ADME NTP Study S0212 1-Amino-2,4-dibromoanthraquinone

The contractor used the abbreviation of ADBAQ for the test article.
Sex/Species: adult male F344 rats.
Vehicle: intravenous, rat serum; oral, corn oil.

CASRN 81-49-2

Radiolabeled with carbon-14 only in the rings; 1-Amino-2,4-dibromoanthraquinone, [Ring-UL-^{14}C]

Studies Performed:

- Single 0.4 mg/kg intravenous dose to rats with sacrifice at 72 hours postdose. (n = 3)
- Single 0.4 mg/kg intravenous dose to rats with sacrifice at 0.25, 0.75, 2, 6, or 24 hours postdose. (n = 3 per time point)
- Single 0.4 mg/kg intravenous dose to rats for bile collection with sacrifice at 6 hours postdose. (n = 3)
- Single 0.5, 2.0, 20.0, or 200.0 mg/kg oral gavage dose to rats with sacrifice 9 days postdose. (n = 3)

The amount of ADBAQ absorbed was calculated by comparing the urinary excretion or the excretion in breath of ^{14}C following an oral dose to that excreted following the 0.4 mg/kg intravenous dose. The breath excretion data was fitted to the equation: mg/kg absorbed = 6.68 log dose (mg/kg) – 0.263 (r = 0.999). At doses much below 2 mg/kg, this equation is not valid.

The elimination half-lives of ADBAQ in adipose, liver, and kidney are approximately 11, 38, and 90 hours, respectively.

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Table 1

Average Cumulative Excretion of Total ^{14}C After Intravenous Administration of 0.4 mg/kg of [^{14}C] ADBAQ (% Dose ± S.D.)[a]

Time (hr)	Urine	Feces	Breath	Total
1	0.37 ± 0.33			
2	1.1 ± 0.5			
3	1.9 ± 1.7			
4	2.6 ± 1.9			
5	3.3 ± 0.8			
6	3.4 ± 0.9			
7	4.4 ± 2.3			
8	4.5 ± 2.4	0.1 ± 0.1		
20.5	11.4 ± 0.4	23.2 ± 20.3		
24	12.0 ± 0.3		4.6 ± 0.2	
29	12.6 ± 0.2	36.5 ± 12.4		
44.5	13.9 ± 0.6	52.6 ± 4.9		
48			5.4 ± 0.3	
53	14.2 ± 0.5	53.3 ± 5.1		
72	14.8 ± 0.6	56.5 ± 4.9	5.8 ± 0.4	77.1 ± 4.3

[a]Tables in the origimal report Appendix have data from individual rats.

Table 2.

Cumulative Excretion of Total ^{14}C after Oral Administration of [^{14}C]ADBAQ[a]
(% Dose)

Dose (mg/kg)	2.0				23			
Excreta	Urine	Feces	Breath	Total	Urine	Feces	Breath	Total
Time (hr)								
6	0.34 ± 0.48			0.34 ± 0.48	0.00	0.00 ± 0.00		0.00 ± 0.00
7	0.38 ± 0.50			0.38 ± 0.50				
8	3.06 ± 0.17	0.17 ± 0.21		3.24 ± 0.05				
20.5	9.36 ± 1.81	34.1 ± 10.70		43.5 ± 11.1	6.40 ± 1.49	44.4 ± 22.7		50.8 ± 21.3
24	9.73 ± 1.83		4.45 ± 0.14	48.3 ± 11.4	7.44 ± 1.94		1.66 ± 0.22	53.5 ± 20.6
28.5	10.1 ± 1.9	50.5 ± 5.9		65.3 ± 5.2	7.94 ± 1.82	56.6 ± 15.6		66.2 ± 13.7
44.5	10.9 ± 1.9	56.8 ± 7.4		72.1 ± 7.10	10.0 ± 1.5	67.8 ± 8.4		79.5 ± 7.3
48			5.00 ± 0.19	72.7 ± 7.1			2.03 ± 0.33	80.0 ± 7.3
52.5	11.1 ± 1.9			72.9 ± 7.0	10.5 ± 1.5			80.3 ± 7.2
72	11.5 ± 1.9	60.9 ± 6.7	5.22 ± 0.20	77.7 ± 6.1	10.8 ± 1.6	75.0 ± 4.1	2.15 ± 0.36	88.0 ± 3.0

