

Table 56

Two generation reproductive toxicity study of NP by oral administration in rats
 Water multiple T-maze test in F1 females; Mean \pm S.D. (N)

Compound	Nonylphenol				
	0 ^a	2	10	50	
<u>The first day</u>					
1st trial	55 \pm 20 13 \pm 6	(28) 55 \pm 13 12 \pm 4	(18) 76 \pm 34 18 \pm 9	(21) 80 \pm 35 * 17 \pm 8	(20)
2nd trial	56 \pm 37 12 \pm 10	(26) 84 \pm 49 17 \pm 11	(18) 60 \pm 28 14 \pm 6	(21) 57 \pm 29 12 \pm 6	(21)
3rd trial	50 \pm 37 10 \pm 9	(29) 58 \pm 33 10 \pm 7	(18) 42 \pm 26 9 \pm 7	(24) 40 \pm 31 8 \pm 7	(21)
<u>The second day</u>					
1st trial	37 \pm 19 8 \pm 6	(26) 44 \pm 33 8 \pm 9	(20) 54 \pm 40 12 \pm 13	(24) 40 \pm 25 7 \pm 6	(22)
2nd trial	33 \pm 19 6 \pm 6	(29) 30 \pm 19 6 \pm 5	(19) 30 \pm 29 6 \pm 11	(25) 25 \pm 15 4 \pm 5	(23)
3rd trial	24 \pm 20 4 \pm 5	(29) 27 \pm 25 4 \pm 5	(20) 19 \pm 16 3 \pm 5	(25) 21 \pm 15 3 \pm 5	(23)
<u>The third day</u>					
1st trial	35 \pm 33 7 \pm 10	(29) 33 \pm 34 4 \pm 5	(20) 17 \pm 11 * 2 \pm 4	(24) 19 \pm 13 3 \pm 4	(23)
2nd trial	17 \pm 9 2 \pm 2	(29) 23 \pm 19 2 \pm 4	(20) 18 \pm 23 2 \pm 4	(25) 12 \pm 4 1 \pm 2	(23)
3rd trial	15 \pm 6 1 \pm 2	(29) 18 \pm 8 2 \pm 3	(20) 14 \pm 7 1 \pm 2	(25) 13 \pm 6 1 \pm 2	(23)

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

*: significant difference from control, p<0.05

Table 57

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

Spontaneous motor activity test of F1 males; Mean ± S.D. (N)

Compound	Nonylphenol			
	0 ^a	2	10	50
Wheel cage activity (count/24hours)	1881 ± 681 (29)	1501 ± 666 (20)	1752 ± 486 (25)	1963 ± 616 (23)

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

Table 58

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

Spontaneous motor activity test of F1 females; Mean \pm S.D. (N)

Compound	Nonylphenol			
	0 ^a	2	10	50
Wheel cage activity (count/24hours)	3798 \pm 1592 (29)	4540 \pm 1387 (20)	3935 \pm 1621 (25)	3856 \pm 1466 (23)

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

Table 59

Two generation reproductive toxicity study of NP by oral administration in rats
Organ weight of F1 males at 10 weeks of age; Mean \pm S.D. (N)

Compound	Nonylphenol				
	0 ^a	2	10	50	
Dose (mg/kg)					
Terminal body weight (g)	417.6 \pm 29.7 (29)	418.8 \pm 28.4 (20)	435.5 \pm 39.9 (25)	425.2 \pm 40.9 (23)	
Testes (g)	3.32 \pm 0.24 b (29) 0.80 \pm 0.08 c (29)	3.15 \pm 0.71 (20) 0.75 \pm 0.17 (20)	3.30 \pm 0.23 (25) 0.76 \pm 0.06 (25)	3.22 \pm 0.25 (23) 0.76 \pm 0.09 (23)	
Epididymides (g)	0.93 \pm 0.09 (29) 0.22 \pm 0.02 (29)	0.93 \pm 0.09 (20) 0.22 \pm 0.02 (20)	0.97 \pm 0.08 (25) 0.22 \pm 0.02 (25)	0.93 \pm 0.08 (23) 0.22 \pm 0.02 (23)	
Prostate glands (g)	0.50 \pm 0.11 (29) 0.12 \pm 0.03 (29)	0.47 \pm 0.09 (20) 0.11 \pm 0.03 (20)	0.49 \pm 0.11 (25) 0.11 \pm 0.02 (25)	0.48 \pm 0.10 (23) 0.11 \pm 0.02 (23)	
Seminal vesicle (g)	1.30 \pm 0.23 (29) 0.31 \pm 0.05 (29)	1.24 \pm 0.18 (20) 0.30 \pm 0.04 (20)	1.29 \pm 0.31 (25) 0.30 \pm 0.07 (25)	1.28 \pm 0.22 (23) 0.30 \pm 0.05 (23)	

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

b: absolute weight

c: relative weight (g per 100g body weight)

