Summary of Feed Carcinogenicity Study of 2-Amino-4-Chlorophenol in B6D2F1 Mice

September 2008

Japan Bioassay Research Center

Japan Industrial Safety and Health Association

PREFACE

The tests were contracted and supported by the Ministry of Health, Labour and Welfare of Japan. The tests were conducted by Japan Bioassay Research Center (JBRC) and the report was prepared by JBRC and peer reviewed by outside expert pathologist. Complete report was submitted to Ministry of Health, Labour and Welfare of Japan on September 30, 2008.

This English Summary was translated by JBRC from Japanese complete report.

Summary of Feed Carcinogenicity Study of 2-Amino-4-chlorophenol in B6D2F1 MICE

Purpose, materials and methods

2-Amino-4-chlorophenol (ACP, CAS No. 95-85-2) is a crystalline solid with a melting point of 137°C. It is insoluble in water.

The carcinogenicity and chronic toxicity of ACP (greater than 99.1% pure) were examined by feeding groups of B6D2F1/Crlj mice ACP-containing diets for 2 years (104 weeks). Each group of test animals consisted of either 50 male or 50 female mice. The dietary concentration of ACP was 0, 512, 1280, or 3200 ppm (w/w). Both sexes were exposed to each concentration of ACP. The highest dose level was chosen so as not to exceed the maximum tolerated dose (MTD), based on both growth rate and toxicity in a previous 13-week toxicity study. The identity of the ACP used in these experiments was confirmed by both infrared spectrometry and mass spectrometry, and it was analyzed by gas chromatography before and after its use to affirm its stability. To ensure that the concentration of ACP in the diet remained constant, the concentration of APC in the diet was determined by high performance liquid chromatography at the time of preparation and on the 4th day after preparation; ACP-containing food was stored at room temperature. The animals were observed daily for clinical signs and mortality. Body weight and food consumption were measured once a week for the first 14 weeks and every 4 weeks thereafter. All animals, including those found dead or in a moribund state as well as those surviving to the end of the 2-year exposure period, underwent complete necropsy. Urinalysis was performed near the end of the administration period. For hematology and blood biochemistry at the terminal necropsy, surviving animals were fasted overnight and bled under deep ether anesthesia. Organs and tissues were removed, weighed and examined for macroscopic lesions at necropsy. The organs and tissues were then fixed and embedded in paraffin. Five µm thick tissue sections were prepared and stained with hematoxylin and eosin and examined microscopically. Incidences of neoplastic lesions were statistically analyzed by Fisher's exact test. Any positive dose-response trends of ACP induction of neoplastic lesions were analyzed by Peto's test. Incidences of non-neoplastic lesions and urinalysis were analyzed by the Chi-square test. Changes in body weight, food consumption, hematological and blood biochemical parameters, and organ weights were analyzed by Dunnett's test. The present studies were conducted in accordance with the Organisation for Economic Co-operation and Development (OECD) Good Laboratory Practice and with reference to the OECD Guideline for Testing of Chemicals 451 "Carcinogenicity Studies".

Results

There was no significant difference in survival rate, body weight or food consumption between any ACP-fed group of either sex and their respective controls.

The incidence of squamous cell papillomas in the forestomach was increased in the 3200 ppm-fed male group compared to their control group. Also, the incidences of squamous cell papillomas in the forestomach in all ACP-fed male groups were higher than the historical control data of the Japan Bioassay Research Center (JBRC). Therefore, the increased incidences of squamous cell papillomas in the forestomach in males is related to ACP administration. A slight increase in the incidence of squamous cell papillomas in the forestomach was also observed in the ACP-fed females, but those incidences were within the range of historical JBRC control data.

Conclusions

In mice, there was some evidence of carcinogenic activity of 2-amino-4-chlorophenol in males, based on an increased incidences of squamous cell papillomas in the forestomach. There was no evidence of carcinogenic activity of 2-amino-4-chlorophenol in females.