Dose (mg/kg)	118				814				1473[b]			
Excreta	Urine	Feces	Breath	Total	Urine	Feces	Breath	Total	Urine	Feces	Breath	Total
Time (hr)												
6	0.04 ± 0.06	0.01 ± 0.01		0 04 ± 0.07	0.07 ± 0.02	0.00 ± 0.00		0.07 ± 0.02	0.01	0.03		0.04
7												
8												
20.5	2.20 ± 0.10	28.6 ± 94		30.8 ± 9.2	0.74 ± 0 30	52.8 ± 20.30		53.6 ± 20.4	0.83	41.10		41.9
24	2.37 ± 0.15		0.44 ± 0.04	31.4 ± 9.2	0.93 ± 0.470		0.07 ± 0.02	53.9 ± 20 5	0.83		0.078	42.0
28.5	2.57 ± 0 23	40.9 ± 8.6		43.9 ± 8.5	1.25 ± 0.44	66.4 ± 12.50		67.7 ± 12.2	1.20	49.8		51.0
44.5	2.97 ± 0.32	61.4 ± 5.7		64 8 ± 5 4	1.91 ± 0.73	78.0 ± 5.20		80.0 ± 4.6	1.85	73.7		75.6
48			0.58 ± 0.04	65.0 ± 5.4			0.13 ± 0.03	80.1 ± 4 6			0.14	75.7
52.5	3 13 ± 0 40			66.8 ± 6.4	2.03 ± 0.76			80.2 ± 4.5	1.97			75.8
72	3.33 ± 0.65	64.7 ± 5.3	0.67 ± 0.07	68.7 ± 4 7	2.32 ± 0.91	83.7 ± 0 6	0.14 ± 0.03	86.2 ± 0.6	2.16	78.2	0.17	80.6

[a] Values are the average for 3 rats ± S.D. Tables in original report Appendix have data from individual rats.

[b] Only 1 rat was dosed at this level.

Table 3. Cumulative Biliary Excretion of ADBAQ and Metabolites After an Intravenous Dose of 0.40 mg/kg of [^{14}C]ADBAQ (% Dose)

End of Collection Period (Hr)	Rat 24	Rat 35	Rat 38	Average ± SD
0.25	7.9	8.7	10.9	9.2 ± 1.6
0.75	23.8	28.1	28.0	26.6 ± 2.4
1.0		33.1	32.4	32.8
2.0	37.7	45.4	45.8	43.0 ± 4.6
3.0	42.2	50.9	51.2	48.1 ± 5.1
4.0	45.1	53.8	53.9	50.9 ± 5.0
5.0	47.2	55.7	55.5	52.8 ± 4.8
6.0	48.8	57.1	56.8	54.2 ± 4.7

Table 4

Excretion of Unmetabolized ADBAQ in Bile and Urine Following a Single Intravenous Dose of 0.4 mg/kg of [^{14}C]ADBAQ

	Collection Period (hr)	Rat No.	ADBAQ (% Dose)	% of Total Excreted ^{14}C Accounted for by ADBAQ
Bile	0-0.25	24	0.2	2.2
	0.75-2.0	24	0.3	2.4
	0-6.0	24	1.5	3.0
	0-6.0	25	1.7	3.0
	0-6.0	38	1.5	2.6
Urine	2.0-3.0	593	0.083	3.2
	0-72	593	0.36	2.5
	0-72	594	0.35	2.3
	0-72	600	0.29	2.0

