

Summary of results (Di-cyclohexyl phthalate)

Generation		Dam: F0 Offspring: F1						
Dose (µg/kg)		0	1.6	8	40	200	500 mg/kg	
Number of pregnant females		12	12	12	12	12	11	
F0	Clinical findings	Salivation	0/12	0/12	0/12	0/12	0/12	11/11
	Found dead		0/12	0/12	0/12	0/12	0/12	0/11
	Body weights	Gestation period	–	–	–	–	–	L
		Lactation period	–	–	–	–	–	–
	Food consumption	Gestation period	–	–	–	–	–	L
		Lactation period	–	–	–	–	–	L
	Delivery and maternal behavior	Delivery index (%)	100	100	100	100	100	100
		Gestation length (day)	22.08 ±0.29	22.00 ±0.00	22.25 ±0.45	22.17 ±0.39	22.17 ±0.39	22.73 ±0.47 H
		Number of Implantation sites	16.83 ±1.40	16.58 ±1.24	15.83 ±1.90	17.42 ±1.78	14.92 ±1.93 L	16.82 ±1.89
		Number of pups delivered	15.83 ±1.40	15.33 ±2.02	13.83 ±1.34	16.42 ±2.11	14.33 ±2.02	12.91 L ±3.08
	Gross findings	Liver Spot, light gray	0/12	1/12	0/12	0/12	0/12	0/11
		Kidney Dilatation, pelvic cavity	0/12	1/12	0/12	0/12	1/12	0/11
		Ureter Dilatation	0/12	1/12	0/12	0/12	1/12	0/11

H : Significantly higher than the control (p<0.01).

L or **L** : Significantly lower than the control (p<0.05 and p<0.01, respectively).

– : No treatment-related alterations.

Summary of results (continued-1)

Generation		Dam: F0					Offspring: F1	
Dose (µg/kg)		0	1.6	8	40	200	500 mg/kg	
Number of pregnant females		12	12	12	12	12	11	
F0	Final body weights (g)	321.3 ±11.9	317.2 ±10.7	317.8 ±14.8	309.2 ±13.8	315.6 ±11.2	310.9 ±16.7	
	Absolute organ weights	Brain (g)	1.92 ±0.08	1.92 ±0.05	1.95 ±0.05	1.95 ±0.03	1.93 ±0.03	1.89 ±0.05
		Pituitary (mg)	11.3 ±1.1	10.9 ±1.1	11.0 ±1.0	11.6 ±1.2	10.7 ±1.8	11.0 ±1.2
		Thyroid (mg)	15.4 ±2.7	17.3 ±3.7	17.2 ±3.2	17.3 ±2.6	15.4 ±2.6	17.5 ±1.9
		Thymus (g)	0.27 ±0.04	0.27 ±0.05	0.26 ±0.06	0.27 ±0.04	0.27 ±0.08	0.22 ±0.06
		Liver (g)	16.57 ±1.35	16.03 ±1.11	16.24 ±1.29	15.59 ±1.10	15.67 ±1.18	18.79 ±1.32 H
		Kidney (g)	2.30 ±0.18	2.28 ±0.21	2.23 ±0.12	2.24 ±0.19	2.27 ±0.18	2.26 ±0.08
		Adrenal (mg)	71.7 ±4.9	72.1 ±7.8	68.6 ±6.7	73.0 ±6.8	70.7 ±6.8	83.3 ±10.0 H
		Ovary (mg)	102.4 ±13.7	93.4 ±16.2	92.2 ±10.3	95.8 ±16.1	93.3 ±17.8	90.0 ±14.5
		Uterus (g)	0.49 ±0.16	0.43 ±0.10	0.47 ±0.12	0.49 ±0.08	0.48 ±0.11	0.42 ±0.05
	Relative organ weights	Brain (g/100 gB.W.)	0.60 ±0.03	0.61 ±0.02	0.61 ±0.03	0.63 ±0.02 H	0.61 ±0.02	0.61 ±0.03
		Pituitary (mg/100 gB.W.)	3.5 ±0.3	3.4 ±0.3	3.5 ±0.3	3.7 ±0.3	3.4 ±0.6	3.5 ±0.4
		Thyroid (mg/100 gB.W.)	4.8 ±0.8	5.5 ±1.1	5.4 ±1.0	5.6 ±0.7	4.9 ±0.8	5.6 ±0.6
		Thymus (g/100 gB.W.)	0.09 ±0.01	0.09 ±0.01	0.08 ±0.02	0.09 ±0.01	0.09 ±0.03	0.07 ±0.02
		Liver (g/100 gB.W.)	5.16 ±0.38	5.06 ±0.36	5.11 ±0.27	5.04 ±0.32	4.97 ±0.39	6.05 ±0.31 H
		Kidney (g/100 gB.W.)	0.72 ±0.06	0.72 ±0.06	0.70 ±0.04	0.73 ±0.05	0.72 ±0.06	0.73 ±0.04
		Adrenal (mg/100 gB.W.)	22.3 ±1.4	22.7 ±2.4	21.6 ±2.4	23.6 ±2.1	22.4 ±2.3	26.9 ±3.3 H
		Ovary (mg/100 gB.W.)	31.9 ±4.6	29.4 ±4.9	29.0 ±3.3	31.0 ±4.9	29.6 ±5.7	29.1 ±5.1
		Uterus (g/100 gB.W.)	0.15 ±0.05	0.13 ±0.03	0.15 ±0.04	0.16 ±0.03	0.15 ±0.03	0.14 ±0.02

