

ADME NTP Study S0053 tert-Butyl perbenzoate

The contractor abbreviated the test article as TBPB.

Sex/Species: adult male F344 rats.

Vehicles: intravenous, 4% rat serum albumin in Sorensen's Buffer; dermal, diethyl ether.

CASRN 614-45-9

Radiolabeled with carbon-14 in the ring; tert-Butyl perbenzoate, [Ring-UL-¹⁴C]-

Studies Performed:

- Single 3.7 mg/kg intravenous dose to rats with sacrifice 24 or 72 hours postdose.
- Single 0.38, 3.4, or 39 mg/kg dermal dose to rats with covered dose site and sacrifice 24 hours postdose.

Sorensen's Buffer is 5 g of NaCl per liter of 0.067 M KH₂PO₄ and 0.067 M Na₂HPO₄ pH 7.4.

The amount of TBPB absorbed was calculated by comparing the urinary excretion of ¹⁴C in 24 hours following a dermal dose to that following the 3.7 mg/kg intravenous dose. The results of these calculations are shown in Table 3. Based on excretion in the urine, 15-16% of each dermal dose was absorbed. The excretion data are fitted well by the equation mg/kg absorbed = 0.166 dose (mg/kg) - 0.034. The assumption for this calculation is that the compound absorbed is TBPB and not decomposition product(s) or metabolite(s).

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Table 1

Average Cumulative Excretion of Total ^{14}C After Intravenous Administration of 3.7 mg/kg of [^{14}C]TBPB (% Dose \pm S.D.)^a

Time (hr)	Urine	Feces	Breath	Total
2	56.1 \pm 22.0			56.1 \pm 22.0
4	76.6 \pm 7.2		0.03 \pm 0.01 ^b	76.6 \pm 7.2
6	78.5 \pm 6.8			78.5 \pm 6.8
8	81.4 \pm 6.4			81.4 \pm 6.4
24	85.0 \pm 4.3	1.0 \pm 1.1		86.0 \pm 4.4
48	87.2 \pm 0.0	1.1 \pm 1.2		88.3 \pm 1.2
72	89.4 \pm 3.9	1.2 \pm 1.2		90.6 \pm 4.1

^aThe original report Appendix has data from individual rats.

^bVolatile organics collected in ethanol traps.

Table 2
 Cumulative Excretion of Total ¹⁴C after Dermal Application of [¹⁴C] TBPB (% Dose ± SD)^a

Dose Applied (mg/kg)	0.377				3.37				38.96				
	Excreta	Urine	Feces	Breath ^b	Total	Urine	Feces	Breath ^b	Total	Urine	Feces	Breath ^b	Total
Time (hr)													
2		0.67±0.58			0.67±0.58	1.01±1.10			1.0 ±1.10	0.16±0.14			0.16±0.14
4		3.76±0.42			3.76±0.42	2.23±1.35			2.23±1.35	0.34±0.42			0.34±0.42
6		4.81±1.03			4.81±1.03	4.48±1.72			4.48±1.72	2.10±1.84			2.10±1.84
8		5.29±1.84	0.00±0.00		5.29±1.84	5.61±3.29	0.30±0.27		5.91±3.56	2.87±1.32	0.17±0.24		3.04±1.56
24		13.1 ±2.7	0.59±0.46	0.51±0.26	14.2 ±3.5	12.7 ±5.8	0.38±0.30	0.092±0.020	13.2 ±6.1	14.31.31	0.39±0.45	0.18±0.08	14.9 ±1.8

^aThe original report Appendix has data from individual rats.

^bCollected via NaOH traps.

