

## ADME NTP Study S0228 Diallyl phthalate

The contractor used the abbreviation of DAP for the test article.

Sex/Species: male F344 rats and B6C3F1 mice.

Vehicle: intravenous, water:ethanol:emulphor (3:2:1); oral, water:ethanol:emulphor (3:2:1).

CASRN 113-17-9

Radiolabeled with carbon-14 position not specified; [<sup>14</sup>C]Diallyl phthalate

Studies Performed:

- Single 10 mg/kg intravenous dose to rats with sacrifice at 0.5, 1, 2, 4, 8, 12, or 24 hours postdose. (n = 3 per time point)
- Single 10 mg/kg intravenous dose to cannulated rats anesthetized with pentobarbital (60 mg/kg) for serial blood samples at 5, 10, 15, 20, and 30 minutes. (n = 3, toxicokinetics)
- Single 10 mg/kg intravenous dose to mice with sacrifice at 0.5, 1, 2, 4, 8, 12, or 24 hours postdose. (n = 3 per time point)
- Single 10 mg/kg intravenous dose to mice with sacrifice at 5, 10, 15, or 30 minutes postdose. (n = 3 per time point, toxicokinetics)
- Single 1, 10, or 100 mg/kg oral gavage dose to rats with sacrifice 24 hours postdose. (n = 3)
- Single 1, 10, or 100 mg/kg oral gavage dose to mice with sacrifice 24 hours postdose. (n = 3)

Toxicokinetics:

Pharmacokinetic parameters were calculated using methods described by Levy, G and Gibaldi, M. 1975. Pharmacokinetics. Concepts in biochemical pharmacology. *Handbook of Experimental Pharmacology*. 28(3):1-34. Springer Verlag, Berlin. Decay curves for <sup>14</sup>C, DAP, and the metabolite monoallylphthalate (MAP) were described by a mono-exponential ( $C = C_0 e^{-kt}$ ) or biexponential ( $C = A e^{-\alpha t} + B e^{-\beta t}$ ) decay curve. The following equations were used for determining rate constants and half-lives:  $\alpha = -\text{slope} \times 2.303$ ;  $t_{1/2}\alpha = \frac{0.693}{\alpha}$ ;  $\beta = -\text{slope} \times 2.303$ ;  $t_{1/2}\beta = \frac{0.693}{\beta}$ .

No DAP was found in blood, liver, kidney, muscle, skin or small intestine 30 minutes after intravenous administration of DAP. Half-life ( $t_{1/2}$ ) of DAP in blood for rats and mice

was ~ 2 minutes. The decay of total  $^{14}\text{C}$  in blood is best described by the biexponential decay curve.

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**Table 1**  
**Disposition of  $^{14}\text{C}$ -Diallylphthalate 24 Hours**  
**After Dosing Mice and Rats<sup>a,b</sup>**

Species	Dose (mg/kg)	Total Recovery of $^{14}\text{C}$	Total $^{14}\text{CO}_2$	Urine $^{14}\text{C}$
Rat	1 (PO)	87.2 $\pm$ 0.6	27.3 $\pm$ 0.0	50.7 $\pm$ 0.8
	10 (PO)	102.1 $\pm$ 1.3	29.6 $\pm$ 1.5	60.0 $\pm$ 5.3
	100 (PO)	96.1 $\pm$ 2.0	25.7 $\pm$ 2.0	58.6 $\pm$ 0.8
	10 (IV)	104.5 $\pm$ 3.6	25.8 $\pm$ 1.2	70.0 $\pm$ 3.6
Mouse	1 (PO)	100.6 $\pm$ 1.8	7.2 $\pm$ 1.0	92.0 $\pm$ 2.9
	10 (PO)	101.4 $\pm$ 1.8	8.3 $\pm$ 0.3	91.5 $\pm$ 2.0
	100 (PO)	102.1 $\pm$ 3.6	12.1 $\pm$ 0.8	87.6 $\pm$ 3.5
	10 (IV)	99.8 $\pm$ 1.2	6.3 $\pm$ 0.29	90.9 $\pm$ 1.1

a Values are calculated as a percent of the dose of  $^{14}\text{C}$  administered.

b Values are the mean of 3 animals + SEM.

