Experiment Number: K08624 | **Toxicokinetics Data Summary** | **Request Date:** 7/11/2023

Route: Dermal, IV | **Compound:** Bis 2-Chloroethoxy Methane/ **Analyte:** Bis 2-Chloroethoxy Methane | **Request Time:** 10:03:16

Species/Strain: Mice/B6C3F1 | **CAS Number:** 111-91-1 | **Lab:** Battelle Columbus

Male

	Treatment Group (mg/kg)		
	50 IV Plasma[a]	**100 IV Plasma[a]**	**300 Dermal Plasma[b]**
Cmax_pred (ug/mL)	38.2 ± 4.7	63.1 ± 10.5	2.42 ± 0.50
Tmax_pred (minute)			11.9 ± 3.7
Cmax_obs (ug/mL)			3.17 ± 0.43
Tmax_obs (minute)			15
Alpha ($minute^{-1}$)			0.0607 ± 0.0373
Alpha Half-life (minute)	4.94 ± 0.34	6.85 ± 0.58	11.4 ± 7.0
Beta ($minute^{-1}$)			0.00309 ± 0.00889
Beta Half-life (minute)	17.8 ± 5.0	28.0 ± 13.2	224 ± 645
k01 ($minute^{-1}$)			0.114 ± 0.114
k01 Half-life (minute)			6.07 ± 6.05
k10 ($minute^{-1}$)	0.136 ± 0.008	0.0989 ± 0.0074	0.0507 ± 0.0398
k10 Half-life (minute)	5.11 ± 0.30	7.01 ± 0.52	13.7 ± 10.7
k12 ($minute^{-1}$)	0.00327 ± 0.00130	0.00174 ± 0.00102	0.00941 ± 0.01064
k21 ($minute^{-1}$)	0.0402 ± 0.0118	0.0253 ± 0.0123	0.00370 ± 0.00978
Cl (mL/min/kg)	178 ± 14	157 ± 18	
Cl2 (mL/min/kg)	4.28 ± 1.55	2.76 ± 1.50	
Cl1_F (mL/min/kg)			3080 ± 970
Cl2_F (mL/min/kg)			571 ± 791
V1 (mL/kg)	1310 ± 160	1590 ± 260	
V2 (mL/kg)	106 ± 23	109 ± 28	
V1_F (mL/kg)			60700 ± 40400
V2_F (mL/kg)			154000 ± 612000
MRT (minute)	7.97 ± 0.41	10.8 ± 0.7	
AUCinf_pred (ug/mL*min)	282 ± 23	638 ± 72	97.5 ± 30.6

Experiment Number: K08624
Route: Dermal, IV
Species/Strain: Mice/B6C3F1

Toxicokinetics Data Summary
Compound: Bis 2-Chloroethoxy Methane/ **Analyte:** Bis 2-Chloroethoxy Methane
CAS Number: 111-91-1

Request Date: 7/11/2023
Request Time: 10:03:16
Lab: Battelle Columbus

Male

	Treatment Group (mg/kg)	
	450 Dermal Plasma[b]	600 Dermal Plasma[b]
Cmax_pred (ug/mL)	4.11 ± 0.50	12.3 ± 2.1
Tmax_pred (minute)	13.7 ± 2.3	14.6 ± 3.1
Cmax_obs (ug/mL)	4.40 ± 1.22	7.98 ± 3.57
Tmax_obs (minute)	10	30
Alpha (minute^{-1})	0.0526 ± 0.0157	0.0498 ± 0.0152
Alpha Half-life (minute)	13.2 ± 3.9	13.9 ± 4.2
Beta (minute^{-1})	0.00244 ± 0.00867	0.00350 ± 0.01301
Beta Half-life (minute)	284 ± 1010	198 ± 734
k01 (minute^{-1})	0.0991 ± 0.0505	0.0918 ± 0.0555
k01 Half-life (minute)	7.00 ± 3.56	7.55 ± 4.56
k10 (minute^{-1})	0.0484 ± 0.0204	0.0488 ± 0.0157
k10 Half-life (minute)	14.3 ± 6.0	14.2 ± 4.6
k12 (minute^{-1})	0.00399 ± 0.00679	0.000979 ± 0.001271
k21 (minute^{-1})	0.00265 ± 0.00903	0.00358 ± 0.01320
Cl1_F (mL/min/kg)	2590 ± 480	1150 ± 180
Cl2_F (mL/min/kg)	214 ± 408	23.2 ± 34.7
V1_F (mL/kg)	53500 ± 18300	23700 ± 9400
V2_F (mL/kg)	80600 ± 427000	6470 ± 33200
AUCinf_pred (ug/mL*min)	174 ± 32	520 ± 80

