

## ADME NTP Study S0816 bis(2-Chloroethoxy)methane

The contract laboratory abbreviation is BCM.

Species: Adult male and female F344 rats and B6C3F1 mice.

Vehicle: intravenous, isotonic saline; oral, water; topical application (dermal), ethanol.

CASRN 111-91-1

Radiolabeled with carbon-14 (uniformly labeled); Bis(2-chloroethoxy)methane-UL-chloroethoxy-<sup>14</sup>C.

Studies performed:

1. Single 10 mg/kg oral gavage dose in male rats with sacrifice 72 hours (h) postdose.
2. Single 0.1 mg/kg oral gavage dose in male rats with sacrifice at 72 hours postdose.
3. Single 1 mg/kg intravenous dose in male rats with sacrifice at 72 hours postdose.
4. Single 10 mg/kg oral gavage dose in male mice with sacrifice at 72 hours postdose.
5. Single 1 mg/kg intravenous dose in male mice with sacrifice at 72 hours postdose.
6. Single 10 mg/kg oral gavage dose in female mice with sacrifice at 72 hours postdose.
7. Single 1 mg/kg intravenous dose in female mice with sacrifice at 72 hours postdose.
8. Single 0.1 mg/kg oral gavage dose in female mice with sacrifice at 72 hours postdose.
9. Single 10 mg/kg dermal dose in male rats with and without protective appliances with sacrifice at 24 hours postdose. The dose site was washed at 6 hours with gauze.
10. Single 0.1 mg/kg dermal study in male rats with and without protective appliances with sacrifice at 24 hours postdose. The dose site was washed at 6 hours with gauze.

11. Single 10 mg/kg dermal dose in male mice with and without protective appliances. Excreta was collected for 24 hours postdose, the dose site washed at 6 hours, and mice were sacrificed and necropsied at 24 hours postdosing.
12. Single 0.1 mg/kg dermal dose in male mice with and without protective appliances. Excreta was collected for 0-6 and 6-50 hours postdose, the dose site was washed at 6 hours, and the mice sacrificed at 50 hours postdose (delay due to bad weather).
13. Single 1 mg/kg intravenous tissue distribution study in male rats with serial sacrifice to 8 hours postdose, selected tissues collected.

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**Table 1**  
**Disposition of Radioactivity 72 h after an Oral Dose**  
**of [<sup>14</sup>C]BCM (10 mg/kg) to Male F-344 Rats<sup>a</sup>**

**Cumulative Excretion of Radioactivity**

End of Collection Period	Percent of Dose Recovered in:				Total
	Urine	Volatile Breath	CO <sub>2</sub>	Feces	
8 h	51.8 ± 9.1	0.093 ± 0.015	5.24 ± 1.48		57.2 ± 8.3
24 h	85.0 ± 1.7	0.109 ± 0.016	6.52 ± 1.86	0.37 ± 0.11	92.0 ± 1.3
48 h	89.0 ± 1.7	0.118 ± 0.017	6.94 ± 1.93	0.37 ± 0.10	96.5 ± 1.2
72 h	90.0 ± 1.9	0.122 ± 0.018	7.14 ± 1.97	0.41 ± 0.16	97.7 ± 1.5

**Distribution in Tissues**

Tissue	ng-eq BCM per g Tissue	Tissue/Blood Ratio	% Dose in Total Tissue
Adipose	85 ± 25	0.216 ± 0.061	0.053 ± 0.017
Blood	390 ± 31	Unity	0.182 ± 0.015
Brain	128 ± 10.6	0.328 ± 0.013	0.007 ± 0.000
Heart	193 ± 22	0.495 ± 0.032	0.006 ± 0.001
Kidney	405 ± 76	1.03 ± 0.13	0.028 ± 0.007
Liver	680 ± 82	1.74 ± 0.094	0.242 ± 0.039
Lung	288 ± 47	0.735 ± 0.063	0.010 ± 0.002
Muscle	93 ± 12	0.239 ± 0.011	0.402 ± 0.051
Skin	329 ± 24	0.843 ± 0.012	0.501 ± 0.038
Spleen	342 ± 43	0.875 ± 0.048	0.007 ± 0.001
Testis	233 ± 24	0.570 ± 0.019	0.024 ± 0.003
Thymus gland	658 ± 98	1.69 ± 0.30	0.008 ± 0.001
<b>Total in tissues</b>			<b>1.48 ± 0.17</b>

a N=4

**Table 2**  
**Disposition of Radioactivity 72 h after an Oral Dose**  
**of [<sup>14</sup>C]BCM (0.1 mg/kg) to Male F-344 Rats<sup>a</sup>**