H: Significantly higher than the control (p<0.01).

Summary of results (continued-2)

Generation		Dam: F0 Offspring: F1							
Dose (µg/kg)		0	1.6	8	40	200	500 mg/kg		
F0	*1	Liver	Necrosis, hepatocyte focal	0/12	0/12	0/12	1/12	0/11	0/11
			Necrosis, hepatocyte massive	0/12	1/12	0/12	0/12	0/11	0/11
			Hypertrophy, hepatocyte, centrilobular	0/12	0/12	0/12	0/12	0/11	5/11 H
		Kidney	Tubule, basophilic	0/12	0/12	0/12	0/12	0/11	1/11
			Cast, proteinaceous	0/12	0/12	0/12	0/12	0/11	1/11
			hydronephrosis	0/12	0/12	0/12	0/12	1/11	0/11
		Ureter	Dilatation, lumen	0/12	0/12	0/12	0/12	1/11	0/11
		Ovary	Cyst, follicular	0/12	0/12	1/12	0/12	0/11	0/11
		Uterus		–	–	–	–	–	–
		Cervix of uterus		–	–	–	–	–	–
		Vagina		–	–	–	–	–	–
		Pituitary	Cvst. anterior lobe	4/12	2/12	1/12	1/12	1/11	4/11
			Cvst. intermediate lobe	0/12	0/12	1/12	0/12	0/11	1/11
		Thyroid		–	–	–	–	–	–
		Parathyroid		–	–	–	–	–	–
		Adrenal		–	–	–	–	–	–

H : Significantly higher than the control (p<0.05).

– : No treatment-related alterations.

*1 : Histopathological findings

Summary of results (continued-3)

Generation		Dam: F0 Offspring: F1								
Dose (µg/kg)		0	1.6	8	40	200	500 mg/kg			
F1	Sex ratio (male/female)		0.95	1.23	1.01	0.80	0.91	1.36		
	Viability (%)									
			LD0	99.47	99.46	99.40	98.48	98.84	96.48	
			LD4	97.35	98.91	99.39	95.36	89.41	97.08	
			LD22	100	100	98.96	100	100	98.84	
	Body weights (g)	Male	LD0	6.1 ±0.3	6.1 ±0.2	6.3 ±0.3	5.9 ±0.4	6.2 ±0.5	5.8 ±0.3 L	
			LD4	9.1 ±0.8	9.4 ±0.9	10.1 ±1.0 H	9.2 ±1.0	9.3 ±1.1	8.9 ±0.9	
			LD7	14.5 ±1.4	14.8 ±2.2	16.0 ±1.3	14.6 ±1.7	14.9 ±2.1	14.0 ±1.7	
			LD14	30.9 ±1.9	31.2 ±3.7	32.6 ±2.0	31.4 ±1.9	31.6 ±2.5	28.0 ±1.3 L	
			LD21	50.9 ±2.8	50.7 ±5.3	52.8 ±3.7	51.3 ±3.3	51.0 ±3.9	46.9 ±3.1	
			After weaning	–	–	–	–	–	D	
			LD0	5.7 ±0.3	5.7 ±0.2	5.9 ±0.3	5.6 ±0.3	5.7 ±0.4	5.4 ±0.3	
		LD4	8.6 ±0.7	8.8 ±0.9	9.5 ±1.2	8.6 ±1.1	8.9 ±1.0	8.2 ±0.9		
		LD7	13.8 ±1.5	14.2 ±2.3	15.0 ±1.3	13.7 ±2.0	14.4 ±2.2	12.9 ±1.9		
		LD14	29.3 ±1.8	30.2 ±4.0	30.7 ±1.9	29.7 ±2.5	30.4 ±2.4	26.4 ±1.5 L		
		LD21	47.9 ±2.2	48.1 ±5.1	49.6 ±3.5	48.7 ±3.8	48.7 ±3.9	44.0 ±3.3		
		After weaning	–	–	–	–	–	D		
		Anogenital distances (mm)	Male	LD0	3.14 ±0.20	3.24 ±0.18	3.22 ±0.23	3.30 ±0.21	3.48 ±0.24 H	2.94 ±0.24
				LD4	4.60 ±0.29	4.72 ±0.26	4.83 ±0.18	4.90 ±0.40 H	5.13 ±0.25 H	4.48 ±0.29
	Female		LD0	1.49 ±0.08	1.57 ±0.21	1.49 ±0.13	1.58 ±0.14	1.63 ±0.13	1.66 ±0.13 H	
LD4			2.27 ±0.16	2.35 ±0.13	2.33 ±0.15	2.42 ±0.20	2.54 ±0.14 H	2.43 ±0.18		

