

## ADME NTP Study S0088 beta-Bromo-beta-nitrostyrene

The contract laboratory used the abbreviation BNS for the test article.

Sex/Species: adult male F344 rats.

Vehicles: intravenous, Emulphor EL-620:serum 1:4 (v/v); oral, corn oil (dried by heating); dermal, acetone (dried over molecular sieves).

CASRN 7166-19-0

Radiolabeled with carbon-14 in the  $\beta$  position; beta-Bromo-beta-nitrostyrene, [ $\beta$ - $^{14}\text{C}$ ]-

Radiolabeled with tritium at the C4-ring position; beta-Bromo-beta-nitrostyrene, [ring 4- $^3\text{H}$ ]-

### Studies Performed:

- Single intravenous administration of 10 mg/kg [ $^3\text{H}/^{14}\text{C}$ ]BNS to rats with sacrifice 0.25, 0.75, 2, 6, 24, and 72 hours (h) postdose.
- Single intravenous administration of 10 mg/kg [ $^3\text{H}/^{14}\text{C}$ ]BNS with sacrifice 6 hours postdose (bile collection study, n=2). (Table 4)
- Single oral gavage administration of 1.2, 12, and 120 mg/kg [ $^3\text{H}/^{14}\text{C}$ ]BNS to rats with sacrifice 24 hours postdose.
- Single oral gavage administration of 1.0, 10, and 98 mg/kg [ $^3\text{H}/^{14}\text{C}$ ]BNS to rats with sacrifice 72 hours postdose.
- Single oral gavage administration 10 mg/kg [ $^3\text{H}/^{14}\text{C}$ ]BNS to rats pretreated with antibiotic for four days with sacrifice 24 hours postdose. (Table 5)
- Single dermal administration of 0.1, 1.0, or 10 mg/cm<sup>2</sup> (~ 0.90, 7.4, 86 mg/kg, respectively) [ $^3\text{H}/^{14}\text{C}$ ]BNS to rats with covered dose site and sacrifice 24 hours postdose.

The actual ratio of [ $^3\text{H}$ ] to [ $^{14}\text{C}$ ]BNS in the dosing solutions was not specified. Water caused some decomposition of the BNS and care was taken to remove water from the stock solvents and route vehicles.

Stability studies showed that essentially all the BNS at a concentration of 0.17 mg/mL added to whole blood was degraded within 5 minutes and that BNS was highly unstable in liver homogenates and small intestinal contents but was stable in the stomach contents. No attempts were made to extract the parent compound from tissues or excreta.

Antibiotics (100 mg/kg lincomycin and 100 mg/kg neomycin) were orally administered to four rats for four days to deplete their intestinal microflora populations. On day 5, the animals were administered 10 mg/kg [ $^3\text{H}/^{14}\text{C}$ ]BNS by oral gavage.

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Table 1

Cumulative Excretion of Total  $^3\text{H}/^{14}\text{C}$  After Intravenous Administration of [ $^3\text{H}/^{14}\text{C}$ ]DNS to Male F344 Rats (% Dose)<sup>a</sup>

Dose (mg/kg)	Time (h)	Urine		Feces		Breath			Total	
		$^3\text{H}$	$^{14}\text{C}$	$^3\text{H}$	$^{14}\text{C}$	$^3\text{H}$	Volatiles $^{14}\text{C}$	$\text{CO}_2$ $^{14}\text{C}$	$^3\text{H}$	$^{14}\text{C}$
9.7	.75	29.2 ± 4.1 <sup>b</sup>	7.0 ± 1.1 <sup>b</sup>		NA <sup>c</sup>		NA	NA	29.2 ± 4.1	7.0 ± 1.1
9.2	2	61.8 ± 40.0 <sup>d</sup>	15.8 ± 10.6 <sup>d</sup>	1.6 ± 3.1	.4 ± .8	<0.1	1.2 ± 0.7	.5 ± .2	63.4 ± 36.1	17.9 ± 9.3
9.6	6	28.5 ± 23.8 <sup>d</sup>	8.4 ± 5.4 <sup>d</sup>	0 ± 0	.1 ± .1	.1 ± .1	5.2 ± .2	1.7 ± .4	28.6 ± 20.6	15.4 ± 3.6
8.5	0-6	51.3 ± 7.9	14.3 ± 3.0			<0.1	6.0 ± 0.3	2.1 ± 0.2		
	6-12	61.5 ± 4.4	19.2 ± 2.2			<0.1	10.6 ± 0.4	4.3 ± 0.4		
	12-24	67.5 ± 3.8 <sup>d</sup>	24.0 ± 2.4 <sup>d</sup>	10.3 ± 2.1	11.3 ± 1.6 <sup>e</sup>	.1 ± 0	12.8 ± 1.2	7.1 ± 2.1	77.9 ± 5.5	55.2 ± 1.9
9.1	0-6	55.7 ± 2.6	15.6 ± 1.0			<0.1	5.6 ± 0.8	3.0 ± 0.3		
	6-12	66.9 ± 2.2	21.6 ± 0.7			<0.1	10.7 ± 1.4	5.6 ± 0.5		
	12-24	70.5 ± 2.0	24.8 ± 0.9	8.9 ± 1.1	10.5 ± 1.0 <sup>e</sup>	<0.1	15.6 ± 2.0	8.5 ± 0.8	79.4 ± 1.1	58.5 ± 1.4
	24-30	71.3 ± 2.1	25.6 ± 0.9			<0.1	16.6 ± 2.0	10.8 ± 2.3		
	30-48	72.8 ± 2.1	27.3 ± 0.5	10.3 ± 1.3	12.6 ± 1.0	<0.1	18.0 ± 2.0	14.5 ± 2.6	83.1 ± 1.1	72.4 ± 3.3
	48-72	74.2 ± 2.1	28.6 ± 0.6	10.6 ± 1.3	13.3 ± 1.1			17.9 ± 2.6	84.8 ± 1.1	77.3 ± 3.4

<sup>a</sup> Values are mean ± SD for 4 animals.<sup>b</sup> Represents urine extracted from bladder at sacrifice.<sup>c</sup> Sample not collected or not analyzed.<sup>d</sup> Represents urine collected from metabolism cage and bladder urine at sacrifice.<sup>e</sup> Feces were collected over time periods 0-24, 24-48 and 48-72 h.

Table 2

Recovery of Total  $^3\text{H}$  and  $^{14}\text{C}$  After IV Administration of [ $^3\text{H}/^{14}\text{C}$ ]BNS to F344 Male Rats (% Dose)<sup>a</sup>

Dose (mg/kg)	Excreta Isotope	Urine		Feces		Breath			Tissues <sup>b</sup>		Total <sup>c</sup>		
		$^3\text{H}$	$^{14}\text{C}$	$^3\text{H}$	$^{14}\text{C}$	$^3\text{H}$	Volatiles $^{14}\text{C}$	$\text{CO}_2$ $^{14}\text{C}$	$^3\text{H}$	$^{14}\text{C}$	$^3\text{H}$	$^{14}\text{C}$	
	Time (h)												
9.5	0.25		NA <sup>d</sup>		NA <sup>d</sup>		NA <sup>d</sup>		NA <sup>d</sup>	80.5 <sup>f</sup>	76.7 <sup>f</sup>	80.5	76.7
9.7	0.75	29.2 ± 4.1	7.0 ± 1.1		NA <sup>d</sup>		NA <sup>d</sup>		NA <sup>d</sup>	51.9 <sup>e</sup>	53.4 <sup>e</sup>	81.1	60.4
9.2	2	61.8 ± 40.0	15.8 ± 10.6	1.6 ± 3.1	0.4 ± 0.8	<0.1	1.2 ± 0.7	0.5 ± 0.2	31.9 <sup>f</sup>	39.0 <sup>f</sup>	95.3	56.9	
9.6	6	28.5 ± 23.8	8.4 ± 5.4	0	0.1 ± 0.1	0.1 ± 0.1	5.2 ± 0.2	1.7 ± 0.4	20.5 <sup>f</sup>	31.5 <sup>f</sup>	49.1	46.9	
8.5	24	67.5 ± 3.8	24.0 ± 2.4	10.3 ± 2.1	11.3 ± 1.6	0.1 ± 0	12.8 ± 1.2	7.1 ± 2.1	14.7 <sup>f</sup>	18.6 <sup>f</sup>	92.6	73.8	
9.1	72	74.2 ± 2.1	28.6 ± 0.6	10.6 ± 1.3	13.3 ± 1.1	0.1 ± 0	18.0 ± 2.0	17.9 ± 2.6	7.3 <sup>e</sup>	12.1 <sup>e</sup>	92.2	89.9	

<sup>a</sup>  $\bar{X} \pm \text{SD}$  for 4 rats, except where noted.<sup>b</sup> Mean % dose for each tissue from 3 rats was calculated and then summed to get this value.<sup>c</sup>  $\bar{X}$  values for excreta and tissues were summed to get this total.<sup>d</sup> Not collected.<sup>e</sup> Sum of dose residing in following tissues: muscle, skin, adipose, blood, liver kidney, lung, heart, brain, eye, trachea, reproductive organs and GI tract.<sup>f</sup> Sum of dose residing in selected tissue, including muscle, skin, adipose, blood, liver, GI tract and GI tract contents.

Table 3

Cumulative Excretion of Total  $^3\text{H}$  and  $^{14}\text{C}$  After Oral Administration of [ $^3\text{H}/^{14}\text{C}$ ]BNS to Male F344 Rats (% Dose)<sup>a</sup>