**Table 2**  
**Accumulative Excretion of  $^{14}\text{CO}_2$  After Dosing Rats  
 With Diallylphthalate  
 Low Dose (1 mg/kg PO)**

Time (Hr)	<u>Rate</u>			Mean $\pm$ SEM
	1	2	3	
1	4.1	1.3	2.9	2.8 $\pm$ 0.8
2	8.5	4.7	6.0	6.4 $\pm$ 1.1
3	10.8	8.0	9.3	9.4 $\pm$ 0.8
4	12.5	10.8	12.0	11.8 $\pm$ 0.5
5	13.8	13.9	15.1	14.3 $\pm$ 0.4
6	—	16.0	17.4	16.7 $\pm$ 0.7
8	17.3	20.1	22.1	19.8 $\pm$ 1.4
12	24.6	24.9	25.4	25.0 $\pm$ 0.2
24	27.4	27.3	27.3	27.3 $\pm$ 0.0

**Table 3**  
**Accumulative Excretion of  $^{14}\text{CO}_2$  After Dosing Rats**  
**With Diallylphthalate**  
**Medium Dose (10 mg/kg PO)**

Time (Hr)	<u>Rat</u>			Mean $\pm$ SEM
	1	2	3	
1	8.0	2.3	1.8	4.0 $\pm$ 2.0
2	16.2	7.9	4.6	9.6 $\pm$ 3.5
3	19.4	13.4	7.9	13.6 $\pm$ 3.3
4	20.8	17.6	11.1	16.5 $\pm$ 2.9
5	22.1	20.6	13.8	18.8 $\pm$ 2.6
6	22.8	22.4	17.5	20.9 $\pm$ 1.7
8	23.9	25.0	24.3	24.4 $\pm$ 0.32
12	25.2	27.9	29.1	27.4 $\pm$ 1.15
24	26.7	30.2	31.8	29.6 $\pm$ 1.5

**Table 4**  
**Accumulative Excretion of  $^{14}\text{CO}_2$  After Dosing Rats  
 With Diallylphthalate  
 High Dose (100 mg/kg PO)**

Time (Hr)	Rat			Mean $\pm$ SEM
	1	2	3	
1	0.28	0.49	0.93	0.57 $\pm$ 0.19
2	0.92	1.2	3.8	2.0 $\pm$ 0.92
3	2.3	2.0	7.6	4.0 $\pm$ 1.8
4	5.4	3.2	10.1	6.2 $\pm$ 2.0
5	7.7	4.6	12.4	8.2 $\pm$ 2.3
6	9.7	6.1	14.0	9.9 $\pm$ 2.3
8	13.2	8.7	16.6	12.8 $\pm$ 2.29
12	21.5	14.6	21.8	19.3 $\pm$ 2.35
24	25.7	25.3	26.0	25.7 $\pm$ 2.0

**Table 5**  
**Accumulative Excretion of  $^{14}\text{CO}_2$  After Dosing Rats  
 With Diallylphthalate  
 Medium Dose (10 mg/kg I.V.)**

Time (Hr)	Rat			Mean $\pm$ SEM
	1	2	3	
1	7.6	8.7	8.9	8.4 $\pm$ 0.4
2	14.1	13.8	16.9	14.9 $\pm$ 0.99
3	17.4	16.4	19.8	17.9 $\pm$ 1.0
4	19.2	17.9	22.1	19.7 $\pm$ 1.2
5	20.5	19.2	23.0	20.9 $\pm$ 1.1
6	21.4	19.9	24.3	21.9 $\pm$ 1.3
8	22.4	21.1	25.4	23.0 $\pm$ 1.3
12	23.7	22.6	26.9	24.4 $\pm$ 1.3
24	25.3	24.0	28.2	25.8 $\pm$ 1.2

**Table 6**  
**Accumulative Excretion of  $^{14}\text{CO}_2$  After Dosing Mice**  
**With Diallylphthalate**  
**Low Dose (1 mg/kg PO)**

Time (Hr)	Mouse			Mean $\pm$ SEM
	1	2	3	
1	0.5	0.5	0.9	0.6 $\pm$ 0.1
2	1.3	1.6	1.8	1.6 $\pm$ 0.1
3	2.2	3.7	3.2	3.0 $\pm$ 0.4
4	3.1	5.0	4.6	4.2 $\pm$ 0.6
5	3.6	5.8	6.0	5.1 $\pm$ 0.8
6	3.9	6.2	6.5	5.5 $\pm$ 0.8
8	4.3	6.8	7.3	6.1 $\pm$ 0.9
12	4.8	7.3	8.0	6.7 $\pm$ 1.0
24	5.4	7.7	8.6	7.2 $\pm$ 1.0

**Table 7**  
**Accumulative Excretion of  $^{14}\text{CO}_2$  After Dosing Mice**  
**With Diethylphthalate**  
**Medium Dose (10 mg/kg PO)**