Table 3

Calculated Absorption of Dermal Doses of [¹⁴C]TBPB
Based on Excretion in Urine

Dermal Dose (mg/kg)	% Absorbed	mg/kg Absorbed
0.377	15.1	0.0569
3.37	14.7	0.495
38.96	16.5	6.43

Table 4

Concentration of Total ^{14}C in Blood and Plasma after Administration of [^{14}C]TBPB^a

Time (hr)	Dose ^b (mg)kg	Route	ng-eq/g		% Dose/g	
			Plasma	Blood	Plasma	Blood
24	3.9	IV	74.9 ± 8.0	51.7 ± 4.0	0.0074 ± 0.0005	0.0051 ± 0.0003
72	3.7	IV	44.7 ± 2.3	25.4 ± 1.0	0.0043 ± 0.0003	0.0025 ± 0.0002
24	0.38	Dermal	1.45 ± 0.32	1.05 ± 0.13	0.0015 ± 0.0004	0.0010 ± 0.0001
24	3.4	Dermal	1.30 ± 0.0	10.9 ± 0.6	0.0013 ± 0.0000	0.0011 ± 0.0000
24	39.0	Dermal	121 ± 29	141 ± 18	0.0012 ± 0.0003	0.0012 ± 0.0002

^a Average ± SD Data from individual rats can be found in the original report Appendix.^b Applied dose.

Table 5
 Concentration of ^{14}C Labeled Compounds in Tissues after Intravenous
 Administration of [^{14}C]TBPB (3.7-3.9 mg/kg)

Tissue	ng-eq/g (TBR)			
	24 hr		72 hr	
Skin, ear	50 ± 28	(.95±.50)	40 ± 32	(1.6 ± 1.2)
ear	44 ± 23	(.84±.39)	33 ± 12	(1.3 ± 0.4)
belly	66 ± 72	(1.22±1.24)	680 ± 830	(26 ± 32)
hindquarters	68 ± 8	(1.33±0.77)	110 ± 80	(4.4 ± 3.2)
back of neck	32 ± 9	(0.62±0.12)	29 ± 14	(1.0 ± 0.5)
Esophagus	77 ± 94	(3.28±0.07)		
Stomach	13 ± 8	(0.25±0.12)		
Liver	32 ± 3	(0.61±0.02)	15 ± 1.0	(0.60±0.04)
Lung	35 ± 6	(0.58±0.14)		
Heart	22 ± 6	(0.43±0.09)		
Kidneys	35 ± 17	(0.66±0.27)		
Adipose, kidney	18 ± 7	(0.35±0.15)	9.1± 1.7	(0.36±0.06)
epididymis	9.8± 7.2	(0.18±0.12)	12 ± 4.0	(0.45±0.14)
mesenteric	32 ± 5.3	(0.62±0.14)	22 ± 11	(0.84±0.42)
Adrenals	37 ± 4.6	(0.73±0.09)		
Small Intestines, full	536 ± 783	(4.83±6.90)		
clean	47 ± 22	(0.45±0.16)		
Large Intestines, full	69 ± 17	(1.34±0.32)		
clean	22 ± 1	(0.43±0.01)		
Cecum	79 ± 34	(1.49±0.52)		
Seminal Vesicles	16 ± 8	(0.31±0.13)		
Testes	18 ± 7	(0.35±0.15)		
Prostate	17 ± 6	(0.32±0.10)		
Muscle, neck	9.4± 7.0	(0.17±0.12)	8.4± 3.1	(0.33±0.11)
hindleg	8.0± 5.2	(0.16±0.09)	6.7± 7.5	(0.26±0.29)
abdominal	8.3± 2.7	(0.16±0.04)	6.4± 0.9	(0.25±0.04)
Brain	11 ± 3	(0.21±0.04)		
Eyes	12 ± 4	(0.23±0.06)		
Spleen	17 ± 2	(0.33±0.03)		
Trachea	47 ± 27	(0.88±0.42)		

Table 6

Concentration of ^{14}C -Labeled Compounds in Selected Tissues 24 hr after Dermal Administration of [^{14}C]TBPB