H or **H** Significantly higher than the control (p<0.05 and p<0.01, respectively).

L or **L**; Significantly lower than the control (p<0.05 and p<0.01, respectively).

D : Decreasing tendency.

– : No treatment-related alterations.

Summary of results (continued-4)

Generation				Dam: F0 Offspring: F1					
Dose (µg/kg)				0	1.6	8	40	200	500 mg/kg
F1	Nipple appearance(%)	Male	LD12	0	0	0	0	0	0
		Female	LD12	100	100	100	100	100	100
	Sexual development (day)	Male	Preputial separation	42.04 ±1.94	41.88 ±2.44	41.92 ±1.72	41.38 ±1.93	42.14 ±2.10	41.55 ±1.79
		Female	Vaginal opening	31.00 ±1.64	31.25 ±2.05	30.58 ±1.41	30.96 ±1.76	30.91 ±1.44	30.33 ±1.39
	Fertility	Count of estrus		3.58 ±0.51	3.75 ±0.45	3.75 ±0.45	3.75 ±0.45	3.73 ±0.47	3.73 ±0.65
		Estrous cycle (day)		4.00 ±0.00	4.00 ±0.00	4.00 ±0.00	4.00 ±0.00	4.00 ±0.00	3.97 ±0.10
		Copulation index (%)	Male	100	100	100	100	90.91	72.73D
			Female	100	100	100	100	90.91	72.73D
		Fertility index (%)		91.67	91.67	91.67	100	100	62.50D
		Number of corpora lutea		16.27 ±1.62	16.82 ±1.25	15.27 ±2.80	15.42 ±1.82	16.00 ±1.56	16.80 ±2.17
		Number of implantations		15.55 ±1.81	16.09 ±1.45	16.00 ±1.90	16.25 ±1.82	15.40 ±2.12	16.60 ±1.95
		Dead embryo index (%)		5.85	12.43 H	8.33	2.16	10.39	9.64
		Number of live embryo		14.64 ±1.91	14.09 ±1.58	14.00 ±3.29	15.08 ±2.23	13.80 ±2.39	15.00 ±2.00
		Number of epidermal sperm (x10 ⁶ /cauda)		625.6 ±98.5	681.1 ±79.2	712.5 ±59.0	670.1 ±65.2	692.3 ±96.9	309.5D ±367.0
Sperm motility (%)		97.78	98.66	97.83	98.15	97.57	54.60D		
Abnormal sperm index (%)		1.81	2.11	2.28	2.22	2.18	2.00		

H : Significantly higher than the control (p<0.05).

D : Decreasing tendency.

Summary of results (continued-5)

Generation				Dam: F0 Offspring: F1								
Dose (µg/kg)				0	1.6	8	40	200	500 mg/kg			
F1	*1	Male	Kidney	Defect	0/25	0/26	0/23	0/22	0/21	2/24		
				Dilatation, pelvic cavity	0/25	0/26	0/23	0/22	0/21	1/24		
			Ureter	Dilatation	0/25	0/26	0/23	0/22	0/21	1/24		
			Testis	Small	0/25	0/26	0/23	0/22	1/21	0/24		
			Epididymis	Small	0/25	0/26	0/23	0/22	0/21	15/24		
		Female	Kidney	Dilatation, pelvic cavity	0/23	1/22	0/24	1/26	0/23	1/18		
				Ureter	Dilatation	0/23	1/22	0/24	0/26	0/23	1/18	
			Uterus	Small	0/23	0/22	0/24	0/26	0/23	1/18		
			*2	Male	Kidney	Defect	0/12	0/12	0/12	0/12	0/11	1/11
						Ureter	Dilatation	0/12	0/12	0/12	0/12	0/11
	Testis	Small			0/12	0/12	0/12	0/12	0/11	8/11		
	Epididymis	Small			0/12	0/12	0/12	0/12	0/11	8/11		
	Seminal vesicle	Small			0/12	0/12	0/12	0/12	0/11	1/11		
		Defect		0/12	0/12	0/12	0/12	0/11	1/11			
	Female	Kidney		Defect	0/12	0/12	0/12	0/12	0/11	1/10		
				Ureter	Dilatation	0/12	0/12	0/12	0/12	0/11	1/10	
		Ovary		Defect	0/12	0/12	0/12	0/12	0/11	1/10		
		Oviduct		Defect	0/12	0/12	0/12	0/12	0/11	1/10		
		Uterus	Defect, uterine bone	0/12	0/12	0/12	0/12	0/11	1/10			
	*3	Male	Kidney	Defect	0/12	0/12	0/12	0/12	0/12	1/11		
				Enlargement	0/12	0/12	0/12	0/12	0/12	1/11		
				Dilatation, pelvic cavity	0/12	1/12	0/12	0/12	0/12	0/11		
			Ureter	Dilatation	0/12	1/12	0/12	0/12	0/12	0/11		
			Testis	Small	0/12	0/12	0/12	0/12	0/12	8/11		
Epididymis			Small	0/12	0/12	0/12	0/12	0/12	8/11			
			Defect	0/12	0/12	0/12	0/12	0/12	2/11			
Seminal vesicle		Defect	0/12	0/12	0/12	0/12	0/12	1/11				
Female		All organs and tissues	-	-	-	-	-	-				

