

Summary of results (Di-(2-ethylhexyl) adipate)

Generation		Dam: F0 Offspring: F1						
Dose (µg/kg)		0	15	150	1500	15000	600 mg/kg	
Number of pregnant females		12	12	11	12	12	11	
F0	Clinical findings		-	-	-	-	-	-
	Body weights (g)	Gestation Day 21	408 ±23	421 ±19	419 ±17	421 ±25	417 ±24	420 ±21
		Lactation Day 0	289 ±19	295 ±16	299 ±17	295 ±16	289 ±21	291 ±11
		Lactation Day 22	349 ±22	358 ±20	350 ±11	354 ±17	340 ±21	347 ±11
	Body Weight gains (g)	Gestation Day 0-21	140 ±20	150 ±17	151 ±12	152 ±19	151 ±18	151 ±15
		Lactation Day 0-22	60 ±24	63 ±17	51 ±15	59 ±15	51 ±25	56 ±12
	Food consumption (g)	Gestation Day 18-19	24 ±3	24 ±3	25 ±4	24 ±4	26 ±4	24 ±4
		Lactation Day 18-19	69 ±9	68 ±11	66 ±10	65 ±11	72 ±10	61 ±9
	Reproduction	Gestation index (%)	100	100	100	100	100	100
		Gestation length (days)	22.2 ±0.3	22.4 ±0.4	22.1 ±0.5	22.1 ±0.3	22.3 ±0.3	22.2 ±0.3
		Number of implantation sites	16.2 ±2.4	15.9 ±2.9	15.8 ±1.7	16.6 ±1.9	15.8 ±1.5	16.5 ±1.5
		Number of live pups at birth	14.5 ±2.2	14.1 ±3.0	13.8 ±1.3	15.0 ±2.1	14.3 ±2.0	13.6 ±3.1

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).

- : No treatment-related alterations.

D or I : Decreasing or increasing tendency.

Summary of result (continued-1)

Generation		Dam: F0 Offspring: F1						
Dose ($\mu\text{g}/\text{kg}$)		0	15	150	1500	15000	600 mg/kg	
Number of pregnant females		12	12	11	12	12	11	
F0	Absolute organ weights	Pituitary (mg)	13.7 ± 1.3	13.7 ± 1.1	13.6 ± 1.9	14.4 ± 1.6	13.2 ± 1.8	13.4 ± 1.1
		Liver (g)	16.50 ± 1.86	16.62 ± 1.23	16.56 ± 1.24	16.07 ± 1.30	16.41 ± 1.31	17.96 I ± 1.16
		Ovary (mg)	78.4 ± 13.5	82.9 ± 12.5	82.3 ± 10.3	84.6 ± 10.4	79.2 ± 7.5	87.7 ± 9.6
		Uterus (g)	0.31 ± 0.14	0.31 ± 0.07	0.27 ± 0.04	0.31 ± 0.06	0.27 ± 0.05	0.33 ± 0.09
	Relative Organ weights	Pituitary (mg%)	3.9 ± 0.3	3.8 ± 0.3	3.9 ± 0.6	4.1 ± 0.4	3.9 ± 0.5	3.9 ± 0.3
		Liver (g%)	4.72 ± 0.29	4.65 ± 0.23	4.73 ± 0.33	4.54 ± 0.31	4.83 ± 0.31	5.18 H ± 0.30
		Ovary (mg%)	22.4 ± 3.4	23.2 ± 3.7	23.6 ± 3.4	23.9 ± 3.1	23.3 ± 2.1	25.3 ± 2.5
		Uterus (g%)	0.09 ± 0.04	0.09 ± 0.02	0.08 ± 0.01	0.09 ± 0.02	0.08 ± 0.01	0.09 ± 0.02
	Gross findings Abnormal		0/12	0/12	0/11	0/12	0/12	0/11
	Histopathological Findings	Liver						
		Necrosis, hepatocyte, focal	0/12	1/12	0/11	1/12	3/12	1/11
		Cellular, infiltration, lymphoid cell, Glisson's sheath	4/12	7/12	4/11	3/12	4/12	4/11
		Microgranuloma	1/12	0/12	1/11	2/12	0/12	0/11
	Proliferation, bile duct	5/12	3/12	2/11	1/12	4/12	8/11	
	Dilatation, sinusoid, focal	0/12	0/12	0/11	1/12	0/12	0/11	

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).