End of Collection Period	Percent of Dose Recovered in:						Total
	Urine*	Volatile Breath*	CO <sub>2</sub> *	Feces*	Blood	Carcass	
8 h	63.2 ± 1.7	0.05 ± 0.01	2.42 ± 0.45				65.7 ± 1.7
24 h	90.8 ± 0.7	0.06 ± 0.01	3.05 ± 0.58	0.87 ± 0.81			94.7 ± 0.7
48 h	93.7 ± 0.6	0.06 ± 0.01	3.27 ± 0.60	1.03 ± 0.80			98.0 ± 0.7
72 h	94.6 ± 0.6	0.07 ± 0.01	3.42 ± 0.60	1.08 ± 0.82	0.20 ± 0.0	2.48 ± 0.35	99.1 ± 0.6

<sup>a</sup> N=4

\*cumulative

Table 3

Disposition of Radioactivity 72 h after an Intravenous Dose  
of [<sup>14</sup>C]BCM (1 mg/kg) to Male F-344 Rats<sup>a</sup>

End of Collection Period	Percent of Dose Recovered in:						Total
	Urine*	Volatile Breath*	CO <sub>2</sub> *	Feces*	Blood	Carcass	
8 h	59.8 ± 8.3	0.18 ± 0.01	2.63 ± 0.95				62.6 ± 7.92
24 h	90.6 ± 3.4	0.20 ± 0.01	3.27 ± 1.09	0.50 ± 0.12			94.6 ± 2.80
48 h	95.7 ± 2.5	0.20 ± 0.02	3.51 ± 1.15	0.73 ± 0.21			100 ± 1.46
72 h	96.6 ± 2.3	0.21 ± 0.02	3.66 ± 1.18	0.76 ± 0.21	0.24 ± 0.03	1.11 ± 0.34	101 ± 1.29

<sup>a</sup> N=4

\*cumulative

Table 4

Disposition of Radioactivity 72 h after an Oral Dose of [<sup>14</sup>C]BCM (10 mg/kg) to Male B6C3F<sub>1</sub> MiceCumulative Excretion of Radioactivity<sup>a</sup>

End of Collection Period	Percent of Dose Recovered in:				Total
	Urine	Volatile Breath	CO <sub>2</sub>	Feces	
8 h	21.4 ± 19.7	0.082 ± 0.03	10.6 ± 1.3		32.0 ± 20.8
24 h	41.0 ± 17.1	0.101 ± 0.024	11.6 ± 1.5	20.6 ± 12.7	73.4 ± 9.3
48 h	45.6 ± 17.5	0.110 ± 0.026	12.4 ± 1.6	23.7 ± 14.9	81.8 ± 5.5
72 h	52.7 ± 17.2	0.113 ± 0.028	12.7 ± 1.6	24.5 ± 15.6	90.0 ± 2.8

Distribution in Tissues<sup>b</sup>

Tissue	ng-eq BCM per g Tissue	Tissue/Blood Ratio	% Dose in Total Tissue
Adipose	190 ± 14.8	1.18 ± 0.034	0.153 ± 0.008
Blood	162 ± 17.2	Unity	0.101 ± 0.008
Brain	92.5 ± 0.344	0.576 ± 0.0593	0.015 ± 0.000
Heart	138 ± 4.19	0.859 ± 0.0658	0.007 ± 0.001
Kidney	400 ± 44.3	2.48 ± 0.0096	0.056 ± 0.005
Liver	467 ± 86.3	2.88 ± 0.227	0.182 ± 0.011
Lung	212 ± 10.9	1.31 ± 0.0727	0.013 ± 0.001
Muscle	102 ± 4.07	0.633 ± 0.0928	0.376 ± 0.025
Skin	213 ± 1.12	1.33 ± 0.149	0.254 ± 0.007
Spleen	208 ± 10.5	1.29 ± 0.0726	0.005 ± 0.000
Testis	113 ± 5.32	0.707 ± 0.108	0.007 ± 0.001
Thymus gland	277 ± 10.2	1.72 ± 0.121	0.006 ± 0.000
Total in tissues			1.18 ± 0.01

a N=4

b N=2 for tissue data. Tissues from two animals were lost due to a shaker accident.

**Table 5**  
**Disposition of Radioactivity 72 h after an Intravenous Dose**  
**of [<sup>14</sup>C]BCM (1 mg/kg) to Male B6C3F<sub>1</sub> Mice<sup>a</sup>**  
**Cumulative Excretion of Radioactivity**

End of Collection Period	Percent of Dose Recovered in:				Total
	Urine	Volatile Breath	CO <sub>2</sub>	Feces	
8 h	36.8 ± 26.1	0.91 ± 0.60	6.77 ± 0.91		44.5 ± 25.8
24 h	53.8 ± 27.9	0.97 ± 0.63	7.51 ± 1.10	16.7 ± 25.7	79.0 ± 11.0
48 h	58.6 ± 26.8	1.00 ± 0.65	8.32 ± 1.54	19.5 ± 25.7	87.5 ± 9.9
72 h	65.8 ± 26.5	1.01 ± 0.65	8.61 ± 1.55	20.3 ± 25.8	95.7 ± 4.4