Dose (mg/kg)	Excreta Isotope	Urine		Feces		Breath			Total	
		$^3\text{H}$	$^{14}\text{C}$	$^3\text{H}$	$^{14}\text{C}$	$^3\text{H}$	Volatiles $^{14}\text{C}$	$\text{CO}_2$ $^{14}\text{C}$	$^3\text{H}$	$^{14}\text{C}$
	Time (h)									
1.0	0-6	5.1 ± 10.2	3.5 ± 7.0	c	c	0.002 ± 0.001	0.87 ± 0.16	0.37 ± 0.10		
	6-12	41.5 ± 18.1	28.9 ± 11.1			0.005 ± 0.003	2.40 ± 0.53	0.99 ± 0.07		
	12-24	49.1 ± 18.0	37.3 ± 8.5	30.6 ± 3.2	32.6 ± 4.9	0.008 ± 0.004	4.79 ± 1.55	2.03 ± 0.073	79.8 ± 16.9	76.8 ± 6.0
	24-30	49.4 ± 18.1	37.6 ± 8.6			0.009 ± 0.004	5.10 ± 0.55	2.34 ± 0.13		
	30-48	49.4 ± 18.2	38.2 ± 8.6	32.5 ± 3.1	34.9 ± 4.7	0.010 ± 0.005	5.62 ± 0.53	2.64 ± 0.18	82.4 ± 17.6	81.6 ± 6.5
	48-72	50.1 ± 18.2	38.6 ± 8.6	32.8 ± 3.2	35.4 ± 4.8	d	d	3.11 ± 0.29	82.9 ± 17.8	82.7 ± 6.3
1.2 <sup>b</sup>	0-6	25.6 ± 7.0	19.9 ± 4.9	c	c	.0 ± .0	.5 ± .1	.2 ± .0	25.6 ± 7.0	20.6 ± 4.9
	6-12	39.3 ± 7.8	30.0 ± 5.6			.0 ± .0	1.6 ± .6	.8 ± .1	39.3 ± 7.8	32.4 ± 6.3
	12-24	56.6 ± 4.2	43.2 ± 2.7	30.6 ± 11.2	31.2 ± 11.1	.0 ± .0	4.3 ± .5	1.7 ± .3	87.3 ± 7.8	80.3 ± 9.2
10.0	0-6	25.9 ± 3.6	20.9 ± 3.1	c	c	0.002 ± 0.001	0.62 ± 0.16	1.41 ± 0.27		
	6-12	57.4 ± 4.1	47.9 ± 3.6			0.004 ± 0.001	1.96 ± 0.52	2.05 ± 0.38		
	12-24	64.2 ± 4.0	55.0 ± 3.7	27.1 ± 5.0	28.2 ± 5.0	0.005 ± 0.001	3.22 ± 1.03	3.04 ± 0.54	91.4 ± 4.3	88.7 ± 4.4
	24-30	64.8 ± 3.8	55.6 ± 3.6			0.006 ± 0.001	3.37 ± 1.18	3.82 ± 0.49		
	30-48	65.3 ± 3.7	56.1 ± 3.4	34.0 ± 10.6	35.3 ± 10.9	0.006 ± 0.001	3.41 ± 1.19	4.50 ± 0.20	99.2 ± 9.0	94.9 ± 2.6
	48-72	65.5 ± 3.8	56.4 ± 3.4	34.3 ± 10.6	35.6 ± 10.9	d	d	4.81 ± 0.26	99.8 ± 9.0	95.5 ± 2.5
12.0 <sup>b</sup>	0-6	18.7 ± 2.9	15.0 ± 2.3	c	c	.0 ± .0	.4 ± .1	.2 ± .1	18.7 ± 2.8	15.6 ± 2.2
	6-12	39.3 ± 10.9	29.5 ± 7.4			.0 ± .0	1.5 ± .7	.9 ± .1	39.4 ± 10.9	31.9 ± 6.7
	12-24	54.7 ± 2.8	42.0 ± .7	31.4 ± 1.2	32.7 ± 1.6	.1 ± .0	3.7 ± 1.2	2.4 ± .3	86.3 ± 1.7	80.8 ± .8
98.2	0-6	7.5 ± 4.5	5.6 ± 3.5	c	c	0.003 ± 0.001	0.48 ± 0.09	0.18 ± 0.03		
	6-12	41.1 ± 3.1	29.1 ± 2.7			0.008 ± 0.002	2.27 ± 0.39	0.70 ± 0.13		
	12-24	49.5 ± 3.5	37.0 ± 3.9	37.2 ± 2.7	39.1 ± 2.7	0.011 ± 0.001	4.37 ± 0.61	1.66 ± 0.27	86.8 ± 1.3	82.1 ± 1.8
	24-30	50.1 ± 3.5	37.5 ± 3.6			0.012 ± 0.001	4.69 ± 0.61	1.97 ± 0.35		
	30-48	50.6 ± 3.4	38.2 ± 3.5	39.4 ± 2.9	41.4 ± 2.9	0.014 ± 0.002	4.86 ± 0.62	2.47 ± 0.33	89.9 ± 0.7	87.1 ± 1.1
	48-72	50.8 ± 3.6	38.5 ± 3.5	39.5 ± 2.8	41.6 ± 2.9	d	d	2.67 ± 0.39	90.4 ± 0.7	87.7 ± 1.2
118 <sup>b</sup>	0-6	12.8 ± 2.5	10.3 ± 2.3	c	c	.0 ± .0	.4 ± .0	.2 ± .0	12.8 ± 2.5	10.9 ± 2.2
	6-12	33.4 ± 1.3	25.8 ± .8			.0 ± .0	1.9 ± .2	.6 ± .1	33.5 ± 6.3	28.3 ± .9
	12-24	43.7 ± 1.0	34.5 ± .5	28.4 ± 3.5	32.3 ± 3.7	.0 ± .0	4.8 ± .5	1.4 ± .2	72.2 ± 3.6	73.0 ± 3.8

<sup>a</sup> Average ± SD for 4 rats, except where noted.<sup>b</sup> Average ± SD for 3 rats.<sup>c</sup> Feces collection intervals were 0-24, 24-48 and 48-72 h.<sup>d</sup> Volatile breath collection discontinued at 48 h.

Table 4

Cumulative Excretion of Total  $^3\text{H}$  and  $^{14}\text{C}$  in Bile Following Oral Administration of 9.1 mg/kg [ $^3\text{H}/^{14}\text{C}$ ]BNS to F344-M Rats (% Dose)<sup>a</sup>

End of Collection Period (h)	$^3\text{H}$	$^{14}\text{C}$
0-1	0.12 ± 0.10	0.11 ± 0.10
1-2	0.32 ± 0.23	0.30 ± 0.23
2-3	0.55 ± 0.31	0.52 ± 0.32
3-4	0.76 ± 0.37	0.72 ± 0.37
4-5	0.98 ± 0.34	0.93 ± 0.35
5-6	1.16 ± 0.27	1.09 ± 0.30

<sup>a</sup> Values are mean ± range for two rats.

Table 5

Cumulative Excretion of Total  $^3\text{H}$  and  $^{14}\text{C}$  after Oral Administration of 10 mg/kg<sup>a</sup> [ $^3\text{H}/^{14}\text{C}$ ]BNS to Antibiotic-Treated and Non-Treated P344-M Rats (% Dose)<sup>b</sup>

Treatment	Time (h)	Urine		Feces		Breath			Total	
		$^3\text{H}$	$^{14}\text{C}$	$^3\text{H}$	$^{14}\text{C}$	Volatiles $^3\text{H}$	$^{14}\text{C}$	$^{14}\text{CO}_2$	$^3\text{H}$	$^{14}\text{C}$
Antibiotic-Treated	0-6	1.4 ± 2.9	1.1 ± 2.2		<sup>c</sup>	<0.1	0.5 ± 0.1	0.2 ± 0.0		
	6-12	53.4 ± 13.2	44.5 ± 10.9			<0.1	2.1 ± 0.6	0.5 ± 0.2		
	12-24	70.1 ± 5.5	59.2 ± 4.7	6.7 ± 3.3	6.3 ± 3.1	<0.1	4.9 ± 1.3	1.0 ± 0.4	71.5 ± 2.7	71.5 ± 2.7
Non-Treated	0-6	18.7 ± 2.9	15.0 ± 2.3		<sup>c</sup>	<0.1	0.4 ± 0.1	0.2 ± 0.1		
	6-12	39.3 ± 10.9	29.5 ± 7.4			<0.1	1.5 ± 0.7	0.9 ± 0.1		
	12-24	54.7 ± 2.8	42.0 ± 0.7	31.4 ± 1.2	32.7 ± 1.6	<0.1	3.7 ± 1.2	2.4 ± 0.3	86.3 ± 1.7	80.8 ± 0.8

<sup>a</sup> Actual dose to non-treated animals was 12 mg/kg.

<sup>b</sup>  $\bar{X} \pm \text{SD}$  for 4 rats in antibiotic treated group and for 3 rats in non-treated group.

<sup>c</sup> Feces collection interval was 0-24 h.

Table 6

Recovery of Total <sup>3</sup>H and <sup>14</sup>C After Oral Administration of [<sup>3</sup>H/<sup>14</sup>C]BNS to P344 Male Rats (% Dose)<sup>a</sup>

Dose (mg/kg)	Excreta Isotope	Urine		Feces		Breath			Tissues		Total <sup>c</sup>	
		<sup>3</sup> H	<sup>14</sup> C	<sup>3</sup> H	<sup>14</sup> C	<sup>3</sup> H	Volatiles <sup>14</sup> C	CO <sub>2</sub> <sup>14</sup> C	<sup>3</sup> H	<sup>14</sup> C	<sup>3</sup> H	<sup>14</sup> C
	Time (h)											
1.0	72	50.1 ± 18.2	38.6 ± 8.6	32.8 ± 3.2	35.4 ± 4.8	.010 ± .005	5.62 ± .53	3.11 ± .29	.874 <sup>d</sup>	2.6 <sup>d</sup>	83.8	85.3
1.2	24	56.6 ± 4.2 <sup>b</sup>	43.2 ± 2.7 <sup>b</sup>	30.6 ± 11.2 <sup>b</sup>	31.2 ± 11.1 <sup>b</sup>	0.00 ± 0.0 <sup>b</sup>	4.3 ± .5 <sup>b</sup>	1.7 ± .3 <sup>b</sup>	8.6 <sup>d,e</sup>	11.6 <sup>d,e</sup>	95.9	91.9
10	72	65.5 ± 3.8	56.4 ± 3.4	34.3 ± 10.6	35.6 ± 10.9	.006 ± .001	3.41 ± 1.19	4.81 ± .26	.47 <sup>d</sup>	1.0 <sup>d</sup>	100.3	96.5
12	24	54.7 ± 2.8 <sup>b</sup>	42.0 ± .7 <sup>b</sup>	31.4 ± 1.2 <sup>b</sup>	32.7 ± 1.6 <sup>b</sup>	.1 ± .0 <sup>b</sup>	3.7 ± 1.2 <sup>b</sup>	2.4 ± .3 <sup>b</sup>	6.2 <sup>d,e</sup>	8.4 <sup>d,e</sup>	92.5	89.2
98	72	50.8 ± 3.6	38.5 ± 3.5	39.5 ± 2.8	41.6 ± 2.9	.014 ± .002	4.86 ± .62	2.67 ± .39	.55 <sup>d</sup>	1.4 <sup>d</sup>	91.0	89.1
118	24	43.7 ± 1.0 <sup>b</sup>	34.5 ± .5 <sup>b</sup>	28.4 ± 3.5 <sup>b</sup>	32.3 ± 3.7 <sup>b</sup>	.0 ± .0 <sup>b</sup>	4.8 ± .5 <sup>b</sup>	1.4 ± .2 <sup>b</sup>	6.7 <sup>d,e</sup>	9.5 <sup>d,e</sup>	78.9	82.5

<sup>a</sup>  $\bar{X} \pm SD$  for 4 rats, except where noted.

<sup>b</sup> Mean of dose for each tissue from 3 rats was calculated and then summed to get this value.

<sup>c</sup>  $\bar{X}$  values for excreta and tissues were summed to get this total.

<sup>d</sup> Sum of dose residing in following tissues: muscle, skin, adipose, blood, liver kidney, lung, heart, brain, eye, trachea, reproductive organs and GI tract.

<sup>e</sup> Sum of dose residing in selected tissue, including muscle, skin, adipose, blood, liver, GI tract and GI tract contents.



Table 7

Cumulative Excretion of Total  $^3\text{H}/^{14}\text{C}$  After Dermal Administration of [ $^3\text{H}/^{14}\text{C}$ ]BNS to Male F344 Rats (% Dose)<sup>a</sup>

Dose ( $\mu\text{g}/\text{cm}^2$ )	Time (h)	Urine		Feces		Breath			Total	
		$^3\text{H}$	$^{14}\text{C}$	$^3\text{H}$	$^{14}\text{C}$	$^3\text{H}$ Volatiles	$^{14}\text{C}$	$\text{CO}_2$ $^{14}\text{C}$	$^3\text{H}$	$^{14}\text{C}$
0.10	0-6	18.6 ± 5.4	1.6 ± .7			.8 ± .6	6.7 ± 2.2	1.4 ± .7	19.4 ± 5.3	9.8 ± 2.8
	6-12	36.2 ± 4.6	4.7 ± 1.0			1.2 ± .5	12.6 ± 2.0	4.7 ± 1.9	37.4 ± 4.2	22.0 ± 1.6
	12-24	45.7 <sup>b</sup> ± 3.2	8.1 <sup>b</sup> ± 1.0	1.7 ± .5	3.7 ± .4	1.4 ± .5	16.6 ± 2.8	9.7 ± 2.3	48.8 ± 2.5	38.1 ± .9
1.0	0-6	9.2 ± 5.0	.6 ± .4			.1 ± .0	1.3 ± .3	.7 ± .2	9.2 ± 5.0	2.7 ± .3
	6-12	18.8 ± 4.1	1.9 ± .8			.1 ± .1	3.7 ± .7	3.3 ± .5	18.9 ± 4.2	8.9 ± .4
	12-24	44.8 <sup>b</sup> ± .8	7.5 <sup>b</sup> ± .5	.8 ± .2	3.7 ± .5	.3 ± .1	7.7 ± 1.4	9.5 ± .8	45.9 ± 1.1	28.4 ± .7
10	0-6	1.6 ± 1.0	.1 ± .0			.0 ± .0	.1 ± .1	.1 ± .0	1.6 ± 1.0	.2 ± .1
	6-12	3.6 ± .6	.2 ± .1			.1 ± .1	.4 ± .1	.2 ± .1	3.7 ± .6	.8 ± .2
	12-24	7.4 <sup>b</sup> ± .6	.7 <sup>b</sup> ± .1	.2 ± .1	.2 ± .1	.2 ± .1	.9 ± .2	.8 ± .3	7.8 ± .6	2.5 ± .5

<sup>a</sup> Values are mean ± SD for 4 animals.<sup>b</sup> Represents urine collected from metabolism cage and bladder urine collected at sacrifice.

