

o-クロロニトロベンゼンのラットを用いた
経口投与による 13 週間毒性試験（混餌試験）報告書

試験番号： 0439

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TABLE 1 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF MALE RATS IN THE 13-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

| Week on Study | Control | | 63 ppm | | | 250 ppm | | | 1000 ppm | | | 2000 ppm | | | 4000 ppm | | |
|------------------|-----------------|-------------------|------------|-----------------------|-------------------|------------|-----------------------|-------------------|------------|-----------------------|-------------------|------------|-----------------------|-------------------|------------|-----------------------|-------------------|
| | Av. Wt. <10> | No. of Surviv. | Av. Wt. | % of cont. <10> | No. of Surviv. | Av. Wt. | % of cont. <10> | No. of Surviv. | Av. Wt. | % of cont. <10> | No. of Surviv. | Av. Wt. | % of cont. <10> | No. of Surviv. | Av. Wt. | % of cont. <10> | No. of Surviv. |
| 0 | 127 (10) | 10 / 10 | 127 (10) | 100 | 10 / 10 | 127 (10) | 100 | 10 / 10 | 127 (10) | 100 | 10 / 10 | 127 (10) | 100 | 10 / 10 | 127 (10) | 100 | 10 / 10 |
| 1 | 154 (10) | 10 / 10 | 156 (10) | 101 | 10 / 10 | 156 (10) | 101 | 10 / 10 | 154 (10) | 100 | 10 / 10 | 148 (10) | 96 | 10 / 10 | 133 (10) | 86 | 10 / 10 |
| 2 | 180 (10) | 10 / 10 | 182 (10) | 101 | 10 / 10 | 182 (10) | 101 | 10 / 10 | 181 (10) | 101 | 10 / 10 | 173 (10) | 96 | 10 / 10 | 154 (10) | 86 | 10 / 10 |
| 3 | 202 (10) | 10 / 10 | 207 (10) | 102 | 10 / 10 | 202 (10) | 100 | 10 / 10 | 204 (10) | 101 | 10 / 10 | 194 (10) | 96 | 10 / 10 | 172 (10) | 85 | 10 / 10 |
| 4 | 219 (10) | 10 / 10 | 225 (10) | 103 | 10 / 10 | 219 (10) | 100 | 10 / 10 | 221 (10) | 101 | 10 / 10 | 213 (10) | 97 | 10 / 10 | 187 (10) | 85 | 10 / 10 |
| 5 | 230 (10) | 10 / 10 | 236 (10) | 103 | 10 / 10 | 231 (10) | 100 | 10 / 10 | 234 (10) | 102 | 10 / 10 | 225 (10) | 98 | 10 / 10 | 199 (10) | 87 | 10 / 10 |
| 6 | 242 (10) | 10 / 10 | 248 (10) | 102 | 10 / 10 | 243 (10) | 100 | 10 / 10 | 245 (10) | 101 | 10 / 10 | 237 (10) | 98 | 10 / 10 | 207 (10) | 86 | 10 / 10 |
| 7 | 254 (10) | 10 / 10 | 261 (10) | 103 | 10 / 10 | 257 (10) | 101 | 10 / 10 | 259 (10) | 102 | 10 / 10 | 249 (10) | 98 | 10 / 10 | 217 (10) | 85 | 10 / 10 |
| 8 | 265 (10) | 10 / 10 | 273 (10) | 103 | 10 / 10 | 268 (10) | 101 | 10 / 10 | 272 (10) | 103 | 10 / 10 | 260 (10) | 98 | 10 / 10 | 228 (10) | 86 | 10 / 10 |
| 9 | 272 (10) | 10 / 10 | 283 (10) | 104 | 10 / 10 | 276 (10) | 101 | 10 / 10 | 280 (10) | 103 | 10 / 10 | 269 (10) | 99 | 10 / 10 | 236 (10) | 87 | 10 / 10 |
| 10 | 281 (10) | 10 / 10 | 290 (10) | 103 | 10 / 10 | 284 (10) | 101 | 10 / 10 | 288 (10) | 102 | 10 / 10 | 277 (10) | 99 | 10 / 10 | 242 (10) | 86 | 10 / 10 |
| 11 | 289 (10) | 10 / 10 | 297 (10) | 103 | 10 / 10 | 291 (10) | 101 | 10 / 10 | 294 (10) | 102 | 10 / 10 | 282 (10) | 98 | 10 / 10 | 247 (10) | 85 | 10 / 10 |
| 12 | 295 (10) | 10 / 10 | 304 (10) | 103 | 10 / 10 | 297 (10) | 101 | 10 / 10 | 300 (10) | 102 | 10 / 10 | 289 (10) | 98 | 10 / 10 | 250 (10) | 85 | 10 / 10 |
| 13 | 298 (10) | 10 / 10 | 307 (10) | 103 | 10 / 10 | 300 (10) | 101 | 10 / 10 | 301 (10) | 101 | 10 / 10 | 289 (10) | 97 | 10 / 10 | 248 (10) | 83 | 10 / 10 |

< > : No.of effective animals, () : No.of measured animals, Av.Wt.:Averaged body weight (Unit : g) .

TABLE 2 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF FEMALE RATS IN THE 13-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

