

2-アミノ-4-クロロフェノールのマウスを用いた
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：0550

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TABLE 1 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF MALE MICE
IN THE 13-WEEK FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

| Week on Study | Control | | 512 ppm | | | 1280 ppm | | | 3200 ppm | | | 8000 ppm | | | 20000 ppm | | |
|------------------|-----------------|-------------------|-----------------|---------------|-------------------|-----------------|---------------|-------------------|-----------------|---------------|-------------------|-----------------|---------------|-------------------|-----------------|---------------|-------------------|
| | Av. Wt. <10> | 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 | 23.8 (10) | 10 / 10 | 23.7 (10) | 100 | 10 / 10 | 23.8 (10) | 100 | 10 / 10 | 23.8 (10) | 100 | 10 / 10 | 23.8 (10) | 100 | 10 / 10 | 23.7 (10) | 100 | 10 / 10 |
| 1 | 25.1 (10) | 10 / 10 | 24.8 (10) | 99 | 10 / 10 | 25.0 (10) | 100 | 10 / 10 | 24.6 (10) | 98 | 10 / 10 | 24.5 (10) | 98 | 10 / 10 | 22.3 (10) | 89 | 10 / 10 |
| 2 | 26.4 (10) | 10 / 10 | 26.0 (10) | 98 | 10 / 10 | 26.2 (10) | 99 | 10 / 10 | 26.0 (10) | 98 | 10 / 10 | 25.7 (10) | 97 | 10 / 10 | 24.2 (10) | 92 | 10 / 10 |
| 3 | 26.7 (10) | 10 / 10 | 26.1 (10) | 98 | 10 / 10 | 26.3 (9) | 99 | 9 / 10 | 26.1 (10) | 98 | 10 / 10 | 26.1 (10) | 98 | 10 / 10 | 24.6 (10) | 92 | 10 / 10 |
| 4 | 27.2 (10) | 10 / 10 | 28.0 (9) | 103 | 9 / 10 | 26.8 (9) | 99 | 9 / 10 | 26.6 (10) | 98 | 10 / 10 | 26.8 (10) | 99 | 10 / 10 | 24.8 (10) | 91 | 10 / 10 |
| 5 | 28.5 (10) | 10 / 10 | 29.1 (9) | 102 | 9 / 10 | 28.0 (9) | 98 | 9 / 10 | 28.0 (10) | 98 | 10 / 10 | 27.6 (10) | 97 | 10 / 10 | 24.9 (10) | 87 | 10 / 10 |
| 6 | 28.2 (10) | 10 / 10 | 28.6 (9) | 101 | 9 / 10 | 27.6 (9) | 98 | 9 / 10 | 27.4 (10) | 97 | 10 / 10 | 27.4 (10) | 97 | 10 / 10 | 25.5 (9) | 90 | 9 / 10 |
| 7 | 29.1 (10) | 10 / 10 | 30.3 (9) | 104 | 9 / 10 | 29.4 (9) | 101 | 9 / 10 | 29.2 (10) | 100 | 10 / 10 | 28.4 (10) | 98 | 10 / 10 | 25.7 (9) | 88 | 9 / 10 |
| 8 | 29.8 (10) | 10 / 10 | 31.0 (9) | 104 | 9 / 10 | 29.7 (9) | 100 | 9 / 10 | 29.7 (10) | 100 | 10 / 10 | 28.8 (10) | 97 | 10 / 10 | 27.4 (9) | 92 | 9 / 10 |
| 9 | 30.4 (10) | 10 / 10 | 31.1 (9) | 102 | 9 / 10 | 30.6 (9) | 101 | 9 / 10 | 30.3 (10) | 100 | 10 / 10 | 29.5 (10) | 97 | 10 / 10 | 27.3 (9) | 90 | 9 / 10 |
| 10 | 31.9 (10) | 10 / 10 | 32.1 (9) | 101 | 9 / 10 | 31.5 (9) | 99 | 9 / 10 | 31.1 (10) | 97 | 10 / 10 | 30.4 (10) | 95 | 10 / 10 | 25.2 (9) | 79 | 9 / 10 |
| 11 | 31.8 (10) | 10 / 10 | 32.3 (9) | 102 | 9 / 10 | 31.5 (9) | 99 | 9 / 10 | 31.5 (10) | 99 | 10 / 10 | 29.7 (10) | 93 | 10 / 10 | 27.1 (9) | 85 | 9 / 10 |
| 12 | 32.3 (10) | 10 / 10 | 32.9 (9) | 102 | 9 / 10 | 31.2 (9) | 97 | 9 / 10 | 31.5 (10) | 98 | 10 / 10 | 30.8 (10) | 95 | 10 / 10 | 27.8 (9) | 86 | 9 / 10 |
| 13 | 32.9 (10) | 10 / 10 | 33.2 (9) | 101 | 9 / 10 | 32.4 (9) | 98 | 9 / 10 | 31.5 (10) | 96 | 10 / 10 | 30.8 (10) | 94 | 10 / 10 | 28.1 (9) | 85 | 9 / 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 MICE
IN THE 13-WEEK FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

