

## ADME NTP Study S0611 Lauric acid diethanolamine condensate

The contract laboratory abbreviation for the test article is LDEA.

Sex/Species: adult male F344 rats and B6C3F1 mice.

Vehicles: intravenous, water:Emulphor 10:1; oral gavage, water; dermal, 95% ethanol.

CASRN 120-40-1

Radiolabeled with carbon-14 randomly on the diethanolamine (DEA) moiety; [<sup>14</sup>C]Lauric acid diethanolamine condensate.

### Lauric acid diethanolamine condensate Studies Performed:

1. Single 25 mg/kg intravenous administration in rats with sacrifice 72 hours postdose. (Tables 1 and 2)
2. Single 25 mg/kg intravenous administration in rats with serial sacrifice at 0.25, 0.75, 2, 6, and 24 hours. (Tables 3 and 4)
3. Single 1000 mg/kg oral gavage administration in rats with sacrifice 72 hours postdose. (Table 5)
4. Single 25 or 400 mg/kg dermal administration in rats with sacrifice 72 hours postdose (with dose site covered – Tables 6, 7, 8, and 9)
5. Single 100 mg/kg dermal administration in rats with blood collection up to 24 hours. (with dose site covered – Tables 10 and 11)
6. Repeat 25 mg/kg/day dermal exposure in rats for up to 3 weeks with (Table 12) and without (Table 13) covered dose sites; determination of percent absorption at 6, 24, 48, and 72 hours after each radiolabeled dose.
7. Single 50 mg/kg intravenous administration in mice with serial sacrifice at 0.25, 0.75, 2, 6, 24, and 72 hours postdose. (Table 14)
8. Single 50 mg/kg dermal administration in mice with sacrifice 72 hours postdose (with dose site covered – Table 15)
9. Single 100 mg/kg dermal administration in mice with sacrifice 72 hours postdose (with dose site covered – Table 16)
10. Single 200 mg/kg dermal administration in mice with sacrifice 72 hours postdose (with dose site covered – Table 17)
11. Single 800 mg/kg dermal administration in mice with sacrifice 72 hours postdose (with dose site covered – Table 18)

In the repeat dermal dose study, two groups of rats (with and without protective appliances) were dosed 5 days per week for 19 days (25/mg/kg/day) with Day 1 being a Monday. Radiolabeled doses were applied on days 3, 7, and 17. Animals were housed in metabolism cages for 72 hours after each radiolabeled dose to allow for collection of urine and feces. In addition to the initial dose area preparation, the dose site area of each rat was clipped and washed with water soaked gauzes on days 8 and 15 (new foam appliance were added after washing for the protected dose site group). Animals were sacrificed 72 hours after application of the last radiolabeled dose.

Serial blood samples were taken (Tables 4, 10, 11, and 14) but no pharmacokinetic analysis was performed.

Note on Accessibility: Persons with disabilities or using assistive technology may find some documents are not fully accessible. For assistance, contact [Central Data Management](#) or use our [contact form](#) and identify the documents/pages for which access is required. We will assist you in accessing the content of the files. NIEHS has helpful information on accessibility.

**Table 1****Cumulative Excretion of Radioactivity 72 h after Intravenous Administration of [<sup>14</sup>C]LDEA (25 mg/kg) to Male F-344 Rats<sup>a</sup>**

End of Collection Period (h)	Percent of Dose Recovered in:				
	Urine	Feces	Breath	CO <sub>2</sub>	Total
6 h	51.7 ± 13.6				51.7 ± 13.6
8 h			0.0 ± 0.0	0.1 ± 0.0	51.8 ± 13.6
24 h	81.2 ± 4.0	4.5 ± 1.1	0.0 ± 0.0	0.2 ± 0.0	85.9 ± 3.5
32 h			0.0 ± 0.0	0.2 ± 0.0	85.9 ± 3.5
48 h	84.7 ± 2.6	6.4 ± 0.8	0.0 ± 0.0	0.2 ± 0.0	91.2 ± 1.9
56 h			0.0 ± 0.0	0.3 ± 0.0	91.3 ± 1.9
72 h	86.1 ± 2.1	6.6 ± 0.8	0.0 ± 0.0	0.3 ± 0.0	93.0 ± 1.4

<sup>a</sup> N=4

**Table 2****Tissue Distribution of Radioactivity 72 h after Intravenous Administration of [<sup>14</sup>C]LDEA (25 mg/kg) to Male F-344 Rats<sup>a</sup>**

Tissue	ng-eq LDEA per g Tissue	Tissue/Blood Ratio	% Dose in Total Tissue
Adipose	3389 ± 830	48 ± 12	1.04 ± 0.23
Adrenal gland	2490 ± 580	35 ± 8	0.00324 ± 0.00172
Blood	71 ± 1	unity	0.016 ± 0.001
Brain	317 ± 36	4.5 ± 0.5	0.00970 ± 0.00139
Kidney	1576 ± 63	22 ± 1	0.0498 ± 0.002
Liver	4228 ± 785	59 ± 11	0.659 ± 0.137
Lung	483 ± 34	6.8 ± 0.5	0.0127 ± 0.0009
Muscle	174 ± 16	2.4 ± 0.2	0.366 ± 0.037
Prostate	796 ± 142	11 ± 2	0.00337 ± 0.00071
Seminal vesicle	608 ± 60	8.5 ± 0.9	0.00567 ± 0.00177
Skin	939 ± 135	13 ± 2	0.705 ± 0.137
Spleen	492 ± 26	6.9 ± 0.4	0.00514 ± 0.00017
Testis	192 ± 15	2.7 ± 0.2	0.00946 ± 0.00097
Total in Tissue			2.9 ± 0.3

<sup>a</sup> N=4

**Table 3**

Cumulative Excretion of Radioactivity after Intravenous Administration of [<sup>14</sup>C]LDEA (25 mg/kg) to Male F-344 Rats

End of Collection Period	Percent of Dose Recovered in:		
	Urine	Feces	Total
<b>15 min</b>			
15 min	3.0 ± 0.7	a	3.0 ± 0.7
<b>45 min</b>			
45 min	14.8 ± 7.9	0.3 ± 0.5	15.0 ± 8.1
<b>2 h</b>			
2 h	24.5 ± 13.9	a	24.5 ± 13.9
<b>6 h</b>			
6 h	71.4 ± 1.3	0.0 ± 0.0	71.4 ± 1.3
<b>24 h</b>			
24 h	81.3 ± 2.1	7.0 ± 0.8	88.3 ± 1.6

<sup>a</sup> No sample collected.

