ADME NTP Study S0008 Acrylamide

Sex/Species: male F344 rats.
Vehicle: intravenous, not specified; oral, water.

CASRN 79-06-1

Radiolabeled with carbon-14, no specified location; [^{14}C]Acrylamide

Studies Performed:

- Single 1.0, 10, or 100 mg/kg oral gavage dose to rats with sacrifice 7 days postdose. (n = 3 per group)

- Single 10 mg/kg intravenous dose to rats with sacrifice at 0.25, 0.5, 1, 2, 4, 8, 12, 24, 48, 72, 120, or 168 hours postdose. (n = 3 per time point)

- Single 10 mg/kg intravenous dose to rats with sacrifice at 0.25, 0.5, 1, 2, 4, 8, 12, 24, 48, 72, 120, or 168 hours postdose. (repeat treatment set; n = 2 per time point)

- Single 10 mg/kg intravenous dose to rats with sacrifice at 6 hours. (n = 4; bile collection)

The percent of parent acrylamide present in each tissue equaled the percent of parent acrylamide in each tissue extract multiplied by that sample's extraction efficiency (Table 11). Parent acrylamide present in fresh tissue samples (except urine) were obtained from a repeat treatment set of intravenously administered rats for analysis (n = 2). For acrylamide as ^{14}C equivalents, the tissue samples of the first treatment set were used (n = 3). Parent acrylamide was separated by HPLC and quantified by liquid scintillation counting.

For bile, the elimination of acrylamide as ^{14}C equivalents peaks at approximately 2 hours at 7.5% of the dose and declines with time. The cumulative % dose in bile is 16.07 and 10.76% for rats numbered A and B, respectively. The total % of dose as parent acrylamide in bile are 1.3 and 0.73% for a third and fourth rat, respectively. Most bile data was presented in figures and is not shown here.

Toxicokinetics:

The elimination of acrylamide as ^{14}C equivalents follows a biphasic, first order kinetic pattern. Several equations were used to model all the tissues:

- $X = A_1e^{-a_1t} + A_2e^{-a_2t}$ was used for all tissues except fat, liver, kidney, testes, and plasma.

- $X = A_1e^{-a_1t} + A_2e^{-a_2t} - (A_1 + A_2)e^{-a_3t}$ was used for fat, liver, kidney, testes, and plasma.

- $X = A_1(e^{-a_2t} - e^{-a_1t})$ was used for blood data. However, the elimination phase could not be accurately determined.

- $X = A_1(1 - e^{-a_1t})$ was used to model subsequent blood data (Table 10).

In several tissues the terminal half-lives are inaccurate due to an insufficient number of data points on the terminal portion of the elimination curve.

The elimination of the parent acrylamide follows a monophasic, first order kinetic pattern. The elimination of parent from tissues parallels that from blood (with $t_{1/2}$ = ~ 2 hours).

- $X = A_1e^{-a_1t}$ was used to model liver, muscle, skin, and blood.

- $X = A_1(e^{-a_1t} - e^{-a_3t})$ was used to model the kidney and testes which also had an absorption phase.

- $U = A_1(1 - e^{-a_1t})$ was used to model the urine elimination curve for parent acrylamide.

Data for fat, small intestine and intestinal contents did not follow any trend, and could not be fitted with any equations for parent acrylamide.

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Table 1. Percentage of dose found in excreta vs time from male Fisher 344 rats (n=3) orally administered acrylamide.

Low Dose = 1 mg/kg[a]	Percent of Dose ± Standard Deviation		
Time (Days)	Urine	Feces	Total
1	56.30±13.34	4.85±2.82	60.88±16.16
2	5.27±1.95	1.47±0.61	6.74±2.56
3	3.50±0.98	0.19±0.01	3.69±0.99
4	1.50±0.06	0.26±0.09	1.75±0.15
5	0.54±0.13	0.26±0.07	0.80±0.20
6 & 7	0	0.57±0.10	0.57±0.10
Cumulative	67.11±13.06	7.32±3.21	74.43±16.27[b]
Medium Dose = 10 mg/kg[a]			
Time (Da	Urine	Feces	Total
1	48.81±11.75	4.73±0.30	53.54±12.05
2	2.64±1.25	0.51±0.07	3.15±1.32
3	2.84±1.32	0.61±0.29	3.45±1.61
4	1.91±0.56	0.32±0.04	2.23±0.60
5	1.42±0.28	0.30±0.09	1.72±0.36
6 & 7	1.06±0.66	0.40±0.15	1.46±0.81
Cumulative	58.68±12.79	6.87±0.71	65.55±13.50[b]
High Dose = 100 mg/kg[a]			
Time (Days)	Urine	Feces	Total
1	66.12±12.32	0.74±0.33	66.86±12.65
2	6.75±2.90	0.23±0.09	6.98±2.99
3	3.84±1.21	0.32±0.23	4.16±1.24
4	1.11±0.15	0.43±0.18	1.54±0.33
5	0.95±0.22	0.26±0.08	1.21±0.30
6 & 7	0.67±0.26	0.28±0.11	0.94±0.37
Cumulative	79.44±10.60	2.25±0.37	81.69±10.97[b]

[a] All doses include a ^{14}C tracer ≅ 40 μCi/kg.