Two generation reproductive toxicity study of NP by oral administration in rats
 Organ weight of F1 females at 10 weeks of age; Mean \pm S.D. (N)

Compound	Nonylphenol				
	0 ^a	2	10	50	
Terminal body weight (g)	265.9 \pm 22.6 (29)	254.5 \pm 23.4 (20)	269.8 \pm 21.6 (25)	263.9 \pm 24.3 (23)	
Uterus (g)	0.44 \pm 0.14 b (29) 0.17 \pm 0.05 c (29)	0.47 \pm 0.14 (20) 0.18 \pm 0.05 (20)	0.49 \pm 0.16 (25) 0.18 \pm 0.06 (25)	0.44 \pm 0.17 (23) 0.17 \pm 0.07 (23)	
Uterus (diestrus) (g)	0.40 \pm 0.09 (18) 0.15 \pm 0.04 (18)	0.43 \pm 0.13 (9) 0.17 \pm 0.05 (9)	0.39 \pm 0.09 (12) 0.14 \pm 0.04 (12)	0.37 \pm 0.10 (16) 0.14 \pm 0.04 (16)	
Uterus (proestrus) (g)	0.79 \pm 0.08 (3) 0.29 \pm 0.02 (3)	0.62 \pm 0.28 (3) 0.24 \pm 0.10 (3)	0.67 \pm 0.12 (8) 0.26 \pm 0.04 (8)	0.68 \pm 0.17 (5) 0.26 \pm 0.06 (5)	
Uterus (estrus) (g)	0.41 \pm 0.03 (8) 0.16 \pm 0.01 (8)	0.44 \pm 0.05 (8) 0.18 \pm 0.03 (8)	0.40 \pm 0.05 (5) 0.16 \pm 0.02 (5)	0.44 (2) 0.17 (2)	
Ovaries (mg)	96.1 \pm 21.3 (29) 36.4 \pm 8.3 (29)	96.2 \pm 13.3 (20) 37.9 \pm 5.3 (20)	98.5 \pm 17.1 (25) 36.6 \pm 6.2 (25)	93.7 \pm 17.4 (23) 35.5 \pm 6.2 (23)	

a: vehicle control, corn oil (2 mL/kg)
 b: absolute weight
 c: relative weight (g or mg per 100g body weight)

Table 61

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

Macroscopic findings of F1 males at 10 weeks of age

Compound	Nonylphenol			
	0 ^a	2	10	50
Dose (mg/kg)				
Number of F1 males examined	29	19	25	23
Number of F1 males showing abnormalities	1	2	1	0
Types and number				
Dilatation of renal pelvis	1	1	1	0
Pale color of spleen	0	1	0	0

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

Table 62

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

Macroscopic findings of F1 females at 10 weeks of age

Compound	Nonylphenol			
Dose (mg/kg)	0 ^a	2	10	50
Number of F1 females examined	29	19	25	23
Number of F1 females showing abnormalities	2	2	0	0
Types and number				
Dilatation of renal pelvis	2	1	0	0
Pale color and nodule in spleen	0	1	0	0

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

Table 63

Two generation reproductive toxicity study of NP by oral administration in rats
 Estrous cycle of F1 females

Compound	Nonylphenol				
	0 ^a	2	10	25	50
Dose (mg/kg)					
Number of females examined	30	21	25	25	23
Mean length of estrous cycle in days	4.3 ± 0.6	4.1 ± 0.3	4.1 ± 0.3	4.1 ± 0.3	4.3 ± 0.6
Number of animals showing each type of cycle during pre-mating period					
4-day cycle	21	18	21	21	15
5-day cycle	2	1	0	0	1
4/5-day cycle	2	0	1	1	3
Monoestrus	2	1	1	1	2
Irregular	3	1	2	2	2
Number of vaginal estrus during mating period	1.1 ± 0.4	1.0 ± 0.2	1.1 ± 0.4	1.1 ± 0.4	1.1 ± 0.3
Mean±S.D.					

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

Table 64

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

Reproductive performance of F1 animals

Compound	Nonylphenol			
	0 ^a	2	10	50
Dose (mg/kg)				
Number of pairs examined (A)	30	21	25	23
Number of pairs successful copulation (B)	29	21	21	22
Copulation index [(B/A)×100,%]	96.7	100.0	84.0	95.7
Number of pregnant females (C)	23	18	19	19
Fertility index [(C/B)×100,%]	79.3	85.7	90.5	86.4
Pairing days until copulation	3.8 ± 2.6	2.8 ± 1.4	2.7 ± 2.1	2.7 ± 1.4
Mean ± S.D.				