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|-----------|--|
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TABLE C 1

BODY WEIGHT CHANGES AND

SURVIVAL ANIMAL NUMBERS: MALE

STUDY NO. : 0580
ANIMAL : MOUSE BEDZF1/Cr1,i[Cr.j.:BDF1]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

PAGE: 1

| | No. of | Surviv. | | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 50/50 | 20/20 | 20/20 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 49/50 | 48/50 | 48/50 | 48/50 | 47/50 | 47/50 | 47/50 | 47/50 | 47/50 | 47/50 | 45/50 | 45/50 | 42/50 | 40/50 | 38/20 | 36/50 | 35/50 |
|-----------------|-------------|----------|----------|------------|-------|-----------|-------|----------|----------|-----------|-------|-----------|--------|-------|-----------|-------|-----------|-------|-------|-------|-------|-------|-------|------------|-------|-------|-------------------------------|-------|-----------|------------|------------|-----------|------------|-------|--------|------------|---------|-------|-----------|---------------|
| 9700 bbm | % of | cont. | <20> | | | 86 (09 | | 26) 97 | | | | | | | | | | | | | | | | | | | (48) 96 | | | | | (47) 98 | | | 15) 66 | | 101 (0) | | | 35) 106 |
| | Av. Wt. | | | | | | | | | | | | 31.1 (| | | | | | | | | | | 46.2 (4 | | | 49.3 (4 | | | | | | | | | | | | | $\overline{}$ |
| | f No. of | | | | | | | | | | | | | | | | 20/20 | | | | | | | | | | 50/50 | | | | | | | | • | | 40/20 | | | |
| | Av. Wt. % o | cont | <95> | | (20) | (20) | (20) | (20) | (20) | | (20) | (20) | (20) | (20) | (20) | (20) | (20) | (20) | (20) | | (20) | (20) | (20) | (20) | (20) | (20) | 49. 3 (50) 95 50 c (50) 07 | (40) | | (47) | (46) | (45) | (45) | (44) | (43) | (41) | (40) | (38) | 4 (38) | |
| | No. of | Surviv. | | 50/50 | 50/50 | 20/20 | 20/20 | 20/20 | 20/20 | 20/20 | 20/20 | 20/20 | 20/20 | 20/20 | 20/20 | 20/20 | 20/20 | 20/20 | 20/20 | 50/50 | 49/50 | 49/50 | 49/20 | 49/50 | 49/50 | 49/50 | 49/50 40/50 | 49/50 | 49/50 | 48/50 | 48/50 | 46/50 | 45/50 | 45/50 | 45/50 | 43/50 | 40/20 | 38/20 | 35/50 | 34/50 |
| | % of | cont. | <20> | 100 | 66 | 66 | 66 | 86 | 66 | 66 | 86 | 66 | 66 | 66 | 97 | 26 | 66 | 66 | 001 | 66 | 66 | 66 | 100 | 100 | 88 | 86 S | 0 20 | 8 8 | 86 | 86 | 66 | 66 | 66 | 100 | 100 | 102 | 109 | 107 | 109 | 109 |
| | Av. Wt. | | | 24.0 (50) | _ | 26.1 (50) | _ | _ | _ | 29.4 (50) | _ | 30.9 (50) | _ | - | 32.0 (50) | _ | _ | _ | _ | | | | | - | _ | | 49.5 (49) | | | | 52.9 (48) | _ | 54.4 (45) | | | | | on. | 55.1 (35) | 53.0 (34) |
| | t. No. of | Surviv. | <50> | (50) 50/50 | | (20) | (20) | (20) | (20) | (20) | (20) | _ | (20) | (20) | (20) | (20) | | (20) | _ | (20) | (20) | (20) | (48) | (49) 49/50 | | | (48) 48/50 | | | (45) 45/50 | (43) 43/50 | | (43) 43/50 | • | _ | (37) 37/50 | | | _ | (33) 33/20 |
| | Av. Wt. | Week Day | on Study | 0-0 24.0 | | | | 4-7 28.2 | 5-7 29.1 | | | | | | 11-7 33.0 | | 13-7 35.0 | | | | | | | 38-7 47.5 | | | 54-7 59.1 | | 62-7 52.8 | | | 74-7 54.4 | | | | | | | | 104-7 48.8 |