[b] Analysis of variance between doses shows no significant differences in excreta.

Table 2. Summary of the % dose recovered in tissues and excreta vs time from rats (n=3) following oral administration of acrylamide.

Tissue	Percent of Dose ± Standard Deviation		
	Low Dose 1 mg/kg	Medium Dose 10 mg/kg	High Dose 100 mg/kg
Brain	0.152±0.036	0.107±0.025	0.098±0.014
Lung	0.169±0.061	0.113±0.031	0.094±0.041
Liver	1.07±0.154	0.905±0.217	0.717±0.482
Kidney	0.219±0.021	0.192±0.039	0.125±0.039
Small Intestine	0.275±0.099	0.183±0.038	0.159±0.076
Fat	0.876±0.157	0.615±0.364	0.442±0.236
Muscle	4.93±0.799	4.21±0.691	3.46±1.01
Skin	2.02±1.32	2.58±1.33	0.820±0.243
Sciatic Nerve	0.006±0.004	0.004±0.002	0.003±0.001
Spinal Cord	0.026±0.015	0.024±0.016	0.008±0.002
Blood	10.08±5.19	8.13±2.10	5.85±3.61
Subtotal	19.83±7.37	17.34±3.41	11.81±5.36
Urine	67.11±13.06	58.68±12.79	79.44±10.60
Feces	7.32±3.21	6.87±0.71	2.25±0.37
Total	94.26±15.34	82.89±13.26	93.50±11.88

Table 3. nMoles acrylamide as ^{14}C equivalents excreted over 7 days following oral administration of acrylamide (n=3).

	Mean nMoles ± Standard Deviation		
Low Dose = 1 mg/kg			
Time (Days)	Urine	Feces	Total
1	996±172	82.5±53.4	1,078±225
2	94.8±38.5	25.9±10.2	121±48.7
3	62.0±16.1	3.4±0.3	65.4±16.4
4	26.8±1.92	4.5±1.4	31.3±3.32
5	9.52±1.91	4.6±1.1	14.1±3.01
6 & 7	0	10.2±2.2	10.2±2.2
Medium Dose = 10 mg/kg			
Time (Days)	Urine	Feces	Total
1	9,227±2,444	893±90	10,120±2,534
2	490±204	96.3±17.2	586±221
3	527±216	115±58	642±274
4	356±84	61.1±10.0	417±94
5	267±52	56.7±12.7	324±64
6 & 7	201±130	76.4±31.3	277±161
High Dose = 100 mg/kg			
Time (Days)	Urine	Feces	Total
1	124,144±31,547	1,400±726	125,544±32,273
2	12,462±4,974	436±184	12,898±5,158
3	7,213±2,259	596±94	7,809±2,353
4	2,072±308	810±335	2,882±643
5	1,756±279	477±163	2,233±442
6 & 7	1,217±391	507±174	1,724±565

Table 4. nMoles acrylamide as ^{14}C equivalents recovered in tissues 7 days after oral administration of acrylamide.

Tissue	Mean nMoles ± Standard Deviation		
	Low Dose 1 mg/kg	Medium Dose 10 mg/kg	High Dose 100 mg/kg
Brain	2.7±0.7	20.0±3.6	184.5±38.4
Lung	3.0±1.0	21.4±6.4	173.6±74.2
Liver	19.1±3.5	169.3±30.8	1,307±804.5
Kidney	3.9±0.5	36.1±6.8	233.6±75.4
Small Intestine	4.9±1.6	34.3±6.4	291.4±121.1
Fat	15.5±2.0	113.8±62.6	809.7±389.2
Muscle	88.3±17.6	791.6±108.4	6,461±2,033
Skin	36.3±24.9	483.8±247.8	1,545±563
Sciatic Nerve	0.1±0.1	0.7±0.4	5.5±3.2
Spinal Cord	0.5±0.3	4.4±2.7	14.9±5.7
Blood	182.0±99.8	1519±310	10,955±7,052

Table 5. Tissue to blood ratios 7 days following oral administration of acrylamide.

Tissue	Mean ± Standard Deviation (n=3)		
	Low Dose 1 mg/kg	Medium Dose 10 mg/kg	High Dose 100 mg/kg
Brain	0.126±0.024	0.107±0.020	0.142±0.015
Lung	0.208±0.025	0.194±0.035	0.222±0.090
Liver	0.203±0.031	0.211±0.042	0.236±0.161
Kidney	0.197±0.012	0.217±0.036	0.193±0.067
Small Intestine	0.046±0.004	0.046±0.006	0.051±0.011
Fat	0.112±0.020	0.097±0.054	0.097±0.052
Muscle	0.088±0.014	0.094±0.014	0.107±0.030
Skin	0.088±0.014	0.094±0.014	0.107±0.030
Sciatic Nerve	0.191±0.127	0.163±0.050	0.126±0.029
Spinal Cord	0.148±0.070	0.149±0.039	0.125±0.041
Blood	1	1	1

Table 6. Summary of percentage of dose and nMoles acrylamide as ^{14}C equivalents excreted over time following iv administration of 10 mg/kg acrylamide to male Fisher 344 rats (n=3).

