TABLE 5. Data of Diisononylphthalate Study – From Puberty to Final Necropsy-

	Diisononylphthalate (ppm)			
	0	400	4000	20000
No of rats	8	8	8	8
Body weight gain , PD21-PD77 (g/day)				
Males				
PD21-PD42	7.9 ± 0.3 *	8.3 ± 0.6	7.5 ± 0.6	6.5 ± 0.7**
PD42-PD77	6.6 ± 0.5	6.9 ± 0.5	6.7 ± 0.8	6.4 ± 0.5
Females				
PD21-PD42	5.9 ± 0.5	6.2 ± 0.3	5.9 ± 0.8	5.2 ± 0.7
PD42-PD77	3.0 ± 0.4	3.2 ± 0.4	3.1 ± 0.3	3.0 ± 0.4
Onset of puberty				
Vaginal opening				
Age (day)	36.0 ± 1.3	34.8 ± 0.7	35.5 ± 0.8	35.8 ± 0.7
Body weight (g)	139.5 ± 13.1	133.7 ± 5.9	129.5 ± 11.8	112.7 ± 20.8*
Preputial separation				
Age (day)	41.8 ± 0.5	41.9 ± 0.4	42.1 ± 0.6	42.3 ± 0.5
Body weight (g)	216.0 ± 9.3	225.1 ± 14.5	205.2 ± 15.2	177.3 ± 17.2**
Estrous cyclicity				
Normal	8/8	8/8	8/8	8/8
Organ weights, final necropsy				
Males (No. of rats)	5	5	5	5
Body weight (g)	504.3 ± 27.2	527.0 ± 24.7	478.6 ± 57.6	456.4 ± 17.9
Brain				
Absolute (g)	2.06 ± 0.09	2.13 ± 0.09	2.11 ± 0.06	2.00 ± 0.05
Relative (g/100g BW)	0.41 ± 0.03	0.40 ± 0.02	0.45 ± 0.05	0.43 ± 0.01
Pituitary				
Absolute (mg)	15.0 ± 2.0	16.4 ± 2.1	14.6 ± 2.2	14.2 ± 1.8
Relative (mg/100g BW)	2.99 ± 0.52	3.11 ± 0.40	3.07 ± 0.45	3.11 ± 0.40
Adrenals				
Absolute (mg)	47.8 ± 6.5	52.4 ± 9.6	53.8 ± 8.8	52.2 ± 5.9
Relative (mg/100g BW)	9.5 ± 1.0	10.0 ± 2.1	11.3 ± 1.7	11.5 ± 1.4
Testes				
Absolute (g)	3.11 ± 0.54	3.43 ± 0.17	3.16 ± 0.14	2.92 ± 0.32
Relative (g/100g BW)	0.61 ± 0.09	0.65 ± 0.03	0.67 ± 0.07	0.64 ± 0.07
Prostate				
Absolute (g)	0.69 ± 0.17	0.66 ± 0.12	0.63 ± 0.10	0.56 ± 0.25
Relative (g/100g BW)	0.14 ± 0.03	0.13 ± 0.02	0.13 ± 0.02	0.12 ± 0.05
Females (No. of rats)	5	5	5	5
Body weight (g)	307.5 ± 23.2	314.2 ± 20.5	304.0 ± 34.2	292.3 ± 23.7
Brain				
Absolute (g)	1.96 ± 0.08	1.93 ± 0.09	1.98 ± 0.08	1.92 ± 0.13
Relative (g/100g BW)	0.64 ± 0.06	0.62 ± 0.05	0.66 ± 0.07	0.65 ± 0.10
Pituitary				
Absolute (mg)	16.8 ± 2.2	17.2 ± 1.6	16.4 ± 2.7	17.2 ± 2.9
Relative (mg/100g BW)	5.48 ± 0.70	5.48 ± 0.49	5.38 ± 0.51	5.87 ± 0.72
Adrenals				
Absolute (mg)	59.6 ± 12.5	55.8 ± 9.54	63.8 ± 14.8	56.6 ± 6.8
Relative (mg/100g BW)	19.5 ± 4.6	17.8 ± 3.3	20.9 ± 3.6	19.6 ± 3.6
Ovaries				
Absolute (mg)	94.6 ± 14.0	92.0 ± 15.0	92.6 ± 5.8	88.6 ± 11.9
Relative (mg/100g BW)	30.9 ± 5.1	29.4 ± 5.1	30.7 ± 3.5	30.7 ± 6.0
Uterus				
Absolute (g)	0.46 ± 0.10	0.42 ± 0.06	0.47 ± 0.12	0.47 ± 0.12
Relative (g/100g BW)	0.15 ± 0.02	0.13 ± 0.01	0.16 ± 0.05	0.16 ± 0.05

* Mean ± SD

* $p < 0.05$ compared to controls

** $p < 0.01$ compared to controls

TABLE 6. Histopathological Findings in Endocrine/Reproductive Organs at 11 weeks in Diisononylphthatate Study

	Diisononylphthalate (ppm)			
	0	400	4000	20000
Males (No. of rats examined)	(5)	(5)	(5)	(5)
Testis				
- Degeneration of dividing spermatocytes at stage XIV (±/+) [a]	0	0	0	4 (0/4)
- Vacuolar degeneration of Sertoli cells (±)	0	0	0	4 (4)
Epididymis				
- Scattered cell debris in tubules (±)	0	0	0	4 (4)
Females (No. of rats examined)	(5)	(5)	(5)	(5)
Ovary				
- Decrease in corpora lutea (±/+)	0	2 [b] (2/0) [c]	1 (1/0)	4 (3/1)