Time (Hr)	<u>Mouse</u>			Mean $\pm$ SEM
	1	2	3	
1	0.5	0.5	0.7	0.6 $\pm$ 0.1
2	2.4	1.3	2.0	1.9 $\pm$ 0.3
3	4.3	2.7	3.6	3.5 $\pm$ 0.5
4	5.4	3.9	4.6	4.6 $\pm$ 0.4
5	6.0	5.0	5.2	5.4 $\pm$ 0.3
6	6.6	5.6	5.7	6.0 $\pm$ 0.3
8	7.1	6.3	6.4	6.6 $\pm$ 0.3
12	7.6	7.0	7.1	7.2 $\pm$ 0.2
24	8.2	7.7	8.9	8.3 $\pm$ 0.3

Table 8

**Accumulative Excretion of  $^{14}\text{CO}_2$  After Dosing Mice  
With Diallylphthalate  
High Dose (100 mg/kg PO)**

Time (Hr)	Mouse			Mean $\pm$ SEM
	1	2	3	
1	0.5	0.6	0.4	0.5 $\pm$ 0.1
2	1.8	2.0	1.7	1.8 $\pm$ 0.1
3	3.2	3.3	3.5	3.3 $\pm$ 0.1
4	5.0	4.8	5.8	5.2 $\pm$ 0.3
5	6.7	5.8	7.2	6.6 $\pm$ 0.4
6	7.9	7.3	7.3	7.5 $\pm$ 0.2
8	9.6	10.3	8.3	9.4 $\pm$ 0.6
12	10.5	13.0	10.0	11.2 $\pm$ 0.9
24	11.9	13.6	10.7	12.1 $\pm$ 0.8

**Table 9**  
**Accumulative Excretion of  $^{14}\text{CO}_2$  After Dosing Mice**  
**With Dialylphthalate**  
**Medium Dose (10 mg/kg I.V.)**

Time (Hr)	<u>Mouse</u>			Mean $\pm$ SEM
	1	2	3	
1	1.1	1.4	1.0	1.2 $\pm$ 0.1
2	1.8	2.9	1.8	2.2 $\pm$ 0.4
3	2.8	4.0	2.6	3.1 $\pm$ 0.4
4	4.0	4.6	3.4	4.0 $\pm$ 0.4
5	4.5	4.9	3.9	4.4 $\pm$ 0.3
6	4.8	5.1	4.2	4.7 $\pm$ 0.3
8	5.2	5.4	4.9	5.2 $\pm$ 0.2
12	5.8	5.8	5.3	5.6 $\pm$ 0.2
24	6.8	6.2	5.8	6.3 $\pm$ 0.29

Table 10  
**Summary of the percent of dose in tissues and excreta vs time  
from rats (n=3) administered Diallylphthalate (10mg/kg I.V.)**

Tissue	30 min	1 hr	2 hr	4 hr	8 hr	12 hr	24 hr
Blood	4.6 $\pm$ 0.7	2.8 $\pm$ 0.1	2.4 $\pm$ 0.12	1.5 $\pm$ 0.03	0.72 $\pm$ 0.02	0.63 $\pm$ 0.07	0.4 $\pm$ 0.06
Brain	0.16 $\pm$ 0.01	0.25 $\pm$ 0.4	0.24 $\pm$ 0.01	0.19 $\pm$ 0.01	0.07 $\pm$ 0.01	0.06 $\pm$ 0.01	0.04 $\pm$ 0.01
Lung	0.23 $\pm$ 0.03	0.20 $\pm$ 0.02	0.14 $\pm$ 0.01	0.10 $\pm$ 0.01	0.07 $\pm$ 0.00	0.06 $\pm$ 0.00	0.09 $\pm$ 0.00
Liver	6.6 $\pm$ 0.6	5.0 $\pm$ 0.1	3.7 $\pm$ 0.3	3.0 $\pm$ 0.2	1.3 $\pm$ 0.09	0.90 $\pm$ 0.01	0.65 $\pm$ 0.03
Kidney	2.6 $\pm$ 0.6	1.4 $\pm$ 0.1	0.88 $\pm$ 0.05	0.58 $\pm$ 0.07	0.23 $\pm$ 0.00	0.16 $\pm$ 0.01	0.12 $\pm$ 0.00
Spleen	0.09 $\pm$ 0.00	0.34 $\pm$ 0.02	0.09 $\pm$ 0.1	0.04 $\pm$ 0.1	0.04 $\pm$ 0.01	0.04 $\pm$ 0.00	0.02 $\pm$ 0.00
Testes	0.62 $\pm$ 0.06	0.47 $\pm$ 0.03	0.42 $\pm$ 0.02	0.31 $\pm$ 0.03	0.12 $\pm$ 0.00	0.10 $\pm$ 0.01	0.08 $\pm$ 0.01
Small Intestine	8.1 $\pm$ 2.7	7.9 $\pm$ 1.4	2.7 $\pm$ 0.2	1.7 $\pm$ 0.53	0.79 $\pm$ 0.06	0.68 $\pm$ 0.02	0.39 $\pm$ 0.05
Muscle	11.4 $\pm$ 0.61	10.8 $\pm$ 0.6	11.3 $\pm$ 0.7	6.4 $\pm$ 0.33	2.6 $\pm$ 0.21	2.4 $\pm$ 0.4	1.93 $\pm$ 0.05
Skin	5.1 $\pm$ 0.70	5.3 $\pm$ 0.2	3.8 $\pm$ 0.5	3.4 $\pm$ 0.18	1.6 $\pm$ 0.30	1.8 $\pm$ 0.1	1.2 $\pm$ 0.23
Fat	0.60 $\pm$ 0.12	1.1 $\pm$ 0.1	0.53 $\pm$ 0.08	0.64 $\pm$ 0.15	0.72 $\pm$ 0.12	0.66 $\pm$ 0.13	0.67 $\pm$ 0.12
Intestinal Contents	4.7 $\pm$ 0.6	5.7 $\pm$ 2.8	6.6 $\pm$ 2.6	1.03 $\pm$ 0.42	0.23 $\pm$ 0.04	0.12 $\pm$ 0.05	1.8 $\pm$ 0.15
Urine	9.9 $\pm$ 8.7	29.7 $\pm$ 5.8	37.1 $\pm$ 5.1	54.2 $\pm$ 3.5	54.1 $\pm$ 1.3	64.8 $\pm$ 9.0	70.0 $\pm$ 3.6

