

I-Addendum 11 Histopathological examinations of offspring - individual findings

continued

Sex	Exp.group (mg/kg/day)	Animal No.	Fate	Histopathological findings <sup>a)</sup>
Female	BPA 40	623	ta	Ovary Decreased corpora lutea ++ Increased follicular atresia ++ Uterus Tall columnar surface epithelial cells + Vagina Mucification of epitheum ++
		624	ta	No abnormalities detected
		627	ta	Ovary Increased follicular atresia +
		628	ta	Ovary Decreased corpora lutea +++ Increased follicular atresia ++ Vagina Hyperplasia of epithelium + Mucification of epitheum ± Squamous epithelial cyst + Pituitary gland Hemorrhage +
		631	ta	Ovary Decreased corpora lutea ++ Increased follicular atresia ++ Uterus Tall columnar surface epithelial cells + Vagina Hyperplasia of epithelium +
		632	ta	Ovary Decreased corpora lutea +++ Increased follicular atresia ++ Uterus Tall columnar surface epithelial cells + Vagina Hyperplasia of epithelium +
		636	ta	Ovary Decreased corpora lutea +++ Increased follicular atresia ++ Uterus Squamous metaplasia of glandular epithelium + Tall columnar surface epithelial cells + Vagina Hyperplasia of epithelium +

a) Organs/tissues examined as follows: ovaries, uterus, vagina and pituitary gland.

ta, terminal autopsy.

±, very slight; +, slight; ++, moderate; +++, severe.

I-Addendum 11 Histopathological examinations of offspring - individual findings

continued

Sex	Exp.group (mg/kg/day)	Animal No.	Fate	Histopathological findings <sup>a)</sup>
Female	BPA 40	637	ta	Ovary Decreased corpora lutea +++ Increased follicular atresia ++ Uterus Tall columnar surface epithelial cells + Vagina Hyperplasia of epithelium +
		638	ta	Ovary Decreased corpora lutea +++ Increased follicular atresia ++ Uterus Squamous metaplasia of glandular epithelium + Tall columnar surface epithelial cells + Vagina Hyperplasia of epithelium + Polyp +
		639	ta	Ovary Decreased corpora lutea +++ Increased follicular atresia ++ Uterus Tall columnar surface epithelial cells + Vagina Hyperplasia of epithelium + Mucification of epithelium +
		643	ta	No abnormalities detected
		644	ta	Ovary Increased follicular atresia +
		648	ta	Ovary Decreased corpora lutea +++ Increased follicular atresia ++ Uterus Tall columnar surface epithelial cells + Vagina Hyperplasia of epithelium + Mucification of epithelium +
		649	ta	No abnormalities detected
		653	ta	Ovary Decreased corpora lutea +++ Increased follicular atresia ++ Vagina Hyperplasia of epithelium +

a) Organs/tissues examined as follows: ovaries, uterus, vagina and pituitary gland.

ta, terminal autopsy.

+, slight; ++, moderate; +++, severe.

**I-Addendum 11 Histopathological examinations of offspring - Individual findings**  
**continued**

<b>Sex</b>	<b>Exp.group (mg/kg/day)</b>	<b>Animal No.</b>	<b>Fate</b>	<b>Histopathological findings<sup>a)</sup></b>
<b>Female</b>	<b>BPA 40</b>	654	ta	Ovary Decreased corpora lutea +++ Increased follicular atresia ++ Vagina Mucification of epithelium ++
		658	ta	No abnormalities detected
		659	ta	No abnormalities detected
		663	ta	No abnormalities detected
		664	ta	No abnormalities detected
		666	ta	No abnormalities detected
		668	ta	No abnormalities detected
		669	ta	Uterus Tall columnar surface epithelial cells + Vagina Mucification of epithelium ++
		671	ta	No abnormalities detected

a) Organs/tissues examined as follows: ovaries, uterus, vagina and pituitary gland.

ta, terminal autopsy.

+, slight; ++, moderate; +++, severe.