| Week on Study | Control | | 512 ppm | | | 1280 ppm | | | 3200 ppm | | | 8000 ppm | | | 20000 ppm | | |
|------------------|-----------------|-------------------|-----------------|---------------|-------------------|-----------------|---------------|-------------------|-----------------|---------------|-------------------|-----------------|---------------|-------------------|-----------------|---------------|-------------------|
| | Av. Wt. <10> | 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 | 18.8 (10) | 10 / 10 | 18.8 (10) | 100 | 10 / 10 | 18.8 (10) | 100 | 10 / 10 | 18.8 (10) | 100 | 10 / 10 | 18.8 (10) | 100 | 10 / 10 | 18.8 (10) | 100 | 10 / 10 |
| 1 | 20.2 (10) | 10 / 10 | 20.2 (10) | 100 | 10 / 10 | 19.4 (10) | 96 | 10 / 10 | 20.0 (10) | 99 | 10 / 10 | 19.9 (10) | 99 | 10 / 10 | 18.6 (10) | 92 | 10 / 10 |
| 2 | 21.0 (10) | 10 / 10 | 20.7 (10) | 99 | 10 / 10 | 20.5 (10) | 98 | 10 / 10 | 21.2 (10) | 101 | 10 / 10 | 20.5 (10) | 98 | 10 / 10 | 20.2 (10) | 96 | 10 / 10 |
| 3 | 21.3 (10) | 10 / 10 | 20.5 (10) | 96 | 10 / 10 | 20.7 (10) | 97 | 10 / 10 | 20.5 (10) | 96 | 10 / 10 | 20.9 (10) | 98 | 10 / 10 | 19.8 (10) | 93 | 10 / 10 |
| 4 | 21.3 (10) | 10 / 10 | 21.9 (10) | 103 | 10 / 10 | 21.4 (10) | 100 | 10 / 10 | 21.3 (10) | 100 | 10 / 10 | 21.0 (10) | 99 | 10 / 10 | 20.2 (10) | 95 | 10 / 10 |
| 5 | 22.0 (10) | 10 / 10 | 22.3 (10) | 101 | 10 / 10 | 22.4 (10) | 102 | 10 / 10 | 22.0 (10) | 100 | 10 / 10 | 21.8 (10) | 99 | 10 / 10 | 20.1 (10) | 91 | 10 / 10 |
| 6 | 20.8 (10) | 10 / 10 | 21.6 (10) | 104 | 10 / 10 | 21.1 (10) | 101 | 10 / 10 | 21.2 (10) | 102 | 10 / 10 | 20.7 (10) | 100 | 10 / 10 | 19.1 (8) | 92 | 8 / 10 |
| 7 | 22.1 (10) | 10 / 10 | 22.6 (10) | 102 | 10 / 10 | 22.3 (10) | 101 | 10 / 10 | 22.5 (10) | 102 | 10 / 10 | 21.8 (10) | 99 | 10 / 10 | 20.8 (7) | 94 | 7 / 10 |
| 8 | 21.7 (10) | 10 / 10 | 21.8 (10) | 100 | 10 / 10 | 22.0 (10) | 101 | 10 / 10 | 22.8 (10) | 105 | 10 / 10 | 21.4 (10) | 99 | 10 / 10 | 21.8 (7) | 100 | 7 / 10 |
| 9 | 22.5 (10) | 10 / 10 | 22.3 (10) | 99 | 10 / 10 | 22.9 (10) | 102 | 10 / 10 | 22.9 (10) | 102 | 10 / 10 | 22.7 (10) | 101 | 10 / 10 | 22.8 (7) | 101 | 7 / 10 |
| 10 | 22.5 (10) | 10 / 10 | 22.5 (10) | 100 | 10 / 10 | 22.7 (10) | 101 | 10 / 10 | 22.8 (10) | 101 | 10 / 10 | 21.5 (10) | 96 | 10 / 10 | 20.2 (7) | 90 | 7 / 10 |
| 11 | 23.2 (10) | 10 / 10 | 23.8 (10) | 103 | 10 / 10 | 23.4 (10) | 101 | 10 / 10 | 23.2 (10) | 100 | 10 / 10 | 22.6 (10) | 97 | 10 / 10 | 22.9 (7) | 99 | 7 / 10 |
| 12 | 23.6 (10) | 10 / 10 | 23.5 (10) | 100 | 10 / 10 | 23.1 (10) | 98 | 10 / 10 | 24.0 (10) | 102 | 10 / 10 | 22.7 (10) | 96 | 10 / 10 | 23.0 (7) | 97 | 7 / 10 |
| 13 | 23.7 (10) | 10 / 10 | 23.8 (10) | 100 | 10 / 10 | 23.9 (10) | 101 | 10 / 10 | 24.2 (10) | 102 | 10 / 10 | 22.5 (10) | 95 | 10 / 10 | 22.9 (7) | 97 | 7 / 10 |

