Table 48

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

Spontaneous motor activity in F_1 females; Mean±S.D. (N)

Compound	Butyl benzyl phthalate			
Dose (mg/kg)	0[a]	20	100	500
Wheel cage activity (counts/24hour)	3211 ± 956 (22)	3164 ± 1239 (19)	4093 ± 1905 (23)	4890 ± 2189 * (24)

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

*: significant difference from control, $p<0.05$

Table 49

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

Sexual maturation of F1 males

Compound	Butyl benzyl phthalate			
Dose (mg/kg)	0[a]	20	100	500
Preputial separation				
Number of animals examined	22	20	23	24
Age (day)	43.2 ± 1.5	43.4 ± 1.5	43.3 ± 1.5	44.5 ± 2.3 *
Body weight (g)	238.7 ± 17.9	233.3 ± 14.7	228.9 ± 18.0	235.8 ± 20.2
Morphological observations at 10 weeks of age				
Number of pups examined	22	19	23	24
External abnormalities				
Number of pups	0	0	0	0
Visceral abnormalities				
Number of pups	0	0	0	2
Types and number				
Atrophy seminal vesicle	1	0	0	1
Atrophy testis	1	0	0	2
Atrophy epididymis	1	0	0	2
Visceral variations				
Number of pups	1	0	2	3
Types and number				
Dilatation of renal pelvis	1	0	2	3

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

*: significant difference from control, $p<0.05$

Table 50

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

Sexual maturation of F_1 females

Compound	Butyl benzyl phthalate			
Dose (mg/kg)	0[a]	20	100	500
Vaginal opening				
Number of animals examined	22	20	23	24
Age (day)	33.1 ± 1.4	33.6 ± 2.5	33.5 ± 2.0	34.0 ± 2.1
Body weight (g)	121.5 ± 10.5	129.2 ± 16.1	121.7 ± 9.9	126.5 ± 14.1
Morphological observations at 10 weeks of age				
Number of pups examined	22	19	23	24
External abnormalities				
Number of pups	0	0	0	0
Visceral abnormalities				
Number of pups	0	0	0	2
Types and number				
Hydronephrosis	0	0	0	1
Dilatation of uterus	0	0	0	1

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

Table 51

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

Organ weight of F_1 males at 10 weeks of age; Mean±S.D. (N)

Compound		Butyl benzyl phthalate			
Dose (mg/kg)		0[a]	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 [b] (22)	3.43 ± 0.30 (19)	3.48 ± 0.35 (23)	3.25 ± 0.49 (24)
		0.76 ± 0.06 [c] (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 F1 females at 10 weeks of age; Mean±S.D. (N)

Compound		Butyl benzyl phthalate			
Dose (mg/kg)		0[a]	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 [b] (22)	0.47 ± 0.21 (19)	0.49 ± 0.21 (23)	0.50 ± 0.17 (23)
		0.19 ± 0.09 [c] (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_1 females

Compound	Butyl benzyl phthalate			
Dose (mg/kg)	0[a]	20	100	500
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_1 animals

Compound	Butyl benzyl phthalate			
Dose (mg/kg)	0[a]	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 Mean±S.D.	3.6 ± 2.8 (22)	4.3 ± 3.1 (18)	3.0 ± 2.3 (21)	3.2 ± 3.0 (22)
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 Mean±S.D.	3.6 ± 2.8 (22)	4.3 ± 3.1 (19)	3.0 ± 2.3 (22)	3.2 ± 3.0 (22)