- : No treatment-related alterations.

D or I : Decreasing or increasing tendency.

Summary of result (continued-2)

Generation			Dam: F0				Offspring: F1		
Dose ($\mu\text{g}/\text{kg}$)			0	15	150	1500	15000	600 mg/kg	
Number of litters			12	12	11	12	12	11	
F1	No. of stillbirths		0.1 ± 0.3	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	0.1 ± 0.3	0.9 <u>H</u> ± 1.4	
	Sex ratio (M/M+F)		0.52	0.50	0.46	0.47	0.48	0.42	
	General signs		M	-	-	-	-	-	
			F	-	-	-	-	-	
	Birth index (%)		90.0 ± 7.4	88.6 ± 10.2	88.0 ± 9.9	90.4 ± 6.4	90.2 ± 11.4	82.7 D ± 18.1	
	Viability index (%)	Day 4	93.5 ± 10.4	92.5 ± 9.2	97.0 ± 6.9	95.1 ± 6.4	94.5 ± 9.7	87.0 ± 12.2	
	Weaning index (%)	Day 22	100.0 ± 0.0	97.3 ± 4.9	99.1 ± 3.0	95.0 ± 8.0	98.3 ± 3.9	93.6 L ± 6.7	
	Body weights (g)	M	Day 0	5.9 ± 0.5	6.1 ± 0.4	6.1 ± 0.3	6.0 ± 0.3	6.0 ± 0.4	5.6 ± 0.3
			Day 22	37.0 ± 4.4	35.4 ± 4.9	36.0 ± 4.4	38.9 ± 8.4	36.8 ± 4.8	33.5 ± 4.6
			Day 70	324 ± 20	327 ± 22	335 ± 25	340 ± 33	331 ± 21	314 ± 19
		F	Day 0	5.6 ± 0.5	5.8 ± 0.5	5.7 ± 0.3	5.5 ± 0.2	5.7 ± 0.4	5.3 ± 0.3
			Day 22	35.9 ± 4.2	33.0 ± 4.4	35.7 ± 5.2	34.5 ± 5.2	37.8 ± 4.9	34.3 ± 5.9
			Day 70	222 ± 13	221 ± 15	219 ± 12	220 ± 16	225 ± 10	215 ± 14
	Body weight gains (g)	M	Day 0-22	31.1 ± 4.2	29.2 ± 4.7	29.8 ± 4.2	32.9 ± 8.3	30.8 ± 4.6	27.9 ± 4.7
			Day 22-70	287 ± 18	292 ± 19	299 ± 23	301 ± 27	294 ± 20	280 ± 16
		F	Day 0-22	30.4 ± 4.1	27.2 ± 4.1	30.0 ± 5.1	29.0 ± 5.1	32.1 ± 4.8	29.0 ± 5.8
			Day 22-70	186 ± 11	188 ± 13	183 ± 11	185 ± 14	187 ± 11	180 ± 13
	AGD (mm)	M	Day 0	2.82 ± 0.28	2.86 ± 0.25	2.81 ± 0.26	2.82 ± 0.18	2.80 ± 0.23	2.85 ± 0.17
			Day 4	4.16 ± 0.27	4.40 ± 0.28	4.38 ± 0.28	4.34 ± 0.43	4.40 ± 0.28	4.23 ± 0.48
		F	Day 0	1.17 ± 0.12	1.16 ± 0.20	1.24 ± 0.22	1.18 ± 0.14	1.20 ± 0.14	1.26 ± 0.23
Day 4			1.86 ± 0.22	1.88 ± 0.28	2.04 ± 0.16	1.97 ± 0.22	2.00 ± 0.22	1.94 ± 0.32	
Gross findings (day 4) Abnormal			0/41	0/39	0/37	0/51	0/41	0/23	
Nipples	M	Day 13 (%)	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	
	F	Day 13 (%)	95 ± 12	98 ± 6	98 ± 6	98 ± 6	98 ± 6	90 ± 22	

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).