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

TABLE 3 FOOD CONSUMPTION CHANGES OF MALE MICE IN THE 13-WEEK FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

| Week on Study | Control | | 512 ppm | | | 1280 ppm | | | 3200 ppm | | | 8000 ppm | | | 20000 ppm | | |
|---------------|-----------------|----------------|------------|--------------------|----------------|------------|--------------------|----------------|------------|--------------------|----------------|------------|--------------------|----------------|------------|--------------------|----------------|
| | Av. Fc. <10> | No. of Surviv. | Av. Fc. | % of cont. <10> | No. of Surviv. | Av. Fc. | % of cont. <10> | No. of Surviv. | Av. Fc. | % of cont. <10> | No. of Surviv. | Av. Fc. | % of cont. <10> | No. of Surviv. | Av. Fc. | % of cont. <10> | No. of Surviv. |
| 1 | 4.0 (10) | 10 / 10 | 3.9 (10) | 98 | 10 / 10 | 4.0 (10) | 100 | 10 / 10 | 3.9 (10) | 98 | 10 / 10 | 4.0 (10) | 100 | 10 / 10 | 3.8 (10) | 95 | 10 / 10 |
| 2 | 3.6 (10) | 10 / 10 | 3.9 (10) | 108 | 10 / 10 | 3.9 (10) | 108 | 10 / 10 | 4.2 (10) | 117 | 10 / 10 | 3.9 (10) | 108 | 10 / 10 | 3.8 (10) | 106 | 10 / 10 |
| 3 | 3.5 (10) | 10 / 10 | 3.6 (10) | 103 | 10 / 10 | 3.6 (9) | 103 | 9 / 10 | 3.7 (10) | 106 | 10 / 10 | 3.8 (10) | 109 | 10 / 10 | 3.5 (10) | 100 | 10 / 10 |
| 4 | 3.6 (10) | 10 / 10 | 4.0 (9) | 111 | 9 / 10 | 3.7 (9) | 103 | 9 / 10 | 3.8 (10) | 106 | 10 / 10 | 3.9 (10) | 108 | 10 / 10 | 3.6 (10) | 100 | 10 / 10 |
| 5 | 3.7 (10) | 10 / 10 | 4.2 (9) | 114 | 9 / 10 | 3.8 (9) | 103 | 9 / 10 | 4.1 (10) | 111 | 10 / 10 | 3.9 (10) | 105 | 10 / 10 | 3.6 (10) | 97 | 10 / 10 |
| 6 | 3.9 (10) | 10 / 10 | 3.8 (9) | 97 | 9 / 10 | 3.7 (9) | 95 | 9 / 10 | 3.9 (10) | 100 | 10 / 10 | 4.1 (10) | 105 | 10 / 10 | 3.9 (9) | 100 | 9 / 10 |
| 7 | 4.3 (10) | 10 / 10 | 4.3 (9) | 100 | 9 / 10 | 4.3 (9) | 100 | 9 / 10 | 4.3 (10) | 100 | 10 / 10 | 4.0 (10) | 93 | 10 / 10 | 3.3 (9) | 77 | 9 / 10 |
| 8 | 4.1 (10) | 10 / 10 | 4.3 (9) | 105 | 9 / 10 | 4.1 (9) | 100 | 9 / 10 | 4.4 (10) | 107 | 10 / 10 | 4.1 (10) | 100 | 10 / 10 | 4.8 (9) | 117 | 9 / 10 |
| 9 | 3.5 (10) | 10 / 10 | 3.9 (9) | 111 | 9 / 10 | 4.1 (9) | 117 | 9 / 10 | 4.2 (10) | 120 | 10 / 10 | 4.1 (10) | 117 | 10 / 10 | 4.4 (9) | 126 | 9 / 10 |
| 10 | 4.1 (10) | 10 / 10 | 4.1 (9) | 100 | 9 / 10 | 4.1 (9) | 100 | 9 / 10 | 4.1 (10) | 100 | 10 / 10 | 4.3 (10) | 105 | 10 / 10 | 3.3 (9) | 80 | 9 / 10 |
| 11 | 3.7 (10) | 10 / 10 | 4.1 (9) | 111 | 9 / 10 | 3.9 (9) | 105 | 9 / 10 | 4.4 (10) | 119 | 10 / 10 | 3.7 (10) | 100 | 10 / 10 | 4.1 (9) | 111 | 9 / 10 |
| 12 | 3.9 (10) | 10 / 10 | 4.1 (9) | 105 | 9 / 10 | 3.8 (9) | 97 | 9 / 10 | 3.8 (10) | 97 | 10 / 10 | 4.2 (10) | 108 | 10 / 10 | 4.1 (9) | 105 | 9 / 10 |
| 13 | 3.9 (10) | 10 / 10 | 4.1 (9) | 105 | 9 / 10 | 4.0 (9) | 103 | 9 / 10 | 3.8 (10) | 97 | 10 / 10 | 3.9 (10) | 100 | 10 / 10 | 3.6 (9) | 92 | 9 / 10 |