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

Table 65

Two generation reproductive toxicity study of NP by oral administration in rats
 Body weight of F1 dams during gestation period; Mean±S.D. (N)

Compound	Nonylphenol			
	0 ^a	2	10	50
Days of gestation				
0	299.9 ± 34.1 (23)	291.5 ± 22.5 (18)	304.0 ± 26.9 (19)	286.7 ± 26.8 (19)
7	327.1 ± 33.9 (23)	320.2 ± 25.0 (18)	329.7 ± 28.1 (19)	309.0 ± 30.0 (19)
14	361.2 ± 35.1 (23)	354.0 ± 30.7 (18)	362.2 ± 30.3 (19)	337.9 ± 34.9 (19)
20	435.2 ± 35.3 (23)	420.7 ± 57.3 (18)	429.8 ± 44.7 (19)	407.6 ± 37.3 * (19)

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

*: significant difference from control, p<0.05

Table 66

Two generation reproductive toxicity study of NP by oral administration in rats
 Body weight gain of F1 dams during gestation period; Mean±S.D. (N)

Compound	Nonylphenol				
	0 ^a	2	10	50	
Days of gestation					
0~7	27.3 ± 6.2 (23)	29.2 ± 6.3 (18)	25.8 ± 9.2 (19)	24.2 ± 11.1 (19)	
0~14	61.3 ± 8.6 (23)	66.4 ± 9.3 (18)	60.8 ± 7.3 (19)	56.8 ± 13.0 (19)	
0~20	135.3 ± 14.6 (23)	145.4 ± 16.9 (18)	135.2 ± 14.6 (19)	118.6 ± 27.9 (19)	

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

Table 67

Two generation reproductive toxicity study of NP by oral administration in rats
 Body weight of F1 dams during lactation period; Mean±S.D. (N)

Compound	Nonylphenol				
	0 ^a	2	10	50	
Days of lactation					
0	338.5 ± 39.6 (23)	332.2 ± 26.3 (18)	345.7 ± 35.8 (19)	332.4 ± 35.6 (19)	
4	342.8 ± 36.2 (23)	340.9 ± 25.2 (18)	352.6 ± 25.4 (19)	335.1 ± 27.1 (19)	
7	349.2 ± 31.9 (23)	350.4 ± 21.3 (17)	359.0 ± 24.6 (19)	345.5 ± 27.7 (19)	
14	366.5 ± 29.9 (23)	371.5 ± 21.1 (17)	380.9 ± 27.6 (19)	364.9 ± 32.3 (19)	
21	351.6 ± 29.3 (23)	349.5 ± 19.0 (17)	364.1 ± 22.9 (19)	358.4 ± 31.1 (19)	

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

Table 68

Two generation reproductive toxicity study of NP by oral administration in rats
 Body weight gain of F1 dams during lactation period; Mean±S.D. (N)

Compound	Nonylphenol			
	0 ^a	2	10	50
Days of lactation				
0~4	4.3 ± 15.3 (23)	8.7 ± 19.6 (18)	6.9 ± 15.4 (19)	2.7 ± 18.8 (19)
0~7	10.6 ± 16.8 (23)	18.4 ± 14.9 (17)	13.2 ± 19.2 (19)	13.1 ± 17.9 (19)
0~14	28.0 ± 20.5 (23)	39.6 ± 19.5 (17)	35.1 ± 20.8 (19)	32.5 ± 25.5 (19)
0~20	13.0 ± 23.5 (23)	17.6 ± 18.3 (17)	18.4 ± 19.4 (19)	26.0 ± 25.7 (19)

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

Table 69

Two generation reproductive toxicity study of NP by oral administration in rats
 Food consumption of F1 dams during gestation period; Mean±S.D. (N)

Compound	Nonylphenol				
	0 ^a	2	10	50	
Days of gestation					
1~2	22.5 ± 3.3 (23)	21.7 ± 2.6 (18)	22.2 ± 3.4 (19)	21.3 ± 3.5 (19)	
7~8	24.3 ± 2.7 (23)	25.2 ± 2.4 (18)	23.4 ± 4.8 (19)	23.2 ± 4.5 (19)	
13~14	25.1 ± 2.7 (23)	25.7 ± 2.6 (18)	26.0 ± 2.2 (19)	24.6 ± 3.1 (19)	
19~20	23.5 ± 2.4 (23)	24.5 ± 3.2 (18)	25.2 ± 2.2 (19)	22.8 ± 5.5 (19)	

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

Table 70

Two generation reproductive toxicity study of NP by oral administration in rats
 Food consumption of F1 dams during lactation period; Mean±S.D. (N)

Compound	Nonylphenol			
	0 ^a	2	10	50
Days of lactation				
3~4	34.6 ± 9.6 (23)	36.7 ± 9.3 (18)	39.6 ± 5.3 (19)	35.5 ± 7.1 (19)
6~7	42.1 ± 7.5 (23)	46.6 ± 3.3 (17)	47.1 ± 6.4 (19)	43.8 ± 7.9 (19)
9~10	50.4 ± 4.8 (23)	55.0 ± 6.4 (17)	55.6 ± 6.6 (19)	53.5 ± 8.2 (19)