| Week on Study | Control | | | 63 ppm | | | 250 ppm | | | 1000 ppm | | | 2000 ppm | | | 4000 ppm | | |
|------------------|-----------------|-------------------|-------------------|-----------------|---------------|-------------------|-----------------|---------------|-------------------|-----------------|---------------|-------------------|-----------------|---------------|-------------------|-----------------|---------------|-------------------|
| | Av. Wt. <10> | No. of Surviv. | No. of Surviv. | Av. Wt. <10> | % of cont. | No. of Surviv. | Av. Wt. <10> | % of cont. | No. of Surviv. | Av. Wt. <10> | % of cont. | No. of Surviv. | Av. Wt. <10> | % of cont. | No. of Surviv. | Av. Wt. <10> | % of cont. | No. of Surviv. |
| 0 | 99 (10) | 10 / 10 | 10 / 10 | 99 (10) | 100 | 10 / 10 | 99 (10) | 100 | 10 / 10 | 99 (10) | 100 | 10 / 10 | 99 (10) | 100 | 10 / 10 | 99 (10) | 100 | 10 / 10 |
| 1 | 112 (10) | 10 / 10 | 10 / 10 | 113 (10) | 101 | 10 / 10 | 113 (10) | 101 | 10 / 10 | 111 (10) | 99 | 10 / 10 | 108 (10) | 96 | 10 / 10 | 99 (10) | 88 | 10 / 10 |
| 2 | 122 (10) | 10 / 10 | 10 / 10 | 123 (10) | 101 | 10 / 10 | 124 (10) | 102 | 10 / 10 | 121 (10) | 99 | 10 / 10 | 119 (10) | 98 | 10 / 10 | 110 (10) | 90 | 10 / 10 |
| 3 | 132 (10) | 10 / 10 | 10 / 10 | 132 (10) | 100 | 10 / 10 | 132 (10) | 100 | 10 / 10 | 128 (10) | 97 | 10 / 10 | 127 (10) | 96 | 10 / 10 | 118 (10) | 89 | 10 / 10 |
| 4 | 139 (10) | 10 / 10 | 10 / 10 | 140 (10) | 101 | 10 / 10 | 139 (10) | 100 | 10 / 10 | 135 (10) | 97 | 10 / 10 | 132 (10) | 95 | 10 / 10 | 123 (10) | 88 | 10 / 10 |
| 5 | 145 (10) | 10 / 10 | 10 / 10 | 145 (10) | 100 | 10 / 10 | 146 (10) | 101 | 10 / 10 | 139 (10) | 96 | 10 / 10 | 137 (10) | 94 | 10 / 10 | 128 (10) | 88 | 10 / 10 |
| 6 | 149 (10) | 10 / 10 | 10 / 10 | 149 (10) | 100 | 10 / 10 | 149 (10) | 100 | 10 / 10 | 144 (10) | 97 | 10 / 10 | 141 (10) | 95 | 10 / 10 | 131 (10) | 88 | 10 / 10 |
| 7 | 152 (10) | 10 / 10 | 10 / 10 | 153 (10) | 101 | 10 / 10 | 154 (10) | 101 | 10 / 10 | 148 (10) | 97 | 10 / 10 | 146 (10) | 96 | 10 / 10 | 136 (10) | 89 | 10 / 10 |
| 8 | 156 (10) | 10 / 10 | 10 / 10 | 158 (10) | 101 | 10 / 10 | 157 (10) | 101 | 10 / 10 | 150 (10) | 96 | 10 / 10 | 148 (10) | 95 | 10 / 10 | 137 (10) | 88 | 10 / 10 |
| 9 | 160 (10) | 10 / 10 | 10 / 10 | 162 (10) | 101 | 10 / 10 | 163 (10) | 102 | 10 / 10 | 154 (10) | 96 | 10 / 10 | 152 (10) | 95 | 10 / 10 | 141 (10) | 88 | 10 / 10 |
| 10 | 165 (10) | 10 / 10 | 10 / 10 | 166 (10) | 101 | 10 / 10 | 165 (10) | 100 | 10 / 10 | 158 (10) | 96 | 10 / 10 | 155 (10) | 94 | 10 / 10 | 144 (10) | 87 | 10 / 10 |
| 11 | 167 (10) | 10 / 10 | 10 / 10 | 167 (10) | 100 | 10 / 10 | 168 (10) | 101 | 10 / 10 | 160 (10) | 96 | 10 / 10 | 157 (10) | 94 | 10 / 10 | 145 (10) | 87 | 10 / 10 |
| 12 | 169 (10) | 10 / 10 | 10 / 10 | 168 (10) | 99 | 10 / 10 | 170 (10) | 101 | 10 / 10 | 163 (10) | 96 | 10 / 10 | 159 (10) | 94 | 10 / 10 | 147 (10) | 87 | 10 / 10 |
| 13 | 169 (10) | 10 / 10 | 10 / 10 | 168 (10) | 99 | 10 / 10 | 170 (10) | 101 | 10 / 10 | 162 (10) | 96 | 10 / 10 | 160 (10) | 95 | 10 / 10 | 147 (10) | 87 | 10 / 10 |

< > : No.of effective animals, () : No.of measured animals, Av.Wt.:Averaged body weight (Unit : g) .

TABLE 3 FOOD CONSUMPTION CHANGES OF MALE RATS IN THE 13-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

| Week on Study | Control | | 63 ppm | | | 250 ppm | | | 1000 ppm | | | 2000 ppm | | | 4000 ppm | | |
|------------------|-----------------|------------------------------|-------------|-----------------------|------------------------------|-------------|-----------------------|------------------------------|-------------|-----------------------|------------------------------|-------------|-----------------------|------------------------------|-------------|-----------------------|------------------------------|
| | Av. FC. <10> | No. of Surviv. 10 / 10 | Av. FC. | % of cont. <10> | No. of Surviv. 10 / 10 | Av. FC. | % of cont. <10> | No. of Surviv. 10 / 10 | Av. FC. | % of cont. <10> | No. of Surviv. 10 / 10 | Av. FC. | % of cont. <10> | No. of Surviv. 10 / 10 | Av. FC. | % of cont. <10> | No. of Surviv. 10 / 10 |
| 1 | 12.4 (10) | 10 / 10 | 12.6 (10) | 102 | 10 / 10 | 12.6 (10) | 102 | 10 / 10 | 12.3 (10) | 99 | 10 / 10 | 11.2 (10) | 90 | 10 / 10 | 8.4 (10) | 68 | 10 / 10 |
| 2 | 13.1 (10) | 10 / 10 | 13.5 (10) | 103 | 10 / 10 | 13.5 (10) | 103 | 10 / 10 | 13.6 (10) | 104 | 10 / 10 | 13.4 (10) | 102 | 10 / 10 | 11.8 (10) | 90 | 10 / 10 |
| 3 | 13.7 (10) | 10 / 10 | 14.3 (10) | 104 | 10 / 10 | 14.0 (10) | 102 | 10 / 10 | 14.4 (10) | 105 | 10 / 10 | 14.0 (10) | 102 | 10 / 10 | 12.2 (10) | 89 | 10 / 10 |
| 4 | 13.9 (10) | 10 / 10 | 14.5 (10) | 104 | 10 / 10 | 14.5 (10) | 104 | 10 / 10 | 14.5 (10) | 104 | 10 / 10 | 14.0 (10) | 101 | 10 / 10 | 12.4 (10) | 89 | 10 / 10 |
| 5 | 13.6 (10) | 10 / 10 | 14.1 (10) | 104 | 10 / 10 | 14.0 (10) | 103 | 10 / 10 | 14.0 (10) | 103 | 10 / 10 | 14.0 (10) | 103 | 10 / 10 | 12.5 (10) | 92 | 10 / 10 |
| 6 | 13.4 (10) | 10 / 10 | 13.8 (10) | 103 | 10 / 10 | 13.6 (10) | 101 | 10 / 10 | 14.0 (10) | 104 | 10 / 10 | 13.9 (10) | 104 | 10 / 10 | 12.4 (10) | 93 | 10 / 10 |
| 7 | 13.7 (10) | 10 / 10 | 14.2 (10) | 104 | 10 / 10 | 14.1 (10) | 103 | 10 / 10 | 14.5 (10) | 106 | 10 / 10 | 14.2 (10) | 104 | 10 / 10 | 12.5 (10) | 91 | 10 / 10 |
| 8 | 13.3 (10) | 10 / 10 | 13.8 (10) | 104 | 10 / 10 | 13.9 (10) | 105 | 10 / 10 | 14.5 (10) | 109 | 10 / 10 | 13.9 (10) | 105 | 10 / 10 | 12.6 (10) | 95 | 10 / 10 |
| 9 | 13.4 (10) | 10 / 10 | 13.8 (10) | 103 | 10 / 10 | 13.9 (10) | 104 | 10 / 10 | 14.0 (10) | 104 | 10 / 10 | 14.0 (10) | 104 | 10 / 10 | 12.4 (10) | 93 | 10 / 10 |
| 10 | 13.8 (10) | 10 / 10 | 13.9 (10) | 101 | 10 / 10 | 13.9 (10) | 101 | 10 / 10 | 14.2 (10) | 103 | 10 / 10 | 14.1 (10) | 102 | 10 / 10 | 12.8 (10) | 93 | 10 / 10 |
| 11 | 13.9 (10) | 10 / 10 | 14.0 (10) | 101 | 10 / 10 | 13.7 (10) | 99 | 10 / 10 | 13.9 (10) | 100 | 10 / 10 | 13.8 (10) | 99 | 10 / 10 | 12.6 (10) | 91 | 10 / 10 |
| 12 | 13.6 (10) | 10 / 10 | 14.0 (10) | 103 | 10 / 10 | 13.6 (10) | 100 | 10 / 10 | 13.9 (10) | 102 | 10 / 10 | 13.9 (10) | 102 | 10 / 10 | 12.2 (10) | 90 | 10 / 10 |
| 13 | 13.6 (10) | 10 / 10 | 13.8 (10) | 101 | 10 / 10 | 13.3 (10) | 98 | 10 / 10 | 13.6 (10) | 100 | 10 / 10 | 13.6 (10) | 100 | 10 / 10 | 11.9 (10) | 88 | 10 / 10 |