- : No treatment-related alterations.

D or I : Decreasing or increasing tendency.

Summary of result (continued-3)

Generation			Dam: F0 Offspring: F1					
Dose ($\mu\text{g}/\text{kg}$)			0	15	150	1500	15000	600 mg/kg
Number of litters			12	12	11	12	12	11
F1	M	Cleavage of balanopreputial gland (days)	50.7 ± 2.0	51.2 ± 3.1	50.5 ± 2.6	49.8 ± 2.5	50.4 ± 2.4	52.2 ± 2.8
	F	Opening of vaginal orifice (days)	35.6 ± 1.8	36.4 ± 2.1	35.2 ± 2.2	35.6 ± 2.4	35.5 ± 3.0	35.7 ± 2.1
		Estrous cycle (days)	4.24 ± 0.42	4.34 ± 0.70	4.32 ± 0.53	4.24 ± 0.43	4.19 ± 0.40	4.15 ± 0.19

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).

– : No treatment-related alterations.

D or I : Decreasing or increasing tendency.

Summary of result (continued -4)

Generation		Dam: F0 Offspring: F1						
Dose (µg/kg)		0	15	150	1500	15000	600 mg/kg	
Number of litters		13	13	11	12	13	12	
*1	*2	Pituitary (mg)	1.8 ±0.3	1.8 ±0.4	1.8 ±0.4	2.0 ±0.4	1.7 ±0.4	1.5 ±0.3
		Thyroid (mg)	4.5 ±0.6	4.6 ±0.7	4.4 ±0.8	4.5 ±0.8	4.4 ±0.6	4.0 ±0.9
		Liver (g)	1.64 ±0.27	1.62 ±0.31	1.61 ±0.28	1.84 ±0.38	1.65 ±0.30	1.43 ±0.28
		Adrenal (mg)	8.4 ±1.6	9.2 ±3.0	10.0 ±2.4	10.5 ±2.8	10.3 ±2.3	7.6 ±1.7
		Testis (mg)	125 ±33	132 ±50	133 ±29	149 ±48	131 ±43	103 ±37
		Epididymis (mg)	31.5 ±3.1	31.7 ±5.8	30.4 ±4.3	32.6 ±5.3	31.0 ±4.2	27.8 ±3.7
		Seminal vesicle (mg)	24.4 ±5.5	22.3 ±5.3	25.9 ±4.1	26.1 ±3.8	25.3 ±6.0	23.8 ±5.9
		Ventral prostate (mg)	8.2 ±2.2	6.9 ±2.5	7.9 ±3.2	7.1 ±2.7	7.2 ±2.4	6.0 ±2.1
	*3	Pituitary (mg%)	4.9 ±0.6	5.1 ±1.1	5.1 ±0.8	5.3 ±1.4	4.5 ±0.8	5.0 ±1.0
		Thyroid (mg%)	12.0 ±1.8	12.9 ±1.9	12.2 ±1.9	11.8 ±2.8	12.1 ±2.2	12.8 ±1.9
		Liver (g%)	4.40 ±0.49	4.52 ±0.42	4.44 ±0.45	4.72 ±0.39	4.50 ±0.31	4.54 ±0.26
		Adrenal (mg%)	22.6 ±4.3	25.5 ±6.5	27.4 ±3.8	26.8 ±3.5	28.1 H ±5.3	24.5 ±5.5
		Testis (mg%)	333 ±71	356 ±90	363 ±47	375 ±58	352 ±93	323 ±92
		Epididymis (mg%)	85.2 ±11.2	90.4 ±19.2	84.2 ±8.5	86.5 ±21.6	85.4 ±11.1	89.5 ±12.0
		Seminal vesicle (mg%)	65.6 ±13.8	64.1 ±18.7	71.8 ±9.8	69.3 ±15.4	69.3 ±14.5	76.0 ±15.1
		Ventral prostate (mg%)	21.8 ±4.4	19.0 ±6.2	21.4 ±6.5	17.9 ±4.9	19.8 ±6.3	19.0 ±4.9
Gross findings Abnormal		0/13	0/13	0/11	0/12	0/13	0/12	
*4	Liver Hematopoiesis, extramedullary Testis	6/13 –	5/13 –	5/11 –	4/12 –	8/13 –	4/12 –	

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).