Table 8

Recovery of Total  $^3\text{H}$  and  $^{14}\text{C}$  After Dermal Application of [ $^3\text{H}/^{14}\text{C}$ ]BNS to F344 Male Rats (% Dose)<sup>a</sup>

Dose (mg/cm <sup>2</sup> )	Urine		Feces		Breath			Tissues <sup>b</sup>		Non-absorbed Dose		Total <sup>c</sup>	
	$^3\text{H}$	$^{14}\text{C}$	$^3\text{H}$	$^{14}\text{C}$	$^3\text{H}$	$^{14}\text{C}$	$^{14}\text{CO}_2$	$^3\text{H}$	$^{14}\text{C}$	$^3\text{H}$	$^{14}\text{C}$	$^3\text{H}$	$^{14}\text{C}$
0.1	45.7 ± 3.2	8.1 ± 1.0	1.7 ± .5	3.7 ± .4	1.4 ± .5	16.6 ± 2.8	9.7 ± 2.3	7.0 <sup>d</sup>	15.2 <sup>d</sup>	18.4 ± .7	18.7 ± 1.5	74.2	72.0
1.0	44.8 ± .8	7.5 ± .5	.8 ± .2	3.7 ± .5	.3 ± .1	7.7 ± 1.4	9.5 ± .8	8.9 <sup>d,e</sup>	21.1 <sup>d,e</sup>	39.4 ± 2.7	37.7 ± 2.2	94.2	87.2
10	7.4 ± .6	.7 ± .1	.2 ± .1	.2 ± .1	.2 ± .1	.9 ± .2	.8 ± .3	1.5 <sup>d</sup>	1.5 <sup>d</sup>	86.1 ± .6	88.1 ± 1.5	93.8	92.1

<sup>a</sup>  $\bar{X} \pm \text{SD}$  for 4 rats, except where noted.

<sup>b</sup> Mean % dose for each tissue from 3 rats was calculated and then summed to get this value.

<sup>c</sup>  $\bar{X}$  values for excreta and tissues were summed to get this total.

<sup>d</sup> Includes dose site skin, as well as muscle, skin, adipose, blood, liver, kidney, lung, heart, brain, eye, reproductive organs and GI tract.

<sup>e</sup> Includes tissues in note d above and GI tract contents.

Table 9

Amount of  $^3\text{H}$ -Labeled Compounds in Tissues After Intravenous Administration  
of 9.1 - 9.7 mg/kg of [ $^3\text{H}/^{14}\text{C}$ ]BNS to Fischer 344 Male Rats (% Dose)<sup>a</sup>

Time (h)	0.25	0.75	2	6	24	72
Tissue Name	% Dose in Total Tissue					
Average Adipose <sup>b</sup>	7.42 ± 0.43	8.39 ± 1.05	5.65 ± 2.23	1.75 ± 0.57	0.243 ± 0.032	0.013 ± 0.050
Adrenal gland		0.011				0.002
Bladder		0.171				0.003
Blood <sup>b</sup>	30.5 ± 3.2	16.9 ± 2.1	14.20 ± 2.00	11.8 ± 6.7	10.2 ± 0.5	4.41 ± 0.51
Brain		0.122				0.017
Cecum		0.087				0.015
Esophagus	0.038 ± 0.009	0.032	0.012 ± 0.004	0.006 ± 0.001	0.004 ± 0.001	0.005
Eye		0.011				0.002
Heart		0.185				0.038
Intestine, large		0.126				0.014
Intestine, small		1.69				0.049
Kidney	7.67 ± 1.30	2.14	1.18 ± 0.33	0.477 ± 0.090	0.148 ± 0.015	0.088
Liver	7.53 ± 1.36	2.83 ± 0.218	2.11 ± 0.22	1.53 ± 0.68	0.920 ± 0.379	0.363 ± 0.032
Lung		0.284				0.071
Average Muscle <sup>b</sup>	17.3 ± 0.5	12.4 ± 1.6	5.39 ± 1.42	2.95 ± 0.49	2.09 ± 0.10	1.32 ± 0.09
Plasma	5.04 ± 0.35	2.85 ± 0.43	1.44 ± 0.45	0.689 ± 0.050	0.412 ± 0.057	0.232 ± 0.046
Prostate		0.102				0.006
Seminal vesicle		0.087				0.006
Average Skin <sup>b</sup>	9.56 ± 0.65	5.59 ± 1.50	2.37 ± 0.70	1.07 ± 0.11	0.689 ± 0.032	0.054 ± 0.008
Spleen	0.218 ± 0.014	0.415	0.855 ± 0.207	0.840 ± 0.227	0.355 ± 0.031	0.155
Stomach	0.199 ± 0.066	0.163	0.076 ± 0.014	0.037 ± 0.007	0.017 ± 0.003	0.015
Testis		0.172				0.029
Trachea	0.023 ± 0.010	0.017	0.013 ± 0.003	0.010 ± 0.005	0.005 ± 0.002	0.008
Total, excluding plasma	80.5%	51.9%	31.9%	20.5%	14.7%	7.29%

<sup>a</sup> Values are mean ± SD for 3 animals, except where SD value is absent. Values for these data are mean for 2 animals.

<sup>b</sup> Total adipose tissue assumed to be 10% of body weight; blood = 6.3%; muscle = 50%; skin = 15%.

Table 10

Amount of  $^{14}\text{C}$ -Labeled Compounds in Tissues After Intravenous Administration  
of 9.1 - 9.7 mg/kg of [ $^3\text{H}/^{14}\text{C}$ ]BNS to Fischer 344 Male Rats (% Dose)<sup>a</sup>

Time (h)	0.25	0.75	2	6	24	72
Tissue Name	% Dose in Total Tissue					
Average Adipose <sup>b</sup>	7.39 ± 0.61	8.28 ± 1.11	5.59 ± 1.83	2.11 ± 0.47	0.461 ± 0.081	0.370 ± 0.060
Adrenal gland		0.011				0.003
Bladder		0.089				0.006
Blood <sup>b</sup>	31.0 ± 2.7	18.7 ± 1.4	16.0 ± 2.0	13.5 ± 6.2	10.7 ± 0.51	5.10 ± 0.54
Brain		0.154				0.021
Cecum		0.094				0.041
Esophagus	0.032 ± 0.008	0.033	0.015 ± 0.003	0.014 ± 0.006	0.020 ± 0.015	0.014
Eye		0.012				0.004
Heart		0.205				0.062
Intestine, large		0.131				0.056
Intestine, small		1.68				0.175
Kidney	5.19 ± 0.25	1.51	1.02 ± 0.330	0.546 ± 0.089	0.224 ± 0.015	0.178
Liver	7.46 ± 1.27	3.30 ± 0.29	2.94 ± 0.118	2.62 ± 0.69	1.47 ± 0.37	0.861 ± 0.036
Lung		0.301				0.127
Average Muscle <sup>b</sup>	16.2 ± 0.8	11.7 ± 1.3	7.94 ± 1.08	8.25 ± 0.42	3.37 ± 0.26	2.63 ± 0.07
Plasma	4.28 ± 0.23	3.34 ± 0.91	2.14 ± 0.90	1.41 ± 0.08	0.772 ± 0.129	0.505 ± 0.096
Prostate		0.083				0.018
Seminal vesicle		0.059				0.037
Average Skin	9.02 ± 0.36	6.13 ± 1.22	4.30 ± 0.94	3.37 ± 0.41	1.84 ± 0.12	1.98 ± 0.39
Spleen	0.215 ± 0.011	0.453	0.941 ± 0.197	0.911 ± 0.195	0.383 ± 0.027	0.186
Stomach	0.184 ± 0.063	0.240	0.171 ± 0.086	0.139 ± 0.005	0.156 ± 0.057	0.192
Testis		0.217				0.074
Trachea	0.023 ± 0.009	0.017	0.018 ± 0.005	0.015 ± 0.006	0.008 ± 0.003	0.014
Total, excluding plasma	76.7%	53.4%	39.0%	31.5%	18.6%	12.5%

<sup>a</sup> Values are mean ± SD for 3 animals, except where SD value is absent. Values for these data are mean for 2 animals.

<sup>b</sup> Total adipose tissue assumed to be 10% of body weight; blood = 6.3%; muscle = 50%; skin = 15%.

Table 11

Concentration of <sup>3</sup>H-Labeled Compounds in Tissues After Intravenous Administration  
of 9.1 - 9.7 mg/kg of [<sup>3</sup>H/<sup>14</sup>C]BNS to Fischer 344 Male Rats (ng-eq/g)<sup>a</sup>

Time (h)	0.25	0.75	2	6	24	72
Tissue Name	ng-eq Compound per g Tissue					
Adipose, epididymal		6320 ± 483				105 ± 32
Adipose, kidney		8660 ± 2200				79 ± 2
Adipose, mesenteric		9460 ± 2350				207 ± 104
Average Adipose	6960 ± 339	8150 ± 1630	5120 ± 2030	1610 ± 448	205 ± 29	130 ± 67
Adrenal gland		7260				724
Bladder		40800				1010
Blood	45400 ± 4500	26000 ± 3900	20400 ± 2930	17100 ± 9110	13700 ± 1340	6930 ± 621
Brain		1880				265
Cecum		4490				611
Esophagus	6000 ± 1940	5220	2220 ± 862	908 ± 211	538 ± 157	767
Eye		1410				205
Heart		5670				1080
Intestine, large		4710				493
Intestine, small		21600				517
Kidney	101000 ± 12100	28200	16700 ± 4790	6580 ± 1880	1930 ± 298	1130
Liver	20600 ± 2920	7530 ± 745	5710 ± 233	4350 ± 1700	2620 ± 1040	963 ± 58
Lung		8200				1880
Muscle, abdom.oblig		2750 ± 438				235 ± 37
Muscle, hind leg		1940 ± 344				248 ± 11
Muscle, trapezius		2510 ± 431				300 ± 20
Average Muscle	3230 ± 42	2400 ± 416	974 ± 257	547 ± 61	351 ± 20	261 ± 35
Plasma	14400 ± 682	8410 ± 1160	3970 ± 1250	1960 ± 122	1070 ± 218	704 ± 154
Prostate		6380				292
Seminal vesicle		3520				222
Skin, ear		3750 ± 884				406 ± 48
Skin, hindquarters		4570 ± 1460				325 ± 55
Skin, neck/shoulder		2560 ± 1250				352 ± 78
Average Skin	5970 ± 434	3620 ± 1010	1430 ± 424	666 ± 90	389 ± 41	361 ± 41
Spleen	12200 ± 637	18800	40500 ± 9530	39100 ± 6850	13900 ± 1220	6980
Stomach	6300 ± 2040	4680	2340 ± 578	1030 ± 98	428 ± 42	452
Testis		1820				264
Trachea	10400 ± 623	5380	4090 ± 1200	1390 ± 314	1190 ± 478	1420

<sup>a</sup> Values are mean ± SD for 3 animals, except where SD value is absent. Values for these data are mean for 2 animals.