Dose (mg/kg)	ng-eq/g (TBR) ^b					
	0.377		3.37		39.0	
Skin, ear	14 ± 2	(13 ± 2)	120 ± 40	(14 ± 4)	860 ± 290	(6.2 ± 2.1)
ear	12 ± 5	(11 ± 6)	74 ± 9	(10 ± 7)	1,100 ± 410	(8.1 ± 3.1)
belly	17 ± 4	(16 ± 3)	540 ± 290	(57 ± 14)	5,000 ± 2,800	(40 ± 26)
hindquarters	14 ± 3	(13 ± 3)	110 ± 70	(14 ± 6)	860 ± 240	(6.0 ± 1.1)
back of neck	7.6 ± 1.9	(7.3 ± 1.6)	32 ± 10	(4.1 ± 2.0)	450 ± 80	(3.2 ± 0.8)
Esophagus	3.2 ± 0.3	(3.1 ± 0.1)	65 ± 76	(6.2 ± 5.9)	470 ± 360	(3.1 ± 2.3)
Stomach	2.9 ± 2.3	(2.8 ± 2.3)	49 ± 36	(5.9 ± 3.3)	210 ± 50	(1.5 ± 0.2)
Liver	2.3 ± 1.5	(2.2 ± 1.6)	32 ± 17	(4.1 ± 2.4)	140 ± 8	(1.1 ± 0.01)
Lung	1.1 ± 0.4	(1.0 ± 0.3)	10 ± 6.5	(1.1 ± 0.4)	86 ± 13	(0.63 ± 0.18)
Heart	0.94 ± 0.32	(0.93 ± 0.31)	3.9 ± 2.5	(0.47 ± 0.06)	52 ± 4	(0.37 ± 0.04)
Kidneys	4.5 ± 0.9	(4.2 ± 0.5)	33 ± 12	(3.8 ± 0.5)	540 ± 132	(3.8 ± 0.9)
Adipose, kidney	1.4 ± 0.4	(1.3 ± 0.5)	4.8 ± 1.8	(0.56 ± 0.11)	720 ± 770	(5.7 ± 6.7)
epididymis	1.4 ± 0.8	(1.4 ± 0.7)	10 ± 7	(1.0 ± 0.4)	530 ± 160	(3.7 ± 0.8)
mesenteric	1.2 ± 0.5	(1.3 ± 0.8)	15 ± 14	(1.5 ± 1.1)	150 ± 36	(1.1 ± 0.2)
Adrenals	0.90 ± 0.05	(0.87 ± 0.11)	5.0 ± 2.9	(0.54 ± 0.15)	99 ± 21	(0.72 ± 0.14)
Small Intestine, full	8.9 ± 12	(7.9 ± 11)	29 ± 42	(3.4 ± 3.9)	400 ± 430	(2.7 ± 2.8)
clean	1.8 ± 1.0	(1.7 ± 1.0)	63 ± 42	(7.1 ± 4.4)	880 ± 2,100	(5.9 ± 13.2)
Large Intestine, full	6.6 ± 1.8	(6.3 ± 1.0)	59 ± 60	(6.5 ± 5.1)	1,800 ± 2,500	(15 ± 21)
clean	1.1 ± 0.1	(1.1 ± 0.2)	6.5 ± 4.0	(0.69 ± 0.25)	4,200 ± 7,100	(35 ± 59)
Cecum	7.3 ± 3.2	(7.3 ± 4.1)	41 ± 44	(4.6 ± 3.9)	730 ± 320	(5.7 ± 2.2)
Seminal Vesicles	2.3 ± 2.6	(2.3 ± 2.5)	14 ± 16	(1.3 ± 1.3)	1,500 ± 2,000	(9.9 ± 13)
Testes	0.35 ± 0.11	(0.33 ± 0.07)	2.0 ± 1.0	(0.23 ± 0.04)	150 ± 70	(1.1 ± 0.6)
Prostate	4.0 ± 5.2	(3.9 ± 5.0)	95 ± 150	(8.8 ± 13)	230 ± 200	(1.6 ± 1.2)
Muscle, neck	0.87 ± 0.64	(0.81 ± 0.51)	6.1 ± 4.1	(0.63 ± 0.26)	320 ± 400	(2.6 ± 3.4)
hind leg	0.48 ± 0.08	(0.45 ± 0.05)	3.1 ± 3.4	(0.60 ± 0.13)	380 ± 180	(2.7 ± 1.4)
abdominal	1.1 ± 0.5	(1.1 ± 0.6)	8.2 ± 4.2	(0.98 ± 0.38)	970 ± 840	(5.9 ± 7.6)
Brain	0.16 ± 0.01	(0.15 ± 0.02)	1.3 ± 0.4	(0.20 ± 0.10)	120 ± 10	(0.89 ± 0.02)
Eyes	0.74 ± 0.32	(0.69 ± 0.23)	5.8 ± 1.7	(0.79 ± 0.54)	180 ± 80	(1.3 ± 0.5)
Spleen	0.50 ± 0.01	(0.48 ± 0.07)	4.0 ± 1.1	(0.48 ± 0.10)	41 ± 6	(0.30 ± 0.03)
Trachea	2.2 ± 0.0	(2.1 ± 0.2)	33 ± 29	(3.4 ± 0.3)	210 ± 80	(1.4 ± 0.5)
SITE OF DOSE						
Muscle Under Dose Site	1.1 ± 0.3	(1.0 ± 0.3)	4.3 ± 3.1	(0.43 ± 0.22)	110 ± 50	(0.75 ± 0.32)
Subcutaneous Fat Under Dose Site	6.3 ± 3.4	(6.5 ± 4.2)	20 ± 9	(2.2 ± 0.2)	390 ± 170	(2.7 ± 1.0)
Brown Fat Under Dose Site	16 ± 8	(15 ± 9)	51 ± 14	(7.3 ± 5.8)	1,700 ± 1,700	(15 ± 6)
Dermis Under Dose Site	4,500 ± 4,300	(4,100 ± 3,700)	5,400 ± 7,300	(1,000 ± 1,600)	64,000 ± 170,000	(4,600 ± 1,700)
Dose Site	1,900 ± 700	(1,800 ± 700)	21,000 ± 13,000	(2,100 ± 700)	240,000 ± 59,000	(1,800 ± 500)