Time (Days)	Urine		Feces		Total	
	% Dose Mean ± SD	nMoles Mean ± SD	% Dose Mean ± SD	nMoles Mean ± SD	% Dose Mean ± SD	nMoles Mean ± SD
1	62.00 ±15.33	13,067 ±4,888	4.82 ±3.09	923 ±420	66.82 ±18.42	13,990 ±5,308
2	4.01 ±1.01	836 ±300	0.577 ±0.090	119 ±27.4	4.59 ±1.91	955 ±327
3	1.40 ±0.18	294 ±82.0	0.216 ±0.077	46.4 ±22.2	1.62 ±0.257	340 ±104
4	1.11 ±0.12	230 ±56.1	0.109 ±0.048	23.7 ±13.0	1.22 ±0.168	254 ±69.1
5	1.38 ±0.68	301 ±177	0.131 ±0.019	27.2 ±6.54	1.51 ±0.699	328 ±183
6	0.599 ±0.014	124 ±25.2	0.074 ±0.018	15.4 ±5.79	0.673 ±0.032	139 ±31.0
7	0.416 ±0.069	87.7 ±28.2	0.087 ±0.044	18.1 ±10.5	0.503 ±0.113	106 ±38.7
Cumulative	70.92 ±16.54	14,940 ±4,901	6.01 ±3.04	1,173 ±421.9	76.93 ±19.58	16,113 ±5,323

Table 7.1 Summary of the % dose recovered in tissues and excreta versus time from rats following iv administration of 10 mg/kg acrylamide (n=3).

Tissue	15 min	30 min	1 hr	2 hr	4 hr	8 hr	12 hr	1 day	2 days	3 days	5 days	7 days
Brain	0.857 ±0.082	(0.737)	0.831 ±0.053	0.766 ±0.177	0.740 ±0.064	0.439 ±0.070	0.282 ±0.044	0.143 ±0.096	0.146 ±0.005	0.119 ±0.004	0.088 ±0.013	0.074 ±0.010
Lung	0.920 ±0.114	(0.637)	0.737 ±0.051	0.5611 ±0.116	0.494 ±0.03	0.251 ±0.058	0.227 ±0.076	0.159 ±0.008	0.175 ±0.033	0.147 ±0.095	0.132 ±0.033	0.082 ±0.020
Liver	6.25 ±1.02	(5.57)	6.95 ±0.46	6.55 ±0.40	5.36 ±0.37	2.77 ±0.30	2.02 ±0.45	1.58 ±0.09	1.13 ±0.071	0.945 ±0.162	0.700 ±0.492	0.342 ±0.091
Kidney	1.42 ±0.19	(1.24)	1.89 ±0.21	1.77 ±0.361	1.34 ±0.23	0.755 ±0.047	0.472 ±0.021	0.323 ±0.060	0.2461 ±0.0261	0.182 ±0.004	0.176 ±0.0571	0.107 ±0.009
Small Intestine	4.511 ±0.37	(4.49)	3.301 ±1.48	4.241 ±0.98	2.31 ±0.21	1.62 ±0.36	0.728 ±0.252	0.432 ±0.010	0.185 ±0.026	0.192 ±0.026	0.115 ±0.038	0.098 ±0.039
Fat	1.53 ±0.46	(1.20)	6.62 ±5.50	3.57 ±3.45	3.37 ±2.11	0.758 ±0.133	1.16 ±1.13	0.524 ±0.054	0.3011 ±0.110	0.408 ±0.159	1.02 ±1.17	0.293 ±0.100
Muscle	46.6 ±4.0	(50.2)	43.1 ±1.9	41.61 ±1.84	16.5 ±5.7	13.5 ±3.4	10.82 ±1.29	7.82 ±0.15	5.67 ±0.341	4.59 ±0.63	4.68 ±0.50	4.19 ±2.36
Skin	13.191 ±2.03	(16.1)	15.4 ±3.2	9.94 ±2.39	14.6 ±3.4	7.39 ±4.27	5.97 ±1.14	7.30 ±1.12	4.01 ±3.45	1.92 ±0.52	4.46 ±1.61	1.98 ±1.36
Sciatic Nerve	01019 ±0.006	(0.013)	0.018 ±0.003	0.016 ±0.003	0.012 ±0.005	0.010 ±0.003	0.007 ±0.003	0.0031 ±0.002	0:002 ±0.001	0.003 ±0.0003	0.002 ±0.001	0.002 ±0.0002
Spinal Cord	0.149 ±0.063	(0.203)	0.115 ±0.049	0.171 ±0.017	0.092 ±0.015	0.075 ±0.0041	0.049 ±0.036	0.026 ±0.010	0.027 ±0.014	0.019 ±0.011	0.0181 ±0.006	0.021 ±0.010
Testes	1.41* ±0142	1.65* ±0.45	1.82 ±0.35	1.69* ±0.42	1.53*1 ±0.24	1.33* ±0.06	0.79* ±0.14	0.45* ±0.03	--	(0.22)	--	--
Blood	9.07 ±3.01	(9.56)	11.8 ±0.5	12.1 ±1.5	13.3 ±0.9	10.7 ±1.4	11.4 ±0.6	11.8 ±0.6	12.5 ±1.0	11.7 ±1.2	10.6 ±1.9	12.4 ±1.9
Plasma	2.90* ±0.37	3.05 ±0.37	3.39* ±0.791	2.95*1 ±0.39	1.74* ±0.12	0.91* ±0.12	0.50* ±0.15	0.29* ±0.10	--	(0.13)	--	--
Intestinal contents & feces	3.14 ±1.07	(2.99)	5.89 ±0.55	4.96 ±0.67	3.79 ±0.47	1.96 ±0.49	3.79 ±1.82	0.448 ±0.016	0.260 ±0.023	0.150 ±0.006	0.142 ±0.071	--
Urine & bladder contents	0.478 ±0.635	(3.82)	4.22 ±2.12	9.38 ±2.59	(22.35)	51.2 ±3.25	50.8 ±6.0	(0.068)	(0.048)	0.083 ±0.119	0.017	--
Injection site	3.31 ±1.29	(4.25)	2.41 ±0.47	1.57 ±0.34	1.16 ±0.56	0.690 ±0.049	1.04 ±0.50	0.763 ±0.294	0.663 ±0.347	0.558 ±0.273	0.417 ±0.039	0.504 ±0.116
Subtotal	92.30 ±5.27	(102.6)	110.3 ±1.4	98.92 ±2.50	(98.12)	96.07 ±3.65	89.48 ±6.78	81.93 ±1.66	25.31 ±3.62	21.231 ±0.461	22.53 ±3.73	20.93 ±3.36
Cumulative mean urine	--	--	--	--	--	--	--	62.00 ±15.33	65.99 ±15.36	67.52 ±15.37	69.92 ±15.37	71.08 ±16.92
Cumulative mean feces	--	--	--	--	--	--	--	4.32 ±3.09	5.40 ±3.09	5.62 ±3.09	5.87 ±3.09	6.02 ±3.04
Total % dose recovered	92.30 ±5.27	(102.6)	110.3 ±1.4	98.92 ±2.50	(98.12)	96.07 ±3.65	89.48 ±6.78	98.75 ±15.73	96.701 ±16.08	94.36 ±15.68	98.32 ±16.12	98.03 ±19.09