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

Table 71

Two generation reproductive toxicity study of NP by oral administration in rats
Organ weight of F1 dams; Mean \pm S.D. (N)

Compound	Nonylphenol				
	Dose (mg/kg)	$\bar{0}^a$			
		2	10	50	
Terminal body weight (g)	351.6 \pm 29.3	(23) 349.5 \pm 19.0	(17) 364.1 \pm 22.9	(19) 358.4 \pm 31.1	(19)
Brain (g)	1.89 \pm 0.07 b 0.54 \pm 0.04 c	(23) 1.88 \pm 0.09 0.54 \pm 0.03	(17) 1.91 \pm 0.07 0.53 \pm 0.04	(19) 1.91 \pm 0.10 0.54 \pm 0.04	(19)
Heart (g)	1.13 \pm 0.10 0.32 \pm 0.02	(23) 1.17 \pm 0.07 0.34 \pm 0.02	(17) 1.16 \pm 0.09 0.32 \pm 0.03	(19) 1.18 \pm 0.13 0.33 \pm 0.03	(19)
Lung (g)	1.10 \pm 0.12 0.31 \pm 0.02	(23) 1.08 \pm 0.08 0.31 \pm 0.01	(17) 1.11 \pm 0.08 0.31 \pm 0.02	(19) 1.11 \pm 0.09 0.31 \pm 0.02	(19)
Liver (g)	15.28 \pm 1.32 4.35 \pm 0.26	(23) 14.48 \pm 1.14 4.15 \pm 0.35	(17) 15.70 \pm 1.46 4.32 \pm 0.39	(19) 16.32 \pm 1.69 4.55 \pm 0.31	(19)
Spleen (g)	0.69 \pm 0.13 0.20 \pm 0.03	(23) 0.62 \pm 0.06 0.18 \pm 0.02	(17) 0.74 \pm 0.09 0.20 \pm 0.02	(19) 0.70 \pm 0.12 0.20 \pm 0.03	(19)
Kidney (g)	2.33 \pm 0.16 0.67 \pm 0.04	(23) 2.38 \pm 0.14 0.68 \pm 0.05	(17) 2.42 \pm 0.18 0.67 \pm 0.05	(19) 2.34 \pm 0.22 0.65 \pm 0.04	(19)

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

b: absolute weight

c: relative weight (g per 100g body weight)

Table 71 (continued)

Two generation reproductive toxicity study of NP by oral administration in rats
Organ weight of F1 dams; Mean \pm S.D. (N)

Compound	Nonylphenol				
	0 ^a	2	10	50	
Terminal body weight (g)	351.6 \pm 29.3 (23)	349.5 \pm 19.0 (17)	364.1 \pm 22.9 (19)	358.4 \pm 31.1 (19)	(19)
Adrenal glands (mg)	74.2 \pm 8.8 (23)	73.8 \pm 11.8 (17)	74.0 \pm 11.2 (19)	76.0 \pm 8.8 (19)	(19)
	21.2 \pm 2.9	21.2 \pm 3.8	20.3 \pm 2.7	21.3 \pm 2.7	
Thymus (mg)	187.9 \pm 66.1 (23)	193.4 \pm 54.7 (17)	179.3 \pm 53.2 (19)	176.3 \pm 53.1 (19)	(19)
	53.1 \pm 17.1	55.6 \pm 16.4	49.4 \pm 14.7	49.3 \pm 14.5	
Ovary (mg)	108.7 \pm 34.4 (23)	98.7 \pm 12.4 (17)	101.3 \pm 13.4 (19)	85.1 \pm 12.3 ** (19)	(19)
	30.9 \pm 9.9	28.4 \pm 4.1	27.9 \pm 3.7	23.7 \pm 2.7 **	
Uterus (g)	0.40 \pm 0.09 (23)	0.43 \pm 0.12 (17)	0.40 \pm 0.06 (19)	0.39 \pm 0.10 (19)	(19)
	0.12 \pm 0.03	0.13 \pm 0.03	0.11 \pm 0.02	0.11 \pm 0.03	
Thyroid glands (mg)	16.5 \pm 3.5 (23)	15.9 \pm 2.2 (17)	16.4 \pm 3.0 (19)	18.2 \pm 3.1 (19)	(19)
	4.7 \pm 0.9	4.5 \pm 0.7	4.5 \pm 0.7	5.1 \pm 0.9	
Pituitary gland (mg)	14.5 \pm 3.5 (23)	12.7 \pm 2.1 (17)	14.1 \pm 3.0 (19)	14.4 \pm 2.2 (19)	(19)
	4.1 \pm 0.9	3.6 \pm 0.5	3.9 \pm 0.7	4.0 \pm 0.6	

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, $p < 0.01$

Table 72

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

Serum concentrations of prolactin (PRL), luteinizing hormone (LH), follicle-stimulating hormone (FSH), thyroid stimulating hormone (TSH), triiodothyronine (T₃), thyroxine (T₄), estradiol in F₁ females; Mean±S.D. (N)