– : No treatment-related alterations.

D or I : Decreasing or increasing tendency.

*1 :F1 male at weaning

*2 : Absolute organ weights

*3 : Relative organ weights

*4 : Histopathological findings

Summary of result (continued -5)

Generation		Dam: F0 Offspring: F1						
Dose (µg/kg)		0	15	150	1500	15000	600 mg/kg	
Number of litters		13	15	14	14	13	14	
*1	*2	Pituitary (mg)	2.2 ±0.4	2.1 ±0.4	2.1 ±0.6	2.0 ±0.4	2.2 ±0.4	1.7 <u>L</u> ±0.3
		Thyroid (mg)	3.8 ±0.9	3.9 ±0.8	4.2 ±0.7	4.3 ±0.8	4.7 H ±1.1	4.2 ±0.6
		Liver (g)	1.60 ±0.24	1.44 ±0.28	1.56 ±0.14	1.57 ±0.25	1.69 ±0.19	1.47 ±0.27
		Adrenal (mg)	9.1 ±2.5	9.6 ±3.0	9.8 ±1.9	8.9 ±2.7	10.0 ±2.2	8.3 ±2.8
		Ovary (mg)	5.8 ±2.2	4.7 ±1.5	5.5 ±1.4	4.9 ±1.9	5.7 ±1.4	4.8 ±1.3
		Uterus (mg)	34.8 ±10.0	27.2 ±7.9	28.0 ±4.3	29.4 ±12.5	29.0 ±9.1	25.9 L ±4.7
	*3	Pituitary (mg%)	6.1 ±0.7	6.7 ±1.2	6.2 ±1.5	5.8 ±0.9	5.9 ±0.6	5.4 ±1.4
		Thyroid (mg%)	10.6 ±2.6	12.6 ±3.0	12.2 ±2.8	12.9 ±2.6	12.4 ±2.1	13.4H ±2.4
		Liver (g%)	4.40 ±0.33	4.51 ±0.30	4.54 ±0.42	4.61 ±0.39	4.50 ±0.19	4.61 ±0.21
		Adrenal (mg%)	25.2 ±7.2	30.2 ±8.1	28.3 ±4.2	26.2 ±7.4	26.6 ±4.0	25.3 ±5.7
		Ovary (mg%)	15.6 ±4.4	14.5 ±3.5	16.0 ±4.1	13.8 ±3.1	15.1 ±3.2	14.9 ±2.6
		Uterus (mg%)	95.1 ±22.2	85.3 ±18.6	81.5 ±12.3	84.4 ±20.8	76.8L ±18.4	82.2 ±14.9
	Gross findings Abnormal		0/13	0/15	0/14	0/14	0/13	0/14
	*4	Liver						
		Necrosis, hepatocyte, focal	0/13	0/15	0/14	1/14	0/13	0/14
		Hematopoiesis, extramedullary	10/13	7/15	8/14	5/14	8/13	6/14
		Ovary, uterus	–	–	–	–	–	–

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).

– : No treatment-related alterations.

D or I : Decreasing or increasing tendency.

*1 :F1 male at weaning

*2 : Absolute organ weights

*3 : Relative organ weights

*4 : Histopathological findings

Summary of result (icontinued-6)