-: No treatment-related alterations.

*1 :Gross findings (Day 22)

*2 :Gross findings (Day 70)

*3 :Gross findings (after the mating period)

Summary of results (continued-6)

Generation			Dam: F0					Offspring: F1		
Dose ($\mu\text{g}/\text{kg}$)			0	1.6	8	40	200	500 mg/kg		
F1	Final body weights(g)	Male	56.5 ± 4.2	56.6 ± 6.0	58.1 ± 4.8	56.6 ± 4.2	56.0 ± 5.9	51.9 ± 3.8 L		
	Day 22	Female	53.2 ± 4.2	52.7 ± 5.6	53.4 ± 4.7	52.6 ± 4.5	53.5 ± 4.7	48.5 ± 5.1 L		
	*1	Male	Brain (g)	1.50 ± 0.05	1.50 ± 0.06	1.53 ± 0.05	1.51 ± 0.05	1.50 ± 0.05	1.46 ± 0.04 L	
			Epididymis (mg)	39.4 ± 5.3	38.5 ± 4.4	38.1 ± 4.2	38.9 ± 3.8	36.8 ± 5.5	26.8 ± 9.1 L	
			Testis (mg)	224.9 ± 21.9	223.5 ± 37.1	231.6 ± 24.4	224.1 ± 14.8	213.3 ± 45.5	206.1 ± 23.2 L	
		Female	Brain (g)	1.45 ± 0.04	1.45 ± 0.07	1.46 ± 0.05	1.45 ± 0.05	1.44 ± 0.05	1.40 ± 0.05 L	
			Ovary (mg)	10.2 ± 2.8	10.5 ± 2.8	10.6 ± 2.3	10.5 ± 3.0	10.3 ± 3.1	9.5 ± 2.9	
			Uterus (mg)	44.5 ± 7.7	46.1 ± 15.4	47.3 ± 10.6	47.3 ± 10.8	44.8 ± 10.7	44.6 ± 10.1	
	*2	Male	Brain (g/100 gBW)	2.66 ± 0.15	2.67 ± 0.25	2.65 ± 0.17	2.68 ± 0.15	2.69 ± 0.23	2.82 ± 0.17 H	
			Epididymis (mg/100 gBW)	69.6 ± 7.3	68.4 ± 7.3	65.7 ± 5.7	68.9 ± 6.4	65.6 ± 7.4	51.6 ± 16.8 L	
			Testis (mg/100 gBW)	397.5 ± 21.3	393.6 ± 40.6	399.0 ± 31.1	396.9 ± 23.5	377.5 ± 62.5	397.0 ± 34.2	
		Female	Brain (g/100 gBW)	2.73 ± 0.22	2.77 ± 0.26	2.75 ± 0.19	2.77 ± 0.18	2.72 ± 0.22	2.90 ± 0.23	
			Ovary (mg/100 gBW)	19.1 ± 4.8	19.9 ± 4.9	19.7 ± 3.4	19.8 ± 4.7	19.1 ± 4.7	19.4 ± 4.9	
			Uterus (mg/100 gBW)	83.7 ± 13.2	87.2 ± 25.6	88.1 ± 16.0	89.5 ± 16.4	83.4 ± 15.8	91.4 ± 15.6	

H : Significantly higher than from the control ($p < 0.05$).

L or **L** : Significantly lower than the control ($p < 0.05$ and $p < 0.01$, respectively).

