

Table 51

Two generation reproductive toxicity study of BBP by oral administration in rats  
Organ weight of F<sub>1</sub> males at 10 weeks of age; Mean±S.D. (N)

Compound	Butyl benzyl phthalate			
	0 <sup>a</sup>	20	100	500
Terminal body weight (g)	454.1 ± 43.4 (22)	454.2 ± 40.6 (19)	453.4 ± 38.5 (23)	423.2 ± 49.9 * (24)
Testes (g)	3.43 ± 0.24 <sup>b</sup> (22)	3.43 ± 0.30 (19)	3.48 ± 0.35 (23)	3.25 ± 0.49 (24)
	0.76 ± 0.06 <sup>c</sup> (22)	0.76 ± 0.10 (19)	0.77 ± 0.07 (23)	0.78 ± 0.15 (24)
Epididymides (g)	0.97 ± 0.08 (22)	0.98 ± 0.09 (19)	0.99 ± 0.09 (23)	0.84 ± 0.13 ** (24)
	0.21 ± 0.02 (22)	0.22 ± 0.02 (19)	0.22 ± 0.01 (23)	0.20 ± 0.04 (24)
Prostate glands (g)	0.45 ± 0.11 (22)	0.52 ± 0.10 (19)	0.53 ± 0.15 (23)	0.42 ± 0.10 (24)
	0.10 ± 0.02 (22)	0.12 ± 0.02 (19)	0.12 ± 0.03 (23)	0.10 ± 0.03 (24)
Seminal vesicle (g)	1.30 ± 0.27 (22)	1.35 ± 0.25 (19)	1.40 ± 0.24 (23)	1.09 ± 0.16 ** (24)
	0.29 ± 0.05 (22)	0.30 ± 0.05 (19)	0.31 ± 0.06 (23)	0.26 ± 0.05 (24)

a: vehicle control, corn oil (2 mL/kg)

b: absolute weight

c: relative weight (g per 100g body weight)

\*: significant difference from control, p<0.05

\*\*: significant difference from control, p<0.01

Table 52

Two generation reproductive toxicity study of BBP by oral administration in rats  
Organ weight of F<sub>1</sub> females at 10 weeks of age; Mean±S.D. (N)

Compound	Butyl benzyl phthalate				
	0 <sup>a</sup>	20	100	500	
Terminal body weight (g)	285.4 ± 21.8 (22)	281.4 ± 25.1 (19)	277.4 ± 22.7 (23)	260.5 ± 18.4 ** (24)	
Uterus (g)	0.53 ± 0.25 <sup>b</sup> (22)	0.47 ± 0.21 (19)	0.49 ± 0.21 (23)	0.50 ± 0.17 (23)	
	0.19 ± 0.09 <sup>c</sup> (22)	0.17 ± 0.07 (19)	0.18 ± 0.08 (23)	0.19 ± 0.06 (23)	
Uterus (diestrus) (g)	0.44 ± 0.10 (14)	0.36 ± 0.09 (12)	0.45 ± 0.17 (15)	0.44 ± 0.09 (10)	
	0.16 ± 0.04 (14)	0.13 ± 0.03 (12)	0.16 ± 0.06 (15)	0.17 ± 0.04 (10)	
Uterus (proestrus) (g)	0.86 ± 0.35 (5)	0.84 ± 0.13 (4)	0.87 ± 0.18 (3)	0.80 ± 0.29 (3)	
	0.31 ± 0.13 (5)	0.28 ± 0.06 (4)	0.31 ± 0.08 (3)	0.30 ± 0.09 (3)	
Uterus (estrus) (g)	0.39 ± 0.07 (3)	0.42 ± 0.02 (3)	0.39 ± 0.05 (5)	0.48 ± 0.09 (10)	
	0.13 ± 0.03 (3)	0.16 ± 0.02 (3)	0.14 ± 0.02 (5)	0.19 ± 0.04 * (10)	
Ovary (mg)	102.8 ± 15.4 (22)	107.4 ± 17.3 (19)	100.7 ± 13.7 (23)	87.9 ± 9.2 ** (24)	
	34.7 ± 8.1 (22)	38.2 ± 5.2 (19)	36.3 ± 4.4 (23)	33.9 ± 4.3 (24)	

a: vehicle control, corn oil (2 mL/kg)

b: absolute weight

c: relative weight (g or mg per 100g body weight)

\*: significant difference from control, p<0.05

\*\* : significant difference from control, p<0.01

Table 53

Two generation reproductive toxicity study of BBP by oral administration in rats  
Estrous cycle of F<sub>1</sub> females