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

TABLE 4 FOOD CONSUMPTION CHANGES OF FEMALE MICE IN THE 13-WEEK FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

| Week on Study | Control | | 512 ppm | | | 1280 ppm | | | 3200 ppm | | | 8000 ppm | | | 20000 ppm | | |
|------------------|-----------------|-------------------|------------|-----------------------|-------------------|------------|-----------------------|-------------------|------------|-----------------------|-------------------|------------|-----------------------|-------------------|------------|-----------------------|-------------------|
| | Av. Fc. <10> | No. of Surviv. | Av. Fc. | % of cont. <10> | No. of Surviv. | Av. Fc. | % of cont. <10> | No. of Surviv. | Av. Fc. | % of cont. <10> | No. of Surviv. | Av. Fc. | % of cont. <10> | No. of Surviv. | Av. Fc. | % of cont. <10> | No. of Surviv. |
| 1 | 3.8 (10) | 10 / 10 | 3.7 (7) | 97 | 10 / 10 | 3.2 (10) | 84 | 10 / 10 | 3.5 (10) | 92 | 10 / 10 | 3.5 (10) | 92 | 10 / 10 | 3.5 (10) | 92 | 10 / 10 |
| 2 | 3.6 (10) | 10 / 10 | 3.3 (10) | 92 | 10 / 10 | 3.1 (10) | 86 | 10 / 10 | 3.5 (10) | 97 | 10 / 10 | 3.2 (10) | 89 | 10 / 10 | 3.2 (10) | 89 | 10 / 10 |
| 3 | 3.4 (10) | 10 / 10 | 3.4 (10) | 100 | 10 / 10 | 3.3 (10) | 97 | 10 / 10 | 3.1 (10) | 91 | 10 / 10 | 3.4 (10) | 100 | 10 / 10 | 3.1 (10) | 91 | 10 / 10 |
| 4 | 3.3 (10) | 10 / 10 | 3.6 (10) | 109 | 10 / 10 | 3.2 (10) | 97 | 10 / 10 | 3.4 (10) | 103 | 10 / 10 | 3.2 (10) | 97 | 10 / 10 | 3.3 (10) | 100 | 10 / 10 |
| 5 | 3.6 (10) | 10 / 10 | 3.7 (10) | 103 | 10 / 10 | 3.6 (10) | 100 | 10 / 10 | 3.5 (10) | 97 | 10 / 10 | 3.5 (10) | 97 | 10 / 10 | 3.4 (9) | 94 | 10 / 10 |
| 6 | 3.4 (10) | 10 / 10 | 3.8 (10) | 112 | 10 / 10 | 3.5 (10) | 103 | 10 / 10 | 3.4 (8) | 100 | 10 / 10 | 3.4 (10) | 100 | 10 / 10 | 3.5 (8) | 103 | 8 / 10 |
| 7 | 3.7 (10) | 10 / 10 | 4.1 (10) | 111 | 10 / 10 | 3.5 (10) | 95 | 10 / 10 | 3.9 (10) | 105 | 10 / 10 | 3.6 (10) | 97 | 10 / 10 | 3.3 (7) | 89 | 7 / 10 |
| 8 | 3.8 (10) | 10 / 10 | 3.8 (10) | 100 | 10 / 10 | 3.7 (10) | 97 | 10 / 10 | 4.0 (10) | 105 | 10 / 10 | 3.7 (10) | 97 | 10 / 10 | 4.3 (7) | 113 | 7 / 10 |
| 9 | 3.7 (10) | 10 / 10 | 4.0 (10) | 108 | 10 / 10 | 3.9 (10) | 105 | 10 / 10 | 3.8 (10) | 103 | 10 / 10 | 4.0 (10) | 108 | 10 / 10 | 4.2 (7) | 114 | 7 / 10 |
| 10 | 3.6 (10) | 10 / 10 | 3.8 (10) | 106 | 10 / 10 | 3.7 (10) | 103 | 10 / 10 | 3.7 (10) | 103 | 10 / 10 | 3.4 (10) | 94 | 10 / 10 | 3.1 (7) | 86 | 7 / 10 |
| 11 | 4.0 (10) | 10 / 10 | 4.1 (10) | 103 | 10 / 10 | 3.9 (10) | 98 | 10 / 10 | 3.7 (10) | 93 | 10 / 10 | 3.5 (10) | 88 | 10 / 10 | 3.9 (7) | 98 | 7 / 10 |
| 12 | 3.9 (10) | 10 / 10 | 3.9 (10) | 100 | 10 / 10 | 3.7 (10) | 95 | 10 / 10 | 3.8 (10) | 97 | 10 / 10 | 3.6 (10) | 92 | 10 / 10 | 3.5 (7) | 90 | 7 / 10 |
| 13 | 3.8 (10) | 10 / 10 | 3.8 (10) | 100 | 10 / 10 | 3.7 (10) | 97 | 10 / 10 | 3.9 (10) | 103 | 10 / 10 | 3.4 (10) | 89 | 10 / 10 | 3.4 (7) | 89 | 7 / 10 |

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

TABLE 5 HEMATOLOGY OF MALE MICE IN THE 13-WEEK FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

| Group Name | Control | 512 ppm | 1280 ppm | 3200 ppm | 8000 ppm | 20000 ppm |
|---------------------------------------|------------------|------------------|------------------|------------------|--------------------|--------------------|
| No. of examined animals | 9 | 9 | 9 | 10 | 10 | 9 |
| RED BLOOD CELL ($10^6/\mu\text{L}$) | 10.52 \pm 0.32 | 10.66 \pm 0.20 | 10.48 \pm 0.38 | 10.20 \pm 0.29 | 9.78 \pm 0.26 ** | 9.21 \pm 0.25 ** |
| HEMOGLOBIN (g/dL) | 15.8 \pm 0.5 | 16.0 \pm 0.3 | 15.6 \pm 0.6 | 15.5 \pm 0.6 | 15.2 \pm 0.4 * | 16.1 \pm 0.3 |
| HEMATOCRIT (%) | 47.6 \pm 1.7 | 48.0 \pm 0.6 | 46.5 \pm 1.4 | 46.3 \pm 1.4 | 44.6 \pm 1.0 * | 41.2 \pm 0.4 ** |
| MCH (pg) | 15.1 \pm 0.1 | 15.1 \pm 0.2 | 14.9 \pm 0.3 | 15.1 \pm 0.3 | 15.5 \pm 0.2 ** | 17.5 \pm 0.3 ** |
| MCHC (g/dL) | 33.3 \pm 0.7 | 33.5 \pm 0.3 | 33.5 \pm 0.7 | 33.4 \pm 0.3 | 34.0 \pm 0.4 * | 39.2 \pm 0.7 ** |
| PLATELET ($10^3/\mu\text{L}$) | 1415 \pm 71 | 1381 \pm 83 | 1383 \pm 51 | 1310 \pm 94 * | 1401 \pm 105 | 1451 \pm 105 |
| RETICULOCYTE (%) | 2.1 \pm 0.3 | 2.0 \pm 0.3 | 2.3 \pm 0.3 | 2.6 \pm 0.5 | 3.7 \pm 0.7 ** | 6.1 \pm 1.4 ** |
| Differential WBC (%) | | | | | | |
| EOSINO | 2 \pm 1 | 1 \pm 1 | 2 \pm 1 | 1 \pm 1 | 1 \pm 1 * | 0 \pm 1 * |