Table 12

Concentration of  $^{14}\text{C}$ -Labeled Compounds in Tissues After Intravenous Administration  
of 9.1 - 9.7 mg/kg of [ $^3\text{H}/^{14}\text{C}$ ]BNS to Fischer 344 Male Rats (ng-eq/g)<sup>a</sup>

Time (h)	0.25	0.75	2	6	24	72
Tissue Name	ng-eq Compound per g Tissue					
Adipose, epididymal		6390 ± 434				267 ± 22
Adipose, kidney		8610 ± 2220				258 ± 20
Adipose, mesenteric		9470 ± 2490				579 ± 128
Average Adipose	6940 ± 515	8160 ± 1590	5110 ± 1670	2000 ± 362	406 ± 86	368 ± 183
Adrenal gland		7420				1550
Bladder		21500				2160
Blood	46200 ± 3780	29100 ± 2900	23300 ± 2910	20100 ± 8620	14900 ± 1420	8110 ± 751
Brain		2400				342
Cecum		4940				1650
Esophagus	4980 ± 1680	5470	2620 ± 699	2290 ± 828	2830 ± 2020	2290
Eye		1550				434
Heart		6380				1790
Intestine, large		4910				1860
Intestine, small		21800				1850
Kidney	69100 ± 1410	20400	14600 ± 4950	7660 ± 1870	3020 ± 422	2310
Liver	20500 ± 2660	8920 ± 846	8090 ± 453	7640 ± 1520	4350 ± 1080	2320 ± 135
Lung		8790				3430
Muscle, abdom.oblig		2270 ± 223				491 ± 76
Muscle, hind leg		2020 ± 381				482 ± 40
Muscle, trapezius		2610 ± 368				614 ± 22
Average Muscle	3040 ± 120	2300 ± 298	1450 ± 188	1580 ± 162	590 ± 54	529 ± 74
Plasma	12300 ± 258	9980 ± 2595	5970 ± 2450	4110 ± 353	2090 ± 463	1560 ± 336
Prostate		5140				949
Seminal vesicle		2420				1270
Skin, ear		4300 ± 776				1220 ± 167
Skin, hindquarters		4850 ± 1210				1450 ± 206
Skin, neck/shoulder		2960 ± 1220				1320 ± 528
Average Skin	5660 ± 292	4040 ± 974	2620 ± 558	2150 ± 286	1080 ± 120	1330 ± 117
Spleen	12000 ± 333	20800	45100 ± 9360	43500 ± 5600	15600 ± 1180	8520
Stomach	5860 ± 1960	7140	5400 ± 3080	4020 ± 198	4140 ± 1310	5660
Testis		2330				681
Trachea	8460 ± 867	5310	4370 ± 1100	2150 ± 414	2160 ± 444	2520

<sup>a</sup> Values are mean ± SD for 3 animals, except where SD value is absent. Values for these data are mean for 2 animals.

Table 13

Tissue-Blood Ratio of  $^3\text{H}$ -Labeled Compounds After Intravenous Administration  
of 9.1 - 9.7 mg/kg of [ $^3\text{H}/^{14}\text{C}$ ]BNS to Fischer 344 Male Rats<sup>a</sup>

Time (h)	0.25	0.75	2	6	24	72
Tissue Name	Tissue-Blood Ratio					
Adipose, epididymal		0.25 ± 0.05				0.02 ± 0.00
Adipose, kidney		0.33 ± 0.06				0.01 ± 0.00
Adipose, mesenteric		0.36 ± 0.04				0.03 ± 0.01
Average Adipose	0.16 ± 0.02	0.31 ± 0.06	0.25 ± 0.06	0.11 ± 0.05	0.02 ± 0.00	0.02 ± 0.01
Adrenal gland		0.31				0.10
Bladder		1.58				0.14
Blood	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00
Brain		0.08				0.04
Cecum		0.19				0.08
Esophagus	0.13 ± 0.04	0.22	0.12 ± 0.03	0.07 ± 0.04	0.04 ± 0.01	0.11
Eye		0.06				0.03
Heart		0.24				0.15
Intestine, large		0.20				0.07
Intestine, small		0.90				0.07
Kidney	2.23 ± 0.14	1.20	0.84 ± 0.34	0.60 ± 0.60	0.14 ± 0.01	0.16
Liver	0.45 ± 0.03	0.29 ± 0.04	0.28 ± 0.03	0.29 ± 0.10	0.19 ± 0.08	0.14 ± 0.05
Lung		0.35				0.26
Muscle, abdom.oblig.		0.11 ± 0.03				0.03 ± 0.00
Muscle, hind leg		0.07 ± 0.00				0.04 ± 0.00
Muscle, trapezius		0.10 ± 0.01				0.04 ± 0.00
Average Muscle	0.07 ± 0.01	0.09 ± 0.02	0.05 ± 0.01	0.04 ± 0.03	0.03 ± 0.00	0.04 ± 0.01
Plasma	0.32 ± 0.02	0.33 ± 0.10	0.20 ± 0.06	0.16 ± 0.137	0.08 ± 0.01	0.10 ± 0.02
Prostate		0.27				0.04
Seminal vesicle		0.15				0.03
Skin, ear		0.14 ± 0.01				0.06 ± 0.01
Skin, hindquarters		0.17 ± 0.03				0.05 ± 0.01
Skin, neck/shoulder		0.10 ± 0.04				0.05 ± 0.01
Average Skin	0.13 ± 0.01	0.14 ± 0.04	0.07 ± 0.01	0.06 ± 0.05	0.03 ± 0.01	0.05 ± 0.01
Spleen	0.27 ± 0.01	0.79	2.02 ± 0.63	2.87 ± 1.65	1.02 ± 0.13	0.96
Stomach	0.14 ± 0.03	0.20	0.12 ± 0.03	0.08 ± 0.06	0.03 ± 0.00	0.06
Testis		0.08				0.04
Trachea	0.23 ± 0.03	0.23	0.20 ± 0.03	0.10 ± 0.05	0.09 ± 0.03	0.20

<sup>a</sup> Values are mean ± SD for 3 animals, except where SD value is absent. Values for these data are mean for 2 animals.

Table 14

Tissue Blood Ratio of  $^{14}\text{C}$ -Labeled Compounds After Intravenous Administration  
of 9.1 - 9.7 mg/kg of [ $^3\text{H}/^{14}\text{C}$ ]HNS to Fischer 344 Male Rats<sup>a</sup>

Time (h)	0.25	0.75	2	6	24	72
Tissue Name	Tissue-Blood Ratio					
Adipose, epididymal		0.22 ± 0.03				0.03 ± 0.00
Adipose, kidney		0.29 ± 0.05				0.03 ± 0.00
Adipose, mesenteric		0.32 ± 0.05				0.07 ± 0.01
Average Adipose	0.15 ± 0.02	0.28 ± 0.05	0.22 ± 0.05	0.11 ± 0.04	0.03 ± 0.00	0.05 ± 0.02
Adrenal gland		0.27				0.19
Bladder		0.76				0.25
Blood	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00
Brain		0.09				0.04
Cecum		0.18				0.19
Esophagus	0.11 ± 0.03	0.20	0.11 ± 0.02	0.12 ± 0.03	0.19 ± 0.15	0.27
Eye		0.06				0.05
Heart		0.23				0.21
Intestine, large		0.18				0.22
Intestine, small		0.79				0.22
Kidney	1.51 ± 0.15	0.75	0.65 ± 0.30	0.49 ± 0.39	0.20 ± 0.01	0.27
Liver	0.44 ± 0.02	0.31 ± 0.04	0.35 ± 0.05	0.43 ± 0.17	0.29 ± 0.08	0.29 ± 0.02
Lung		0.32				0.40
Muscle, abdom.oblig.		0.08 ± 0.00				0.06 ± 0.01
Muscle, hind leg		0.07 ± 0.01				0.06 ± 0.01
Muscle, trapezius		0.09 ± 0.01				0.08 ± 0.01
Average Muscle	0.07 ± 0.01	0.08 ± 0.01	0.06 ± 0.01	0.10 ± 0.07	0.04 ± 0.00	0.07 ± 0.01
Plasma	0.27 ± 0.02	0.35 ± 0.12	0.26 ± 0.10	0.25 ± 0.16	0.14 ± 0.02	0.19 ± 0.03
Prostate		0.19				0.11
Seminal vesicle		0.09				0.15
Skin, ear		0.15 ± 0.01				0.15 ± 0.02
Skin, hindquarters		0.17 ± 0.02				0.18 ± 0.02
Skin, neck/shoulder		0.10 ± 0.04				0.16 ± 0.05
Average Skin	0.12 ± 0.01	0.14 ± 0.03	0.11 ± 0.02	0.13 ± 0.09	0.07 ± 0.00	0.16 ± 0.01
Spleen	0.26 ± 0.01	0.76	1.98 ± 0.60	2.46 ± 1.04	1.05 ± 0.10	1.00
Stomach	0.13 ± 0.03	0.26	0.23 ± 0.13	0.24 ± 0.15	0.28 ± 0.10	0.67
Testis		0.09				0.08
Trachea	0.18 ± 0.02	0.19	0.19 ± 0.03	0.12 ± 0.04	0.14 ± 0.02	0.30

<sup>a</sup> Values are mean ± SD for 3 animals, except where SD value is absent. Values for these data are mean for 2 animals.



Table 15

$^3\text{H}/^{14}\text{C}$  Ratio in Tissues After Intravenous Administration  
of 9.1 - 9.7 mg/kg of [ $^3\text{H}/^{14}\text{C}$ ]BNS to Fischer 344 Male Rats<sup>a</sup>

Time (h)	.25	.75	2	6	24	72
Tissue Name	$^3\text{H}/^{14}\text{C}$ Ratio					
Adipose, epididymal		0.99				0.39
Adipose, kidney		1.01				0.31
Adipose, mesenteric		1.00				0.36
Average, Adipose	1.00	1.00	1.00	0.80	0.51	0.35
Adrenal gland		0.98				0.47
Bladder		1.90				0.47
Blood	0.98	0.89	0.88	0.85	0.92	0.85
Brain		0.78				0.78
Cecum		0.91				0.37
Esophagus	1.21	0.96	0.85	0.40	0.19	0.34
Eye		0.91				0.47
Heart		0.89				0.60
Intestine, large		0.96				0.27
Intestine, small		0.99				0.28
Kidney	1.47	1.38	1.14	0.86	0.64	0.49
Liver	1.01	0.85	0.71	0.57	0.60	0.42
Lung		0.93				0.55
Muscle, abdom.oblig.		1.21				0.48
Muscle, hind leg		0.96				0.52
Muscle, trapezius		0.96				0.49
Average Muscle	1.06	1.04	0.67	0.35	0.60	0.49
Plasma	1.18	0.84	0.67	0.48	0.51	0.45
Prostate		1.24				0.31
Seminal vesicle		1.45				0.18
Skin, ear		0.87				0.33
Skin, hindquarters		0.94				0.22
Skin, neck/shoulder		0.87				0.27
Average Skin	1.06	0.90	0.55	0.31	0.36	0.27
Spleen	1.01	0.90	0.90	0.90	0.89	0.82
Stomach	1.08	0.66	0.43	0.26	0.10	0.08
Testis		0.78				0.39
Trachea	1.23	1.01	0.94	0.65	0.55	0.56

<sup>a</sup> Values calculated by equation: [Avg ng-eq  $^3\text{H}/\text{g}$  tissue]/[Avg ng-eq  $^{14}\text{C}/\text{g}$  tissue]

Table 16

Amount of  $^3\text{H}$ -Labeled Compounds in Tissues 24 h After Oral  
Administration of [ $^3\text{H}/^{14}\text{C}$ ]BNS to Fischer 344 Male Rats (% Dose)<sup>a</sup>

Dose (mg/kg)		120	12	1.2
Tissue Name	N	% Dose in Total Tissue		
Adipose <sup>b</sup>	3	0.101 ± 0.031	0.063 ± 0.010	0.084 ± 0.040
Adrenal gland	3	0.000 ± 0.000		
Bladder	3	0.001 ± 0.000		
Blood <sup>b</sup>	3	0.226 ± 0.018	0.230 ± 0.011	0.239 ± 0.018
Brain	3	0.005 ± 0.000		
Cecum	3	0.300 ± 0.059	0.156 ± 0.081	0.238 ± 0.073
Esophagus	3	0.002 ± 0.000	0.001 ± 0.000	0.002 ± 0.001
Eye	3	0.001 ± 0.000		
Heart	3	0.004 ± 0.001		
Intestine, large	3	0.167 ± 0.056	0.152 ± 0.081	0.169 ± 0.133
Intestine, small	3	0.069 ± 0.036	0.042 ± 0.004	0.062 ± 0.014
Kidney	3	0.020 ± 0.003		
Liver	3	0.070 ± 0.016	0.081 ± 0.009	0.089 ± 0.007
Lung	3	0.012 ± 0.002		
Muscle <sup>b</sup>	3	0.408 ± 0.078	0.478 ± 0.036	0.441 ± 0.014
Plasma	3	0.035 ± 0.002	0.043 ± 0.003	0.046 ± 0.003
Prostate	3	0.002 ± 0.001		
Seminal vesicle	3	0.007 ± 0.002		
Skin <sup>b</sup>	3	0.109 ± 0.006	0.140 ± 0.011	0.147 ± 0.015
Spleen	3	0.005 ± 0.001		
Stomach	3	0.087 ± 0.019	0.196 ± 0.023	0.321 ± 0.074
Testis	3	0.007 ± 0.000		
Trachea	3	0.001 ± 0.000		
Contents, Cecum	3	3.17 ± 1.17	2.87 ± 1.42	3.11 ± 2.59
Contents, Lg Int	3	1.69 ± 0.362	1.56 ± 1.45	3.30 ± 2.23
Contents, Sm Int	3	0.167 ± 0.041	0.124 ± 0.031	0.152 ± 0.027
Contents, Stomach	3	0.023 ± 0.010	0.022 ± 0.003	0.054 ± 0.007
Contents, Bladder	3	0.042 ± 0.006	0.045 ± 0.005	0.219 ± 0.215
Total, excluding plasma		6.69	6.16	8.63

<sup>a</sup> Values are mean ± SD for N animals.