* (n=4)

Values in parentheses are the average of 2 rats.

Table 8. Summary of nMoles acrylamide as ^{14}C equivalents (mean±S.D.) found in tissues following iv administration of 10 mg/kg acrylamide to rats (n=3).

Tissue	15 min	30 min*	1 hr	2 hr	4 hr	8 hr	12 hr	1 day	2 days	3 days	5 days	7 days
Brain	195.6 ±9.6	(184.9)	215.0 ±23.5	183.7 ±42.4	185.2 ±10.9	110.5 ±20.8	72.19 ±14.36	47.89 ±4.52	35.46 ±0.47	25.86 ±0.82	20.45 ±3.46	15.68 ±4.74
Lung	209.9 ±16.7	(157.8)	179.0 ±2.9	134.6 ±27.9	123.8 ±5.7	60.52 ±15.76	58.48 ±22.20	39.77 ±3.08	40.15 ±8.78	32.11 ±20.67	30.91 ±8.42	16.88 ±4.44
Liver	1427 ±211	(1393)	1692 ±72	1572 ±96	1345 ±85	662.6 ±57.5	513.8 ±124.2	396.7 ±9.0	259.2 ±9.8	206.1 ±35.4	164.9 ±120.6	73.15 ±29.73
Kidney	323.9 ±42.6	(310.0)	386.3 ±37.6	425.0 ±20.7	337.0 ±67.1	181.5 ±19.0	120.1 ±6.6	81.52 ±18.34	56.27 ±3.74	39.75 ±0.95	41.02 ±14.28	22.14 ±4.83
Small Intestine	1029 ±175	(1114)	913.1 ±303.2	1017 ±234	580.3 ±78.6	391.0 ±103.7	183.4 ±53.3	108.3 ±6.7	42.27 ±4.81	41.93 ±5.59	26.97 ±9.78	20.91 ±10.68
Fat	347.1 ±89.0	(301.0)	1566 ±1217	857.0 ±827.8	846.3 ±531.3	181.4 ±29.9	284.9 ±263.9	131.1 ±9.0	69.03 ±25.25	88.91 ±34.61	235.5 ±267.8	58.22 ±7.84
Muscle	10644 ±1352	(12621)	11718 ±1048	9983 ±441	6696 ±1723	3748 ±971	2691 ±196	1960 ±74	1299 ±84	715.1 ±552.8	1091 ±139	852.9 ±523.6
Skin	3031 ±588	(4069)	3780 ±940	2386 ±692	3681 ±973	1885 ±996	1519 ±305	1834 ±321	913 ±789	327.7 ±262.9	1044 ±406	568.0 ±253.7
Sciatic Nerve	4.25 ±1.23	(3.24)	4.42 ±0.43	3.85 ±0.79	2.99 ±1.35	2.31 ±0.85	1.52 ±0.71	0.77 ±0.51	0.50 ±0.21	0.72 ±0.07	0.49 ±0.19	0.31 ±0.06
Spinal cord	33.78 ±13.58	(50.41)	28.16 ±12.67	41.13 ±4.15	22.99 ±3.97	18.05 ±1.40	16.50 ±6.78	6.48 ±2.12	5.98 ±2.85	4.11 ±2.43	4.19 ±1.27	4.34 ±2.55
Blood	2077 ±697	(2406)	2874 ±227	2910 ±350	3323 ±121	2569 ±230	2903 ±277	2974 ±261	2866 ±360	2550 ±266	2550 ±266	2610 ±826