**Distribution in Tissues**

Tissue	ng-eq BCM per g Tissue	Tissue/Blood Ratio	% Dose in Total Tissue
Adipose	27.5 ± 14.4	1.45 ± 0.730	0.291 ± 0.0149
Blood	19.0 ± 3.47	Unity	0.156 ± 0.019
Brain	7.04 ± 0.898	0.378 ± 0.064	0.018 ± 0.003
Heart	13.5 ± 2.60	0.714 ± 0.083	0.009 ± 0.002
Kidney	43.3 ± 1.31	2.33 ± 0.37	0.075 ± 0.006
Liver	37.0 ± 8.27	1.94 ± 0.11	0.186 ± 0.022
Lung	20.5 ± 3.67	1.08 ± 0.07	0.016 ± 0.002
Muscle	8.87 ± 1.64	0.468 ± 0.039	0.433 ± 0.066
Skin	14.1 ± 3.69	0.739 ± 0.101	0.222 ± 0.051
Spleen	15.6 ± 2.17	0.828 ± 0.058	0.005 ± 0.001
Testis	7.45 ± 1.24	0.396 ± 0.058	0.007 ± 0.001
Thymus gland	22.8 ± 1.30	1.24 ± 0.28	0.005 ± 0.002
Total in tissues			1.42 ± 0.22

a N=4

Table 6

Disposition of Radioactivity 72 h after an Oral Dose of [ $^{14}\text{C}$ ]BCM (10 mg/kg) to Female B6C3F<sub>1</sub> Mice<sup>a</sup>

## Cumulative Excretion of Radioactivity

End of Collection Period	Percent of Dose Recovered in:			Total
	Urine	CO <sub>2</sub>	Feces	
8 h	9.35 ± 14.5	7.81 ± 2.04		17.2 ± 12.5
24 h	34.9 ± 21.7	9.46 ± 2.14	16.5 ± 9.3	60.9 ± 15.9
48 h	43.9 ± 24.8	10.3 ± 2.1	20.5 ± 11.5	74.7 ± 16.5
72 h	56.8 ± 18.4	10.7 ± 2.2	24.7 ± 14.2	92.2 ± 4.7

## Distribution in Tissues

Tissue	ng-eq BCM per g Tissue	Tissue/Blood Ratio	% Dose in Total Tissue
Adipose	219 ± 66	1.86 ± 0.54	0.159 ± 0.092
Blood	118 ± 8.88	Unity	0.0812 ± 0.004
Brain	88.5 ± 21.9	0.752 ± 0.173	0.020 ± 0.006
Heart	98.6 ± 9.23	0.841 ± 0.089	0.006 ± 0.001
Kidney	307 ± 99.7	2.61 ± 0.81	0.044 ± 0.013
Liver	364 ± 25.6	3.10 ± 0.15	0.145 ± 0.020
Lung	183 ± 29.2	1.56 ± 0.24	0.012 ± 0.002
Muscle	67.8 ± 9.83	0.582 ± 0.118	0.283 ± 0.070
Ovaries	215 ± 46.5	1.82 ± 0.33	0.001 ± 0.000
Skin	122 ± 18.8	1.05 ± 0.20	0.163 ± 0.037
Spleen	166 ± 23.3	1.41 ± 0.20	0.004 ± 0.001
Thymus gland	319 ± 152	2.72 ± 1.27	0.004 ± 0.003
Total in tissues			0.935 ± 0.24

a N=4



Table 7

Disposition of Radioactivity 72 h after an Intravenous Dose  
of [<sup>14</sup>C]BCM (1 mg/kg) to Female B6C3F<sub>1</sub> Mice<sup>a</sup>

End of Collection Period	Percent of Dose Recovered in:						Total
	Urine*	Volatile Breath*	CO <sub>2</sub> *	Feces*	Blood	Carcass	
8 h	27.0 ± 17.2	0.27 ± 0.02	3.52 ± 1.54				30.7 ± 16.4
24 h	52.0 ± 26.6	0.30 ± 0.03	4.17 ± 1.81	15.2 ± 10.2			71.7 ± 15.8
48 h	63.5 ± 25.2	0.31 ± 0.03	4.52 ± 1.98	17.3 ± 11.9			85.6 ± 132.1
72 h	71.5 ± 20.5	0.32 ± 0.03	4.70 ± 2.05	17.9 ± 12.5	0.05 ± 0.02	0.77 ± 0.22	94.4 ± 8.00

<sup>a</sup> N=4

\*cumulative

Bis(2-chloroethoxy)methane (BCM)

Table 8

Disposition of Radioactivity 72 h after an Oral Dose  
of [<sup>14</sup>C]BCM (0.1 mg/kg) to Female B6C3F<sub>1</sub> Mice<sup>a</sup>

End of Collection Period	Percent of Dose Recovered in:					Total
	Urine*	CO <sub>2</sub> *	Feces*	Blood	Carcass	
8 h	18.3 ± 27.1	4.96 ± 0.43				23.3 ± 26.9
24 h	40.2 ± 25.4	5.73 ± 0.62	8.47 ± 5.98			54.4 ± 21.9
48 h	46.2 ± 22.5	6.18 ± 0.76	11.1 ± 5.4			63.5 ± 18.7
72 h	65.6 ± 14.7	6.52 ± 0.78	14.6 ± 6.3	0.08 ± 0.02	0.96 ± 0.38	86.7 ± 9.6