<sup>b</sup> The total quantities of some tissues were estimated as percentages of total body weight. These are as follows: adipose: 10%; blood: 6.3%; muscle: 50%; skin: 15%.

Table 17

Amount of  $^{14}\text{C}$ -Labeled Compounds in Tissues 24 h After Oral Administration of [ $^3\text{H}/^{14}\text{C}$ ]BNS to Fischer 344 Male Rats (% Dose)<sup>a</sup>

Dose (mg/kg)		120	12	1.2
Tissue Name	N	% Dose in Total Tissue		
Adipose <sup>b</sup>	3	0.201 ± 0.023	0.157 ± 0.010	0.201 ± 0.018
Adrenal gland	3	0.001 ± 0.000		
Bladder	3	0.002 ± 0.000		
Blood <sup>b</sup>	3	0.470 ± 0.039	0.424 ± 0.093	0.596 ± 0.131
Brain	3	0.011 ± 0.001		
Cecum	3	0.364 ± 0.066	0.182 ± 0.086	0.268 ± 0.072
Esophagus	3	0.004 ± 0.001	0.004 ± 0.001	0.005 ± 0.001
Eye	3	0.002 ± 0.000		
Heart	3	0.010 ± 0.001		
Intestine, large	3	0.205 ± 0.065	0.187 ± 0.093	0.195 ± 0.135
Intestine, small	3	0.112 ± 0.040	0.117 ± 0.026	0.124 ± 0.014
Kidney	3	0.048 ± 0.001		
Liver	3	0.261 ± 0.033	0.312 ± 0.033	0.332 ± 0.060
Lung	3	0.032 ± 0.005		
Muscle <sup>b</sup>	3	0.883 ± 0.183	0.901 ± 0.075	0.983 ± 0.232
Plasma	3	0.123 ± 0.012	0.139 ± 0.029	0.174 ± 0.037
Prostate	3	0.005 ± 0.001		
Seminal vesicle	3	0.017 ± 0.003		
Skin <sup>b</sup>	3	0.507 ± 0.050	0.588 ± 0.140	0.830 ± 0.200
Spleen	3	0.010 ± 0.000		
Stomach	3	0.153 ± 0.028	0.264 ± 0.061	0.434 ± 0.113
Testis	3	0.023 ± 0.003		
Trachea	3	0.002 ± 0.000		
Contents, Cecum	3	3.75 ± 1.42	3.06 ± 1.48	3.25 ± 2.59
Contents, Lg Int	3	1.99 ± 0.413	1.67 ± 1.52	3.49 ± 2.31
Contents, Sm Int	3	0.234 ± 0.038	0.179 ± 0.032	0.189 ± 0.021
Contents, Stomach	3	0.147 ± 0.039	0.258 ± 0.038	0.450 ± 0.096
Contents, Bladder	3	0.054 ± 0.006	0.058 ± 0.008	0.246 ± 0.235
Total, excluding plasma		11.6	8.36	9.49

<sup>a</sup> Values are mean ± SD for N animals.

<sup>b</sup> The total quantities of some tissues were estimated as percentages of total body weight. These are as follows: adipose: 10%; blood: 6.3%; muscle: 50%; skin: 15%.

Table 18

Amount of  $^3\text{H}$ -Labeled Compounds in Tissues 72 h After Oral  
Administration of [ $^3\text{H}/^{14}\text{C}$ ]BNS to Fischer 344 Male Rats (% Dose)<sup>a</sup>

Dose (mg/kg)		98	10	1.0
Tissue Name	N	% Dose in Total Tissue		
Adipose <sup>b</sup>	3	0.023 ± 0.002	0.011 ± 0.004	0.032 ± 0.007
Adrenal gland	2	<0.001	<0.001	<0.001
Bladder	2	<0.001	<0.001	<0.001
Blood	3	0.137 ± 0.022	0.064 ± 0.005	0.154 ± 0.015
Brain	2	0.002	0.003	0.004
Cecum	2	0.003	0.007	0.003
Esophagus	2	<0.001	<0.001	<0.001
Eye	2	<0.001	<0.001	<0.001
Heart	2	0.002	0.002	0.002
Intestine, large	2	0.002	0.002	0.003
Intestine, small	2	0.008	0.007	0.009
Kidney	2	0.008	0.007	0.013
Liver	3	0.047 ± 0.002	0.029 ± 0.004	0.058 ± 0.004
Lung	2	0.003	0.002	0.004
Muscle <sup>b</sup>	3	0.179 ± 0.055	0.218 ± 0.036	0.397 ± 0.024
Plasma	3	0.027 ± 0.002	0.024	0.033 ± 0.004
Prostate	2	0.001	0.001	0.001
Seminal vesicle	2	0.001	<0.001	0.001
Skin <sup>b</sup>	3	0.077 ± 0.008	0.092 ± 0.042	0.170 ± 0.063
Spleen	2	0.002	0.002	0.002
Stomach	2	0.046	0.015	0.011
Testis	2	0.006	0.008	0.008
Trachea	2	<0.001	<0.001	<0.001
Total, excluding plasma		0.548	0.470	0.874

<sup>a</sup> Values are mean ± SD for N animals; for N=2, mean only.

<sup>b</sup> The total quantities of some tissues were estimated as percentages of total body weight. These are as follows: adipose: 10%; blood: 6.3%; muscle: 50%; skin: 15%.

Table 19

Amount of  $^{14}\text{C}$ -Labeled Compounds in Tissues 72 h After Oral Administration of [ $^3\text{H}/^{14}\text{C}$ ]BNS to Fischer 344 Male Rats (% Dose)<sup>a</sup>

Dose (mg/kg)		98	10	1.0
Tissue Name	N	% Dose in Total Tissue		
Adipose <sup>b</sup>	3	0.077 ± 0.017	0.087 ± 0.018	0.145 ± 0.040
Adrenal gland	2	0.001	0.001	0.001
Bladder	2	0.001	0.001	0.003
Blood <sup>b</sup>	3	0.216 ± 0.029	0.129 ± 0.020	0.349 ± 0.009
Brain	2	0.003	0.004	0.006
Cecum	2	0.013	0.010	0.012
Esophagus	2	0.003	0.002	0.004
Eye	2	0.001	0.001	0.002
Heart	2	0.006	0.004	0.008
Intestine, large	2	0.015	0.007	0.015
Intestine, small	2	0.044	0.027	0.049
Kidney	2	0.016	0.018	0.039
Liver	3	0.136 ± 0.011	0.080 ± 0.015	0.182 ± 0.008
Lung	2	0.016	0.010	0.019
Muscle <sup>b</sup>	3	0.472 ± 0.096	0.307 ± 0.054	0.789 ± 0.021
Plasma	3	0.051 ± 0.004	0.044	0.136 ± 0.006
Prostate	2	0.004	0.003	0.003
Seminal vesicle	2	0.005	0.002	0.011
Skin <sup>b</sup>	3	0.272 ± 0.014	0.267 ± 0.002	0.671 ± 0.068
Spleen	2	0.007	0.004	0.008
Stomach	2	0.116	0.064	0.087
Testis	2	0.012	0.013	0.022
Trachea	2	0.002	0.001	0.002
Total, excluding plasma		1.44%	1.04%	2.56%

<sup>a</sup> Values are mean ± SD for N animals; for N=2, mean only.

<sup>b</sup> The total quantities of some tissues were estimated as percentages of total body weight. These are as follows: adipose: 10%; blood: 6.3%; muscle: 50%; skin: 15%.

Table 20

Concentration of  $^3\text{H}$ -Labeled Compounds in Tissues 24 h After Oral Administration of [ $^3\text{H}/^{14}\text{C}$ ]BNS to Fischer 344 Male Rats (ng-eq/g)<sup>a</sup>

Dose (mg/kg)		120	12	1.2
Tissue Name	N	ng-eq Compound per g Tissue		
Adipose	3	1200 ± 336	77 ± 16	10 ± 5
Adrenal gland	3	884 ± 627		
Bladder	3	3980 ± 1240		
Blood	3	4330 ± 437	445 ± 14	46 ± 4
Brain	3	797 ± 64		
Cecum	3	134000 ± 31500	7460 ± 3090	1090 ± 486
Esophagus	3	2500 ± 157	179 ± 38	32 ± 12
Eye	3	660 ± 80		
Heart	3	1500 ± 184		
Intestine, large	3	69400 ± 15500	5120 ± 2950	687 ± 651
Intestine, small	3	8680 ± 3530	528 ± 54	64 ± 13
Kidney	3	3060 ± 296		
Liver	3	2420 ± 466	265 ± 19	30 ± 3
Lung	3	2400 ± 27		
Muscle	3	985 ± 209	117 ± 5	11 ± 1
Plasma	3	1290 ± 119	158 ± 4	17 ± 2
Prostate	3	1190 ± 230		
Seminal vesicle	3	2010 ± 185		
Skin	3	873 ± 57	114 ± 4	12 ± 1
Spleen	3	2760 ± 568		
Stomach	3	24900 ± 2690	7240 ± 120	1170 ± 157
Testis	3	857 ± 123		
Trachea	3	2720 ± 2220		
Contents, Cecum	3	244000 ± 68000	18700 ± 6040	3240 ± 1840
Contents, Lg Int	3	281000 ± 50400	25900 ± 11200	8150 ± 5860
Contents, Sm Int	3	9930 ± 1660	842 ± 97	137 ± 13
Contents, Stomach	3	3660 ± 1050	367 ± 130	84 ± 35
Contents, Bladder	3	23500 ± 1450	2780 ± 970	639 ± 391

<sup>a</sup> Values are mean ± SD for N animals.

Table 21

Concentration of  $^{14}\text{C}$ -Labeled Compounds in Tissues 24 h After Oral Administration of [ $^3\text{H}/^{14}\text{C}$ ]BNS to Fischer 344 Male Rats (ng-eq/g)<sup>a</sup>

Dose (mg/kg)		120	12	1.2
Tissue Name	N	ng-eq Compound per g Tissue		
Adipose	3	2410 ± 250	192 ± 17	24 ± 2
Adrenal gland	3	3820 ± 88		
Bladder	3	6710 ± 2350		
Blood	3	8980 ± 975	817 ± 144	115 ± 27
Brain	3	1940 ± 152		
Cecum	3	163000 ± 38400	8690 ± 3190	1230 ± 507
Esophagus	3	6220 ± 1360	804 ± 217	82 ± 25
Eye	3	1930 ± 264		
Heart	3	3820 ± 514		
Intestine, large	3	85500 ± 17600	6310 ± 3370	784 ± 678
Intestine, small	3	14100 ± 3370	1450 ± 174	130 ± 10
Kidney	3	7430 ± 313		
Liver	3	9020 ± 883	1020 ± 63	110 ± 22
Lung	3	6340 ± 511		
Muscle	3	2130 ± 489	220 ± 13	24 ± 6
Plasma	3	4500 ± 538	516 ± 89	65 ± 15
Prostate	3	3360 ± 639		
Seminal vesicle	3	4820 ± 210		
Skin	3	4060 ± 491	476 ± 95	67 ± 17
Spleen	3	5980 ± 188		
Stomach	3	43900 ± 6070	9760 ± 1980	1580 ± 180
Testis	3	2930 ± 686		
Trachea	3	5940 ± 2250		
Contents, Cecum	3	288000 ± 82900	20000 ± 6120	3450 ± 2000
Contents, Lg Int	3	330000 ± 58400	27900 ± 11400	8680 ± 6280
Contents, Sm Int	3	13900 ± 1250	1230 ± 44	171 ± 22
Contents, Stomach	3	25600 ± 10300	4480 ± 1960	714 ± 355
Contents, Bladder	3	30200 ± 1850	3460 ± 642	726 ± 416

<sup>a</sup> Values are mean ± SD for N animals.