Generation			Dam: F0 Offspring: F1							
Dose (µg/kg)			0	15	150	1500	15000	600 mg/kg		
Number of litters			12	12	11	12	12	11		
*1	*2	Pituitary (mg)	11.5 ±1.4	11.3 ±1.4	11.6 ±1.2	12.0 ±1.2	12.1 ±1.4	10.7 ±1.5		
		Thyroid (mg)	16.2 ±2.8	15.1 ±2.0	15.8 ±3.7	16.2 ±3.7	15.8 ±1.5	15.1 ±3.4		
		Liver (g)	12.99 ±1.92	13.16 ±1.02	13.56 ±1.65	13.20 ±1.83	13.16 ±2.12	12.87 ±2.06		
		Adrenal (mg)	44.1 ±5.1	47.3 ±6.1	44.3 ±8.4	45.9 ±4.9	41.4 ±7.1	44.0 ±5.8		
		Testis (mg)	2.59 ±0.31	2.45 ±0.34	2.51 ±0.54	2.67 ±0.22	2.64 ±0.27	2.61 ±0.20		
		Epididymis (mg)	673 ±77	668 ±112	660 ±133	689 ±103	692 ±85	647 ±96		
		Seminal vesicle (mg)	1.34 ±0.27	1.34 ±0.28	1.35 ±0.41	1.35 ±0.31	1.41 ±0.20	1.19 ±0.26		
		Ventral prostate (mg)	403 ±73	399 ±80	424 ±131	416 ±98	409 ±60	375 ±82		
	*3	Pituitary (mg%)	3.5 ±0.3	3.4 ±0.4	3.5 ±0.4	3.5 ±0.3	3.6 ±0.3	3.4 ±0.2		
		Thyroid (mg%)	4.9 ±0.7	4.5 ±0.5	4.7 ±1.0	4.7 ±1.0	4.7 ±0.5	4.8 ±1.0		
		Liver (g%)	3.88 ±0.39	3.95 ±0.23	4.07 ±0.21	3.85 ±0.32	3.98 ±0.43	4.05 ±0.29		
		Adrenal (mg%)	13.2 ±1.3	14.2 ±1.6	13.3 ±2.2	13.4 ±0.9	12.3 ±2.0	13.9 ±1.2		
		Testis (mg%)	0.77 ±0.06	0.74 ±0.10	0.75 ±0.14	0.79 ±0.07	0.79 ±0.06	0.83 ±0.05		
		Epididymis (mg%)	202 ±16	200 ±29	196 ±28	201 ±22	205 ±21	204 ±21		
		Seminal vesicle (mg%)	0.40 ±0.06	0.40 ±0.07	0.39 ±0.09	0.39 ±0.08	0.42 ±0.05	0.37 ±0.06		
		Ventral prostate (mg%)	120 ±17	119 ±19	124 ±27	121 ±23	121 ±15	117 ±16		
	Gross findings			0/23	0/20	1/18	0/21	0/22	0/16	
	Testis Small and softness Epididymis, seminal vesicle and prostate Small			0/23	0/20	0/18	1/21	0/22	0/16	
	*4	Liver	Necrosis, hepatocyte, focal	1/12	0/12	1/11	0/12	0/12	0/11	
			Microgranuloma	1/12	1/12	1/11	2/12	1/12	4/11	
		Testis	Cellular infiltration, lymphoid cell, Glisson's sheath	9/12	9/12	5/11	7/12	8/12	7/11	
			Atrophy, seminiferous tubule	1/12	4/12	1/11	2/12	2/12	1/11	
	Seminiferous tubuli (%)			75.9 ±2.4	76.4 ±2.4	75.5 ±2.8	74.9 ±3.1	77.4 ±3.8	76.3 ±2.4	
	Testosterone (ng/mL)			2.09 ±0.89	1.48 ±0.61	1.49 ±0.70	0.96 <u>L</u> ±0.37	1.18 <u>L</u> ±0.57	0.99 <u>L</u> ±0.44	
	mRNA expression (%)		Testis	AR	0.0406 ±0.0060	0.0418 ±0.0061	0.0423 ±0.0057	0.0453 ±0.0060	0.0414 ±0.0049	0.0437 ±0.0079

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).

– : No treatment-related alterations.

D or I : Decreasing or increasing tendency.

*1 : F1 female on Day 70

*2 : Absolute organ weights

*3 : Relative organ weights

*4 : Histopathological findings

Summary of result (continued-7)