Compound	Butyl benzyl phthalate			
	0 <sup>a</sup>	20	100	500
Dose (mg/kg)				
Number of females examined	22	20	23	24
Mean length of estrous cycle in days	4.0 ± 0.2	4.4 ± 0.5	4.0 ± 0.1	4.2 ± 0.3
Number of animals showing each type of cycle during treatment period				
4-day cycle	21	10	20	18
5-day cycle	1	5		2
4/5-day cycle		2	2	4
Monoestrus		2	1	
Irregular				
Anestrus		1		
Number of vaginal estrus during mating period				
period; Mean±S.D.	1.2 ± 0.4	1.2 ± 0.4	1.1 ± 0.5	1.3 ± 0.6

a: vehicle control, corn oil (2 mL/kg)

Table 54

Two generation reproductive toxicity study of BBP by oral administration in rats  
 Reproductive performance of F<sub>1</sub> animals

Compound	Butyl benzyl phthalate			
	0 <sup>a</sup>	20	100	500
Number of males examined (A)	22	19	23	24
Number of males successful copulation (B)	22	18	21	22
Copulation index [(B/A) × 100, %]	100.0	94.7	91.3	91.7
Number of pregnant females (C)	17	13	19	16
Fertility index [(B/A) × 100, %]	77.3	72.2	90.5	72.7
Pairing days until copulation	3.6 ± 2.8 ( 22)	4.3 ± 3.1 ( 18)	3.0 ± 2.3 ( 21)	3.2 ± 3.0 ( 22)
MeantS.D.				
Number of females examined (A)	22	20	24	24
Number of females successful copulation (B)	22	19	22	22
Copulation index [(B/A) × 100, %]	100.0	95.0	91.7	91.7
Number of pregnant females (C)	17	14	20	16
Fertility index [(B/A) × 100, %]	77.3	73.7	90.9	72.7
Pairing days until copulation	3.6 ± 2.8 ( 22)	4.3 ± 3.1 ( 19)	3.0 ± 2.3 ( 22)	3.2 ± 3.0 ( 22)
MeantS.D.				

a: vehicle control, corn oil (2 mL/kg)

Table 55\*

Two generation reproductive toxicity study of BBP by oral administration in rats  
 Summary of macroscopic findings in F1 males adult

Group Grade	0 mg/kg		20 mg/kg		100 mg/kg		500 mg/kg	
	-	+	-	+	-	+	-	+
(Testis)	[22]		[20]		[23]		[24]	
Small, right side	22	0	20	0	23	0	20	4
Small, bilateral	22	0	20	0	23	0	23	1
Area, pale, right side	22	0	20	0	23	0	23	1
Defect, right side	22	0	20	0	23	0	23	1
Enlargement, left side (Epididymis)	22	0	20	0	23	0	23	1
Small, right side (Prostate)	[22]	0	[20]	0	[23]	0	[24]	4
Small (Kidney)	[22]	0	[20]	0	[23]	0	[24]	1
Enlargement Dilatation, renal pelvis, bilateral	[22]	0	[20]	0	[23]	0	[24]	1
Dilatation, renal pelvis, right side	20	2	20	0	23	0	23	1
Cyst, bilateral (Spleen)	22	0	18	2	23	0	24	0
Deformity	[22]	0	[20]	0	[23]	1	[24]	0
	22	0	20	0	22	1	24	0

-, Negative; +, Positive

[ ], Number of animals examined

Table 56

Two generation reproductive toxicity study of BBP by oral administration in rats  
Summary of macroscopic findings in F1 females adult

Group Grade	0 mg/kg		20 mg/kg		100 mg/kg		500 mg/kg	
	-	+	-	+	-	+	-	+
(Kidney)	[22]		[20]		[23]		[24]	
Dilatation, renal pelvis, bilateral	22	0	20	0	22	1	24	0
Dilatation, renal pelvis, right side	20	2	20	0	23	0	23	1
Dilatation, renal pelvis, left side	22	0	19	1	23	0	24	0
Pale, cortex	22	0	20	0	22	1	24	0
(Thymus)	[22]		[20]		[23]		[24]	
Small	21	1	20	0	23	0	24	0
(Lung)	[22]		[20]		[23]		[24]	
Spot, red	22	0	20	0	23	0	23	1

-, Negative; +, Positive

[ ], Number of animals examined

Table 57

Two generation reproductive toxicity study of BBP by oral administration in rats  
Organ weight of F<sub>1</sub> adult males; Mean±S.D. (N)