[a] Grade of the findings; ±, very slight; and +, slight

[b] Total No. of animals with each finding

[c] No. of animals in each grade

TABLE 7. Data of Genistein Study -From Birth to Prepubertal Necropsy-

	Genistein (ppm)			
	0	20	200	1000
No. of litters	5	5	5	5
Maternal body weight gain (g/day)				
Gestational period	14.1 ± 2.4[a]	14.4 ± 2.8	12.7 ± 1.2	11.8 ± 2.1
Lactational period	0.6 ± 2.2	0.2 ± 4.4	1.6 ± 2.9	1.7 ± 3.6
Maternal food consumption (g/day)				
Gestational period	24.7 ± 1.8	23.4 ± 1.6	23.8 ± 0.5	23.4 ± 1.3
Lactational period	35.2 ± 1.4	35.5 ± 0.5	37.4 ± 0.8	37.0 ± 1.3
Calculated maternal intake (mg/kg/day)				
Gestational period	0	1.3 ± 0.7	13.7 ± 0.7	66.6 ± 4.0
Lactational period	0	2.1 ± 1.1	23.0 ± 1.8	113.1 ± 7.1
No. of live offspring	13.2 ± 0.8	13.4 ± 1.1	12.4 ± 1.5	14.2 ± 1.3
Body weight , PD2 (g)				
Males	7.4 ± 0.8	7.4 ± 0.5	7.6 ± 0.7	7.0 ± 0.6
Females	6.9 ± 0.4	7.0 ± 0.6	7.2 ± 0.6	6.7 ± 0.7
AGD, PD2 (mm)				
Males	3.1 ± 0.4	3.5 ± 0.2	3.4 ± 0.2	3.2 ± 0.3
Females	1.2 ± 0.2	1.4 ± 0.3	1.3 ± 0.0	1.3 ± 0.2
Body weight gain (g/day)				
Males				
PD2-PD10	1.6 ± 0.2	1.3 ± 0.0	1.7 ± 0.2	1.3 ± 0.2
PD10-PD21	2.8 ± 0.4	2.7 ± 0.8	3.2 ± 0.7	2.2 ± 0.5
Females				
PD2-PD10	1.6 ± 0.3	1.3 ± 0.1	1.6 ± 0.2	1.3 ± 0.2
PD10-PD21	2.8 ± 0.4	2.8 ± 0.7	3.4 ± 0.8	2.5 ± 0.5
Organ weights, prepubertal necropsy				
Males (No. of rats)	5	5	5	5
Body weight (g)	53.7 ± 2.1	49.3 ± 9.9	58.0 ± 9.9	46.3 ± 4.4
Brain				
Absolute (g)	1.46 ± 0.06	1.46 ± 0.06	1.52 ± 0.08	1.42 ± 0.06
Relative (g/100g BW)	2.73 ± 0.14	3.07 ± 0.61	2.68 ± 0.50	3.09 ± 0.29
Adrenals				
Absolute (mg)	15.2 ± 2.8	12.0 ± 3.8	17.4 ± 3.4	14.0 ± 2.0
Relative (mg/100g BW)	28.4 ± 5.5	25.0 ± 5.0	30.3 ± 4.8	30.8 ± 7.4
Testes				
Absolute (g)	0.28 ± 0.04	0.24 ± 0.05	0.31 ± 0.06	0.25 ± 0.05
Relative (g/100g BW)	0.53 ± 0.07	0.49 ± 0.04	0.53 ± 0.03	0.53 ± 0.07
Females (No. of rats)	5	5	5	5
Body weight (g)	51.2 ± 3.3	44.7 ± 12.6	49.6 ± 12.2	41.5 ± 4.2
Brain				
Absolute (g)	1.45 ± 0.03	1.39 ± 0.09	1.41 ± 0.08	1.40 ± 0.06
Relative (g/100g BW)	2.84 ± 0.16	3.31 ± 0.92	2.96 ± 0.61	3.14 ± 0.22
Adrenals				
Absolute (mg)	14.0 ± 1.2	13.0 ± 3.3	12.0 ± 3.6	11.4 ± 2.1
Relative (mg/100g BW)	27.5 ± 3.2	29.0 ± 3.0	24.1 ± 4.8	25.9 ± 6.6
Ovaries				
Absolute (mg)	15.8 ± 2.4	13.0 ± 4.0	19.4 ± 5.1	16.2 ± 2.4
Relative (mg/100g BW)	32.1 ± 4.5	30.0 ± 5.1	39.3 ± 5.9	36.3 ± 5.2
Uterus				
Absolute (g)	48.4 ± 12.4	52.0 ± 11.9	56.6 ± 8.7	48.8 ± 4.9
Relative (g/100g BW)	95.2 ± 27.7	120.0 ± 17.4	120.2 ± 38.2	109.0 ± 5.9

[a] Mean ± SD

TABLE 8. Data of Genistein Study –From Puberty to Final Necropsy-

	Genistein (ppm)			
	0	20	200	1000
No of rats	8	8	8	8
Body weight gain (g/day)				
Males				
PD21-PD42	7.1 ± 0.5 [a]	6.4 ± 0.5	7.1 ± 0.9	6.2 ± 0.3*
PD42D77	7.3 ± 0.7	6.5 ± 0.7	6.5 ± 0.6	6.4 ± 0.6
Females				
PD21-PD42	5.3 ± 0.4	5.1 ± 0.5	4.9 ± 0.2	4.8 ± 0.3
PD42-PD77	3.5 ± 0.6	3.1 ± 0.3	2.9 ± 0.3	3.1 ± 0.6
Onset of puberty				
Vaginal opening				
Age (day)	34.9 ± 0.6	35.0 ± 1.1	36.0 ± 1.7	35.8 ± 1.6
Body weight (g)	116.8 ± 5.7	110.1 ± 12.1	120.1 ± 13.5	112.9 ± 12.4
Preputial separation				
Age (day)	41.6 ± 1.1	42.0 ± 0.9	41.0 ± 0.0	41.9 ± 0.6
Body weight (g)	195.8 ± 11.8	179.9 ± 12.9	194.7 ± 26.0	170.5 ± 7.0*
Estrous cyclicity				
Normal	8/8	8/8	8/8	8/8
Organ weights, final necropsy				
Males (No. of rats)	5	5	5	5
Body weight (g)	558.0 ± 45.5	470.7 ± 43.1**	482.1 ± 36.2*	465.1 ± 36.0**
Brain				
Absolute (g)	2.05 ± 0.07	2.04 ± 0.16	2.04 ± 0.07	2.05 ± 0.10
Relative (g/100g BW)	0.37 ± 0.04	0.44 ± 0.01*	0.43 ± 0.04	0.44 ± 0.05
Pituitary				
Absolute (mg)	15.0 ± 1.6	14.2 ± 1.8	12.8 ± 1.9	12.2 ± 0.8*
Relative (mg/100g BW)	2.69 ± 0.24	3.01 ± 0.12*	2.65 ± 0.24	2.63 ± 0.07
Adrenals				
Absolute (mg)	42.8 ± 6.0	42.0 ± 2.8	46.8 ± 7.1	47.0 ± 4.2
Relative (mg/100g BW)	7.7 ± 0.8	9.0 ± 1.0	9.7 ± 1.3*	10.1 ± 1,0**
Testes				
Absolute (g)	3.37 ± 0.20	3.08 ± 0.14	3.40 ± 0.26	3.11 ± 0.28
Relative (g/100g BW)	0.61 ± 0.02	0.66 ± 0.06	0.71 ± 0.08	0.67 ± 0.08
Prostate				
Absolute (g)	0.83 ± 0.17	0.68 ± 0.12	0.78 ± 0.17	0.84 ± 0.10
Relative (g/100g BW)	0.15 ± 0.02	0.15 ± 0.03	0.16 ± 0.02	0.18 ± 0.02
Females (No. of rats)	5	5	5	5
Body weight (g)	297.7 ± 31.7	276.7 ± 40.4	271.2 ± 7.62	264.1 ± 17.1
Brain				
Absolute (g)	1.93 ± 0.11	1.91 ± 0.19	1.98 ± 0.05	1.87 ± 0.10
Relative (g/100g BW)	0.65 ± 0.05	0.70 ± 0.05	0.73 ± 0.04	0.71 ± 0.04
Pituitary				
Absolute (mg)	15.8 ± 1.9	14.8 ± 2.6	15.0 ± 2.0	15.6 ± 0.9
Relative (mg/100g BW)	5.32 ± 0.59	5.35 ± 0.60	5.53 ± 0.70	5.92 ± 0.35
Adrenals				
Absolute (mg)	59.2 ± 2.9	49.8 ± 7.4	56.6 ± 9.3	59.8 ± 7.2
Relative (mg/100g BW)	20.1 ± 2.6	18.3 ± 3.9	20.9 ± 3.8	22.6 ± 1.9
Ovaries				
Absolute (mg)	81.6 ± 14.4	80.2 ± 10.7	76.2 ± 11.3	72.8 ± 7.9
Relative (mg/100g BW)	27.3 ± 2.6	29.7 ± 7.1	28.1 ± 4.0	27.6 ± 2.9
Uterus				
Absolute (g)	0.50 ± 0.13	0.45 ± 0.13	0.44 ± 0.06	0.48 ± 0.13
Relative (g/100g BW)	0.17 ± 0.05	0.17 ± 0.07	0.17 ± 0.18	0.18 ± 0.06

[a] Mean ± SD

* $p < 0.05$ compared to controls

** $p < 0.01$ compared to controls

TABLE 9. Histopathological Findings in Endocrine/Reproductive Organs at 11 weeks in Genistein Study

	Genistein (ppm)			
	0	20	200	1000
Males (No. of rats examined)	(5)	(5)	(5)	(5)
No abnormalities	5	5	5	5
Females (No. of rats examined)	(5)	(5)	(5)	(5)
Ovary				
- Increase in follicles * (±/+) [a]	0	0	2 [b] (0/2) [c]	1 (0/1)