Compound	Nonylphenol			
	0 ^a	2	10	50
PRL (ng/mL)	264.4 ± 284.9 (23)	85.8 ± 83.0 (16)	248.2 ± 368.9 (19)	203.6 ± 209.8 (19)
LH (ng/mL)	13.4 ± 2.1 (23)	12.7 ± 2.0 (17)	13.8 ± 1.5 (19)	12.8 ± 2.1 (19)
FSH (ng/mL)	238.8 ± 47.2 (23)	286.5 ± 59.3 * (17)	269.1 ± 47.3 (19)	244.6 ± 70.3 (19)
TSH (ng/mL)	16.1 ± 3.8 (23)	20.1 ± 2.8 ** (17)	17.3 ± 2.5 (19)	18.1 ± 3.4 (19)
T ₃ (ng/mL)	0.9 ± 0.2 (22)	0.7 ± 0.2 * (12)	0.8 ± 0.1 (17)	0.7 ± 0.2 ** (16)
T ₄ (ng/mL)	51.8 ± 11.3 (23)	54.1 ± 13.1 (17)	47.6 ± 6.1 (19)	48.4 ± 11.0 (19)
Estradiol (pg/mL)	13.4 ± 7.4 (14)	11.2 ± 7.4 (6)	18.9 ± 4.9 (3)	10.3 ± 7.7 (13)

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

* : significant difference from control, p<0.05

** : significant difference from control, p<0.01

Table 73

Two generation reproductive toxicity study of NP by oral administration in rats
 Macroscopic findings in F1 females

Group Grade	0 mg/kg		2 mg/kg		10 mg/kg		50 mg/kg	
	-	+	-	+	-	+	-	+
(Liver)	[30]	0	[21]	1	[25]	0	[23]	0
Pale (Stomach)	[30]	0	[21]	1	[25]	0	[23]	0
Nodule, mucosa, glandular stomach	30	0	21	0	23	0	21	1
(Adrenal gland)	[30]	0	[21]	1	[25]	0	[23]	0
Enlargement (Spleen)	[30]	0	[21]	1	[25]	0	[23]	0
Dark (Thymus)	[30]	0	[21]	1	[25]	0	[23]	0
Small	30	0	20	1	23	0	22	0

-, Negative; +, Positive
 [], Number of animals examined

Table 75

Two generation reproductive toxicity study of NP by oral administration in rats
Development of F2 offspring up to weaning; MeantS.D. (N)

Compound	Nonylphenol			
	0 ^a	2	10	50
Gestation period; days	22.0 ± 0.4 (23)	22.1 ± 0.3 (18)	22.0 ± 0.5 (19)	21.9 ± 0.2 (19)
Implantations	14.9 ± 2.6 (23)	15.2 ± 1.6 (18)	14.6 ± 1.5 (19)	12.5 ± 3.3 * (19)
Delivery index; dams A)	100	100	100	100
Day 0				
Fetuses delivered	13.5 ± 2.3 (23)	14.3 ± 2.2 (18)	13.3 ± 1.8 (19)	11.5 ± 3.0 * (19)
Delivery index; fetuses B)	91.5 ± 10.8 (23)	94.3 ± 9.3 (18)	91.1 ± 8.4 (19)	92.6 ± 7.4 (19)
Live newborns	13.2 ± 2.2 (23)	14.2 ± 2.3 (18)	13.2 ± 1.6 (19)	11.3 ± 2.9 * (19)
Birth index C)	89.7 ± 11.3 (23)	93.2 ± 10.4 (18)	90.4 ± 7.8 (19)	91.0 ± 6.9 (19)
Viability index D)	97.9 ± 4.3 (23)	98.8 ± 3.8 (18)	99.3 ± 2.0 (19)	98.3 ± 3.3 (19)
Day 4				
Live offspring	12.9 ± 2.4 (23)	13.8 ± 2.0 (18)	12.7 ± 1.7 (19)	11.3 ± 2.9 * (19)
Viability index E)	97.6 ± 7.2 (23)	98.0 ± 4.9 (18)	96.5 ± 9.7 (19)	99.6 ± 1.8 (19)
Offspring after culling	8.0 ± 0.2 (23)	8.0 ± 0.0 (18)	8.0 ± 0.0 (19)	7.6 ± 1.0 (19)
Males	4.0 ± 0.6 (23)	3.9 ± 1.0 (18)	4.1 ± 0.5 (19)	3.9 ± 0.7 (19)
Females	4.0 ± 0.7 (23)	4.1 ± 1.0 (18)	3.9 ± 0.5 (19)	3.7 ± 0.7 (19)
Day 21				
Live offspring	7.8 ± 0.7 (23)	7.6 ± 1.9 (18)	7.9 ± 0.3 (19)	7.6 ± 1.0 (19)
Males	4.0 ± 0.6 (23)	3.7 ± 1.0 (18)	4.0 ± 0.5 (19)	3.9 ± 0.7 (19)
Females	3.9 ± 0.8 (23)	3.8 ± 1.0 (18)	3.9 ± 0.5 (19)	3.7 ± 0.7 (19)
Weaning index F)	98.4 ± 7.8 (23)	94.4 ± 23.6 (18)	98.7 ± 3.9 (19)	100.0 ± 0.0 (19)