**Table 4**

**Distribution of Radioactivity after Intravenous Administration of [14C]LDEA (25 mg/kg) to Male F-344 Rats<sup>a</sup>**

Tissue	ng-eq LDEA per g Tissue	Tissue/Blood Ratio	% Dose in Total Tissue
<b>15 minutes</b>			
Adipose	11800 ± 3000	0.844 ± 0.090	3.23 ± 0.79
Adrenal gland	43500 ± 5800	3.17 ± 0.12	0.0306 ± 0.0049
Blood	13800 ± 2100	unity	2.81 ± 0.40
Brain	41400 ± 6100	3.01 ± 0.03	1.10 ± 0.16
Kidney	93600 ± 12500	6.18 ± 0.32	2.72 ± 0.33
Liver	200000 ± 34000	14.7 ± 2.7	28.7 ± 4.1
Lung	26900 ± 2700	1.97 ± 0.23	0.471 ± 0.142
Muscle	15900 ± 2100	1.16 ± 0.02	29.8 ± 3.7
Plasma	17600 ± 6300	1.25 ± 0.30	1.59 ± 0.56
Prostate	25600 ± 4500	1.86 ± 0.04	0.111 ± 0.030
Seminal vesicle	17900 ± 2600	1.30 ± 0.15	0.180 ± 0.005
Skin	14200 ± 2500	1.03 ± 0.03	9.50 ± 1.56
Spleen	21100 ± 4000	1.53 ± 0.09	0.181 ± 0.032
Testis	10300 ± 1700	0.748 ± 0.032	0.405 ± 0.068
<b>Total in Tissue</b>			<b>80.9 ± 8.8</b>
<b>45 minutes</b>			
Adipose	8800 ± 5110	1.56 ± 0.59	2.44 ± 1.42
Adrenal gland	10900 ± 3700	2.05 ± 0.09	0.00854 ± 0.00371
Blood	5310 ± 1830	unity	1.09 ± 0.37
Brain	13500 ± 7300	2.39 ± 0.69	0.349 ± 0.179
Kidney	88000 ± 28700	16.7 ± 1.3	2.44 ± 0.86
Liver	206000 ± 102000	36.9 ± 7.8	33.1 ± 15.6
Lung	11500 ± 3200	2.22 ± 0.20	0.259 ± 0.118
Muscle	4040 ± 2120	0.726 ± 0.215	7.69 ± 4.04
Plasma	10900 ± 5500	1.98 ± 0.56	0.990 ± 0.501
Prostate	23200 ± 11400	4.26 ± 0.90	0.109 ± 0.051
Seminal vesicle	11900 ± 6300	2.18 ± 0.70	0.116 ± 0.051
Skin	6380 ± 3250	1.14 ± 0.28	4.29 ± 2.19
Spleen	4420 ± 1630	0.825 ± 0.055	0.0413 ± 0.0158
Testis	6160 ± 3170	1.10 ± 0.28	0.260 ± 0.137
<b>Total in Tissue</b>			<b>53.0 ± 25.3</b>

**Table 4 (continued)**

**Distribution of Radioactivity after Intravenous Administration of  
[<sup>14</sup>C]LDEA (25 mg/kg) to Male F-344 Rats**

Tissue	ng-eq LDEA per g Tissue	Tissue/Blood Ratio	% Dose in Total Tissue
<b>2 hours</b>			
Adipose	5150 ± 2660	1.74 ± 0.46	1.41 ± 0.70
Adrenal gland	8860 ± 7990	2.88 ± 1.85	0.00589 ± 0.00459
Blood	2810 ± 830	unity	0.573 ± 0.158
Brain	3640 ± 1090	1.31 ± 0.17	0.0918 ± 0.251
Kidney	48800 ± 20500	17.1 ± 3.1	1.33 ± 0.49
Liver	106000 ± 35800	37.1 ± 4.2	15.6 ± 5.4
Lung	6970 ± 2680	2.51 ± 0.66	0.128 ± 0.036
Muscle	1480 ± 440	0.543 ± 0.159	2.78 ± 0.75
Plasma	4560 ± 1420	1.61 ± 0.05	0.411 ± 0.120
Prostate	61400 ± 84600	17.7 ± 22.7	0.265 ± 0.323
Seminal vesicle	21600 ± 33000	6.15 ± 8.91	0.323 ± 0.515
Skin	4010 ± 2580	1.34 ± 0.50	2.65 ± 1.64
Spleen	2410 ± 690	0.871 ± 0.164	0.0227 ± 0.0053
Testis	2020 ± 810	0.703 ± 0.079	0.0850 ± 0.0300
Total in Tissue			25.4 ± 9.4
<b>6 hours</b>			
Adipose	8260 ± 1610	12.9 ± 3.15	2.32 ± 0.43
Adrenal gland	2830 ± 590	4.39 ± 0.77	0.00205 ± 0.00052
Blood	644 ± 29	unity	0.135 ± 0.007
Brain	682 ± 14	1.06 ± 0.03	0.0183 ± 0.0008
Kidney	7870 ± 190	12.2 ± 0.7	0.222 ± 0.006
Liver	24400 ± 2700	37.9 ± 2.5	3.75 ± 0.25
Lung	2170 ± 160	3.37 ± 0.25	0.0547 ± 0.0084
Muscle	343 ± 22	0.534 ± 0.057	0.662 ± 0.045
Plasma	913 ± 76	1.42 ± 0.10	0.0845 ± 0.0085
Prostate	2730 ± 780	4.26 ± 1.22	0.0112 ± 0.0053
Seminal vesicle	2290 ± 2300	3.54 ± 3.51	0.0278 ± 0.0256
Skin	2620 ± 270	4.08 ± 0.49	1.79 ± 0.15
Spleen	1050 ± 30	1.63 ± 0.10	0.00988 ± 0.00027
Testis	484 ± 48	0.753 ± 0.073	0.0210 ± 0.0012
Total in Tissue			9.11 ± 0.25