Mean \pm S.D.Significant difference: * : $p \leq 0.05$ ** : $p \leq 0.01$ Test of Dunnett

TABLE 6 HEMATOLOGY OF FEMALE MICE IN THE 13-WEEK FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

| Group Name | Control | 512 ppm | 1280 ppm | 3200 ppm | 8000 ppm | 20000 ppm |
|---------------------------------------|------------------|------------------|------------------|------------------|---------------------|--------------------|
| No. of examined animals | 10 | 10 | 10 | 8 | 10 | 7 |
| RED BLOOD CELL ($10^6/\mu\text{L}$) | 10.80 \pm 0.29 | 10.74 \pm 0.34 | 10.67 \pm 0.28 | 10.61 \pm 0.21 | 10.12 \pm 0.30 ** | 9.68 \pm 0.49 ** |
| HEMOGLOBIN (g/dL) | 16.5 \pm 0.4 | 16.3 \pm 0.5 | 16.3 \pm 0.5 | 16.1 \pm 0.3 | 15.7 \pm 0.5 ** | 16.8 \pm 1.1 |
| HEMATOCRIT (%) | 49.0 \pm 1.1 | 48.3 \pm 1.2 | 47.8 \pm 1.3 | 48.1 \pm 1.1 | 46.5 \pm 1.2 ** | 44.6 \pm 2.5 ** |
| MCH (pg) | 15.3 \pm 0.1 | 15.2 \pm 0.1 | 15.3 \pm 0.2 | 15.2 \pm 0.1 | 15.5 \pm 0.2 | 17.3 \pm 0.6 ** |
| MCHC (g/dL) | 33.8 \pm 0.5 | 33.8 \pm 0.3 | 34.1 \pm 0.3 | 33.5 \pm 0.4 | 33.7 \pm 0.4 | 37.6 \pm 0.8 ** |
| RETICULOCYTE (%) | 2.2 \pm 0.6 | 2.2 \pm 0.5 | 1.9 \pm 0.4 | 2.5 \pm 0.8 | 4.1 \pm 1.2 ** | 7.3 \pm 1.4 ** |
| Differential WBC (%) | | | | | | |
| MONO | 3 \pm 1 | 2 \pm 1 | 2 \pm 1 | 2 \pm 1 | 1 \pm 1 ** | 1 \pm 1 ** |

Mean \pm S.D.Significant difference: * : $p \leq 0.05$ ** : $p \leq 0.01$ Test of Dunnett

TABLE 7 BIOCHEMISTRY OF MALE MICE IN THE 13-WEEK FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

| Group Name | Control | 512 ppm | 1280 ppm | 3200 ppm | 8000 ppm | 20000 ppm |
|-------------------------|-------------|-------------|-------------|-------------|-------------|---------------|
| No. of examined animals | 10 | 9 | 9 | 10 | 10 | 9 |
| T-BILIRUBIN (mg/dL) | 0.13 ± 0.02 | 0.14 ± 0.01 | 0.14 ± 0.03 | 0.13 ± 0.02 | 0.15 ± 0.03 | 0.16 ± 0.02 * |

Mean ± S.D.
Significant difference: * : $p \leq 0.05$ ** : $p \leq 0.01$ Test of Dunnett

TABLE 8 BIOCHEMISTRY OF FEMALE MICE IN THE 13-WEEK FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

| Group Name | Control | 512 ppm | 1280 ppm | 3200 ppm | 8000 ppm | 20000 ppm |
|-------------------------|-------------|-------------|-------------|-------------|-------------|--------------|
| No. of examined animals | 10 | 9 | 10 | 8 | 10 | 7 |
| T-BILIRUBIN (mg/dL) | 0.14 ± 0.02 | 0.15 ± 0.06 | 0.13 ± 0.01 | 0.13 ± 0.01 | 0.14 ± 0.04 | 0.18 ± 0.05 |
| GLUCOSE (mg/dL) | 131 ± 23 | 140 ± 25 | 136 ± 20 | 153 ± 31 | 142 ± 23 | 180 ± 22 ** |
| T-CHOLESTEROL (mg/dL) | 72 ± 6 | 72 ± 10 | 70 ± 7 | 76 ± 15 | 81 ± 12 | 93 ± 13 ** |
| PHOSPHOLIPID (mg/dL) | 143 ± 9 | 144 ± 14 | 138 ± 12 | 148 ± 25 | 157 ± 19 | 171 ± 18 ** |
| UREA NITROGEN (mg/dL) | 19.0 ± 2.4 | 19.2 ± 2.0 | 19.0 ± 3.3 | 19.5 ± 2.0 | 20.2 ± 2.3 | 27.4 ± 8.0 * |

Mean ± S.D.
Significant difference: * : $p \leq 0.05$ ** : $p \leq 0.01$ Test of Dunnett