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 implantations) 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 live 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)

* : significant difference from control, p<0.05

Table 76

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

Body weight of F₂ offspring up to weaning; Mean±S.D. (N)

Compound	Nonylphenol				
	Dose (mg/kg)	0 ^a	2	10	50
Day 0					
Male		6.6 ± 0.5 (23)	6.5 ± 0.4 (18)	6.7 ± 0.4 (19)	6.8 ± 0.5 (19)
Female		6.3 ± 0.4 (23)	6.1 ± 0.4 (18)	6.3 ± 0.4 (19)	6.4 ± 0.4 (19)
Day 4 (After culling)					
Male		10.2 ± 1.6 (23)	10.0 ± 1.2 (18)	10.5 ± 1.0 (19)	10.7 ± 1.5 (19)
Female		9.7 ± 1.5 (23)	9.5 ± 1.2 (18)	9.9 ± 1.0 (19)	10.4 ± 1.5 (19)
Day 7					
Male		17.1 ± 2.7 (23)	17.0 ± 1.0 (17)	17.2 ± 1.6 (19)	16.9 ± 1.8 (19)
Female		16.3 ± 3.4 (23)	16.2 ± 1.1 (17)	16.4 ± 1.4 (19)	16.5 ± 1.9 (19)
Day 14					
Male		34.4 ± 3.4 (23)	35.2 ± 1.8 (17)	35.9 ± 3.1 (19)	34.0 ± 3.9 (19)
Female		33.1 ± 3.4 (23)	34.0 ± 1.9 (17)	34.2 ± 3.0 (19)	33.3 ± 3.6 (19)
Day 21					
Male		56.1 ± 5.8 (23)	58.2 ± 3.5 (17)	58.6 ± 5.5 (19)	55.7 ± 6.7 (19)
Female		53.6 ± 5.6 (23)	54.9 ± 6.1 (17)	55.1 ± 5.1 (19)	53.5 ± 5.8 (19)

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

Table 77

Two generation reproductive toxicity study of NP by oral administration in rats
 Morphological observations of F2 live pups at birth

Compound	Nonylphenol		
Dose (mg/kg)	0 ^a	2	10
Number of live pups examined	304	255	251
<u>External abnormalities</u>			
Number of pups	0	0	0

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

b: animal no., FB02014FB001

Table 78

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

Morphological observations of F2 dead pups during lactation period

Compound	Nonylphenol			
	0 ^a	2	10	50
Number of dead pups ^b	17	17	14	5
Number of dead pups collected	10	10	3	5
Number of dead pups observed	7	1	6	11
<u>External abnormalities</u>				
Number of pups	0	1	0	0
<u>Types and number</u>				
Emaciation	0	1	0	1
<u>Visceral abnormalities</u>				
Number of pups	0	0	0	0

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

b: including missing pup

Table 79

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

Morphological observations of F2 pups culled on postnatal day 4

Compound	Nonylphenol		
Dose (mg/kg)	0 ^a	2	10
Number of pups examined	114	105	89
<u>External abnormalities</u>			
Number of pups	0	0	0
<u>Visceral abnormalities</u>			
Number of pups	0	0	0

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

b: animal no., FB03013EB001

Table 80

Two generation reproductive toxicity study of NP by oral administration in rats
 Morphological observations of F2 weanlings on postnatal day 21

Compound	Nonylphenol		
Dose (mg/kg)	0 ^a	2	10
Number of weanlings examined	180	136	150
<u>External abnormalities</u>			
Number of weanlings	0	0	0
<u>Visceral abnormalities</u>			
Number of weanlings	3	1	1
<u>Types and number</u>			
Dilatation of the renal pelvis	2	1	0
Small testis	1	0	1

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

Table 81

Two generation reproductive toxicity study of NP by oral administration in rats
Organ weight of F1 males; Mean \pm S.D. (N)

