

Table 16

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

Body weight gain of F<sub>0</sub> females during lactation period; Mean±S.D. (N)

| Compound          | Nonylphenol       |                   |                     |                   |                  |
|-------------------|-------------------|-------------------|---------------------|-------------------|------------------|
|                   | 0 <sup>a</sup>    | 2                 | 10                  | 50                | 250 <sup>b</sup> |
| Days of lactation |                   |                   |                     |                   |                  |
| 0~4               | 10.7 ± 16.4 ( 30) | 10.1 ± 12.6 ( 21) | 0.6 ± 12.3 * ( 25)  | 13.4 ± 14.8 ( 24) |                  |
| 0~7               | 16.2 ± 15.1 ( 30) | 15.9 ± 10.8 ( 21) | 7.1 ± 14.7 * ( 25)  | 20.7 ± 14.3 ( 23) |                  |
| 0~14              | 29.9 ± 15.3 ( 30) | 31.9 ± 13.3 ( 21) | 19.6 ± 13.9 * ( 25) | 34.4 ± 17.3 ( 23) |                  |
| 0~21              | 17.5 ± 18.6 ( 30) | 19.3 ± 12.8 ( 21) | 7.3 ± 17.7 ( 25)    | 22.2 ± 20.8 ( 23) |                  |

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

b: animals were necropsied before mating.

\*: significant difference from control, p&lt;0.05

Table 17

Two generation reproductive toxicity study of NP by oral administration in rats  
 Food consumption of F<sub>0</sub> females during pre-mating period; Mean±S.D. (N)

| Compound          | Nonylphenol      |                  |                  |                  |                     |
|-------------------|------------------|------------------|------------------|------------------|---------------------|
|                   | 0 <sup>a</sup>   | 2                | 10               | 50               | 250                 |
| Days of treatment |                  |                  |                  |                  |                     |
| 1-2               | 17.9 ± 3.3 ( 35) | 19.0 ± 2.5 ( 25) | 17.0 ± 3.0 ( 25) | 17.4 ± 2.9 ( 25) | 15.6 ± 2.6 ** ( 25) |
| 4-5               | 17.2 ± 2.8 ( 35) | 16.7 ± 2.7 ( 25) | 16.8 ± 3.5 ( 25) | 16.8 ± 2.6 ( 25) | 6.4 ± 5.2 ** ( 25)  |
| 8-9               | 18.3 ± 2.4 ( 35) | 18.3 ± 2.4 ( 25) | 17.5 ± 3.1 ( 25) | 17.2 ± 2.6 ( 25) | 11.7 ± 7.2 ** ( 12) |
| 11-12             | 17.7 ± 3.1 ( 35) | 17.5 ± 3.0 ( 25) | 17.0 ± 3.6 ( 25) | 17.1 ± 2.3 ( 25) | 16.5 ± 2.4 ( 9)     |

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

\*\* : significant difference from control, p<0.01

Table 18

Two generation reproductive toxicity study of NP by oral administration in rats  
 Food consumption of F<sub>0</sub> females during gestation period; Mean±S.D. (N)

| Compound          | Nonylphenol     |                 |                 |                 |
|-------------------|-----------------|-----------------|-----------------|-----------------|
|                   | 0 <sup>a</sup>  | 2               | 10              | 50              |
| Dose (mg/kg)      | 0               | 2               | 10              | 50              |
| Days of gestation |                 |                 |                 |                 |
| 1~2               | 22.6 ± 2.2 (30) | 22.8 ± 3.1 (22) | 21.7 ± 2.6 (25) | 21.0 ± 2.6 (25) |
| 7~8               | 23.4 ± 2.6 (30) | 23.3 ± 3.3 (22) | 24.0 ± 3.1 (25) | 22.4 ± 2.7 (25) |
| 13~14             | 22.5 ± 2.8 (30) | 23.2 ± 2.0 (22) | 23.4 ± 2.6 (25) | 24.0 ± 3.0 (25) |
| 19~20             | 22.4 ± 2.2 (30) | 22.0 ± 3.0 (22) | 22.8 ± 2.6 (25) | 20.7 ± 3.1 (25) |

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

b: animals were necropsied before mating.

Table 19

Two generation reproductive toxicity study of NP by oral administration in rats  
 Food consumption of F0 females during lactation period; Mean±S.D. (N)

| Compound          | Nonylphenol      |                  |                  |                  |
|-------------------|------------------|------------------|------------------|------------------|
|                   | 0 <sup>a</sup>   | 2                | 10               | 50               |
| Dose (mg/kg)      |                  |                  |                  | 250 <sup>b</sup> |
| Days of lactation |                  |                  |                  |                  |
| 3~4               | 36.2 ± 7.0 ( 30) | 35.6 ± 5.4 ( 21) | 35.7 ± 5.3 ( 25) | 34.6 ± 6.6 ( 24) |
| 6~7               | 41.7 ± 5.2 ( 30) | 41.9 ± 4.6 ( 21) | 42.5 ± 4.3 ( 25) | 41.2 ± 4.0 ( 23) |
| 9~10              | 49.2 ± 6.3 ( 30) | 48.7 ± 5.0 ( 21) | 49.5 ± 3.8 ( 25) | 48.0 ± 5.6 ( 23) |

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

b: animals were necropsied before mating.