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TABLE C 2

BODY WEIGHT CHANGES AND

SURVIVAL ANIMAL NUMBERS: FEMALE

PAGE: 2

STUDY NO. : 0580
ANIMAL : MOUSE BEDZH:J/Cr1,i[Cr.j:EDF1]
UNIT : E
REPORT TYPE : A1 104
SEX : FEMALE

| Week-Day on Study | | | | | | | | | | | |
|----------------------|-----------|---------|------------|-------|---------|-----------|------|--------|-----------|-------|---------|
| Week-Day on Study | Av. Wt. | No. of | Av. Wt. | Jo % | No. of | Av. Wt. | Jo % | No. of | Av. Wt. | 36 | No of |
| on Study | | Surviv. | | cont. | Surviv. | | COD | Surviv | | cont | Survivi |
| | ~ | <20> | | <20> | | | <20> | : : | | (20°) | |
| 0-0 | 19.2 (50) | 50/50 | 19. 2 (50) | 100 | 20/20 | | 100 | 50/50 | - 1 | 001 | 50/50 |
| 1-7 | _ | 50/50 | 20.1 (50) | 100 | 20/20 | | 66 | 50/50 | | 86 | 50/50 |
| 2-2 | 20.3 (50) | 50/50 | 20.5 (50) | 101 | 50/50 | 20.2 (50) | 100 | 50/50 | | 100 | 50/50 |
| 3-7 | _ | 50/50 | _ | 100 | 20/20 | | 100 | 20/20 | | 66 | 50/50 |
| 4-7 | ~ | 50/50 | _ | 100 | 20/20 | | 100 | 50/50 | | 100 | 50/50 |
| 22 | 22.1 (50) | 50/50 | _ | 100 | 20/20 | | 100 | 20/20 | | 66 | 50/50 |
| 2-9 | _ | 20/20 | 22.3 (50) | 66 | 20/20 | | 100 | 20/20 | | 100 | 50/50 |
| 2-2 | _ | 20/20 | _ | 101 | 20/20 | | 100 | 20/20 | | 100 | 50/50 |
| 2-8 | 23.6 (50) | 50/50 | 23.7 (50) | 100 | 50/50 | | 86 | 50/50 | | 100 | 50/50 |
| 2-6 | 24.0 (50) | 50/50 | 24.2 (50) | 101 | 50/50 | | 86 | 20/20 | | 66 | 50/50 |
| 7-01 | _ | 50/50 | 24.7 (50) | 102 | 50/50 | | 66 | 50/50 | | 100 | 50/50 |
| 117 | 24.7 (50) | 20/20 | | 100 | 50/50 | | 97 | 50/50 | _ | 86 | 50/50 |
| 127 | 24.8 (50) | 50/50 | 25.1 (50) | 101 | 20/20 | | 66 | 50/50 | _ | 100 | 50/50 |
| 73-7 | 25.8 (50) | 20/20 | _ | 100 | 20/20 | | 26 | 20/20 | _ | 86 | 20/20 |
| 14-7 | _ | 20/20 | _ | 100 | 20/20 | 25.6 (50) | 97 | 50/50 | 25.8 (50) | 86 | 50/50 |
| 18-7 | 27.5 (50) | 20/20 | 27.9 (50) | 101 | 50/50 | | 86 | 50/50 | _ | 66 | 50/50 |
| 22-7 | _ | 20/20 | _ | 101 | 50/50 | | 66 | 20/20 | | 100 | 49/50 |
| 26-7 | _ | 20/20 | _ | 101 | 20/20 | | 86 | 50/50 | | 26 | 49/50 |
| 30-7 | _ | 20/20 | 32.7 (50) | 102 | 20/20 | | 66 | 50/50 | _ | 86 | 49/50 |
| 34-7 | _ | 50/50 | _ | 101 | 50/50 | | 86 | 20/20 | _ | 16 | 49/50 |
| 38-7 | _ | 50/50 | 35.3 (50) | 102 | 20/20 | | 66 | 20/20 | _ | 100 | 49/50 |
| 42-7 | 35.9 (50) | 50/50 | - | 103 | 20/20 | 35.4 (50) | 66 | 20/20 | _ | 101 | 48/50 |
| 46-7 | _ | 20/20 | - | 102 | 20/20 | | 86 | 50/50 | _ | 102 | 48/50 |
| 2-05 | _ | 20/20 | _ | 104 | 20/20 | | 66 | 20/20 | _ | 102 | 48/50 |
| 54-7 | _ | 20/20 | _ | 103 | 20/20 | | 66 | 20/20 | _ | 101 | 48/50 |
| 287 | 38.8 (50) | 20/20 | 39.8 (49) | 103 | 49/50 | | 66 | 20/20 | _ | 101 | 48/50 |
| 627 | | 50/50 | _ | 102 | 48/50 | | 66 | 49/50 | _ | 102 | 48/50 |
| 2-99 | | 49/50 | 41.1 (47) | 104 | 47/50 | | 66 | 49/20 | _ | 102 | 48/50 |
| 2-02 | | 49/50 | | 105 | 47/50 | | 101 | 49/20 | _ | 103 | 47/50 |
| 747 | | 49/50 | _ | 104 | 47/50 | | 101 | 48/50 | _ | 102 | 47/50 |
| 2-82 | | 48/50 | | 102 | 46/50 | | 86 | 47/50 | _ | 100 | 46/50 |
| 2-28 | 10.1 (48) | 48/50 | 42.5 (44) | 901 | 44/50 | | 100 | 47/50 | _ | 102 | 44/50 |
| 2-98 | 39.8 (47) | 47/50 | 42.8 (43) | 108 | 43/50 | 10.8 (44) | 103 | 44/50 | _ | 102 | 41/50 |
| 2-06 | 39.9 (45) | 45/50 | 43.3 (41) | 601 | 41/50 | | 104 | 40/20 | _ | 103 | 38/50 |
| 94-7 | 39.0 (41) | 41/50 | 41.7 (39) | 107 | 39/50 | | 106 | 36/50 | _ | 103 | 36/50 |
| 286 | 40.8 (36) | 36/20 | 41.6 (34) | 102 | 34/50 | 0 | 100 | 33/20 | _ | 86 | 34/50 |
| 102-7 | 40.5 (34) | 34/50 | _ | 102 | 29/50 | 41.5 (30) | 102 | 30/20 | 38.8 (30) | 96 | 30/50 |
| 104-7 | 39.6 (34) | 34/50 | 39.1 (28) | 66 | 28/50 | 9.6 | 103 | 28/50 | _ | 96 | 30/50 |