Compound	Nonylphenol				
	Dose (mg/kg)	0 ^a	2	10	50
Terminal body weight (g)	599.5 \pm 71.3 (30)	630.0 \pm 50.8 (21)	604.8 \pm 64.9 (25)	596.4 \pm 56.1 (23)	
Brain (g)	2.05 \pm 0.09 b (29) 0.34 \pm 0.03 c (29)	2.03 \pm 0.09 (21) 0.32 \pm 0.03 (21)	2.06 \pm 0.08 (25) 0.35 \pm 0.04 (25)	2.08 \pm 0.11 (23) 0.35 \pm 0.03 (23)	
Heart (g)	1.57 \pm 0.14 (30) 0.26 \pm 0.02 (30)	1.66 \pm 0.16 (21) 0.26 \pm 0.02 (21)	1.52 \pm 0.16 (25) 0.25 \pm 0.02 (25)	1.59 \pm 0.17 (23) 0.27 \pm 0.02 (23)	
Lung (g)	1.42 \pm 0.15 (30) 0.24 \pm 0.02 (30)	1.39 \pm 0.11 (21) 0.22 \pm 0.02 (21)	1.45 \pm 0.22 (25) 0.24 \pm 0.03 (25)	1.40 \pm 0.08 (23) 0.24 \pm 0.02 (23)	
Liver (g)	21.04 \pm 3.16 (30) 3.50 \pm 0.23 (30)	21.59 \pm 2.10 (21) 3.31 \pm 0.57 (21)	21.82 \pm 3.25 (25) 3.60 \pm 0.33 (25)	22.26 \pm 2.81 (23) 3.73 \pm 0.27 * (23)	
Spleen (g)	0.92 \pm 0.16 (30) 0.15 \pm 0.02 (30)	0.92 \pm 0.10 (21) 0.15 \pm 0.02 (21)	0.91 \pm 0.10 (25) 0.15 \pm 0.01 (25)	0.93 \pm 0.18 (23) 0.16 \pm 0.03 (23)	
Kidneys (g)	3.41 \pm 0.43 (30) 0.57 \pm 0.07 (30)	3.55 \pm 0.34 (21) 0.56 \pm 0.03 (21)	3.52 \pm 0.41 (25) 0.59 \pm 0.07 (25)	3.71 \pm 0.35 (23) 0.62 \pm 0.04 ** (23)	
Adrenal glands (mg)	56.0 \pm 9.3 (30) 9.4 \pm 1.6 (30)	60.1 \pm 10.2 (21) 9.6 \pm 1.9 (21)	57.2 \pm 12.1 (25) 9.4 \pm 1.5 (25)	53.6 \pm 9.9 (23) 9.0 \pm 1.5 (23)	
Thymus (mg)	303.7 \pm 62.8 (30) 50.9 \pm 10.1 (30)	273.1 \pm 58.5 (21) 43.2 \pm 8.5 * (21)	307.3 \pm 81.6 (25) 50.6 \pm 10.7 (25)	267.7 \pm 70.1 (23) 45.1 \pm 12.3 (23)	

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

b: absolute weight

c: relative weight (g or mg per 100g body weight)

*: significantly difference from control, p<0.05

**: significantly difference from control, p<0.01

Table 81 (continued)

Two generation reproductive toxicity study of NP by oral administration in rats
Organ weight of F1 males; Mean \pm S.D. (N)

Compound	Nonylphenol				
	0 ^a	2	10	50	
Terminal body weight (g)	599.5 \pm 71.3 (30)	630.0 \pm 50.8 (21)	604.8 \pm 64.9 (25)	596.4 \pm 56.1 (23)	
Testes (g)	3.61 \pm 0.25 b (30) 0.61 \pm 0.07 c (30)	3.52 \pm 0.36 (21) 0.56 \pm 0.06 (21)	3.47 \pm 0.31 (25) 0.58 \pm 0.08 (25)	3.45 \pm 0.28 (23) 0.58 \pm 0.08 (23)	
Epididymides (g)	1.32 \pm 0.10 (30) 0.22 \pm 0.02 (30)	1.40 \pm 0.14 (21) 0.22 \pm 0.02 (21)	1.30 \pm 0.11 (25) 0.22 \pm 0.03 (25)	1.27 \pm 0.10 (23) 0.21 \pm 0.02 (23)	
Ventral prostate (g)	0.70 \pm 0.14 (30) 0.12 \pm 0.02 (30)	0.65 \pm 0.16 (21) 0.10 \pm 0.03 (21)	0.69 \pm 0.33 (25) 0.12 \pm 0.06 (25)	0.64 \pm 0.15 (23) 0.11 \pm 0.02 (23)	
Seminal vesicle (g)	1.80 \pm 0.25 (30) 0.30 \pm 0.05 (30)	1.88 \pm 0.24 (21) 0.30 \pm 0.05 (21)	1.87 \pm 0.28 (25) 0.31 \pm 0.06 (25)	1.80 \pm 0.34 (23) 0.30 \pm 0.05 (23)	
Prostate and seminal vesicle (g)	2.99 \pm 0.38 (30) 0.50 \pm 0.07 (30)	3.03 \pm 0.38 (21) 0.48 \pm 0.08 (21)	3.08 \pm 0.50 (25) 0.52 \pm 0.11 (25)	2.90 \pm 0.43 (23) 0.49 \pm 0.07 (23)	
Thyroid glands (mg)	20.1 \pm 4.6 (30) 3.4 \pm 0.9 (30)	22.7 \pm 4.5 (21) 3.6 \pm 0.8 (21)	21.3 \pm 4.8 (25) 3.5 \pm 0.8 (25)	21.6 \pm 4.9 (23) 3.6 \pm 0.7 (23)	
Pituitary gland (mg)	12.3 \pm 2.1 (30) 2.0 \pm 0.3 (30)	12.2 \pm 2.2 (21) 2.0 \pm 0.4 (21)	12.4 \pm 1.6 (25) 2.0 \pm 0.3 (25)	13.5 \pm 1.8 (23) 2.3 \pm 0.3 (23)	