Generation		Dam: F0 Offspring: F1						
Dose (µg/kg)		0	15	150	1500	15000	600 mg/kg	
Number of litters		12	12	11	12	12	11	
*1	*2	Pituitary (mg)	11.9 ±1.2	10.2• □ ±1.7	11.5 ±1.8	11.6 ±1.5	11.6 ±1.3	11.2 ±1.0
		Thyroid (mg)	14.7 ±3.1	15.2 ±2.9	15.3 ±2.2	15.9 ±2.5	16.5 ±3.4	14.7 ±3.2
		Liver (g)	9.28 ±0.77	9.11 ±1.28	9.02 ±1.05	9.18 ±1.18	9.49 ±1.04	9.35 ±0.74
		Adrenal (mg)	59.8 ±6.7	63.4 ±8.2	58.7 ±5.2	62.1 ±8.0	62.0 ±7.9	62.6 ±8.4
		Ovary (mg)	99.7 ±17.7	89.4 ±17.9	93.2 ±16.8	99.7 ±15.7	107.5 ±13.1	108.7 ±14.7
		Uterus (mg)	637 ±89	596 ±135	579 ±99	596 ±58	617 ±97	579 ±84
	*3	Pituitary (mg%)	5.2 ±0.4	4.6 ±0.8	5.1 ±0.7	5.1 ±0.5	5.0 ±0.4	4.9 ±0.4
		Thyroid (mg%)	6.5 ±1.3	6.9 ±1.4	6.9 ±1.0	7.0 ±0.8	7.1 ±1.3	6.5 ±1.2
		Liver (mg%)	4.08 ±0.23	4.09 ±0.34	4.03 ±0.25	4.00 ±0.20	4.08 ±0.22	4.11 ±0.23
		Adrenal (mg%)	26.3 ±2.5	28.5 ±2.3	26.3 ±2.2	27.2 ±3.7	26.7 ±2.8	27.5 ±3.2
		Ovary (mg%)	43.8 ±7.4	40.1 ±6.2	41.6 ±6.6	43.4 ±4.0	46.4 ±5.3	47.9 ±6.8
		Uterus (mg%)	280 ±38	269 ±59	258 ±28	263 ±36	266 ±38	254 ±34
Gross findings Abnormal		0/23	0/21	0/22	0/21	0/22	0/18	
*4	Liver Necrosis, hepatocyte, focal	0/12	0/12	0/11	1/12	0/12	0/11	
	Microgranuloma	3/12	3/12	0/11	1/12	1/12	0/11	
	Cellular infiltration, lymphoid cell, Glisson's sheath	6/12	10/12	6/11	6/12	6/12	9/11	
	Ovary, uterus	–	–	–	–	–	–	

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).

– : No treatment-related alterations.

D or I : Decreasing or increasing tendency.

*1 : F1 female on Day 70

*2 : Absolute organ weights

*3 : Relative organ weights

*4 : Histopathological findings

Summary of result (continued-8)

Generation		Dam: F0 Offspring: F1						
Dose ($\mu\text{g}/\text{kg}$)		0	15	150	1500	15000	600 mg/kg	
Number of litters		12	12	11	12	12	11	
*1	*2	Ovary						
		Ratio of corpus lutea (%)	43.4 ± 12.9	43.2 ± 10.2	43.3 ± 8.7	49.1 ± 8.1	47.5 ± 11.5	52.6 ± 11.2
		Number of corpus lutea /mm ²	1.20 ± 0.21	1.15 ± 0.30	1.15 ± 0.40	1.17 ± 0.20	1.34 ± 0.24	1.22 ± 0.31
		Uterus						
		Thickness (mm)	1.134 ± 0.21	1.112 ± 0.24	1.150 ± 0.25	1.192 ± 0.17	1.175 ± 0.19	1.219 ± 0.10
		Thickness of endometrium (mm)	5	2	0	9	2	9
	Cell height of epithelium (i m)	0.679 ± 0.17	0.672 ± 0.19	0.699 ± 0.17	0.733 ± 0.13	0.709 ± 0.13	0.730 ± 0.10	
		0	4	7	6	9	2	
		27.6 ± 4.7	29.7 ± 7.5	27.1 ± 3.7	30.0 ± 4.7	29.5 ± 4.3	27.6 ± 4.4	
	Estradiol (pg/mL)		68.9 ± 28.4	58.1 ± 28.7	56.3 ± 36.5	70.2 ± 30.7	68.1 ± 24.0	73.6 ± 36.7
mRNA expression (%)	Ovary	ER α	0.0137 ± 0.0115	0.0087 ± 0.0032	0.0099 ± 0.0027	0.0099 ± 0.0033	0.0088 ± 0.0021	0.0076 L ± 0.0026
		ER β	0.0154 ± 0.0064	0.0112 ± 0.0062	0.0165 ± 0.0068	0.0139 ± 0.0047	0.0139 ± 0.0064	0.0129 ± 0.0051

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).