<sup>a</sup> N=4

\*cumulative

Table 9

Disposition of Dermal Doses of [<sup>14</sup>C]BCM in Male F-344 Rats<sup>a</sup>

	10 mg/kg		0.1 mg/kg	
	with appliances	without appliances	with appliances	without appliances
<b>Absorbed</b>				
Urine	13.60 ± 1.88	39.43 ± 9.69	14.33 ± 5.38	36.78 ± 4.28
CO <sub>2</sub>	0.45 ± 0.15	1.80 ± 0.59	0.36 ± 0.15	0.97 ± 0.22
Feces	0.60 ± 0.57	1.19 ± 0.36	0.27 ± 0.08	0.96 ± 0.34
Tissues	0.55 ± 0.13	1.52 ± 0.45	0.51 ± 0.13	1.27 ± 0.19
Dose site	0.24 ± 0.09	0.29 ± 0.14	0.25 ± 0.18	0.24 ± 0.09
Total Absorbed	15.44 ± 2.55	44.23 ± 10.73	15.73 ± 5.82	40.23 ± 4.32
<b>Unabsorbed</b>				
Skin gauzes	0.62 ± 0.11	1.40 ± 0.91	2.15 ± 1.04	1.54 ± 0.57
Appliance	52.10 ± 9.99		51.50 ± 9.19	
Total unabsorbed	52.72 ± 10.09	1.40 ± 0.91	53.65 ± 9.95	1.54 ± 0.57
<b>Volatiles</b>	18.73 ± 1.18	46.95 ± 3.01	18.78 ± 4.80	44.53 ± 5.64
<b>Total Recovery</b>	86.88 ± 12.26	92.58 ± 10.71	88.15 ± 14.60	86.29 ± 9.05

<sup>a</sup> N=4. Data are mean ± SD of percent of dose recovered. Excreta were collected for 24 h postdosing. Tissues were sampled at 24 h postdosing.

Table 10

**Distribution of Radioactivity in Tissues of Rats 24 h  
after Dermal Administration of [<sup>14</sup>C]BCM (10 mg/kg)<sup>a</sup>**

Tissue	ng-eq BCM per g Tissue	Tissue/Blood Ratio	% Dose in Total Tissue
<b>With appliances</b>			
Adipose	17.4 ± 5.57	0.216 ± 0.028	0.013 ± 0.000
Blood	79.8 ± 19.0	Unity	0.045 ± 0.01
Brain	49.0 ± 8.21	0.624 ± 0.081	0.004 ± 0.000
Heart	40.0 ± 8.01	0.505 ± 0.043	0.001 ± 0.000
Kidney	267 ± 10.0	3.27 ± 0.49	0.022 ± 0.008
Liver	240 ± 42.1	3.04 ± 0.28	0.103 ± 0.026
Lung	88.8 ± 14.7	1.13 ± 0.09	0.004 ± 0.001
Muscle	16.0 ± 3.06	0.203 ± 0.029	0.084 ± 0.023
Skin	131 ± 26.7	1.68 ± 0.34	0.246 ± 0.075
Spleen	87.1 ± 16.5	1.10 ± 0.07	0.002 ± 0.000
Testis	40.0 ± 9.3	0.502 ± 0.021	0.005 ± 0.001
Thymus gland	1080 ± 171	14.3 ± 4.7	0.015 ± 0.003
Total in tissues			0.55 ± 0.129
<b>Without appliances</b>			
Adipose	62.9 ± 19.3	0.322 ± 0.1100	0.053 ± 0.022
Blood	197 ± 38.6	Unity	0.122 ± 0.040
Brain	130 ± 41.6	0.649 ± 0.096	0.011 ± 0.004
Heart	101 ± 23.9	0.510 ± 0.056	0.004 ± 0.001
Kidney	614 ± 193	3.06 ± 0.36	0.054 ± 0.025
Liver	587 ± 134	2.97 ± 0.19	0.267 ± 0.102
Lung	202 ± 42.1	1.02 ± 0.04	0.009 ± 0.003
Muscle	49.4 ± 19.8	0.263 ± 0.139	0.280 ± 0.119
Skin	331 ± 66.7	1.69 ± 0.28	0.668 ± 0.222
Spleen	233 ± 49.3	1.18 ± 0.05	0.006 ± 0.002
Testis	97.1 ± 38.0	0.481 ± 0.119	0.013 ± 0.006
Thymus gland	3320 ± 1250	16.6 ± 4.52	0.051 ± 0.023
Total in tissues			1.52 ± 0.45

<sup>a</sup> N=4

Table 11

Distribution of Radioactivity in Tissues of Rats 24 h after Dermal Administration of [<sup>14</sup>C]BCM (0.1 mg/kg)<sup>a</sup>