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TABLE C 3

BODY WEIGHT CHANGES: MALE

| Group Name Administration week-day. Courtrol 24.0± 0.8 25.4± 1.2 26.4± 1.3 27.3± 1.4 28.2± 1.5 512 ppm 24.0± 0.8 25.1± 1.0 26.1± 0.9 27.0± 1.1 27.7± 1.3 1280 ppm 24.0± 0.8 25.1± 1.0 25.8± 1.3* 27.0± 1.4 27.9± 1.5 3200 ppm 24.0± 0.8 24.7± 1.2** 25.8± 1.2** 26.6± 1.6 27.3± 1.9** | UNIT : R REPORT TYPE : AI 104 SEX : MALE | | | | | | | PAGE : |
|---|--|-----------------------|---------------------|-----------|-----------------|-----------|------------|---------------|
| 24.0± 0.8 25.4± 1.2 26.4± 1.3 27.3± 1.4 28.2± 24.0± 0.8 25.1± 1.0 26.1± 0.9 27.0± 1.1 27.7± 24.0± 0.8 25.1± 1.0 25.8± 1.3* 27.0± 1.4 27.9± 24.0± 0.8 24.7± 1.2** 25.8± 1.2* 26.6± 1.6 27.3± | roup Name | Administration 0-0 | week-day | 2-7 | 3-7 | 4-7 | £5 | 2-9 |
| 24.0± 0.8 25.1± 1.0 26.1± 0.9 27.0± 1.1 27.7± 24.0± 0.8 25.1± 1.0 25.8± 1.3* 27.0± 1.4 27.9± 24.0± 0.8 24.7± 1.2* 25.8± 1.2* 26.6± 1.6 27.3± | Control | 24.0± 0.8 | | 26.4士 1.3 | 27.3± 1.4 | | 29.1± 1.6 | 29.7± 1.6 |
| 24.0± 0.8 25.1± 1.0 25.8± 1.3* 27.0± 1.4 27.9± 24.0± 0.8 24.7± 1.2* 25.8± 1.2* 26.6± 1.6 27.3± | 512 ppm | 24.0 ± 0.8 | | | | | 28.7 ± 1.4 | 29.4 ± 1.4 |
| 24.0± 0.8 24.7± 1.2** 25.8± 1.2* 26.6± 1.6 27.3± | 1280 ppm | 24.0± 0.8 | | | 27.0± 1.4 | 27.9± 1.5 | 28.8 1.8 | 29.5± 1.8 |
| | 3200 ppm | 24.0± 0.8 | | | 26.6± 1.6 | | 28.4± 1.7 | 29.1± 2.0 |
| | | | | | | | | |
| Significant difference : $\star:P \le 0.05$ $\star\star:P \le 0.01$ Test of Dunnett | Significant difference : | | 5 : P ≤ 0.01 | | Test of Dunnett | | | |