**Table 4 (continued)**

**Distribution of Radioactivity after Intravenous Administration of  
[<sup>14</sup>C]LDEA (25 mg/kg) to Male F-344 Rats**

Tissue	ng-eq LDEA per g Tissue	Tissue/Blood Ratio	% Dose in Total Tissue
<b>24 hours</b>			
Adipose	6080 ± 750	34.0 ± 6.0	1.70 ± 0.21
Adrenal gland	2000 ± 220	11.3 ± 2.3	0.00158 ± 0.00019
Blood	181 ± 22	unity	0.0376 ± 0.0043
Brain	353 ± 11	1.97 ± 0.19	0.00960 ± 0.00066
Kidney	1540 ± 100	8.59 ± 0.48	0.0430 ± 0.0011
Liver	5820 ± 520	32.7 ± 5.9	0.899 ± 0.110
Lung	850 ± 170	4.73 ± 0.89	0.0174 ± 0.0020
Muscle	216 ± 2	1.21 ± 0.16	0.416 ± 0.006
Plasma	261 ± 36	1.44 ± 0.03	0.0240 ± 0.0032
Prostate	1090 ± 310	6.23 ± 2.55	0.00465 ± 0.00060
Seminal vesicle	421 ± 54	2.37 ± 0.55	0.00641 ± 0.00085
Skin	1670 ± 170	9.39 ± 1.91	1.14 ± 0.12
Spleen	680 ± 20	3.81 ± 0.44	0.00606 ± 0.00008
Testis	204 ± 4	1.14 ± 0.13	0.00905 ± 0.00025
<b>Total in Tissue</b>			<b>4.32 ± 0.28</b>

<sup>a</sup> N=3



Table 5

Disposition of Radioactivity following Oral Administration  
of [<sup>14</sup>C]LDEA (1000 mg/kg) to Male F-344 Rats<sup>a</sup>

Tissue	ng-eq LDEA per g Tissue	Tissue/Blood Ratio	% Dose in Total Tissue
Adipose	391000 ± 33000	55.5 ± 7.8	2.81 ± 0.38
Blood	7090 ± 790	unity	0.0378 ± 0.0059
Kidney	129000 ± 2000	18.4 ± 2.1	0.0882 ± 0.0044
Liver	321000 ± 26000	45.8 ± 8.0	1.34 ± 0.11
			Total in tissues = 4.27 ± 0.49

Percent of Dose Appearing in:

End of Collection Period (h)	Urine	Feces	Total
6	9.7 ± 1.8	—	9.7 ± 1.8
24	60.4 ± 6.9	3.7 ± 1.8	64.1 ± 7.5
48	74.4 ± 3.5	8.7 ± 0.8	83.2 ± 2.7
72	79.0 ± 1.6	9.3 ± 1.0	88.3 ± 0.6

<sup>a</sup> N=3

**Table 6**

**Cumulative Excretion of Radioactivity 72 h after Dermal Administration of [<sup>14</sup>C]LDEA to Male F-344 Rats<sup>a</sup>**

**25 mg/kg**

Collection Interval	Percent of Dose Recovered in:		
	Urine	Feces	Total
0-6 h	ND <sup>b</sup>		ND
6-24 h	32 ± .7	0.1 ± 0.0	3.4 ± 0.7
24-48 h	10.7 ± 2.4	0.6 ± 0.1	11.3 ± 2.5
48-72 h	19.7 ± 5.2	1.1 ± 0.2	20.9 ± 5.3

**400 mg/kg**

Collection Interval	Percent of Dose Recovered in:		
	Urine	Feces	Total
0-6 h	ND <sup>b</sup>		ND
6-24 h	3.9 ± 2	0.1 ± 0.0	4.0 ± 2.1
24-48 h	11.9 ± 5.3	0.4 ± 0.2	12.3 ± 5.5
48-72 h	24.1 ± 9.4	0.9 ± 0.3	25.0 ± 9.7

<sup>a</sup> N=4

<sup>b</sup> ND = none detected

**Table 7**  
**Disposition of Radioactivity 72 h after Dermal Application**  
**of [<sup>14</sup>C]LDEA to Male F-344 Rats<sup>a</sup>**

	% Dose Appearing In:	
	25 mg/kg	400 mg/kg
<b>Absorbed</b>		
Tissues	0.82 ± 0.19	1.1 ± 0.3
Urine	19.7 ± 5.2	24.1 ± 9.4
Feces	1.1 ± 0.2	0.9 ± 0.3
Dose site	4.65 ± 1.16	3.17 ± 1.17
<b>Total</b>	<b>26.3 ± 6.4</b>	<b>29.2 ± 9.6</b>
<b>Unabsorbed</b>		
Appliance	22.6 ± 11.3	25.0 ± 6.5
Skin Wash	41.0 ± 9.5	31.9 ± 6.3
Gauze	5.50 ± 1.63	6.35 ± 6.10
<b>Total</b>	<b>69.1 ± 6.0</b>	<b>63.3 ± 9.7</b>
<b>Total Recovery</b>	<b>95.4 ± 0.9</b>	<b>92.5 ± 0.6</b>