Compound	Butyl benzyl phthalate			
	0 <sup>a</sup>	20	100	500
Terminal body weight (g)	662.9 ± 67.6 (22)	637.1 ± 49.6 (20)	613.4 ± 55.3* (23)	580.0 ± 52.7** (24)
Brain (g)	2.10 ± 0.06 <sup>b</sup> (22)	2.10 ± 0.07 (20)	2.08 ± 0.06 (23)	2.07 ± 0.09 (24)
	0.32 ± 0.03 <sup>c</sup> (22)	0.33 ± 0.03 (20)	0.34 ± 0.03 (23)	0.36 ± 0.04** (24)
Heart (g)	1.73 ± 0.16 (22)	1.67 ± 0.13 (20)	1.61 ± 0.17* (23)	1.53 ± 0.18** (24)
	0.26 ± 0.02 (22)	0.26 ± 0.02 (20)	0.26 ± 0.02 (23)	0.26 ± 0.02 (24)
Lung (g)	1.49 ± 0.12 (22)	1.50 ± 0.09 (20)	1.41 ± 0.09 (23)	1.41 ± 0.18 (24)
	0.23 ± 0.02 (22)	0.24 ± 0.02 (20)	0.23 ± 0.02 (23)	0.24 ± 0.03* (24)
Liver (g)	23.60 ± 2.77 (22)	23.56 ± 2.56 (20)	21.74 ± 3.09 (23)	23.67 ± 3.74 (24)
	3.57 ± 0.35 (22)	3.70 ± 0.29 (20)	3.54 ± 0.38 (23)	4.09 ± 0.59** (24)
Spleen (g)	1.00 ± 0.09 (22)	0.94 ± 0.13 (20)	0.97 ± 0.13 (23)	0.88 ± 0.12** (24)
	0.15 ± 0.02 (22)	0.15 ± 0.02 (20)	0.16 ± 0.02 (23)	0.15 ± 0.02 (24)
Kidneys (g)	3.62 ± 0.32 (22)	3.63 ± 0.25 (20)	3.66 ± 0.38 (23)	3.76 ± 0.56 (24)
	0.55 ± 0.04 (22)	0.57 ± 0.05 (20)	0.60 ± 0.06* (23)	0.65 ± 0.07** (24)
Adrenal glands (mg)	58.1 ± 6.4 (22)	59.1 ± 7.2 (20)	54.7 ± 8.6 (23)	55.1 ± 6.2 (24)
	8.8 ± 1.1 (22)	9.3 ± 1.0 (20)	8.9 ± 1.3 (23)	9.5 ± 1.1 (24)
Thymus (mg)	376.1 ± 95.5 (22)	360.7 ± 96.9 (20)	307.3 ± 46.4 (23)	330.6 ± 77.2 (24)
	57.1 ± 14.3 (22)	57.1 ± 17.0 (20)	50.4 ± 8.3 (23)	56.9 ± 12.1 (24)
Testes (g)	3.75 ± 0.34 (22)	3.74 ± 0.19 (20)	3.63 ± 0.27 (23)	3.30 ± 0.64** (24)
	0.57 ± 0.07 (22)	0.59 ± 0.06 (20)	0.60 ± 0.06 (23)	0.57 ± 0.12 (24)
Epididymides (g)	1.38 ± 0.11 (22)	1.34 ± 0.09 (20)	1.31 ± 0.08 (23)	1.09 ± 0.23** (24)
	0.21 ± 0.02 (22)	0.21 ± 0.02 (20)	0.21 ± 0.02 (23)	0.19 ± 0.04 (24)
Ventral prostate (g)	0.71 ± 0.10 (22)	0.69 ± 0.11 (19)	0.66 ± 0.10 (23)	0.61 ± 0.14* (23)
	0.11 ± 0.01 (22)	0.11 ± 0.02 (19)	0.11 ± 0.02 (23)	0.10 ± 0.02 (23)
Seminal vesicle (g)	1.99 ± 0.40 (22)	1.94 ± 0.43 (19)	1.98 ± 0.29 (23)	1.80 ± 0.42 (24)
	0.30 ± 0.06 (22)	0.31 ± 0.06 (19)	0.32 ± 0.05 (23)	0.31 ± 0.07 (24)
Prostate and seminal vesicle (g)	3.17 ± 0.42 (22)	3.02 ± 0.39 (20)	3.20 ± 0.33 (23)	2.81 ± 0.56* (24)
	0.48 ± 0.06 (22)	0.48 ± 0.07 (20)	0.52 ± 0.06 (23)	0.49 ± 0.09 (24)
Thyroid glands (mg)	21.0 ± 4.7 (22)	21.6 ± 4.3 (20)	22.1 ± 2.7 (23)	22.5 ± 4.5 (24)
	3.2 ± 0.7 (22)	3.4 ± 0.7 (20)	3.6 ± 0.6 (23)	3.9 ± 0.8** (24)
Pituitary gland (mg)	12.4 ± 1.6 (22)	12.5 ± 1.5 (20)	12.2 ± 1.6 (23)	12.3 ± 1.3 (24)
	1.9 ± 0.3 (22)	2.0 ± 0.2 (20)	2.0 ± 0.2 (23)	2.1 ± 0.2** (24)

a: vehicle control, corn oil (2 mL/kg)

b: absolute weight

c: relative weight (mg per 100g body weight)