[a] Grade of the findings; ±, very slight; and +, slight

[b] Total No. of animals with each finding

[c] No. of animals in each grade

* Composed mainly of primary and secondary follicles

TABLE 10. Data of Nonylphenol Study -From Birth to Prepubertal Necropsy-

	Nonylphenol (ppm)			
	0	60	600	3000
No. of dams	6	6	5	6
Maternal body weight gain (g/day)				
Gestational period	13.8 ± 1.4	12.6 ± 2.2	13.8 ± 1.2	10.3 ± 1.8**
Lactational period	6.4 ± 2.3	4.0 ± 0.7	5.5 ± 2.2	5.7 ± 1.5
Maternal food consumption (g/day)				
Gestational period	28.3 ± 1.4	27.5 ± 1.9	28.2 ± 1.7	30.7 ± 5.4
Lactational period	51.8 ± 3.9	50.6 ± 4.8	48.7 ± 1.8	47.2 ± 5.4
Calculated maternal intake (mg/kg/day)				
Gestational period	0	4.8 ± 2.5	48.2 ± 2.7	270.4 ± 55.9
Lactational period	0	9.1 ± 4.8	87.2 ± 3.1	455.3 ± 36.3
No. of live offspring	12.0 ± 1.3	12.4 ± 2.5	11.8 ± 1.5	13.0 ± 1.3
Body weight , PD2 (g)				
Males	7.8 ± 0.8	8.0 ± 0.8	7.7 ± 1.0	7.0 ± 0.8
Females	7.5 ± 0.7	7.7 ± 0.9	7.3 ± 1.1	6.7 ± 0.8
AGD, PD2 (mm)				
Males	3.2 ± 0.5	3.2 ± 0.2	3.0 ± 0.3	3.0 ± 0.2
Females	1.3 ± 0.1	1.2 ± 0.1	1.2 ± 0.1	1.1 ± 0.2**
Body weight gain (g/day)				
Males				
PD2-PD10	1.6 ± 0.2	1.5 ± 0.3	1.6 ± 0.2	1.2 ± 0.5
PD10-PD21	2.5 ± 0.4	2.1 ± 0.6	2.8 ± 0.2	2.4 ± 0.3
Females				
PD2-PD10	1.5 ± 0.2	1.6 ± 0.2	1.5 ± 0.2	1.1 ± 0.4
PD10-PD21	2.4 ± 0.4	2.0 ± 0.8	2.7 ± 0.3	2.5 ± 0.2
Organ weights, prepubertal necropsy				
Males (No. of rats)	5	5	5	5
Body weight (g)	74.2 ± 5.8	68.5 ± 7.6	77.4 ± 5.6	64.4 ± 11.4
Brain				
Absolute (g)	1.54 ± 0.06	1.54 ± 0.08	1.58 ± 0.04	1.50 ± 0.09
Relative (g/100g BW)	2.08 ± 0.13	2.27 ± 0.21	2.05 ± 0.16	2.37 ± 0.32
Adrenals				
Absolute (mg)	21.0 ± 2.0	18.6 ± 3.6	21.4 ± 4.7	17.4 ± 4.0
Relative (mg/100g BW)	28.4 ± 1.1	27.3 ± 5.9	27.5 ± 5.1	26.9 ± 3.1
Testes				
Absolute (g)	0.47 ± 0.11	0.41 ± 0.07	0.46 ± 0.04	0.40 ± 0.11
Relative (g/100g BW)	0.63 ± 0.10	0.59 ± 0.05	0.60 ± 0.05	0.61 ± 0.08
Females (No. of rats)	5	5	5	5
Body weight (g)	71.7 ± 4.8	63.4 ± 5.2	72.2 ± 7.9	59.2 ± 8.7*
Brain				
Absolute (g)	1.53 ± 0.08	1.48 ± 0.04	1.51 ± 0.06	1.48 ± 0.05
Relative (g/100g BW)	2.14 ± 0.07	2.35 ± 0.19	2.10 ± 0.15	2.53 ± 0.33*
Adrenals				
Absolute (mg)	18.4 ± 2.3	15.6 ± 2.5	20.0 ± 5.1	15.0 ± 4.4
Relative (mg/100g BW)	25.7 ± 3.7	24.5 ± 2.2	27.6 ± 5.8	25.1 ± 4.4
Ovaries				
Absolute (mg)	33.8 ± 5.0	32.0 ± 5.7	33.2 ± 3.8	27.0 ± 4.5
Relative (mg/100g BW)	47.3 ± 7.9	50.3 ± 5.7	46.2 ± 5.8	45.9 ± 6.7
Uterus				
Absolute (mg)	48.4 ± 12.3	49.4 ± 13.2	44.8 ± 7.5	42.8 ± 6.9
Relative (mg/100g BW)	67.7 ± 17.7	77.6 ± 18.8	61.9 ± 6.0	72.7 ± 8.6

¹ Mean ± SD

* $p < 0.05$ compared to controls

** $p < 0.01$ compared to controls

TABLE 11. Data of Nonylphenol Study –From Puberty to Final Necropsy-

	Nonylphenol (ppm)			
	0	60	600	3000
No of rats	8	8	8	8
Body weight gain (g/day)				
Males				
PD21-PD48	8.0 ± 0.4	7.4 ± 0.7	7.2 ± 0.6*	7.3 ± 0.5*
PD48-PD63	8.5 ± 0.7	7.6 ± 1.3	7.5 ± 0.5	8.3 ± 0.9
PD63-PD77	5.1 ± 1.0	4.8 ± 0.8	5.0 ± 0.6	4.7 ± 0.9
Females				
PD21-PD48	5.5 ± 0.1	5.7 ± 0.6	5.7 ± 0.6	5.9 ± 0.5
PD48-PD63	3.6 ± 0.4	3.5 ± 0.8	3.3 ± 0.3	3.7 ± 0.6
PD63-PD77	2.5 ± 0.5	2.2 ± 0.8	2.3 ± 0.4	2.0 ± 0.6
Onset of puberty				
Vaginal opening				
Age (day)	33.8 ± 1.7	33.1 ± 1.8	35.4 ± 2.2	34.0 ± 0.5
Body weight (g)	118.0 ± 10.3	112.3 ± 18.1	126.8 ± 16.0	113.2 ± 4.9
Preputial separation				
Age (day)	40.8 ± 0.9	41.6 ± 1.5	41.9 ± 1.4	42.3 ± 1.3
Body weight (g)	205.8 ± 9.1	197.4 ± 15.9	196.6 ± 17.3	197.3 ± 8.8
Estrous cyclicity				
Normal	7/8	7/8	8/8	7/8
Irregular	1/8	1/8	0/8	1/8
Extended estrous	0/8	0/8	0/8	0/8
Extended diestrous	1/8	1/8	0/8	1/8
Persistent diestrous	0/8	0/8	0/8	0/8
Organ weights, final necropsy				
Males (No. of rats)	5	5	5	5
Body weight (g)	469.1 ± 22.2	422.1 ± 55.7	441.6 ± 24.7	434.5 ± 30.5
Brain				
Absolute (g)	1.99 ± 0.05	2.04 ± 0.05	2.01 ± 0.08	2.00 ± 0.09
Relative (g/100g BW)	0.43 ± 0.03	0.49 ± 0.07	0.46 ± 0.03	0.46 ± 0.04
Pituitary				
Absolute (mg)	13.6 ± 1.1	12.8 ± 1.6	13.0 ± 1.4	13.4 ± 1.5
Relative (mg/100g BW)	2.91 ± 0.33	3.06 ± 0.45	2.94 ± 0.27	3.09 ± 0.30
Adrenals				
Absolute (mg)	59.6 ± 7.0	49.0 ± 3.5	50.2 ± 7.3	53.4 ± 9.8
Relative (mg/100g BW)	12.8 ± 1.9	11.7 ± 1.0	11.4 ± 1.5	12.2 ± 1.3
Testes				
Absolute (g)	3.26 ± 0.37	2.70 ± 1.02	3.08 ± 0.15	2.89 ± 0.21
Relative (g/100g BW)	0.69 ± 0.05	0.62 ± 0.20	0.70 ± 0.04	0.67 ± 0.08
Prostate				
Absolute (g)	0.53 ± 0.14	0.49 ± 0.12	0.44 ± 0.11	0.59 ± 0.05
Relative (g/100g BW)	0.11 ± 0.03	0.11 ± 0.02	0.10 ± 0.03	0.14 ± 0.01
Females (No. of rats)	5	5	5	5
Body weight (g)	272.5 ± 4.2	271.7 ± 29.9	267.7 ± 19.6	267.1 ± 19.3
Brain				
Absolute (g)	1.91 ± 0.09	1.88 ± 0.05	1.90 ± 0.06	1.88 ± 0.07
Relative (g/100g BW)	0.70 ± 0.03	0.70 ± 0.06	0.71 ± 0.04	0.71 ± 0.06
Pituitary				
Absolute (mg)	16.0 ± 2.4	14.4 ± 2.5	15.8 ± 1.6	16.8 ± 1.6
Relative (mg/100g BW)	5.87 ± 0.86	5.28 ± 0.50	5.91 ± 0.52	6.28 ± 0.30
Adrenals				
Absolute (mg)	60.2 ± 6.0	56.6 ± 8.8	59.4 ± 7.1	69.0 ± 5.5
Relative (mg/100g BW)	22.1 ± 1.9	20.9 ± 3.2	22.1 ± 1.0	25.9 ± 2.3*
Ovaries				
Absolute (mg)	102.0 ± 18.5	92.8 ± 10.7	88.8 ± 10.5	98.6 ± 24.5
Relative (mg/100g BW)	37.4 ± 6.5	34.2 ± 3.1	33.2 ± 3.2	36.8 ± 8.1
Uterus				
Absolute (g)	0.46 ± 0.09	0.42 ± 0.08	0.38 ± 0.02	0.47 ± 0.12
Relative (g/100g BW)	0.17 ± 0.35	0.16 ± 0.03	0.14 ± 0.01	0.17 ± 0.03