*1: Absolute organ weights (Day 22)

*2: Relative organ weights (Day 22)

Summary of results (continued-7)

Generation			Dam: F0					Offspring: F1		
Dose ($\mu\text{g}/\text{kg}$)			0	1.6	8	40	200	500 mg/kg		
F1	Final body weights(g) Day 70	Male	391.4 ± 18.4	401.7 ± 15.3	395.8 ± 28.1	396.2 ± 29.9	398.2 ± 31.0	369.9 ± 22.2		
		Female	252.1 ± 20.0	245.6 ± 20.2	256.5 ± 18.8	266.9 ± 17.4	260.6 ± 19.3	244.6 ± 17.1		
*1	Male	Brain (g)	2.04 ± 0.06	2.03 ± 0.05	2.05 ± 0.09	2.05 ± 0.08	2.04 ± 0.04	1.95 ± 0.08 L		
		Pituitary (mg)	11.6 ± 0.6	10.1 ± 1.2 L	10.9 ± 0.7	10.7 ± 0.7 L	11.0 ± 1.5	10.0 ± 0.5 L		
		Thyroid (mg)	16.4 ± 3.0	17.7 ± 3.1	17.8 ± 3.9	16.4 ± 3.8	16.4 ± 2.5	15.4 ± 2.5		
		Liver (g)	17.52 ± 2.30	17.62 ± 1.48	17.59 ± 1.82	17.37 ± 2.15	17.57 ± 2.37	16.49 ± 1.33		
		Kidney (g)	3.27 ± 0.28	3.26 ± 0.27	3.25 ± 0.17	3.22 ± 0.35	3.26 ± 0.37	2.77 ± 0.31 L		
		Adrenal (mg)	55.1 ± 3.9	58.2 ± 5.6	55.1 ± 5.1	54.2 ± 4.8	56.4 ± 6.0	55.2 ± 6.2		
		Seminal vesicle (g)	1.73 ± 0.32	1.67 ± 0.25	1.64 ± 0.30	1.66 ± 0.24	1.57 ± 0.40	1.30 ± 0.27 L		
		Prostate (g)	0.77 ± 0.10	0.70 ± 0.13	0.77 ± 0.12	0.78 ± 0.06	0.82 ± 0.13	0.59 ± 0.09 L		
		Epididymis (g)	0.82 ± 0.04	0.79 ± 0.07	0.86 ± 0.05	0.78 ± 0.05	0.89 ± 0.31	0.58 ± 0.54 L		
		Testis (g)	2.76 ± 0.15	2.71 ± 0.11	2.81 ± 0.10	2.64 ± 0.14	2.73 ± 0.12	1.88 ± 0.53 L		
		Levator ani muscle (g)	0.87 ± 0.09	0.83 ± 0.07	0.93 ± 0.10	0.87 ± 0.07	0.84 ± 0.09	0.70 ± 0.08 L		
		Female	Brain (g)	1.85 ± 0.08	1.87 ± 0.08	1.89 ± 0.06	1.90 ± 0.06	1.91 ± 0.05	1.79 ± 0.07	
			Pituitary (mg)	9.3 ± 0.8	9.0 ± 0.9	9.5 ± 1.3	9.7 ± 1.1	9.5 ± 0.8	8.8 ± 1.7	
			Thyroid (mg)	13.4 ± 3.1	13.1 ± 2.0	13.1 ± 2.6	14.8 ± 3.6	13.7 ± 3.0	13.7 ± 3.9	
Liver (g)	11.84 ± 1.18		11.84 ± 0.86	12.72 ± 1.28	13.23 ± 1.24 H	12.68 ± 1.43	12.39 ± 1.29			
Kidney (g)	1.81 ± 0.17		1.84 ± 0.12	1.90 ± 0.18	1.96 ± 0.15	1.91 ± 0.13	1.68 ± 0.18			
Adrenal (mg)	70.5 ± 6.1		71.1 ± 5.5	73.4 ± 7.7	74.2 ± 9.2	72.8 ± 7.6	75.7 ± 11.0			
Ovary (mg)	112.0 ± 14.4		106.6 ± 10.0	105.6 ± 15.1	108.1 ± 11.8	115.1 ± 13.5	100.6 ± 20.6			
Uterus (mg)	0.74 ± 0.09	0.72 ± 0.09	0.74 ± 0.11	0.74 ± 0.07	0.73 ± 0.06	0.76 ± 0.18				

L: Significantly lower than the control ($p < 0.01$).

L: Significantly lower than the control ($p < 0.05$).