\*: significant difference from control, p&lt;0.05

\*\*: significant difference from control, p&lt;0.01

Table 58

Two generation reproductive toxicity study of BBP by oral administration in rats  
Organ weight of F<sub>1</sub> females on day 21 of lactation; Mean±S.D. (N)

Compound	Butyl benzyl phthalate				
	0 <sup>a</sup>	20	100	500	
Dose (mg/kg)					
Terminal body weight (g)	360.7 ± 21.1 (16)	364.3 ± 19.3 (15)	366.0 ± 25.3 (21)	362.3 ± 28.5 (17)	
Brain	1.92 ± 0.07 <sup>b</sup> (16) 0.54 ± 0.03 <sup>c</sup>	1.93 ± 0.05 (15) 0.53 ± 0.03	1.92 ± 0.06 (21) 0.53 ± 0.03	1.95 ± 0.09 (17) 0.54 ± 0.03	
Heart	1.15 ± 0.07 (16) 0.32 ± 0.02	1.19 ± 0.12 (15) 0.33 ± 0.02	1.16 ± 0.10 (21) 0.32 ± 0.02	1.15 ± 0.07 (17) 0.32 ± 0.02	
Lung	1.14 ± 0.07 (16) 0.32 ± 0.02	1.14 ± 0.10 (15) 0.31 ± 0.02	1.14 ± 0.07 (21) 0.31 ± 0.02	1.12 ± 0.10 (17) 0.31 ± 0.03	
Liver	15.65 ± 1.03 (16) 4.34 ± 0.21	15.70 ± 1.49 (15) 4.31 ± 0.30	15.38 ± 1.40 (21) 4.21 ± 0.35	15.75 ± 1.30 (17) 4.35 ± 0.26	
Spleen	0.70 ± 0.09 (16) 0.19 ± 0.02	0.67 ± 0.09 (15) 0.18 ± 0.02	0.74 ± 0.13 (21) 0.20 ± 0.03	0.71 ± 0.11 (17) 0.20 ± 0.03	
Kidneys	2.35 ± 0.14 (16) 0.65 ± 0.04	2.37 ± 0.21 (15) 0.65 ± 0.05	2.49 ± 0.28 (21) 0.68 ± 0.07	2.45 ± 0.15 (17) 0.68 ± 0.06	
Adrenal glands	71.5 ± 6.4 (16) 19.9 ± 2.0	67.9 ± 8.2 (15) 18.7 ± 2.4	71.2 ± 10.3 (21) 19.5 ± 2.4	73.0 ± 11.0 (17) 20.2 ± 2.8	
Thymus	207.8 ± 61.5 (16) 57.4 ± 16.4	218.7 ± 70.4 (15) 60.2 ± 19.2	181.0 ± 43.6 (21) 49.4 ± 11.1	233.8 ± 71.2 (17) 64.7 ± 20.3	
Ovary	96.7 ± 12.3 (16) 26.8 ± 3.1	98.7 ± 19.0 (15) 27.1 ± 4.6	105.2 ± 11.3 (21) 28.8 ± 2.5	94.1 ± 13.1 (17) 26.1 ± 4.0	
Uterus	0.43 ± 0.12 (16) 0.12 ± 0.03	0.43 ± 0.19 (15) 0.12 ± 0.06	0.44 ± 0.09 (21) 0.12 ± 0.02	0.43 ± 0.07 (17) 0.12 ± 0.02	
Thyroid glands	18.8 ± 2.7 (16) 5.2 ± 0.9	17.2 ± 3.2 (15) 4.7 ± 0.9	18.5 ± 3.9 (21) 5.1 ± 1.2	19.5 ± 2.9 (17) 5.4 ± 0.8	
Pituitary gland	14.2 ± 2.2 (16) 4.0 ± 0.7	14.6 ± 2.6 (15) 4.0 ± 0.7	14.2 ± 2.1 (21) 3.9 ± 0.5	13.3 ± 1.6 (17) 3.7 ± 0.4	

a: vehicle control, corn oil (2 mL/kg)

b: absolute weight

c: relative weight (mg per 100g body weight)



Table 59  
 †  
 Two generation reproductive toxicity study of BBP by oral administration in rats  
 Summary of histopathological findings in F1 male adult