* Values in parentheses are the average of 2 rats.

Table 9. Tissue (g):Blood (ml) ratios ± S.D. following iv administration of 10 mg/kg acrylamide to rats (n=3).

Tissue	15 min	30 min*	1 hr	2 hr	4 hr	8 hr	12 hr	1 day	2 days	3 days	5 days	7 days
Brain	0.94 ±0.23	(0.85)	0.72 ±0.09	0.66 ±0.20	0.56 ±0.07	0.41 ±0.12	0.24 ±0.02	0.15 ±0.01	0.11 ±0.02	0.09 ±0.01	0.09 ±0.02	0.06 ±0.00
Lung	1.23 ±0.46	(0.90)	0.91 ±0.04	0.64 ±0.09	0.58 ±0.05	0.37 ±0.05	0.28 ±0.08	0.21 ±0.04	0.23 ±0.07	0.16 ±0.03	0.23 ±0.03	0.15 ±0.05
Liver	1.36 ±0.33	(1.17)	1.20 ±0.04	1.00 ±0.12	0.80 ±0.03	0.58 ±0.07	0.36 ±0.07	0.26 ±0.04	0.17 ±0.03	0.16 ±0.04	0.15 ±0.05	0.10 ±0.02
Kidney	1.50 ±0.26	(1.19)	1.35 ±0.21	1.45 ±0.14	1.09 ±0.19	0.74 ±0.20	0.41 ±0.01	0.28 ±0.04	0.22 ±0.03	0.16 ±0.02	0.18 ±0.01	0.12 ±0.00
Small Intestine	1.30 ±0.44	(1.17)	1.31 ±0.35	1.16 ±0.10	0.71 ±0.06	0.44 ±0.11	0.23 ±0.05	0.14 ±0.01	0.08 ±0.02	0.04 ±0.01	0.05 ±0.01	0.03 ±0.01
Fat	0.23 ±0.10	(0.17)	0.73 ±0.61	0.40 ±0.41	0.32 ±0.20	0.09 ±0.02	0.13 ±0.14	0.06 ±0.01	0.03 ±0.01	0.04 ±0.01	0.14 ±0.18	0.03 ±0.02
Muscle	1.01 ±0.40	(0.95)	0.74 ±0.04	0.62 ±0.05	0.36 ±0.10	0.27 ±0.09	0.17 ±0.03	0.12 ±0.01	0.08 ±0.01	0.07 ±0.02	0.08 ±0.02	0.06 ±0.03
Skin	0.89 ±0.33	(0.95)	0.74 ±0.17	0.47 ±0.16	0.62 ±0.16	0.42 ±0.23	0.29 ±0.05	0.35 ±0.04	0.19 ±0.17	0.09 ±0.03	0.23 ±0.04	0.15 ±0.12
Sciatic Nerve	0.98 ±0.38	(0.53)	0.73 ±0.20	0.53 ±0.11	0.43 ±0.15	0.32 ±0.08	0.24 ±0.12	0.10 ±0.04	0.09 ±0.05	0.13 ±0.02	0.08 ±0.03	0.05 ±0.01
Spinal Cord	0.62 ±0.21	(0.81)	0.71 ±0.21	0.66 ±0.11	0.38 ±0.04	0.30 ±0.05	0.15 ±0.10	0.11 ±0.03	0.10 ±0.02	0.07 ±0.05	0.10 ±0.05	0.07 ±0.03
Blood	1	1	1	1	1	1	1	1	1	1	1	1

* Values in parentheses represent average of 2 rats.