Experiment Number: K08624
Route: Dermal, IV
Species/Strain: Mice/B6C3F1

Toxicokinetics Data Summary
Compound: Bis 2-Chloroethoxy Methane/ **Analyte:** Bis 2-Chloroethoxy Methane
CAS Number: 111-91-1

Request Date: 7/11/2023
Request Time: 10:03:16
Lab: Battelle Columbus

Female

	Treatment Group (mg/kg)		
	50 IV Plasma[a]	**300 Dermal Plasma[b]**	**600 Dermal Plasma[b]**
Cmax_pred (ug/mL)	30.4 ± 5.8	5.58 ± 0.92	15.5 ± 1.8
Tmax_pred (minute)		9.36 ± 2.01	14.1 ± 1.8
Cmax_obs (ug/mL)		6.69 ± 1.76	15.7 ± 5.0
Tmax_obs (minute)		10	15
Alpha ($minute^{-1}$)		0.0824 ± 0.0312	0.0547 ± 0.0106
Alpha Half-life (minute)	4.63 ± 0.72	8.41 ± 3.18	12.7 ± 2.4
Beta ($minute^{-1}$)		0.00841 ± 0.00406	0.00453 ± 0.00235
Beta Half-life (minute)	23.7 ± 47.7	82.4 ± 39.7	153 ± 79
k01 ($minute^{-1}$)		0.137 ± 0.094	0.0900 ± 0.0342
k01 Half-life (minute)		5.06 ± 3.46	7.71 ± 2.93
k10 ($minute^{-1}$)	0.142 ± 0.018	0.0782 ± 0.0291	0.0536 ± 0.0103
k10 Half-life (minute)	4.86 ± 0.62	8.87 ± 3.30	12.9 ± 2.5
k12 ($minute^{-1}$)	0.00561 ± 0.00248	0.00377 ± 0.00213	0.000965 ± 0.000264
k21 ($minute^{-1}$)	0.0307 ± 0.0628	0.00886 ± 0.00435	0.00462 ± 0.00240
Cl (mL/min/kg)	234 ± 25		
Cl2 (mL/min/kg)	9.21 ± 3.54		
Cl1_F (mL/min/kg)		1960 ± 260	959 ± 98
Cl2_F (mL/min/kg)		94.2 ± 33.3	17.2 ± 4.2
V1 (mL/kg)	1640 ± 320		
V2 (mL/kg)	300 ± 585		
V1_F (mL/kg)		25000 ± 10800	17900 ± 4600
V2_F (mL/kg)		10600 ± 5100	3730 ± 2210
MRT (minute)	8.30 ± 3.21		
AUCinf_pred (ug/mL*min)	214 ± 23	153 ± 20	626 ± 64

Experiment Number: K08624
Route: Dermal, IV
Species/Strain: Mice/B6C3F1

Toxicokinetics Data Summary
Compound: Bis 2-Chloroethoxy Methane/ **Analyte:** Bis 2-Chloroethoxy Methane
CAS Number: 111-91-1

Request Date: 7/11/2023
Request Time: 10:03:16
Lab: Battelle Columbus

Male

	Treatment Group (mg/kg)		
	50 IV Heart[c]	**300 Dermal Heart[d]**	**600 Dermal Heart[d]**
Cmax_obs (ug/g)	39.3	2.51	9.95
Tmax_obs (minute)	3.90	18.0	14.0
Half-life (minute)	8.88	23.5	25.5