<sup>a</sup> N=4

**Table 8**

**Tissue Distribution of Radioactivity 72 h after Dermal Administration of [<sup>14</sup>C]LDEA (25 mg/kg) to Male F-344 Rats<sup>a</sup>**

Tissue	ng-eq LDEA per g Tissue	Tissue/Blood Ratio	% Dose in Total Tissue
Adipose	490 ± 180	7.7 ± 2.2	0.15 ± 0.05
Adrenal gland	430 ± 80	7.0 ± 1.4	0.00043 ± 0.00007
Blood	64 ± 19	unity	0.014 ± 0.004
Brain	67 ± 14	1.1 ± 0.2	0.0020 ± 0.0005
Kidney	1118 ± 257	18 ± 3	0.0343 ± 0.0076
Liver	2487 ± 445	40 ± 6	0.374 ± 0.064
Lung	338 ± 75	5.7 ± 2.3	0.00852 ± 0.00325
Muscle	56 ± 11	0.90 ± 0.12	0.12 ± 0.02
Prostate	512 ± 509	7.0 ± 5.2	0.00182 ± 0.00204
Seminal vesicle	339 ± 220	4.8 ± 2.0	0.00360 ± 0.00255
Skin	160 ± 40	2.5 ± 0.4	0.12 ± 0.03
Spleen	226 ± 31	3.7 ± 1.1	0.00205 ± 0.00038
Testis	74 ± 26	1.1 ± 0.1	0.0035 ± 0.0013
Total in Tissue =			0.82 ± 0.17

<sup>a</sup> N=4

Table 9

Tissue Distribution of Radioactivity 72 h after Dermal Administration of [<sup>14</sup>C]LDEA (400 mg/kg) to Male F-344 Rats<sup>a</sup>

Tissue	ng-eq LDEA per g Tissue	Tissue/Blood Ratio	% Dose in Total Tissue
Adipose	10700 ± 4900	6.5 ± 1.2	0.197 ± 0.087
Adrenal gland	10000 ± 4000	6.5 ± 1.0	0.00066 ± 0.00031
Blood	1600 ± 500	unity	0.022 ± 0.007
Brain	1970 ± 520	1.2 ± 0.1	0.00363 ± 0.00102
Kidney	37750 ± 7500	24 ± 3	0.0624 ± 0.0135
Liver	52410 ± 13540	33 ± 3	0.445 ± 0.113
Lung	5550 ± 1630	3.5 ± 0.6	0.00887 ± 0.00237
Muscle	1400 ± 300	0.87 ± 0.14	0.17 ± 0.03
Prostate	4200 ± 1400	2.6 ± 0.5	0.00145 ± 0.00026
Seminal vesicle	3550 ± 490	2.3 ± 0.6	0.00174 ± 0.00042
Skin	3500 ± 900	2.2 ± 0.2	0.16 ± 0.04
Spleen	4400 ± 940	2.8 ± 0.6	0.00241 ± 0.00060
Testis	1600 ± 300	1.0 ± 0.2	0.00417 ± 0.00090
Total in Tissue =			1.1 ± 0.3

<sup>a</sup> N=4

Table 10

Plasma and Blood Levels of LDEA Equivalents following Dermal Administration of [14C]LDEA (100 mg/kg) to Male F-344 Rats

Blood  
(ng/g blood)

Collection time	Rat 1	Rat 2	Rat 3	Rat 4	Mean ± Standard Deviation
15 min	2.43	5.87	3.84	9.81	5.49 ± 3.21
6 h	44.9	117	244	302	177 ± 117
24 h	405	464	626	834	582 ± 192
30 h	483	476	633	805	599 ± 155
48 h	547	621	680	826	669 ± 118
72 h	550	473	552	726	575 ± 107

Plasma  
(ng/g plasma)

Collection time	Rat 1	Rat 2	Rat 3	Rat 4	Mean ± Standard Deviation
15 min	4.21	b	7.13	4.83	4.04 ± 2.97
6 h	66.5	175	342	400	246 ± 153
24 h	574	587	863	1160	796 ± 278
30 h	615	644	837	1120	803 ± 231
48 h	688	802	882	1100	867 ± 173
72 h	600	549	674	826	662 ± 121

a N=4

b Below level of quantitation.

Table 11

Composition of LDEA Equivalents in Plasma following Dermal Administration of [<sup>14</sup>C]LDEA (100 mg/kg) to Male F-344 Rats

Rat 2

Collection time	LDEA (nmole/g plasma)	Metabolites nmole eq / g plasma
15 min	0.047	0.081
6 h	0.132	0.559
24 h	0.237	1.52
30 h	0.213	1.44
48 h	0.293	1.89
72 h	0.191	1.24

Rat 1

Collection time	LDEA (nmole/g plasma)	Metabolites nmole eq / g plasma
24 h	0.210	1.25
72 h	0.241	1.21

Rat 3

Collection time	LDEA (nmole/g plasma)	Metabolites nmole eq / g plasma
24 h	0.423	2.11
72 h <sup>1</sup>	—	—

<sup>1</sup> HPLC malfunction, sample consumed.