< > : No.of effective animals, () : No.of measured animals Av.FC.:Averaged food consumption (Unit : g) .

TABLE 4 FOOD CONSUMPTION CHANGES OF FEMALE RATS IN THE 13-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

| Week on Study | Control | | 63 ppm | | | 250 ppm | | | 1000 ppm | | | 2000 ppm | | | 4000 ppm | | |
|------------------|-----------------|---------------------------|-------------|-----------------------|---------------------------|-------------|-----------------------|---------------------------|------------|-----------------------|---------------------------|------------|-----------------------|---------------------------|------------|-----------------------|---------------------------|
| | Av. FC. <10> | No. of Surviv. / 10 | Av. FC. | % of cont. <10> | No. of Surviv. / 10 | Av. FC. | % of cont. <10> | No. of Surviv. / 10 | Av. FC. | % of cont. <10> | No. of Surviv. / 10 | Av. FC. | % of cont. <10> | No. of Surviv. / 10 | Av. FC. | % of cont. <10> | No. of Surviv. / 10 |
| 1 | 9.5 (10) | 10 / 10 | 9.4 (10) | 99 | 10 / 10 | 9.2 (10) | 97 | 10 / 10 | 8.8 (10) | 93 | 10 / 10 | 8.0 (10) | 84 | 10 / 10 | 6.3 (10) | 66 | 10 / 10 |
| 2 | 10.0 (10) | 10 / 10 | 10.5 (10) | 105 | 10 / 10 | 9.6 (10) | 96 | 10 / 10 | 9.5 (10) | 95 | 10 / 10 | 9.5 (10) | 95 | 10 / 10 | 8.7 (10) | 87 | 10 / 10 |
| 3 | 10.0 (10) | 10 / 10 | 10.0 (10) | 100 | 10 / 10 | 10.0 (10) | 100 | 10 / 10 | 9.5 (10) | 95 | 10 / 10 | 9.5 (10) | 95 | 10 / 10 | 8.6 (10) | 86 | 10 / 10 |
| 4 | 10.2 (10) | 10 / 10 | 10.0 (10) | 98 | 10 / 10 | 10.1 (10) | 99 | 10 / 10 | 9.7 (10) | 95 | 10 / 10 | 9.4 (10) | 92 | 10 / 10 | 8.7 (10) | 85 | 10 / 10 |
| 5 | 9.8 (10) | 10 / 10 | 9.8 (10) | 100 | 10 / 10 | 9.9 (10) | 101 | 10 / 10 | 9.4 (10) | 96 | 10 / 10 | 9.3 (10) | 95 | 10 / 10 | 8.6 (10) | 88 | 10 / 10 |
| 6 | 9.6 (10) | 10 / 10 | 10.0 (10) | 104 | 10 / 10 | 9.4 (10) | 98 | 10 / 10 | 9.3 (10) | 97 | 10 / 10 | 9.7 (10) | 101 | 10 / 10 | 8.2 (10) | 85 | 10 / 10 |
| 7 | 9.4 (10) | 10 / 10 | 9.6 (10) | 102 | 10 / 10 | 9.6 (10) | 102 | 10 / 10 | 9.4 (10) | 100 | 10 / 10 | 9.5 (10) | 101 | 10 / 10 | 8.5 (10) | 90 | 10 / 10 |
| 8 | 9.0 (10) | 10 / 10 | 9.7 (10) | 108 | 10 / 10 | 9.2 (10) | 102 | 10 / 10 | 8.8 (10) | 98 | 10 / 10 | 8.9 (10) | 99 | 10 / 10 | 8.0 (10) | 89 | 10 / 10 |
| 9 | 9.0 (10) | 10 / 10 | 9.1 (10) | 101 | 10 / 10 | 9.4 (10) | 104 | 10 / 10 | 9.0 (10) | 100 | 10 / 10 | 9.5 (10) | 106 | 10 / 10 | 8.0 (10) | 89 | 10 / 10 |
| 10 | 9.3 (10) | 10 / 10 | 9.4 (10) | 101 | 10 / 10 | 9.5 (10) | 102 | 10 / 10 | 9.2 (10) | 99 | 10 / 10 | 9.3 (10) | 100 | 10 / 10 | 8.1 (10) | 87 | 10 / 10 |
| 11 | 9.6 (10) | 10 / 10 | 9.6 (10) | 100 | 10 / 10 | 9.6 (10) | 100 | 10 / 10 | 9.1 (10) | 95 | 10 / 10 | 9.2 (10) | 96 | 10 / 10 | 8.2 (10) | 85 | 10 / 10 |
| 12 | 9.3 (10) | 10 / 10 | 9.0 (10) | 97 | 10 / 10 | 9.1 (10) | 98 | 10 / 10 | 8.9 (10) | 96 | 10 / 10 | 9.1 (10) | 98 | 10 / 10 | 7.9 (10) | 85 | 10 / 10 |
| 13 | 9.4 (10) | 10 / 10 | 9.0 (10) | 96 | 10 / 10 | 9.1 (10) | 97 | 10 / 10 | 8.8 (10) | 94 | 10 / 10 | 9.3 (10) | 99 | 10 / 10 | 8.1 (10) | 86 | 10 / 10 |

