± 0.0041			
t _{1/2} (k ₁₀) (minute)	20.0 ± 2.4			
k ₁₂ (minute ⁻¹)	0.00460 ± 0.00137			
k ₂₁ (minute ⁻¹)	0.00976 ± 0.00149			
Cl (mL/min/kg)	55.9 ± 5.1			
Cl ₂ (mL/min/kg)	7.44 ± 1.93			

Experiment Number: C99028

Route: Dermal, IV

Species/Strain: Rat/F344

Toxicokinetics Data Summary

Test Compound: Bis 2-Chloroethoxy Methane

CAS Number: 111-91-1

Date Report Requested: 02/07/2017

Time Report Requested: 14:10:39

Lab: Battelle Columbus

Male

Treatment Groups (mg/kg)

20 IV^e, #

Plasma

V ₁ (mL/kg)	1620 ± 290
V ₂ (mL/kg)	762 ± 143
MRT (minute)	42.5 ± 3.3
AUC _{inf} (ug/mL*min)	357 ± 32

Experiment Number: C99028

Route: Dermal, IV

Species/Strain: Rat/F344

Toxicokinetics Data Summary

Test Compound: Bis 2-Chloroethoxy Methane

CAS Number: 111-91-1

Date Report Requested: 02/07/2017

Time Report Requested: 14:10:39

Lab: Battelle Columbus

Male

Treatment Groups (mg/kg)

20 IV c. #

Thymus

C_{max}(obs) 48.7 ug/g

T_{max}(obs) (minute) 14.8

t_{1/2} (minute) 80.5

Experiment Number: C99028

Route: Dermal, IV

Species/Strain: Rat/F344

Toxicokinetics Data Summary

Test Compound: Bis 2-Chloroethoxy Methane

CAS Number: 111-91-1

Date Report Requested: 02/07/2017

Time Report Requested: 14:10:39

Lab: Battelle Columbus

Female

Treatment Groups (mg/kg)

100^{a, #}

400^{b, *}

400^{a, #}

20 IV^{f, #}

Heart

C _{max} (obs)	8.87 ug/g	6.80 ug/g	20.4 ug/g	11.6 ug/g
T _{max} (obs) (minute)	15.5	360	34.7	15.0
t _{1/2} (minute)	63.0	548	387	68.1

Experiment Number: C99028

Route: Dermal, IV

Species/Strain: Rat/F344

Toxicokinetics Data Summary

Test Compound: Bis 2-Chloroethoxy Methane

CAS Number: 111-91-1

Date Report Requested: 02/07/2017

Time Report Requested: 14:10:39

Lab: Battelle Columbus

Female

Treatment Groups (mg/kg)

100^{b, #}

400^{b, *}

400^{a, #}

20 IV^{c, #}

Liver

$C_{\max(\text{obs})}$	2.26 ug/g	123 ug/g	14.5 ug/g	1.70 ug/g
$T_{\max(\text{obs})}$ (minute)	34.3	480	64.0	14.8
$t_{1/2}$ (minute)	46.7	373	199	25.7

Experiment Number: C99028

Route: Dermal, IV

Species/Strain: Rat/F344

Toxicokinetics Data Summary

Test Compound: Bis 2-Chloroethoxy Methane

CAS Number: 111-91-1

Date Report Requested: 02/07/2017

Time Report Requested: 14:10:39

Lab: Battelle Columbus

Female

Treatment Groups (mg/kg)