I-Addendum 11 Histopathological examinations of offspring - individual findings

continued

Sex	Exp.group (mg/kg/day)	Animal No.	Fate	Histopathological findings <sup>a)</sup>
Female	BPA 400	673	ta	Ovary Increased follicular atresia + Vagina Mucification of epithelium +
		674	ta	Ovary Decreased corpora lutea +++ Increased follicular atresia ++ Uterus Tall columnar glandular epithelial cells + Tall columnar surface epithelial cells + Vagina Hyperplasia of epithelium +
		678	ta	No abnormalities detected
		679	ta	No abnormalities detected
		683	ta	Ovary Decreased corpora lutea +++ Increased follicular atresia ++ Uterus Squamous metaplasia of glandular epithelium ++ Tall columnar surface epithelial cells + Vagina Hyperplasia of epithelium + Mucification of epithelium ±
		684	ta	Ovary Decreased corpora lutea +++ Increased follicular atresia ++ Uterus Tall columnar surface epithelial cells + Vagina Hyperplasia of epithelium +
		688	ta	Ovary Decreased corpora lutea +++ Increased follicular atresia ++ Uterus Tall columnar surface epithelial cells + Vagina Hyperplasia of epithelium +
		689	ta	Ovary Decreased corpora lutea +++ Increased follicular atresia ++ Uterus Tall columnar surface epithelial cells + Vagina Hyperplasia of epithelium +

a) Organs/tissues examined as follows: ovaries, uterus, vagina and pituitary gland.

ta, terminal autopsy.

±, very slight; +, slight; ++, moderate; +++, severe.

I-Addendum 11 Histopathological examinations of offspring - individual findings  
continued

Sex	Exp.group (mg/kg/day)	Animal No.	Fate	Histopathological findings <sup>a)</sup>
Female	BPA 400	693	ia	Lung Nephroblastoma (metastasis) Kidney Nephroblastoma Vagina Vaginitis + Pituitary gland Rathke's pouch remnant +
		694	ta	No abnormalities detected
		698	ta	No abnormalities detected
		699	ta	Ovary Decreased corpora lutea +++ Increased follicular atresia ++ Uterus Squamous metaplasia of glandular epithelium + Tall columnar surface epithelial cells +
		703	ta	No abnormalities detected
		704	ta	Ovary Decreased corpora lutea +++ Increased follicular atresia ++ Uterus Tall columnar glandular epithelial cells + Tall columnar surface epithelial cells + Vagina Hyperplasia of epithelium +
		708	ta	No abnormalities detected
		709	ta	Ovary Decreased corpora lutea +++ Increased follicular atresia ++ Uterus Tall columnar surface epithelial cells + Vagina Hyperplasia of epithelium + Mucification of epithelium +
		713	ta	Ovary Decreased corpora lutea +++ Increased follicular atresia ++ Uterus Tall columnar glandular epithelial cells + Tall columnar surface epithelial cells ++ Vagina Hyperplasia of epithelium +
		714	ta	Ovary Hemorrhage +

a) Organs/tissues examined as follows: ovaries, uterus, vagina, pituitary gland and macroscopic lesions.

ta, terminal autopsy.

+, slight; ++, moderate; +++, severe.

I-Addendum 11 Histopathological examinations of offspring - individual findings

continued

Sex	Exp.group (mg/kg/day)	Animal No.	Fate	Histopathological findings <sup>a)</sup>
Female	EE 0.05	718	ta	Ovary Decreased corpora lutea +++ Increased follicular atresia ++ Uterus Squamous metaplasia of glandular epithelium + Vagina Hyperplasia of epithelium + Mucification of epithelium +
		719	ta	Ovary Decreased corpora lutea +++ Increased follicular atresia ++ Vagina Hyperplasia of epithelium +
		723	ta	Ovary Decreased corpora lutea +++ Increased follicular atresia ++ Vagina Hyperplasia of epithelium +
		724	ta	Ovary Decreased corpora lutea +++ Increased follicular atresia ++ Uterus Tall columnar surface epithelial cells + Vagina Hyperplasia of epithelium +
		728	ta	Ovary Decreased corpora lutea ++ Increased follicular atresia + Vagina Hyperplasia of epithelium + Mucification of epithelium ±
		729	ta	Vagina Mucification of epithelium +
		733	ta	No abnormalities detected
		734	ta	Vagina Mucification of epithelium ++
		738	ta	Vagina Mucification of epithelium ++
		739	ta	Vagina Mucification of epithelium ±

a) Organs/tissues examined as follows: ovaries, uterus, vagina and pituitary gland.