Table 5

Recovery of Radioactivity after Administration of ADBAQ to Rats

Time (hr)	Route	Dose (mg/kg)	% Dose[a] Recovered in						
			Urine	Feces	Breath	Selected Tissues	Cage Washes	Carcass	Total
0.25	IV	0.4				35.6 ± 2.5		51.4 ± 2.5	87.0 ± 3.5
0.75	IV	0.4				11.6 ± 0.46		73.2 ± 2.0	84.8 ± 2.1
2.0	IV	0.4				9.67 ± 0.61		71.3 ± 0.8	81.0 ± 1.0
6.0	IV	0.4	2.89 ± 1.31	0.80 ± 1.36		7.96 ± 0.55	1.51 ± 0.30	60.6 ± 2.7	73.8 ± 3.3
24.0	IV	0.4	11.0 ± 1.2	43.2 ± 9.7	4.75 ± 0.04	4.39 ± 0.08	3.38 ± 3.33	15.3 ± 4.3	82.0 ± 11.2
72.0	IV	0.4	14.8 ± 0.6	56.5 ± 4.9	5.8 ± 0.4	2.94 ± 0.24		3.32 ± 0.06	83.4 ± 4.1
72.0	Oral	2.0	11.5 ± 1.9	60.9 ± 6.7	5.22 ± 0.20	2.49 ± 0.36	0.87 ± 0.50	3.05 ± 0.33	84.0 ± 7.0
72.0	Oral	23	10.8 ± 1.6	75.0 ± 4.1	2.15 ± 0.36	1.49 ± 0.54	1.37 ± 0.86		90.8 ± 4.3
72.0	Oral	118	3.33 ± 0.65	64.7 ± 5.3	0.67 ± 0.07	0.33 ± 0.05	0.25 ± 0.16		69.3 ± 5.3
72.0	Oral	814[b]	2.32 ± 0.91	83.7 ± 0.6	0.14 ± 0.03	0.54 ± 0.59	0.21 ± 0.08	0.13 ± 0.06	87.0 ± 1.9
72.0	Oral	1473[b]	2.16	78.2	0.17	0.52	0.42		81.5[b]

[a]Average for 3 rats ± SD. Tables in original report Appendix have data from individual rats.

[b]Only 1 rat was dosed at this level.

Table 6. Calculated Absorption of Oral Doses of [^{14}C]ADBAQ

Dose mg/kg	% absorbed based on excretion in		mg/kg absorbed based on excretion in	
	Breath	Urine	Breath	Urine
2.0	90	78	1.8	1.6
23	37	74	8.5	17
118	12	21	14	25
814	2.4	15	19	122
1473[a]	2.9	15	43	220

[a]Based on a single animal.

Table 7

Concentration of Total ^{14}C in Blood, Plasma and Red Blood Cells (RBC) after Administration of [^{14}C]ADBAQ[E]

Time (hr)	Dose & Route (mg/kg)	Note	ng-eq/g			% Dose/g		
			Plasma	RBC	Blood	Plasma	RBC	Blood
0.125	0.4 IV	A	390 ± 10			0.37 ± 0.10		
0.25	0.4 IV	B	210 ± 10	190 ± 10	200 ± 10	0.24 ± 0.03	0.22 ± 0.02	0.23 ± 0.02
0.5	0.4 IV	C	330			0.31		
0.75	0.4 IV	B	240 ± 20	71 ± 5	150 ± 10	0.23 ± 0.03	0.07 ± 0.2	0.15 ± 0.02
1.5	0.4 IV	A	280 ± 40			0.26 ± 0.05		
2.0	0.4 IV	B	310 ± 10	58 ± 2	160 ± 6	0.32 ± 0.01	0.06 ± 0.00	0.16 ± 0.01
2.5	0.4 IV	A	290 ± 20			0.27 ± 0.03		
3.5	0.4 IV	A	303 ± 30			0.28 ± 0.02		
4.5	0.4 IV	A	280 ± 0			0.26 ± 0.01		
5.5	0.4 IV	A	240 ± 20			0.22 ± 0.01		
6.0	0.4 IV	B	290 ± 60	29 ± 8	140 ± 20	0.33 ± 0.07	0.04 ± 0.01	0.16 ± 0.02
24.0	0.4 IV	B	160 ± 20	18 ± 7	76 ± 9	0.18 ± 0.02	0.02 ± 0.01	0.08 ± 0.01
72.0	0.4 IV	B	59 ± 4	9.4 ± 1.4		0.06 ± 0.00	0.009 ± 0.001	
72.0	2.0 Oral	B	240 ± 110	54 ± 5	150 ± 50	0.05 ± 0.02	0.01 ± 0.00	0.03 ± 0.01
72.0	23 Oral	B	910 ± 340	270 ± 40	680 ± 210	0.02 ± 0.01	0.006 ± 0.001	0.01 ± 0.00
72.0	118 Oral	B	600 ± 150	900 ± 150	650 ± 140	0.003 ± 0.002	0.003 ± 0.001	0.002 ± 0.004
72.0	814 Oral	B	1800 ± 1300	1100 ± 300	1600 ± 800	0.0007 ± 0.0004	0.0005 ± 0.0001	0.0006 ± 0.0003
72.0	1473 Oral	D	2300	2500	3300	0.0005	0.0006	0.0008