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 −	0 mg/kg +	20 mg/kg −	20 mg/kg +	100 mg/kg −	100 mg/kg +	500 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	22	0	20	0	23	0	23	1
(Epididymis)	[22]		[20]		[23]		[24]	
Small, right side	22	0	20	0	23	0	20	4
(Prostate)	[22]		[20]		[23]		[24]	
Small	22	0	20	0	23	0	23	1
(Kidney)	[22]		[20]		[23]		[24]	
Enlargement	22	0	20	0	23	0	23	1
Dilatation, renal pelvis, bilateral	20	2	20	0	23	0	23	1
Dilatation, renal pelvis, right side	22	0	18	2	23	0	24	0
Cyst, bilateral	22	0	20	0	22	1	24	0
(Spleen)	[22]		[20]		[23]		[24]	
Deformity	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 −	0 mg/kg +	20 mg/kg −	20 mg/kg +	100 mg/kg −	100 mg/kg +	500 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_1 adult males; Mean±S.D. (N)

Compound		Butyl benzyl phthalate			
Dose (mg/kg)		0[a]	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 [b] (22)	2.10 ± 0.07 (20)	2.08 ± 0.06 (23)	2.07 ± 0.09 (24)
		0.32 ± 0.03 [c] (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, $p<0.05$
**: significant difference from control, $p<0.01$

Table 58

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

Organ weight of F1 females on day 21 of lactation; Mean±S.D. (N)