Table 10. Percentage of dose in blood and plasma vs time after iv administration of acrylamide (10 mg/kg).

Sample time	Rat #	Hematocrit	% of Dose in Blood	mean±Std. Dev.	% of Dose in Plasma	mean±Std. Dev.
15 min.	70	0.43	10.49	11.14±1.54	2.42	2.90±0.37
	71	0.37	9.26		2.86	
	80	0.47	12.37		3.31	
	81	0.43	12.42		3.03	
30 min	73	0.40	11.02	12.61±1.69	2.64	3.05±0.37
	82	0.50	12.45		3.36	
	83	0.47	14.38		3.15	
1 hour	66	0.37	12.73	13.58±1.41	3.17	3.39±0.79
	67	0.47	12.04		2.40	
	77	0.50	14.60		4.24	
	92	0.50	14.95		3.76	
2 hours	64	0.33	11.98	14.35±2.62	3.03	2.95±0.39
	65	0.40	12.37		2.38	
	93	0.50	17.40		3.14	
	94	0.50	15.66		3.25	
4 hours	62	0.33	12.84	14.49±2.12	1.86	1.74±0.12
	63	0.33	12.50		1.82	
	84	0.43	15.96		1.63	
	85	0.43	16.66		1.63	
8 hours	60	0.37	12.00	11.58±2.05	0.88	0.91±0.12
	61	0.33	13.28		1.08	
	86	0.47	12.44		0.81	
	87	0.50	8.61		0.88	
12 hours	75	0.47	12.36	13.64±1.86	0.62	0.50±0.15
	76	0.43	12.69		0.61	
	88	0.50	16.39		0.47	
	89	0 43	13.10		0 30	
1 day	72	0.43	11.27	13.55±2.38	0.36	0.29±0.10
	74	0.43	13.21		0.37	
	90	0.45	12.82		0.16	
	91	0.50	16.90		0.27	
3 days	78	0.43	15.16	(14.86)	0.15	(0.13)
	79	0.43	14.57		0.12	

Table 11. Percentage of parent acrylamide in selected tissues vs time after iv administration of acrylamide (10 mg/kg).

Time	15 min		30 min		1 hour		2 hours		4 hours	
Rat #	80	81	82	83	77	92	93	94	84	85
Tissue	% Parent									
Brain	47.42	49.98	52.64	55.07	*	*	*	*	*	*
Lung	48.42	52.31	47.12	50.22	*	*	*	*	*	*
Liver	26.80	26.80	25.40	22.07	23.07	29.70	19.32	18.87	4.13	3.50
Kidney	31.36	33.87	38.91	38.44	37.72	32.01	22.77	25.72	5.73	6.77
Small Intestine	54.88	53.90	49.71	56.58	45.00	44.66	41.95	49.51	27.98	32.41
Fat	50.49	65.65	58.81	63.57	56.54	44.37	62.28	41.63	30.50	30.85
Muscle	82.89	84.75	92.65	94.05	90.68	77.33	77.13	79.63	63.96	67.51
Skin	73.76	76.20	83.11	86.74	76.91	84.34	82.37	86.56	I.S.	66.50
Spinal Cord	53.88	52.02	65.48	55.63	*	*	*	*	*	*
Testes	N.D.	5.21	4.43	3.85	I.S.	22.26	10.84	11.41	N.D.	4.07
Intestinal Contents	76.96	71.07	58.48	59.99	11.43	66.26	63.00	54.32	28.91	32.27
Blood	48.45	44.17	37.33	35.08	40.60	37.73	27.32	28.31	19.98	11.72

* Tissue not analyzed because contained <1% of the dose.

I.S.= Insufficient sample for analysis.

N.D.= Below our limits of detection (<1% parent in tissue).

Table 11. Percentage of parent acrylamide in selected tissues vs time after iv administration of acrylamide (10 mg/kg)--Continued.

Time	8 hours		12 hours		1 day	
Rat #	86	87	88	89	90	91
Tissue	% Parent					
Liver	1.00	2.26	N.D.	N.D.	N.D.	N.D.
Small Intestine	7.87	12.88	*	*	*	*
Fat	N.D.	26.82	N.D.	N.D.	*	*
Muscle	40.40	39.01	8.43	N.D.	N.D.	N.D.
Skin	29.72	46.78	31.90	32.82	N.D.	N.D.
Testes	1.44	N.D.	*	*	*	*
Intestinal Contents	20.42	24.85	N.D.	N.D.	*	*
Blood	1.61	3.44	N.D.	N.D.	N.D.	N.D.

* Tissue not analyzed because contained <1% of the dose.

I.S. = Insufficient sample for analysis.

N.D. = Below our limits of detection (<1% parent in tissues).

Table 12. Summary of percentage of dose as parent acrylamide in selected tissues vs time after iv administration of acrylamide (10 mg/kg).