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

b: absolute weight

c: relative weight (g or mg per 100g body weight)

Table 82

Two generation reproductive toxicity study of NP by oral administration in rats
Epididymal sperm findings in F1 males

Compound	Nonylphenol			
	0 ^a	2	10	50
Dose (mg/kg)				
Number of F1 males examined	30	21	25	23
% of motile (Mean ± S.D.)	95.5 ± 3.4	96.7 ± 3.9	94.6 ± 6.0	94.8 ± 4.2
% of progressive (Mean ± S.D.)	82.5 ± 6.6	84.2 ± 9.5	81.6 ± 8.1	81.0 ± 6.1
Sperm counts (Mean±S.D.)				
Caudal epididymis weight	0.3033 ± 0.0337 (30)	0.3157 ± 0.027 (20)	0.3086 ± 0.033 (25)	0.2971 ± 0.029 (23)
No. of sperm per caudal epididymis (x10 ⁶)	535.0 ± 155.2 (30)	580.2 ± 169.1 (20)	586.3 ± 169.3 (25)	664.7 ± 175.4 (23)
No. of sperm per caudal epididymis weight (x10 ⁶ /g)	1767.2 ± 436.5 (30)	1847.7 ± 558.7 (20)	1918.5 ± 536.5 (25)	2242.3 ± 582.3** (23)

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

** : significant difference from control, p<0.01

Table 83

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

Serum concentrations of testosterone, luteinizing hormone (LH), follicle-stimulating hormone (FSH), thyroid stimulating hormone (TSH), triiodothyronine (T3), thyroxine (T4) in F1 males; Mean±S.D. (N)

Compound	Nonylphenol			
	0 ^a	2	10	50
Dose (mg/kg)				
Testosterone (ng/mL)	7.6 ± 4.9 (30)	9.7 ± 6.4 (21)	8.1 ± 6.6 (25)	7.0 ± 5.2 (23)
LH (ng/mL)	12.2 ± 2.1 (30)	13.3 ± 2.0 (21)	11.5 ± 1.6 (25)	11.9 ± 1.4 (23)
FSH (ng/mL)	301.7 ± 68.5 (30)	243.5 ± 50.9 * (21)	306.1 ± 77.3 (25)	291.1 ± 80.6 (23)
TSH (ng/mL)	12.6 ± 2.2 (30)	14.1 ± 2.5 (21)	14.1 ± 2.8 (25)	13.5 ± 2.2 (23)
T3 (ng/mL)	0.8 ± 0.1 (30)	0.6 ± 0.1 ** (20)	0.8 ± 0.1 (25)	0.7 ± 0.1 ** (23)
T4 (ng/mL)	76.1 ± 10.1 (30)	75.3 ± 8.4 (21)	73.6 ± 8.9 (25)	76.4 ± 10.6 (23)

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

* : significant difference from control, p<0.05

** : significant difference from control, p<0.01

Table 84

Two generation reproductive toxicity study of NP by oral administration in rats
Macroscopic findings of F1 males

Group Grade	0 mg/kg		2 mg/kg		10 mg/kg		50 mg/kg	
	-	+	-	+	-	+	-	+
(Seminal vessicle)	[30]		[21]		[25]		[23]	
Small, left side	30	0	20	1	25	0	23	0
(Brain)	[30]		[21]		[25]		[23]	
Recessed area	30	0	21	0	24	1	23	0
(Kidney)	[30]		[21]		[25]		[23]	
Dilatation, renal pelvis, bilateral	29	1	21	0	25	0	23	0
Dilatation, renal pelvis, right side	28	2	21	0	22	3	21	2
(Liver)	[30]		[21]		[25]		[23]	
Cyst, left side	29	1	21	0	25	0	23	0
Yellowish/pale	30	0	19	2	25	0	23	0
Pale, cauda lobe	30	0	21	0	25	0	22	1
(Lung)	[30]		[21]		[25]		[23]	
Small, cauda lobe	29	1	21	0	25	0	22	1
Yellowish	30	0	21	0	24	1	23	0
(Spleen)	[30]		[21]		[25]		[23]	
Insufficiency, retraction	30	0	21	0	24	1	23	0
Spot, white, multiple	30	0	21	0	25	0	22	1
(Thymus)	[30]		[21]		[25]		[23]	
Small	30	0	20	1	25	0	23	0

-, Negative; +, Positive
[], Number of animals examined