Experiment Number: K08624
Route: Dermal, IV
Species/Strain: Mice/B6C3F1

Toxicokinetics Data Summary
Compound: Bis 2-Chloroethoxy Methane/ **Analyte:** Bis 2-Chloroethoxy Methane
CAS Number: 111-91-1

Request Date: 7/11/2023
Request Time: 10:03:16
Lab: Battelle Columbus

Female

	Treatment Group (mg/kg)		
	20 IV Heart[c]	**300 Dermal Heart[d]**	**600 Dermal Heart[d]**
Cmax_obs (ug/g)	34.6	6.63	17.5
Tmax_obs (minute)	4.19	14.5	33.0
Half-life (minute)	6.98	10.8	61.9

Experiment Number: K08624
Route: Dermal, IV
Species/Strain: Mice/B6C3F1

Toxicokinetics Data Summary
Compound: Bis 2-Chloroethoxy Methane/ **Analyte:** Bis 2-Chloroethoxy Methane
CAS Number: 111-91-1

Request Date: 7/11/2023
Request Time: 10:03:16
Lab: Battelle Columbus

Male

	Treatment Group (mg/kg)		
	50 IV Liver[c]	**300 Dermal Liver[d]**	**600 Dermal Liver[d]**
Cmax_obs (ug/g)	1.65	3.15	13.2
Tmax_obs (minute)	6.96	17.6	32.3
Half-life (minute)	7.66	26.4	44.3

Experiment Number: K08624
Route: Dermal, IV
Species/Strain: Mice/B6C3F1

Toxicokinetics Data Summary
Compound: Bis 2-Chloroethoxy Methane/ **Analyte:** Bis 2-Chloroethoxy Methane
CAS Number: 111-91-1

Request Date: 7/11/2023
Request Time: 10:03:16
Lab: Battelle Columbus

Female

	Treatment Group (mg/kg)		
	50 IV Liver[c]	**300 Dermal Liver[d]**	**600 Dermal Liver[d]**
Cmax_obs (ug/g)	0.164	3.49	15.6
Tmax_obs (minute)	3.52	14.1	32.3
Half-life (minute)	15.2	24.0	30.7

Experiment Number: K08624
Route: Dermal, IV
Species/Strain: Mice/B6C3F1

Toxicokinetics Data Summary
Compound: Bis 2-Chloroethoxy Methane/ **Analyte:** Bis 2-Chloroethoxy Methane
CAS Number: 111-91-1

Request Date: 7/11/2023
Request Time: 10:03:16
Lab: Battelle Columbus

Male

	Treatment Group (mg/kg)		
	50 IV Thymus[c]	**300 Dermal Thymus[d]**	**600 Dermal Thymus[d]**
Cmax_obs (ug/g)	32.8	3.00	14.0
Tmax_obs (minute)	3.90	13.2	13.9
Half-life (minute)	7.91	14.7	14.5

Experiment Number: K08624
Route: Dermal, IV
Species/Strain: Mice/B6C3F1

Toxicokinetics Data Summary
Compound: Bis 2-Chloroethoxy Methane/ **Analyte:** Bis 2-Chloroethoxy Methane
CAS Number: 111-91-1

Request Date: 7/11/2023
Request Time: 10:03:16
Lab: Battelle Columbus

Female

	Treatment Group (mg/kg)		
	50 IV Thymus[c]	**300 Dermal Thymus[d]**	**600 Dermal Thymus[d]**
Cmax_obs (ug/g)	30.3	5.88	13.7
Tmax_obs (minute)	4.19	14.4	18.6
Half-life (minute)	5.74	14.3	16.7

Experiment Number: K08624
Route: Dermal
Species/Strain: Mice/B6C3F1

Toxicokinetics Data Summary
Compound: Bis 2-Chloroethoxy Methane/ **Analyte:** Thiodiglycolic Acid
CAS Number: 111-91-1