A. Blood from anesthetized animals with biliary canulas. Average of two rats with range.

B. Blood taken by cardiac puncture at sacrifice. Average of three rats ± SD.

C. Blood from anesthetized animals with biliary canulas. Data from one rat.

D. Blood taken by cardiac puncture at sacrifice. Data from one rat.

E. Tables in original report Appendix have data from individual rats.

Table 8

Concentration of Parent Compound in Plasma and Tissue at Various Times Following an Intravenous Dose of [^{14}C]ADBAQ

Substance	Time (hr)	Rat No.	ADBAQ (ng-eq/g tissue)	% of Total ^{14}C in Tissue Accounted for by ADBAQ
Plasma	0.25	36	58.7	22
		37	57.4	22
		19	72.0	37
		23	68.3	35
		Average ± SD	64.1 ± 7.2	29 ± 8
	2.0	26, 27, 28[a]	8.6	2.8
	6.0	16	14.0	4.0
		17	13.1	5.9
		18	11.7	4.2
		Average ± SD	12.9 ± 1.2	4.7 ± 1.0
	24	42	10.5	3.6
		43A	8.2	4.0
		44	11.5	4.3
		Average ± SD	10.1 ± 7	4.0 ± 0.4
Adipose	0.25	19	489	95
		21	576	95
		23	526	94
		Average ± SD	530 ± 44	95 ± 1
	6.0	16	229	95
		17	374	93
		18	243	79
		Average ± SD	282 ± 80	89 ± 9
	24	32	123	91
		33	101	69
		34	112	85
		Average ± SD	112 ± 11	82 ± 11
Liver	0.25	19	175	18
		21	262	23
		23	229	23
		Average ± SD	222 ± 44	21 ± 3
	6.0	16	40	18
		17	29	18
		18	31	18
		Average ± SD	33 ± 6	18 ± 0

Table 8 (continued)

Substance	Time (hr)	Rat No.	ADBAQ (ng-eq/g tissue)	% of Total ^{14}C in Tissue Accounted for by ADBAQ
	24	32	20	17
		33	14	18
		34	29	18
		Average ± SD	21 ± 8	18 ± 1
Muscle	0.25	19	273	88
		21	225	84
		23	184	85
		Average ± SD	227 ± 44	86 ± 2
	6.0	16	5.4	41
		17	8.8	46
		18	10.4	64
		Average ± SD	8.2 ± 2.6	50 ± 12
	24	33	3.4	22
		34	1.1	21
		Average	2.2	22
Skin	0.25	19	223	82
		21	200	82
		23	249	80
		Average ± SD	224 ± 24	81 ± 1
	6.0	16	61	60
		17	40	57
		18	43	50
		Average ± SD	48 ± 11	56 ± 5
	24	32	24	25
		33	24	28
		34	26	25
		Average ± SD	25 ± 1	26 ± 2

[a]Plasma from these animals were combined.

Table 9

Concentration of ^{14}C-Labeled Compounds in Tissues after Intravenous Administration of [^{14}C]ADBAQ (0.4 mg/kg)