EE, Ethinyl estradiol 50 µg/kg/day.

ta, terminal autopsy.

±, very slight; +, slight; ++, moderate; +++, severe.

I-Addendum 11 Histopathological examinations of offspring - individual findings  
continued

Sex	Exp.group (mg/kg/day)	Animal No.	Fate	Histopathological findings <sup>a)</sup>
Female	EE 0.05	743	ta	Ovary Decreased corpora lutea +++ Increased follicular atresia ++ Uterus Tall columnar surface epithelial cells + Vagina Hyperplasia of epithelium + Mucification of epithelium ± Pituitary gland Diffuse hyperplasia in pars distalis +
		744	ta	Ovary Increased follicular atresia + Uterus Atrophy + Vagina Mucification of epithelium ++
		748	ta	Ovary Decreased corpora lutea +++ Increased follicular atresia ++ Uterus Tall columnar surface epithelial cells + Vagina Hyperplasia of epithelium + Mucification of epithelium +
		749	ta	Ovary Decreased corpora lutea +++ Increased follicular atresia ++ Vagina Hyperplasia of epithelium +
		753	ta	Ovary Decreased corpora lutea +++ Increased follicular atresia ++ Uterus Squamous metaplasia of glandular epithelium + Tall columnar surface epithelial cells + Vagina Hyperplasia of epithelium + Mucification of epithelium +
		754	ta	Ovary Decreased corpora lutea +++ Increased follicular atresia ++ Vagina Hyperplasia of epithelium +

a) Organs/tissues examined as follows: ovaries, uterus, vagina and pituitary gland.

EE, Ethinyl estradiol 50 µg/kg/day.

ta, terminal autopsy.

±, very slight; +, slight; ++, moderate; +++, severe.

I-Addendum 11 Histopathological examinations of offspring - individual findings  
continued

Sex	Exp.group (mg/kg/day)	Animal No.	Fate	Histopathological findings <sup>a)</sup>
Female	EE 0.05	758	ta	Vagina Mucification of epithelium +++
		759	ta	No abnormalities detected
		760	ta	No abnormalities detected
		761	ta	Vagina Mucification of epithelium +
		765	ta	Vagina Mucification of epithelium +
		766	ta	Ovary Decreased corpora lutea + Increased follicular atresia + Vagina Mucification of epithelium ++

a) Organs/tissues examined as follows: ovaries, uterus, vagina and pituitary gland.

EE, Ethinyl estradiol 50 µg/kg/day.

ta, terminal autopsy.