Mean ± SD, * $p < 0.05$ compared to controls, ** $p < 0.01$ compared to controls

TABLE 12. Histopathological Findings in Endocrine/Reproductive Organs at 11 weeks in Nonylphenol Study

	Nonylphenol (ppm)			
	0	60	600	3000
Males (No. of rats examined)	(5)	(5)	(5)	(5)
Testis				
- Aspermatogenesis	0	1[d]	0	0
Epididymis				
- Loss of sperm	0	1[d]	0	0
- Cell debris in ducts	0	0	1	0
				0
Seminal vesicles				
- Small in size	0	1[d]	0	0
Females (No. of rats examined)	(5)	(5)	(5)	(5)
Ovary				
- Multiple follicular cysts* (±/+)[a]	1[b] (1/0)[c]	1 (1/0)	1 (0/1)	2 (1/1)
Pituitary				
- Diffuse hyperplasia, anterior lobe	0	0	0	1

[a] Grade of the findings; ±, very slight; and +, slight

[b] Total No. of animals with each finding

[c] No. of animals in each grade

[d] Observed in a same animal

* Composed mainly of primary and secondary follicles

TABLE 13. Data of Bisphenol A Study -From Birth to Prepubertal Necropsy-

	Bisphenol A (ppm)			
	0	60	600	3000
No. of dams	6	5	5	6
Maternal body weight gain (g/day)				
Gestational period	14.8 ± 2.0	16.5 ± 2.7	13.9 ± 2.2	9.2 ± 3.6**
Lactational period	5.2 ± 1.2	6.5 ± 1.6	5.4 ± 2.1	7.4 ± 2.0
Maternal food consumption (g/day)				
Gestational period	29.1 ± 2.3	29.5 ± 1.9	28.6 ± 1.9	26.5 ± 4.0
Lactational period	45.8 ± 3.9	47.0 ± 8.1	44.1 ± 2.5	38.7 ± 7.8
Calculated maternal intake (mg/kg/day)				
Gestational period	0	5.1 ± 0.2	49.1 ± 1.7	231.8 ± 29.7
Lactational period	0	8.5 ± 0.9	80.2 ± 5.5	384.4 ± 60.0
No. of live offspring	12.2 ± 1.5	13.8 ± 2.3	11.8 ± 1.3	14.0 ± 1.1
Body weight , PD2 (g)				
Males	7.6 ± 0.3	6.6 ± 0.5**	7.3 ± 0.5	5.9 ± 0.6**
Females	7.0 ± 0.4	6.3 ± 0.5	7.1 ± 0.5	5.6 ± 0.6**
AGD, PD2 (mm)				
Males	2.9 ± 0.3	3.1 ± 0.3	3.0 ± 0.3	2.9 ± 0.2
Females	1.0 ± 0.1	1.1 ± 0.1	1.1 ± 0.1	1.1 ± 0.1
Body weight gain (g/day)				
Males				
PD2-PD10	1.4 ± 0.2	1.5 ± 0.2	1.4 ± 0.2	1.1 ± 0.2*
PD10-PD21	3.0 ± 0.2	3.0 ± 0.3	3.1 ± 0.3	3.2 ± 0.4
Females				
PD2-PD10	1.4 ± 0.2	1.5 ± 0.1	1.5 ± 0.1	1.0 ± 0.1**
PD10-PD21	2.8 ± 0.2	3.0 ± 0.2	3.1 ± 0.1	3.0 ± 0.2
Organ weights, prepubertal necropsy				
Males (No. of rats)	5	5	5	5
Body weight (g)	91.9 ± 7.9	83.9 ± 7.8	88.9 ± 3.3	77.9 ± 3.2**
Brain				
Absolute (g)	1.60 ± 0.08	1.56 ± 0.04	1.67 ± 0.07	1.55 ± 0.03
Relative (g/100g BW)	1.74 ± 0.09	1.89 ± 0.14	1.87 ± 0.12	1.99 ± 0.09**
Adrenals				
Absolute (mg)	23.0 ± 1.6	23.0 ± 2.8	22.8 ± 1.6	22.2 ± 6.1
Relative (mg/100g BW)	25.1 ± 2.1	27.4 ± 2.7	25.6 ± 1.8	28.3 ± 6.6
Testes				
Absolute (g)	0.63 ± 0.07	0.57 ± 0.06	0.64 ± 0.09	0.55 ± 0.04*
Relative (g/100g BW)	0.69 ± 0.06	0.68 ± 0.02	0.72 ± 0.10	0.64 ± 0.05
Females (No. of rats)	5	5	5	5
Body weight (g)	82.6 ± 5.4	79.0 ± 3.0	80.3 ± 4.1	70.7 ± 5.5**
Brain				
Absolute (g)	1.54 ± 0.05	1.51 ± 0.03	1.55 ± 0.05	1.46 ± 0.05*
Relative (g/100g BW)	1.87 ± 0.09	1.92 ± 0.09	1.93 ± 0.12	2.07 ± 0.14
Adrenals				
Absolute (mg)	23.2 ± 3.3	19.8 ± 2.9	21.2 ± 2.3	19.6 ± 2.7
Relative (mg/100g BW)	28.0 ± 2.8	25.0 ± 2.9	26.5 ± 3.8	27.9 ± 4.9
Ovaries				
Absolute (mg)	23.2 ± 2.2	20.8 ± 3.3	21.4 ± 2.3	21.2 ± 1.8
Relative (mg/100g BW)	28.2 ± 3.0	26.2 ± 3.1	26.6 ± 2.0	30.1 ± 3.0
Uterus				
Absolute (mg)	62.4 ± 14.1	53.4 ± 13.6	48.8 ± 9.0	55.4 ± 9.5
Relative (mg/100g BW)	75.6 ± 16.3	67.2 ± 14.7	60.6 ± 8.9	79.1 ± 17.8