Tissue	ng-eq BCM per g Tissue	Tissue/Blood Ratio	% Dose in Total Tissue
<b>With appliances</b>			
Adipose	0.297 ± 0.055	0.341 ± 0.057	0.018 ± 0.004
Blood	0.874 ± 0.104	Unity	0.040 ± 0.010
Brain	0.553 ± 0.024	0.637 ± 0.060	0.003 ± 0.001
Heart	0.352 ± 0.018	0.405 ± 0.039	0.001 ± 0.000
Kidney	1.97 ± 0.47	2.28 ± 0.65	0.013 ± 0.003
Liver	2.42 ± 0.09	2.79 ± 0.30	0.080 ± 0.019
Lung	0.937 ± 0.153	1.07 ± 0.07	0.003 ± 0.001
Muscle	0.208 ± 0.037	0.240 ± 0.045	0.086 ± 0.016
Skin	1.73 ± 0.30	1.98 ± 0.20	0.259 ± 0.083
Spleen	0.874 ± 0.075	1.00 ± 0.06	0.002 ± 0.000
Testis	0.392 ± 0.039	0.454 ± 0.077	0.004 ± 0.000
Thymus gland	12.6 ± 2.2	14.4 ± 1.19	0.012 ± 0.005
Total in tissues			0.512 ± 0.126
<b>Without appliances</b>			
Adipose	0.988 ± 1.04	0.482 ± 0.514	0.058 ± 0.056
Blood	2.06 ± 0.064	Unity	0.095 ± 0.007
Brain	1.47 ± 0.28	0.712 ± 0.140	0.009 ± 0.002
Heart	0.93 ± 0.13	0.449 ± 0.066	0.002 ± 0.000
Kidney	6.03 ± 1.36	2.93 ± 0.69	0.039 ± 0.004
Liver	10.3 ± 8.42	4.97 ± 4.07	0.317 ± 0.276
Lung	2.18 ± 0.25	1.06 ± 0.13	0.007 ± 0.001
Muscle	0.402 ± 0.079	0.195 ± 0.039	0.172 ± 0.040
Skin	4.06 ± 0.22	1.97 ± 0.13	0.611 ± 0.040
Spleen	2.20 ± 0.370	1.06 ± 0.19	0.004 ± 0.000
Testis	0.858 ± 0.145	0.416 ± 0.076	0.009 ± 0.001
Thymus gland	34.9 ± 4.14	17.0 ± 2.35	0.034 ± 0.004
Total in tissues			1.27 ± 0.19

<sup>a</sup> N=4

Table 12

Disposition of Dermal Doses of [<sup>14</sup>C]BCM in Male B6C3F<sub>1</sub> Mice

	Corrected Data				Uncorrected Data			
	10 mg/kg		0.1 mg/kg		10 mg/kg		0.1 mg/kg	
	with appliances <sup>a,c</sup>	without appliances <sup>b,c</sup>	with appliances <sup>a</sup>	without appliances <sup>a</sup>	with appliances <sup>a,c</sup>	without appliances <sup>b,c</sup>	with appliances <sup>a</sup>	without appliances <sup>a</sup>
<b>Absorbed</b>								
Urine	12.59 ± 5.43	17.47 ± 2.41	8.94 ± 1.48 <sup>d</sup>	12.33 ± 1.32 <sup>d</sup>	14.50 ± 6.82	24.03 ± 6.58	15.05 ± 10.85 <sup>d</sup>	12.33 ± 1.32 <sup>d</sup>
CO <sub>2</sub>	1.10 ± 0.33	1.57 ± 0.81	0.42 ± 0.10 <sup>d</sup>	0.99 ± 0.52 <sup>d</sup>	1.28 ± 0.55	2.0 ± 20.78	0.92 ± 1.07 <sup>d</sup>	0.99 ± 0.52 <sup>d</sup>
Feces	1.75 ± 1.01	1.50 ± 1.77	e	e	1.93 ± 0.96	2.33 ± 1.64	e	e
Tissues	1.63 ± 1.80	0.47 ± 0.34	f	f	1.69 ± 1.74	0.83 ± 0.48	f	f
Dose site	1.25 ± 1.59	0.06 ± 0.04	f	f	1.31 ± 1.55	0.10 ± 0.05	f	f
Total Absorbed	18.30 ± 3.78*	21.07 ± 4.28**	9.36 ± 1.40*	13.32 ± 1.43**	20.71 ± 4.99	28.49 ± 7.09	15.96 ± 11.92	13.32 ± 1.43
<b>Unabsorbed</b>								
Skin gauzes	1.31 ± 0.59	0.27 ± 0.21	1.73 ± 0.82	0.50 ± 0.17	1.48 ± 0.61	0.50 ± 0.35	2.69 ± 1.62	0.50 ± 0.17
Appliance	18.02 ± 9.53		5.50 ± 2.52		20.20 ± 9.60		10.79 ± 11.16	
Total unabsorbed	19.33 ± 9.00	0.27 ± 0.21	7.23 ± 1.98	0.50 ± 0.17	21.67 ± 9.10	0.38 ± 0.38	13.48 ± 12.50	0.50 ± 0.17
<b>Volatiles</b>	35.22 ± 15.63	56.00 ± 6.28	24.23 ± 4.06 <sup>d</sup>	36.70 ± 5.63 <sup>d</sup>	42.23 ± 26.13	77.55 ± 22.60	42.25 ± 33.51 <sup>d</sup>	36.70 ± 5.63 <sup>d</sup>
<b>Total recovery</b>	71.80 ± 11.40	77.35 ± 10.34	40.82 ± 5.87	50.52 ± 6.15	83.54 ± 30.97	106.42 ± 29.42	71.69 ± 57.77	50.52 ± 6.15