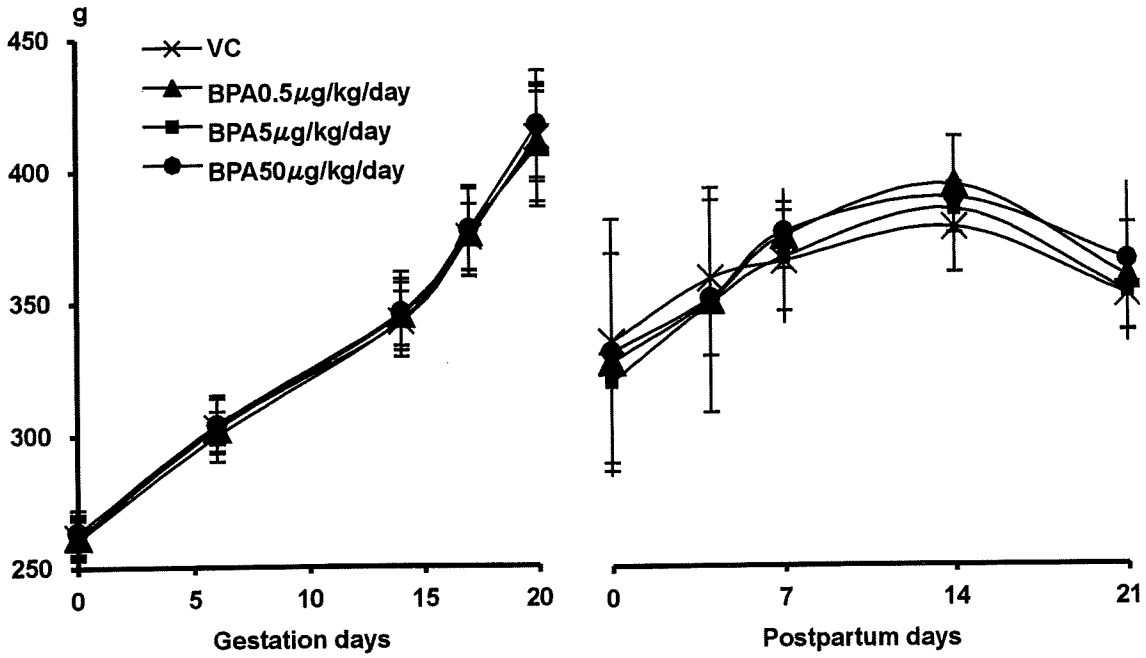
+, slight; ++, moderate; +++, severe.



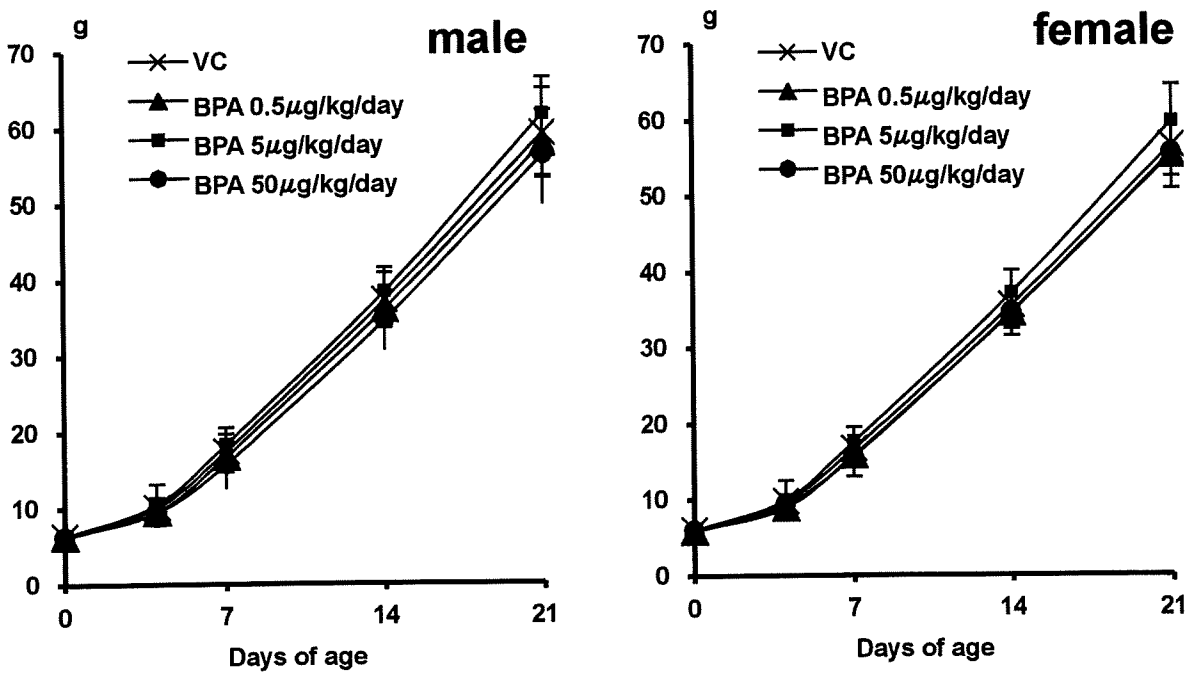
**I-Addendum 11 Histopathological examinations of offspring - individual findings  
continued**