< > : No.of effective animals, () : No.of measured animals Av.FC.:Averaged food consumption (Unit : g) .

TABLE 5 HEMATOLOGY OF MALE RATS IN THE 13-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

| Group Name | Control | 63 ppm | 250 ppm | 1000 ppm | 2000 ppm | 4000 ppm |
|---------------------------------------|-------------|-------------|---------------|----------------|----------------|----------------|
| No. of examined animals | 10 | 10 | 10 | 10 | 10 | 9 |
| Red blood cell ($10^6/\mu\text{L}$) | 9.49 ± 0.19 | 9.44 ± 0.17 | 9.35 ± 0.20 | 8.78 ± 0.11 ** | 8.42 ± 0.20 ** | 7.83 ± 0.33 ** |
| Hemoglobin (g/dL) | 16.0 ± 0.4 | 15.8 ± 0.3 | 15.5 ± 0.4 ** | 14.4 ± 0.2 ** | 13.9 ± 0.3 ** | 14.0 ± 0.5 ** |
| Hematocrit (%) | 46.1 ± 0.8 | 45.8 ± 0.9 | 45.1 ± 0.8 | 43.4 ± 0.5 ** | 41.9 ± 0.8 ** | 42.6 ± 1.1 ** |
| MCV (fL) | 48.6 ± 0.3 | 48.5 ± 0.3 | 48.3 ± 0.4 | 49.4 ± 0.5 | 49.8 ± 0.5 * | 54.5 ± 1.3 ** |
| MCH (pg) | 16.9 ± 0.2 | 16.8 ± 0.2 | 16.5 ± 0.2 ** | 16.4 ± 0.2 ** | 16.5 ± 0.2 ** | 17.9 ± 0.3 ** |
| MCHC (g/dL) | 34.8 ± 0.5 | 34.6 ± 0.4 | 34.2 ± 0.3 * | 33.2 ± 0.3 ** | 33.2 ± 0.3 ** | 32.9 ± 0.4 ** |
| Platelet ($10^3/\mu\text{L}$) | 786 ± 34 | 816 ± 36 | 844 ± 32 * | 830 ± 58 | 788 ± 63 | 654 ± 48 ** |
| Reticulocyte (%) | 1.8 ± 0.2 | 2.0 ± 0.2 | 2.3 ± 0.2 | 3.6 ± 0.3 ** | 4.8 ± 0.6 ** | 8.5 ± 1.1 ** |
| Methemoglobin (%) | 0.3 ± 0.0 | 0.3 ± 0.1 | 0.3 ± 0.1 | 0.4 ± 0.2 | 0.9 ± 0.4 ** | 1.4 ± 0.5 ** |
| APTT (sec) | 26.9 ± 3.5 | 26.7 ± 3.4 | 27.8 ± 5.6 | 22.1 ± 2.6 * | 22.3 ± 5.4 | 25.5 ± 3.0 |
| Differential WBC N-SEG (%) | 19 ± 4 | 16 ± 2 | 17 ± 2 | 14 ± 3 ** | 17 ± 3 | 15 ± 3 ** |

Mean ± S.D.

*) Significant difference, $p < 0.05$ (Test of Dunnett)

**) Significant difference, $p < 0.01$ (Test of Dunnett)

TABLE 6 HEMATOLOGY OF FEMALE RATS IN THE 13-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

| Group Name | Control | 63 ppm | 250 ppm | 1000 ppm | 2000 ppm | 4000 ppm |
|---------------------------------------|-------------|----------------|----------------|----------------|----------------|----------------|
| No. of examined animals | 10 | 10 | 10 | 10 | 10 | 10 |
| Red blood cell ($10^6/\mu\text{L}$) | 8.84 ± 0.22 | 8.54 ± 0.16 ** | 8.48 ± 0.14 ** | 8.03 ± 0.21 ** | 7.67 ± 0.23 ** | 7.20 ± 0.18 ** |
| Hemoglobin (g/dL) | 16.1 ± 0.4 | 15.5 ± 0.3 ** | 15.3 ± 0.3 ** | 14.3 ± 0.4 ** | 13.7 ± 0.4 ** | 13.4 ± 0.4 ** |
| Hematocrit (%) | 44.6 ± 1.3 | 43.4 ± 0.8 | 43.7 ± 0.8 | 41.8 ± 1.2 ** | 40.4 ± 1.0 ** | 40.2 ± 1.1 ** |
| MCV (fL) | 50.4 ± 0.5 | 50.9 ± 0.5 | 51.5 ± 0.4 | 52.0 ± 0.4 ** | 52.7 ± 1.0 ** | 55.8 ± 0.4 ** |
| MCH (pg) | 18.2 ± 0.1 | 18.1 ± 0.1 | 18.0 ± 0.1 | 17.9 ± 0.2 ** | 17.9 ± 0.3 * | 18.6 ± 0.2 |
| MCHC (g/dL) | 36.1 ± 0.5 | 35.6 ± 0.4 | 35.0 ± 0.3 ** | 34.3 ± 0.4 ** | 33.9 ± 0.4 ** | 33.3 ± 0.4 ** |
| Platelet ($10^3/\mu\text{L}$) | 859 ± 57 | 893 ± 59 | 896 ± 52 | 836 ± 70 | 742 ± 30 ** | 598 ± 42 ** |
| Reticulocyte (%) | 1.8 ± 0.2 | 2.1 ± 0.3 | 2.4 ± 0.3 | 3.7 ± 0.6 ** | 4.9 ± 0.6 ** | 7.9 ± 0.9 ** |
| Methemoglobin (%) | 0.3 ± 0.1 | 0.3 ± 0.1 | 0.4 ± 0.1 | 0.5 ± 0.2 | 1.1 ± 0.3 ** | 1.5 ± 0.7 ** |
| Prothrombin time (sec) | 14.8 ± 1.0 | 15.4 ± 0.8 | 15.3 ± 0.8 | 15.5 ± 0.9 | 16.2 ± 1.4 * | 17.9 ± 1.2 ** |

Mean ± S.D.