Data are mean ± SD of percent of dose recovered.

<sup>a</sup> N=4.

<sup>b</sup> N=3. One mouse died due to anesthesia complications during the 6-h dose site wash.

<sup>c</sup> Excreta were collected for 24 h postdosing. Tissues were sampled at 24 h postdosing.

<sup>d</sup> Due to inclement weather, the 6–24 h samples were not collected. Instead a 6–50 h sample was collected. These samples were at room temperature for an undetermined amount of time prior to analysis.

<sup>e</sup> No feces samples were collected.

<sup>f</sup> Due to inclement weather, no tissue samples were collected

\* Values are statistically significantly different, p < 0.05

\*\* Values are statistically significantly different, p < 0.05

Table 13

Distribution of Radioactivity in Tissues of Mice 24 h after Dermal Administration of [<sup>14</sup>C]BCM (10 mg/kg)

Tissue	ng-eq BCM per g Tissue	Tissue/Blood Ratio	% Dose in Total Tissue	% Dose in Total Tissue (corrected)
<b>With appliances<sup>a</sup></b>				
Adipose	97.7 ± 101	1.89 ± 1.05	0.088 ± 0.079	0.084 ± 0.082
Blood	45.7 ± 23.0		0.035 ± 0.014	0.031 ± 0.015
Brain	58.0 ± 10.3	1.45 ± 0.53	0.010 ± 0.002	0.008 ± 0.001
Heart	36.1 ± 26.1	0.748 ± 0.161	0.002 ± 0.001	0.002 ± 0.001
Kidney	466 ± 606	8.04 ± 6.68	0.068 ± 0.084	0.065 ± 0.085
Liver	185 ± 164	3.57 ± 1.35	0.085 ± 0.059	0.079 ± 0.063
Lung	117 ± 92.6	2.40 ± 0.72	0.007 ± 0.006	0.007 ± 0.006
Muscle	74.5 ± 86.8	1.36 ± 0.89	0.310 ± 0.314	0.293 ± 0.324
Skin	833 ± 1010	16.7 ± 14.8	1.06 ± 1.21	1.04 ± 1.23
Spleen	96.8 ± 81.1	1.97 ± 0.68	0.002 ± 0.002	0.002 ± 0.002
Testis	42.3 ± 36.2	0.855 ± 0.299	0.003 ± 0.002	0.003 ± 0.002
Thymus gland	1000 ± 222	24.4 ± 6.47	0.019 ± 0.006	0.016 ± 0.004
		Total in tissues	1.69 ± 1.74	1.63 ± 1.80
<b>Without appliances<sup>b</sup></b>				
Adipose	52.2 ± 22.2	0.698 ± 0.23	0.055 ± 0.015	0.046 ± 0.017
Blood	73.8 ± 10.8	Unity	0.065 ± 0.028	0.050 ± 0.004
Brain	83.1 ± 21.5	1.12 ± 0.16	0.016 ± 0.006	0.013 ± 0.002
Heart	51.1 ± 13.5	0.686 ± 0.102	0.003 ± 0.001	0.002 ± 0.000
Kidney	281 ± 76	3.79 ± 0.10	0.048 ± 0.021	0.038 ± 0.005
Liver	231 ± 76	3.06 ± 0.62	0.137 ± 0.065	0.107 ± 0.029
Lung	119 ± 21	1.61 ± 0.09	0.009 ± 0.004	0.007 ± 0.000
Muscle	36.0 ± 15.5	0.473 ± 0.148	0.186 ± 0.099	0.144 ± 0.054
Skin	152 ± 64	2.03 ± 0.71	0.277 ± 0.218	0.198 ± 0.082
Spleen	101 ± 33	1.36 ± 0.31	0.003 ± 0.000	0.003 ± 0.001
Testis	47.9 ± 11.9	0.643 ± 0.078	0.004 ± 0.002	0.003 ± 0.001
Thymus gland	1320 ± 502	17.8 ± 5.81	0.027 ± 0.012	0.021 ± 0.003
		Total in tissues	0.83 ± 0.48	0.47 ± 0.34