<b>Sex</b>	<b>Exp.group (mg/kg/day)</b>	<b>Animal No.</b>	<b>Fate</b>	<b>Histopathological findings<sup>a)</sup></b>
<b>Male</b>	<b>BPA 0.005</b>	148	ia	Lung Nephroblastoma Kidney Nephroblastoma Adrenal Not available (Not in section)
	<b>BPA 400</b>	320	ia	White mass in the thoracic cavity with reddish hydrothorax Diagnosis: thymoma (possible)

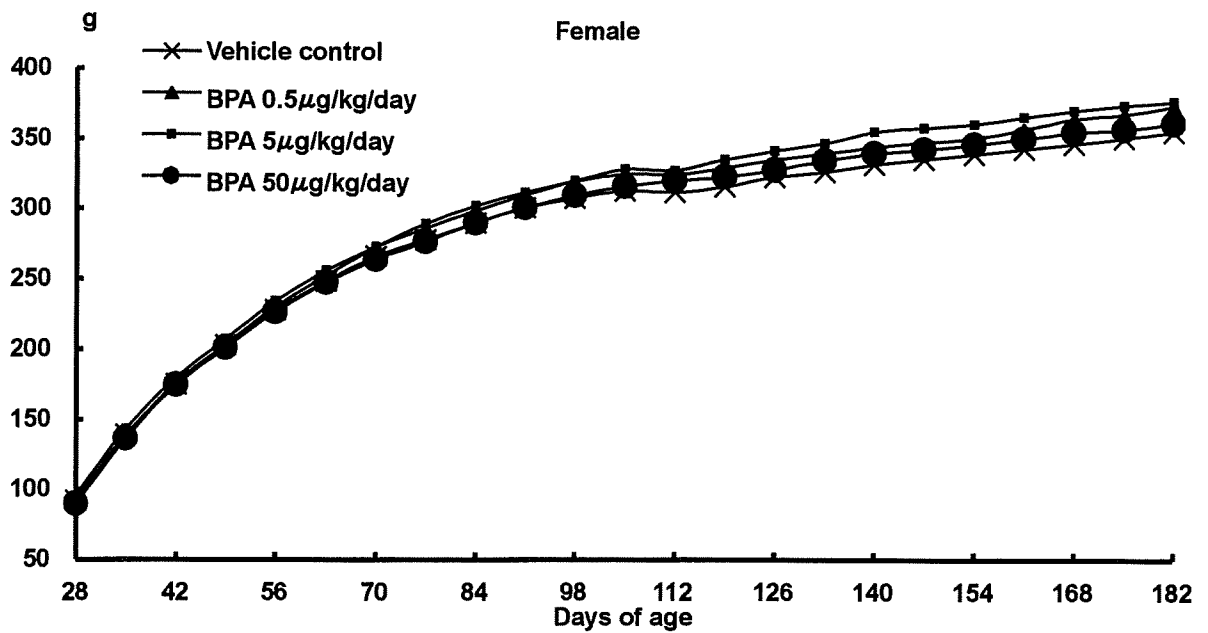
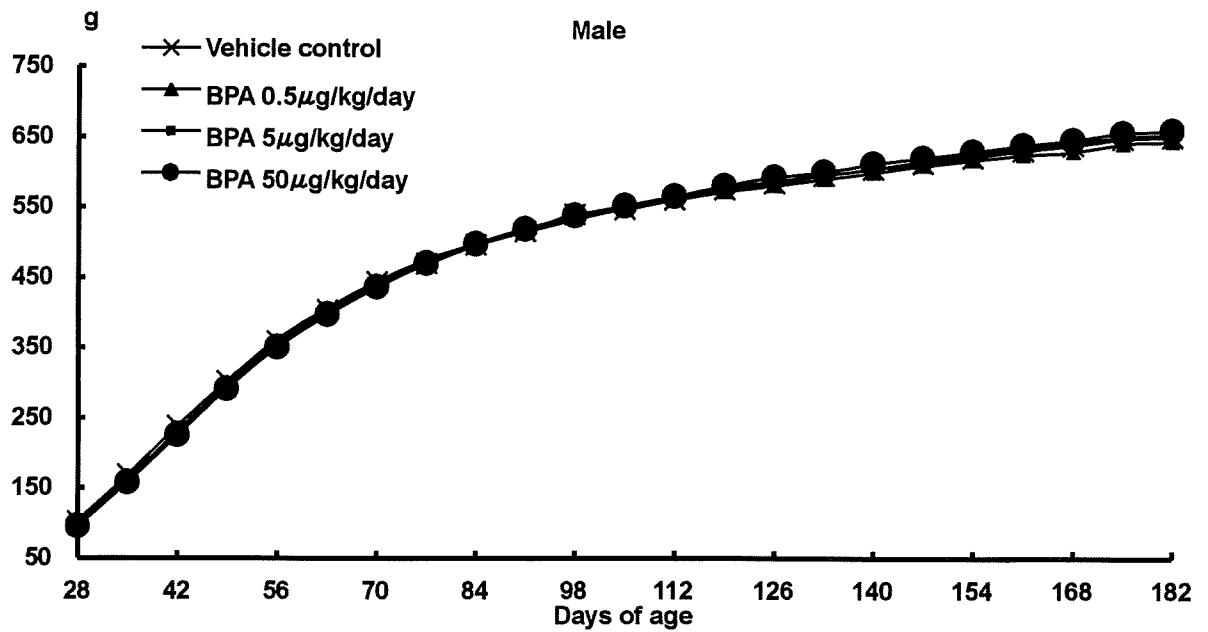
a) Organs/tissues examined as follows: macroscopic lesions.  
ia, interim autopsy.