Request Date: 7/11/2023
Request Time: 10:03:16
Lab: Battelle Columbus

Male

	Treatment Group (mg/kg)		
	300 Dermal Plasma[d]	**450 Dermal Plasma[d]**	**600 Dermal Plasma[d]**
Cmax_pred (ug/mL)	2.32	5.82	7.78
Tmax_obs (minute)	240	90	240
Half-life (minute)	188	195	205

Male

	Treatment Group (mg/kg)	
	300 Dermal Heart[d]	**600 Dermal Heart[d]**
Cmax_obs (ug/g)	0.731	3.12
Tmax_obs (minute)	180	240
Half-life (minute)	448	169

Male

	Treatment Group (mg/kg)	
	300 Dermal Liver[d]	**600 Dermal Liver[d]**
Cmax_obs (ug/g)	48.2	88.2
Tmax_obs (minute)	90	120
Half-life (minute)	140	145

Male

	Treatment Group (mg/kg)	
	300 Dermal Thymus[d]	**600 Dermal Thymus[d]**
Cmax_obs (ug/g)	2.35	10.0
Tmax_obs (minute)	180	480
Half-life (minute)	746	542

Female

	Treatment Group (mg/kg)	
	300 Dermal Plasma[d]	**600 Dermal Plasma[d]**
Cmax_obs (ug/mL)	1.95	4.33
Tmax_obs (minute)	90	90
Half-life (minute)	185	214

Female

	Treatment Group (mg/kg)	
	300 Dermal Heart[d]	**600 Dermal Heart[d]**
Cmax_obs (ug/g)	0.833	2.64
Tmax_obs (minute)	240	240
Half-life (minute)	340	218

Female

	Treatment Group (mg/kg)	
	300 Dermal Liver[d]	**600 Dermal Liver[d]**
Cmax_obs (ug/g)	56.9	93.4
Tmax_obs (minute)	90	120
Half-life (minute)	133	140

Female

	Treatment Group (mg/kg)	
	300 Dermal Thymus[d]	**600 Dermal Thymus[d]**
Cmax_obs (ug/g)	2.94	6.76
Tmax_obs (minute)	240	480
Half-life (minute)	447	300

LEGEND

MODELING SOFTWARE

WinNonlin Version 5.0.1

MODELING METHOD & BEST FIT MODEL

[a]WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA, Two-compartment model with bolus input, first order output, and 1/Yhat2 weighting.

[b]WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA, Two-compartment model with first order input, first order output, and 1/Yhat2 weighting.

[c]WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA, Non-compartment model with bolus input, first order output, and uniform weighting.

[d]WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA, Non-compartment model with first order input, first order output, and uniform weighting.

ANALYTE

Bis 2-Chloroethoxy Methane
Thiodiglycolic Acid

TK PARAMETERS

Cmax = Observed or Predicted Maximum plasma (or tissue) concentration
Tmax = Time at which Cmax predicted or observed occurs
Half-Life = Non-compartmental analysis (NCA) terminal elimination rate constant, NCA ke or kelim
Alpha = Hybrid rate constant of the alpha phase
Alpha Half-life = Half-life for the alpha phase
Beta = Hybrid rate constant of the beta phase
Beta Half-life = Half-life for the beta phase
k01 = Absorption rate constant, ka
k01 Half-life = Half-life of the absorption process to the central compartment
k10 = Elimination rate constant from the central compartment also ke or kelim
k10 Half-life = Half-life for the elimination process from the central compartment
k12 = Distribution rate constant from first to second compartment
k21 = Distribution rate constant from second to first compartment
Cl = Clearance, includes total clearance
Cl2 = Clearance of the secondary compartment
Cl1_F = Apparent clearance of the central compartment, also Cl_F for gavage groups in non-compartmental model
Cl2_F = Apparent clearance of the secondary compartment
V1 = Volume of distribution of the central compartment, includes Vd and V volume of distribution, Vz apparent volume of distribution NCA, Vapp apparent volume of distribution for intravenous studies
V2 = Volume of distribution for the peripheral compartment
V1_F = Apparent volume of distribution for the central compartment includes Vd_F, V_F for oral groups, and Vc_F
V2_F = Apparent volume of distribution for the peripheral compartment
MRT = Mean Residence Time
AUCinf_pred = Area under the plasma concentration versus time curve, AUC, extrapolated to time equals infinity