Time	15 min		30 min		1 hour		2 hours	
Rat #	80	81	82	83	77	92	93	94
Tissue	% of dose as parent							
Brain	0.496	0.434	0.451	0.650	*	*	*	*
Lung	0.279	0.305	0.245	0.300	*	*	*	*
Liver	1.548	1.773	1.227	1.202	1.137	1.758	1.022	0.945
Kidney	0.446	0.464	0.513	0.535	0.588	0.499	0.330	0.328
Small Intestine	1.478	1.233	1.223	1.463	1.417	1.376	1.127	1.119
Fat	1.076	1.064	4.298	1.58	0.775	0.395	1.84	1.87
Muscle	48.15	46.45	45.55	46.55	42.82	38.49	31.78	27.73
Skin	10.19	11.36	12.92	12.82	9.68	12.68	3.73	8.79
Spinal Cord	0.114	0.052	0.099	0.097	*	*	*	*
Testes	ND	0.082	0.088	0.080	I.S.	0.470	0.197	0.253
Intestinal Contents	0.885	1.128	0.856	0.777	0.172	0.442	1.899	0.803
Blood	5.992	5.488	4.649	5.044	5.962	5.641	4.752	4.431

* Tissue not analyzed because contained <1% of the dose.

I.S. = Insufficient sample for analysis.

N.D. = Below our limits of detection (<1% parent in tissue).

Table 12. Summary of percentage of dose as parent acrylamide in selected tissues vs time after iv administration of acrylamide (10 mg/kg)--Continued.

Time	4 hours		8 hours		12 hours		1 day	
Rat #	84	85	86	87	88	89	90	91
Tissue	% of dose as parent							
Liver	0.167	0.175	0.033	0.062	N.D.	N.D.	N.D.	N.D.
Kidney	0.080	0.097	*	*	*	*	*	*
Small Intestine	0.674	0.502	1.17	1.19	*	*	*	*
Fat	1.06	0.226	N.D.	1.39	N.D.	N.D.	*	*
Muscle	17.24	22.26	7.09	6.93	1.02	N.D.	N.D.	N.D.
Skin	I.S.	5.80	3.72	3.22	0.833	0.371	N.D.	N.D.
Testes	N.D.	0.073	0.020	N.D.	*	*	*	*
Intestinal contents	0.569	0.897	0.339	0.524	N.D.	N.D.	*	*
Blood	3.18	1.95	0.200	0.296	N.D.	N.D.	N.D.	N.D.

* Tissue not analyzed because contained <1% of the dose.

I.S. = Insufficient sample for analysis.

N.D. = Below our limits of detection (<1% parent in tissue).

Table 13. Summary of percentage of dose found in selected tissues vs time following iv administration of acrylamide (10 mg/kg).

Time	15 min		30 min		1 hour		2 hours		4 hours	
Rat #	80	81	82	83	77	92	93	94	84	85
Tissue	% of dose									
Brain	1.406	0.869	0.856	1.181						
Lung	0.576	0.583	0.520	0.597						
Liver	5.777	6.615	4.830	5.448	4.927	5.924	5.288	5.003	4.042	5.000
Kidney	1.423	1.371	1.318	1.391	1.558	1.561	1.451	1.274	1.399	1.441
Small Intestine	2.694	2.288	2.461	2.586	3.148	3.083	2.687	2.261	2.410	1.552
Fat	2.131	1.621	7.308	2.480	1.372	0.890	2.95	4.49	3.49	0.731
Muscle	58.09	54.80	49.16	49.38	47.22	49.77	41.21	34.82	26.95	33.01
Skin	13.81	14.91	15.54	14.78	12.59	15.04	4.53	10.16	7.624	8.728
Spinal Cord	0.211	0.100	0.152	0.175						
Testes	1.922	1.574	1.982	2.080		2.111	1.821	2.215	1.259	1.802
Intestinal contents	1.150	1.587	1.464	1.296	1.505	0.667	3.015	3.319	1.973	2.783
Blood	12.37	12.43	12.45	14.38	14.60	14.95	17.40	15.66	15.96	16.66

Table 13. Summary of percentage of dose found in selected tissues vs time following iv administration of acrylamide (10 mg/kg)--Continued.

Time	8 hours		12 hours		1 day		3 days	
Rat #	86	87	88	89	90	91	78	79
Tissue	% of dose							
Liver	3.300	2.739	2.104	1.847	1.316	1.328	1.594	1.152
Small Intestine	1.492	1.484						
Fat	1.220	5.191	2.640	1.064	0.586	0.108	0.937	1.040
Muscle	17.55	17.76	12.14	9.774	8.427	7.595	5.551	6.851
Skin	12.52	6.894	2.609	1.128	1.135	1.780	5.519	0.872
Testes	1.369	1.380	0.996	0.723	0.416	0.561	0.226	0.212
Intestinal Contents	1.659	2.107	0.831	0.452	0.142	0.103	0.249	0.082
Blood	12.44	8.612	16.38	13.10	12.82	16.90	15.16	14.57

Table 14. Percentage of Parent acrylamide in urine 5 days* after iv administration of acrylamide (10 mg/kg).

