

o-クロロニトロベンゼンのマウスを用いた  
経口投与による2週間毒性試験（混餌試験）報告書

試験番号： 0434

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TABLE 1 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF MALE MICE IN THE 2-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

| Week-Day<br>on Study | Control        |                   | 625 ppm    |               |                   | 1250 ppm   |               |                   | 2500 ppm   |               |                   | 5000 ppm   |               |                   | 10000 ppm  |               |                   |
|----------------------|----------------|-------------------|------------|---------------|-------------------|------------|---------------|-------------------|------------|---------------|-------------------|------------|---------------|-------------------|------------|---------------|-------------------|
|                      | Av. Wt.<br><5> | No. of<br>Surviv. | Av. Wt.    | % of<br>cont. | No. of<br>Surviv. | Av. Wt.    | % of<br>cont. | No. of<br>Surviv. | Av. Wt.    | % of<br>cont. | No. of<br>Surviv. | Av. Wt.    | % of<br>cont. | No. of<br>Surviv. | Av. Wt.    | % of<br>cont. | No. of<br>Surviv. |
| 0-0                  | 23.4 ( 5 )     | 5 / 5             | 23.4 ( 5 ) | 100           | 5 / 5             | 23.3 ( 5 ) | 100           | 5 / 5             | 23.3 ( 5 ) | 100           | 5 / 5             | 23.4 ( 5 ) | 100           | 5 / 5             | 23.3 ( 5 ) | 100           | 5 / 5             |
| 1-3                  | 23.6 ( 5 )     | 5 / 5             | 23.7 ( 5 ) | 100           | 5 / 5             | 23.3 ( 5 ) | 99            | 5 / 5             | 22.2 ( 5 ) | 94            | 5 / 5             | 19.7 ( 5 ) | 83            | 5 / 5             | 17.5 ( 5 ) | 74            | 5 / 5             |
| 1-7                  | 24.4 ( 5 )     | 5 / 5             | 24.1 ( 5 ) | 99            | 5 / 5             | 24.1 ( 5 ) | 99            | 5 / 5             | 24.1 ( 5 ) | 99            | 5 / 5             | 21.9 ( 5 ) | 90            | 5 / 5             | 17.2 ( 5 ) | 70            | 5 / 5             |
| 2-3                  | 25.1 ( 5 )     | 5 / 5             | 24.7 ( 5 ) | 98            | 5 / 5             | 24.8 ( 5 ) | 99            | 5 / 5             | 24.7 ( 5 ) | 98            | 5 / 5             | 22.9 ( 5 ) | 91            | 5 / 5             | 16.6 ( 4 ) | 66            | 4 / 5             |
| 2-7                  | 25.7 ( 5 )     | 5 / 5             | 25.4 ( 5 ) | 99            | 5 / 5             | 25.7 ( 5 ) | 100           | 5 / 5             | 25.6 ( 5 ) | 100           | 5 / 5             | 23.5 ( 5 ) | 91            | 5 / 5             | 15.6 ( 3 ) | 61            | 3 / 5             |

< > : No.of effective animals, ( ) : No.of measured animals Av.Wt.:g

TABLE 2 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF FEMALE MICE IN THE 2-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

| Week-Day<br>on Study | Control        |                   | 625 ppm    |               |                   | 1250 ppm   |               |                   | 2500 ppm   |               |                   | 5000 ppm   |               |                   | 10000 ppm  |               |                   |
|----------------------|----------------|-------------------|------------|---------------|-------------------|------------|---------------|-------------------|------------|---------------|-------------------|------------|---------------|-------------------|------------|---------------|-------------------|
|                      | Av. Wt.<br><5> | No. of<br>Surviv. | Av. Wt.    | % of<br>cont. | No. of<br>Surviv. | Av. Wt.    | % of<br>cont. | No. of<br>Surviv. | Av. Wt.    | % of<br>cont. | No. of<br>Surviv. | Av. Wt.    | % of<br>cont. | No. of<br>Surviv. | Av. Wt.    | % of<br>cont. | No. of<br>Surviv. |
| 0-0                  | 18.7 ( 5 )     | 5 / 5             | 18.7 ( 5 ) | 100           | 5 / 5             | 18.7 ( 5 ) | 100           | 5 / 5             | 18.8 ( 5 ) | 101           | 5 / 5             | 18.8 ( 5 ) | 101           | 5 / 5             | 18.7 ( 5 ) | 100           | 5 / 5             |
| 1-3                  | 18.6 ( 5 )     | 5 / 5             | 19.1 ( 5 ) | 103           | 5 / 5             | 18.9 ( 5 ) | 102           | 5 / 5             | 18.8 ( 5 ) | 101           | 5 / 5             | 16.6 ( 5 ) | 89            | 5 / 5             | 13.8 ( 5 ) | 74            | 5 / 5             |
| 1-7                  | 18.7 ( 5 )     | 5 / 5             | 19.8 ( 5 ) | 106           | 5 / 5             | 19.6 ( 5 ) | 105           | 5 / 5             | 20.4 ( 5 ) | 109           | 5 / 5             | 19.2 ( 5 ) | 103           | 5 / 5             | 13.7 ( 5 ) | 73            | 5 / 5             |
| 2-3                  | 18.9 ( 5 )     | 5 / 5             | 19.8 ( 5 ) | 105           | 5 / 5             | 19.8 ( 5 ) | 105           | 5 / 5             | 20.3 ( 5 ) | 107           | 5 / 5             | 19.6 ( 5 ) | 104           | 5 / 5             | 13.3 ( 3 ) | 70            | 3 / 5             |
| 2-7                  | 19.4 ( 5 )     | 5 / 5             | 20.3 ( 5 ) | 105           | 5 / 5             | 20.3 ( 5 ) | 105           | 5 / 5             | 21.1 ( 5 ) | 109           | 5 / 5             | 20.8 ( 5 ) | 107           | 5 / 5             | 13.2 ( 3 ) | 68            | 3 / 5             |