II-Figure 1. Mean body weights of dams  
Not significant



II-Figure 2. Mean body weights of offspring - birth to weaning  
Not significant



II-Figure 3. Mean body weights of offspring - twenty eight to 182 days of age

II-Table 1-1. Body weights of dams - group mean values

Exp.group ( $\mu$ g/kg/day)	Gestational period (days)						Postpartum period (days)					
	0	6	14	17	20		0	4	7	14	21	
Vehicle control 0	Mean (g)	261.8	302.7	342.8	374.5	412.2		311.1	328.2	332.2	341.1	323.3
	S.D.	7.5	6.3	11.1	12.6	17		33	21.1	13.4	12.4	9.9
	n	10	10	10	10	10		10	10	10	10	10
BPA 0.5	Mean (g)	261.6	302.4	345.4	376.1	410.1		305.4	322.1	339.5	353.1	328.2
	S.D.	8.7	12.5	16	16.7	22.4		29.6	30.4	9	13.1	14.5
	n	10	10	10	10	10		8	7	6	6	6
BPA 5	Mean (g)	260.7	300.7	343.3	376.7	408.7		300.1	321.4	333.8	346.5	323.9
	S.D.	7.4	8.6	14	17	22.9		25.6	26.9	18.2	11	13.8
	n	10	10	10	10	10		10	9	8	7	7
BPA 50	Mean (g)	263.5	303.8	346.1	377.4	417.0		308.3	322.8	340.6	349.6	332.6
	S.D.	8.4	9.9	12.6	15.6	20.4		29.4	27.3	11.3	15.5	20.8
	n	10	10	10	10	10		10	10	9	9	9

II-Table 1-2. Body weights of offspring during postpartum period - group mean values