Rat 4

Collection time	LDEA (nmole/g plasma)	Metabolites nmole eq / g plasma
24 h	0.553	2.89
72 h	0.244	1.73

<sup>a</sup> N=4

**Table 12**

**Cumulative Excretion of Radiolabel over 72 h following Successive Dermal Administration of [<sup>14</sup>C]LDEA (25 mg/kg/day) in a 3-Week Repeat Dosing Regimen<sup>a</sup> Male F-344 Rats with Protected Dose Sites Used<sup>b</sup>**

**Day 3**

<b>End of Collection Period(h)</b>	<b>Urine</b>	<b>Feces</b>	<b>Total</b>
6	0.191 ± 0.126		0.191 ± 0.126
24	2.84 ± 1.41	0.0969 ± 0.0474	2.93 ± 1.45
48	6.01 ± 2.44	0.311 ± 0.116	6.32 ± 2.55
72	9.69 ± 3.39	0.520 ± 0.172	10.2 ± 3.56

**Day 10**

<b>End of Collection Period(h)</b>	<b>Urine</b>	<b>Feces</b>	<b>Total</b>
6	0.174 ± 0.0628		0.174 ± 0.0628
24	3.20 ± 1.93	0.0625 ± 0.0465	3.27 ± 1.97
48	7.76 ± 4.26	0.331 ± 0.186	8.09 ± 4.44
72	13.1 ± 6.76	0.684 ± 0.298	13.8 ± 7.03

**Day 17**

<b>End of Collection Period(h)</b>	<b>Urine</b>	<b>Feces</b>	<b>Total</b>
6	0.320 ± 0.373		0.320 ± 0.373
24	5.69 ± 2.42	0.123 ± 0.058	5.81 ± 2.48
48	14.0 ± 6.54	0.521 ± 0.233	14.5 ± 6.76
72	22.4 ± 7.43	0.992 ± 0.389	23.4 ± 7.80

**a** Unlabeled LDEA administered on all days except for Days 3, 10, and 17. [<sup>14</sup>C]LDEA was administered on Days 3, 10, and 17.

**b** N=5



**Table 13****Cumulative Excretion of Radiolabel over 72 h following Successive Dermal Administration of [<sup>14</sup>C]LDEA (25 mg/kg/day) in a 3-Week Repeat Dosing Regimen<sup>a</sup> Male F-344 Rats with Dose Sites Unprotected<sup>b</sup>****Day 3**

End of Collection Period (h)	Urine	Feces	Total
6	11.2 ± 7.50		11.2 ± 7.50
24	57.0 ± 22.1	4.33 ± 2.72	61.3 ± 19.8
48	70.3 ± 16.5	7.71 ± 3.19	78.0 ± 13.3
72	76.5 ± 11.6	8.70 ± 4.34	85.2 ± 7.26

**Day 10**

End of Collection Period (h)	Urine	Feces	Total
6	2.00 ± 1.87		2.00 ± 1.87
24	32.2 ± 10.8	1.82 ± 0.8	34.0 ± 11.4
48	53.1 ± 11.0	5.16 ± 1.64	58.3 ± 11.2
72	65.3 ± 7.42	6.87 ± 1.87	72.1 ± 7.97

**Day 17**

End of Collection Period (h)	Urine	Feces	Total
6	4.36 ± 2.99		4.36 ± 2.99
24	36.3 ± 8.35	1.18 ± 0.21	37.5 ± 8.45
48	55.0 ± 7.00	5.68 ± 2.56	60.7 ± 7.08
72	66.9 ± 5.29	7.24 ± 2.44	74.1 ± 5.72

<sup>a</sup> Unlabeled LDEA administered on all days except for Days 3, 10, and 17. [<sup>14</sup>C]LDEA was administered on Days 3, 10, and 17.

<sup>b</sup> N=5

Table 14

Disposition and Excretion of Radioactivity after Intravenous Administration of [<sup>14</sup>C]LDEA (50 mg/kg) to Male B6C3F1 Mice

End of Collection Period	Percent of Dose Recovered in:		
	Urine	Feces	Total
15 min			
15 min	10.2 ± 13.2	a	10.2 ± 13.2
45 min			
45 min	15.2 ± 7.4	0.0300 ± 0.0117	15.3 ± 7.4
2 h			
2 h	56.6 ± 1.8	0.0812 ± 0.0241	56.7 ± 1.7
6 h			
6 h	71.5 ± 10.8	0.249 ± 0.376	71.8 ± 11.1
24 h			
24 h	87.1 ± 3.7	7.61 ± 1.26	94.7 ± 4.9
72 h			
48 h	72.2 ± 10.4	7.3 ± 3.3	80.7 ± 11.1
72 h	77.3 ± 7.4	12.8 ± 4.4	90.0 ± 6.4

<sup>a</sup> None detected

<sup>b</sup> No sample collected

Tissue	ng-eq LDEA per g Tissue	Tissue/Blood Ratio	% Dose in Total Tissue
15 minutes			
Adipose	34000 ± 9060	1.53 ± 0.39	6.72 ± 1.81
Adrenal gland	74400 ± 6300	3.35 ± 0.23	0.0377 ± 0.00930
Blood	22300 ± 3000	unity	3.42 ± 0.45
Brain	64300 ± 10900	2.87 ± 0.12	2.07 ± 0.28
Kidney	136000 ± 27000	6.06 ± 0.59	4.27 ± 0.84
Liver	255000 ± 11000	11.6 ± 1.3	25.8 ± 2.47
Lung	49600 ± 7000	2.22 ± 0.04	0.547 ± 0.108
Muscle	25700 ± 2700	1.15 ± 0.08	23.3 ± 2.3
Plasma	28700 ± 7600	1.27 ± 0.19	
Prostate	50500 ± 19100	2.27 ± 0.75	0.118 ± 0.052
Seminal vesicle	16100 ± 1300	0.730 ± 0.097	0.263 ± 0.022
Skin	19600 ± 2300	0.882 ± 0.069	5.73 ± 0.62
Spleen	29500 ± 4100	1.32 ± 0.00	0.157 ± 0.025
Testis	16000 ± 2900	0.715 ± 0.041	0.229 ± 0.056
Total in Tissue			72.7 ± 4.2

Table 14 (continued)