Table 20

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

Estrous cycle of F0 females

| Compound  | Nonylphenol    |           |           |           |           |
|---|----------------|-----------|-----------|-----------|-----------|
|   | 0 <sup>a</sup> | 2         | 10        | 50        | 250       |
| Dose (mg/kg)  | 0              | 2         | 10        | 50        | 250       |
| Number of females examined                            | 35             | 25        | 25        | 25        | 25        |
| Mean length of estrous cycle in days                  | 4.0 ± 0.2      | 4.0 ± 0.0 | 4.0 ± 0.0 | 4.0 ± 0.0 | 4.0 ± 0.2 |
| Pre-treatment period; Mean±S.D.                       | 4.0 ± 0.2      | 4.0 ± 0.2 | 4.0 ± 0.2 | 4.2 ± 0.8 | 5.0       |
| Treatment period; Mean±S.D.                           |                |           |           |           |           |
| Number of animals showing each type of cycle          |                |           |           |           |           |
| during pre-treatment period                           | 34             | 25        | 25        | 25        | 24        |
| 4-day cycle   | 1              | 0         | 0         | 0         | 1         |
| 5-day cycle   | 0              | 0         | 0         | 0         | 0         |
| 4/5-day cycle   | 0              | 0         | 0         | 0         | 0         |
| Irregular   |                |           |           |           |           |
| Changes of estrous cycle after treatment              |                |           |           |           |           |
| Number of animals whose estrous cycle was not changed | 33             | 24        | 23        | 24        | 0         |
| Number of animals whose estrous cycle was changed     | 2              | 1         | 2         | 1         | 25        |
| [Pre-treatment]                                       |                |           |           |           |           |
| → 4-day   | 1              | 1         | 1         | 1         | 2         |
| → 4/5-day   | 0              | 0         | 0         | 0         | 0         |
| → irregular   | 0              | 0         | 1         | 0         | 0         |
| → 4-day   | 1              | 0         | 0         | 0         | 0         |
| → 4/5-day   | 0              | 0         | 0         | 0         | 0         |
| → irregular   | 0              | 0         | 0         | 0         | 0         |
| → monoestrus  | 0              | 0         | 0         | 0         | 19        |
| → anestrus  | 0              | 0         | 0         | 0         | 3         |
| → anestrus  | 0              | 0         | 0         | 0         | 1         |
| → 5-day   | 0              | 0         | 0         | 0         | 0         |
| Number of vaginal estrus during mating period         |                |           |           |           |           |
| Mean±S.D.   | 1.1 ± 0.3      | 1.2 ± 0.5 | 1.0 ± 0.2 | 1.0 ± 0.2 | N.E.      |

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

Table 21

Two generation reproductive toxicity study of NP by oral administration in rats  
 Reproductive performance of F<sub>0</sub> animals

| Compound                                  | Nonylphenol    |           |           |           |
|---|----------------|-----------|-----------|-----------|
|   | 0 <sup>a</sup> | 2         | 10        | 50        |
| Number of pairs examined (A)              | 35             | 25        | 25        | 25        |
| Number of pairs successful copulation (B) | 35             | 25        | 25        | 25        |
| Copulation index [(B/A)×100,%]            | 100.0          | 100.0     | 100.0     | 100.0     |
| Number of pregnant females (C)            | 33             | 22        | 25        | 25        |
| Fertility index [(C/B)×100,%]             | 94.3           | 88.0      | 100.0     | 100.0     |
| -----                                     |                |           |           |           |
| Pairing days until copulation             | 2.7 ± 1.8      | 3.2 ± 3.0 | 2.3 ± 1.7 | 2.7 ± 2.4 |
| Mean ± S.D.                               |                |           |           |           |

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

Table 21 (continued)

Two generation reproductive toxicity study of NP by oral administration in rats  
 Reproductive performance of F<sub>0</sub> animals

| Compound                                  | Nonylphenol      |
|---|------------------|
| ng/kg                                     | 250 <sup>a</sup> |
| Number of pairs examined (A)              | 23               |
| Number of pairs successful copulation (B) | 22               |
| Copulation index [(B/A)×100,%]            | 95.7             |
| Number of pregnant females (C)            | 21               |
| Fertility index [(C/B)×100,%]             | 95.5             |
| -----                                     |                  |
| Pairing days until copulation             | 2.9 ± 1.9        |
| Mean ± S.D.                               |                  |

a: Animals were necropsied before mating. Males were mated with intact females.

Table 22

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

Organ weight of F<sub>0</sub> females; Mean  $\pm$  S.D. (N)

| Compound             | Nonylphenol  |   |   |   |                  |
|----------------------|--|---|---|---|------------------|
|                      | 0 <sup>a</sup>                                       | 2   | 10  | 50  | 250 <sup>d</sup> |
| Terminal body weight | (g) 330.2 $\pm$ 17.3 (30)                            | 332.0 $\pm$ 13.2 (21)                         | 327.9 $\pm$ 22.5 (25)                         | 330.8 $\pm$ 15.9 (23)                         | (23)             |
| Brain                | (g) 1.86 $\pm$ 0.08 b (30)<br>0.56 $\pm$ 0.03 c (30) | 1.86 $\pm$ 0.07 (21)<br>0.56 $\pm$ 0.02 (21)  | 1.84 $\pm$ 0.06 (25)<br>0.56 $\pm$ 0.04 (25)  | 1.86 $\pm$ 0.06 (23)<br>0.56 $\pm$ 0.03 (23)  | (23)             |
| Heart                | (g) 1.09 $\pm$ 0.09 (30)<br>0.33 $\pm$ 0.02 (30)     | 1.08 $\pm$ 0.07 (21)<br>0.33 $\pm$ 0.02 (21)  | 1.07 $\pm$ 0.07 (25)<br>0.33 $\pm$ 0.03 (25)  | 1.07 $\pm$ 0.08 (23)<br>0.32 $\pm$ 0.02 (23)  | (23)             |
| Lung                 | (g) 1.11 $\pm$ 0.08 (30)<br>0.34 $\pm$ 0.02 (30)     | 1.08 $\pm$ 0.08 (21)<br>0.33 $\pm$ 0.02 (21)  | 1.11 $\pm$ 0.06 (25)<br>0.34 $\pm$ 0.02 (25)  | 1.10 $\pm$ 0.07 (23)<br>0.33 $\pm$ 0.02 (23)  | (23)             |
| Liver                | (g) 14.18 $\pm$ 0.94 (30)<br>4.30 $\pm$ 0.29 (30)    | 13.84 $\pm$ 1.32 (21)<br>4.17 $\pm$ 0.39 (21) | 14.29 $\pm$ 1.19 (25)<br>4.37 $\pm$ 0.43 (25) | 14.52 $\pm$ 1.46 (23)<br>4.39 $\pm$ 0.39 (23) | (23)             |
| Spleen               | (g) 0.66 $\pm$ 0.12 (30)<br>0.20 $\pm$ 0.03 (30)     | 0.68 $\pm$ 0.12 (21)<br>0.20 $\pm$ 0.04 (21)  | 0.64 $\pm$ 0.08 (25)<br>0.19 $\pm$ 0.03 (25)  | 0.62 $\pm$ 0.07 (23)<br>0.19 $\pm$ 0.02 (23)  | (23)             |
| Kidneys              | (g) 2.09 $\pm$ 0.13 (30)<br>0.64 $\pm$ 0.04 (30)     | 2.20 $\pm$ 0.16 (21)<br>0.66 $\pm$ 0.05 (21)  | 2.16 $\pm$ 0.21 (25)<br>0.66 $\pm$ 0.07 (25)  | 2.08 $\pm$ 0.16 (23)<br>0.63 $\pm$ 0.05 (23)  | (23)             |

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

b: absolute weight

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

d: animals were necropsied before mating.