< > : No.of effective animals, ( ) : No.of measured animals Av.Wt.:g

TABLE 3 FOOD CONSUMPTION CHANGES OF MALE MICE IN THE 2-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

| Week-Day<br>on Study | Control        |                            | 625 ppm        |                      |                            | 1250 ppm       |                      |                            | 2500 ppm       |                      |                            | 5000 ppm       |                      |                            | 10000 ppm      |                      |                            |
|----------------------|----------------|----------------------------|----------------|----------------------|----------------------------|----------------|----------------------|----------------------------|----------------|----------------------|----------------------------|----------------|----------------------|----------------------------|----------------|----------------------|----------------------------|
|                      | Av. Fc.<br><5> | No. of<br>Surviv.<br>5 / 5 | Av. Fc.<br><5> | % of<br>cont.<br><5> | No. of<br>Surviv.<br>5 / 5 | Av. Fc.<br><5> | % of<br>cont.<br><5> | No. of<br>Surviv.<br>5 / 5 | Av. Fc.<br><5> | % of<br>cont.<br><5> | No. of<br>Surviv.<br>5 / 5 | Av. Fc.<br><5> | % of<br>cont.<br><5> | No. of<br>Surviv.<br>5 / 5 | Av. Fc.<br><5> | % of<br>cont.<br><5> | No. of<br>Surviv.<br>5 / 5 |
| 1-3                  | 3.6 ( 5 )      | 5 / 5                      | 3.9 ( 5 )      | 108                  | 5 / 5                      | 3.4 ( 5 )      | 94                   | 5 / 5                      | 2.7 ( 5 )      | 75                   | 5 / 5                      | 1.5 ( 5 )      | 42                   | 5 / 5                      | 0.5 ( 5 )      | 14                   | 5 / 5                      |
| 1-7                  | 4.1 ( 5 )      | 5 / 5                      | 4.1 ( 5 )      | 100                  | 5 / 5                      | 4.3 ( 5 )      | 105                  | 5 / 5                      | 4.7 ( 5 )      | 115                  | 5 / 5                      | 3.9 ( 5 )      | 95                   | 5 / 5                      | 1.9 ( 5 )      | 46                   | 5 / 5                      |
| 2-3                  | 3.7 ( 5 )      | 5 / 5                      | 3.8 ( 5 )      | 103                  | 5 / 5                      | 3.8 ( 5 )      | 103                  | 5 / 5                      | 3.6 ( 5 )      | 97                   | 5 / 5                      | 3.2 ( 5 )      | 86                   | 5 / 5                      | 0.9 ( 4 )      | 24                   | 4 / 5                      |
| 2-7                  | 4.0 ( 5 )      | 5 / 5                      | 4.3 ( 5 )      | 108                  | 5 / 5                      | 4.3 ( 5 )      | 108                  | 5 / 5                      | 4.0 ( 5 )      | 100                  | 5 / 5                      | 3.6 ( 5 )      | 90                   | 5 / 5                      | 1.5 ( 3 )      | 38                   | 3 / 5                      |

< > : No.of effective animals, ( ) : No.of measured animals Av.Fc.:g

TABLE 4 FOOD CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

| Week-Day<br>on Study | Control        |                            | 625 ppm        |                      |                            | 1250 ppm       |                      |                            | 2500 ppm       |                      |                            | 5000 ppm       |                      |                            | 10000 ppm      |                      |                            |
|----------------------|----------------|----------------------------|----------------|----------------------|----------------------------|----------------|----------------------|----------------------------|----------------|----------------------|----------------------------|----------------|----------------------|----------------------------|----------------|----------------------|----------------------------|
|                      | Av. Fc.<br><5> | No. of<br>Surviv.<br>5 / 5 | Av. Fc.<br><5> | % of<br>cont.<br><5> | No. of<br>Surviv.<br>5 / 5 | Av. Fc.<br><5> | % of<br>cont.<br><5> | No. of<br>Surviv.<br>5 / 5 | Av. Fc.<br><5> | % of<br>cont.<br><5> | No. of<br>Surviv.<br>5 / 5 | Av. Fc.<br><5> | % of<br>cont.<br><5> | No. of<br>Surviv.<br>5 / 5 | Av. Fc.<br><5> | % of<br>cont.<br><5> | No. of<br>Surviv.<br>5 / 5 |
| 1-3                  | 3.2 ( 5 )      | 5 / 5                      | 3.4 ( 5 )      | 106                  | 5 / 5                      | 3.1 ( 5 )      | 97                   | 5 / 5                      | 2.8 ( 5 )      | 88                   | 5 / 5                      | 1.8 ( 5 )      | 56                   | 5 / 5                      | 0.7 ( 5 )      | 22                   | 5 / 5                      |
| 1-7                  | 3.7 ( 5 )      | 5 / 5                      | 3.7 ( 5 )      | 100                  | 5 / 5                      | 3.8 ( 5 )      | 103                  | 5 / 5                      | 3.9 ( 5 )      | 105                  | 5 / 5                      | 3.6 ( 5 )      | 97                   | 5 / 5                      | 2.3 ( 5 )      | 62                   | 5 / 5                      |
| 2-3                  | 3.3 ( 5 )      | 5 / 5                      | 3.4 ( 5 )      | 103                  | 5 / 5                      | 3.3 ( 5 )      | 100                  | 5 / 5                      | 3.2 ( 5 )      | 97                   | 5 / 5                      | 2.7 ( 5 )      | 82                   | 5 / 5                      | 1.7 ( 3 )      | 52                   | 3 / 5                      |
| 2-7                  | 3.8 ( 5 )      | 5 / 5                      | 3.8 ( 5 )      | 100                  | 5 / 5                      | 3.8 ( 5 )      | 100                  | 5 / 5                      | 3.5 ( 5 )      | 92                   | 5 / 5                      | 3.3 ( 5 )      | 87                   | 5 / 5                      | 1.6 ( 3 )      | 42                   | 3 / 5                      |