TABLE 9 URINALYSIS OF MALE MICE IN THE 13-WEEK FEED STUDY OF
2-AMINO-4-CHLOROPHENOL

| Group Name | | Control | 512 ppm | 1280 ppm | 3200 ppm | 8000 ppm | 20000 ppm |
|-------------------------|-----------------|-----------------|---------|----------|----------|----------|-----------|
| No. of examined animals | | 10 | 9 | 9 | 10 | 10 | 9 |
| pH | Grade | | | | | | |
| | 5.0 | 0 | 0 | 0 | 0 | 0 | 0 |
| | 6.0 | 0 | 0 | 0 | 1 | 4 | 2 |
| | 6.5 | 0 | 0 | 2 | 1 | 0 | 5 |
| | 7.0 | 3 | 5 | 3 | 2 | 1 | 1 |
| | 7.5 | 4 | 3 | 1 | 3 | 2 | 1 |
| | 8.0 | 2 | 1 | 1 | 3 | 2 | 0 |
| | 8.5 | 1 | 0 | 2 | 0 | 1 | 0 |
| | Chi square test | | | | | | * |
| Protein | — | 0 | 0 | 0 | 0 | 0 | 0 |
| | ± | 0 | 0 | 1 | 0 | 4 | 8 |
| | + | 7 | 9 | 8 | 10 | 6 | 1 |
| | 2+ | 3 | 0 | 0 | 0 | 0 | 0 |
| | 3+ | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4+ | 0 | 0 | 0 | 0 | 0 | 0 |
| | | Chi square test | | | | | * |
| Ketone body | — | 1 | 2 | 3 | 5 | 6 | 6 |
| | ± | 2 | 2 | 4 | 3 | 3 | 3 |
| | + | 7 | 5 | 2 | 2 | 1 | 0 |
| | 2+ | 0 | 0 | 0 | 0 | 0 | 0 |
| | 3+ | 0 | 0 | 0 | 0 | 0 | 0 |
| | 4+ | 0 | 0 | 0 | 0 | 0 | 0 |
| | Chi square test | | | | | * | ** |

Significant difference: * : $p \leq 0.05$ ** : $p \leq 0.01$

TABLE 10 ORGAN WEIGHTS OF MALE MICE IN THE 13-WEEK FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

| Group Name | Control | 512 ppm | 1280 ppm | 3200 ppm | 8000 ppm | 20000 ppm | |
|------------------------|---------------|---------------|---------------|---------------|------------------|------------------|----|
| No. of examined animal | 10 | 9 | 9 | 10 | 10 | 9 | |
| Body weight (g) | 30.6 ± 2.4 | 30.8 ± 2.6 | 30.1 ± 2.4 | 29.6 ± 3.1 | 28.7 ± 2.5 | 25.8 ± 1.0 | ** |
| Lungs (g) | 0.146 ± 0.010 | 0.149 ± 0.007 | 0.143 ± 0.011 | 0.145 ± 0.009 | 0.153 ± 0.016 | 0.147 ± 0.012 | |
| Lungs (%) | 0.479 ± 0.031 | 0.487 ± 0.045 | 0.476 ± 0.039 | 0.495 ± 0.054 | 0.532 ± 0.029 * | 0.572 ± 0.061 ** | ** |
| Kidneys (g) | 0.419 ± 0.033 | 0.447 ± 0.067 | 0.744 ± 0.733 | 0.407 ± 0.029 | 0.409 ± 0.028 | 0.450 ± 0.031 * | * |
| Kidneys (%) | 1.376 ± 0.135 | 1.464 ± 0.299 | 2.583 ± 2.767 | 1.381 ± 0.070 | 1.427 ± 0.065 | 1.744 ± 0.136 ** | ** |
| Spleen (g) | 0.050 ± 0.005 | 0.054 ± 0.008 | 0.054 ± 0.011 | 0.053 ± 0.008 | 0.067 ± 0.005 ** | 0.145 ± 0.023 ** | ** |
| Spleen (%) | 0.162 ± 0.016 | 0.177 ± 0.033 | 0.182 ± 0.047 | 0.178 ± 0.016 | 0.233 ± 0.014 ** | 0.562 ± 0.091 ** | ** |
| Liver (g) | 1.094 ± 0.073 | 1.126 ± 0.071 | 1.077 ± 0.101 | 1.088 ± 0.127 | 1.116 ± 0.108 | 1.214 ± 0.068 * | * |
| Liver (%) | 3.583 ± 0.193 | 3.662 ± 0.230 | 3.579 ± 0.184 | 3.673 ± 0.144 | 3.891 ± 0.204 ** | 4.702 ± 0.207 ** | ** |
| Brain (g) | 0.437 ± 0.009 | 0.447 ± 0.013 | 0.448 ± 0.018 | 0.441 ± 0.010 | 0.441 ± 0.014 | 0.432 ± 0.014 | |
| Brain (%) | 1.438 ± 0.128 | 1.458 ± 0.137 | 1.495 ± 0.103 | 1.505 ± 0.152 | 1.545 ± 0.125 | 1.674 ± 0.103 ** | ** |

Mean ± S.D.