Compound		Butyl benzyl phthalate			
Dose (mg/kg)		0[a]	20	100	500
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	(g)	1.92 ± 0.07 (16)[b]	1.93 ± 0.05 (15)	1.92 ± 0.06 (21)	1.95 ± 0.09 (17)
		0.54 ± 0.03[c]	0.53 ± 0.03	0.53 ± 0.03	0.54 ± 0.03
Heart	(g)	1.15 ± 0.07 (16)	1.19 ± 0.12 (15)	1.16 ± 0.10 (21)	1.15 ± 0.07 (17)
		0.32 ± 0.02	0.33 ± 0.02	0.32 ± 0.02	0.32 ± 0.02
Lung	(g)	1.14 ± 0.07 (16)	1.14 ± 0.10 (15)	1.14 ± 0.07 (21)	1.12 ± 0.10 (17)
		0.32 ± 0.02	0.31 ± 0.02	0.31 ± 0.02	0.31 ± 0.03
Liver	(g)	15.65 ± 1.03 (16)	15.70 ± 1.49 (15)	15.38 ± 1.40 (21)	15.75 ± 1.30 (17)
		4.34 ± 0.21	4.31 ± 0.30	4.21 ± 0.35	4.35 ± 0.26
Spleen	(g)	0.70 ± 0.09 (16)	0.67 ± 0.09 (15)	0.74 ± 0.13 (21)	0.71 ± 0.11 (17)
		0.19 ± 0.02	0.18 ± 0.02	0.20 ± 0.03	0.20 ± 0.03
Kidneys	(g)	2.35 ± 0.14 (16)	2.37 ± 0.21 (15)	2.49 ± 0.28 (21)	2.45 ± 0.15 (17)
		0.65 ± 0.04	0.65 ± 0.05	0.68 ± 0.07	0.68 ± 0.06
Adrenal glands	(mg)	71.5 ± 6.4 (16)	67.9 ± 8.2 (15)	71.2 ± 10.3 (21)	73.0 ± 11.0 (17)
		19.9 ± 2.0	18.7 ± 2.4	19.5 ± 2.4	20.2 ± 2.8
Thymus	(mg)	207.8 ± 61.5 (16)	218.7 ± 70.4 (15)	181.0 ± 43.6 (21)	233.8 ± 71.2 (17)
		57.4 ± 16.4	60.2 ± 19.2	49.4 ± 11.1	64.7 ± 20.3
Ovary	(mg)	96.7 ± 12.3 (16)	98.7 ± 19.0 (15)	105.2 ± 11.3 (21)	94.1 ± 13.1 (17)
		26.8 ± 3.1	27.1 ± 4.6	28.8 ± 2.5	26.1 ± 4.0
Uterus	(g)	0.43 ± 0.12 (16)	0.43 ± 0.19 (15)	0.44 ± 0.09 (21)	0.43 ± 0.07 (17)
		0.12 ± 0.03	0.12 ± 0.06	0.12 ± 0.02	0.12 ± 0.02
Thyroid glands	(mg)	18.8 ± 2.7 (16)	17.2 ± 3.2 (15)	18.5 ± 3.9 (21)	19.5 ± 2.9 (17)
		5.2 ± 0.9	4.7 ± 0.9	5.1 ± 1.2	5.4 ± 0.8
Pituitary gland	(mg)	14.2 ± 2.2 (16)	14.6 ± 2.6 (15)	14.2 ± 2.1 (21)	13.3 ± 1.6 (17)
		4.0 ± 0.7	4.0 ± 0.7	3.9 ± 0.5	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 −	±	+	++	+++	Pos.	20 mg/kg −	±	+	++	+++	Pos.	100 mg/kg −	±	+	++	+++	Pos.	500 mg/kg −	±	+	++	+++	Pos.
(Testis)	[10]						[10]						[10]						[10]					
Atrophy, seminiferous tubule, right side	10	0	0	0	0	0	10	0	0	0	0	0	10	0	0	0	0	0	4	1	1	0	4*	6##
Decrease, germ cell, seminiferous tubule, right side	10	0	0	0	0	0	10	0	0	0	0	0	10	0	0	0	0	0	6	0	0	0	4	4#
Edema, interstitium, right side	10	0	0	0	0	0	10	0	0	0	0	0	10	0	0	0	0	0	6	0	0	4	0	4#
Spermatic granuloma, rete testis, right side	10	0	0	0	0	0	10	0	0	0	0	0	10	0	0	0	0	0	9	0	1	0	0	1
Atrophy, seminiferous tubule, left side	10	0	0	0	0	0	10	0	0	0	0	0	10	0	0	0	0	0	7	2	1	0	0	3
Dilatation, seminiferous tubule, diffuse, left side	10	0	0	0	0	0	10	0	0	0	0	0	10	0	0	0	0	0	9	0	0	1	0	1
Decrease, germ cell, seminiferous tubule, left side	10	0	0	0	0	0	10	0	0	0	0	0	10	0	0	0	0	0	9	1	0	0	0	1
Defect, right side	10	0	0	0	0	0	10	0	0	0	0	0	10	0	0	0	0	0	9	0	0	0	1	1
Multinucleated giant cell, seminiferous tubule, left side	10	0	0	0	0	0	10	0	0	0	0	0	10	0	0	0	0	0	9	0	1	0	0	1
(Epididymis)	[10]						[10]						[10]						[10]					
Decrease, sperm, lumen, with cell debris, unilateral	10	0	0	0	0	0	10	0	0	0	0	0	10	0	0	0	0	0	5	0	0	0	5	5#
(Prostate: ventral lobe)	[10]						[0]						[0]						[10]					
Cellular infiltration, lymphocyte, interstitium	7	2	1	0	0	3													6	2	0	2	0	4
Cellular infiltration, lymphocyte /plasma cell, epithelium	8	1	1	0	0	2													8	0	2	0	0	2
(Seminal vesicle & coagulating gland)	[10]						[0]						[0]						[10]					
No remarkable change																			[10]					
(Liver)	[10]						[0]						[0]						10	0	0	0	0	0
Fatty change, periportal	8	0	2	0	0	2																		
(Kidney)	[10]						[0]						[0]						[10]					
Basophilic tubule, cortex	0	7	3	0	0	10													0	5	5	0	0	10
Eosinophilic body	7	1	1	1	0	3													9	1	0	0	0	1
Mineralization	6	4	0	0	0	4													7	3	0	0	0	3
Dilatation, renal pelvis	9	0	1	0	0	1													9	1	0	0	0	1
Fibrosis, focal, subcapsule	9	1	0	0	0	1													10	0	0	0	0	0
Cast, hyalin, cortex/medulla	8	2	0	0	0	2													6	3	1	0	0	4
Cellular infiltration, lymphocyte, interstitium	10	0	0	0	0	0													9	1	0	0	0	1
(Mammary gland)	[10]						[0]						[0]						[10]					
No remarkable change																			[10]					
(Thyroid gland)	[10]						[0]						[0]						10	0	0	0	0	0
Ectopic thymus	9	1	0	0	0	1																		
(Parathyroid gland)	[8]						[0]						[0]						[8]					
No remarkable change																								
(Pituitary gland)	[10]						[0]						[0]						[10]					
No remarkable change																								
(Adrenal gland)	[10]						[0]						[0]						[10]					
No remarkable change																								