Table 22 (continued)

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

Organ weight of F<sub>0</sub> females; Mean ± S.D. (N)

| Compound                 | Nonylphenol                             |   |                                       |   |                  |
|--------------------------|---|---|---------------------------------------|---|------------------|
|                          | 0 <sup>a</sup>                          | 2                                       | 10                                    | 50                                      | 250 <sup>d</sup> |
| Terminal body weight (g) | 330.2 ± 17.3 (30)                       | 332.0 ± 13.2 (21)                       | 327.9 ± 22.5 (25)                     | 330.8 ± 15.9 (23)                       |                  |
| Adrenal glands (mg)      | 65.1 ± 10.3 b (30)<br>19.8 ± 3.3 c (30) | 66.7 ± 8.4 (21)<br>20.1 ± 2.5 (21)      | 63.3 ± 7.9 (25)<br>19.4 ± 2.5 (25)    | 66.6 ± 11.4 (23)<br>20.1 ± 3.0 (23)     |                  |
| Thymus (mg)              | 183.2 ± 49.9 (30)<br>55.5 ± 15.2 (30)   | 174.7 ± 56.6 (21)<br>52.7 ± 17.4 (21)   | 161.7 ± 47.1 (25)<br>49.7 ± 15.9 (25) | 164.1 ± 57.2 (23)<br>49.9 ± 18.0 (23)   |                  |
| Ovaries (mg)             | 89.8 ± 11.8 (30)<br>27.2 ± 3.5 (30)     | 93.3 ± 11.5 (21)<br>28.1 ± 3.6 (21)     | 88.2 ± 8.5 (25)<br>27.0 ± 3.0 (25)    | 74.2 ± 10.1** (23)<br>22.5 ± 3.4** (23) |                  |
| Uterus (g)               | 0.36 ± 0.07 (30)<br>0.11 ± 0.02 (30)    | 0.42 ± 0.09* (21)<br>0.13 ± 0.03** (21) | 0.36 ± 0.07 (25)<br>0.11 ± 0.02 (25)  | 0.40 ± 0.10 (23)<br>0.12 ± 0.03 (23)    |                  |
| Thyroid gland (mg)       | 14.0 ± 2.8 (30)<br>4.3 ± 0.9 (30)       | 14.7 ± 4.2 (21)<br>4.4 ± 1.3 (21)       | 14.4 ± 2.2 (25)<br>4.4 ± 0.7 (25)     | 14.6 ± 2.9 (23)<br>4.4 ± 0.9 (23)       |                  |
| Pituitary gland (mg)     | 13.5 ± 2.4 (30)<br>4.1 ± 0.7 (30)       | 13.6 ± 2.0 (21)<br>4.1 ± 0.6 (21)       | 13.1 ± 1.7 (25)<br>4.0 ± 0.5 (25)     | 13.7 ± 1.7 (23)<br>4.2 ± 0.6 (23)       |                  |

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

b: absolute weight

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

d: animals were necropsied before mating.

\*: significant difference from control, p&lt;0.05

\*\*: significant difference from control, p&lt;0.01

Table 23 - 1

Two generation reproductive toxicity study of NP by oral administration in rats  
 Summary of macroscopic findings in Fo females at the end of the dosing period

| Group<br>Grade                           | 0 mg/kg |    | 2 mg/kg |    | 10 mg/kg |   | 50 mg/kg |    |   |
|--|---------|----|---------|----|----------|---|----------|----|---|
|  | -       | +  | -       | +  | -        | + | -        | +  |   |
| (Uterus)                                 | [35]    | 34 | [25]    | 25 | [25]     | 0 | [25]     | 25 | 0 |
| Retention, fluid, lumen                  |         | 1  |         |    |          |   |          |    |   |
| (Kidney)                                 | [35]    | 35 | [25]    | 25 | [25]     | 0 | [25]     | 22 | 3 |
| Pale, cortex                             |         | 0  |         |    |          |   |          | 24 | 1 |
| Soft                                     |         | 0  |         |    |          |   |          | 24 | 1 |
| Area, pale                               |         | 0  |         |    |          |   |          | 25 | 0 |
| Area, mottled, cortex                    |         | 34 |         |    |          | 0 |          | 25 | 0 |
| Cyst, left side                          |         | 0  |         |    |          | 1 |          | 25 | 0 |
| (Liver)                                  | [35]    | 35 | [25]    | 25 | [25]     | 0 | [25]     | 24 | 1 |
| Pale                                     |         | 0  |         |    |          |   |          | 24 | 1 |
| (Stomach)                                | [35]    | 35 | [25]    | 25 | [25]     | 0 | [25]     | 24 | 1 |
| Thickening, mucosa,<br>glandular stomach |         | 0  |         |    |          | 1 |          | 24 | 1 |
| Area, dark, mucosa,<br>glandular stomach |         | 0  |         |    |          | 0 |          | 24 | 1 |
| (Adrenal gland)                          | [35]    | 35 | [25]    | 25 | [25]     | 0 | [25]     | 23 | 2 |
| Enlargement                              |         | 0  |         |    |          | 1 |          | 23 | 2 |
| (Thymus)                                 | [35]    | 33 | [25]    | 25 | [25]     | 0 | [25]     | 20 | 5 |
| Small                                    |         | 2  |         |    |          | 4 |          | 20 | 5 |

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

Table 23 - 2

Two generation reproductive toxicity study of NP by oral administration in rats  
Summary of macroscopic findings in F0 females