< > : No.of effective animals, ( ) : No.of measured animals Av.Fc.:g

TABLE 5 HEMATOLOGY OF MALE MICE IN THE 2-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

| Group Name                            | Control          | 625 ppm          | 1250 ppm        | 2500 ppm          | 5000 ppm        | 10000 ppm          |
|---------------------------------------|------------------|------------------|-----------------|-------------------|-----------------|--------------------|
| No. of examined animals               | 5                | 5                | 5               | 5                 | 5               | 3                  |
| Red blood cell ( $10^6/\mu\text{L}$ ) | 10.24 $\pm$ 0.42 | 10.10 $\pm$ 0.48 | 9.63 $\pm$ 0.36 | 9.30 $\pm$ 0.28 * | 9.54 $\pm$ 0.29 | 7.50 $\pm$ 0.99 ** |
| Hematocrit (%)                        | 48.4 $\pm$ 1.9   | 47.6 $\pm$ 2.2   | 45.2 $\pm$ 1.9  | 44.9 $\pm$ 2.8    | 49.7 $\pm$ 1.4  | 29.8 $\pm$ 1.6 **  |
| WBC ( $10^3/\mu\text{L}$ )            | 1.96 $\pm$ 0.73  | 1.58 $\pm$ 0.90  | 2.06 $\pm$ 0.47 | 2.24 $\pm$ 0.84   | 3.03 $\pm$ 1.53 | 7.10 $\pm$ 0.94 ** |
| Differential WBC (%)                  |                  |                  |                 |                   |                 |                    |
| N-SEG                                 | 14 $\pm$ 4       | 15 $\pm$ 4       | 10 $\pm$ 2      | 14 $\pm$ 3        | 16 $\pm$ 3      | 71 $\pm$ 5 **      |
| LYMPHO                                | 83 $\pm$ 5       | 80 $\pm$ 6       | 85 $\pm$ 3      | 82 $\pm$ 5        | 77 $\pm$ 5      | 18 $\pm$ 2 **      |

Mean  $\pm$  S.D.\*) Significant difference,  $p < 0.05$  (Test of Dunnett)\*\*) Significant difference,  $p < 0.01$  (Test of Dunnett)TABLE 6 HEMATOLOGY OF FEMALE MICE IN THE 2-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

| Group Name                            | Control         | 625 ppm         | 1250 ppm           | 2500 ppm           | 5000 ppm           | 10000 ppm          |
|---------------------------------------|-----------------|-----------------|--------------------|--------------------|--------------------|--------------------|
| No. of examined animals               | 5               | 5               | 5                  | 5                  | 5                  | 3                  |
| Red blood cell ( $10^6/\mu\text{L}$ ) | 9.95 $\pm$ 0.26 | 9.88 $\pm$ 0.12 | 9.26 $\pm$ 0.19 ** | 8.67 $\pm$ 0.14 ** | 8.91 $\pm$ 0.22 ** | 5.38 $\pm$ 0.37 ** |
| Hematocrit (%)                        | 47.5 $\pm$ 0.9  | 46.8 $\pm$ 0.5  | 44.8 $\pm$ 1.3 **  | 43.8 $\pm$ 1.0 **  | 46.8 $\pm$ 1.7     | 32.8 $\pm$ 1.8 **  |
| MCV (fL)                              | 47.8 $\pm$ 0.7  | 47.4 $\pm$ 0.4  | 48.3 $\pm$ 0.5     | 50.5 $\pm$ 1.3     | 52.5 $\pm$ 1.0 *   | 61.1 $\pm$ 2.5 **  |

Mean  $\pm$  S.D.\*) Significant difference,  $p < 0.05$  (Test of Dunnett)\*\*) Significant difference,  $p < 0.01$  (Test of Dunnett)