*) Significant difference, $p < 0.05$ (Test of Dunnett)

**) Significant difference, $p < 0.01$ (Test of Dunnett)

TABLE 7 BIOCHEMISTRY OF MALE RATS IN THE 13-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

| Group Name | Control | 63 ppm | 250 ppm | 1000 ppm | 2000 ppm | 4000 ppm |
|-------------------------|-------------|--------------|---------------|---------------|----------------|----------------|
| No. of examined animals | 10 | 10 | 10 | 10 | 10 | 9 |
| Total protein (g/dL) | 6.1 ± 0.2 | 6.4 ± 0.1 ** | 6.6 ± 0.2 ** | 7.1 ± 0.1 ** | 7.3 ± 0.2 ** | 7.1 ± 0.2 ** |
| Albumin (g/dL) | 3.8 ± 0.1 | 4.0 ± 0.1 ** | 4.2 ± 0.1 ** | 4.6 ± 0.1 ** | 4.6 ± 0.1 ** | 4.4 ± 0.1 ** |
| A/G ratio | 1.7 ± 0.1 | 1.7 ± 0.1 | 1.8 ± 0.1 ** | 1.8 ± 0.1 ** | 1.8 ± 0.1 ** | 1.6 ± 0.1 |
| T-bilirubin (mg/dL) | 0.11 ± 0.01 | 0.12 ± 0.01 | 0.12 ± 0.01 | 0.16 ± 0.01 * | 0.30 ± 0.08 ** | 0.69 ± 0.13 ** |
| Glucose (mg/dL) | 174 ± 10 | 175 ± 10 | 176 ± 13 | 175 ± 28 | 162 ± 8 | 150 ± 6 ** |
| T-cholesterol (mg/dL) | 60 ± 4 | 72 ± 8 | 85 ± 6 | 132 ± 6 ** | 181 ± 17 ** | 240 ± 22 ** |
| Triglyceride (mg/dL) | 44 ± 13 | 47 ± 17 | 55 ± 8 | 68 ± 16 | 101 ± 8 ** | 168 ± 29 ** |
| Phospholipid (mg/dL) | 110 ± 7 | 125 ± 13 | 145 ± 8 | 221 ± 14 ** | 316 ± 28 ** | 433 ± 27 ** |
| GOT (IU/L) | 60 ± 5 | 73 ± 24 | 74 ± 23 | 67 ± 13 | 139 ± 53 ** | 223 ± 32 ** |
| GPT (IU/L) | 40 ± 4 | 45 ± 9 | 45 ± 9 | 59 ± 12 * | 205 ± 77 ** | 448 ± 71 ** |
| LDH (IU/L) | 160 ± 22 | 183 ± 43 | 192 ± 45 | 151 ± 10 | 182 ± 40 | 219 ± 27 ** |
| ALP (IU/L) | 248 ± 17 | 235 ± 16 | 207 ± 10 * | 208 ± 13 * | 298 ± 12 | 482 ± 39 * |
| γ-GTP (IU/L) | 2 ± 1 | 1 ± 1 | 2 ± 1 | 5 ± 2 | 56 ± 17 ** | 398 ± 64 ** |
| CPK (IU/L) | 103 ± 23 | 94 ± 8 | 93 ± 12 | 82 ± 6 ** | 78 ± 5 ** | 100 ± 15 |
| Urea nitrogen (mg/dL) | 19.8 ± 1.7 | 20.0 ± 1.6 | 19.7 ± 1.7 | 20.8 ± 2.2 | 21.0 ± 1.4 | 21.9 ± 1.3 * |
| Sodium (mEq/L) | 142 ± 1 | 142 ± 1 | 142 ± 2 | 142 ± 1 | 141 ± 1 | 140 ± 1 ** |
| Chloride (mEq/L) | 107 ± 1 | 106 ± 1 | 106 ± 1 | 105 ± 1 ** | 104 ± 2 ** | 104 ± 1 ** |
| Calcium (mg/dL) | 10.1 ± 0.2 | 10.2 ± 0.2 | 10.3 ± 0.1 ** | 10.7 ± 0.1 ** | 10.9 ± 0.2 ** | 10.8 ± 0.1 ** |

Mean ± S.D.

*) Significant difference, p<0.05 (Test of Dunnett)

**) Significant difference, p<0.01 (Test of Dunnett)

TABLE 8 BIOCHEMISTRY OF FEMALE RATS IN THE 13-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