Table 10  
 Summary of the percent of dose in tissues and excreta versus time from rats (n=3)  
 administered 10 mg/kg Diallylphthalate intravenously (continued)<sup>a</sup>

Tissue	<b>30 min</b>	<b>1 hr</b>	<b>2 hr</b>	<b>4 hr</b>	<b>8 hr</b>	<b>12 hr</b>	<b>24 hr</b>
Tail	1.7 ± 0.41	1.2 ± 0.13	0.59 ± 0.23	0.1 ± 0.01	0.32 ± 0.24	0.59 ± 0.18	No data
Total Recovery	56.4 ± 6.8	72.6 ± 6.9	70.7 ± 8.4	73.3 ± 2.9	62.9 ± 1.4	72.9 ± 8.6	7.4 ± 0.2 (without urine <sup>b</sup> )

<sup>a</sup>Excreta includes urine only. Bile, feces, <sup>14</sup>CO<sub>2</sub>, and volatile organics were not collected.

<sup>b</sup>Urine value for 24 hour time point is 70.0 ± 3.6.

**Table 11**  
**Summary of the percent of dose in tissues and excreta vs time**  
**from mice (n=3) administered Diallylphthalate (10mg/kg I.V.)**

Tissue	30 min	1 hr	2 hr	4 hr	8 hr	12 hr	24 hr
Blood	2.1 $\pm$ 0.2 (n=6)	1.1 $\pm$ 0.1 (n=6)	0.55 $\pm$ 0.02	0.33 $\pm$ 0.02	0.25 $\pm$ 0.03	0.21 $\pm$ 0.01	0.11 $\pm$ 0.01
Brain	0.12 $\pm$ 0.01	0.10 $\pm$ 0.02	0.07 $\pm$ 0.01	0.04 $\pm$ 0.01	0.03 $\pm$ 0.00	0.02 $\pm$ 0.00	0.02 $\pm$ 0.00
Lung	0.21 $\pm$ 0.04	0.12 $\pm$ 0.01	0.11 $\pm$ 0.02	0.07 $\pm$ 0.01	0.04 $\pm$ 0.00	0.03 $\pm$ 0.00	0.03 $\pm$ 0.00
Liver	3.8 $\pm$ 0.4 (n=6)	1.7 $\pm$ 0.1 (n=6)	1.1 $\pm$ 0.1	0.57 $\pm$ 0.02	0.30 $\pm$ 0.02	0.29 $\pm$ 0.04	0.17 $\pm$ 0.02
Kidney	3.6 $\pm$ 0.5 (n=6)	1.8 $\pm$ 0.2 (n=6)	0.49 $\pm$ 0.01	0.23 $\pm$ 0.02	0.17 $\pm$ 0.02	0.16 $\pm$ 0.02	0.07 $\pm$ 0.01
Spleen	0.08 $\pm$ 0.01	0.09 $\pm$ 0.01	0.05 $\pm$ 0.00	0.02 $\pm$ 0.00	0.01 $\pm$ 0.00	0.02 $\pm$ 0.00	0.01 $\pm$ 0.00
Testes	0.24 $\pm$ 0.12	0.10 $\pm$ 0.02	0.06 $\pm$ 0.01	0.02 $\pm$ 0.00	0.02 $\pm$ 0.00	0.01 $\pm$ 0.00	0.01 $\pm$ 0.00
Small Intestine	13.55 $\pm$ 4.64 (n=6)	4.6 $\pm$ 1.1 (n=6)	1.0 $\pm$ 0.1	1.4 $\pm$ 0.6	0.31 $\pm$ 0.03	0.38 $\pm$ 0.15	0.14 $\pm$ 0.01
Muscle	7.6 $\pm$ 0.8 (n=6)	5.5 $\pm$ 0.8 (n=5)	1.7 $\pm$ 0.1	0.93 $\pm$ 0.09	0.64 $\pm$ 0.06	0.55 $\pm$ 0.02	0.55 $\pm$ 0.22
Skin	4.60 $\pm$ 0.74 (n=6)	3.6 $\pm$ 0.09 (n=6)	0.80 $\pm$ 0.09	0.75 $\pm$ 0.27	0.33 $\pm$ 0.01	0.48 $\pm$ 0.04	0.25 $\pm$ 0.11
Fat	0.61 $\pm$ 0.14	0.51 $\pm$ 0.16	0.22 $\pm$ 0.04	0.12 $\pm$ 0.00	0.12 $\pm$ 0.00	0.12 $\pm$ 0.01	0.28 $\pm$ 0.21
Bile	0.71 $\pm$ 0.2	0.6 $\pm$ 0.12 (n=2)	0.11 $\pm$ 0.02 (n=2)	0.54 $\pm$ 0.09 (n=2)	0.15 $\pm$ 0.07	0.05 $\pm$ 0.02	---
Urine	36.3 $\pm$ 10.3	62.1 $\pm$ 1.0	72.7 $\pm$ 4.1	78.7 $\pm$ 3.3	70.2 $\pm$ 13.5	83.4 $\pm$ 3.6	90.9 $\pm$ 1.1