| Group<br>Grade                            | 250 mg/kg |    |
|---|-----------|----|
|   | -         | +  |
| (Ovary)                                   | [25]      |    |
| Small                                     | 23        | 2  |
| (Uterus)                                  | [25]      |    |
| Dilatation, lumen                         | 22        | 3  |
| Retention, regrad                         | 24        | 1  |
| (Kidney)                                  | [25]      |    |
| Rough surface                             | 23        | 2  |
| Enlargement                               | 19        | 6  |
| Pale                                      | 23        | 2  |
| Area, pale/vitish cloudy, cortex          | 13        | 12 |
| Soft                                      | 23        | 2  |
| Whitish cloudy, medulla                   | 23        | 2  |
| (Liver)                                   | [25]      |    |
| Dark                                      | 23        | 2  |
| Pale                                      | 24        | 1  |
| Indistinct, lobular pattern               | 24        | 1  |
| Congestion                                | 21        | 4  |
| (Spleen)                                  | [25]      |    |
| Small                                     | 12        | 13 |
| Indistinct, follicle                      | 21        | 4  |
| Elevated area                             | 24        | 1  |
| (Thymus)                                  | [25]      |    |
| Small                                     | 9         | 16 |
| (Lung)                                    | [25]      |    |
| Dark                                      | 24        | 1  |
| Area, dark                                | 22        | 3  |
| Emphysema                                 | 23        | 2  |
| (Heart)                                   | [25]      |    |
| Retention, blood                          | 22        | 3  |
| (Pancreas)                                | [25]      |    |
| Pale                                      | 21        | 4  |
| (Adrenal gland)                           | [25]      |    |
| Enlargement                               | 9         | 16 |
| (Pituitary gland)                         | [25]      |    |
| Enlargement                               | 24        | 1  |
| (Thyroid gland)                           | [25]      |    |
| Small, left side                          | 24        | 1  |
| (Stomach)                                 | [25]      |    |
| Whitish cloudy, mucosa, glandular stomach | 24        | 1  |
| Soft red/brown, mucosa, glandular stomach | 22        | 3  |
| Accumulation, gas                         | 22        | 3  |
| Decrease, content                         | 21        | 4  |
| (Urinary bladder)                         | [25]      |    |
| Retention, urine                          | 24        | 1  |
| (Bone marrow)                             | [25]      |    |
| Pale                                      | 24        | 1  |
| (Skin)                                    | [25]      |    |
| Alopecia                                  | 19        | 6  |
| Soiled fur                                | 8         | 17 |

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

Table 24-1

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

## Summary of histopathological findings in F0 female

| Group<br>Grade                            | 0 mg/kg |     |   | 2 mg/kg |     |   | 10 mg/kg |     |   | 50 mg/kg |     |   |      |
|---|---------|-----|---|---------|-----|---|----------|-----|---|----------|-----|---|------|
|   | -       | +/- | + | -       | +/- | + | -        | +/- | + | -        | +/- | + | Pos. |
| (Ovary)                                   | [ 9 ]   |     |   | [ 0 ]   |     |   | [ 0 ]    |     |   | [ 9 ]    |     |   |      |
| Decrease, vesicular follicle              | 9       | 0   | 0 | 0       | 0   | 0 | 0        | 0   | 0 | 8        | 0   | 1 | 0    |
| Increase, atresia, follicle               | 7       | 1   | 1 | 0       | 0   | 2 |          |     |   | 9        | 0   | 0 | 0    |
| (Oviduct)                                 | [ 9 ]   |     |   | [ 0 ]   |     |   | [ 0 ]    |     |   | [ 9 ]    |     |   |      |
| No remarkable change                      | [ 9 ]   |     |   | [ 0 ]   |     |   | [ 0 ]    |     |   | [ 9 ]    |     |   |      |
| (Uterus: horn & cervix)                   | [ 9 ]   |     |   | [ 0 ]   |     |   | [ 0 ]    |     |   | [ 9 ]    |     |   |      |
| No remarkable change                      | [ 9 ]   |     |   | [ 0 ]   |     |   | [ 0 ]    |     |   | [ 9 ]    |     |   |      |
| (Vagina)                                  |         | 2   | 2 | 3       | 2   | 0 |          |     |   |          | 2   | 1 | 3    |
| Mucification, epithelium                  |         | 5   | 4 | 0       | 0   | 0 |          |     |   |          | 6   | 2 | 1    |
| Cornification, epithelium                 |         | 8   | 0 | 0       | 1   | 0 |          |     |   |          | 9   | 0 | 0    |
| Cyst, lamina propria                      | [ 9 ]   |     |   | [ 0 ]   |     |   | [ 0 ]    |     |   | [ 9 ]    |     |   |      |
| (Mammary gland)                           | [ 9 ]   |     |   | [ 9 ]   |     |   | [ 10 ]   |     |   | [ 9 ]    |     |   |      |
| Atrophy, focal                            |         | 9   | 0 | 1       | 0   | 0 |          |     |   |          | 9   | 0 | 0    |
| (Liver)                                   |         |     |   |         |     |   |          |     |   |          |     |   |      |
| Hepertrophy, hepatocyte,<br>centrilobular | [ 9 ]   |     |   | [ 0 ]   |     |   | [ 0 ]    |     |   | [ 9 ]    |     |   |      |
| (Kidney)                                  |         | 9   | 0 | 0       | 0   | 0 |          |     |   |          | 6   | 3 | 0    |
| Hepertrophy, hepatocyte,<br>centrilobular |         |     |   |         |     |   |          |     |   |          |     |   |      |
| (Kidney)                                  |         | 6   | 3 | 0       | 0   | 0 |          |     |   |          | 8   | 1 | 0    |
| Basophilic tubule, cortex                 |         | 8   | 1 | 0       | 0   | 0 |          |     |   |          | 9   | 0 | 0    |
| Cast, cortex                              | [ 9 ]   |     |   | [ 0 ]   |     |   | [ 0 ]    |     |   | [ 9 ]    |     |   |      |
| (Spleen)                                  |         |     |   |         |     |   |          |     |   |          |     |   |      |
| Hematopoiesis, extramedullary             |         | 0   | 3 | 6       | 0   | 0 |          |     |   |          | 0   | 3 | 6    |
| Deposit, pigment, brown                   |         | 0   | 0 | 8       | 1   | 0 |          |     |   |          | 0   | 0 | 8    |
| (Spleen)                                  |         |     |   |         |     |   |          |     |   |          |     |   |      |
| Hematopoiesis, extramedullary             |         |     |   |         |     |   |          |     |   |          |     |   |      |
| Deposit, pigment, brown                   |         |     |   |         |     |   |          |     |   |          |     |   |      |

-, Negative; +/-, Very slight; +, Slight; ++, Moderate; +++ Severe; Pos., Total of positive grade

[ ], Number of animals examined

Table 24-1 (continued)