' Mean ± SD

* $p < 0.05$ compared to controls

** $p < 0.01$ compared to controls

TABLE 14. Data of Bisphenol A Study –From Puberty to Final Necropsy-

	Bisphenol A (ppm)			
	0	60	600	3000
No of rats	8	8	8	8
Body weight gain (g/day)				
Males				
PD21-PD42	7.1 ± 0.1	7.1 ± 0.6	7.6 ± 0.6	6.7 ± 0.5
PD42-PD63	8.5 ± 0.5	8.0 ± 0.6	8.2 ± 0.7	7.7 ± 0.8
PD63-PD77	5.6 ± 0.6	5.4 ± 0.6	5.4 ± 0.8	4.7 ± 0.6
Females				
PD21-PD42	4.9 ± 0.4	4.9 ± 0.4	5.6 ± 0.4	4.7 ± 0.5
PD42-PD63	3.9 ± 0.4	3.6 ± 0.6	4.0 ± 0.5	3.5 ± 0.8
PD63-PD77	2.8 ± 0.5	2.5 ± 0.5	2.7 ± 0.4	2.2 ± 0.6
Onset of puberty				
Vaginal opening				
Age (day)	35.4 ± 2.2	34.9 ± 0.6	34.6 ± 1.4	36.6 ± 1.8
Body weight (g)	121.6 ± 12.9	122.5 ± 7.4	132.6 ± 6.6	122.4 ± 9.3
Preputial separation				
Age (day)	42.0 ± 2.0	40.6 ± 1.9	40.3 ± 2.2	42.0 ± 1.3
Body weight (g)	211.0 ± 25.9	195.5 ± 19.5	207.6 ± 24.1	199.2 ± 24.7
Estrous cyclicity				
Normal	7/8	6/8	8/8	8/8
Irregular	1/8	2/8	0/8	0/8
Extended estrous	0/8	0/8	0/8	0/8
Extended diestrous	1/8	2/8	0/8	0/8
Persistent diestrous	0/8	0/8	0/8	0/8
Organ weights, final necropsy				
Males (No. of rats)	5	5	5	5
Body weight (g)	470.7 ± 25.5	461.7 ± 35.1	466.3 ± 47.8	414.8 ± 37.7
Brain				
Absolute (g)	1.95 ± 0.19	2.02 ± 0.08	2.06 ± 0.06	1.98 ± 0.09
Relative (g/100g BW)	0.42 ± 0.05	0.44 ± 0.03	0.45 ± 0.05	0.48 ± 0.03
Pituitary				
Absolute (mg)	13.2 ± 1.6	13.8 ± 2.5	12.0 ± 1.6	10.6 ± 2.5
Relative (mg/100g BW)	2.82 ± 0.45	3.00 ± 0.55	2.58 ± 0.23	2.54 ± 0.48
Adrenals				
Absolute (mg)	57.6 ± 4.4	53.4 ± 5.0	49.8 ± 6.9	47.8 ± 4.4*
Relative (mg/100g BW)	12.3 ± 1.0	11.6 ± 1.1	10.7 ± 0.8	11.6 ± 1.0
Testes				
Absolute (g)	3.22 ± 0.20	3.34 ± 0.44	3.08 ± 0.17	2.95 ± 0.40
Relative (g/100g BW)	0.69 ± 0.03	0.72 ± 0.09	0.66 ± 0.06	0.71 ± 0.06
Prostate				
Absolute (g)	0.67 ± 0.04	0.64 ± 0.17	0.54 ± 0.05	0.59 ± 0.15
Relative (g/100g BW)	0.14 ± 0.01	0.14 ± 0.03	0.12 ± 0.01	0.14 ± 0.03
Females (No. of rats)	5	5	5	5
Body weight (g)	273.5 ± 14.9	283.9 ± 18.2	288.6 ± 23.6	238.6 ± 29.4
Brain				
Absolute (g)	1.87 ± 0.11	1.92 ± 0.07	1.92 ± 0.02	1.82 ± 0.08
Relative (g/100g BW)	0.48 ± 0.07	0.51 ± 0.04	0.67 ± 0.07	0.69 ± 0.09
Pituitary				
Absolute (mg)	13.0 ± 1.9	14.4 ± 2.1	13.2 ± 2.6	11.4 ± 1.1
Relative (mg/100g BW)	4.76 ± 0.68	5.05 ± 0.43	4.55 ± 0.68	4.79 ± 0.28
Adrenals				
Absolute (mg)	55.4 ± 2.4	60.4 ± 7.4	64.2 ± 1.9	59.8 ± 7.6
Relative (mg/100g BW)	20.3 ± 1.4	21.3 ± 2.2	22.4 ± 2.0	25.4 ± 5.1
Ovaries				
Absolute (mg)	91.0 ± 19.0	94.8 ± 13.3	88.2 ± 8.7	81.8 ± 12.0
Relative (mg/100g BW)	33.2 ± 5.8	33.6 ± 6.0	30.7 ± 3.3	34.6 ± 6.5
Uterus				
Absolute (g)	0.45 ± 0.16	0.51 ± 0.13	0.45 ± 0.03	0.45 ± 0.05
Relative (g/100g BW)	0.17 ± 0.07	0.18 ± 0.04	0.16 ± 0.02	0.19 ± 0.03

Mean ± SD, * $p < 0.05$ compared to controls, ** $p < 0.01$ compared to controls

TABLE 15. Histopathological Findings in Endocrine/Reproductive Organs at 11 weeks in Bisphenol A Study

	Bisphenol A (ppm)			
	0	20	200	1000
Males (No. of rats examined)	(5)	(5)	(5)	(5)
No abnormalities	5	5	5	5
Females (No. of rats examined)	(5)	(5)	(5)	(5)
No abnormalities	5	5	5	5