Tissue	ng-eq/g (TBR)[a]					
	0.25 hr	0.75 hr	2.0 hr	6.0 hr	24.0 hr	72.0 hr
Liver	1500 ± 100 (7.4 ± 0.4)	880 ± 50 (5.7 ± 0.3)	770 ± 80 (5.1 ± 0.5)	550 ± 80 (4.1 ± 0.1)	360 ± 20 (4.8 ± 0.4)	160 ± 40 (5.2 ± 0.6)[b]
Skin (Belly)	390 ± 150 (2.0 ± 0.8)	610 ± 190 (4.1 ± 1.6)	360 ± 130 (2.3 ± 0.8)	79 ± 4 (0.59 ± 0.08)	59 ± 18 (0.78 ± 0.28)	19 ± 5 (0.60 ± 0.12)[b]
(Hindquarters)	220 ± 10 (1.1 ± 0.1)	260 ± 50 (1.7 ± 0.3)	140 ± 60 (0.88 ± 0.38)	43 ± 10 (0.31 ± 0.03)	24 ± 3 (0.31 ± 0.03)	20 ± 2 (0.64 ± 0.04)[b]
(Back of Neck)	260 ± 60 (1.3 ± 0.3)	280 ± 80 (1.8 ± 0.5)	110 ± 50 (0.70 ± 0.29)	55 ± 11 (0.40 ± 0.02)	27 ± 1 (0.35 ± 0.05)	24 ± 6 (0.82 ± 0.14)[b]
Muscle (Neck)	260 ± 50 (1.2 ± 0.3)	180 ± 70 (1.2 ± 0.6)	44 ± 19 (0.29 ± 0.13)	32 ± 2 (0.24 ± 0.04)	22 ± 11 (0.27 ± 0.10)	18 ± 7 (0.52 ± 0.24)[b]
(Hind leg)	180 ± 20 (0.91 ± 0.07)	84 ± 14 (0.56 ± 0.13)	31 ± 8 (0.20 ± 0.04)	16 ± 3 (0.12 ± 0.03)	17 ± 7 (0.22 ± 0.10)	5.9 ± 2.5 (0.20 ± 0.08)[b]
(Abdomen)	180 ± 30 (0.90 ±0.12)	120 ± 30 (0.76 ± 0.18)	57 ± 29 (0.37 ± 0.19)	17 ± 3 (0.12 ± 0.01)	16 ± 3 (0.22 0.06)	11 ± 5 (0.36 ± 0.16)[b]
Lungs	1200 ± 60 (5.9 ± 0.2)	260 ± 90 (1.6 ± 0.6)	150 ± 20 (0.97 ± 0.12)	130 ± 10 (0.95 ± 0.18)	56 ± 17 (0.74 ± 0.19)	23 ± 3 (0.78 ± 0.14)[b]
Heart	340 ± 50 (1.7 ± 0.2)	180 ± 50 (1.2 ± 0.3)	71 ± 8 (0.46 ± 0.05)	62 ± 9 (0.46 ± 0.05)	38 ± 2 (0.50 ± 0.04)	19 ± 2 (0.62 ± 0.1)[b]
Kidneys	590 ± 30 (3.0 ± 0.2)	450 ± 30 (3.0 ± 0.2)	380 ± 20 (2.5 ± 0.1)	340 ± 20 (2.5 ± 0.3)	270 ± 10 (3.6 ± 0.3)	200 ± 20 (6.6 ± 0.6)[b]
Adipose (Kidney)	840 ± 340 (4.2 ± 1.9)	1000 ± 500 (7.1 ± 4.4)	650 ± 160 (4.2 ± 1.0)	380 ± 140 (2.9 ± 1.3)	120 ± 20 (1.6 ± 0.4)	15 ± 6 (0.62 ± 0.10)[b]