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

Summary of histopathological findings in F<sub>0</sub> female

| Group<br>Grade                              | 0 mg/kg |     |   | 2 mg/kg |     |      | 10 mg/kg |     |   | 50 mg/kg |     |      |       |     |   |    |     |      |   |
|---|---------|-----|---|---------|-----|------|----------|-----|---|----------|-----|------|-------|-----|---|----|-----|------|---|
|   | -       | +/- | + | ++      | +++ | Pos. | -        | +/- | + | ++       | +++ | Pos. | -     | +/- | + | ++ | +++ | Pos. |   |
| (Lung)                                      | [ 9 ]   |     |   |         |     |      | [ 0 ]    |     |   |          |     |      | [ 9 ] |     |   |    |     |      |   |
| Accumulation, foam cell                     | 0       | 3   | 5 | 1       | 0   | 9    |          |     |   |          |     |      |       | 3   | 3 | 3  | 0   | 0    | 6 |
| Hemorrhage, focal                           | 6       | 2   | 1 | 0       | 0   | 3    |          |     |   |          |     |      |       | 7   | 2 | 0  | 0   | 0    | 2 |
| Cellular infiltration,<br>neutrophil, focal | 7       | 2   | 0 | 0       | 0   | 2    |          |     |   |          |     |      |       | 7   | 2 | 0  | 0   | 0    | 2 |
| Mineralization, artery                      | 7       | 2   | 0 | 0       | 0   | 2    |          |     |   |          |     |      |       | 8   | 1 | 0  | 0   | 0    | 1 |
| Metaplasia, osseous                         | 6       | 3   | 0 | 0       | 0   | 3    |          |     |   |          |     |      |       | 9   | 0 | 0  | 0   | 0    | 0 |
| (Thymus)                                    | [ 9 ]   |     |   |         |     |      | [ 0 ]    |     |   |          |     |      | [ 9 ] |     |   |    |     |      | 1 |
| Atrophy<br>(Urinary bladder)                | [ 9 ]   |     |   |         |     | 1    | [ 0 ]    |     |   |          |     |      | [ 9 ] |     |   |    |     |      |   |
| No remarkable change<br>(Thyroid gland)     | [ 9 ]   |     |   |         |     |      | [ 0 ]    |     |   |          |     |      | [ 9 ] |     |   |    |     |      |   |
| No remarkable change<br>(Parathyroid gland) | [ 9 ]   |     |   |         |     |      | [ 0 ]    |     |   |          |     |      | [ 9 ] |     |   |    |     |      |   |
| No remarkable change<br>(Pituitary gland)   | [ 9 ]   |     |   |         |     |      | [ 0 ]    |     |   |          |     |      | [ 9 ] |     |   |    |     |      |   |
| No remarkable change<br>(Adrenal gland)     | [ 9 ]   |     |   |         |     |      | [ 0 ]    |     |   |          |     |      | [ 9 ] |     |   |    |     |      |   |
| No remarkable change<br>(Heart)             | [ 9 ]   |     |   |         |     |      | [ 0 ]    |     |   |          |     |      | [ 9 ] |     |   |    |     |      |   |
| No remarkable change                        | [ 9 ]   |     |   |         |     |      | [ 0 ]    |     |   |          |     |      | [ 9 ] |     |   |    |     |      |   |

-, Negative; +/-, Very slight; +, Slight; ++, Moderate; +++, Severe; Pos., Total of positive grade

[ ], Number of animals examined

Table 24-2  
Two generation reproductive toxicity study of NP by oral administration in rats  
Summary of histopathological findings in F0 female

| Group                                    | 0 mg/kg |     |   |    |     | 2 mg/kg |       |     |   |    | 10 mg/kg |       |       |     |   | 50 mg/kg |     |      |       |     |   |    |     |      |       |
|--|---------|-----|---|----|-----|---------|-------|-----|---|----|----------|-------|-------|-----|---|----------|-----|------|-------|-----|---|----|-----|------|-------|
|  | -       | +/- | + | ++ | +++ | Pos.    | -     | +/- | + | ++ | +++      | Pos.  | -     | +/- | + | ++       | +++ | Pos. | -     | +/- | + | ++ | +++ | Pos. |       |
| (Uterus: horn & cervix)                  | [ 1 ]   |     |   |    |     | 0       | [ 0 ] |     |   |    |          | 0     | [ 1 ] |     |   |          |     | 0    | [ 1 ] |     |   |    |     | 0    | [ 1 ] |
| Hemorrhage, endometrium                  |         |     |   |    |     | 0       |       |     |   |    |          | 0     |       |     |   |          |     | 0    |       |     |   |    |     | 0    |       |
| (Vagina)                                 | [ 1 ]   |     |   |    |     | 1       | [ 0 ] |     |   |    |          | 1     | [ 1 ] |     |   |          |     | 0    | [ 1 ] |     |   |    |     | 0    | [ 1 ] |
| Mucification, epithelium                 |         |     |   |    |     | 1       |       |     |   |    | 1        |       |       |     |   |          |     | 0    |       |     |   |    |     | 0    |       |
| Cornification, epithelium                |         |     |   |    |     | 0       |       |     |   |    | 0        |       |       |     |   |          |     | 0    |       |     |   |    |     | 0    |       |
| Cyst, lamina propria                     |         |     |   |    |     | 0       |       |     |   |    | 0        |       |       |     |   |          |     | 0    |       |     |   |    |     | 0    |       |
| (Liver)                                  | [ 1 ]   |     |   |    |     | 0       | [ 1 ] |     |   |    |          | 0     | [ 1 ] |     |   |          |     | 0    | [ 1 ] |     |   |    |     | 0    | [ 1 ] |
| Hepertrophy, hepatocyte, centrilobular   |         |     |   |    |     | 0       |       |     |   |    | 0        |       |       |     |   |          |     | 1    |       |     |   |    |     | 0    |       |
| Fatty change, periportal                 |         |     |   |    |     | 0       |       |     |   |    | 0        |       |       |     |   |          |     | 1    |       |     |   |    |     | 0    |       |
| (Kidney)                                 | [ 1 ]   |     |   |    |     | 0       | [ 0 ] |     |   |    | 0        | [ 1 ] |       |     |   |          |     | 0    | [ 1 ] |     |   |    |     | 0    | [ 1 ] |
| Basophilic tubule, cortex                |         |     |   |    |     | 0       |       |     |   |    | 1        |       |       |     |   |          |     | 0    |       |     |   |    |     | 0    |       |
| Degeneration, vacuolar, proximal tubule  |         |     |   |    |     | 0       |       |     |   |    | 0        |       |       |     |   |          |     | 0    |       |     |   |    |     | 0    |       |
| Degeneration, fatty, proximal tubule     |         |     |   |    |     | 0       |       |     |   |    | 0        |       |       |     |   |          |     | 0    |       |     |   |    |     | 0    |       |
| Cast, cortex                             |         |     |   |    |     | 0       |       |     |   |    | 1        |       |       |     |   |          |     | 0    |       |     |   |    |     | 0    |       |
| Mineralization, papilla & renal pelvis   |         |     |   |    |     | 0       |       |     |   |    | 1        |       |       |     |   |          |     | 0    |       |     |   |    |     | 0    |       |
| (Spleen)                                 | [ 1 ]   |     |   |    |     | 0       | [ 0 ] |     |   |    | 0        | [ 0 ] |       |     |   |          |     | 0    | [ 1 ] |     |   |    |     | 0    | [ 1 ] |
| Hematopoiesis, extramedullary            |         |     |   |    |     | 0       |       |     |   |    | 1        |       |       |     |   |          |     | 0    |       |     |   |    |     | 0    |       |
| Deposit, pigment, brown                  |         |     |   |    |     | 0       |       |     |   |    | 1        |       |       |     |   |          |     | 0    |       |     |   |    |     | 0    |       |
| (Lung)                                   | [ 1 ]   |     |   |    |     | 0       | [ 0 ] |     |   |    | 1        | [ 0 ] |       |     |   |          |     | 0    | [ 1 ] |     |   |    |     | 0    | [ 1 ] |
| Accumulation, foam cell                  |         |     |   |    |     | 0       |       |     |   |    | 1        |       |       |     |   |          |     | 0    |       |     |   |    |     | 0    |       |
| Hemorrhage, focal                        |         |     |   |    |     | 1       |       |     |   |    | 0        |       |       |     |   |          |     | 0    |       |     |   |    |     | 0    |       |
| Cellular infiltration, neutrophil, focal |         |     |   |    |     | 1       |       |     |   |    | 0        |       |       |     |   |          |     | 0    |       |     |   |    |     | 0    |       |
| Mineralization, artery                   |         |     |   |    |     | 1       |       |     |   |    | 0        |       |       |     |   |          |     | 0    |       |     |   |    |     | 0    |       |
| Metaplasia, osseous                      |         |     |   |    |     | 1       |       |     |   |    | 0        |       |       |     |   |          |     | 0    |       |     |   |    |     | 0    |       |
| (Thymus)                                 | [ 1 ]   |     |   |    |     | 1       | [ 0 ] |     |   |    | 0        | [ 0 ] |       |     |   |          |     | 0    | [ 1 ] |     |   |    |     | 0    | [ 1 ] |
| Atrophy                                  |         |     |   |    |     | 1       |       |     |   |    | 0        |       |       |     |   |          |     | 0    |       |     |   |    |     | 0    |       |