TABLE 7 BIOCHEMISTRY OF MALE MICE IN THE 2-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

| Group Name              | Control     | 625 ppm     | 1250 ppm    | 2500 ppm     | 5000 ppm       | 10000 ppm      |
|-------------------------|-------------|-------------|-------------|--------------|----------------|----------------|
| No. of examined animals | 5           | 5           | 5           | 5            | 5              | 3              |
| Total protein (g/dL)    | 4.8 ± 0.1   | 4.8 ± 0.1   | 5.0 ± 0.1   | 5.3 ± 0.1 ** | 5.6 ± 0.1 **   | 5.6 ± 0.1 **   |
| Albumin (g/dL)          | 2.9 ± 0.1   | 2.9 ± 0.1   | 3.0 ± 0.1   | 3.2 ± 0.1 ** | 3.5 ± 0.1 **   | 3.6 ± 0.1 **   |
| A/G ratio               | 1.5 ± 0.1   | 1.5 ± 0.1   | 1.6 ± 0.1   | 1.5 ± 0.1    | 1.6 ± 0.1 *    | 1.8 ± 0.1 **   |
| T-Bilirubin (mg/dL)     | 0.15 ± 0.02 | 0.15 ± 0.01 | 0.18 ± 0.01 | 0.20 ± 0.01  | 0.33 ± 0.02 ** | 0.88 ± 0.33 ** |
| Glucose (mg/dL)         | 322 ± 16    | 303 ± 27    | 295 ± 26    | 281 ± 26     | 233 ± 16 **    | 61 ± 68 **     |
| T-Cholesterol (mg/dL)   | 93 ± 7      | 122 ± 11    | 160 ± 7     | 226 ± 23 **  | 340 ± 43 **    | 201 ± 16       |
| Phospholipid (mg/dL)    | 204 ± 10    | 246 ± 13    | 292 ± 11    | 374 ± 31 **  | 519 ± 45 **    | 281 ± 40       |
| GOT (IU/L)              | 31 ± 2      | 28 ± 2      | 29 ± 2      | 34 ± 8       | 52 ± 5         | 689 ± 549      |
| GPT (IU/L)              | 18 ± 1      | 22 ± 3      | 27 ± 4      | 46 ± 18 *    | 94 ± 12 **     | 877 ± 716 **   |
| LDH (IU/L)              | 185 ± 18    | 171 ± 12    | 187 ± 32    | 254 ± 58     | 423 ± 53 *     | 11703 ± 7593 * |
| $\gamma$ -GTP(IU/L)     | 1 ± 1       | 1 ± 1       | 1 ± 0       | 2 ± 0        | 17 ± 1         | 12 ± 6         |
| CPK (IU/L)              | 61 ± 18     | 72 ± 24     | 52 ± 12     | 74 ± 25      | 80 ± 22        | 941 ± 660 *    |
| Urea Nitrogen(mg/L)     | 23.0 ± 4.6  | 24.3 ± 2.5  | 23.0 ± 3.1  | 20.1 ± 7.6   | 20.8 ± 1.5     | 45.1 ± 25.2    |
| Potassium (mEq/L)       | 4.8 ± 0.6   | 4.8 ± 0.2   | 4.6 ± 0.2   | 4.5 ± 0.3    | 5.1 ± 0.6      | 6.0 ± 0.2 **   |
| Chloride (mEq/L)        | 118 ± 1     | 118 ± 2     | 117 ± 2     | 115 ± 2      | 113 ± 1 *      | 116 ± 6        |
| Calcium(mg/dL)          | 9.1 ± 0.1   | 9.2 ± 0.1   | 9.4 ± 0.2   | 9.7 ± 0.2 ** | 9.5 ± 0.2 **   | 10.1 ± 0.1 **  |

Mean ± S.D.

\*) Significant difference, p&lt;0.05 (Test of Dunnett)

\*\*) Significant difference, p&lt;0.01 (Test of Dunnett)

TABLE 8 BIOCHEMISTRY OF FEMALE MICES IN THE 2-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