Table 7

Concentration of ^{14}C -Labeled Compounds in Tissues After Intravenous Administration of 3.7-3.9 mg/kg of [^{14}C]TBPB (% Dose in the Entire Tissue)^a

Tissue	24 hr	72 hr
Skin ^b	0.20 \pm 0.14	0.21 \pm 0.22 ^c
Esophagus	0.0010 \pm 0.0011	
Stomach	0.0045 \pm 0.0036	
Liver	0.027 \pm 0.005	0.013 \pm 0.000
Lung	0.0033 \pm 0.0005	
Heart	0.0017 \pm 0.0005	
Kidneys ^b	0.0064 \pm 0.0002	
Adipose ^b	0.051 \pm 0.006	0.040 \pm 0.026
Adrenals	0.0002 \pm 0.0001	
Cecum	0.045 \pm 0.013	
Seminal vesicles	0.0007 \pm 0.0004	
Testes	0.0036 \pm 0.0004	
Prostate	0.0003 \pm 0.0002	
Muscle ^b	0.11 \pm 0.06	0.11 \pm 0.01
Brain	0.0017 \pm 0.0007	
Eyes	0.0003 \pm 0.0001	
Spleen	0.0011 \pm 0.0001	
Trachea	0.0007 \pm 0.0004	
Tail	0.12 \pm 0.08	0.16 \pm 0.14

^aThe original report Appendix has data from individual rats.

^bAdipose assumed to be 10% of body weight; muscle, 50% of body weight; skin, 15% of body weight.

^cBelly was omitted due to possible contamination from urine.

Table 8

Concentration of ^{14}C -Labeled Compounds in Tissues After Dermal Administration of [^{14}C]TBPB (% Dose in the Entire Tissue)

Tissue	0.38 mg/kg dose	3.4 mg/kg dose	39 mg/kg dose
Skin ^b	0.51 \pm 0.16	0.54 \pm 0.70	0.63 \pm 0.80
Liver	0.020 \pm 0.012	0.028 \pm 0.016	0.011 \pm 0.001
Adipose ^b	0.034 \pm 0.013	0.026 \pm 0.024	0.14 \pm 0.09
Muscle ^b	0.10 \pm 0.05	0.085 \pm 0.045	0.70 \pm 0.70

^aDose applied.

^bAdipose assumed to be 10% of body weight; muscle, 50% of body weight; skin, 15% of body weight.