*1: Absolute organ weights (Day 70)

Summary of results (continued-8)

Generation		Dam: F0 Offspring: F1							
Dose (µg/kg)		0	1.6	8	40	200	500 mg/kg		
F1	*1	Male	Brain (g/100 gB.W.)	0.52 ±0.02	0.51 ±0.02	0.52 ±0.03	0.52 ±0.03	0.52 ±0.04	0.53 ±0.04
			Pituitary (mg/100 gB.W.)	2.9 ±0.2	2.5 ±0.3 L	2.8 ±0.2	2.7 ±0.2	2.8 ±0.3	2.7 ±0.2
			Thyroid (mg/100 gB.W.)	4.2 ±0.7	4.4 ±0.7	4.5 ±1.0	4.1 ±1.0	4.1 ±0.5	4.2 ±0.7
			Liver (g/100 gB.W.)	4.47 ±0.44	4.38 ±0.28	4.44 ±0.25	4.38 ±0.32	4.40 ±0.31	4.46 ±0.26
			Kidney (g/100 gB.W.)	0.84 ±0.04	0.81 ±0.05	0.82 ±0.05	0.81 ±0.04	0.82 ±0.06	0.75 ±0.06 L
			Adrenal (mg/100 gB.W.)	14.1 ±1.1	14.5 ±1.9	14.0 ±1.2	13.7 ±1.3	14.2 ±1.2	15.0 ±1.6
			Seminal vesicle (g/100 gB.W.)	0.44 ±0.08	0.41 ±0.06	0.42 ±0.07	0.42 ±0.06	0.40 ±0.11	0.35 ±0.07 L
			Prostate (g/100 gB.W.)	0.20 ±0.03	0.17 ±0.03	0.20 ±0.03	0.20 ±0.02	0.21 ±0.03	0.16 ±0.02 L
			Epididymis (g/100 gB.W.)	0.21 ±0.01	0.20 ±0.02	0.22 ±0.02	0.20 ±0.02	0.22 ±0.07	0.16 ±0.15 L
			Testis (g/100 gB.W.)	0.71 ±0.04	0.68 ±0.03	0.71 ±0.05	0.67 ±0.05	0.69 ±0.05	0.51 ±0.14 L
			Levator ani muscle (g/100 gB.W.)	0.22 ±0.02	0.21 ±0.01	0.24 ±0.03	0.22 ±0.03	0.21 ±0.03	0.19 ±0.02 L
			Female	Brain (g/100 gB.W.)	0.74 ±0.05	0.76 ±0.06	0.74 ±0.05	0.72 ±0.06	0.74 ±0.04
	Pituitary (mg/100 gB.W.)	3.7 ±0.2		3.7 ±0.3	3.7 ±0.4	3.7 ±0.3	3.7 ±0.3	3.6 ±0.6	
	Thyroid (mg/100 gB.W.)	5.3 ±1.3		5.3 ±0.7	5.1 ±1.0	5.6 ±1.5	5.3 ±1.1	5.6 ±1.5	
	Liver (g/100 gB.W.)	4.70 ±0.25		4.83 ±0.29	4.96 ±0.33	4.95 ±0.28	4.86 ±0.30	5.06 ±0.31 H	
	Kidney (g/100 gB.W.)	0.72 ±0.03		0.75 ±0.04	0.74 ±0.03	0.74 ±0.04	0.74 ±0.05	0.69 ±0.06	
	Adrenal (mg/100 gB.W.)	28.1 ±2.6		29.0 ±1.8	28.6 ±2.7	27.8 ±3.0	28.0 ±2.6	30.9 ±3.6	
	Ovary (mg/100 gB.W.)	44.6 ±5.5		43.6 ±4.6	41.1 ±4.4	40.5 ±2.9 L	44.2 ±4.0	41.2 ±8.1	
	Uterus (mg/100 gB.W.)	0.30 ±0.05		0.29 ±0.04	0.29 ±0.04	0.28 ±0.03	0.28 ±0.01	0.31 ±0.07	

H : Significantly higher than the control (p<0.05).

L or L : Significantly lower than the control (p<0.05 and p<0.01, respectively).

*1 :Relative organ weights (day 70)

Summary of results (continued-9)