– : No treatment-related alterations.

D or I : Decreasing or increasing tendency.

*1 : F1 female on Day 70

*2 : Histopathological findings

Summary of result (continued-9)

Generation		Dam: F0 Offspring: F1						
Dose (µg/kg)		0	15	150	1500	15000	600 mg/kg	
*1	Female	Number of litters	24	22	22	23	24	19
		Copulation index (%)	100.0	95.5	100.0	100.0	95.8	89.5
		Number of days till copulation	3.0 ±1.8	2.6 ±1.2	2.8 ±1.1	2.6 ±1.0	2.6 ±1.2	2.4 ±1.5
		Fertility index (%)	100.0	100.0	95.5	95.7	100.0	100.0
	Male	Number of litters	24	22	22	23	24	19
		Gross findings						
		Kidney						
		Dilatation, right pelvis	2/24	0/22	0/22	0/23	0/24	0/19
		Testis						
		Large	0/24	1/22	0/22	0/23	0/24	0/19
		Small	1/24	0/22	0/22	1/23	1/24	0/19
		Epididymis						
		Small	1/24	1/22	0/22	1/23	1/24	0/19
		Motile sperm rate (%)	82.8 ±7.3	77.6 ±12.9	80.3 ±8.1	83.0 ±7.7	80.9 ±5.9	79.7 ±8.8
		Progressive sperm rate (%)	15.5 ±10.2	13.1 ±10.3	14.2 ±12.1	19.0 ±11.8	16.0 ±11.5	15.3 ±10.7
		Curvilinear velocity (?m/s)	297.3 ±34.1	287.9 ±36.2	287.3 ±41.0	305.7 ±33.1	298.3 ±34.7	298.8 ±28.8
		Sperm abnormal rate (%)	5.8 ±2.5	8.0 ±12.3	4.8 ±2.1	5.2 ±3.1	5.5 ±3.5	3.7 <u>L</u> ±2.9
		Head abnormal rate (%)	5.5 ±2.4	7.7 ±12.4	4.3 ±1.8	4.8 ±2.9	5.2 ±3.3	3.3 <u>L</u> ±2.5
	Tail abnormal rate (%)	0.3 ±0.4	0.3 ±0.5	0.5 ±0.7	0.4 ±0.4	0.3 ±0.5	0.3 ±0.7	
	Number of sperms (x 10 ⁶)	208.0 ±65.4	212.4 ±39.6	212.6 ±34.9	212.4 ±57.3	223.3 ±38.3	192.1 ±50.2	
	Number of sperms/g (x 10 ⁶)	897.8 ±252. 9	932.9 ±136. 8	926.2 ± 94.0	906.2 ±171. 6	949.1 ±125. 5	878.7 ±148. 0	
	Female	Number of litters	24	21	21	22	23	17
		Gross findings Abnormal	0/24	0/21	0/21	0/22	0/23	0/17
		Number of corpora lutea	14.4 ±2.4	14.6 ±2.2	14.3 ±1.9	14.8 ±2.8	14.2 ±1.5	13.9 ±1.8
		Number of implantation sites	12.6 ±2.7	13.2 ±2.5	13.0 ±2.2	12.6 ±3.3	12.7 ±2.1	12.2 ±2.2
		Pre-implantation loss rate	12.9 ±11.1	9.3 ±11.2	9.7 ±9.2	15.6 ±14.1	10.7 ±10.5	12.2 ±12.1
		Post-implantation loss rate	6.7 ±10.0	10.8 ±11.1	6.4 ±8.5	4.8 ±5.3	6.9 ±6.4	6.3 ±8.0
		Number of live embryos	11.7 ±2.8	11.7 ±2.2	12.1 ±2.2	12.0 ±3.2	11.8 ±1.9	11.5 ±2.3

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).

- : No treatment-related alterations.

D or I : Decreasing or increasing tendency.

*1 : F1 reproductive performance