| Group Name | Control | 63 ppm | 250 ppm | 1000 ppm | 2000 ppm | 4000 ppm |
|-------------------------|-------------|-------------|--------------|---------------|---------------|----------------|
| No. of examined animals | 10 | 10 | 10 | 10 | 10 | 10 |
| Total protein (g/dL) | 6.2 ± 0.1 | 6.3 ± 0.2 | 6.5 ± 0.2 ** | 6.9 ± 0.2 ** | 7.1 ± 0.2 ** | 7.1 ± 0.2 ** |
| Albumin (g/dL) | 3.8 ± 0.1 | 3.9 ± 0.1 | 4.1 ± 0.2 ** | 4.4 ± 0.1 ** | 4.5 ± 0.1 ** | 4.5 ± 0.1 ** |
| A/G ratio | 1.6 ± 0.1 | 1.6 ± 0.1 | 1.7 ± 0.1 * | 1.8 ± 0.1 ** | 1.7 ± 0.1 ** | 1.7 ± 0.1 * |
| T-bilirubin (mg/dL) | 0.15 ± 0.02 | 0.14 ± 0.02 | 0.14 ± 0.01 | 0.17 ± 0.01 | 0.21 ± 0.03 * | 0.41 ± 0.04 ** |
| Glucose (mg/dL) | 135 ± 13 | 145 ± 15 | 154 ± 15 ** | 144 ± 10 | 149 ± 8 | 144 ± 10 |
| T-cholesterol (mg/dL) | 73 ± 7 | 82 ± 11 | 101 ± 9 | 135 ± 15 ** | 161 ± 21 ** | 187 ± 22 ** |
| Triglyceride (mg/dL) | 17 ± 5 | 19 ± 7 | 19 ± 6 | 27 ± 10 | 41 ± 17 ** | 77 ± 31 ** |
| Phospholipid (mg/dL) | 141 ± 11 | 153 ± 19 | 176 ± 15 | 227 ± 25 ** | 275 ± 35 ** | 351 ± 33 ** |
| GOT (IU/L) | 69 ± 14 | 65 ± 8 | 66 ± 12 | 68 ± 6 | 77 ± 10 | 132 ± 34 ** |
| GPT (IU/L) | 36 ± 9 | 33 ± 4 | 37 ± 9 | 40 ± 7 | 60 ± 16 ** | 144 ± 37 ** |
| ALP (IU/L) | 178 ± 20 | 164 ± 18 | 153 ± 29 | 153 ± 21 | 189 ± 21 | 322 ± 28 ** |
| γ-GTP (IU/L) | 1 ± 1 | 2 ± 1 | 2 ± 1 | 7 ± 2 * | 46 ± 22 ** | 263 ± 48 ** |
| Urea nitrogen (mg/dL) | 18.7 ± 2.2 | 18.0 ± 1.0 | 18.8 ± 1.7 | 20.1 ± 1.5 | 20.4 ± 0.8 | 22.4 ± 3.4 ** |
| Chloride (mEq/L) | 107 ± 1 | 107 ± 1 | 107 ± 1 | 106 ± 1 | 106 ± 1 | 105 ± 1 ** |
| Calcium (mg/dL) | 9.9 ± 0.2 | 10.0 ± 0.2 | 10.1 ± 0.3 | 10.3 ± 0.2 ** | 10.5 ± 0.3 ** | 10.6 ± 0.2 ** |

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

TABLE 9 URINALYSIS OF MALE RATS IN THE 13-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

| Group Name | | Control | 63 ppm | 250 ppm | 1000 ppm | 2000 ppm | 4000 ppm |
|--|-----------------|---------|--------|---------|----------|----------|----------|
| Number of examined animals | | 10 | 10 | 10 | 10 | 10 | 10 |
| | Grade | | | | | | |
| pH | 6.0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6.5 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 7.0 | 0 | 0 | 0 | 0 | 0 | 2 |
| | 7.5 | 0 | 0 | 1 | 2 | 3 | 7 |
| | 8.0 | 5 | 4 | 4 | 7 | 7 | 1 |
| | 8.5 | 5 | 6 | 5 | 1 | 0 | 0 |
| | Chi square test | | | | | * | ** |
| Significant difference : * : p<0.05 ** : p<0.01 | | | | | | | |

TABLE 10 URINALYSIS OF FEMALE RATS IN THE 13-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

| Group Name | | Control | 63 ppm | 250 ppm | 1000 ppm | 2000 ppm | 4000 ppm |
|--|-----------------|---------|--------|---------|----------|----------|----------|
| Number of examined animals | | 10 | 10 | 10 | 10 | 10 | 10 |
| | Grade | | | | | | |
| pH | 6.0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6.5 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 7.0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 7.5 | 0 | 1 | 0 | 0 | 1 | 1 |
| | 8.0 | 7 | 4 | 2 | 4 | 9 | 7 |
| | 8.5 | 3 | 5 | 8 | 6 | 0 | 2 |
| | Chi square test | | | * | | | |
| Significant difference : * : p<0.05 ** : p<0.01 | | | | | | | |

TABLE 11 ORGAN WEIGHTS OF MALE RATS IN THE 13-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

| Group Name | Control | 63 ppm | 250 ppm | 1000 ppm | 2000 ppm | 4000 ppm |
|-------------------------|---------------|------------------|------------------|-------------------|-------------------|-------------------|
| No. of examined animals | 10 | 10 | 10 | 10 | 10 | 10 |
| Body weight (g) | 281 ± 16 | 290 ± 14 | 281 ± 14 | 282 ± 14 | 269 ± 11 | 229 ± 9 ** |
| Thymus (g) | 0.196 ± 0.022 | 0.214 ± 0.017 | 0.189 ± 0.022 | 0.199 ± 0.022 | 0.191 ± 0.020 | 0.170 ± 0.015 * |
| Thymus (%) | 0.070 ± 0.008 | 0.074 ± 0.006 | 0.067 ± 0.009 | 0.071 ± 0.006 | 0.071 ± 0.006 | 0.074 ± 0.006 |
| Testes (g) | 2.912 ± 0.107 | 3.034 ± 0.100 | 3.036 ± 0.099 | 3.069 ± 0.199 | 3.107 ± 0.128 * | 1.457 ± 0.194 ** |
| Testes (%) | 1.041 ± 0.069 | 1.048 ± 0.045 | 1.084 ± 0.049 | 1.091 ± 0.077 | 1.155 ± 0.033 ** | 0.635 ± 0.084 ** |
| Heart (g) | 0.874 ± 0.051 | 0.908 ± 0.045 | 0.905 ± 0.025 | 0.913 ± 0.041 | 0.897 ± 0.044 | 0.804 ± 0.037 ** |
| Heart (%) | 0.312 ± 0.015 | 0.313 ± 0.012 | 0.323 ± 0.015 | 0.324 ± 0.008 | 0.334 ± 0.015 ** | 0.350 ± 0.012 ** |
| Lungs (g) | 0.975 ± 0.051 | 0.987 ± 0.040 | 0.968 ± 0.047 | 0.985 ± 0.039 | 0.972 ± 0.044 | 0.949 ± 0.047 |
| Lungs (%) | 0.347 ± 0.008 | 0.341 ± 0.009 | 0.345 ± 0.010 | 0.350 ± 0.013 | 0.362 ± 0.012 * | 0.414 ± 0.012 ** |
| Kidneys (g) | 1.777 ± 0.082 | 1.829 ± 0.068 | 1.849 ± 0.091 | 1.986 ± 0.108 ** | 2.045 ± 0.093 ** | 2.231 ± 0.125 ** |
| Kidneys (%) | 0.634 ± 0.021 | 0.632 ± 0.028 | 0.660 ± 0.028 | 0.705 ± 0.022 * | 0.760 ± 0.019 ** | 0.973 ± 0.048 ** |
| Spleen (g) | 0.517 ± 0.033 | 0.552 ± 0.032 | 0.560 ± 0.028 | 0.679 ± 0.038 ** | 1.010 ± 0.076 ** | 1.579 ± 0.163 ** |
| Spleen (%) | 0.184 ± 0.008 | 0.191 ± 0.009 | 0.200 ± 0.010 | 0.241 ± 0.011 ** | 0.376 ± 0.025 ** | 0.687 ± 0.050 ** |
| Liver (g) | 6.823 ± 0.524 | 7.762 ± 0.492 ** | 8.646 ± 0.460 ** | 10.997 ± 0.721 ** | 13.502 ± 0.477 ** | 15.148 ± 0.820 ** |
| Liver (%) | 2.430 ± 0.075 | 2.677 ± 0.073 | 3.083 ± 0.085 * | 3.900 ± 0.098 ** | 5.023 ± 0.211 ** | 6.603 ± 0.226 ** |
| Brain (g) | 1.877 ± 0.046 | 1.879 ± 0.048 | 1.866 ± 0.036 | 1.882 ± 0.037 | 1.847 ± 0.042 | 1.806 ± 0.062 ** |
| Brain (%) | 0.670 ± 0.037 | 0.649 ± 0.030 | 0.666 ± 0.032 | 0.669 ± 0.031 | 0.687 ± 0.021 | 0.788 ± 0.027 ** |