(Epididymis)	360 ± 70 (1.8 ± 0.4)	700 ± 220 (4.6 ± 1.6)	600 ± 210 (3.9 ± 1.3)	330 ± 90 (2.6 ± 1.0)	140 ± 40 (1.8 ± 0.8)	15 ± 5 (0.50 ± 0.22)[b]
(Mesenteric)	800 ± 130 (4.0 ± 0.8)	1100 ± 500 (7.2 ± 3.6)	920 ± 29 (5.9 ± 0.2)	320 ± 140 (2.4 ± 1.3)	95 ± 36 (1.2 ± 0.4)	12 ± 5 (0.40 ± 0.20)[b]
Adrenals	5200 ± 2600 (26 ± 15)	2600 ± 500 (17 ± 5)	1500 ± 260 (9.7 ± 2.0)	420 ± 170 (3.0 ± 0.8)	70 ± 9 (0.95 ± 0.22)	28 ± 6 (0.92 ± 0.20)[b]
Brain	350 ± 10 (1.7 ± 0.2)	170 ± 10 (1.1 ± 0.1)	37 ± 4 (0.26 ± 0.04)	8.7 ± 2.1 (0.05 ± 0.03)	4.6 ± 0.6 (0.06 ± 0.01)	4.5 ± 2.4 (0.10 ± 0.02)[b]
Eyes	110 ± 20 (0.55 ± 0.14)					13 ± 11 (0.42 ± 0.32)[b]
Esophagus	210 ± 20 (1.1 ± 0.1)					17 ± 3 (0.56 ± 0.04)[b]
Stomach	78 ± 10 (0.40 ± 0.04)					26 ± 27 (0.80 ± 0.80)[b]
Small Intestines	1500 ± 100 (7.8 ± 1.0)					27 ± 4 (0.91 ± 0.16)[b]
Large Intestines	140 ± 30 (0.69 ± 0.12)					32 ± 13 (1.08 ± 0.52)[b]
Cecum	60 ± 20 (0.30 ± 0.10)					--
Seminal Vesicles	120 ± 10 (0.61 ± 0.02)					21 ± 3 (0.70 ± 0.10)[b]
Testes	130 ± 10 (0.66 ± 0.04)					20 ± 1 (0.58 ± 0.02)[b]
Prostate	230 ± 30 (1.2 ± 0.2)					10 ± 7 (0.32 ± 0.22)[b]
Plasma	210 ± 10 (1.1 ± 0.0)	240 ± 20 (1.4 ± 0.3)	310 ± 10 (2.0 ± 0.1)	290 ± 60 (2.1 ± 0.1)	160 ± 20 (2.0 ± 0.1)	59 ± 4 (2.0 ± 0.0)[b]
RBC	190 ± 10 (0.98 ± 0.03)	71 ± 5 (0.46 ± 0.07)	58 ± 2 (0.37 ± 0.01)	29 ± 8 (0.21 ± 0.06)	18 ± 7 (0.23 ± 0.06)	9.4 ± 1.4 (0.32 ± 0.02)[b]
Blood	190 ± 10 (1.0 ± 0.0)	150 ± 10 (1.0 ± 0.0)	160 ± 6 (1.0 ± 0.0)	140 ± 2 (1.0 ± 0.0)	76 ± 9 (1.0 ± 0.0)	--
Plasma/Blood	1.1	1.6	1.9	2.1	2.1	--