-, Negative; +/-, Very slight; +, Slight; ++, Moderate; +++, Severe; Pos., Total of positive grade  
[ ], Number of animals examined

Table 24 - 3

Two generation reproductive toxicity study of NP by oral administration in rats  
 Summary of histopathological findings in F0 female of 250 mg/kg

| Group<br>Grade  | 250 mg/kg |     |    |    |     | Pos. |    |
|---|-----------|-----|----|----|-----|------|----|
|   | -         | +/- | +  | ++ | +++ |      |    |
| (Ovary)   | [25]      | 16  | 7  | 2  | 0   | 0    | 9  |
| Decrease, corpus luteum   |           |     |    |    |     |      |    |
| Increase, atrecia, follicle                                     |           | 18  | 7  | 0  | 0   | 0    | 7  |
| Decrease, vesicular follicle                                    |           | 21  | 3  | 1  | 0   | 0    | 4  |
| Increase, interstitial gland                                    |           | 16  | 7  | 2  | 0   | 0    | 9  |
| (Oviduct)   | [25]      |     |    |    |     |      |    |
| No remarkable change  |           |     |    |    |     |      |    |
| (Uterus: horn & cervix)   | [25]      | 0   | 17 | 8  | 0   | 0    | 25 |
| Hyperplasia, luminal epithelial cell                            |           | 24  | 1  | 0  | 0   | 0    | 1  |
| Metaplasia, squamous, luminal epithelium                        |           | 9   | 4  | 12 | 0   | 0    | 16 |
| Increase, endmetrium  |           | 18  | 4  | 1  | 2   | 0    | 7  |
| Dilatation, lumen   | [25]      |     |    |    |     |      |    |
| (Vagina)  | [25]      | 14  | 1  | 5  | 5   | 0    | 11 |
| Mucification, epithelium  |           | 8   | 15 | 2  | 0   | 0    | 17 |
| Cornification, epithelium                                       | [25]      |     |    |    |     |      |    |
| (Adrenal gland)   | [25]      | 3   | 7  | 9  | 6   | 0    | 22 |
| Hypertrophy, cortical cell                                      |           |     |    |    |     |      |    |
| (Parathyroid gland)   | [25]      |     |    |    |     |      |    |
| No remarkable change  |           |     |    |    |     |      |    |
| (Thyroid gland)   | [22]      | 21  | 1  | 0  | 0   | 0    | 1  |
| Ectopic thymus  | [25]      |     |    |    |     |      |    |
| (Liver)   | [25]      | 0   | 3  | 21 | 1   | 0    | 25 |
| Hypertrophy, hepatocyte, centrilobular                          |           | 23  | 2  | 0  | 0   | 0    | 2  |
| Degeneration, granular, eosinophilic, hepatocyte, centrilobular |           | 24  | 0  | 1  | 0   | 0    | 1  |
| Microgranuloma  |           | 21  | 3  | 1  | 0   | 0    | 4  |
| Mitosis, hepatocyte   |           | 14  | 5  | 6  | 0   | 0    | 11 |
| Fatty change, periportal  | [25]      |     |    |    |     |      |    |
| (Spleen)  | [25]      | 6   | 5  | 6  | 7   | 1    | 19 |
| Atrophy   |           | 7   | 13 | 5  | 0   | 0    | 18 |
| Hematopoiesis, extramedullary                                   |           | 0   | 0  | 4  | 21  | 0    | 25 |
| Deposit, pigment, brown   |           |     |    |    |     |      |    |
| (Thymus)  | [23]      | 6   | 4  | 3  | 5   | 5    | 17 |
| Atrophy, with pyknosis/decrease of lymphocyte                   |           |     |    |    |     |      |    |

-, Negative; +/-, Very slight; +, Slight; ++, Moderate; +++, Severe; Pos., Total of positive grade