Disposition and Excretion of Radioactivity after Intravenous Administration of [<sup>14</sup>C]LDEA (50 mg/kg) to Male B6C3F1 Mice

Tissue	ng-eq LDEA per g Tissue	Tissue/Blood Ratio	% Dose in Total Tissue
<b>45 minutes</b>			
Adipose	27500 ± 4700	3.32 ± 0.90	5.45 ± 1.0
Adrenal gland	35200 ± 7700	4.16 ± 0.50	0.0136 ± 0.0042
Blood	8440 ± 1340	unity	1.30 ± 0.21
Brain	15600 ± 2000	1.86 ± 0.21	0.454 ± 0.064
Kidney	123000 ± 76000	14.0 ± 6.6	3.75 ± 2.41
Liver	193000 ± 25000	23.1 ± 3.5	19.7 ± 2.7
Lung	15400 ± 1600	1.84 ± 0.11	0.177 ± 0.019
Muscle	5150 ± 470	0.617 ± 0.086	4.66 ± 0.34
Plasma	14200 ± 3800	1.67 ± 0.22	
Prostate	82400 ± 45700	10.5 ± 6.9	0.253 ± 0.172
Seminal vesicle	11200 ± 6500	1.44 ± 1.04	0.146 ± 0.086
Skin	8460 ± 1380	1.00 ± 0.07	2.47 ± 0.38
Spleen	6180 ± 250	0.742 ± 0.091	0.0338 ± 0.0029
Testis	9700 ± 2160	1.17 ± 0.32	0.144 ± 0.037
Total in Tissue			38.6 ± 5.3
<b>2 hours</b>			
Adipose	18000 ± 8000	4.74 ± 3.62	3.60 ± 1.62
Adrenal gland	20500 ± 9200	5.07 ± 3.10	0.0120 ± 0.0084
Blood	4820 ± 2320	unity	0.748 ± 0.364
Brain	3780 ± 800	0.848 ± 0.197	0.132 ± 0.041
Kidney	32200 ± 7400	7.32 ± 2.38	1.03 ± 0.237
Liver	78400 ± 21000	18.5 ± 8.4	8.15 ± 1.91
Lung	9130 ± 1710	2.06 ± 0.53	0.109 ± 0.023
Muscle	3130 ± 1320	0.796 ± 0.485	2.87 ± 1.20
Plasma	8220 ± 2140	2.00 ± 1.18	
Prostate	25800 ± 4100	5.97 ± 2.04	0.0948 ± 0.0336
Seminal vesicle	2700 ± 1300	0.0705 ± 0.567	0.0397 ± 0.0174
Skin	9210 ± 8340	2.37 ± 2.26	2.72 ± 2.45
Spleen	2890 ± 200	0.686 ± 0.287	0.0142 ± 0.0038
Testis	3580 ± 1780	0.931 ± 0.765	0.0565 ± 0.0277
Total in Tissue			19.5 ± 5.1

Table 14 (continued)

Disposition and Excretion of Radioactivity after Intravenous Administration of [<sup>14</sup>C]LDEA (50 mg/kg) to Male B6C3F1 Mice

Tissue	ng-eq LDEA per g Tissue	Tissue/Blood Ratio	% Dose in Total Tissue
<b>6 hours</b>			
Adipose	20400 ± 6700	11.2 ± 3.7	4.07 ± 1.31
Adrenal gland	13000 ± 3400	7.45 ± 3.14	0.00917 ± 0.00370
Blood	2050 ± 1080	unity	0.318 ± 0.166
Brain	903 ± 137	0.583 ± 0.420	0.0327 ± 0.0042
Kidney	10900 ± 2000	7.01 ± 5.08	0.340 ± 0.063
Liver	19200 ± 500	12.6 ± 9.3	1.90 ± 0.20
Lung	5580 ± 920	3.36 ± 1.83	0.0672 ± 0.0170
Muscle	4100 ± 4040	2.25 ± 1.61	3.76 ± 3.66
Plasma	2590 ± 1340	1.27 ± 0.04	
Prostate	39700 ± 26000	17.7 ± 5.5	0.169 ± 0.109
Seminal vesicle	8950 ± 6900	3.95 ± 2.12	0.123 ± 0.081
Skin	7170 ± 6240	3.80 ± 2.34	2.12 ± 1.82
Spleen	2030 ± 990	1.12 ± 0.46	0.0105 ± 0.0032
Testis	2280 ± 1440	1.04 ± 0.22	0.0360 ± 0.0238
Total in Tissue			13.0 ± 6.2
<b>24 hours</b>			
Adipose	4640 ± 1370	35.4 ± 14.0	0.931 ± 0.277
Adrenal gland	2610 ± 780	19.9 ± 8.7	0.00170 ± 0.00042
Blood	136 ± 20	unity	0.0212 ± 0.0029
Brain	337 ± 94	2.45 ± 0.42	0.0125 ± 0.0036
Kidney	1880 ± 90	14.0 ± 1.7	0.0604 ± 0.0035
Liver	4560 ± 760	33.4 ± 1.9	0.492 ± 0.049
Lung	2590 ± 210	19.2 ± 1.9	0.0300 ± 0.0044
Muscle	265 ± 104	1.96 ± 0.78	0.242 ± 0.089
Plasma	197 ± 23	1.45 ± 0.05	
Prostate	724 ± 260	5.28 ± 1.53	0.00254 ± 0.00145
Seminal vesicle	265 ± 49	1.96 ± 0.44	0.00407 ± 0.00072
Skin	533 ± 180	3.86 ± 1.04	0.157 ± 0.051
Spleen	524 ± 19	3.89 ± 0.61	0.00371 ± 0.00132
Testis	224 ± 31	1.65 ± 0.17	0.00369 ± 0.00048
Total in Tissue			1.97 ± 0.32

Table 14 (continued)