Rat #	19	20	21	
1	2.27	2.43	2.70	2.47±0.22
2	7.07	2.55	2.30	3.97±2.68
3	2.53	1.73	2.81	2.36±0.56
4	2.32	1.70	2.88	2.30±0.59
5	3.36	0.46	0.36	1.39±1.70

* The % Parent excreted after 5 days was below the acceptable detection limits.

Table 15. Percentage of dose as parent acrylamide in urine 5 days* after iv administration of acrylamide (10 mg/kg).

Rat #	19	20	21	
Time (days)	Percentage of dose			Mean ± S.D.
1	1.18	1.93	1.47	1.53 ±0.38
2	0.255	0.132	0.075	0.154±0.091
3	0.032	0.028	0.038	0.033±0.005
4	0.024	0.017	0.036	0.026±0.010
5	0.023	0.007	0.007	0.012±0.009

* The % Parent excreted after 5 days was below the acceptable detection limits.

Table 16. Total ^{14}C in Tissues.

Organ	A_1 %	a_1 hr^{-1}	$T_{1/2}^{a_1}$ hr	A_2	a_2 hr^{-1}	$T_{1/2}^{a_2}$ hr	a_3 hr^{-1}	r
Brain	0.781 ±0.069	0.13643 ±0.02217	5.08 ±0.83	0.158 ±0.024	0.004488 ±0.001408	154.44 ±48.45	-	0.993
Sciatic nerve	0.0150 ±0.0019	0.11947 ±0.02867	5.80 ±1.39	0.0032 ±0.0007	0.003855 ±0.002087	179.80 ±97.34	-	0.985
Spinal cord	0.148 ±0.018	0.14462 ±0.03027	4.79 ±1.00	0.0235 ±0.0051	0.001213 ±0.00198	571.43 ±933.70	-	0.983
Lung	0.650 ±0.072	0.25580 ±0.05365	2.71 ±0.57	0.201 ±0.023	0.004652 ±0.001139	149.00 ±36.48	-	0.989
Small intestine	4.427 ±0.395	0.16247 ±0.01846	4.27 ±0.49	0.299 ±0.055	0.007070 ±0.001668	98.04 ±23.13	-	0.996
Skin	11.153 ±2.438	0.06236 ±0.03464	11.12 ±6.17	2.816 ±1.301	0.00003209 ±0.00493915	21600.1†	-	0.922
Muscle	46.905 ±3.028	0.19941 ±0.01952	3.48 ±0.34	6.762 ±0.651	0.003145 ±0.000922	220.40 ±64.61	-	0.996
Fat	7.917 ±10.633	0.28462 ±0.20340	2.44 ±1.74	0.497 ±0.227	0.003417 ±0.004723	202.85 ±280.38	1.01983 ±0.98339	0.928
Liver	6.490 ±1.074	0.21007 ±0.04930	3.30 ±0.77	1.865 ±0.248	0.009491 ±0.001289	73.03 ±9.92	4.98589 ±1.84736	0.994
Kidney	1.717 ±0.287	0.16814 ±0.03686	4.12 ±0.90	0.321 ±0.055	0.006175 ±0.001611	112.25 ±29.29	3.97024 ±1.42253	0.991
Testes	1.800 ±0.279	0.08371 ±0.02921	8.28 ±2.89	0.212 ±0.320	0.00002793 ±0.020286	24817.3 ±1.8 E7	4.775 ±1.110	0.995
Plasma	3.869 ±0.305	0.25058 ±0.02314	2.77 ±0.26	0.400 ±0.059	0.01559 ±0.00261	44.46 ±7.44	4.793 ±0.964	0.999
Blood *	11.719 ±0.370	5.28626 ±0.94247	-	-	0.000001102 ±0.000421887	628990†	-	0.738
Blood **	13.633 ±0.391	6.571 ±1.364	-	-	-	-	-	0.688

* Data obtained from Table 7.

** Data obtained from Table 10.

† The terminal slope cannot be accurately determined.

Table 17. Parent Acrylamide.

Organ	A_1	a_1	$T_{1/2}^{a_1}$	a_3	r
	%	hr^{-1}	hr	hr^{-1}	
Liver	1.875 ±0.254	0.48291 ±0.03592	1.44 ±0.11	-	0.973
Muscle	55.809 ±4.421	0.29554 ±0.01610	2.35 ±0.13	-	0.984
Skin	12.920 ±2.037	0.23369 ±0.02702	2.97 ±0.34	-	0.934
Blood	7.936 ±1.096	0.40138 ±0.03662	1.73 ±0.16	-	0.961
Kidney	1.136 ±0.136	0.63591 ±0.03961	1.09 ±0.07	2.974 ±0.415	0.994
Testes	1.159 ±5.617	0.50698 ±0.49899	1.37 ±1.35	1.159 ±5.617	0.881
Urine	1.733 ±0.012	0.08832 ±0.00445	7.85 ±0.40	-	0.981