[ ], Number of animals examined

Table 24 - 3 (continued)  
 Two generation reproductive toxicity study of NP by oral administration in rats  
 Summary of histopathological findings in F0 female of 250 mg/kg

| Group<br>Grade   | 250 mg/kg |     |    |    |     |    | Pos. |
|--|-----------|-----|----|----|-----|----|------|
|  | -         | +/- | +  | ++ | +++ |    |      |
| (Kidney)   | [25]      |     |    |    |     |    |      |
| Basophilic tubule, cortex  | 5         | 2   | 9  | 8  | 1   | 20 |      |
| Basophilic tubule, medulla & papilla   | 3         | 8   | 9  | 5  | 0   | 22 |      |
| Alteration, cytoplasmic, ralefaction & vacuolation, proximal & distal tubule, cortex | 0         | 3   | 5  | 12 | 5   | 25 |      |
| Dilatation, distal tubule, cortex & medulla  | 3         | 7   | 9  | 6  | 0   | 22 |      |
| Dilatation, collecting tubule, medulla & papilla                                     | 12        | 6   | 4  | 3  | 0   | 13 |      |
| Cell debris, lumen, distal & collecting tubule                                       | 5         | 8   | 11 | 1  | 0   | 20 |      |
| Necrosis, epithelium, proximal tubule, cortex  | 4         | 12  | 2  | 3  | 4   | 21 |      |
| Necrosis, epithelium, distal & collecting tubule                                     | 6         | 17  | 2  | 0  | 0   | 19 |      |
| Mitosis, epithelium, collecting tubule, medulla & papilla                            | 5         | 11  | 9  | 0  | 0   | 20 |      |
| Cast, hyalin, cortex   | 22        | 1   | 2  | 0  | 0   | 3  |      |
| Cellular infiltration, neutrophil, lumen, distal & collecting tubule                 | 12        | 8   | 5  | 0  | 0   | 13 |      |
| Cellular infiltration, neutrophil, epithelium & interstitium, cortex                 | 22        | 2   | 1  | 0  | 0   | 3  |      |
| Cellular infiltration, neutrophil, epithelium & interstitium, medulla/papilla        | 7         | 12  | 6  | 0  | 0   | 18 |      |
| Hyperplasia, transitional epithelium, renal pelvis                                   | 16        | 9   | 0  | 0  | 0   | 9  |      |
| Mineralization   | 6         | 14  | 4  | 1  | 0   | 19 |      |
| (Urinary bladder)  | [20]      |     |    |    |     |    |      |
| Hyperplasia, transitional, epithelium, diffuse                                       | 4         | 14  | 2  | 0  | 0   | 16 |      |
| (Mammary gland)  | [24]      |     |    |    |     |    |      |
| Hyperplasia  | 19        | 5   | 0  | 0  | 0   | 5  |      |
| (Pancreas)   | [ 4]      |     |    |    |     |    |      |
| No remarkable change   | [24]      |     |    |    |     |    |      |
| (Heart)  | [25]      |     |    |    |     |    |      |
| No remarkable change   | [25]      |     |    |    |     |    |      |
| (Lung)   | [ 2]      |     |    |    |     |    |      |
| No remarkable change   | [ 2]      |     |    |    |     |    |      |
| (Pituitary gland)  | [ 2]      |     |    |    |     |    |      |
| No remarkable change   | [ 2]      |     |    |    |     |    |      |
| (Stomach)  | [ 2]      |     |    |    |     |    |      |
| Erosion, mucosa, glandular stomach   | 1         | 1   | 0  | 0  | 0   | 1  |      |
| Metaplasia, squamous, focal, mucosa, squamous hyperplasia, mucosa, forestomach       | 1         | 1   | 0  | 0  | 0   | 1  |      |
| Squamous hyperplasia, mucosa, forestomach  | 0         | 0   | 2  | 0  | 0   | 2  |      |

-, Negative; +/-, Very slight; +, Slight; ++, Moderate; +++, Severe; Pos., Total of positive grade  
 [ ], Number of animals examined



Table 25

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 (T<sub>3</sub>), thyroxine (T<sub>4</sub>), estradiol in F<sub>0</sub> females; Mean±S.D. (N)

| Compound               | Nonylphenol       |                      |                   |                   |  |
|------------------------|-------------------|----------------------|-------------------|-------------------|--|
|                        | 0 <sup>a</sup>    | 2                    | 10                | 50                |  |
| PRL (ng/mL)            | 75.8 ± 67.7 (30)  | 124.8 ± 152.3 (21)   | 76.9 ± 144.4 (25) | 79.3 ± 68.0 (23)  |  |
| LH (ng/mL)             | 10.7 ± 2.9 (30)   | 11.9 ± 3.9 (21)      | 12.0 ± 2.4 (25)   | 12.8 ± 2.6 (23)   |  |
| FSH (ng/mL)            | 268.9 ± 97.8 (30) | 195.8 ± 52.3 ** (21) | 305.8 ± 94.4 (25) | 304.2 ± 92.3 (23) |  |
| TSH (ng/mL)            | 17.2 ± 3.3 (30)   | 12.9 ± 2.4 ** (21)   | 17.9 ± 2.7 (25)   | 17.0 ± 2.5 (23)   |  |
| T <sub>3</sub> (ng/mL) | 1.2 ± 0.2 (30)    | 1.2 ± 0.3 (21)       | 1.1 ± 0.2 (25)    | 1.0 ± 0.2 ** (23) |  |
| T <sub>4</sub> (ng/mL) | 66.3 ± 12.9 (30)  | 50.7 ± 10.4 ** (21)  | 68.6 ± 11.5 (25)  | 66.3 ± 11.9 (23)  |  |
| Estradiol (pg/mL)      | 15.3 ± 6.6 (5)    | 11.0 ± 2.9 (10)      | 19.9 ± 9.0 (4)    | 14.3 ± 6.7 (8)    |  |

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

\*\* : significant difference from control, p&lt;0.01

Table 25 (continued)

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 (T<sub>3</sub>), thyroxine (T<sub>4</sub>), estradiol in F<sub>0</sub> females; Mean ± S.D. (N)

| Compound               | Nonylphenol   |      |
|------------------------|---------------|------|
| Dose (mg/kg)           | 250           |      |
| PRL (ng/mL)            | 254.5 ± 225.8 | (19) |
| LH (ng/mL)             | 17.6 ± 8.9    | (19) |
| FSH (ng/mL)            | 478.2 ± 319.8 | (19) |
| TSH (ng/mL)            | 27.2 ± 8.2    | (19) |
| T <sub>3</sub> (ng/mL) | 1.2 ± 0.2     | (19) |
| T <sub>4</sub> (ng/mL) | 67.8 ± 28.4   | (19) |
| Estradiol (pg/mL)      | 26.3 ± 14.7   | (5)  |

Data of 250 mg/kg group was excluded from statistical evaluation.