TK PARAMETERS PROTOCOL

TK_INTRAVENOUS PLASMA

ANALYSIS METHOD

Following blood collection, each animal was terminated with CO2 and the heart, thymus, and liver were collected. Blood collection time points for this group are 2, 5, 10, 15, 20, 30, 40, 50, 60, and 90 minutes. SE is the standard error of the mean. Parameter estimates are reported to three significant figures. Cmax (predicted) based on the model prediction at time 0 minutes.

50 mg/kg Male and Female

Animals were given a single bolus injection of Bis 2-Chloroethoxy Methane (CEM) through a jugular catheter. Concentrations time data sets were evaluated using non-compartmental analysis and, when possible, compartmental models. WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA

ANALYSIS METHOD

Following blood collection, each animal was terminated with CO2 and the heart, thymus, and liver were collected. Blood collection time points for this group are 5, 10, 15, 30, 45, 60, 90, 120, 180, 240, and 360 minutes. SE is the standard error of the mean. Parameter estimates are reported to three significant figures. Cmax (predicted) based on the model prediction at time 0 minutes.

100 mg/kg Male

Animals were given a single bolus injection of Bis 2-Chloroethoxy Methane (CEM) through a jugular catheter. Concentrations time data sets were evaluated using non-compartmental analysis and, when possible, compartmental models. WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA

TK_DERMAL PLASMA

ANALYSIS METHOD

Following blood collection, each animal was terminated with CO2 and the heart, thymus, and liver were collected. Blood collection time points for this group are 5, 10, 15, 30, 60, 90, 120, 180, and 240 minutes. SE is the standard error of the mean. Parameter estimates are reported to three significant figures except for observed Tmax.

300 mg/kg Male and Female, 450 mg/kg Male

Animals were given a single dermal administration of Bis 2-Chloroethoxy Methane (CEM) in 95 percent ethanol. Concentrations time data sets were evaluated using non-compartmental analysis and, when possible, compartmental models. WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA

ANALYSIS METHOD

Following blood collection, each animal was terminated with CO2 and the heart, thymus, and liver were collected. Blood collection time points for this group are 5, 10, 15, 30, 60, 90, 120, 180, 240, and 360 minutes. SE is the standard error of the mean. Parameter estimates are reported to three significant figures except for observed Tmax.

600 mg/kg Male and Female

Animals were given a single dermal administration of Bis 2-Chloroethoxy Methane (CEM) in 95 percent ethanol. Concentrations time data sets were evaluated using non-compartmental analysis and, when possible, compartmental models. WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA

TK PARAMETERS PROTOCOL (cont'd)

TK_INTRAVENOUS HEART

ANALYSIS METHOD

Following blood collection, each animal was terminated with CO2 and the heart, thymus, and liver were collected. Blood collection time points for this group are 2, 5, 10, 15, 20, 30, 40, 50, 60, and 90 minutes. Parameter estimates are reported to three significant figures. Non-compartmental analysis does not calculate a standard error.

50 mg/kg Male and Female

Animals were given a single bolus injection of Bis 2-Chloroethoxy Methane (CEM) through a jugular catheter. Concentrations time data sets were evaluated using non-compartmental analysis and, when possible, compartmental models using WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA

TK_DERMAL HEART

ANALYSIS METHOD

Following blood collection, each animal was terminated with CO2 and the heart, thymus, and liver were collected. Blood collection time points for this group are 5, 10, 15, 30, 60, 90, 120, 180, and 240 minutes. Parameter estimates are reported to three significant figures. Non-compartmental analysis does not calculate a standard error.