| Group Name              | Control     | 625 ppm     | 1250 ppm    | 2500 ppm    | 5000 ppm       | 10000 ppm      |
|-------------------------|-------------|-------------|-------------|-------------|----------------|----------------|
| No. of examined animals | 5           | 5           | 5           | 5           | 5              | 3              |
| Total protein (g/dL)    | 4.7 ± 0.0   | 4.8 ± 0.1   | 5.0 ± 0.3   | 5.1 ± 0.1   | 5.5 ± 0.2 **   | 5.8 ± 0.2 **   |
| Albumin (g/dL)          | 3.0 ± 0.1   | 3.1 ± 0.1   | 3.2 ± 0.2   | 3.2 ± 0.1   | 3.6 ± 0.1 **   | 4.0 ± 0.4 **   |
| A/G ratio               | 1.8 ± 0.1   | 1.9 ± 0.1   | 1.8 ± 0.2   | 1.7 ± 0.1   | 1.8 ± 0.2      | 2.3 ± 0.4 *    |
| T-Bilirubin (mg/dL)     | 0.17 ± 0.01 | 0.17 ± 0.03 | 0.19 ± 0.03 | 0.21 ± 0.01 | 0.26 ± 0.04 ** | 0.65 ± 0.15 ** |
| Glucose (mg/dL)         | 280 ± 33    | 261 ± 19    | 257 ± 17    | 257 ± 8     | 226 ± 18 **    | 85 ± 29 **     |
| T-Cholesterol (mg/dL)   | 74 ± 5      | 112 ± 13    | 136 ± 11    | 204 ± 13 *  | 318 ± 31 **    | 244 ± 7 **     |
| Phospholipid (mg/dL)    | 163 ± 14    | 218 ± 20    | 241 ± 17    | 322 ± 6 *   | 486 ± 56 **    | 345 ± 22 *     |
| GOT (IU/L)              | 45 ± 8      | 35 ± 5      | 36 ± 3      | 38 ± 2      | 61 ± 19        | 130 ± 30       |
| GPT (IU/L)              | 24 ± 8      | 22 ± 5      | 26 ± 2      | 42 ± 3      | 111 ± 45 **    | 116 ± 50 *     |
| LDH (IU/L)              | 268 ± 50    | 204 ± 28    | 194 ± 22    | 250 ± 34    | 343 ± 118      | 3398 ± 305     |
| γ-GTP(IU/L)             | 1 ± 1       | 1 ± 0       | 1 ± 1       | 1 ± 0       | 20 ± 3         | 29 ± 7 *       |
| CPK (IU/L)              | 119 ± 76    | 52 ± 20     | 59 ± 20     | 65 ± 23     | 61 ± 26        | 262 ± 50       |
| Urea Nitrogen(mg/L)     | 21.9 ± 1.8  | 18.2 ± 3.5  | 16.6 ± 1.2  | 17.0 ± 2.9  | 20.4 ± 3.2     | 37.9 ± 11.0    |
| Sodium (mEq/L)          | 148 ± 3     | 148 ± 1     | 148 ± 1     | 148 ± 1     | 149 ± 1        | 152 ± 1 **     |
| Potassium (mEq/L)       | 4.6 ± 0.3   | 4.4 ± 0.4   | 4.7 ± 0.4   | 4.2 ± 0.2   | 4.8 ± 0.7      | 5.7 ± 0.6 *    |
| Chloride (mEq/L)        | 120 ± 2     | 119 ± 1     | 119 ± 2     | 117 ± 1 *   | 115 ± 1 **     | 115 ± 3 **     |
| Calcium(mg/dL)          | 9.1 ± 0.1   | 9.2 ± 0.3   | 9.1 ± 0.3   | 9.5 ± 0.1 * | 9.6 ± 0.3 **   | 9.4 ± 0.2      |

Mean ± S.D.

\*) Significant difference, p&lt;0.05 (Test of Dunnett)

\*\*) Significant difference, p&lt;0.01 (Test of Dunnett)

TABLE 9 ORGAN WEIGHTS OF MALE MICE IN THE 2-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

| Group Name              | Control       | 625 ppm         | 1250 ppm         | 2500 ppm         | 5000 ppm          | 10000 ppm        |
|-------------------------|---------------|-----------------|------------------|------------------|-------------------|------------------|
| No. of examined animals | 5             | 5               | 5                | 5                | 5                 | 3                |
| Body weight (g)         | 25.5 ± 0.9    | 25.1 ± 1.3      | 25.4 ± 1.1       | 25.4 ± 1.1       | 23.3 ± 0.9 *      | 15.4 ± 0.7 **    |
| Thymus (g)              | 0.056 ± ##### | 0.054 ± #####   | 0.056 ± #####    | 0.054 ± #####    | 0.028 ± ##### **  | 0.007 ± ##### ** |
| Thymus (%)              | 0.220 ± ##### | 0.214 ± #####   | 0.219 ± #####    | 0.212 ± #####    | 0.120 ± ##### **  | 0.043 ± ##### ** |
| Adrenals (g)            | 0.009 ± ##### | 0.008 ± #####   | 0.008 ± #####    | 0.008 ± #####    | 0.008 ± #####     | 0.009 ± #####    |
| Adrenals (%)            | 0.037 ± ##### | 0.034 ± #####   | 0.031 ± #####    | 0.032 ± #####    | 0.035 ± #####     | 0.056 ± ##### ** |
| Testes (g)              | 0.197 ± ##### | 0.182 ± #####   | 0.195 ± #####    | 0.186 ± #####    | 0.182 ± #####     | 0.056 ± ##### ** |
| Testes (%)              | 0.773 ± ##### | 0.722 ± #####   | 0.770 ± #####    | 0.736 ± #####    | 0.782 ± #####     | 0.360 ± ##### ** |
| Heart (g)               | 0.142 ± ##### | 0.141 ± #####   | 0.139 ± #####    | 0.141 ± #####    | 0.130 ± #####     | 0.130 ± #####    |
| Heart (%)               | 0.557 ± ##### | 0.559 ± #####   | 0.546 ± #####    | 0.557 ± #####    | 0.559 ± #####     | 0.842 ± ##### ** |
| Lungs (g)               | 0.155 ± ##### | 0.148 ± #####   | 0.157 ± #####    | 0.148 ± #####    | 0.149 ± #####     | 0.146 ± #####    |
| Lungs (%)               | 0.610 ± ##### | 0.588 ± #####   | 0.620 ± #####    | 0.582 ± #####    | 0.639 ± #####     | 0.948 ± ##### *  |
| Kidneys (g)             | 0.363 ± ##### | 0.379 ± #####   | 0.402 ± #####    | 0.388 ± #####    | 0.375 ± #####     | 0.313 ± #####    |
| Kidneys (%)             | 1.427 ± ##### | 1.510 ± #####   | 1.581 ± ##### *  | 1.529 ± #####    | 1.609 ± ##### *   | 2.031 ± ##### ** |
| Spleen (g)              | 0.048 ± ##### | 0.056 ± #####   | 0.072 ± #####    | 0.112 ± ##### ** | 0.145 ± ##### **  | 0.111 ± #####    |
| Spleen (%)              | 0.190 ± ##### | 0.221 ± #####   | 0.282 ± ##### ** | 0.442 ± ##### ** | 0.623 ± ##### **  | 0.720 ± ##### ** |
| Liver (g)               | 1.316 ± ##### | 1.563 ± ##### * | 1.825 ± ##### ** | 2.229 ± ##### ** | 2.378 ± ##### **  | 1.512 ± #####    |
| Liver (%)               | 5.180 ± ##### | 6.211 ± ##### * | 7.188 ± ##### ** | 8.783 ± ##### ** | 10.213 ± ##### ** | 9.790 ± ##### ** |
| Brain (g)               | 0.446 ± ##### | 0.435 ± #####   | 0.438 ± #####    | 0.437 ± #####    | 0.427 ± #####     | 0.419 ± #####    |
| Brain (%)               | 1.752 ± ##### | 1.733 ± #####   | 1.727 ± #####    | 1.722 ± #####    | 1.834 ± #####     | 2.715 ± ##### ** |