Disposition and Excretion of Radioactivity after Intravenous Administration of [<sup>14</sup>C]LDEA (50 mg/kg) to Male B6C3F1 Mice

Tissue	ng-eq LDEA per g Tissue		Tissue/Blood Ratio		% Dose in Total Tissue	
<b>72 hours</b>						
Adipose	2560 ±	1230	26.8 ±	10.7	0.524 ±	0.236
Adrenal gland	2180 ±	1650	22.5 ±	16.5	0.00233 ±	0.00186
Blood	93 ±	16	unity		0.0149 ±	0.0025
Brain	443 ±	132	4.73 ±	1.13	0.0151 ±	0.0039
Kidney	1540 ±	360	16.9 ±	4.8	0.0506 ±	0.0104
Liver	2670 ±	680	29.0 ±	7.7	0.345 ±	0.066
Lung	1490 ±	340	16.2 ±	4.1	0.0170 ±	0.0024
Muscle	248 ±	47	2.72 ±	0.62	0.235 ±	0.0318
Prostate	866 ±	249	9.24 ±	1.83	0.00311 ±	0.00094
Seminal vesicle	562 ±	153	6.11 ±	1.64	0.00675 ±	0.00188
Skin	414 ±	162	4.37 ±	1.24	0.126 ±	0.046
Spleen	450 ±	54	4.95 ±	0.96	0.00345 ±	0.00089
Testis	404 ±	64	4.38 ±	0.57	0.00598 ±	0.00049
Total in tissues =					1.35 ±	0.33

Table 15

Disposition of Radioactivity following Dermal Administration  
of [<sup>14</sup>C]LDEA (50 mg/kg) to Male B6C3F1 Mice<sup>a</sup>

Tissue	ng-eq LDEA per g Tissue	Tissue/Blood Ratio	% Dose in Total Tissue
Adipose	810 ± 174	13.5 ± 8.6	0.214 ± 0.039
Adrenal gland	549 ± 311	7.30 ± 3.44	0.0005 ± 0.0003
Blood	116 ± 137	unity	0.0236 ± 0.0270
Brain	137 ± 98	1.65 ± 0.56	0.00599 ± 0.00389
Kidney	1740 ± 1890	16.7 ± 4.1	0.0737 ± 0.0756
Liver	2280 ± 2450	22.2 ± 6.6	0.300 ± 0.301
Lung	504 ± 334	6.35 ± 2.72	0.00847 ± 0.00524
Muscle	160 ± 64	2.36 ± 1.36	0.194 ± 0.072
Prostate	362 ± 137	5.50 ± 3.48	0.00051 ± 0.00038
Seminal vesicle	269 ± 105	3.90 ± 1.96	0.00381 ± 0.00187
Skin	243 ± 121	3.41 ± 1.90	0.0949 ± 0.0448
Spleen	223 ± 88	3.27 ± 1.82	0.00136 ± 0.00043
Testis	147 ± 14	2.49 ± 1.62	0.00298 ± 0.00039
Total in tissue =			0.923 ± 0.546

Percent of Dose Appearing in:

End of Collection Period (h)	Urine	Feces	Total
6	1.3 ± 1.4	—	1.3 ± 1.4
24	15.8 ± 4.3	2.5 ± 1.9	18.4 ± 5.4
48	22.2 ± 5.9	7.0 ± 2.5	29.2 ± 8.1
72	32.2 ± 7.5	10.3 ± 2.1	42.6 ± 9.3

% Dose Appearing In:	
<b>Absorbed</b>	
Tissues	0.923 ± 0.546
Urine	32.2 ± 7.5
Feces	10.3 ± 2.1
Dose site	5.63 ± 0.98
<b>Total</b>	49.1 ± 9.5
<b>Unabsorbed</b>	
Appliance	0.810 ± 0.967
Skin wash	40.4 ± 7.3
Gauze	1.27 ± 0.65
<b>Total</b>	42.5 ± 6.6
<b>Total Recovery</b>	91.6 ± 6.5

<sup>a</sup> N=4

**Table 16**

**Disposition of Radioactivity following Dermal Administration  
of [<sup>14</sup>C]LDEA (100 mg/kg) to Male B6C3F1 Mice**

Tissue	ng-eq LDEA per g Tissue	Tissue/Blood Ratio	% Dose in Total Tissue
Adipose	2980 ± 1480	23.3 ± 8.1	0.289 ± 0.149
Adrenal gland	1970 ± 210	15.9 ± 1.6	0.00060 ± 0.00026
Blood	125 ± 22	unity	0.00936 ± 0.00184
Brain	304 ± 41	2.44 ± 0.11	0.00529 ± 0.00065
Kidney	2410 ± 200	19.5 ± 2.1	0.0357 ± 0.0047
Liver	4080 ± 150	33.4 ± 6.4	0.167 ± 0.014
Lung	1400 ± 240	11.2 ± 1.0	0.00840 ± 0.00124
Muscle	291 ± 97	2.29 ± 0.41	0.129 ± 0.046
Prostate	1040 ± 250	8.58 ± 2.83	0.00072 ± 0.00047
Seminal vesicle	658 ± 191	5.29 ± 1.36	0.00316 ± 0.00082
Skin	373 ± 17	3.06 ± 0.70	0.0531 ± 0.0024
Spleen	693 ± 147	5.53 ± 0.61	0.00174 ± 0.00033
Testis	386 ± 44	3.11 ± 0.26	0.00280 ± 0.00039
Total in Tissue			0.699 ± 0.193

**Percent of Dose Appearing in:**

End of Collection Period (h)	Urine	Feces	Total
6	ND <sup>a</sup>	-	ND
24	23.4 ± 7.7	3.1 ± 0.5	26.5 ± 8.1
48	32.9 ± 14.4	13.0 ± 6.4	45.9 ± 10.5
72	48.6 ± 13.2	16.6 ± 7.8	65.2 ± 7.9