Mean ± S.D.
^{*}) Significant difference, p<0.05 (Test of Dunnett)
^{**}) Significant difference, p<0.01 (Test of Dunnett)

TABLE 12 ORGAN WEIGHTS OF FEMALE RATS IN THE 13-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

| Group Name | Control | 63 ppm | 250 ppm | 1000 ppm | 2000 ppm | 4000 ppm |
|-------------------------|---------------|---------------|-----------------|------------------|------------------|------------------|
| No. of examined animals | 10 | 10 | 10 | 10 | 10 | 10 |
| Body weight (g) | 157 ± 6 | 158 ± 7 | 158 ± 7 | 152 ± 11 | 147 ± 10 * | 135 ± 9 ** |
| Thymus (g) | 0.182 ± 0.019 | 0.174 ± 0.013 | 0.174 ± 0.013 | 0.166 ± 0.012 | 0.165 ± 0.010 | 0.153 ± 0.018 ** |
| Thymus (%) | 0.115 ± 0.010 | 0.110 ± 0.008 | 0.110 ± 0.009 | 0.110 ± 0.007 | 0.112 ± 0.009 | 0.114 ± 0.012 |
| Adrenals (g) | 0.049 ± 0.003 | 0.050 ± 0.005 | 0.049 ± 0.005 | 0.049 ± 0.004 | 0.047 ± 0.005 | 0.040 ± 0.007 ** |
| Adrenals (%) | 0.031 ± 0.002 | 0.031 ± 0.003 | 0.031 ± 0.003 | 0.032 ± 0.003 | 0.032 ± 0.003 | 0.030 ± 0.004 |
| Heart (g) | 0.580 ± 0.022 | 0.584 ± 0.039 | 0.595 ± 0.036 | 0.579 ± 0.032 | 0.593 ± 0.043 | 0.550 ± 0.039 |
| Heart (%) | 0.369 ± 0.015 | 0.370 ± 0.022 | 0.376 ± 0.022 | 0.383 ± 0.016 | 0.404 ± 0.026 ** | 0.409 ± 0.019 ** |
| Lungs (g) | 0.722 ± 0.038 | 0.712 ± 0.035 | 0.715 ± 0.025 | 0.709 ± 0.033 | 0.695 ± 0.046 | 0.657 ± 0.042 ** |
| Lungs (%) | 0.459 ± 0.017 | 0.452 ± 0.026 | 0.452 ± 0.018 | 0.469 ± 0.022 | 0.473 ± 0.016 | 0.489 ± 0.021 ** |
| Kidneys (g) | 1.074 ± 0.054 | 1.080 ± 0.062 | 1.113 ± 0.071 | 1.196 ± 0.062 ** | 1.244 ± 0.078 ** | 1.313 ± 0.085 ** |
| Kidneys (%) | 0.683 ± 0.019 | 0.685 ± 0.034 | 0.703 ± 0.027 | 0.791 ± 0.036 ** | 0.846 ± 0.022 ** | 0.977 ± 0.050 ** |
| Spleen (g) | 0.365 ± 0.033 | 0.350 ± 0.027 | 0.374 ± 0.027 | 0.448 ± 0.031 | 0.593 ± 0.057 ** | 0.898 ± 0.122 ** |
| Spleen (%) | 0.232 ± 0.016 | 0.222 ± 0.014 | 0.236 ± 0.013 | 0.296 ± 0.012 * | 0.402 ± 0.021 ** | 0.666 ± 0.061 ** |
| Liver (g) | 3.779 ± 0.180 | 4.038 ± 0.163 | 4.544 ± 0.240 | 5.700 ± 0.536 ** | 6.948 ± 0.625 ** | 8.636 ± 0.754 ** |
| Liver (%) | 2.402 ± 0.060 | 2.562 ± 0.065 | 2.870 ± 0.041 * | 3.758 ± 0.099 ** | 4.718 ± 0.240 ** | 6.417 ± 0.287 ** |
| Brain (g) | 1.740 ± 0.061 | 1.709 ± 0.066 | 1.711 ± 0.033 | 1.738 ± 0.051 | 1.735 ± 0.045 | 1.681 ± 0.041 |
| Brain (%) | 1.108 ± 0.058 | 1.085 ± 0.051 | 1.083 ± 0.049 | 1.152 ± 0.074 | 1.183 ± 0.079 | 1.255 ± 0.083 ** |

Mean ± S.D.
^{*)} Significant difference, p<0.05 (Test of Dunnett)
^{**)} Significant difference, p<0.01 (Test of Dunnett)