Mean ± S.D.

\*) Significant difference, p&lt;0.05 (Test of Dunnett)

\*\*) Significant difference, p&lt;0.01 (Test of Dunnett)



TABLE 10 ORGAN WEIGHTS OF FEMALE MICE IN THE 2-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

| Group Name              | Control       | 625 ppm          | 1250 ppm         | 2500 ppm         | 5000 ppm          | 10000 ppm         |
|-------------------------|---------------|------------------|------------------|------------------|-------------------|-------------------|
| No. of examined animals | 5             | 5                | 5                | 5                | 5                 | 3                 |
| Body weight (g)         | 19.3 ± 0.7    | 20.3 ± 0.7       | 20.0 ± 0.6       | 20.8 ± 0.8 **    | 20.5 ± 0.7 *      | 13.0 ± 0.4 **     |
| Thymus (g)              | 0.069 ± 0.005 | 0.075 ± 0.008    | 0.073 ± 0.007    | 0.073 ± 0.008    | 0.054 ± 0.008 **  | 0.008 ± 0.003 **  |
| Thymus (%)              | 0.361 ± 0.032 | 0.372 ± 0.041    | 0.365 ± 0.026    | 0.350 ± 0.026    | 0.263 ± 0.037 **  | 0.059 ± 0.020 **  |
| Ovaries (g)             | 0.027 ± 0.003 | 0.025 ± 0.006    | 0.025 ± 0.006    | 0.030 ± 0.007    | 0.027 ± 0.005     | 0.007 ± 0.002 **  |
| Ovaries (%)             | 0.138 ± 0.014 | 0.124 ± 0.029    | 0.126 ± 0.029    | 0.141 ± 0.029    | 0.132 ± 0.027     | 0.051 ± 0.018 **  |
| Heart (g)               | 0.112 ± 0.009 | 0.118 ± 0.012    | 0.119 ± 0.013    | 0.118 ± 0.013    | 0.114 ± 0.004     | 0.090 ± 0.004 *   |
| Heart (%)               | 0.583 ± 0.032 | 0.583 ± 0.049    | 0.597 ± 0.066    | 0.568 ± 0.049    | 0.554 ± 0.030     | 0.692 ± 0.036 *   |
| Lungs (g)               | 0.134 ± 0.005 | 0.144 ± 0.015    | 0.138 ± 0.009    | 0.138 ± 0.010    | 0.141 ± 0.009     | 0.116 ± 0.006     |
| Lungs (%)               | 0.694 ± 0.024 | 0.712 ± 0.074    | 0.688 ± 0.033    | 0.663 ± 0.042    | 0.686 ± 0.045     | 0.893 ± 0.067 **  |
| Kidneys (g)             | 0.251 ± 0.008 | 0.265 ± 0.015    | 0.271 ± 0.021    | 0.266 ± 0.012    | 0.274 ± 0.020     | 0.244 ± 0.007     |
| Kidneys (%)             | 1.307 ± 0.072 | 1.306 ± 0.083    | 1.355 ± 0.101    | 1.280 ± 0.038    | 1.333 ± 0.073     | 1.879 ± 0.031 **  |
| Spleen (g)              | 0.053 ± 0.004 | 0.067 ± 0.004    | 0.104 ± 0.018    | 0.141 ± 0.015 ** | 0.172 ± 0.010 **  | 0.133 ± 0.004 *   |
| Spleen (%)              | 0.274 ± 0.014 | 0.329 ± 0.017 ** | 0.519 ± 0.086 ** | 0.678 ± 0.068 ** | 0.836 ± 0.032 **  | 1.028 ± 0.016 **  |
| Liver (g)               | 0.925 ± 0.079 | 1.291 ± 0.088 ** | 1.394 ± 0.095 ** | 1.746 ± 0.122 ** | 2.111 ± 0.138 **  | 1.402 ± 0.031 **  |
| Liver (%)               | 4.803 ± 0.379 | 6.357 ± 0.368 ** | 6.978 ± 0.438 ** | 8.382 ± 0.303 ** | 10.281 ± 0.359 ** | 10.819 ± 0.414 ** |
| Brain (g)               | 0.425 ± 0.023 | 0.446 ± 0.011    | 0.431 ± 0.009    | 0.435 ± 0.013    | 0.417 ± 0.017     | 0.396 ± 0.016     |
| Brain (%)               | 2.208 ± 0.078 | 2.200 ± 0.088    | 2.157 ± 0.073    | 2.088 ± 0.045    | 2.031 ± 0.091 *   | 3.055 ± 0.201 **  |