Vehicle control	Sex	Postpartum period (days)				
		0 (g)	4 (g)	7 (g)	14 (g)	21 (g)
	Mean	6.39	10.14	17.50	37.28	59.14
	S.D.	0.57	1.25	2.23	3.51	5.92
	Number of Dams	10	10	10	10	10
	Mean	6.06	9.79	16.71	35.50	56.48
	S.D.	0.48	1.29	2.27	3.03	5.75
	Number of Dams	10	10	10	10	10

Mean values represent means of litter means within each group

II-Table 1-2. Body weights of offspring during postpartum period - group mean values  
continued

		Postpartum period (days)				
		0	4	7	14	21
Sex	(g)	6.31	9.49	16.76	36.07	57.79
Male	Mean	6.31	9.49	16.76	36.07	57.79
	S.D.	0.31	1.21	1.97	2.41	4.34
	Number of Dams	8	6	6	6	6
Female	Mean	5.91	8.96	15.87	34.49	55.21
	S.D.	0.26	1.09	1.59	2.09	2.84
	Number of Dams	8	6	6	6	6

Mean values represent means of litter means within each group

II-Table 1-2. Body weights of offspring during postpartum period - group mean values  
continued

		Postpartum period (days)				
		0 (g)	4 (g)	7 (g)	14 (g)	21 (g)
Sex	Mean	6.40	10.45	18.41	38.36	61.67
	S.D.	0.59	2.69	2.13	3.1	4.78
	Number of Dams	10	8	7	7	7
Female	Mean	6.05	9.94	17.64	37.10	59.60
	S.D.	0.64	2.52	1.83	2.94	4.8
	Number of Dams	10	8	7	7	7

Mean values represent means of litter means within each group

III-Table 1-2. Body weights of offspring during postpartum period - group mean values  
continued

Sex	0 (g)	4 (g)	7 (g)	Postpartum period (days)		
				14 (g)	21 (g)	21 (g)
Male	Mean 6.27	9.53	15.73	34.63	56.25	
	S.D. 0.77	2.05	3.22	4.01	6.54	
	Number of Dams 10	9	9	9	9	
Female	Mean 5.99	9.44	15.70	34.62	55.49	
	S.D. 0.82	1.97	2.69	3.19	4.69	
	Number of Dams 10	9	9	9	9	

Mean values represent means of litter means within each group



ii-Table1-3. Body weights of offspring in post weaning development - group mean values

		days after birth																						
		28	35	42	49	56	63	70	77	84	91	98	105	112	119	126	133	140	147	154	161	168	175	182
Sex	Mean	101.9	168.6	237.7	301.8	358.2	402.8	443.5	469.9	496.1	515.6	539.1	546.5	560.1	574.5	584.3	594.5	603.7	611.8	620.8	630.3	637.8	646.7	649.9
	S.D.	10.6	16.4	21.1	27.3	30.8	36.1	45.7	42.0	44.5	46.6	47.4	50.6	54.6	56.0	56.6	57.9	59.4	60.7	61.5	62.7	62.9	64.3	63.8
	n	19	19	19	19	19	19	19	19	19	19	19	19	19	19	19	19	19	19	19	19	19	19	19
Female	Mean	92.1	138.8	174.7	202.7	227.8	248.2	266.0	277.7	289.9	300.5	307.6	312.7	311.7	315.8	322.7	326.3	331.6	335.5	338.9	342.7	346.1	350.3	355.0
	S.D.	7.9	9.7	12.1	14.6	16.1	17.4	19.3	21.2	22.8	24.3	25.4	25.1	23.4	24.9	25.8	26.0	26.1	27.1	29.4	28.2	29.4	30.9	32.9
	n	46	46	46	46	46	46	46	46	46	46	31	31	31	30	31	31	31	31	31	31	31	31	31

Unit: gram

II-Table1-3. Body weights of offspring in post weaning development - group mean values  
continued