Generation				Dam: F0 Offspring: F1						
Dose (µg/kg)				0	1.6	8	40	200	500 mg/kg	
F1	*1	Male	Liver	Necrosis, hepatocyte, focal	1/12	0/12	0/12	0/12	0/11	0/11
			Kidney	Hydronephrosis	0/12	0/12	0/12	0/12	0/11	2/11
			Ureter	Dilatation	1/12	0/12	0/12	0/12	0/11	1/11
			Testis	Hypoplasia	0/12	0/12	0/12	0/12	1/12	0/11
			Epididymis	Hypoplasia/Agenesis	0/12	0/12	0/12	0/12	0/11	12/19 H
			Prostate		–	–	–	–	–	–
			Coagulating gland		–	–	–	–	–	–
			Seminal vesicle		–	–	–	–	–	–
			Pituitary	Cyst, anterior lobe	0/12	0/11	0/12	1/12	0/11	0/11
			Thyroid		–	–	–	–	–	–
		Adrenal		–	–	–	–	–	–	
		Brain		–	–	–	–	–	–	
		Female	Liver		–	–	–	–	–	–
			Kidney	Hydronephrosis	0/12	1/12	0/12	1/13	0/11	1/10
			Ovary		–	–	–	–	–	–
			Oviduct		–	–	–	–	–	–
			Uterus	Hypoplasia / Atresia of uterine horn	0/12	0/11	0/12	0/12	0/11	1/10
			Cervix of uterus		–	–	–	–	–	–
			Vagina		–	–	–	–	–	–
			Pituitary	Cyst, anterior lobe	0/12	0/11	0/13	1/12	0/11	0/10
Thyroid			–	–	–	–	–	–		
Adrenal			–	–	–	–	–	–		
Brain		–	–	–	–	–	–			

H: Significantly higher than the control (p<0.01).

– : No treatment-related alterations.

*1 : Histopathological findings (Day 22)

Summary of results (continued-10)

Generation				Dam: F0		Offspring: F1				
Dose (µg/kg)				0	1.6	8	40	200	500 mg/kg	
F1	*1	Male	Liver	Normic hepatocyte focal	1/12	0/12	1/12	0/12	1/11	0/11
				Kidney	Tubule basophilic	3/12	2/12	3/12	2/12	3/11
			Testis	Mineralization, papilla	0/12	0/12	0/12	0/12	0/11	1/11
				Disappearance germ cell seminiferous tubule	0/12	0/12	0/12	0/12	0/11	8/11 H
				Hypertrophy Leydig cell	0/12	0/12	0/12	0/12	0/11	8/11 H
			Epididymis	Formation giant cell, seminiferous tubule	0/12	0/12	0/12	0/12	0/11	8/11 H
				Disappearance, sperm, lumen	0/12	0/12	0/12	0/12	0/11	8/11 H
				Cell debris, lumen	0/12	0/12	0/12	0/12	0/11	4/11 H
				Hemorrhage/A necrosis	0/12	0/12	0/12	0/12	0/11	2/11
				Dilatation, lumen	0/12	0/12	0/12	0/12	0/11	1/11
				Prostate	Cellular infiltration lymphocyte	0/12	0/12	0/12	0/12	1/11
			Coagulating gland		-	-	-	-	-	-
		Seminal vesicle		-	-	-	-	-	-	
		Pituitary	Cyst anterior lobe	1/12	1/12	2/12	1/12	1/11	2/11	
			Cyst intermediate lobe	0/12	0/12	1/12	0/12	0/11	0/11	
		Thyroid		-	-	-	-	-	-	
		Adrenal		-	-	-	-	-	-	
		Female	Liver		-	-	-	-	-	-
				Kidney	Tubule basophilic	1/12	0/12	0/12	2/12	0/11
			Mineralization, papilla		0/12	0/12	0/12	1/12	0/11	4/11 H
			Ovary		-	-	-	-	-	-
			Oviduct		-	-	-	-	-	-
			Uterus		-	-	-	-	-	-
			Cervix of uterus	Cyst squamous epithelial	0/12	0/12	1/12	0/12	0/11	0/9
Vagina			-	-	-	-	-	-		
Pituitary	Cyst anterior lobe		2/12	0/12	0/12	4/12	0/11	1/10		
Thyroid			-	-	-	-	-	-		
Adrenal			-	-	-	-	-	-		

H or **H**: Significantly higher than the control (p<0.05 and p<0.01, respectively).

-: No treatment-related alterations.

*1: Histopathological findings (Day 70)

Summary of results (continued-11)