<sup>a</sup> N=4

<sup>b</sup> N=3

Table 14

Disposition of Radioactivity After an Intravenous Administration of  
[<sup>14</sup>C]BCM (1 mg/kg) to Male Rats

## Distribution in Tissues

Tissue	N	ng-eq BCM per g Tissue	Tissue/Blood Ratio	% Dose in Total Tissue
<b>0.25 h</b>				
Adipose	3	1760 ± 214	2.89 ± 0.427	18.0 ± 2.34
Blood	3	610 ± 18.6	UNITY	4.57 ± 0.0969
Brain	3	350 ± 11.4	0.574 ± 0.0160	0.256 ± 0.0109
Heart	3	481 ± 12.8	0.789 ± 0.00444	0.159 ± 0.00433
Kidney	3	19900 ± 1080	32.6 ± 1.40	17.5 ± 1.08
Liver	3	2420 ± 77.9	3.96 ± 0.193	11.0 ± 0.430
Lung	3	979 ± 71.0	1.60 ± 0.113	0.460 ± 0.278
Muscle	3	379 ± 11.1	0.621 ± 0.00181	15.5 ± 0.307
Skin	3	641 ± 5.18	1.05 ± 0.0290	12.3 ± 0.0966
Spleen	3	396 ± 9.13	0.650 ± 0.0340	0.0897 ± 0.00508
Testis	3	374 ± 63.8	0.611 ± 0.0852	0.414 ± 0.0252
Thymus	3	402 ± 78.4	0.658 ± 0.116	0.121 ± 0.0343
Total in tissues				80.40 ± 2.33
<b>0.5 h</b>				
Adipose	3	1520 ± 221.	2.93 ± 0.687	14.6 ± 2.21
Blood	3	529 ± 76.6	UNITY	3.72 ± 0.562
Brain	3	197 ± 31.4	0.381 ± 0.0993	0.141 ± 0.0333
Heart	3	401 ± 72.5	0.767 ± 0.156	0.125 ± 0.0285
Kidney	3	20700 ± 881	39.6 ± 4.89	16.3 ± 0.687
Liver	3	2800 ± 237	5.43 ± 1.32	11.6 ± 0.640
Lung	3	889 ± 81.7	1.69 ± 0.107	0.389 ± 0.0736
Muscle	3	415 ± 282	0.849 ± 0.708	15.9 ± 10.8
Skin	3	413 ± 51.1	0.786 ± 0.0860	7.46 ± 0.999
Spleen	3	374 ± 26.1	0.719 ± 0.132	0.0808 ± 0.0140
Testis	3	277 ± 40.5	0.531 ± 0.0994	0.302 ± 0.0538
Thymus	3	278 ± 72.7	0.524 ± 0.0873	0.0666 ± 0.0217
Total in tissues				70.38 ± 2.55



**Table 14**  
(continued)

**Disposition of Radioactivity After an Intravenous Administration of  
[<sup>14</sup>C]BCM (1 mg/kg) to Male Rats**

Tissue	N	ng-eq BCM per g Tissue	Tissue/Blood Ratio	% Dose in Total Tissue
<b>1 h</b>				
Adipose	3	663 ± 84.7	1.77 ± 0.404	6.13 ± 2.12
Blood	3	383 ± 53.2	UNITY	2.90 ± 0.412
Brain	3	103 ± 10.7	0.271 ± 0.0460	0.0789 ± 0.0109
Heart	3	253 ± 12.2	0.671 ± 0.119	0.0865 ± 0.00568
Kidney	3	16000 ± 1400	42.6 ± 9.03	14.4 ± 0.771
Liver	3	1790 ± 130	4.77 ± 1.05	8.31 ± 0.420
Lung	3	559 ± 65.0	1.48 ± 0.255	0.290 ± 0.0237
Muscle	3	134 ± 18.4	0.351 ± 0.0240	5.56 ± 0.796
Skin	3	307 ± 12.3	0.810 ± 0.108	5.96 ± 0.220
Spleen	3	397 ± 24.8	1.05 ± 0.210	0.0997 ± 0.00101
Testis	3	276 ± 22.3	0.734 ± 0.157	0.328 ± 0.0177
Thymus	3	410 ± 32.0	1.09 ± 0.244	0.105 ± 0.0222
Total in tissues				44.49 ± 2.84
<b>2 h</b>				
Adipose	3	316 ± 21.2	1.00 ± 0.338	3.23 ± 0.177
Blood	3	343 ± 129	UNITY	2.60 ± 1.08
Brain	3	69.0 ± 8.37	0.222 ± 0.0890	0.0497 ± 0.00753
Heart	3	200 ± 46.9	0.632 ± 0.273	0.0687 ± 0.0169
Kidney	3	9930 ± 2320	32.6 ± 15.0	8.12 ± 2.24
Liver	3	1670 ± 135	5.36 ± 1.98	7.21 ± 0.360
Lung	3	783 ± 614	2.09 ± 0.902	0.413 ± 0.372
Muscle	3	82.2 ± 23.2	0.245 ± 0.0243	3.39 ± 1.09
Skin	3	371 ± 152	1.08 ± 0.0613	7.23 ± 3.24
Spleen	3	571 ± 9.35	1.81 ± 0.583	0.130 ± 0.0110
Testis	3	393 ± 23.9	1.25 ± 0.409	0.461 ± 0.0464
Thymus	3	842 ± 57.5	2.63 ± 0.704	0.206 ± 0.0183
Total in tissues				33.11 ± 3.87