Table 22

Concentration of  $^3\text{H}$ -Labeled Compounds in Tissues 72 h After Oral Administration of [ $^3\text{H}/^{14}\text{C}$ ]BNS to Fischer 344 Male Rats (ng-eq/g)<sup>a</sup>

Dose (mg/kg)		98		10		1.0			
ng-eq Compound per g Tissue									
Tissue Name	N	N		N		N			
Adipose	3	232	± 22	3	12	± 5	3	3	± 1
Adrenal gland	2	394		2	44		2	20	
Bladder	2	1020		2	104		2	25	
Blood	3	2280	± 341	3	114	± 17	3	26	± 2
Brain	2	324		2	43		2	5	
Cecum	2	581		2	197		2	12	
Esophagus	2	311		2	64		2	4	
Eye	2	218		2	45		2	7	
Heart	2	594		2	61		2	7	
Intestine, large	2	423		2	51		2	7	
Intestine, small	2	532		2	48		2	8	
Kidney	2	1030		2	88		2	16	
Liver	3	1320	± 108	3	87	± 9	3	16	± 1
Lung	2	778		2	59		2	10	
Muscle	3	370	± 116	3	47	± 10	3	8	±
Plasma	3	864	± 58	2	83		3	11	± 1
Prostate	2	258		2	39		2	7	
Seminal vesicle	2	291		2	31		2	5	
Skin	3	534	± 65	3	70	± 29	3	12	± 4
Spleen	2	1090		2	76		2	12	
Stomach	2	9620		2	328		2	28	
Testis	2	539		2	67		2	8	
Trachea	2	405		2	37		2	8	

<sup>a</sup> Values are mean ± SD for N animals; for N=2, mean only.



Table 23

Concentration of  $^{14}\text{C}$ -Labeled Compounds in Tissues 72 h After Oral Administration of [ $^3\text{H}/^{14}\text{C}$ ]BNS to Fischer 344 Male Rats (ng-eq/g)<sup>a</sup>

Dose (mg/kg)	98		10		1.0	
Tissue Name	ng-eq Compound per g Tissue					
	N		N		N	
Adipose	3	796 ± 185	3	96 ± 17	3	15 ± 4
Adrenal gland	2	2270	2	233	2	57
Bladder	2	2970	2	258	2	76
Blood	3	3620 ± 370	3	233 ± 29	3	58 ± 1
Brain	2	482	2	52	2	8
Cecum	2	2390	2	321	2	41
Esophagus	2	3560	2	323	2	63
Eye	1	986	2	74	2	22
Heart	2	1900	2	134	2	28
Intestine, large	2	3320	2	188	2	40
Intestine, small	2	3030	2	200	2	44
Kidney	2	1960	2	230	2	51
Liver	3	3780 ± 472	3	243 ± 14	3	49 ± 2
Lung	2	3900	2	243	2	56
Muscle	3	976 ± 173	3	67 ± 9	3	16 ± 1
Plasma	3	1620 ± 90	2	153	3	43 ± 2
Prostate	2	1970	2	159	2	36
Seminal vesicle	2	2430	2	180	2	42
Skin	3	1890 ± 140	3	199 ± 14	3	47 ± 5
Spleen	2	2950	2	189	2	41
Stomach	2	22900	2	1400	2	230
Testis	2	1150	2	109	2	21
Trachea	2	2270	2	268	2	46

<sup>a</sup> Values are mean ± SD for N animals; for N=2, mean only.

Table 24

Tissue-Blood Ratio of  $^3\text{H}$ -Labeled Compounds 24 h After Oral Administration of [ $^3\text{H}/^{14}\text{C}$ ]BNS to Fischer 344 Male Rats<sup>a</sup>

Dose (mg/kg)		120	12	1.2
Tissue Name	N	Tissue-Blood Ratio		
Adipose	3	0.29 ± 0.11	0.17 ± 0.03	0.23 ± 0.13
Adrenal gland	3	0.21 ± 0.16		
Bladder	3	0.91 ± 0.21		
Blood	3	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00
Brain	3	0.19 ± 0.01		
Cecum	3	31.1 ± 7.0	16.9 ± 7.4	23.9 ± 11.6
Esophagus	3	0.58 ± 0.05	0.40 ± 0.09	0.69 ± 0.27
Eye	3	0.15 ± 0.02		
Heart	3	0.35 ± 0.06		
Intestine, large	3	16.3 ± 5.2	11.4 ± 6.6	15.6 ± 15.8
Intestine, small	3	2.08 ± 1.09	1.19 ± 0.12	1.39 ± 0.21
Kidney	3	0.72 ± 0.15		
Liver	3	0.56 ± 0.10	0.59 ± 0.03	0.64 ± 0.01
Lung	3	0.56 ± 0.06		
Muscle	3	0.23 ± 0.04	0.26 ± 0.02	0.23 ± 0.01
Plasma	3	0.30 ± 0.01	0.36 ± 0.02	0.37 ± 0.01
Prostate	3	0.27 ± 0.03		
Seminal vesicle	3	0.47 ± 0.07		
Skin	3	0.20 ± 0.01	0.26 ± 0.01	0.26 ± 0.01
Spleen	3	0.65 ± 0.21		
Stomach	3	5.82 ± 1.22	16.3 ± 0.4	25.6 ± 5.0
Testis	3	0.20 ± 0.02		
Trachea	3	0.67 ± 0.61		
Contents, Cecum	3	56.5 ± 14.3	42.3 ± 14.8	69.4 ± 36.4
Contents, Lg Int	3	65.9 ± 17.5	58.2 ± 25.3	173. ± 116.
Contents, Sm Int	3	2.33 ± 0.64	1.90 ± 0.27	2.99 ± 0.45
Contents, Stomach	3	0.84 ± 0.17	0.82 ± 0.27	1.80 ± 0.61
Contents, Bladder	3	5.48 ± 0.81	6.29 ± 2.32	14.2 ± 9.7

<sup>a</sup> Values are mean ± SD for N animals.

Table 25

Tissue-Blood Ratio of  $^{14}\text{C}$ -Labeled Compounds 24 h After Oral Administration of [ $^3\text{H}/^{14}\text{C}$ ]BNS to Fischer 344 Male Rats<sup>a</sup>

Dose (mg/kg)		120	12	1.2
Tissue Name	N	Tissue-Blood Ratio		
Adipose	3	0.27 ± 0.05	0.24 ± 0.07	0.22 ± 0.04
Adrenal gland	3	0.43 ± 0.04		
Bladder	3	0.74 ± 0.22		
Blood	3	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00
Brain	3	0.22 ± 0.02		
Cecum	3	18.1 ± 3.2	10.6 ± 3.1	11.1 ± 6.0
Esophagus	3	0.69 ± 0.08	1.03 ± 0.41	0.72 ± 0.20
Eye	3	0.22 ± 0.03		
Heart	3	0.43 ± 0.04		
Intestine, large	3	9.73 ± 3.01	8.32 ± 5.31	7.73 ± 8.04
Intestine, small	3	1.61 ± 0.58	1.83 ± 0.53	1.16 ± 0.19
Kidney	3	0.83 ± 0.06		
Liver	3	1.01 ± 0.01	1.27 ± 0.19	0.97 ± 0.04
Lung	3	0.71 ± 0.02		
Muscle	3	0.23 ± 0.03	0.27 ± 0.04	0.21 ± 0.02
Plasma	3	0.50 ± 0.03	0.63 ± 0.03	0.56 ± 0.02
Prostate	3	0.37 ± 0.05		
Seminal vesicle	3	0.54 ± 0.04		
Skin	3	0.45 ± 0.01	0.58 ± 0.03	0.58 ± 0.03
Spleen	3	0.67 ± 0.10		
Stomach	3	4.91 ± 0.71	12.0 ± 1.6	14.2 ± 3.8
Testis	3	0.32 ± 0.05		
Trachea	3	0.68 ± 0.31		
Contents, Cecum	3	31.9 ± 6.9	24.8 ± 7.8	29.7 ± 14.5
Contents, Lg Int	3	37.2 ± 9.3	36.7 ± 21.6	73.8 ± 47.0
Contents, Sm Int	3	1.57 ± 0.32	1.53 ± 0.28	1.53 ± 0.32
Contents, Stomach	3	2.81 ± 0.86	5.47 ± 2.17	6.02 ± 1.67
Contents, Bladder	3	3.40 ± 0.49	4.33 ± 1.21	6.85 ± 5.21

<sup>a</sup> Values are mean ± SD for N animals.

Table 26

Tissue-Blood Ratio of  $^3\text{H}$ -Labeled Compounds 72 h After Oral  
Administration of [ $^3\text{H}/^{14}\text{C}$ ]BNS to Fischer 344 Male Rats<sup>a</sup>

Dose (mg/kg)		98	10	1.0
Tissue Name	N	Tissue Blood Ratio		
Adipose	3	0.10 ± 0.02	0.10 ± 0.04	0.13 ± 0.02
Adrenal gland	2	0.18	0.37	0.76
Bladder	2	0.46	0.85	0.91
Blood	3	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00
Brain	2	0.15	0.36	0.19
Cecum	2	0.26	1.67	0.43
Esophagus	2	0.14	0.53	0.14
Eye	2	0.10	0.37	0.25
Heart	2	0.27	0.50	0.28
Intestine, large	2	0.19	0.42	0.26
Intestine, small	2	0.25	0.41	0.29
Kidney	2	0.47	0.74	0.61
Liver	3	0.58 ± 0.07	0.77 ± 0.04	0.61 ± 0.03
Lung	2	0.35	0.48	0.39
Muscle	3	0.16 ± 0.03	0.42 ± 0.08	0.32 ± 0.01
Plasma	2	0.38 ± 0.04	0.65	0.41 ± 0.02
Prostate	2	0.12	0.31	0.25
Seminal vesicle	2	0.13	0.25	0.17
Skin	3	0.24 ± 0.06	0.63 ± 0.32	0.48 ± 0.23
Spleen	2	0.50	0.63	0.44
Stomach	2	4.00	2.98	1.01
Testis	2	0.25	0.54	0.28
Trachea	2	0.18	0.31	0.29

<sup>a</sup> Values are mean ± SD for N animals; for N=2, mean value only.

Table 27

Tissue-Blood Ratio of  $^{14}\text{C}$ -Labeled Compounds 72 h After Oral  
Administration of [ $^3\text{H}/^{14}\text{C}$ ]BNS to Fischer 344 Male Rats<sup>a</sup>

Dose (mg/kg)		98	10	1.0
Tissue Name	N	Tissue Blood Ratio		
Adipose	3	0.22 ± 0.06	0.41 ± 0.03	0.26 ± 0.02
Adrenal gland	2	0.62	0.95	0.97
Bladder	2	0.80	1.05	1.31
Blood	3	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00
Brain	2	0.13	0.21	0.15
Cecum	2	0.65	1.31	0.70
Esophagus	2	0.96	1.34	1.08
Eye	2	0.25	0.29	0.38
Heart	2	0.52	0.54	0.49
Intestine, large	2	0.90	0.77	0.69
Intestine, small	2	0.83	0.82	0.75
Kidney	2	0.49	0.93	0.87
Liver	3	1.04 ± 0.03	1.05 ± 0.11	0.85 ± 0.04
Lung	2	1.06	0.98	0.96
Muscle	3	0.27 ± 0.02	0.29 ± 0.01	0.28 ± 0.01
Plasma	2	0.45 ± 0.02	0.68	0.75 ± 0.03
Prostate	2	0.54	0.64	0.62
Seminal vesicle	2	0.66	0.72	0.72
Skin	3	0.53 ± 0.09	0.86 ± 0.14	0.81 ± 0.10
Spleen	2	0.80	0.76	0.71
Stomach	2	6.17	5.54	3.97
Testis	2	0.31	0.45	0.35
Trachea	2	0.62	1.09	0.79

<sup>a</sup> Values are mean ± SD for N animals; for N=2, mean only.