100 d, #

200 d, #

400 b, *

400 d, #

Plasma

	100 d, #	200 d, #	400 b, *	400 d, #
$C_{\max(\text{pred})}$ (ug/mL)	9.41 ± 1.48	9.97 ± 1.24		15.0 ± 2.2
$T_{\max(\text{pred})}$ (minute)	15.2 ± 3.4	20.9 ± 3.4		27.2 ± 6.9
$C_{\max(\text{obs})}$			10.8 ug/mL	
$T_{\max(\text{obs})}$ (minute)			360	
$t_{1/2}$ (minute)			386	
Alpha (minute ⁻¹)	0.0513 ± 0.0410	0.0395 ± 0.0293		0.00985 ± 0.00119
$t_{1/2(\text{Alpha})}$ (minute)	13.5 ± 10.8	17.6 ± 13.0		70.4 ± 8.5
Beta (minute ⁻¹)	0.00916 ± 0.00355	0.00608 ± 0.00215		0.00122 ± 4.4E-4
$t_{1/2(\text{Beta})}$ (minute)	75.7 ± 29.3	114 ± 40		570 ± 205
k_{01} (minute ⁻¹)	0.0860 ± 0.0852	0.0586 ± 0.0496		0.0924 ± 0.0380
$t_{1/2(k01)}$ (minute)	8.06 ± 7.98	11.8 ± 10.0		7.50 ± 3.08
k_{10} (minute ⁻¹)	0.0445 ± 0.0323	0.0358 ± 0.0250		0.00914 ± 0.00106
$t_{1/2(k10)}$ (minute)	15.6 ± 11.3	19.4 ± 13.5		75.8 ± 8.8
k_{12} (minute ⁻¹)	0.00544 ± 0.00789	0.00304 ± 0.00401		0.000608 ± 0.000179
k_{21} (minute ⁻¹)	0.0106 ± 0.0051	0.00670 ± 0.00272		0.00131 ± 0.00049

Experiment Number: C99028

Route: Dermal, IV

Species/Strain: Rat/F344

Toxicokinetics Data Summary

Test Compound: Bis 2-Chloroethoxy Methane

CAS Number: 111-91-1

Date Report Requested: 02/07/2017

Time Report Requested: 14:10:39

Lab: Battelle Columbus

Female

Treatment Groups (mg/kg)

100 d, # 200 d, # 400 b, * 400 d, #

Plasma

Cl _{1(F)} (mL/min/kg)	223 ± 31	321 ± 43	188 ± 25
Cl _{2(F)} (mL/min/kg)	27.3 ± 22.6	27.2 ± 20.2	12.5 ± 4.2
V _{1(F)} (mL/kg)	5020 ± 3900	8950 ± 6460	20500 ± 4300
V _{2(F)} (mL/kg)	2590 ± 1170	4070 ± 1840	9520 ± 3710
AUC _{int} (ug/mL*min)	448 ± 63	624 ± 84	2130 ± 280

Experiment Number: C99028

Route: Dermal, IV

Species/Strain: Rat/F344

Toxicokinetics Data Summary

Test Compound: Bis 2-Chloroethoxy Methane

CAS Number: 111-91-1

Date Report Requested: 02/07/2017

Time Report Requested: 14:10:39

Lab: Battelle Columbus

Female

Treatment Groups (mg/kg)

	20 IV ^{e, #}		40 IV ^{e, #}		100 ^{a, #}	400 ^{b, *}
	Plasma				Thymus	
C _{max(pred)} (ug/mL)	13.2	± 2.3	24.1	± 2.8		
T _{max(pred)} (minute)						
C _{max(obs)}					8.37 ug/g	11.0 ug/g
T _{max(obs)} (minute)					15.6	480
t _{1/2} (minute)					43.8	652
t _{1/2(Alpha)} (minute)	13.7	± 1.7	22.6	± 2.0		
t _{1/2(Beta)} (minute)	68.5	± 6.9	86.7	± 7.9		
k ₁₀ (minute ⁻¹)	0.0424	± 0.0046	0.0273	± 0.0020		
t _{1/2(k10)} (minute)	16.3	± 1.8	25.4	± 1.9		
k ₁₂ (minute ⁻¹)	0.00611	± 0.00156	0.00238	± 0.00063		
k ₂₁ (minute ⁻¹)	0.0120	± 0.0015	0.00898	± 0.00102		
Cl (mL/min/kg)	64.1	± 5.5	45.4	± 3.0		
Cl ₂ (mL/min/kg)	9.22	± 2.09	3.95	± 0.93		