−, 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 −	±	+	++	+++	Pos.	20 mg/kg −	±	+	++	+++	Pos.	100 mg/kg −	±	+	++	+++	Pos.	500 mg/kg −	±	+	++	+++	Pos.
(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	9	1	0	0	0	1													10	0	0	0	0	0
(Kidney)	[10]						[0]						[0]						[10]					
Basophilic tubule, cortex	6	4	0	0	0	4													5	5	0	0	0	5
Mineralization, papilla	8	1	1	0	0	2													10	0	0	0	0	0
Dilatation, renal pelvis, right side	9	0	1	0	0	1													10	0	0	0	0	0
Dilatation, collecting tubule, medulla & papilla	10	0	0	0	0	0													9	1	0	0	0	1
(Mammary gland)	[10]						[0]						[0]						[10]					
No remarkable change																								
(Thyroid gland)	[10]						[0]						[0]						[10]					
Ectopic thymus	10	0	0	0	0	0													9	1	0	0	0	1
(Parathyroid gland)	[9]						[0]						[0]						[8]					
No remarkable change																								
(Pituitary gland)	[10]						[0]						[0]						[10]					
No remarkable change																								
(Adrenal gland)	[10]						[0]						[0]						[10]					
No remarkable change																								
(Thymus)	[1]						[0]						[0]						[0]					
Atrophy	0	1	0	0	0	1																		

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

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Epididymal sperm findings in F_1 males at 18-19 weeks of age; Mean±S.D.

Compound	Butyl benzyl phthalate											
Dose (mg/kg)	0[a]			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[b]	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 ($x10^6$/g)

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Serum concentrations of testosterone, luteinizing hormone (LH), follicle-stimulating hormone (FSH), thyroid-stimulating hormone (TSH), triiodothyronine (T3), thyroxine (T4) in F_1 adult males; Mean±S.D. (N)

Compound	Butyl benzyl phthalate			
Dose (mg/kg)	0[a]	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, $p<0.05$
**: significant difference from control, $p<0.01$

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Serum concentrations of prolactin (PRL), luteinizing hormone (LH), follicle-stimulating hormone (FSH), thyroid-stimulating hormone (TSH), triiodothyronine (T3), thyroxine (T4), estradiol in F_1 adult females; Mean±S.D. (N)

Compound		Butyl benzyl phthalate			
Dose (mg/kg)		0[a]	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)

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Development F_2 offspring up to weaning; Mean±S.D. (N)

Compound	Butyl benzyl phthalate			
Dose (mg/kg)	0[a]	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 implantatios) 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)

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Body weight of F_2 offspring up to weaning; Mean±S.D. (Litter)

Compound	Butyl benzyl phthalate			
Dose (mg/kg)	0[a]	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)

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Morphological observations of F_2 live pups at birth

Compound	Butyl benzyl phthalate			
Dose (mg/kg)	0[a]	20	100	500
Number of live pups examined	210	204	249	198
External abnormalities				
Number of pups	0	0	0	2
Types and number				
Dwarf runt	0	0	0	1
Filamentous tail	0	0	0	1
Anal atresia	0	0	0	1

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Morphological observations of F_2 dead pups during lactation period

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

a: vehicle control, corn oil (2 mL/kg)
b: including missing pups