Group Grade	0 mg/kg			20 mg/kg			100 mg/kg			500 mg/kg		
	-	±	+	-	±	+	-	±	+	-	±	+
(Testis)	[10]			[10]			[10]			[10]		
Atrophy, seminiferous tubule, right side	10	0	0	10	0	0	10	0	0	4	1	0
Decrease, germ cell, seminiferous tubule, right side	10	0	0	10	0	0	10	0	0	6	0	0
Edema, interstitium, right side	10	0	0	10	0	0	10	0	0	6	0	0
Spermatogenic granuloma, rete testis, right side	10	0	0	10	0	0	10	0	0	9	0	1
Atrophy, seminiferous tubule, left side	10	0	0	10	0	0	10	0	0	7	2	1
Dilatation, seminiferous tubule, diffuse, left side	10	0	0	10	0	0	10	0	0	9	0	0
Decrease, germ cell, seminiferous tubule, left side	10	0	0	10	0	0	10	0	0	9	1	0
Defect, right side	10	0	0	10	0	0	10	0	0	9	0	0
Multinucleated giant cell, seminiferous tubule, left side	10	0	0	10	0	0	10	0	0	9	0	1
(Epididymis)	[10]			[10]			[10]			[10]		
Decrease, sperm, lumen, with cell debris, unilateral	10	0	0	10	0	0	10	0	0	5	0	0
(Prostate: ventral lobe)	[10]			[0]			[0]			[10]		
Cellular infiltration, lymphocyte, interstitium	7	2	1	7	2	1	7	2	1	6	2	0
Cellular infiltration, lymphocyte /plasma cell, epithelium	8	1	1	8	1	1	8	1	1	8	0	2
(Seminol vesicle & coagulating gland)	[10]			[0]			[0]			[10]		
No remarkable change	[10]			[10]			[10]			[10]		
(Liver)	8	0	2	8	0	2	8	0	2	10	0	0
Fatty change, periportal	[10]			[0]			[0]			[10]		
(Kidney)	0	7	3	0	7	3	0	7	3	0	5	0
Basophilic tubule, cortex	7	1	1	7	1	1	7	1	1	9	1	0
Eosinophilic body	6	4	0	6	4	0	6	4	0	7	3	0
Mineralization	9	0	1	9	0	1	9	0	1	9	1	0
Dilatation, renal pelvis	9	1	0	9	1	0	9	1	0	10	0	0
Fibrosis, focal, subcapsule	8	2	0	8	2	0	8	2	0	6	3	1
Cast, hyalin, cortex/medulla	10	0	0	10	0	0	10	0	0	9	1	0
Cellular infiltration, lymphocyte, interstitium	[10]			[0]			[0]			[10]		
(Mammary gland)	[10]			[0]			[0]			[10]		
No remarkable change	[10]			[0]			[0]			[10]		
(Thyroid gland)	9	1	0	9	1	0	9	1	0	10	0	0
Ectopic thymus	[8]			[0]			[0]			[8]		
(Parathyroid gland)	[10]			[0]			[0]			[10]		
No remarkable change	[10]			[0]			[0]			[10]		
(Pituitary gland)	[10]			[0]			[0]			[10]		
No remarkable change	[10]			[0]			[0]			[10]		
(Adrenal gland)	[10]			[0]			[0]			[10]		
No remarkable change	[10]			[0]			[0]			[10]		

- , Negative; ±, Very slight; †, Slight; ††, Moderate; †††, Severe; Pos., Total of positive grade  
 † †, Number of animals examined  
 \*, Significantly different from control p<0.05 (Two-tailed Mann-Whitney U test)  
 #, Significantly different from control p<0.05 (One-tailed Fisher exact test)  
 ##, Significantly different from control p<0.01 (One-tailed Fisher exact test)

Table 60  
Two generation reproductive toxicity study of BBP by oral administration in rats  
Summary of histopathological findings in F1 female adult