[a] Values are the averages for 3 rats ± SD. TBR = tissue-blood ratio. Tables in original report Appendix have data from individual rats.

[b] Calculated from tissue plasma ratios (TPR) using the equation [^{14}C]plasma = 2[^{14}C]blood

Table 10

Concentration of ^{14}C-Labeled Compounds in Selected Tissues 72 hr after Oral Administration of [^{14}C]ADBAQ[a]

	ng-eq/g (TBR)[b]				
Dose (mg/kg)	2.0	23	118	814	1473
Liver	940 ± 220 (6.7 ± 2.0)	4100 ± 1200 (6.0 ± 1.0)	4700 ± 600 (7.4 ± 1.4)	14000 ± 6000 (9.7 ± 2.1)	25000 (7.6)
Skin (Belly)	68 ± 13 (0.50 ± 0.22)	520 ± 80 (0.76 ± 0.22)	540 ± 40 (0.87 ± 0.20)	1700 ± 500 (1.2 ± 0.4)	3600 (1.1)
(Hindquarters)	80 ± 7 (0.57 ± 0.15)	550 ± 190 (0.89 ± 0.53)	570 ± 40 (0.92 ± 0.25)	1600 ± 600 (1.1 ± 0.2)	2900 (0.87)
(Back of Neck)	99 ± 4 (0.73 ± 0.23)	530 ± 100 (0.81 ± 0.22)	610 ± 30 (0.98 ± 0.28)	1400 ± 200 (1.1 ± 0.6)	4200 (1.3)
Muscle (Neck)	44 ± 10 (0.31 ± 0.04)	270 ± 140 (0.41 ± 0.23)	250 ± 50 (0.39 ± 0.02)	700 ± 170 (0.57 ± 0.38)	1500 (0.45)
(Hind Leg)	32 ± 6 (0.23 ± 0.05)	160 ± 30 (0.24 ± 0.04)	160 ± 20 (0.25 ± 0.02)	690 ± 290 (0.49 ± 0.14)	2700 (0.80)
(Abdomen)	38 ± 10 (0.27 ± 0.07)	200 ± 40 (0.31 ± 0.041)	250 ± 40 (0.40 ± 0.12)	2400 ± 2900 (1.4 ± 1.1)	2200 (0.67)
Lungs	130 ± 40 (1.0 ± 0.4)	--	--	--	--
Heart	85 ± 14 (0.61 ± 0.14)	--	--	--	--
Kidneys	990 ± 200 (6.8 ± 2.4)	5300 ± 1100 (8.0 ± 0.9)	6200 ± 200 (9.9 ± 2.7)	16000 ± 5000 (12 ± 4)	25000 (7.3)
Adipose (Kidney)	39 ± 2 (0.29 ± 0.09)	370 ± 140 (0.60 ± 0.32)	670 ± 190 (1.0 ± 0.3)	1200 ± 300 (0.93 ± 0.41)	6700 (2.0)
(Epididymis)	48 ± 17 (0.38 ± 0.26)	550 ± 480 (0.90 ± 0.81)	1600 ± 500 (2.5 ± 0.8)	2000 ± 800 (1.3 ± 0.9)	9600 (2.9)
(Mesenteric)	36 ± 5 (0.26 ± 0.06)	280 ± 60 (0.38 ± 0.04)	580 ± 190 (0.9 ± 0.2)	1200 ± 400 (0.90 ± 0.35)	4000 (1.2)
Adrenals	230 ± 90 (1.4 ± 0.5)	--	--	--	--
Brain	13 ± 3 (0.09 ± 0.03)	--	--	--	--
Eyes	46 ± 5 (0.33 ± 0.13)	--	--	--	--
Esophagus	57 ± 40 (0.48 ± 0.44)	--	--	--	--
Stomach	33 ± 7 (0.25 ± 0.12)	--	--	--	--
Small Intestines	130 ± 30 (0.98 ± 0.39)	630 ± 180 (0.94 ± 0.14)	710 ± 40 (1.1 ± 0.2)	4200 ± 4100 (2.4 ± 1.3)	7000 (2.1)
Large Intestines	410 ± 230 (2.5 ± 1.5)	2200 ± 560 (4.6 ± 0.4)	4600 ± 1100 (7.7 ± 1.3)	25000 ± 35000 (17 ± 19)	230000 (69)
Cecum	--	2700 ± 1800 (3.7 ± 1.4)	5700 ± 2600 (8.5 ± 2.4)	360000 ± 560000 (160 ± 250)	120000 (36)
Seminal Vesicles	76 ± 4 (0.56 ± 0.19)	--	--	--	--
Testes	68 ± 6 (0.49 ± 0.12)	--	--	--	--
Prostate	63 ± 14 (0.47 ± 0.19)	--	--	--	--
Plasma	240 ± 110 (1.6 ± 0.5)	910 ± 340 (1.3 ± 0.1)	600 ± 150 (0.93 ± 0.03)	1800 ± 1300 (1.0 ± 0.3)	2300 (0.70)
RBC	54 ± 5 (0.39 ± 0.11)	270 ± 40 (0.41 ± 0.07)	900 ± 150 (1.3 ± 0.3)	1100 ± 300 (0.74 ± 0.22)	2500 (0.76)
Blood	150 ± 50 (1.0 ± 0.0)	680 ± 210 (1.0 ± 0.0)	650 ± 140 (1.0 ± 0.0)	1600 ± 800 (1.0 ± 0.0)	3300 (1.0)

[a]Values are the average for 3 rats ± SD except that only one rat was dosed at 1473 mg/kg. See Tables A19-A23 in Appendix for data from individual rats.

[b]Tissue:blood ratio.

Table 11

Amount of ^{14}C Contained in Selected Tissues after Intravenous Administration of 0.4 mg/kg of [^{14}C]ADBAQ.[a]

Values are the average percent dose ± SD in the entire tissue for 3 rats.