Table 12  
 Total recoveries of the percent of dose in tissues and excreta versus time from mice (n=3)  
 administered 10 mg/kg Diallylphthalate intravenously<sup>a,b</sup>

Tissue	<b>30 min</b>	<b>1 hr</b>	<b>2 hr</b>	<b>4 hr</b>	<b>8 hr</b>	<b>12 hr</b>	<b>24 hr</b>
Total Recovery	75.81 ± 10.2	62.59 ± 21.7	79.1 ± 3.9	83.6 ± 3.7	73.3 ± 13.4	85.7 ± 3.4	93.04 ± 1.47

<sup>a</sup>Values are % of dose and are from the original set of intravenous distribution studies with n =3 at each time point unless no sample was collected for one of the mice. Excreta is represented by urine and bile only.

<sup>b</sup>These recovery values represents the recovery summation for Table 11 (except for 30 minute and 1 hour time points), Table 13, and Table 14. Additional data was added to Table 13 and 14 data for the Table 11 summary.

**Table 13**  
**Mouse - DAP Kinetics**  
**Percent of Dose in Tissues and Excreta**  
**1/2 Hour After I.V. Administration of Diethylphthalate**

Tissue*	0.5-1	0.5-2	0.5-3	X $\pm$ SEM
Blood	2.42	2.60	2.04	2.35 $\pm$ 0.17
Brain	0.12	0.14	0.09	0.12 $\pm$ 0.01
Lung	0.26	0.22	0.14	0.21 $\pm$ 0.04
Liver	4.88	4.55	3.39	4.27 $\pm$ 0.45
Kidney	5.25	4.77	2.81	4.28 $\pm$ 0.75
Spleen	0.10	0.08	0.06	0.08 $\pm$ 0.01
Testes	0.48	0.12	0.11	0.24 $\pm$ 0.12
Small Intestine	22.62	14.77	6.20	14.53 $\pm$ 4.7
Muscle	8.71	7.13	5.38	7.07 $\pm$ 0.96
Skin	4.98	3.22	2.81	3.67 $\pm$ 0.67
Fat	0.77	0.72	0.34	0.61 $\pm$ 0.14
Bile	0.57	1.1	0.45	0.71 $\pm$ 0.20
Urine	17.7	53.3	38.0	36.3 $\pm$ 10.3
Total	69.98	95.65	61.8	75.81 $\pm$ 10.2

\*Values are % of dose

**Table 14**  
**Mouse - DAP Kinetics**  
**Percent of Dose in Tissues and Excreta**  
**1 Hour After I.V. Administration of Diallylphthalate**