Group Grade	0 mg/kg		20 mg/kg		100 mg/kg		500 mg/kg	
	-	±	-	±	-	±	-	±
(Ovary)	[10]		[0]		[0]		[10]	
No remarkable change (Uterus)	[10]		[0]		[0]		[10]	
No remarkable change (Vagina)	[10]		[0]		[0]		[10]	
No remarkable change (Liver)	[10]		[0]		[0]		[10]	
Granulation & necrosis, subcapsule, focal (Kidney)	[10]	9 1 0 0 0 1	[0]		[0]		[10]	10 0 0 0 0 0
Basophilic tubule, cortex	[10]	6 4 0 0 0 4	[0]		[0]		[10]	5 0 0 0 5
Mineralization, papilla	[10]	8 1 1 0 0 2					[10]	10 0 0 0 0 0
Dilatation, renal pelvis, right side	[10]	9 0 1 0 0 1					[10]	10 0 0 0 0 0
Dilatation, collecting tubule, medulla & papilla (Mammary gland)	[10]	10 0 0 0 0 0	[0]		[0]		[10]	9 1 0 0 0 1
No remarkable change (Thyroid gland)	[10]		[0]		[0]		[10]	
Ectopic thymus (Parathyroid gland)	[9]	10 0 0 0 0 0	[0]		[0]		[8]	9 1 0 0 0 1
No remarkable change (Pituitary gland)	[10]		[0]		[0]		[10]	
No remarkable change (Adrenal gland)	[10]		[0]		[0]		[10]	
No remarkable change (Thymus)	[11]	0 1 0 0 0 1	[0]		[0]		[0]	
Atrophy								

- , Negative; ±, Very slight; +, Slight; ++, Moderate; +++, Severe; Pos., Total of positive grade  
[ ], Number of animals examined

Table 61

Two generation reproductive toxicity study of BBP by oral administration in rats  
Epididymal sperm findings in F1 males at 18-19 weeks of age; Mean±S.D.

Compound	Butyl benzyl phthalate				
	0 <sup>a</sup>	20	100	500	
% of motile	95 ± 4 ( 22)	96 ± 4 ( 20)	97 ± 2 ( 23)	88 ± 22 ( 24)	
% of progressive	83 ± 8 ( 22)	83 ± 8 ( 20)	85 ± 7 ( 23)	77 ± 21 ( 24)	
Sperm counts <sup>b</sup>	1876.6 ± 390.8 ( 22)	1708.0 ± 370.2 ( 20)	1802.9 ± 310.9 ( 23)	1710.1 ± 531.1 ( 24)	

a: vehicle control, corn oil (2 mL/kg)

b: number of sperm per caudal epidymis weight (x10<sup>6</sup>/g)

Table 62

Two generation reproductive toxicity study of BBP by oral administration in rats

Serum concentrations of testosterone, luteinizing hormone (LH), follicle-stimulating hormone (FSH), thyroid-stimulating hormone (TSH), triiodothyronine (T3), thyroxine (T4) in F1 adult males; Mean±S.D. (N)

Compound	Butyl benzyl phthalate				
	0 <sup>a</sup>	20	100	500	
Testosterone (ng/mL)	6.6 ± 2.9 ( 22)	8.1 ± 3.3 ( 20)	7.1 ± 5.2 ( 23)	3.7 ± 3.3 ** ( 24)	
LH (ng/mL)	14.5 ± 3.3 ( 22)	16.4 ± 2.6 ( 20)	13.2 ± 4.7 ( 23)	11.4 ± 2.0 ** ( 24)	
FSH (ng/mL)	244 ± 42 ( 22)	237 ± 59 ( 20)	228 ± 37 ( 23)	256 ± 57 ( 24)	
TSH (ng/mL)	14.5 ± 2.6 ( 22)	16.2 ± 2.4 ( 20)	14.6 ± 2.2 ( 23)	15.2 ± 2.8 ( 24)	
T3 (ng/mL)	0.7 ± 0.1 ( 22)	0.8 ± 0.1 * ( 20)	0.8 ± 0.1 * ( 23)	0.8 ± 0.1 ( 24)	
T4 (ng/mL)	67 ± 13 ( 22)	74 ± 9 ( 20)	66 ± 7 ( 23)	53 ± 7 ** ( 24)	

a: vehicle control, corn oil (2 mL/kg)

\*: significant difference from control, p&lt;0.05

\*\*: significant difference from control, p&lt;0.01

Table 63

Two generation reproductive toxicity study of BBP by oral administration in rats

Serum concentrations of prolactin (PRL), luteinizing hormone (LH), follicle-stimulating hormone (FSH), thyroid-stimulating hormone (TSH), triiodothyronine (T3), thyroxine (T4), estradiol in F<sub>1</sub> adult females; Mean±S.D. (N)