Significant difference: * : $p \leq 0.05$ ** : $p \leq 0.01$ Test of Dunnett

TABLE 11 ORGAN WEIGHTS OF FEMALE MICE IN THE 13-WEEK FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

| Group Name | Control | 512 ppm | 1280 ppm | 3200 ppm | 8000 ppm | 20000 ppm | |
|------------------------|---------------|---------------|---------------|---------------|------------------|------------------|----|
| No. of examined animal | 10 | 10 | 10 | 10 | 10 | 7 | |
| Body weight (g) | 21.2 ± 1.3 | 21.1 ± 1.2 | 21.0 ± 1.4 | 21.9 ± 1.6 | 20.5 ± 0.8 | 20.5 ± 0.7 | |
| Kidneys (g) | 0.293 ± 0.014 | 0.298 ± 0.012 | 0.284 ± 0.018 | 0.308 ± 0.020 | 0.292 ± 0.010 | 0.315 ± 0.020 * | * |
| Kidneys (%) | 1.386 ± 0.045 | 1.412 ± 0.092 | 1.356 ± 0.060 | 1.408 ± 0.081 | 1.426 ± 0.044 | 1.538 ± 0.130 * | * |
| Spleen (g) | 0.054 ± 0.005 | 0.057 ± 0.004 | 0.052 ± 0.006 | 0.056 ± 0.007 | 0.071 ± 0.013 * | 0.153 ± 0.015 ** | ** |
| Spleen (%) | 0.254 ± 0.019 | 0.268 ± 0.020 | 0.250 ± 0.019 | 0.257 ± 0.029 | 0.344 ± 0.053 ** | 0.744 ± 0.069 ** | ** |
| Liver (g) | 0.877 ± 0.027 | 0.880 ± 0.047 | 0.857 ± 0.091 | 0.916 ± 0.090 | 0.895 ± 0.071 | 1.036 ± 0.067 ** | ** |
| Liver (%) | 4.148 ± 0.141 | 4.166 ± 0.175 | 4.085 ± 0.248 | 4.179 ± 0.229 | 4.368 ± 0.231 | 5.043 ± 0.240 ** | ** |

Mean ± S.D.

Significant difference: * : $p \leq 0.05$ ** : $p \leq 0.01$ Test of Dunnett

TABLE 12 INCIDENCES OF SELECTED LESIONS OF MALE MICE IN THE 13-WEEK FEED STUDY OF 2-AMINO-4-CHLOROPHENOL (DEAD AND MORIBUND ANIMALS)

| Group Name | Control | | | | 512 ppm | | | | 1280 ppm | | | | 3200 ppm | | | | 8000 ppm | | | | 20000 ppm | | | |
|------------------------------|---------|---|---|---|---------|---|---|---|----------|---|---|---|----------|---|---|---|----------|---|---|---|-----------|---|---|---|
| Number of examined animals | 0 | | | | 1 | | | | 1 | | | | 0 | | | | 0 | | | | 1 | | | |
| Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| thymus | | | | | <1> | | | | <1> | | | | | | | | <1> | | | | | | | |
| atrophy | — | | | | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | — | | | | — | | | | 0 | 0 | 1 | 0 |
| spleen | | | | | <1> | | | | <1> | | | | | | | | <1> | | | | | | | |
| deposit of hemosiderin | — | | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | — | | | | — | | | | 0 | 0 | 1 | 0 |
| extramedullary hematopoiesis | — | | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | — | | | | — | | | | 0 | 0 | 1 | 0 |
| heart | | | | | <1> | | | | <1> | | | | | | | | <1> | | | | | | | |
| myocardial necrosis | — | | | | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | — | | | | — | | | | 0 | 0 | 0 | 0 |
| myocarditis | — | | | | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | — | | | | — | | | | 0 | 0 | 0 | 0 |
| stomach | | | | | <1> | | | | <1> | | | | | | | | <1> | | | | | | | |
| hyperplasia:forestomach | — | | | | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | — | | | | — | | | | 0 | 1 | 0 | 0 |
| kidney | | | | | <1> | | | | <1> | | | | | | | | <1> | | | | | | | |
| hydronephrosis | — | | | | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | — | | | | — | | | | 1 | 0 | 0 | 0 |
| mineralization:cortex | — | | | | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | — | | | | — | | | | 0 | 0 | 0 | 0 |

Grade 1: Slight 2: Moderate 3: Marked 4: Severe
 < > : Number of animals examined at the site
 — : All animals survived at the terminal necropsy

TABLE 13 INCIDENCES OF SELECTED LESIONS OF MALE MICE IN THE 13-WEEK FEED STUDY OF 2-AMINO-4-CHLOROPHENOL (SACRIFICED ANIMALS)

| Group Name | Control | | | | 512 ppm | | | | 1280 ppm | | | | 3200 ppm | | | | 8000 ppm | | | | 20000 ppm | | | |
|-------------------------------------|---------|---|---|---|---------|---|---|---|----------|---|---|---|----------|---|---|------|----------|---|---|------|-----------|---|---|------|
| Number of examined animals | 10 | | | | 9 | | | | 9 | | | | 10 | | | | 10 | | | | 9 | | | |
| Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| spleen | <10> | | | | <9> | | | | <9> | | | | <10> | | | | <10> | | | | <9> | | | |
| deposit of hemosiderin | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 10 | 0 | 0 | 0 ** | 10 | 0 | 0 | 0 ** | 0 | 9 | 0 | 0 ** |
| extramedullary hematopoiesis | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 5 | 0 | 0 | 0 | 10 | 0 | 0 | 0 ** | 2 | 8 | 0 | 0 ** | 0 | 0 | 9 | 0 ** |
| stomach | <10> | | | | <9> | | | | <9> | | | | <10> | | | | <10> | | | | <9> | | | |
| erosion:forestomach | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 |
| ulcer:forestomach | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 0 | 0 | 0 |
| hyperplasia:forestomach | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 7 | 1 | 0 | 0 ** | 4 | 4 | 0 | 0 ** | 0 | 0 | 9 | 0 ** |
| liver | <10> | | | | <9> | | | | <9> | | | | <10> | | | | <10> | | | | <9> | | | |
| deposit of hemosiderin | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 9 | 0 | 0 | 0 ** |
| swelling:centeral | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 6 | 0 | 0 | 0 * | 7 | 0 | 0 | 0 ** |
| kidney | <10> | | | | <9> | | | | <9> | | | | <10> | | | | <10> | | | | <9> | | | |
| hydronephrosis | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| inflammatory polyp | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| urinary bladder | <10> | | | | <9> | | | | <9> | | | | <10> | | | | <10> | | | | <9> | | | |
| hyperplasia:transitional epithelium | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 4 | 0 | 0 | 0 | 8 | 0 | 0 | 0 ** |
| swelling:transitional epithelium | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 5 | 0 | 0 | 0 * | 5 | 4 | 0 | 0 ** | 1 | 8 | 0 | 0 ** |