300 mg Male and Female

Animals were given a single dermal administration of Bis 2-Chloroethoxy Methane (CEM) in 95 percent ethanol. Concentrations time data sets were evaluated using non-compartmental analysis and, when possible, compartmental models. WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA

TK PARAMETERS PROTOCOL (cont'd)

ANALYSIS METHOD

Following blood collection, each animal was terminated with CO2 and the heart, thymus, and liver were collected. Blood collection time points for this group are 5, 10, 15, 30, 60, 90, 120, 180, 240, and 360 minutes. Parameter estimates are reported to three significant figures. Non-compartmental analysis does not calculate a standard error.

600 mg/kg Male and Female

Animals were given a single bolus injection of Bis 2-Chloroethoxy Methane (CEM) through a jugular catheter. Concentrations time data sets were evaluated using non-compartmental analysis and, when possible, compartmental models using WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA

TK_DERMAL LIVER

ANALYSIS METHOD

Following blood collection, each animal was terminated with CO2 and the heart, thymus, and liver were collected. Blood collection time points for this group are 2, 5, 10, 15, 20, 30, 40, 50, 60, and 90 minutes. Parameter estimates are reported to three significant figures. Non-compartmental analysis does not calculate a standard error.

50 mg/kg Male and Female

Animals were given a single bolus injection of Bis 2-Chloroethoxy Methane (CEM) through a jugular catheter. Concentrations time data sets were evaluated using non-compartmental analysis and, when possible, compartmental models using WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA

TK PARAMETERS PROTOCOL (cont'd)

ANALYSIS METHOD

Following blood collection, each animal was terminated with CO2 and the heart, thymus, and liver were collected. Blood collection time points for this group are 5, 10, 15, 30, 60, 90, 120, 180, and 240 minutes. Parameter estimates are reported to three significant figures. Non-compartmental analysis does not calculate a standard error.

300 mg Male and Female

Animals were given a single dermal administration of Bis 2-Chloroethoxy Methane (CEM) in 95 percent ethanol. Concentrations time data sets were evaluated using non-compartmental analysis and, when possible, compartmental models. WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA

ANALYSIS METHOD

Following blood collection, each animal was terminated with CO2 and the heart, thymus, and liver were collected. Blood collection time points for this group are 5, 10, 15, 30, 60, 90, 120, 180, 240, and 360 minutes. Parameter estimates are reported to three significant figures. Non-compartmental analysis does not calculate a standard error.

600 mg/kg Male and Female

Following blood collection, each animal was terminated with CO2 and the heart, thymus, and liver were collected. Blood collection time points for this group are 5, 10, 15, 30, 60, 90, 120, 180, 240, and 360 minutes. Parameter estimates are reported to three significant figures. Non-compartmental analysis does not calculate a standard error.

TK PARAMETERS PROTOCOL (cont'd)

TK_INTRAVENOUS THYMUS

ANALYSIS METHOD

Following blood collection, each animal was terminated with CO2 and the heart, thymus, and liver were collected. Blood collection time points for this group are 2, 5, 10, 15, 20, 30, 40, 50, 60, and 90 minutes. Parameter estimates are reported to three significant figures. Non-compartmental analysis does not calculate a standard error.

50 mg/kg Male and Female

Animals were given a single bolus injection of Bis 2-Chloroethoxy Methane (CEM) through a jugular catheter. Concentrations time data sets were evaluated using non-compartmental analysis and, when possible, compartmental models using WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA

TK_DERMAL THYMUS

ANALYSIS METHOD

Following blood collection, each animal was terminated with CO2 and the heart, thymus, and liver were collected. Blood collection time points for this group are 5, 10, 15, 30, 60, 90, 120, 180, and 240 minutes. Parameter estimates are reported to three significant figures. Non-compartmental analysis does not calculate a standard error.

300 mg Male and Female

Animals were given a single dermal administration of Bis 2-Chloroethoxy Methane (CEM) in 95 percent ethanol. Concentrations time data sets were evaluated using non-compartmental analysis and, when possible, compartmental models. WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA

TK PARAMETERS PROTOCOL

ANALYSIS METHOD

Following blood collection, each animals was terminated with CO2 and the heart, thymus, and liver were collected. Blood collection time points for this group are 5, 10, 15, 30, 60, 90, 120, 180, 240, and 360 minutes. Parameter estimates are reported to three significant figures. Non-compartmental analysis does not calculate a standard error.