Table 26

Two generation reproductive toxicity study of NP by oral administration in rats  
Development of F1 offspring up to weaning; Means±D. (N)

| Compound                   | Nonylphenol       |                   |                  |                   |                  |
|----------------------------|-------------------|-------------------|------------------|-------------------|------------------|
|                            | 0 <sup>a</sup>    | 2                 | 10               | 50                | 250 <sup>b</sup> |
| Gestation period; days     | 22.1 ± 0.4 ( 30)  | 22.0 ± 0.4 ( 22)  | 21.8 ± 0.4 ( 25) | 22.0 ± 0.4 ( 25)  |                  |
| Implantations              | 15.3 ± 1.5 ( 30)  | 14.3 ± 2.4 ( 22)  | 14.7 ± 1.9 ( 25) | 14.3 ± 2.2 ( 25)  |                  |
| Delivery index; dams A)    | 100               | 100               | 100              | 100               |                  |
| Day 0                      |                   |                   |                  |                   |                  |
| Fetuses delivered          | 13.9 ± 2.4 ( 30)  | 13.4 ± 2.6 ( 22)  | 14.0 ± 1.6 ( 25) | 12.8 ± 2.7 ( 25)  |                  |
| Delivery index; fetuses B) | 90.9 ± 13.5 ( 30) | 93.3 ± 6.5 ( 22)  | 95.2 ± 5.6 ( 25) | 89.9 ± 13.6 ( 25) |                  |
| Live newborns              | 13.7 ± 2.3 ( 30)  | 12.9 ± 2.7 ( 22)  | 13.7 ± 1.8 ( 25) | 12.3 ± 2.7 ( 25)  |                  |
| Birth index C)             | 89.7 ± 13.4 ( 30) | 90.3 ± 11.8 ( 22) | 93.6 ± 7.8 ( 25) | 86.3 ± 15.2 ( 25) |                  |
| Viability index D)         | 98.8 ± 3.4 ( 30)  | 96.8 ± 10.7 ( 22) | 98.3 ± 5.9 ( 25) | 96.1 ± 9.2 ( 25)  |                  |
| Day 4                      |                   |                   |                  |                   |                  |
| Live offspring             | 13.5 ± 2.2 ( 30)  | 12.5 ± 3.7 ( 22)  | 13.4 ± 1.8 ( 25) | 11.2 ± 4.2 ( 25)  |                  |
| Viability index E)         | 98.7 ± 3.1 ( 30)  | 94.8 ± 21.4 ( 22) | 98.1 ± 3.8 ( 25) | 91.0 ± 27.5 ( 25) |                  |
| Offspring after culling    | 7.9 ± 0.7 ( 30)   | 7.9 ± 0.4 ( 21)   | 8.0 ± 0.0 ( 25)  | 8.0 ± 0.2 ( 23)   |                  |
| Males                      | 3.9 ± 0.6 ( 30)   | 4.0 ± 0.9 ( 21)   | 3.8 ± 0.8 ( 25)  | 4.0 ± 0.2 ( 23)   |                  |
| Females                    | 4.0 ± 0.3 ( 30)   | 3.9 ± 0.9 ( 21)   | 4.2 ± 0.8 ( 25)  | 4.0 ± 0.3 ( 23)   |                  |
| Day 21                     |                   |                   |                  |                   |                  |
| Live offspring             | 7.9 ± 0.7 ( 30)   | 7.9 ± 0.4 ( 21)   | 8.0 ± 0.0 ( 25)  | 8.0 ± 0.2 ( 23)   |                  |
| Males                      | 3.9 ± 0.6 ( 30)   | 4.0 ± 0.9 ( 21)   | 3.8 ± 0.8 ( 25)  | 4.0 ± 0.2 ( 23)   |                  |
| Females                    | 4.0 ± 0.3 ( 30)   | 3.9 ± 0.9 ( 21)   | 4.2 ± 0.8 ( 25)  | 4.0 ± 0.3 ( 23)   |                  |
| Weaning index F)           | 100               | 100               | 100              | 100               |                  |

A): Delivery index; dams = (no. of dams having live newborns / no. of pregnant females)

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 4) 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)

b: animals were necropsied before mating

Table 27

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

Body weight of F1 offspring up to weaning; Mean±S.D. (N)

| Compound              | Nonylphenol      |                  |                  |                  |
|-----------------------|------------------|------------------|------------------|------------------|
|                       | 0 <sup>a</sup>   | 2                | 10               | 50               |
| Day 0                 |                  |                  |                  |                  |
| Male                  | 6.6 ± 0.5 ( 30)  | 6.5 ± 0.6 ( 22)  | 6.6 ± 0.4 ( 25)  | 6.5 ± 0.6 ( 25)  |
| Female                | 6.3 ± 0.5 ( 30)  | 6.2 ± 0.6 ( 22)  | 6.2 ± 0.4 ( 25)  | 6.2 ± 0.6 ( 25)  |
| Day 4 (After culling) |                  |                  |                  |                  |
| Male                  | 10.3 ± 1.4 ( 30) | 10.3 ± 1.2 ( 21) | 10.2 ± 1.0 ( 25) | 10.7 ± 1.6 ( 23) |
| Female                | 9.9 ± 1.3 ( 30)  | 9.7 ± 1.3 ( 21)  | 9.9 ± 1.0 ( 25)  | 10.3 ± 1.5 ( 23) |
| Day 7                 |                  |                  |                  |                  |
| Male                  | 16.9 ± 1.8 ( 30) | 16.8 ± 1.5 ( 21) | 17.0 ± 1.2 ( 25) | 17.0 ± 1.8 ( 23) |
| Female                | 16.3 ± 1.7 ( 30) | 16.0 ± 1.6 ( 21) | 16.2 ± 1.2 ( 25) | 16.4 ± 1.6 ( 23) |
| Day 14                |                  |                  |                  |                  |
| Male                  | 34.1 ± 2.7 ( 30) | 33.6 ± 2.7 ( 21) | 34.4 ± 2.3 ( 25) | 33.3 ± 2.5 ( 23) |
| Female                | 33.2 ± 2.7 ( 30) | 32.4 ± 2.8 ( 21) | 33.1 ± 2.5 ( 25) | 32.5 ± 2.4 ( 23) |
| Day 21                |                  |                  |                  |                  |
| Male                  | 56.0 ± 4.3 ( 30) | 55.2 ± 4.0 ( 21) | 55.3 ± 4.5 ( 25) | 54.7 ± 4.1 ( 23) |
| Female                | 53.9 ± 4.3 ( 30) | 53.2 ± 4.8 ( 21) | 53.4 ± 4.1 ( 25) | 52.7 ± 3.2 ( 23) |

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

b: animals were necropsied before mating