TABLE 13 INCIDENCES OF SELECTED LESIONS OF MALE RATS IN THE 13-WEEK
FEED STUDY OF *o*-CHLORONITROBENZENE

| Group | | Control | 63 ppm | 250 ppm | 1000 ppm | 2000 ppm | 4000 ppm |
|--|-----------------|--------------|------------|------------|----------|----------|----------|
| Number of examined animals | | 10 | 10 | 10 | 10 | 10 | 10 |
| Organ | Grade | | | | | | |
| Findings | | | | | | | |
| Bone marrow | | | | | | | |
| Erythropoiesis : increased | 1+ | 0 | 0 | 0 | 0 | 10 | 10 |
| | Chi Square test | | | | | ** | ** |
| Spleen | | | | | | | |
| Deposit of hemosiderin | 1+ | 0 | 0 | 10 | 10 | 10 | 10 |
| | Chi Square test | | | ** | ** | ** | ** |
| Increased extramedullary hematopoiesis | 1+ | 0 | 0 | 0 | 10 | 10 | 10 |
| | Chi Square test | | | | ** | ** | ** |
| Engorgement of erythrocyte | 1+ | 0 | 0 | 10 | 10 | 0 | 0 |
| | 2+ | 0 | 0 | 0 | 0 | 10 | 0 |
| | 3+ | 0 | 0 | 0 | 0 | 0 | 10 |
| | Chi Square test | | | ** | ** | ** | ** |
| Capsule hyperplasia | 1+ | 0 | 0 | 0 | 0 | 9 | 0 |
| | 2+ | 0 | 0 | 0 | 0 | 1 | 10 |
| | Chi Square test | | | | | ** | ** |
| Liver | | | | | | | |
| Necrosis : single cell | 1+ | 0 | 0 | 0 | 8 | 10 | 10 |
| | Chi Square test | | | | ** | ** | ** |
| Deposit of hemosiderin | 1+ | 0 | 0 | 0 | 5 | 10 | 10 |
| | Chi Square test | | | | * | ** | ** |
| Hydropic change : central | 1+ | 0 | 0 | 0 | 7 | 0 | 0 |
| | 2+ | 0 | 0 | 0 | 0 | 10 | 6 |
| | 3+ | 0 | 0 | 0 | 0 | 0 | 4 |
| | Chi Square test | | | | ** | ** | ** |
| Hepatocellular hypertrophy : central | 1+ | 0 | 0 | 0 | 0 | 10 | 0 |
| | 2+ | 0 | 0 | 0 | 0 | 0 | 10 |
| | Chi Square test | | | | | ** | ** |
| Kidney | | | | | | | |
| Eosinophilic body | 1+ | 4 | 2 | 6 | 4 | 0 | 0 |
| | 2+ | 6 | 8 | 4 | 6 | 0 | 0 |
| | Chi Square test | | | | | ** | ** |
| Hyaline cast | 1+ | 0 | 0 | 0 | 1 | 8 | 5 |
| | Chi Square test | | | | | ** | * |
| Deposit of brown pigment : proximal tubule | 1+ | 0 | 0 | 0 | 10 | 0 | 0 |
| | 2+ | 0 | 0 | 0 | 0 | 10 | 0 |
| | 3+ | 0 | 0 | 0 | 0 | 0 | 10 |
| | Chi Square test | | | | ** | ** | ** |
| Testis | | | | | | | |
| Germ cell necrosis | 1+ | 2 | 0 | 0 | 0 | 0 | 4 |
| | 2+ | 0 | 0 | 0 | 1 | 0 | 5 |
| | 3+ | 0 | 0 | 0 | 0 | 0 | 1 |
| | Chi Square test | | | | | | ** |
| Epididymis | | | | | | | |
| Decreased : sperma | 1+ | 0 | 0 | 0 | 0 | 0 | 0 |
| | 2+ | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3+ | 0 | 0 | 0 | 0 | 0 | 10 |
| | Chi Square test | | | | | | ** |
| Debris of spermatic elements | 1+ | 0 | 0 | 0 | 0 | 0 | 8 |
| | 2+ | 0 | 0 | 0 | 0 | 0 | 1 |
| | Chi Square test | | | | | | ** |
| Grade | 1+: Slight | 2+: Moderate | 3+: Marked | 4+: Severe | | | |
| Significant difference | * : p<0.05 | ** : p<0.01 | | | | | |

TABLE 14 INCIDENCES OF SELECTED LESIONS OF FEMALE RATS IN THE 13-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

| Group | | Control | 63 ppm | 250 ppm | 1000 ppm | 2000 ppm | 4000 ppm |
|--|-----------------|--------------|------------|------------|----------|----------|----------|
| Number of examined animals | | 10 | 10 | 10 | 10 | 10 | 10 |
| Organ | Grade | | | | | | |
| Findings | | | | | | | |
| Bone marrow | | | | | | | |
| Erythropoiesis : increased | 1+ | 0 | 0 | 0 | 0 | 10 | 10 |
| | Chi Square test | | | | | ** | ** |
| Spleen | | | | | | | |
| Deposit of hemosiderin | 1+ | 0 | 0 | 10 | 10 | 10 | 10 |
| | Chi Square test | | | ** | ** | ** | ** |
| Increased extramedullary hematopoiesis | 1+ | 0 | 0 | 0 | 10 | 10 | 10 |
| | Chi Square test | | | | ** | ** | ** |
| Engorgement of erythrocyte | 1+ | 0 | 0 | 9 | 10 | 0 | 0 |
| | 2+ | 0 | 0 | 0 | 0 | 10 | 0 |
| | 3+ | 0 | 0 | 0 | 0 | 0 | 10 |
| | Chi Square test | | | ** | ** | ** | ** |
| Capsule hyperplasia | 1+ | 0 | 0 | 0 | 0 | 6 | 6 |
| | 2+ | 0 | 0 | 0 | 0 | 0 | 4 |
| | Chi Square test | | | | | * | ** |
| Liver | | | | | | | |
| Necrosis : single cell | 1+ | 0 | 0 | 0 | 8 | 9 | 10 |
| | Chi Square test | | | | ** | ** | ** |
| Deposit of hemosiderin | 1+ | 0 | 0 | 0 | 10 | 10 | 10 |
| | Chi Square test | | | | ** | ** | ** |
| Hydropic change : central | 1+ | 0 | 0 | 0 | 1 | 7 | 0 |
| | 2+ | 0 | 0 | 0 | 0 | 3 | 5 |
| | 3+ | 0 | 0 | 0 | 0 | 0 | 5 |
| | Chi Square test | | | | | ** | ** |
| Hepatocellular hypertrophy : central | 1+ | 0 | 0 | 0 | 0 | 2 | 10 |
| | Chi Square test | | | | | | ** |
| Kidney | | | | | | | |
| Deposit of brown pigment : proximal tubule | 1+ | 0 | 0 | 10 | 10 | 0 | 0 |
| | 2+ | 0 | 0 | 0 | 0 | 10 | 0 |
| | 3+ | 0 | 0 | 0 | 0 | 0 | 10 |
| | Chi Square test | | | ** | ** | ** | ** |
| Grade | 1+: Slight | 2+: Moderate | 3+: Marked | 4+: Severe | | | |
| Significant difference | * : p<0.05 | ** : p<0.01 | | | | | |