Compound	Butyl benzyl phthalate			
	0 <sup>a</sup>	20	100	500
PRL (ng/mL)	111.1 ± 130.5 ( 16)	47.5 ± 84.8 ( 15)	53.6 ± 72.9 ( 21)	148.6 ± 146.3 ( 17)
LH (ng/mL)	11.9 ± 1.9 ( 16)	10.5 ± 2.0 ( 15)	12.2 ± 2.1 ( 21)	12.3 ± 2.3 ( 17)
FSH (ng/mL)	241 ± 47 ( 16)	224 ± 46 ( 15)	219 ± 65 ( 21)	220 ± 56 ( 17)
TSH (ng/mL)	15.9 ± 2.8 ( 16)	15.3 ± 1.7 ( 15)	15.0 ± 2.2 ( 21)	14.5 ± 2.5 ( 17)
T3 (ng/mL)	0.7 ± 0.1 ( 14)	0.7 ± 0.1 ( 15)	0.7 ± 0.2 ( 21)	0.7 ± 0.1 ( 17)
T4 (ng/mL)	48 ± 12 ( 16)	55 ± 27 ( 15)	53 ± 11 ( 21)	54 ± 11 ( 17)
Estradiol (pg/mL)	16.3 ± 8.5 ( 5)	14.5 ± 7.6 ( 11)	14.5 ± 11.6 ( 8)	11.5 ± 6.6 ( 3)

a: vehicle control, corn oil (2 mL/kg)

Table 64

Two generation reproductive toxicity study of BBP by oral administration in rats  
Development F<sub>2</sub> offspring up to weaning; Mean±S.D. (N)

Compound	Butyl benzyl phthalate				
	0 <sup>a</sup>	20	100	500	
Gestation period; days	21.9 ± 0.6 (16)	22.0 ± 0.4 (15)	21.9 ± 0.4 (21)	22.1 ± 0.2 (17)	
Implantations	13.9 ± 2.6 (16)	14.6 ± 2.1 (15)	13.4 ± 3.1 (21)	13.1 ± 3.1 (17)	
Delivery index; dam A)	100.0	100.0	100.0	100.0	
Day 0					
Fetuses delivered	13.3 ± 2.6 (16)	13.9 ± 2.2 (15)	12.1 ± 3.2 (21)	11.8 ± 3.2 (17)	
Delivery index; fetuses B)	95.8 ± 4.7 (16)	95.0 ± 7.8 (15)	90.0 ± 9.3 (21)	90.1 ± 12.5 (17)	
Live newborns	13.1 ± 2.8 (16)	13.6 ± 2.3 (15)	11.9 ± 3.1 (21)	11.6 ± 3.3 (17)	
Birth index C)	94.2 ± 5.8 (16)	93.1 ± 8.3 (15)	88.3 ± 9.7 (21)	88.7 ± 14.5 (17)	
Viability index D)	98.3 ± 5.2 (16)	98.0 ± 3.6 (15)	98.1 ± 3.5 (21)	98.0 ± 5.2 (17)	
Day 4					
Live offspring	12.8 ± 2.7 (16)	12.9 ± 2.7 (15)	11.8 ± 3.1 (21)	11.4 ± 3.3 (17)	
Viability index E)	97.8 ± 4.8 (16)	95.4 ± 12.8 (15)	99.7 ± 1.5 (21)	97.6 ± 5.1 (17)	
Offspring after culling	8.0 ± 0.0 (16)	7.9 ± 0.3 (15)	7.8 ± 0.6 (21)	7.7 ± 1.0 (17)	
Males	3.9 ± 0.3	4.1 ± 0.6	3.8 ± 1.0	3.9 ± 1.1	
Females	4.1 ± 0.3	3.9 ± 0.6	4.0 ± 0.7	3.8 ± 1.0	
Day 21					
Live offspring	8.0 ± 0.0 (16)	7.9 ± 0.3 (15)	7.8 ± 0.6 (21)	7.6 ± 1.2 (17)	
Males	3.9 ± 0.3	4.1 ± 0.6	3.8 ± 1.0	3.9 ± 1.1	
Females	4.1 ± 0.3	3.9 ± 0.6	4.0 ± 0.7	3.8 ± 1.0	
Weaning index F)	100.0 ± 0.0 (16)	100.0 ± 0.0 (15)	100.0 ± 0.0 (21)	98.5 ± 6.1 (17)	

A): Delivery index; dams = (no. of dams having live newborns / no. of pregnant females) x 100

B): Delivery index; fetuses = (no. of fetuses delivered / no. of implantations) x 100

C): Birth index = (no. of live newborns / no. of implantations) x 100

D): Viability index; Day 0 = (no. of live newborns / no. of offspring delivered) x 100

E): Viability index; Day 4 = (no. of live offspring on day 4 / no. of offspring on day 0) x 100

F): Weaning index = (no. of live offspring at weaning / no. of live offspring on day 4) x 100

a: vehicle control, corn oil (2 mL/kg)

Table 65

Two generation reproductive toxicity study of BBP by oral administration in rats  
 Body weight of F<sub>2</sub> offspring up to weaning; Mean±S.D. (Litter)