Sex	BPA 0.5g/kg/day																						
	days after birth																						
	28	35	42	49	56	63	70	77	84	91	98	105	112	119	126	133	140	147	154	161	168	175	182
Mean	98.4	162.1	230.3	296.0	356.1	400.5	438.9	468.0	495.0	514.1	531.9	547.7	559.2	570.7	579.9	589.4	598.7	608.6	617.1	623.8	629.0	639.7	643.3
S.D.	6.6	11.2	18.0	22.6	27.7	32.6	35.3	36.9	39.9	42.9	44.3	47.8	49.4	53.2	55.5	57.0	58.9	61.1	62.8	65.2	66.7	67.7	68.6
n	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12	12
Mean	90.1	137.3	176.1	203.1	229.8	252.2	272.4	286.1	298.4	309.8	319.2	324.5	323.7	328.7	334.9	339.2	344.1	347.0	350.4	356.5	363.9	367.4	373.1
S.D.	5.2	8.7	12.7	15.9	18.2	23.9	25.7	27.5	27.4	31.5	30.5	28.8	27.7	25.5	26.7	24.7	24.8	26.5	26.9	26.3	26.5	29.6	29.6
n	34	34	34	34	34	34	34	34	34	23	23	23	23	23	23	23	23	23	23	23	23	23	23

Unit: gram

II-Table1-3. Body weights of offspring in post weaning development - group mean values  
continued

Sex	Animal-ID No.	days after birth																						
		28	35	42	49	56	63	70	77	84	91	98	105	112	119	126	133	140	147	154	161	168	175	182
Male	Mean	103.8	168.0	237.8	302.0	362.1	406.2	444.3	475.2	498.0	519.3	536.6	546.2	561.0	577.4	585.6	595.7	604.4	614.7	625.2	635.3	641.3	649.3	652.8
	S.D.	9.0	17.6	24.5	28.7	33.3	36.4	39.4	40.6	42.2	43.3	45.0	48.2	48.6	56.5	53.4	54.0	54.2	55.3	57.2	58.5	57.2	59.1	61.1
	n	14	14	14	14	14	14	14	14	14	14	14	14	14	12	14	14	14	14	14	14	14	14	14
Female	Mean	95.6	142.8	179.5	207.0	234.2	256.0	273.0	289.4	301.9	311.6	319.9	327.9	327.1	334.9	341.0	346.9	354.7	357.7	360.4	365.5	370.0	373.4	376.5
	S.D.	6.9	9.4	12.6	14.7	15.8	16.8	18.4	20.4	20.7	20.9	22.0	23.0	21.5	26.7	28.5	27.9	27.4	28.1	31.0	32.1	32.1	34.6	36.0
	n	35	35	35	35	35	35	35	35	35	35	35	35	35	22	22	22	22	22	22	22	22	22	22

Unit: gram

II-Table1-3. Body weights of offspring in post weaning development - group mean values  
continued

Sex	Animal-ID No.	days after birth																						
		28	35	42	49	56	63	70	77	84	91	98	105	112	119	126	133	140	147	154	161	168	175	182
male	Mean	95.2	157.7	225.5	291.1	350.0	396.9	436.4	469.8	497.0	517.8	537.0	551.0	564.7	579.1	592.2	599.3	611.5	619.3	628.9	637.9	645.2	655.4	668.7
	S.D.	13.6	19.7	22.2	25.7	27.0	28.3	31.3	34.3	35.9	39.3	42.1	44.8	48.5	50.8	51.8	54.1	56.7	57.8	58.2	60.3	61.5	62.5	61.6
	n	18	18	18	18	18	18	18	18	18	18	18	18	18	18	18	18	18	18	18	18	18	18	18
female	Mean	89.7	136.2	174.2	200.7	226.3	247.3	263.7	276.5	289.7	300.8	309.3	315.9	319.9	322.6	327.4	334.5	339.4	342.1	345.6	350.0	354.3	356.4	361.0
	S.D.	6.8	9.7	12.7	14.5	16.9	19.9	20.1	23.2	24.8	23.4	25.0	25.6	27.5	31.0	30.9	31.9	30.5	31.0	33.6	35.6	35.5	37.7	38.1
	n	46	46	46	46	46	46	44	46	46	30	30	30	30	30	30	30	30	30	30	30	30	30	30

Unit: gram