Grade 1: Slight 2: Moderate 3: Marked 4: Severe
 < > : Number of animals examined at the site
 Significant difference ; * : $p \leq 0.05$ ** : $p \leq 0.01$ Test of Chi Square

TABLE 14 INCIDENCES OF SELECTED LESIONS OF FEMALE MICE IN THE 13-WEEK FEED STUDY OF 2-AMINO-4-CHLOROPHENOL (DEAD AND MORIBUND ANIMALS)

| Group Name | Control | | | | 512 ppm | | | | 1280 ppm | | | | 3200 ppm | | | | 8000 ppm | | | | 20000 ppm | | | |
|----------------------------------|---------|---|---|---|---------|---|---|---|----------|---|---|---|----------|---|---|---|----------|---|---|---|-----------|---|-----|---|
| Number of examined animals | 0 | | | | 0 | | | | 0 | | | | 0 | | | | 0 | | | | 3 | | | |
| Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| thymus | | | | | | | | | | | | | | | | | | | | | | | | |
| atrophy | | — | | | | — | | | | — | | | | — | | | | — | | | | | <3> | |
| spleen | | | | | | | | | | | | | | | | | | | | | | | | |
| deposit of hemosiderin | | — | | | | — | | | | — | | | | — | | | | — | | | | | <3> | |
| extramedullary hematopoiesis | | — | | | | — | | | | — | | | | — | | | | — | | | | | 0 | 3 |
| tongue | | | | | | | | | | | | | | | | | | | | | | | | |
| inflammation | | — | | | | — | | | | — | | | | — | | | | — | | | | | <3> | |
| stomach | | | | | | | | | | | | | | | | | | | | | | | | |
| erosion:forestomach | | — | | | | — | | | | — | | | | — | | | | — | | | | | <3> | |
| ulcer:forestomach | | — | | | | — | | | | — | | | | — | | | | — | | | | | 2 | 0 |
| hyperplasia:forestomach | | — | | | | — | | | | — | | | | — | | | | — | | | | | 0 | 0 |
| urinary bladder | | | | | | | | | | | | | | | | | | | | | | | | |
| necrosis:transitional epithelium | | — | | | | — | | | | — | | | | — | | | | — | | | | | <3> | |
| | | | | | | | | | | | | | | | | | | | | | | | 0 | 2 |

Grade 1: Slight 2: Moderate 3: Marked 4: Severe
< > : Number of animals examined at the site
— : All animals survived at the terminal necropsy

TABLE 15 INCIDENCES OF SELECTED LESIONS OF FEMALE MICE IN THE 13-WEEK FEED STUDY OF 2-AMINO-4-CHLOROPHENOL (SACRIFICED ANIMALS)

| Group Name | Control | | | | 512 ppm | | | | 1280 ppm | | | | 3200 ppm | | | | 8000 ppm | | | | 20000 ppm | | | |
|-------------------------------------|---------|---|---|---|---------|---|---|---|----------|---|---|-----|----------|---|---|-----|----------|---|---|-----|-----------|---|---|-----|
| Number of examined animals | 10 | | | | 10 | | | | 10 | | | | 10 | | | | 10 | | | | 7 | | | |
| Grade | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 | 1 | 2 | 3 | 4 |
| spleen | <10> | | | | <10> | | | | <10> | | | | <10> | | | | <10> | | | | <7> | | | |
| deposit of hemosiderin | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 5 | 0 | 0 | 0* | 10 | 0 | 0 | 0** | 3 | 7 | 0 | 0** | 0 | 7 | 0 | 0** |
| extramedullary hematopoiesis | 1 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 9 | 0 | 0 | 0** | 8 | 2 | 0 | 0** | 4 | 5 | 1 | 0** | 0 | 0 | 7 | 0** |
| stomach | <10> | | | | <10> | | | | <10> | | | | <10> | | | | <10> | | | | <7> | | | |
| erosion:forestomach | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| ulcer:forestomach | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 3 | 1 | 0 | 0* |
| hyperplasia:forestomach | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 3 | 3 | 0 | 0* | 5 | 3 | 2 | 0** | 0 | 0 | 7 | 0** |
| liver | <10> | | | | <10> | | | | <10> | | | | <10> | | | | <10> | | | | <7> | | | |
| deposit of hemosiderin | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 7 | 0 | 0 | 0** |
| urinary bladder | <10> | | | | <10> | | | | <10> | | | | <10> | | | | <10> | | | | <7> | | | |
| hyperplasia:transitional epithelium | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 4 | 0 | 0 | 0* |
| necrosis:transitional epithelium | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| swelling:transitional epithelium | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 2 | 0 | 0 | 0 | 7 | 0 | 0 | 0** | 10 | 0 | 0 | 0** | 0 | 7 | 0 | 0** |

Grade 1: Slight 2: Moderate 3: Marked 4: Severe
 < > : Number of animals examined at the site
 Significant difference ; * : $p \leq 0.05$ ** : $p \leq 0.01$ Test of Chi Square