Compound	Butyl benzyl phthalate			
	0 <sup>a</sup>	20	100	500
Day 0				
Male	6.7 ± 0.6 ( 16)	6.7 ± 0.4 ( 15)	6.7 ± 0.6 ( 21)	6.5 ± 0.7 ( 17)
Female	6.3 ± 0.5 ( 16)	6.4 ± 0.5 ( 15)	6.3 ± 0.6 ( 21)	6.1 ± 0.5 ( 17)
Day 4 (After culling)				
Male	10.4 ± 1.5 ( 16)	10.7 ± 1.2 ( 15)	10.9 ± 2.3 ( 21)	10.4 ± 1.6 ( 17)
Female	9.9 ± 1.5 ( 16)	10.3 ± 1.3 ( 15)	10.6 ± 2.2 ( 21)	9.9 ± 1.3 ( 17)
Day 7				
Male	16.8 ± 1.5 ( 16)	17.4 ± 1.6 ( 15)	17.6 ± 2.8 ( 21)	16.5 ± 2.1 ( 17)
Female	16.1 ± 1.5 ( 16)	16.7 ± 1.7 ( 15)	16.8 ± 2.6 ( 21)	15.5 ± 1.7 ( 17)
Day 14				
Male	34.8 ± 2.7 ( 16)	36.4 ± 2.9 ( 15)	36.1 ± 4.0 ( 21)	33.0 ± 5.2 ( 17)
Female	33.5 ± 2.4 ( 16)	36.6 ± 11.3 ( 15)	34.7 ± 4.0 ( 21)	30.8 ± 3.5 ( 17)
Day 21				
Male	57.0 ± 5.0 ( 16)	59.0 ± 4.1 ( 15)	58.6 ± 6.4 ( 21)	52.6 ± 5.8 ( 17)
Female	54.7 ± 4.7 ( 16)	56.7 ± 4.2 ( 15)	55.9 ± 6.6 ( 21)	48.3 ± 5.0 ( 17)

a: vehicle control, corn oil (2 mL/kg)

Table 66

Two generation reproductive toxicity study of BBP by oral administration in rats  
Morphological observations of F<sub>2</sub> live pups at birth

Compound	Butyl benzyl phthalate		
	0 <sup>a</sup>	20	100
Dose (mg/kg)			500
Number of live pups examined	210	204	249
<u>External abnormalities</u>			
Number of pups	0	0	2
<u>Types and number</u>			
Dwarf runt	0	0	1
Filamentous tail	0	0	1
Anal atresia	0	0	1



Table 67

Two generation reproductive toxicity study of BBP by oral administration in rats  
Morphological observations of F<sub>2</sub> dead pups during lactation period

Compound	Butyl benzyl phthalate			
Dose (mg/kg)	0 <sup>a</sup>	20	100	500
Number of dead pups <sup>b</sup>	8	14	6	9
Number of dead pups collected	4	7	4	3
<u>External abnormalities</u>				
Number of pups	2	0	0	0
<u>Types and number</u>				
Open eyelid	2	0	0	0
<u>Visceral abnormalities</u>				
Number of pups	0	0	0	0
<u>Visceral variations</u>				
Number of pups	0	2	0	0
<u>Types and number</u>				
Dilatation of renal pelvis	0	2	0	0

a: vehicle control, corn oil (2 mL/kg)

b: including missing pups

Table 68

Two generation reproductive toxicity study of BBP by oral administration in rats  
Morphological observations of F<sub>2</sub> pups culled on postnatal day 4

Compound	Butyl benzyl phthalate			
Dose (mg/kg)	0 <sup>a</sup>	20	100	500
Number of pups examined	77	75	85	62
<u>External abnormalities</u>				
Number of pups	0	0	0	0
<u>Visceral abnormalities</u>				
Number of pups	0	0	0	0
<u>Visceral variations</u>				
Number of pups	1	0	0	0
<u>Types and number</u>				
Dilatation of renal pelvis	1	0	0	0

a: vehicle control, corn oil (2 mL/kg)

Table 69

Two generation reproductive toxicity study of BBP by oral administration in rats  
Morphological observations of F<sub>2</sub> weanlings

Compound	Butyl benzyl phthalate			
	0 <sup>a</sup>	20	100	500
Number of weanlings examined	128	119	163	130
<u>External abnormalities</u>				
Number of weanlings	0	0	0	1
<u>Types and number</u>				
Anury	0	0	0	1
<u>Visceral abnormalities</u>				
Number of pups	1	0	1	1
<u>Types and number</u>				
Small testis	1	0	1	1
<u>Visceral variations</u>				
Number of pups	3	1	8	0
<u>Types and number</u>				
Red spot thymus	0	0	1	0
Dilatation of renal pelvis	3	1	7	0

a: vehicle control, corn oil (2 mL/kg)