[a] Grade of the findings; ±, very slight; and +, slight

[b] Total No. of animals with each finding

[c] No. of animals in each grade

* Composed mainly of primary and secondary follicles

TABLE 16. Data of Tamoxifen Study -From Birth to Prepubertal Necropsy-

	Tamoxifen (ppm)			
	0	0.005	0.05	0.25
No. of dams	6	6	6	9
Maternal body weight gain (g/day)				
Gestational period	13.9 ± 1.4	13.1 ± 1.1	12.9 ± 2.3	12.3 ± 2.3
Lactational period	6.2 ± 2.0	7.9 ± 1.8	8.7 ± 2.6	4.8 ± 2.2
Maternal food consumption (g/day)				
Gestational period	26.6 ± 3.3	26.4 ± 1.6	26.4 ± 1.0	27.8 ± 1.4
Lactational period	46.8 ± 3.7	51.6 ± 3.7	51.2 ± 4.1	44.3 ± 7.7
Calculated maternal intake (μ g/kg/day)				
Gestational period	0	0.4 ± 0.2	3.8 ± 0.3	20.5 ± 1.8
Lactational period	0	0.8 ± 0.4	8.0 ± 0.7	34.8 ± 6.9
No. of live offspring	13.2 ± 1.0	13.7 ± 0.8	13.3 ± 2.1	10.4 ± 4.1
Body weight , PD2 (g)				
Males	7.3 ± 0.5	6.8 ± 0.7	7.0 ± 1.1	8.4 ± 1.3
Females	7.1 ± 0.5	6.3 ± 0.7	6.6 ± 1.0	7.9 ± 1.2
AGD, PD2 (mm)				
Males	2.9 ± 0.2	2.9 ± 0.2	3.0 ± 0.5	3.1 ± 0.3
Females	1.1 ± 0.1	1.1 ± 0.1	1.1 ± 0.1	1.1 ± 0.2
Body weight gain (g/day)				
Males				
PD2-PD10	1.6 ± 0.2	1.6 ± 0.2	1.6 ± 0.3	1.6 ± 0.4
PD10-PD21	2.5 ± 0.3	2.6 ± 0.2	2.4 ± 0.3	2.4 ± 0.8
Females				
PD2-PD10	1.7 ± 0.2	1.6 ± 0.2	1.6 ± 0.2	1.6 ± 0.4
PD10-PD21	2.5 ± 0.4	2.5 ± 0.2	2.4 ± 0.3	2.3 ± 0.3
Organ weights, prepubertal necropsy				
Males (No. of rats)	5	5	5	5
Body weight (g)	80.3 ± 9.1	78.3 ± 9.4	75.2 ± 5.1	77.5 ± 3.97
Brain				
Absolute (g)	1.57 ± 0.09	1.57 ± 0.10	1.54 ± 0.07	1.66 ± 0.07
Relative (g/100g BW)	1.97 ± 0.13	2.03 ± 0.22	2.05 ± 0.16	2.14 ± 0.06
Adrenals				
Absolute (mg)	21.4 ± 5.0	20.8 ± 4.0	19.4 ± 4.3	22.6 ± 3.9
Relative (mg/100g BW)	26.6 ± 5.8	26.4 ± 2.6	26.0 ± 6.6	29.0 ± 4.1
Testes				
Absolute (g)	0.50 ± 0.09	0.51 ± 0.04	0.45 ± 0.06	0.49 ± 0.04
Relative (g/100g BW)	0.62 ± 0.05	0.66 ± 0.06	0.60 ± 0.08	0.63 ± 0.05
Females (No. of rats)	5	5	5	5
Body weight (g)	74.5 ± 6.7	70.4 ± 2.7	72.4 ± 7.0	71.2 ± 2.7
Brain				
Absolute (g)	1.48 ± 0.05	1.53 ± 0.06	1.47 ± 0.07	1.49 ± 0.07
Relative (g/100g BW)	1.99 ± 0.16	2.17 ± 0.09	2.05 ± 0.16	2.10 ± 0.16
Adrenals				
Absolute (mg)	19.4 ± 0.5	19.4 ± 1.9	18.8 ± 3.0	18.6 ± 0.5
Relative (mg/100g BW)	26.2 ± 2.3	27.6 ± 3.1	26.0 ± 3.9	26.2 ± 1.3
Ovaries				
Absolute (mg)	22.0 ± 6.6	20.6 ± 2.5	19.0 ± 4.2	18.8 ± 1.1
Relative (mg/100g BW)	29.9 ± 6.7	29.2 ± 2.6	26.3 ± 5.7	26.4 ± 1.5
Uterus				
Absolute (mg)	62.8 ± 4.7	62.8 ± 10.7	56.8 ± 8.5	56.4 ± 17.2
Relative (mg/100g BW)	85.2 ± 13.2	88.9 ± 12.4	78.8 ± 12.4	79.1 ± 22.8

* Mean ± SD

* $p < 0.05$ compared to controls

** $p < 0.01$ compared to controls

TABLE 17. Data of Tamoxifen Study –From Puberty to Final Necropsy-

	Tamoxifen (ppm)			
	0	0.005	0.05	0.25
No of rats	8	8	8	8
Body weight gain (g/day)				
Males				
PD28-PD42	9.2 ± 0.8	9.6 ± 0.9	8.5 ± 0.9	8.9 ± 1.2
PD42-PD77	7.3 ± 0.8	7.1 ± 1.4	7.1 ± 0.6	6.9 ± 1.1
Females				
PD28-PD42	3.0 ± 0.3	2.8 ± 0.4	2.7 ± 0.2	2.9 ± 0.4
PD42-PD77	3.2 ± 0.4	3.3 ± 0.5	3.4 ± 0.4	3.5 ± 0.6
Onset of puberty				
Vaginal opening				
Age (day)	34.1 ± 1.2	33.5 ± 0.9	34.5 ± 1.1	33.6 ± 0.9
Body weight (g)	132.6 ± 14.4	117.3 ± 3.6	116.3 ± 10.9	123.2 ± 16.4
Preputial separation				
Age (day)	40.9 ± 0.8	41.3 ± 1.5	41.8 ± 1.2	40.9 ± 1.5
Body weight (g)	197.2 ± 13.7	208.9 ± 22.8	191.5 ± 16.0	206.6 ± 23.8
Estrous cyclicity				
Normal	8/8	7/8	8/8	7/8
Irregular	0/8	1/8	0/8	1/8
Extended estrous	0/8	0/8	0/8	0/8
Extended diestrous	0/8	1/8	0/8	1/8
Persistent diestrous	0/8	0/8	0/8	0/8
Organ weights, final necropsy				
Males (No. of rats)	5	5	5	5
Body weight (g)	467.9 ± 51.0	456.8 ± 63.2	458.5 ± 37.1	449.2 ± 66.5
Brain				
Absolute (g)	2.05 ± 0.05	2.06 ± 0.13	2.05 ± 0.10	2.12 ± 0.05
Relative (g/100g BW)	0.44 ± 0.04	0.46 ± 0.04	0.45 ± 0.02	0.48 ± 0.07
Pituitary				
Absolute (mg)	11.0 ± 2.9	13.0 ± 2.0	10.8 ± 1.1	13.0 ± 3.7
Relative (mg/100g BW)	2.33 ± 0.50	2.85 ± 0.20	2.37 ± 0.29	2.85 ± 0.42
Adrenals				
Absolute (mg)	49.0 ± 8.0	57.8 ± 10.3	49.2 ± 2.9	52.2 ± 8.4
Relative (mg/100g BW)	10.4 ± 0.9	12.7 ± 1.7	10.8 ± 1.1	11.7 ± 1.2
Testes				
Absolute (g)	3.17 ± 0.29	3.31 ± 0.26	3.19 ± 0.41	3.23 ± 0.31
Relative (g/100g BW)	0.68 ± 0.02	0.73 ± 0.11	0.70 ± 0.07	0.73 ± 0.11
Prostate				
Absolute (g)	0.47 ± 0.09	0.53 ± 0.13	0.53 ± 0.12	0.58 ± 0.05
Relative (g/100g BW)	0.10 ± 0.01	0.12 ± 0.03	0.11 ± 0.03	0.12 ± 0.02
Females (No. of rats)	5	5	5	8
Body weight (g)	293.4 ± 37.2	291.0 ± 29.6	282.6 ± 22.1	286.9 ± 42.7
Brain				
Absolute (g)	2.00 ± 0.07	1.99 ± 0.18	1.93 ± 0.09	1.95 ± 0.06
Relative (g/100g BW)	0.69 ± 0.07	0.68 ± 0.10	0.68 ± 0.06	0.66 ± 0.11
Pituitary				
Absolute (mg)	13.8 ± 1.6	14.6 ± 2.1	14.2 ± 1.3	15.0 ± 2.1
Relative (mg/100g BW)	4.74 ± 0.64	5.02 ± 0.54	5.07 ± 0.77	5.27 ± 0.81
Adrenals				
Absolute (mg)	62.6 ± 13.2	68.0 ± 6.2	64.2 ± 8.1	70.4 ± 12.0
Relative (mg/100g BW)	21.3 ± 2.7	23.5 ± 2.4	22.7 ± 2.1	24.7 ± 3.9
Ovaries				
Absolute (mg)	88.2 ± 13.7	100.2 ± 16.9	85.2 ± 4.4	108.6 ± 12.7
Relative (mg/100g BW)	30.1 ± 3.0	35.0 ± 8.3	30.3 ± 2.6	38.1 ± 3.2
Uterus				
Absolute (g)	0.46 ± 0.05	0.51 ± 0.08	0.47 ± 0.07	0.45 ± 0.06
Relative (g/100g BW)	0.16 ± 0.02	0.18 ± 0.02	0.17 ± 0.03	0.16 ± 0.02

' Mean ± SD, * $p < 0.05$ compared to controls, ** $p < 0.01$ compared to controls

TABLE 18. Histopathological Findings in Endocrine/Reproductive Organs at 11 weeks in Tamoxifen Study