Experiment Number: C99028

Route: Dermal, IV

Species/Strain: Rat/F344

Toxicokinetics Data Summary

Test Compound: Bis 2-Chloroethoxy Methane

CAS Number: 111-91-1

Date Report Requested: 02/07/2017

Time Report Requested: 14:10:39

Lab: Battelle Columbus

Female

Treatment Groups (mg/kg)

20 IV e.#

40 IV e.#

Plasma

V ₁ (mL/kg)	1510 ± 260	1660 ± 190
V ₂ (mL/kg)	767 ± 126	440 ± 71
MRT (minute)	35.5 ± 2.6	46.4 ± 2.3
AUC _{inf} (ug/mL*min)	312 ± 27	882 ± 58

Experiment Number: C99028

Route: Dermal, IV

Species/Strain: Rat/F344

Toxicokinetics Data Summary

Test Compound: Bis 2-Chloroethoxy Methane

CAS Number: 111-91-1

Date Report Requested: 02/07/2017

Time Report Requested: 14:10:39

Lab: Battelle Columbus

Female

Treatment Groups (mg/kg)

400 a, #

20 IV c, #

Thymus

C _{max} (obs)	27.6 ug/g	42.7 ug/g
T _{max} (obs) (minute)	34.3	14.9
t _{1/2} (minute)	187	164

Experiment Number: C99028

Route: Dermal, IV

Species/Strain: Rat/F344

Toxicokinetics Data Summary

Test Compound: Bis 2-Chloroethoxy Methane

CAS Number: 111-91-1

Date Report Requested: 02/07/2017

Time Report Requested: 14:10:39

Lab: Battelle Columbus

LEGEND

Data are displayed as mean \pm SEM

MODELING METHOD & BEST FIT MODEL

^a WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA; Non-compartment model with first order input, first order output, and uniform weighting. Non-compartmental analysis does not calculate a standard error.

^b WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA; Non-compartment model with first order input, first order output, and uniform weighting.

^c WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA; Non-compartment model with bolus input, first order output, and 1/Y² weighting. Non-compartmental analysis does not calculate a standard error for half life.

^d WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA; Two-compartment model with first order input, first order output, and 1/Y^{hat}2 weighting.

^e WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA; Two-compartment model with bolus input, first order output, and 1/Y^{hat}2 weighting.

^f WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA; Non-compartment model with bolus input, first order output, and 1/Y² weighting. Non-compartmental analysis does not calculate a standard error for half life. User defined value used for half-life shown here (68.1), NCA gave poor visual fit of terminal phase. NCA half life was 39.1.

ANALYTE

Bis 2-Chloroethoxy Methane

* Thiodiglycolic Acid

TK PARAMETERS

C_{max} = Observed or Predicted Maximum plasma (or tissue) concentration

T_{max} = Time at which C_{max} predicted or observed occurs

t_{1/2} = 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_{1/2(alpha)} = Half-life for the alpha phase

Beta = Hybrid rate constant of the beta phase

t_{1/2(beta)} = Half-life for the beta phase

k₀₁ = Absorption rate constant, k_a

t_{1/2(k01)} = Half-life of the absorption process to the central compartment

k₁₀ = 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

k₁₂ = Distribution rate constant from first to second compartment etc.

k₂₁ = Distribution rate constant from second to first compartment etc.

Cl = Clearance, includes total clearance

Cl₂ = Clearance of the secondary compartment

Experiment Number: C99028

Route: Dermal, IV

Species/Strain: Rat/F344

Toxicokinetics Data Summary

Test Compound: Bis 2-Chloroethoxy Methane

CAS Number: 111-91-1

Date Report Requested: 02/07/2017

Time Report Requested: 14:10:39

Lab: Battelle Columbus

LEGEND

TK PARAMETERS

$Cl_{1(F)}$ = Apparent clearance of the central compartment, also $Cl_{(F)}$ for gavage groups in non-compartmental model

$Cl_{2(F)}$ = Apparent clearance of the secondary compartment

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_2 = Volume of distribution for the peripheral compartment

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

$V_{2(F)}$ = Apparent volume of distribution for the peripheral compartment

MRT = Mean residence time

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

**** END OF REPORT ****