Tissue*	1-1	1-2	1-3	X $\pm$ SEM
Blood	1.35	1.21	0.94	1.17 $\pm$ 0.12
Brain	0.10	0.14	0.07	0.10 $\pm$ 0.02
Lung	0.12	0.15	0.10	0.12 $\pm$ 0.01
Liver	1.67	1.87	1.34	1.63 $\pm$ 0.15
Kidney	2.84	1.98	1.29	2.04 $\pm$ 0.45
Spleen	0.08	0.11	0.08	0.09 $\pm$ 0.01
Testes	0.11	0.13	0.07	0.10 $\pm$ 0.02
Small Intestine	8.53	5.62	4.89	6.35 $\pm$ 1.11
Muscle	4.40	4.30	5.84	4.85 $\pm$ 0.50
Skin	2.75	1.73	2.35	2.28 $\pm$ 0.30
Fat	0.83	0.32	0.39	0.51 $\pm$ 0.16
Bile	0.48	-----	0.71	0.60 $\pm$ 0.12 (N=2)
Urine	51.1	1.6	73.18	62.1 $\pm$ 11.0 (N=2)
Total	76.53	20.0	91.25	62.59 $\pm$ 21.7

\*Values are % of dose

**Table 15**  
**Summary of the Percent of Dose in Tissue and Excreta**  
**From Rats (n=3) 24 Hours After Oral Administration**  
**of Diallylphthalate**

Tissue	Percent of Dose $\pm$ SEM		
	Low (1 mg/kg)	Medium (10 mg/kg)	High (100 mg/kg)
Blood	0.62 $\pm$ 0.05	0.99 $\pm$ 0.62	0.72 $\pm$ 0.09
Brain	0.05 $\pm$ 0.00	0.04 $\pm$ 0.00	0.05 $\pm$ 0.00
Lung	0.06 $\pm$ 0.00	0.07 $\pm$ 0.01	0.06 $\pm$ 0.01
Liver	0.81 $\pm$ 0.05	0.93 $\pm$ 0.09	0.06 $\pm$ 0.10
Kidney	0.15 $\pm$ 0.00	0.17 $\pm$ 0.01	0.19 $\pm$ 0.02
Spleen	0.03 $\pm$ 0.0	0.03 $\pm$ 0.00	0.03 $\pm$ 0.00
Testes	0.08 $\pm$ 0.00	0.08 $\pm$ 0.01	0.09 $\pm$ 0.01
Small Intestine	0.57 $\pm$ 0.04	0.61 $\pm$ 0.04	0.70 $\pm$ 0.15
Muscle	1.88 $\pm$ 0.05	2.3 $\pm$ 0.23	2.2 $\pm$ 0.2
Skin	0.91 $\pm$ 0.18	1.2 $\pm$ 0.3	1.0 $\pm$ 0.07
Fat	0.42 $\pm$ 0.08	0.90 $\pm$ 0.55	0.33 $\pm$ 0.04
Feces	3.07 $\pm$ 0.35	4.38 $\pm$ 2.29	5.2 $\pm$ 1.1
Urine	50.7 $\pm$ 0.8	60.0 $\pm$ 5.3	58.6 $\pm$ 0.8
CO <sub>2</sub>	27.3 $\pm$ 0.0	29.6 $\pm$ 1.5	25.7 $\pm$ 2.0
Total	87.2 $\pm$ 0.6	102.1 $\pm$ 1.3	96.1 $\pm$ 2.0

Table 16

**Summary of the Percent of Dose in Tissues and Excreta  
From Mice (n=3) 24 Hours After Oral Administration  
of Diallylphthalate**

Tissue	Percent of Dose $\pm$ SEM		
	Low Dose (1 mg/kg)	Medium Dose (10 mg/kg)	High Dose (100 mg/kg)
Blood	0.09 $\pm$ 0.01	0.09 $\pm$ 0.06	0.19 $\pm$ 0.02
Brain	0.02 $\pm$ 0.00	0.02 $\pm$ 0.00	0.04 $\pm$ 0.00
Lung	0.02 $\pm$ 0.00	0.04 $\pm$ 0.01	0.02 $\pm$ 0.00
Liver	0.17 $\pm$ 0.02	0.16 $\pm$ 0.02	0.24 $\pm$ 0.02
Kidney	0.04 $\pm$ 0.01	0.14 $\pm$ 0.10	0.07 $\pm$ 0.00
Spleen	0.01 $\pm$ 0.00	0.01 $\pm$ 0.00	0.02 $\pm$ 0.00
Testes	0.01 $\pm$ 0.00	0.01 $\pm$ 0.00	0.02 $\pm$ 0.00
Small Intestine	0.19 $\pm$ 0.04	0.21 $\pm$ 0.01	0.38 $\pm$ 0.03
Muscle	0.37 $\pm$ 0.10	0.43 $\pm$ 0.06	0.77 $\pm$ 0.06
Skin	0.15 $\pm$ 0.02	0.23 $\pm$ 0.03	0.31 $\pm$ 0.12
Fat	0.37 $\pm$ 0.14	0.26 $\pm$ 0.2	0.42 $\pm$ 0.09
Feces	0.48 $\pm$ 0.36	0.79 $\pm$ 0.49	0.40 $\pm$ 0.14
Urine	92.0 $\pm$ 2.9	91.5 $\pm$ 2.0	87.6 $\pm$ 3.5
CO <sub>2</sub>	7.2 $\pm$ 1.0	8.3 $\pm$ 0.3	12.1 $\pm$ 0.8
Total	100.6 $\pm$ 1.8	101.4 $\pm$ 1.8	102.1 $\pm$ 3.6