	Tamoxifen (ppm)			
	0	0.005	0.05	0.25
	0	20	200	1000
Males (No. of rats examined)	(5)	(5)	(5)	(5)
No abnormalities	5	5	5	5
Females (No. of rats examined)	(5)	(5)	(5)	(5)
No abnormalities	5	5	5	5

[a] Grade of the findings; ±, very slight; and +, slight

[b] Total No. of animals with each finding

[c] No. of animals in each grade

* Composed mainly of primary and secondary follicles

TABLE 19. Formulations of Soybean/alfalfa-free Diet

Ingredients	Percentage by weight
Fish meal (60% protein)	14.00
Corn gluten meal (60% protein)	8.00
Ground corn	28.50
Ground wheat	30.62
Wheat middlings	10.00
Brewer dried yeast	2.00
Dry molasses	0.75
Corn oil	2.50
Mineral/Vitamin mixture	3.63

Note. Information provided by the supplier (Oriental Yeast Co Ltd., Tokyo, Japan)

	CRF-1	SF-NIH07	
Ingredients (% by weight)		Ground corn	30.0
		Ground wheat	30.0
		Wheat middlings	12.0
		Fish meal (60% protein)	10.0
		Dried skim milk	5.0
		Lucerne meal	4.0
		Corn gluten meal (60% protein)	3.0
		Brewer dried yeast	2.0
		Dry molasses	0.7
		Corn oil	1.0
		Mineral/Vitamin mixture	2.3
Nutrient standards (%)			
Crude protein	23.1	23.5	
Crude fat	5.9	5.0	
Crude ash	6.5	6.8	
Crude fiber	3.3	3.4	
Phytoestrogen contents (mg/ 100 g)			
Genistin	10.2	< 0.05	
Daidzin	8.7	< 0.05	
Coumestrol	N.R.	0.3	

TABLE 20. Effects of Diets on Perinatal Exposure to Ethinylestradiol -Effects on dams-

	CRF-1		SAF-NIH	
	control	EE (0.5 ppm)	control	EE (0.5 ppm)
No. of dams	7	7	7	7
Calculated EE intake (μg/kg/day)				
GD15-GD20	0	28.5 ± 2.8	0	28.1 ± 4.1
PD2-PD10	0	62.0 ± 10.4	0	66.6 ± 10.5
Body weight gain (g/day)				
GD15-GD20	14.9 ± 0.9 [1]	9.5 ± 1.7**	13.6 ± 2.0	7.5 ± 2.4##
PD2-PD10	3.2 ± 0.7	2.8 ± 2.7	4.8 ± 2.0	3.9 ± 2.8
Food consumption (g/day)				
GD15-GD20	26.6 ± 0.9	19.6 ± 1.7**	25.7 ± 2.5	19.0 ± 3.0##
PD2-PD10	46.2 ± 6.8	39.4 ± 5.7	50.7 ± 4.0	41.1 ± 8.3#

[1] Mean ± SD

*, ** $p < 0.05$ or $p < 0.01$, respectively compared to control (CRF-1)

#, ## $p < 0.05$ or $p < 0.01$, respectively compared to control (SAF-NIH)

TABLE 21. Effects of Diets on Perinatal Exposure to Ethinylestradiol -From Birth to Prepubertal Necropsy-

	CRF-1		SAF-NIH	
	control	EE (0.5 ppm)	control	EE (0.5 ppm)
No. of litters	7	7	7	7
Litter size	12.9 ± 1.2[a]	12.1 ± 2.3	13.0 ± 0.8	12.7 ± 0.8
Body weight , PD2 (g)				
Males	8.4 ± 0.6	7.7 ± 1.1	7.8 ± 1.0	6.6 ± 0.2#
Females	7.9 ± 0.5	7.3 ± 1.2	7.4 ± 0.8	6.4 ± 0.3#
AGD, PD2				
Males				
Absolute (mm)	3.2 ± 0.3	3.1 ± 0.4	3.2 ± 0.3	2.9 ± 0.1#
Relative (mm/g BW)	0.38 ± 0.02	0.41 ± 0.05	0.42 ± 0.03*	0.45 ± 0.02
Females				
Absolute (mm)	1.1 ± 0.1	1.1 ± 0.1	1.2 ± 0.1	1.1 ± 0.1
Relative (mm/g BW)	0.14 ± 0.02	0.15 ± 0.02	0.16 ± 0.01*	0.17 ± 0.01
Body weight gain (g/day)				
Males				
PD2-PD10	1.8 ± 0.5	1.3 ± 0.3	1.7 ± 0.3	1.2 ± 0.3#
PD10-PD21	3.5 ± 0.4	3.1 ± 0.1	2.8 ± 0.3*	2.7 ± 0.3
Females				
PD2-PD10	1.8 ± 0.4	1.3 ± 0.3*	1.8 ± 0.2	1.0 ± 0.3##
PD10-PD21	3.4 ± 0.3	3.1 ± 0.1*	2.7 ± 0.2**	2.7 ± 0.3
Organ weights, prepubertal necropsy				
Males (No. of rats)	5	5	5	5
Body weight (g)	61.4 ± 5.2	53.1 ± 5.9*	58.8 ± 4.3	46.8 ± 1.9##
Adrenals				
Absolute (mg)	19.6 ± 3.8	16.0 ± 3.4	18.6 ± 3.6	14.8 ± 1.1
Relative (mg/100g BW)	31.9 ± 4.8	30.1 ± 5.4	31.4 ± 4.3	31.7 ± 2.6
Testes				
Absolute (g)	0.28 ± 0.02	0.22 ± 0.04*	0.26 ± 0.03	0.20 ± 0.02##
Relative (g/100g BW)	0.45 ± 0.03	0.41 ± 0.04	0.45 ± 0.03	0.42 ± 0.05
Females (No. of rats)	5	5	5	5
Body weight (g)	58.7 ± 5.4	53.2 ± 4.0	56.4 ± 2.9	46.6 ± 2.4##
Adrenals				
Absolute (mg)	16.6 ± 2.7	14.2 ± 2.3	17.4 ± 2.1	14.2 ± 1.6#
Relative (mg/100g BW)	28.3 ± 4.1	26.7 ± 3.4	30.9 ± 4.4	30.4 ± 2.4
Ovaries				
Absolute (mg)	16.0 ± 3.7	10.4 ± 1.5*	18.0 ± 1.6	12.6 ± 2.1##
Relative (mg/100g BW)	27.5 ± 6.9	19.5 ± 1.8*	31.9 ± 3.1	27.1 ± 4.2
Uterus				
Absolute (mg)	36.4 ± 5.9	35.2 ± 3.8	34.2 ± 5.6	33.4 ± 5.5
Relative (mg/100g BW)	62.1 ± 10.2	66.5 ± 8.9	60.5 ± 7.5	71.4 ± 9.2

[a] Mean ± SD

[b] Data were expressed as mean ± SD of litters or individual offspring during lactational period or after weaning, respectively

*, ** $p < 0.05$ or $p < 0.01$, respectively compared to control (CRF-1)

#, ## $p < 0.05$ or $p < 0.01$, respectively compared to control (SAF-NIH)

TABLE 22. Effects of Diets on Perinatal Exposure to Ethinylestradiol –From Puberty to Final Necropsy