Table 14  
(continued)

Disposition of Radioactivity After an Intravenous Administration of  
[<sup>14</sup>C]BCM (1 mg/kg) to Male Rats

Tissue	N	ng-eq BCM per g Tissue	Tissue/Blood Ratio	% Dose in Total Tissue
<b>4 h</b>				
Adipose	3	237 ± 187	0.864 ± 0.659	2.46 ± 1.98
Blood	3	274 ± 41.0	UNITY	2.07 ± 0.345
Brain	3	74.8 ± 5.41	0.277 ± 0.0480	0.0582 ± 0.00312
Heart	3	128 ± 24.9	0.468 ± 0.0551	0.0438 ± 0.0115
Kidney	3	3930 ± 1810	13.9 ± 4.65	3.33 ± 1.42
Liver	3	1200 ± 218	4.49 ± 1.35	5.10 ± 0.477
Lung	3	287 ± 39.9	1.05 ± 0.0570	0.149 ± 0.0393
Muscle	3	76.8 ± 27.9	0.285 ± 0.105	3.17 ± 1.20
Skin	3	334 ± 118	1.23 ± 0.432	6.48 ± 2.40
Spleen	3	476 ± 26.2	1.75 ± 0.177	0.120 ± 0.00523
Testis	3	336 ± 28.7	1.24 ± 0.126	0.413 ± 0.0230
Thymus	3	1140 ± 123	4.27 ± 1.10	0.308 ± 0.0106
Total in tissues				23.70 ± 5.53
<b>8 h</b>				
Adipose	3	41.4 ± 4.39	0.288 ± 0.107	0.409 ± 0.0410
Blood	3	154 ± 38.6	UNITY	1.11 ± 0.285
Brain	3	41.1 ± 4.83	0.278 ± 0.0665	0.0315 ± 0.00295
Heart	3	47.8 ± 6.42	0.319 ± 0.0448	0.0150 ± 0.00107
Kidney	3	1000 ± 60.2	6.80 ± 1.57	0.853 ± 0.0564
Liver	3	532 ± 78.0	3.55 ± 0.574	2.19 ± 0.181
Lung	3	149 ± 13.6	1.02 ± 0.270	0.0639 ± 0.00658
Muscle	3	30.5 ± 15.7	0.192 ± 0.0581	1.21 ± 0.651
Skin	3	214 ± 66.5	1.41 ± 0.331	3.97 ± 1.12
Spleen	3	207 ± 13.5	1.41 ± 0.381	0.0455 ± 0.00330
Testis	3	104 ± 4.43	0.707 ± 0.194	0.124 ± 0.00136
Thymus	3	1040 ± 157	7.06 ± 2.04	0.275 ± 0.0427
Total in tissues				10.30 ± 1.77

Table 15

## Cumulative Percent of Dose Excreted in Urine and Feces of Mice

Study	End of Cumulative Interval (h)	Percent Recovered In:		
		Urine	Feces	Urine + Feces
Male 10 mg/kg oral	24	41.0 ± 17.1	20.6 ± 12.7	61.7 ± 8.4
	48	45.6 ± 17.5	23.7 ± 14.9	69.1 ± 5.1
	72	52.7 ± 17.2	24.5 ± 15.6	77.2 ± 1.9
Male 1 mg/kg iv	24	53.8 ± 27.9	16.7 ± 25.7	70.5 ± 10.8
	48	58.6 ± 26.8	19.5 ± 25.7	78.4 ± 9.8
	72	65.8 ± 26.5	20.3 ± 25.8	86.1 ± 4.6
Female 10 mg/kg oral	24	34.9 ± 21.7	16.6 ± 9.3	51.5 ± 16.4
	48	43.9 ± 24.8	20.5 ± 11.5	64.4 ± 16.9
	72	56.8 ± 18.4	24.7 ± 14.2	81.5 ± 5.2
Female 1 mg/kg iv	24	52.0 ± 26.6	15.2 ± 10.2	67.2 ± 16.5
	48	63.5 ± 25.2	17.3 ± 11.9	80.8 ± 13.5
	72	71.5 ± 20.5	17.9 ± 2.5	89.5 ± 8.3
Female 0.1 mg/kg oral	24	40.2 ± 25.4	8.5 ± 6.0	48.7 ± 22.4
	48	46.2 ± 22.5	11.1 ± 5.4	57.3 ± 19.3
	72	65.6 ± 14.7	14.6 ± 6.3	80.2 ± 10.4