Table 17

**Total  $^{14}\text{C}$ , Diallylphthalate and Monoallylphthalate  
in the Blood of Mice and Rats after I.V. Administration  
of Diallylphthalate <sup>a</sup>**

Time (Min)	Animal	Total $^{14}\text{C}$	Diallylphthalate	Monoallylphthalate
5	Mouse <sup>b</sup>	8.8 $\pm$ 0.8	0.17 $\pm$ 0.05	2.7 $\pm$ 0.6
	Rat <sup>c</sup>	16.1 $\pm$ 1.1	0.45 $\pm$ 0.16	7.6 $\pm$ 0.30
10	Mouse	4.9 $\pm$ 0.6	0.23 $\pm$ 0.04	2.9 $\pm$ 0.4
	Rat	13.8 $\pm$ 0.7	0.06 $\pm$ 0.03	6.7 $\pm$ 0.3
15	Mouse	5.3 $\pm$ 0.2	0.01 $\pm$ 0.01	2.2 $\pm$ 0.2
	Rat	13.8 $\pm$ 0.7	0.06 $\pm$ 0.03	7.4 $\pm$ 0.6
20	Rat	12.0 $\pm$ 1.0	N.D. <sup>d</sup>	6.1 $\pm$ 0.6
30	Mouse	2.1 $\pm$ 0.2	N.D.	0.45 $\pm$ 0.08
	Rat	11.2 $\pm$ 1.4	N.D.	4.3 $\pm$ 0.8

a. Values are calculated as a percent of the dose of  $^{14}\text{C}$  administered.

b. Three mice were used for each time point.

c. Serial blood samples were taken from 3 rats anesthetized with pentobarbital (60 mg/kg).

d. Not detected.

**Table 18**  
**Summary of Total  $^{14}\text{C}$ , Diallylphthalate and Monoallylphthalate  
 in the Blood of Pentobarbital Anesthetized Rats  
 After I.V. Administration of Diallylphthalate.<sup>a</sup>**

Time (Min)	Rat #	Total $^{14}\text{C}$		Diallyl Phthalate		Monoallyl Phthalate	
		Percent Dose	$\bar{X} \pm \text{SEM}$	Percent Dose	$\bar{X} \pm \text{SEM}$	Percent Dose	$\bar{X} \pm \text{SEM}$
5	1	15.6	16.1 $\pm$	0.23	0.45 $\pm$	7.0	7.6 $\pm$
	2	18.2	1.1	0.36	0.16	8.0	0.30
	3	14.5		0.76		7.7	
10	1	15.1	13.8 $\pm$	0.07	0.06 $\pm$	7.4	6.7 $\pm$
	2	13.6	0.7	0.003	0.03	6.3	0.3
	3	12.6		0.12		6.6	
15	1	14.6	13.0 $\pm$	0.00	0.00	8.2	7.4 $\pm$
	2	12.9	0.9	0.00		6.3	0.6
	3	11.4		0.00		7.8	
20	1	13.5	12.0 $\pm$	0.00	0.00	7.1	6.1 $\pm$
	2	12.6	1.0	0.00		6.1	0.6
	3	10.0		0.00		5.0	
30	1	14.0	11.2 $\pm$	0.00	0.00	5.9	4.3 $\pm$
	2	10.0	1.4	0.00		3.6	0.8
	3	9.6		0.00		3.4	

<sup>a</sup> Serial blood samples were taken from 3 rats which were anesthetized with pentobarbital (60 mg/kg).