Table 28

$^3\text{H}/^{14}\text{C}$  Ratio in Tissues 24 h After Oral Administration  
of [ $^3\text{H}/^{14}\text{C}$ ]BNS to Fischer 344 Male Rats<sup>a</sup>

Dose (mg/kg)		120	12	1.2
Tissue Name	N	$^3\text{H}/^{14}\text{C}$ Ratio		
Adipose	3	0.50	0.40	0.42
Adrenal gland	3	0.23		
Bladder	3	0.59		
Blood	3	0.48	0.55	0.40
Brain	3	0.41		
Cecum	3	0.82	0.86	0.89
Esophagus	3	0.40	0.22	0.39
Eye	3	0.34		
Heart	3	0.39		
Intestine, large	3	0.81	0.81	0.88
Intestine, small	3	0.61	0.37	0.49
Kidney	3	0.41		
Liver	3	0.27	0.26	0.27
Lung	3	0.38		
Muscle	3	0.46	0.53	0.46
Plasma	3	0.29	0.31	0.26
Prostate	3	0.36		
Seminal vesicle	3	0.42		
Skin	3	0.22	0.24	0.18
Spleen	3	0.46		
Stomach	3	0.57	0.74	0.74
Testis	3	0.29		
Trachea	3	0.46		
Contents, Cecum	3	0.85	0.94	0.94
Contents, Lg Int	3	0.85	0.93	0.94
Contents, Sm Int	3	0.71	0.69	0.80
Contents, Stomach	3	0.14	0.08	0.12
Contents, Bladder	3	0.78	0.80	0.88

<sup>a</sup> Values calculated by equation:  $[\text{Av ng-eq } ^3\text{H/g tissues}] / [\text{Av ng-eq } ^{14}\text{C/g tissue}]$

Table 29

$^3\text{H}/^{14}\text{C}$  Ratio in Tissues 72 h After Oral Administration  
of [ $^3\text{H}/^{14}\text{C}$ ]BNS to Fischer 344 Male Rats<sup>a</sup>

Dose (mg/kg)	98		10		1.0	
Tissue Name	N	$^3\text{H}/^{14}\text{C}$ Ratio		N		
Adipose	3	0.29	3	0.13	3	0.20
Adrenal gland	2	0.17	2	0.19	2	0.35
Bladder	2	0.35	2	0.40	2	0.33
Blood	3	0.63	3	0.49	3	0.45
Brain	2	0.67	2	0.83	2	0.63
Cecum	2	0.24	2	0.61	2	0.29
Esophagus	2	0.09	2	0.20	2	0.06
Eye	1	0.22	2	0.61	2	0.32
Heart	2	0.31	2	0.46	2	0.25
Intestine, large	2	0.13	2	0.27	2	0.18
Intestine, small	2	0.18	2	0.24	2	0.18
Kidney	2	0.53	2	0.38	2	0.31
Liver	3	0.35	3	0.36	3	0.33
Lung	2	0.20	2	0.24	2	0.18
Muscle	3	0.38	3	0.70	3	0.50
Plasma	3	0.53	2	0.54	3	0.26
Prostate	2	0.13	2	0.25	2	0.19
Seminal vesicle	2	0.12	2	0.17	2	0.12
Skin	3	0.28	3	0.35	3	0.26
Spleen	2	0.37	2	0.40	2	0.29
Stomach	2	0.42	2	0.23	2	0.12
Testis	2	0.47	2	0.62	2	0.38
Trachea	2	0.18	2	0.14	2	0.17

<sup>a</sup> Values calculated by equation:  $[\text{Av ng-eq } ^3\text{H/g tissue}]/[\text{Av ng-eq } ^{14}\text{C/g tissue}]$

Table 30

Amount of  $^3\text{H}$  in Tissues 24 h Following Dermal  
Application of [ $^3\text{H}/^{14}\text{C}$ ]BNS to Male F344 Rats (% Dose)<sup>a</sup>

Dose (mg/cm <sup>2</sup> )		0.1	1.0	10
Tissue Name	N	% Dose in Total Tissue		
Adipose <sup>b</sup>	3	0.187 ± 0.210	0.189 ± 0.031	0.018 ± 0.017
Adrenal gland	3	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000
Bladder	3	0.011 ± 0.012	0.054 ± 0.045	0.006 ± 0.003
Blood <sup>b</sup>	3	0.225 ± 0.112	0.283 ± 0.013	0.016 ± 0.009
Brain	3	0.004 ± 0.001	0.009 ± 0.001	0.001 ± 0.001
Cecum	3	0.023 ± 0.001	0.023 ± 0.003	0.011 ± 0.004
Esophagus	3	0.002 ± 0.002	0.001 ± 0.000	0.000 ± 0.000
Eye	3	0.001 ± 0.001	0.001 ± 0.000	0.001 ± 0.001
Heart	3	0.005 ± 0.002	0.008 ± 0.003	0.002 ± 0.003
Intestine, large	3	0.026 ± 0.024	0.021 ± 0.008	0.004 ± 0.005
Intestine, small	3	0.088 ± 0.003	0.044 ± 0.012	0.019 ± 0.013
Kidney	3	0.042 ± 0.008	0.069 ± 0.014	0.010 ± 0.004
Liver	3	0.118 ± 0.036	0.010 ± 0.005	0.024 ± 0.007
Lung	3	0.020 ± 0.005	0.028 ± 0.006	0.005 ± 0.003
Muscle <sup>b</sup>	3	0.893 ± 0.325	0.690 ± 0.073	0.096 ± 0.104
Plasma	3	0.114	0.374 ± 0.143	0.029 ± 0.002
Prostate	3	0.023 ± 0.037	0.076 ± 0.058	0.000 ± 0.000
Seminal vesicle	3	0.065 ± 0.107	0.015 ± 0.013	0.001 ± 0.000
Skin <sup>b</sup>	3	0.762 ± 0.332	0.285 ± 0.017	0.070 ± 0.050
Spleen	3	0.004 ± 0.004	0.005 ± 0.000	0.005 ± 0.005
Stomach	3	0.012 ± 0.005	0.008 ± 0.002	0.001 ± 0.001
Testis	3	0.072 ± 0.093	0.028 ± 0.020	0.005 ± 0.001
Trachea	3	0.000 ± 0.001	0.001 ± 0.001	0.000 ± 0.001
Contents, Cecum	3	N/A <sup>c</sup>	0.163 ± 0.065	N/A
Contents, Lg Int	3	N/A	0.117 ± 0.074	N/A
Contents, Sm Int	3	N/A	0.089 ± 0.010	N/A
Contents, Stomach	3	N/A	0.024 ± 0.012	N/A
Total, excluding plasma		2.60	2.33	0.282

<sup>a</sup> Average ± SD for N animals; for N=2, mean only.

<sup>b</sup> Total adipose tissue assumed to be 10% of body weight; blood = 6.3%; muscle = 50%; skin = 15%.

<sup>c</sup> Not analyzed.



Table 31

Amount of  $^{14}\text{C}$  in Tissues 24 h Following Dermal  
Application of [ $^3\text{H}/^{14}\text{C}$ ]BNS to Male F344 Rats (% Dose)<sup>a</sup>

Dose (mg/cm <sup>2</sup> )		0.1	1.0	10
Tissue Name	N	% Dose in Total Tissue		
Adipose <sup>b</sup>	3	0.440 ± 0.253	0.823 ± 0.087	0.081 ± 0.014
Adrenal gland	3	0.003 ± 0.001	0.006 ± 0.000	0.000 ± 0.000
Bladder	3	0.010 ± 0.002	0.025 ± 0.011	0.001 ± 0.000
Blood <sup>b</sup>	3	0.798 ± 0.109	1.17 ± 0.08	0.097 ± 0.021
Brain	3	0.023 ± 0.001	0.057 ± 0.007	0.006 ± 0.002
Cecum	3	0.104 ± 0.034	0.183 ± 0.021	0.025 ± 0.004
Esophagus	3	0.013 ± 0.009	0.016 ± 0.002	0.001 ± 0.000
Eye	3	0.003 ± 0.001	0.006 ± 0.001	0.000 ± 0.000
Heart	3	0.036 ± 0.012	0.059 ± 0.011	0.004 ± 0.001
Intestine, large	3	0.108 ± 0.012	0.253 ± 0.095	0.018 ± 0.009
Intestine, small	3	0.387 ± 0.143	0.472 ± 0.067	0.041 ± 0.011
Kidney	3	0.197 ± 0.060	0.286 ± 0.022	0.021 ± 0.003
Liver	3	1.07 ± 0.17	1.71 ± 0.12	0.100 ± 0.022
Lung	3	0.097 ± 0.019	0.217 ± 0.028	0.011 ± 0.001
Muscle <sup>b</sup>	3	2.69 ± 0.23	4.14 ± 0.35	0.261 ± 0.031
Plasma	3	0.400	0.570 ± 0.112	0.042 ± 0.006
Prostate	3	0.022 ± 0.013	0.067 ± 0.009	0.001 ± 0.000
Seminal vesicle	3	0.061 ± 0.039	0.066 ± 0.006	0.002 ± 0.002
Skin <sup>b</sup>	3	1.92 ± 0.54	2.09 ± 0.14	0.142 ± 0.035
Spleen	3	0.040 ± 0.005	0.060 ± 0.013	0.007 ± 0.006
Stomach	3	0.143 ± 0.052	0.209 ± 0.035	0.013 ± 0.009
Testis	3	0.115 ± 0.040	0.122 ± 0.010	0.008 ± 0.003
Trachea	3	0.007 ± 0.006	0.010 ± 0.004	0.001 ± 0.000
Contents, Cecum	3	N/A <sup>c</sup>	0.849 ± 0.131	N/A
Contents, Lg Int	3	N/A	0.740 ± 0.328	N/A
Contents, Sm Int	3	N/A	0.442 ± 0.060	N/A
Contents, Stomach	3	N/A	0.307 ± 0.051	N/A
Total, excluding plasma		8.29	14.4	0.84

<sup>a</sup> Average ± SD for N animals; for N=2, mean only.

<sup>b</sup> Total adipose tissue assumed to be 10% of body weight; blood = 6.3%; muscle = 50%; skin = 15%.

<sup>c</sup> Not analyzed.