Mean ± S.D.  
<sup>\*</sup>) Significant difference, p<0.05 (Test of Dunnett)  
<sup>\*\*</sup>) Significant difference, p<0.01 (Test of Dunnett)

TABLE 11 INCIDENCES OF SELECTED LESIONS OF MALE MICE IN THE 2-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

| Group<br>Number of examined animals<br>Organ | Grade of<br>Nonneoplastic<br>lesion | Control | 625ppm | 1250ppm | 2500ppm | 5000ppm | 10000ppm                          |
|--|-------------------------------------|---------|--------|---------|---------|---------|-----------------------------------|
|  |                                     | 5       | 5      | 5       | 5       | 5       | 5 (2)                             |
| <b>Findings</b>                              |                                     |         |        |         |         |         |                                   |
| Nasal cavity                                 |                                     |         |        |         |         |         |                                   |
| Atrophy:<br>olfactory epithelium             | 1+                                  | 0       | 0      | 0       | 0       | 5       | 5 (2)                             |
| Bone marrow                                  |                                     |         |        |         |         |         |                                   |
| Erythropoiesis:increased                     | 1+                                  | 0       | 0      | 0       | 0       | 0       | 4 (1)                             |
| Thymus                                       |                                     |         |        |         |         |         |                                   |
| Atrophy                                      | 3+                                  | 0       | 0      | 0       | 0       | 0       | 4 <sup>a)</sup> (1) <sup>b)</sup> |
| Spleen                                       |                                     |         |        |         |         |         |                                   |
| deposit of hemosiderin                       | 1+                                  | 0       | 0      | 3       | 0       | 0       | 0 (0)                             |
|  | 2+                                  | 0       | 0      | 0       | 5       | 5       | 4 (1)                             |
| Extramedullary hematopoiesis                 | 1+                                  | 0       | 0      | 1       | 0       | 0       | 0 (0)                             |
|  | 2+                                  | 0       | 0      | 2       | 5       | 5       | 2 (1)                             |
|  | 3+                                  | 0       | 0      | 0       | 0       | 0       | 3 (1)                             |
| Engorgement of erythrocyte                   | 1+                                  | 0       | 0      | 4       | 5       | 5       | 1 (0)                             |
|  | 2+                                  | 0       | 0      | 0       | 0       | 0       | 4 (2)                             |
| Vein   |                                     |         |        |         |         |         |                                   |
| Thrombus                                     | 1+                                  | 0       | 0      | 0       | 0       | 0       | 3 (1)                             |
| Tongue                                       |                                     |         |        |         |         |         |                                   |
| Mineralization                               | 1+                                  | 0       | 0      | 0       | 0       | 0       | 1 (1)                             |
| Stomach                                      |                                     |         |        |         |         |         |                                   |
| Erosion:forestomach                          | 1+                                  | 0       | 0      | 0       | 0       | 0       | 2 (1)                             |
|  | 2+                                  | 0       | 0      | 0       | 0       | 0       | 1 (0)                             |
| Hyperplasia:forestomach                      | 1+                                  | 0       | 0      | 0       | 0       | 1       | 1 (0)                             |
|  | 2+                                  | 0       | 0      | 0       | 1       | 0       | 2 (1)                             |
| Liver  |                                     |         |        |         |         |         |                                   |
| Increase in mitosis                          | 1+                                  | 0       | 0      | 0       | 5       | 5       | 0 (0)                             |
| Necrosis:central                             | 2+                                  | 0       | 0      | 0       | 0       | 0       | 1 (1)                             |
| Necrosis:single cell                         | 1+                                  | 0       | 0      | 0       | 0       | 0       | 4 (1)                             |
| Deposit of hemosiderin                       | 1+                                  | 0       | 0      | 0       | 0       | 0       | 2 (2)                             |
|  | 2+                                  | 0       | 0      | 0       | 0       | 0       | 1 (0)                             |
| Hydropic change:central                      | 2+                                  | 0       | 0      | 0       | 0       | 0       | 3 (2)                             |
| Hepatocellular hypertrophy:<br>central       | 3+                                  | 0       | 5      | 5       | 5       | 5       | 2 (0)                             |
| Testis                                       |                                     |         |        |         |         |         |                                   |
| Germ cell necrosis                           | 1+                                  | 0       | 0      | 0       | 0       | 0       | 2 (1)                             |
|  | 2+                                  | 0       | 0      | 0       | 0       | 0       | 3 (1)                             |
| Epididymis                                   |                                     |         |        |         |         |         |                                   |
| Debris of spermatic elements                 | 1+                                  | 0       | 0      | 0       | 0       | 0       | 3 (1) <sup>c)</sup>               |
|  | 2+                                  | 0       | 0      | 0       | 0       | 0       | 1 (0)                             |
| Brain  |                                     |         |        |         |         |         |                                   |
| Hemorrhage                                   | 1+                                  | 0       | 0      | 0       | 0       | 0       | 1 (1)                             |
| Haderien gland                               |                                     |         |        |         |         |         |                                   |
| Necrosis                                     | 1+                                  | 0       | 0      | 0       | 0       | 0       | 1 (1)                             |
| Muscle                                       |                                     |         |        |         |         |         |                                   |
| Mineralization                               | 1+                                  | 0       | 0      | 0       | 0       | 0       | 3 (1)                             |

Grade : 1+.Slight 2+.Moderate 3+.Marked 4+.Severe  
 ( ) : Number of dead animals.  
 a) : Number of examined animal is 4 according to the atrophy.  
 b) : Number of examined animal is 1 according to the atrophy.  
 c) : Number of examined animal is 1 according to missing.