Table 19

**Summary of Total  $^{14}\text{C}$ , Diallylphthalate and Monoallylphthalate  
in the Blood of Mice after I.V. Administration of Diallylphthalate**

Time (Min)	Rat #	Percent Dose	Total $^{14}\text{C}$	Diallyl Phthalate	Monoallyl Phthalate
			$\bar{X} \pm \text{SEM}$	$\bar{X} \pm \text{SEM}$	$\bar{X} \pm \text{SEM}$
5	1	10.3	8.8 $\pm$	0.24	0.17 $\pm$
	2	7.9	0.8	0.07	0.05
	3	8.2		0.20	
10	4	6.0	4.9 $\pm$	0.22	0.23 $\pm$
	5	4.1	0.6	0.16	0.04
	6	4.6		0.31	
15	7	4.9	5.3 $\pm$	0.00	0.01 $\pm$
	19	5.7	0.2	0.01	0.01
	20	5.3		0.02	
30	14	1.3	2.1 $\pm$	ND <sup>a</sup>	0.40
	15	1.6	0.2	ND	0.35
	16	2.4		ND	0.61
	1	2.4		---	---
	2	2.6		---	---
	3	2.0		---	---
60	10	1.3	1.1 $\pm$	ND	0.11
	13	0.90	0.1	ND	0.06
	18	1.1		ND	0.02
	1	1.4		---	---
	2	1.2		---	---
	3	0.94		---	---
120	1	0.50	0.55 $\pm$		
	2	0.57	0.02		
	3	0.57			
240	1	0.29	0.33 $\pm$		
	2	0.36	0.02		
	3	0.34			
480	1	0.29	0.25 $\pm$		
	2	0.27	0.03		
	3	0.19			
720	1	0.19	0.21 $\pm$		
	2	0.24	0.01		
	3	0.21			
1440	1	0.12	0.11 $\pm$		

a Not Detected

**Table 20**  
**Elimination Constants for Diallylphthalate**  
**and Monoallylphthalate from Blood**  
**after Intravenous Administration**

Species	Compound	A	alpha (min <sup>-1</sup> )	n	r	t-1/2 (min)
rat <sup>a</sup>	DAP <sup>c</sup>	3.4	0.403	2	1.00	1.7
	MAP <sup>d</sup>	8.9	0.022	5	0.91	32
mouse <sup>b</sup>	DAP	1.2	0.283	3	0.82	2.4
	MAP	5.1	0.075	5	0.99	9.3

- a. The values for these calculations are from serial blood samples taken from 3 rats which were anesthetized with pentobarbital (60 mg/kg).
- b. Three mice were used for each time point.
- c. Diallylphthalate.
- d. Monoallylphthalate.

**Table 21**  
**Elimination Constants for Diallylphthalate**  
**(as  $^{14}\text{C}$  Equivalents) from Tissues of Rats**  
**Following Intravenous Administration**

Organ	A	B	alpha	beta	n <sup>a</sup>	r <sup>b</sup>	t-1/2 (hr)	
			(hr <sup>-1</sup> )	(hr <sup>-1</sup> )			alpha	beta
blood	7.3	1.9	1.98	0.0744	5	0.90	0.35	9.3
liver	6.0	3.4	1.146	0.0786	5	0.91	0.37	8.8
kidney	4.9	0.698	1.86	0.0858	5	0.88	0.37	8.1
muscle	1.3	3.01	0.202	0.0185	3	1.00	3.4	37
skin <sup>c</sup>	4.1	--	0.593	--	6	0.88	11.7	--
small intestine	12.2	1.7	0.912	0.0654	4	0.93	0.76	10.6
brain	0.19	0.09	0.129	0.0347	3	0.92	5.4	20
testes <sup>d</sup>	--	0.39	--	0.0798	6	0.88	--	8.7

- a. The number of points used to determine the terminal phase of the decay curve.
- b. Correlation coefficient for the terminal phase of the decay curve.
- c. The data is best described by a monoexponential equation.
- d. Insufficient data to calculate the alpha elimination phase.

**Table 22**  
**Elimination Constants for Diallylphthalate**  
**(as  $^{14}\text{C}$  Equivalents) from Tissues of Mice**  
**Following Intravenous Administration**

Organ	A	B	$\alpha$ $(\text{hr}^{-1})$	$\beta$ $(\text{hr}^{-1})$	n <sup>a</sup>	r <sup>b</sup>	$t_{1/2}$ (hr)	
							alpha	beta
blood	6.6	0.4	1.89	0.0539	4	1.00	0.37	12.8
liver	4.6	0.57	1.08	0.0533	4	0.93	0.64	13
kidney	8.4	0.29	1.79	0.0583	4	0.99	0.39	11.9
muscle	15.5	0.84	1.40	0.0215	4	0.84	0.50	32
skin	17.3	0.71	2.29	0.0442	4	0.71	0.30	15.7
small intestine	56	1.2	2.77	0.096	5	0.90	0.25	7.2
brain	0.11	0.04	0.66	0.0320	4	0.82	1.1	21.7
testes	0.99	0.02	1.30	0.0334	3	0.69	0.53	21
lung <sup>c</sup>	--	0.096	--	0.0612	6	0.84	--	11.3

a. The number of points used to determine the terminal phase of the decay curve.

b. Correlation coefficient for the terminal phase of the decay curve.

c. Insufficient data to calculate the alpha elimination phase.