Table 32

Concentration of  $^3\text{H}$  in Tissues 24 h Following Dermal Application of [ $^3\text{H}/^{14}\text{C}$ ]BNS to Male F344 Rats (ng-eq/g)<sup>a</sup>

Dose (mg/cm <sup>2</sup> )		0.1	1.0	10
Tissue Name	N	ng-eq Compound per g Tissue		
Adipose	3	17 ± 18	148 ± 26	161 ± 156
Adrenal gland	3	8 ± 13	159 ± 44	856 ± 907
Bladder	3	334 ± 372	16900 ± 13000	13700 ± 7000
Blood	3	32 ± 16	350 ± 20	221 ± 126
Brain	3	6 ± 2	106 ± 11	109 ± 88
Cecum	3	83 ± 24	721 ± 161	3570 ± 1410
Esophagus	3	20 ± 21	175 ± 53	443 ± 75
Eye	3	10 ± 9	99 ± 7	71 ± 123
Heart	3	14 ± 7	171 ± 23	521 ± 724
Intestine, large	3	68 ± 53	436 ± 186	932 ± 1140
Intestine, small	3	79 ± 16	413 ± 124	1370 ± 500
Kidney	3	52 ± 6	702 ± 120	1160 ± 328
Liver	3	27 ± 6	212 ± 4	616 ± 186
Lung	3	34 ± 11	253 ± 17	662 ± 373
Muscle	3	16 ± 6	108 ± 12	170 ± 189
Plasma	3	31	888 ± 327	774 ± 77
Prostate	3	174 ± 278	2500 ± 1610	820 ± 760
Seminal vesicle	3	232 ± 383	351 ± 292	236 ± 87
Skin	3	46 ± 21	148 ± 11	412 ± 300
Spleen	3	17 ± 17	198 ± 27	2210 ± 2900
Stomach	3	32 ± 9	169 ± 29	316 ± 282
Testis	3	75 ± 102	232 ± 162	403 ± 103
Trachea	3	7 ± 13	145 ± 60	1280 ± 2210
Contents, Cecum	3	N/A <sup>b</sup>	834 ± 400	N/A
Contents, Lg Int	3	N/A	847 ± 565	N/A
Contents, Sm Int	3	N/A	427 ± 134	N/A
Contents, Stomach	3	N/A	123 ± 35	N/A

<sup>a</sup> Average ± SD for N animals; for N=2, mean only.

<sup>b</sup> Not analyzed.

Table 33

Concentration of  $^{14}\text{C}$  in Tissues 24 h Following Dermal  
Application of [ $^3\text{H}/^{14}\text{C}$ ]BNS to Fischer 344 Male Rats (ng-eq/g)<sup>a</sup>

Dose (mg/cm <sup>2</sup> )		0.1	1.0	10
Tissue Name	N	ng-eq Compound per g Tissue		
Adipose	3	40 ± 23	640 ± 77	711 ± 148
Adrenal gland	3	130 ± 68	2380 ± 316	669 ± 499
Bladder	3	308 ± 63	7830 ± 3140	3000 ± 655
Blood	3	113 ± 14	1450 ± 111	1340 ± 335
Brain	3	36 ± 4	677 ± 77	722 ± 197
Cecum	3	353 ± 117	5690 ± 883	8380 ± 2730
Esophagus	3	189 ± 63	2450 ± 721	1430 ± 244
Eye	3	31 ± 14	470 ± 38	440 ± 171
Heart	3	102 ± 31	1300 ± 37	978 ± 98
Intestine, large	3	306 ± 32	5270 ± 2100	4260 ± 1650
Intestine, small	3	331 ± 93	4430 ± 485	3260 ± 653
Kidney	3	241 ± 64	2920 ± 125	2370 ± 244
Liver	3	245 ± 30	3630 ± 201	2660 ± 719
Lung	3	165 ± 50	1960 ± 70	1600 ± 336
Muscle	3	49 ± 4	643 ± 54	456 ± 71
Plasma	2	109	1350 ± 282	1120 ± 135
Prostate	3	193 ± 78	2270 ± 327	926 ± 425
Seminal vesicle	3	237 ± 119	1590 ± 212	947 ± 499
Skin	3	116 ± 33	1080 ± 86	821 ± 203
Spleen	3	178 ± 28	2350 ± 375	3510 ± 3540
Stomach	3	400 ± 139	4650 ± 505	2770 ± 2150
Testis	3	111 ± 54	1020 ± 53	698 ± 283
Trachea	3	132 ± 73	1410 ± 75	2450 ± 2400
Contents, Cecum	3	N/A <sup>b</sup>	4280 ± 925	N/A
Contents, Lg Int	3	N/A	5190 ± 1880	N/A
Contents, Sm Int	3	N/A	2080 ± 584	N/A
Contents, Stomach	3	N/A	1750 ± 641	N/A

<sup>a</sup> Average ± SD for N animals; for N=2, mean only.

<sup>b</sup> Not analyzed.

Table 34

Tissue-Blood Ratio of  $^3\text{H}$  in Tissues 24 h Following Dermal  
Application of [ $^3\text{H}/^{14}\text{C}$ ]BNS to Male F344 Rats<sup>a</sup>

Dose (mg/cm <sup>2</sup> )		0.1	1.0	10
Tissue Name	N	Tissue-Blood Ratio		
Adipose	2	0.45 ± 0.36	0.42 ± 0.05	1.10 ± 1.03
Adrenal gland	2	0.21 ± 0.35	0.45 ± 0.10	8.1 ± 11.5
Bladder	3	9.06 ± 7.19	46.9 ± 35.2	64.6 ± 7.5
Blood	3	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00
Brain	3	0.27 ± 0.25	0.30 ± 0.01	0.91 ± 0.22
Cecum	3	2.88 ± 0.89	2.05 ± 0.37	19.0 ± 8.6
Esophagus	3	0.50 ± 0.54	0.50 ± 0.14	2.57 ± 1.54
Eye	1	0.24 ± 0.25	0.28 ± 0.10	0.29 ± 0.50
Heart	3	0.61 ± 0.57	0.49 ± 0.06	2.58 ± 2.73
Intestine, large	2	2.13 ± 0.95	1.27 ± 0.62	9.4 ± 14.3
Intestine, small	3	3.06 ± 1.94	1.17 ± 0.29	10.0 ± 10.4
Kidney	3	2.15 ± 1.68	2.02 ± 0.47	8.05 ± 7.93
Liver	3	1.17 ± 1.02	0.61 ± 0.03	3.94 ± 3.06
Lung	3	1.50 ± 1.36	0.72 ± 0.03	4.98 ± 5.27
Muscle	3	0.55 ± 0.12	0.31 ± 0.02	0.83 ± 0.71
Plasma	3	.77	2.58 ± 1.09	4.66 ± 3.12
Prostate	3	4.35 ± 6.00	6.98 ± 4.20	3.89 ± 2.24
Seminal vesicle	3	5.44 ± 8.58	0.98 ± 0.77	1.67 ± 1.62
Skin	3	1.54 ± 0.43	0.42 ± 0.02	1.68 ± 0.88
Spleen	2	0.55 ± 0.34	0.56 ± 0.04	9.8 ± 11.2
Stomach	2	1.43 ± 1.32	0.48 ± 0.06	2.33 ± 2.39
Testis	3	1.92 ± 2.13	0.65 ± 0.42	2.59 ± 2.24
Trachea	1	0.17 ± 0.29	0.41 ± 0.16	5.17 ± 8.95
Contents, Cecum	3	N/A <sup>b</sup>	2.38 ± 1.12	N/A
Contents, Lg Int	3	N/A	2.43 ± 1.60	N/A
Contents, Sm Int	3	N/A	1.21 ± 0.35	N/A
Contents, Stomach	3	N/A	0.36 ± 0.12	N/A

<sup>a</sup> Average ± SD for N animals; for N=2, mean only.

<sup>b</sup> Not analyzed.

Table 35

Tissue-Blood Ratio of  $^{14}\text{C}$  in Tissues 24 h Following Dermal  
Application of [ $^3\text{H}/^{14}\text{C}$ ]BNS to Male F344 Rats<sup>a</sup>

Dose (mg/cm <sup>2</sup> )		0.1	1.0	10
Tissue Name	N	Tissue-Blood Ratio		
Adipose	3	0.37 ± 0.26	0.44 ± 0.02	0.54 ± 0.06
Adrenal gland	3	1.21 ± 0.79	1.65 ± 0.24	0.57 ± 0.53
Bladder	3	2.73 ± 0.54	5.33 ± 1.89	2.31 ± 0.62
Blood	3	1.00 ± 0.00	1.00 ± 0.00	1.00 ± 0.00
Brain	3	0.32 ± 0.02	0.47 ± 0.02	0.54 ± 0.01
Cecum	3	3.16 ± 1.09	3.93 ± 0.47	6.15 ± 0.69
Esophagus	3	1.73 ± 0.76	1.70 ± 0.49	1.14 ± 0.43
Eye	3	0.27 ± 0.10	0.33 ± 0.05	0.32 ± 0.06
Heart	3	0.94 ± 0.40	0.90 ± 0.09	0.76 ± 0.18
Intestine, large	3	2.72 ± 0.34	3.73 ± 1.79	3.49 ± 2.21
Intestine, small	3	3.02 ± 1.20	3.08 ± 0.49	2.52 ± 0.70
Kidney	3	2.19 ± 0.76	2.03 ± 0.24	1.85 ± 0.51
Liver	3	2.20 ± 0.44	2.52 ± 0.25	2.05 ± 0.59
Lung	3	1.51 ± 0.64	1.36 ± 0.12	1.24 ± 0.37
Muscle	3	0.43 ± 0.02	0.45 ± 0.03	0.35 ± 0.05
Plasma	3	0.91	0.93 ± 0.13	0.89 ± 0.35
Prostate	3	1.68 ± 0.52	1.57 ± 0.19	0.76 ± 0.46
Seminal vesicle	3	2.05 ± 0.81	1.11 ± 0.24	0.79 ± 0.54
Skin	3	1.04 ± 0.34	0.75 ± 0.00	0.63 ± 0.17
Spleen	3	1.58 ± 0.29	1.64 ± 0.39	2.39 ± 1.97
Stomach	3	3.62 ± 1.44	3.21 ± 0.14	2.21 ± 1.59
Testis	3	0.96 ± 0.36	0.70 ± 0.02	0.56 ± 0.28
Trachea	3	1.23 ± 0.79	0.98 ± 0.12	1.68 ± 1.32
Contents, Cecum	3	N/A <sup>b</sup>	2.97 ± 0.63	N/A
Contents, Lg Int	3	N/A	3.63 ± 1.37	N/A
Contents, Sm Int	3	N/A	1.43 ± 0.37	N/A
Contents, Stomach	3	N/A	1.20 ± 0.35	N/A

<sup>a</sup> Average ± SD for N animals; for N=2, mean only.

<sup>b</sup> Not analyzed.

Table 36

$^3\text{H}/^{14}\text{C}$  Ratio in Tissues 24 h Following Dermal  
Application of [ $^3\text{H}/^{14}\text{C}$ ]BNS to Fischer 344 Male Rats<sup>a</sup>

Dose (mg/cm <sup>2</sup> )	0.10		1.0		10	
Tissue Name	$^3\text{H}/^{14}\text{C}$ Ratio					
	N		N		N	
Adipose	3	0.43	3	0.23	3	0.23
Adrenal gland	3	0.06	3	0.07	3	1.28
Bladder	3	1.08	3	2.16	3	4.57
Blood	3	0.28	3	0.24	3	0.17
Brain	3	0.17	3	0.16	3	0.15
Cecum	3	0.24	3	0.13	3	0.43
Esophagus	3	0.11	3	0.07	3	0.31
Eye	3	0.32	3	0.21	3	0.16
Heart	3	0.14	3	0.13	3	0.53
Intestine, large	3	0.22	3	0.08	3	0.22
Intestine, small	3	0.24	3	0.09	3	0.42
Kidney	3	0.22	3	0.24	3	0.49
Liver	3	0.11	3	0.06	3	0.23
Lung	3	0.21	3	0.13	3	0.41
Muscle	3	0.33	3	0.17	3	0.37
Plasma	2	0.28	3	0.66	3	0.69
Prostate	3	0.90	3	1.10	3	0.89
Seminal vesicle	3	0.98	3	0.22	3	0.25
Skin	3	0.40	3	0.14	3	0.50
Spleen	3	0.10	3	0.08	3	0.63
Stomach	3	0.08	3	0.04	3	0.11
Testis	3	0.68	3	0.23	3	0.58
Trachea	3	0.05	3	0.10	3	0.52
Contents, Cecum		N/A <sup>b</sup>	3	0.20		N/A <sup>b</sup>
Contents, Lg Int		N/A	3	0.16		N/A
Contents, Sm Int		N/A	3	0.21		N/A
Contents, Stomach		N/A	3	0.07		N/A

<sup>a</sup> Values calculated by equation: [Av ng-eq  $^3\text{H}/\text{g}$  tissue]/[Av ng-eq  $^{14}\text{C}/\text{g}$  tissue]

<sup>b</sup> Not analyzed.