Time (hr)	0.25	0.75	2.0	6.0	24.0	72.0
Adipose[b]	17 ± 3	23 ± 8	18 ± 3	9.0 ± 1.9	3.0 ± 0.3	0.40 ± 0.1
Liver	17 ± 1	9.0 ± 0.4	8.0 ± 0.6	6.6 ± 0.7	3.7 ± 0.1	1.6 ± 0.1
Muscle[b]	27 ± 3	15 ± 3	5.5 ± 2.3	2.8 ± 0.1	2.3 ± 0.4	1.5 ± 0.5
Skin[b]	11 ± 2	14 ± 1	7.7 ± 3.0	2.3 ± 0.3	1.4 ± 0.2	0.91 ± 0.16
Lungs	1.1 ± 0.1	0.39 ± 0.04	0.21 ± 0.02	0.18 ± 0.08	0.06 ± 0.02	0.05 ± 0.00
Heart	0.33 ± 0.06	0.14 ± 0.04	0.06 ± 0.00	0.05 ± 0.01	0.03 ± 0.01	0.02 ± 0.00
Kidneys	1.2 ± 0.0	0.79 ± 0.07	0.70 ± 0.02	0.68 ± 0.02	0.48 ± 0.01	0.43 ± 0.03
Adrenals	0.21 ± 0.02	0.12 ± 0.03	0.07 ± 0.01	0.02 ± 0.01	0.00 ± 0.00	0.00 ± 0.00
Brain	0.67 ± 0.06	0.25 ± 0.03	0.06 ± 0.00	0.02 ± 0.00	0.01 ± 0.00	0.01 ± 0.00
Eyes	0.03 ± 0.00					0.00 ± 0.00
Esophagus	0.03 ± 0.00					0.01 ± 0.01
Stomach	0.46 ± 0.06					0.01 ± 0.01
Small Intestines	13 ± 2					
Large Intestines	0.30 ± 0.16					
Cecum	0.03 ± 0.10					
Seminal Vesicles	0.06 ± 0.01					0.02 ± 0.00
Testes	0.41 ± 0.03					0.05 ± 0.01
Prostate	0.05 ± 0.00					0.01 ± 0.01

[a]Tables in original report Appendix have data from individual rats.

[b]Adipose assumed to be 10% of body weight; muscle - 50% of body weight; skin - 15% of body weight.

Table 12

Amount of ^{14}C Contained in Selected Tissues 72 hr after Oral Administration of [^{14}C]ADBAQ

	% Dose in Tissue[a]				
Dose (mg/kg)	2.0	23	118	814	1473[b]
Adipose[c]	0.20 ± 0.01	0.18 ± 0.07	0.08 ± 0.03	0.20 ± 0.01	0.05
Liver	1.68 ± 0.22	0.70 ± 0.18	0.15 ± 0.01	0.056 ± 0.016	0.065
Muscle[c]	0.94 ± 0.20	0.48 ± 0.12	0.09 ± 0.01	0.07 ± 0.06	0.07
Skin[c]	0.62 ± 0.02	0.35 ± 0.03	0.07 ± 0.01	0.03 ± 0.01	0.04
Lungs	0.048 ± 0.015				
Heart	0.017 ± 0.002				
Kidneys	0.37 ± 0.02	0.18 ± 0.05	0.037 ± 0.002	0.013 ± 0.004	0.012
Adrenals	0.0014 ± 0.0004				
Brain	0.0041 ± 0.0009				
Eyes	0.0024 ± 0.0002				
Esophagus	0.0014 ± 0.0004				
Stomach	0.017 ± 0.004				
Seminal vesicles	0.015 ± 0.002				
Testes	0.037 ± 0.006				
Prostate	0.0086 ± 0.0024				
Small intestines		0.065 ± 0.009	0.015 ± 0.001	0.010 ± 0.006	0.012
Large intestines		0.22 ± 0.11	0.039 ± 0.021	0.044 ± 0.075	0.17
Cecum		0.30 ± 0.20	0.095 ± 0.043	0.42 ± 0.59	0.26

[a]Values are the averages for 3 rats ± SD. Tables in original report Appendix have data from individual rats.

[b]Only 1 rat was dosed at this level.

[c]Adipose assumed to be 10% of body weight; muscle - 50% of body weight; skin - 15% of body weight.