<sup>a</sup> ND=none detected

**% Dose Appearing In:**

<b>Absorbed</b>	
Tissues	0.699 ± 0.193
Urine	48.6 ± 13.2
Feces	16.6 ± 7.8
Dose site	1.02 ± 0.12
<b>Total</b>	<b>66.8 ± 8.2</b>
<b>Unabsorbed</b>	
Appliance cover	0.148 ± 0.137
Skin wash	14.6 ± 6.5
Gauze	1.56 ± 0.86
<b>Total</b>	<b>16.4 ± 7.0</b>
<b>Total Recovery</b>	<b>85.4 ± 34.0</b>

<sup>a</sup> N=4

Table 17

**Disposition of Radioactivity following Dermal Administration  
of [<sup>14</sup>C]LDEA (200 mg/kg) to Male B6C3F1 Mice**

Tissue	ng-eq LDEA per g Tissue	Tissue/Blood Ratio	% Dose in Total Tissue
Adipose	5640 ± 1680	20.5 ± 4.6	0.266 ± 0.071
Adrenal gland	3090 ± 780	11.3 ± 2.1	0.00048 ± 0.00024
Blood	276 ± 67	unity	0.0101 ± 0.0019
Brain	724 ± 116	2.66 ± 0.25	0.00599 ± 0.00094
Kidney	5380 ± 1240	19.7 ± 2.3	0.0412 ± 0.0078
Liver	8280 ± 2380	29.8 ± 2.3	0.167 ± 0.048
Lung	2740 ± 710	9.92 ± 1.34	0.00775 ± 0.00187
Muscle	687 ± 218	2.50 ± 0.58	0.149 ± 0.0414
Prostate	2480 ± 1250	8.75 ± 3.61	0.00093 ± 0.00074
Seminal vesicle	1300 ± 400	4.76 ± 1.32	0.00342 ± 0.00063
Skin	833 ± 193	3.03 ± 0.35	0.0581 ± 0.0110
Spleen	1460 ± 340	5.30 ± 0.59	0.00159 ± 0.00040
Testis	746 ± 153	2.73 ± 0.24	0.00268 ± 0.00040
Total in Tissue			0.714 ± 0.145

**Percent of Dose Appearing in:**

End of Collection Period (h)	Urine	Feces	Total
6	3.4 ± 4.0	-	3.4 ± 4.0
24	27.2 ± 7.7	4.0 ± 1.6	31.2 ± 6.9
48	43.1 ± 10.9	7.4 ± 1.6	50.6 ± 11.0
72	54.7 ± 11.2	14.1 ± 2.9	68.8 ± 11.0

**% Dose Appearing In:**

<b>Absorbed</b>	
Tissues	0.714 ± 0.145
Urine	54.7 ± 11.2
Feces	14.1 ± 2.9
Dose site	1.18 ± 0.46
<b>Total</b>	69.1 ± 13.5
<b>Unabsorbed</b>	
Appliance cover	0.379 ± 0.442
Skin wash	16.1 ± 12.6
Gauze	0.992 ± 0.168
<b>Total</b>	17.4 ± 12.3
<b>Total Recovery</b>	88.3 ± 1.3

<sup>a</sup> N=4



Table 18

Disposition of Radioactivity following Dermal Administration of [<sup>14</sup>C]LDEA (800 mg/kg) to Male B6C3F1 Mice<sup>a</sup>

Tissue	ng-eq LDEA per g Tissue	Tissue/ Blood Ratio	% Dose in Total Tissue
Adipose	18900 ± 8000	15.4 ± 5.5	0.228 ± 0.168
Adrenal gland	14500 ± 3500	12.3 ± 4.6	0.00059 ± 0.00016
Blood	1400 ± 830	unity	0.0150 ± 0.0096
Brain	3320 ± 820	2.91 ± 1.47	0.00828 ± 0.00190
Kidney	27900 ± 8900	22.8 ± 6.6	0.0600 ± 0.0237
Liver	33800 ± 13100	26.4 ± 5.4	0.245 ± 0.124
Lung	10800 ± 2700	9.12 ± 3.38	0.00879 ± 0.00316
Muscle	3720 ± 1220	3.17 ± 1.49	0.232 ± 0.089
Prostate	13700 ± 7400	11.8 ± 7.3	0.00098 ± 0.00068
Seminal vesicle	7740 ± 1460	7.14 ± 3.95	0.00517 ± 0.00211
Skin	10000 ± 3800	11.2 ± 10.8	0.196 ± 0.066
Spleen	6230 ± 410	5.85 ± 3.52	0.00212 ± 0.0008
Testis	4330 ± 520	3.96 ± 2.12	0.00419 ± 0.0006
Total in tissues			= 1.01 ± 0.35

Percent of Dose Appearing in:

End of Collection Period (h)	Urine	Feces	Total
6	1.4 ± 1.0	—	1.4 ± 1.0
24	14.1 ± 2.4	2.6 ± 1.0	16.7 ± 2.3
48	22.1 ± 2.7	4.9 ± 2.2	27.0 ± 1.3
72	36.6 ± 3.1	10.3 ± 4.8	46.9 ± 7.8

% Dose Appearing In:	
<b>Absorbed</b>	
Tissues	1.01 ± 0.35
Urine	36.6 ± 3.1
Feces	10.3 ± 4.8
Dose site	2.30 ± 1.12
<b>Total</b>	50.2 ± 8.8
<b>Unabsorbed</b>	
Appliance	1.43 ± 0.29
Skin wash	33.0 ± 28.0
Gauze	0.790 ± 0.381
<b>Total</b>	35.2 ± 28.5
<b>Total Recovery</b>	85.4 ± 34.0

<sup>a</sup> N=4