	CRF-1		SAF-NIH	
	control	EE (0.5 ppm)	control	EE (0.5 ppm)
No of rats	8	8	8	8
Body weight gain (g/day)				
Males				
PD21-PD42	7.8 ± 0.8 [a]	7.7 ± 0.6	7.9 ± 0.5	6.8 ± 0.4##
PD42-PD63	8.6 ± 0.8	8.4 ± 0.9	8.5 ± 0.8	7.8 ± 0.5
PD63-PD77	5.8 ± 0.7	5.3 ± 0.7	5.6 ± 0.8	5.5 ± 0.6
Females				
PD21-PD42	5.6 ± 0.5	5.5 ± 0.5	5.8 ± 0.5	5.5 ± 0.4
PD42-PD63	3.9 ± 0.4	3.6 ± 0.6	4.1 ± 0.5	4.0 ± 0.6
PD63-PD77	2.8 ± 0.4	2.3 ± 0.6*	2.9 ± 0.5	2.4 ± 0.6
Onset of puberty				
Vaginal opening				
Age (day)	32.6 ± 1.5	27.1 ± 4.2**	30.6 ± 1.9*	30.5 ± 4.2
Body weight (g)	127.4 ± 11.6	81.1 ± 21.2**	111.9 ± 10.6*	97.2 ± 23.0
Preputial separation				
Age (day)	39.3 ± 1.4	40.5 ± 1.6	38.1 ± 1.3	41.0 ± 1.1##
Body weight (g)	209.2 ± 11.0	209.2 ± 23.4	198.1 ± 16.6	193.6 ± 12.1
Estrous cyclicity				
Normal	8/8	0/8	7/8	3/8
Irregular	0/8	8/8	1/8	5/8
Extended diestrous	0/8	0/8	0/8	3/8
Persistent estrous	0/8	6/8	0/8	1/8
Persistent diestrous	0/8	1/8	1/8	0/8
Mixture	0/8	1/8	0/8	1/8
Organ weights, final necropsy				
Males				
Body weight (g)	483.7 ± 46.3	465.7 ± 30.8	482.1 ± 28.9	431.3 ± 24.6##
Pituitary				
Absolute (mg)	13.5 ± 2.4	13.6 ± 1.5	14.5 ± 1.9	15.1 ± 2.4
Relative (mg/100g BW)	2.79 ± 0.41	2.94 ± 0.42	3.04 ± 0.61	3.49 ± 0.44
Adrenals				
Absolute (mg)	50.5 ± 6.3	51.4 ± 7.2	57.0 ± 8.1	58.3 ± 6.8
Relative (mg/100g BW)	10.5 ± 1.2	11.1 ± 1.7	11.8 ± 1.7	13.5 ± 1.3#
Testes				
Absolute (g)	3.26 ± 0.24	3.24 ± 0.24	3.37 ± 0.25	3.24 ± 0.22
Relative (g/100g BW)	0.68 ± 0.05	0.70 ± 0.05	0.70 ± 0.07	0.75 ± 0.05
Epidydimis				
Absolute (g)	1.02 ± 0.06	1.02 ± 0.07	1.04 ± 0.07	1.00 ± 0.08
Relative (g/100g BW)	0.21 ± 0.01	0.22 ± 0.01	0.22 ± 0.02	0.23 ± 0.01
Prostate				
Absolute (g)	0.60 ± 0.13	0.59 ± 0.16	0.65 ± 0.09	0.61 ± 0.13
Relative (g/100g BW)	0.12 ± 0.02	0.13 ± 0.03	0.13 ± 0.02	0.12 ± 0.06
Females				
Body weight (g)	298.3 ± 17.3	271.7 ± 23.6*	304.1 ± 21.7	277.3 ± 25.9#
Pituitary				
Absolute (mg)	17.3 ± 3.0	24.4 ± 6.5*	16.4 ± 1.7	18.5 ± 2.4
Relative (mg/100g BW)	5.76 ± 0.79	9.05 ± 2.51**	5.41 ± 0.67	6.73 ± 1.11#
Adrenals				
Absolute (mg)	68.8 ± 17.3	72.9 ± 10.0	62.8 ± 5.4	71.1 ± 9.4#
Relative (mg/100g BW)	22.9 ± 4.9	27.0 ± 3.9	20.7 ± 1.9	25.8 ± 3.6##
Ovaries				
Absolute (mg)	90.8 ± 9.6	61.1 ± 15.8**	95.4 ± 18.5	100.6 ± 25.8
Relative (mg/100g BW)	30.4 ± 1.9	22.5 ± 5.4**	31.4 ± 6.1	36.0 ± 47.6
Uterus				
Absolute (g)	0.43 ± 0.04	0.45 ± 0.08	0.44 ± 0.05	0.41 ± 0.05
Relative (g/100g BW)	0.15 ± 0.01	0.17 ± 0.03	0.14 ± 0.01	0.15 ± 0.03

[a] Mean ± SD

*, ** $p < 0.05$ or $p < 0.01$, respectively, compared to control (CRF-1)

#, ## $p < 0.05$ or $p < 0.01$, respectively, compared to control (SAF-NIH)

TABLE 23. Effects of Diets on Perinatal Exposure to Ethinylestradiol
-Histopathological Assessment of Endocrine/Reproductive Organs at 11 Weeks of Age-

	CRF-1		SAF-NIH	
	control	EE (0.5 ppm)	control	EE (0.5 ppm)
Males (No. of rats examined)	(5)	(5)	(5)	(5)
No abnormalities	5	5	5	5
Females (No. of rats examined)	(8)	(8)	(8)	(8)
Ovary				
- Multiple follicular cysts (±/+/++/+++) [a]	0	8 [b] (0/1/0/7) [c]	0	3 (0/2/0/1)
Uterus				
- Endometrial hyperplasia (++/+++)	0	7 (3/4)	0	2 (0/2)
- Squamous metaplasia, endometrium (++/+++)	0	4 (3/1 [d])	0	1 (0/1)
Vagina				
- Estrous	0	8	0	1
- Diestrous	8	0	8	6
- Mucosal degeneration associated with scattered keratinization of epithelia (+)	0	0	0	1 (1)
Mammary gland				
- Acinar hyperplasia (+/++/+++)	0	8 (1/6/1)	1 (1/0/0)	4 (3/1/0)
Adrenal				
- Diffuse hyperplasia, cortex (±/+)	0	1 (0/1)	0	0
Pituitary				
- Diffuse hyperplasia, anterior lobe (+/++/+++)	0	8 (0/2/6)	0	3 (1/2/0)

[a] Grade of the findings; ±, very slight; +, slight; ++, moderate; and +++, severe

[b] Total No. of animals with each finding

[c] No. of animals in each grade

[d] Mucosal epithelia were entirely replaced by squamous cells and therefore, the grade of endometrial hyperplasia could not be estimated in this case

Table 24. Summary of perinatal exposure effects of MXC, DINP, Gen, BA, NP or Tam to the offsprings.

Chemical	Dietary dose (ppm)	PND10	Week 3		Age at puberty	Estrous cyclicity	Week 11			
		Gene expression in SDN-POA	Pituitary immuno-histochemistry	BW and organ weight			BW and organ weight	Histopathology	Pituitary immuno-histochemistry	Size of SDN-POA
MXC	24								♀: PRL ↑	
	240									
	1200	♂: GAT-1(↓)	♂: LH ↓, FSH ↓, PRL ↓; ♀: LH ↓	♂, ♀: BW gain ↓; ♂: Testes ↓	♂:delayed; ♀:facilitated	Extended estrous or diestrous	♀: Ovary ↓	Mutliple follicular cysts/ovary; Endometrial hyperplasia/uterus; Diffuse hyperplasia/antrerior pituitary, etc.	♀: FSH ↑, PRL ↑	
DINP	400									
	4000			♂: BW ↓						
	20000			♂, ♀: BW gain ↓, BW ↓; ♂: Testes ↓				Degeneration/dividing spermatocyte, stage XIV; Vacuolar degeneration/Sertoli cells		
Gen	20, 200									
	1000									
NP	60, 600									
	3000									
BA	60, 600									
	3000			♂, ♀: BW gain ↓, BW ↓						
Tam	0.02, 0.2, 1.0									
EE	0.5	♂, ♀: GAT-1 ↓	♀: PRL ↑	♂, ♀: BW ↓	♂: delayed	Persistent estrous/ extended diestrous	♀: Pituitary ↑, ovary ↓, uterus ↑	Mutliple follicular cysts/ovary; Endometrial hyperplasia/uterus; Diffuse hyperplasia/antrerior pituitary, etc.		♂: size ↓

: No obvious change was observed.

: Not examined.