TABLE 12 INCIDENCES OF SELECTED LESIONS OF FEMALE MICE IN THE 2-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

| Group<br>Number of examined animals<br>Organ | Grade of<br>Nonneoplastic<br>lesion | Control | 625ppm | 1250ppm | 2500ppm | 5000ppm | 10000ppm |
|--|-------------------------------------|---------|--------|---------|---------|---------|----------|
|  |                                     | 5       | 5      | 5       | 5       | 5       | 5 (2)    |
| <b>Findings</b>                              |                                     |         |        |         |         |         |          |
| Nasal cavity                                 |                                     |         |        |         |         |         |          |
| Respiratory metaplasia:<br>gland             | 1+                                  | 0       | 0      | 0       | 1       | 0       | 1 (0)    |
| Atrophy:<br>olfactory epithelium             | 1+                                  | 0       | 0      | 0       | 0       | 3       | 4 (1)    |
|  | 2+                                  | 0       | 0      | 0       | 0       | 0       | 1 (1)    |
| Lung   |                                     |         |        |         |         |         |          |
| Congestion                                   | 2+                                  | 0       | 0      | 0       | 0       | 0       | 2 (2)    |
| Bone marrow                                  |                                     |         |        |         |         |         |          |
| Erythropoiesis:increased                     | 1+                                  | 0       | 0      | 0       | 0       | 5       | 4 (1)    |
| Thymus                                       |                                     |         |        |         |         |         |          |
| Atrophy                                      | 3+                                  | 0       | 0      | 0       | 0       | 0       | 5 (2)    |
| Spleen                                       |                                     |         |        |         |         |         |          |
| deposit of hemosiderin                       | 1+                                  | 0       | 0      | 5       | 0       | 0       | 4 (2)    |
|  | 2+                                  | 0       | 0      | 0       | 5       | 5       | 1 (0)    |
| Extramedullary hematopoiesis                 | 1+                                  | 0       | 4      | 0       | 0       | 0       | 0 (0)    |
|  | 2+                                  | 0       | 0      | 5       | 5       | 5       | 1 (1)    |
|  | 3+                                  | 0       | 0      | 0       | 0       | 0       | 4 (1)    |
| Engorgement of erythrocyte                   | 1+                                  | 0       | 0      | 5       | 5       | 5       | 3 (0)    |
|  | 2+                                  | 0       | 0      | 0       | 0       | 0       | 2 (2)    |
| Heart  |                                     |         |        |         |         |         |          |
| Mineralization                               | 1+                                  | 0       | 0      | 0       | 0       | 0       | 4 (2)    |
| Stomach                                      |                                     |         |        |         |         |         |          |
| Erosion:forestomach                          | 1+                                  | 0       | 0      | 1       | 0       | 1       | 1 (0)    |
| Hyperplasia:forestomach                      | 1+                                  | 0       | 0      | 2       | 1       | 0       | 1 (0)    |
|  | 2+                                  | 0       | 0      | 0       | 1       | 2       | 1 (0)    |
| Liver  |                                     |         |        |         |         |         |          |
| Increase in mitosis                          | 1+                                  | 0       | 0      | 0       | 3       | 4       | 0 (0)    |
| Necrosis:central                             | 2+                                  | 0       | 0      | 0       | 0       | 0       | 2 (2)    |
| Deposit of hemosiderin                       | 1+                                  | 0       | 0      | 0       | 0       | 0       | 1 (1)    |
|  | 2+                                  | 0       | 0      | 0       | 0       | 0       | 3 (0)    |
| Hydropic change:central                      | 2+                                  | 0       | 0      | 0       | 0       | 0       | 2 (2)    |
| Hepatocellular hypertrophy:<br>central       | 1+                                  | 0       | 1      | 0       | 0       | 0       | 0 (0)    |
|  | 2+                                  | 0       | 3      | 0       | 0       | 0       | 0 (0)    |
|  | 3+                                  | 0       | 1      | 5       | 5       | 5       | 3 (0)    |
| Kidney                                       |                                     |         |        |         |         |         |          |
| Deposit of hemosiderin                       | 1+                                  | 0       | 0      | 0       | 0       | 0       | 3 (0)    |
| Adrenal                                      |                                     |         |        |         |         |         |          |
| Extramedullary hematopoiesis                 | 1+                                  | 0       | 0      | 0       | 0       | 0       | 1 (0)    |
| Brain  |                                     |         |        |         |         |         |          |
| Hemorrhage                                   | 1+                                  | 0       | 0      | 0       | 0       | 0       | 1 (0)    |
| Muscle                                       |                                     |         |        |         |         |         |          |
| Mineralization                               | 1+                                  | 0       | 0      | 0       | 0       | 0       | 1 (0)    |

Grade : 1+.Slight 2+.Moderate 3+.Marked 4+.Severe

( ) : Number of dead animals.