600 mg Male and Female

Animals were given a single dermal administration of Bis 2-Chloroethoxy Methane (CEM) in 95 percent ethanol. Concentrations time data sets were evaluated using non-compartmental analysis and, when possible, compartmental models. WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA

TK PARAMETERS PROTOCOL (cont'd)

TK_DERMAL PLASMA

ANALYSIS METHOD

Following blood collection, each animal was terminated with CO2 and the heart, thymus, and liver were collected. Blood collection time points for this group are 5, 10, 15, 30, 60, 90, 120, 180, 240, 480, 600, and 720 minutes. Parameter estimates are reported to three significant figures, except for observed Tmax Non-compartmental analysis does not calculate a standard error.

300 mg/kg Male and Female

Animals were given a single dermal administration of Bis 2-Chloroethoxy Methane (CEM) in 95 percent ethanol. Concentrations time data sets were evaluated using non-compartmental analysis and, when possible, compartmental models. WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA

ANALYSIS METHOD

Following blood collection, each animal was terminated with CO2 and the heart, thymus, and liver were collected. Blood collection time points for this group are 5, 10, 15, 30, 60, 90, 120, 180, 240, 360, 480, 600, and 720 minutes. Parameter estimates are reported to three significant figures, except for observed Tmax Non-compartmental analysis does not calculate a standard error.

600 mg/kg Male and Female, 450 mg/kg Male

Animals were given a single dermal administration of Bis 2-Chloroethoxy Methane (CEM) in 95 percent ethanol. Concentrations time data sets were evaluated using non-compartmental analysis and, when possible, compartmental models. WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA

TK PARAMETERS PROTOCOL (cont'd)

TK_DERMAL HEART

ANALYSIS METHOD

Following blood collection, each animal was terminated with CO2 and the heart, thymus, and liver were collected. Blood collection time points for this group are 5, 10, 15, 30, 60, 90, 120, 180, 240, 480, 600, and 720 minutes. Parameter estimates are reported to three significant figures. Non-compartmental analysis does not calculate a standard error.

300 mg/kg, 600 mg/kg Male and Female

Animals were given a single dermal administration of Bis 2-Chloroethoxy Methane (CEM) in 95 percent ethanol. Concentrations time data sets were evaluated using non-compartmental analysis and, when possible, compartmental models. WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA

TK_DERMAL LIVER

ANALYSIS METHOD

Following blood collection, each animals was terminated with CO2 and the heart, thymus, and liver were collected. Blood collection time points for this group are 5, 10, 15, 30, 60, 90, 120, 180, 240, 480, 600, and 720 minutes. Parameter estimates are reported to three significant figures. Non-compartmental analysis does not calculate a standard error.

TK PARAMETERS PROTOCOL (cont'd)

300 mg/kg, 600 mg/kg Male and Female

Animals were given a single dermal administration of Bis 2-Chloroethoxy Methane (CEM) in 95 percent ethanol. Concentrations time data sets were evaluated using non-compartmental analysis and, when possible, compartmental models. WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA

TK_DERMAL THYMUS

ANALYSIS METHOD

Following blood collection, each animal was terminated with CO2 and the heart, thymus, and liver were collected. Blood collection time points for this group are 5, 10, 15, 30, 60, 90, 120, 180, 240, 480, 600, and 720 minutes. Parameter estimates are reported to three significant figures, except for observed Tmax Non-compartmental analysis does not calculate a standard error.

300 mg/kg, 600 mg/kg Male and Female

Animals were given a single dermal administration of Bis 2-Chloroethoxy Methane (CEM) in 95 percent ethanol. Concentrations time data sets were evaluated using non-compartmental analysis and, when possible, compartmental models. WinNonlin, Version 5.0.1, Pharsight Corporation, Mountain View, CA