Generation		Dam: F0 Offspring: F1								
Dose (µg/kg)		0	1.6	8	40	200	500 mg/kg			
F1	*1	Day 22	Male	Testosterone (ng/mL)	n=13 0.07 ±0.06	n=13 0.05 ±0.05	n=12 0.03 ±0.06	n=12 0.03 ±0.04	n=11 0.01 ±0.02 L	n=14 0.01 ±0.03 L
				LH (ng/mL)	n=12 1.50 ±0.36	n=13 1.66 ±0.35	n=11 1.61 ±0.40	n=10 1.64 ±0.42	n=10 1.68 ±0.47	n=10 1.69 ±0.40
				FSH (ng/mL)	n=12 12.40 ±3.49	n=13 12.44 ±2.16	n=11 12.08 ±2.19	n=10 11.64 ±2.25	n=10 13.62 ±2.98	n=10 12.47 ±1.64
		Female	Estradiol-17 ^β (pg/mL)	n=12 16.9 ±10.7	n=11 21.6 ±8.1	n=11 19.1 ±13.9	n=14 19.9 ±15.5	n=12 15.3 ±11.5	n=11 17.5 ±8.3	
			LH (ng/mL)	n=11 1.74 ±1.08	n=11 1.63 ±0.41	n=12 1.63 ±0.38	n=12 1.36 ±0.39	n=11 1.51 ±0.37	n=7 1.37 ±0.35	
			FSH (ng/mL)	n=11 22.12 ±10.98	n=11 20.31 ±9.29	n=12 24.83 ±11.56	n=12 17.97 ±6.66	n=11 22.63 ±10.21	n=7 18.11 ±8.18	
	Day 70	Male	Testosterone (ng/mL)	n=12 4.69 ±1.41	n=12 4.54 ±1.42	n=12 4.98 ±1.36	n=12 4.65 ±2.22	n=11 4.43 ±1.31	n=11 4.07 ±2.00	
			LH (ng/mL)	n=12 1.83 ±0.41	n=12 1.95 ±0.51	n=12 1.82 ±0.30	n=12 1.81 ±0.30	n=11 1.79 ±0.17	n=11 2.11 ±0.53	
			FSH (ng/mL)	n=12 14.73 ±1.67	n=12 14.66 ±1.25	n=12 13.47 ±1.85	n=12 14.27 ±1.03	n=11 14.59 ±0.98	n=11 15.50 ±2.93	
		Female	Estradiol (pg/mL)	n=12 46.3 ±13.5	n=12 45.9 ±16.1	n=12 49.4 ±19.4	n=12 36.8 ±11.5	n=11 43.3 ±13.1	n=10 44.9 ±15.3	
			LH (ng/mL)	n=12 1.64 ±1.61	n=12 1.25 ±0.50	n=12 1.40 ±0.59	n=12 1.55 ±0.18	n=11 1.31 ±0.58	n=10 1.30 ±0.26	
			FSH (ng/mL)	n=12 5.82 ±0.91	n=12 5.80 ±0.72	n=12 6.04 ±0.92	n=12 6.08 ±0.77	n=11 6.24 ±0.67	n=10 6.50 ±0.60	

L : Significantly lower than the control (p<0.05).

*1: Hormone concentrations

Summary of results (continued-12)

Generation				Dam: F0 Offspring: F1						
Dose ($\mu\text{g/kg}$)				0	1.6	8	40	200	500 mg/kg	
F1	*1	Day 70	Prostate	ER^a ($\times 10^{-3}$)	n=12 3.65 ± 1.07	n=12 2.73 ± 0.91	n=12 2.85 ± 1.73	n=12 3.58 ± 1.28	n=11 2.41 ± 0.79	n=11 3.12 ± 0.92
				ER^b ($\times 10^{-3}$)	n=12 236.84 ± 3.69	n=12 253.25 ± 5.13	n=12 207.88 ± 3.67	n=12 208.28 ± 3.86	n=11 231.84 ± 2.88	n=11 271.42 ± 5.38
				AR ($\times 10^{-3}$)	n=12 188.15 ± 21.83	n=12 205.14 ± 21.18	n=12 176.28 ± 19.04	n=12 188.78 ± 35.71	n=11 198.67 ± 32.61	n=11 269.05 ± 40.25 H
				IGF-1 ($\times 10^{-3}$)	n=12 31.10 ± 7.28	n=12 40.60 ± 7.44	n=12 42.76 ± 14.24	n=12 34.76 ± 6.48	n=11 36.15 ± 8.29	n=11 41.15 ± 9.12
			Uterus	ER^a ($\times 10^{-3}$)	n=12 236.68 ± 44.76	n=12 208.32 ± 29.22	n=12 315.81 ± 57.65 H	n=12 289.36 ± 27.94 H	n=11 280.36 ± 22.31 H	n=10 247.38 ± 38.25
				ER^b ($\times 10^{-3}$)	n=12 2.64 ± 2.11	n=12 2.30 ± 2.36	n=12 3.87 ± 5.69	n=12 1.58 ± 0.77	n=11 1.72 ± 0.76	n=10 1.40 ± 0.53
				AR ($\times 10^{-3}$)	n=12 47.98 ± 9.37	n=12 43.34 ± 8.54	n=12 61.85 ± 10.60 H	n=12 61.07 ± 4.42 H	n=11 57.84 ± 7.12 H	n=10 50.26 ± 6.25
				IGF-1 ($\times 10^{-3}$)	n=12 92.60 ± 22.16	n=12 91.04 ± 25.64	n=12 115.65 ± 26.03	n=12 111.63 ± 22.41	n=11 112.22 ± 21.62	n=10 89.38 ± 25.96

H or **H**: Significantly higher than the control ($p < 0.05$ and $p < 0.01$, respectively).

*1: mRNA expression (%)