| STUDY NO. : 0580 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : K REPORT TYPE : A1 104 SEX : MALE | J[Cr.j:BDF1] | | BODY WEIGHT CHANGES ALL ANTMALS | (SUMMARY) | | | PAGE: 2 |
|--|---------------------|--------------------------------|------------------------------------|-----------------|--------------|---------------|--------------|
| Group Name | Administrati 7-7 | Administration week-day 7-7 | L-6 | 701 | 117 | 12-7 | 13-7 |
| Control. | 30.6± 1.7 | 31.2± 1.7 | 31.9± 2.0 | 32.3± 2.3 | 33.0± 2.4 | 34.3± 2.3 | 35.0± 2.6 |
| 512 ppm | 30.0 = 1.7 | 30.9土 1.7 | 31.6± 1.8 | 32.0 ± 2.1 | 32.0 ± 2.1 | 33.4 ± 1.9 | 34.6 ± 2.0 |
| 1280 ppm | 30.2 ± 1.9 | 30.7 ± 2.1 | 31.5± 2.2 | 32.1 ± 2.2 | 32.4± 2.3 | 33.6± 2.6 | 34.5± 2.8 |
| 3200 ppm | 29.8± 2.1 | 30.2 ± 2.4 | 31.1 ± 1.9 | 32.0 ± 2.1 | 32.1± 2.1 | 33.4 ± 2.3 | 34.1± 2.4 |
| | | | | | | | |
| Significant difference : | *: P ≤ 0.05 | ** : P ≤ 0.01 | | Test of Dunnett | | ALC | |
| (HAN260) | | | | | | | BAIS 4 |

| TRAIMING : MOOSE DOES IVELIJIES JEDITIJ UNIT : K REPORT TYPE : Al 104 SEX : MALE | 1.0d.j.b0r1.j | | ALL MALMALS | | | | PAG | PAGE: 3 |
|---|-----------------------------|----------------|-------------|-----------------|------------|----------------|-----------|---------|
| Group Name | Administration week-day14-7 | n week-day18-7 | 22-7 | 267 | 30-7 | 34-7 | 38-7 | |
| Control | 35.4± 2.7 | 37.8± 3.8 | 40.0± 4.3 | 42.9± 4.9 | 44.5± 4.9 | 46.3 ± 4.5 | 47.5± 4.5 | |
| 512 ppm | 35.2± 2.2 | 37.9± 2.5 | 39.4± 3.9 | 42.5± 3.2 | 44.1± 3.3 | 46.1± 3.4 | 47.5± 3.5 | |
| 1280 թթա | 35.1 ± 2.8 | 37.7± 3.4 | 39.4士 4.0 | 42.0± 4.1 | 43.7 ± 4.3 | 44.8+ 4.2 | 46.2± 4.2 | |
| 3200 ppm | 34.8± 2.4 | 37.6± 2.8 | 39.1± 3.3 | 41.4± 4.1 | 43.0± 4.0 | 44.2± 4.3* | 46.2± 4.5 | |
| | | | | | | | | |
| Significant difference ; | *:P≤0.05 | ‡: P ≤ 0.01 | | Test of Dunnett | | | | |
| (HAN260) | 7,777 | | | | | | | BAIS 4 |

| ANIMAL : MOUSE BGD2F1/Cr1j[Crj:BDF1] UNIT : R REPORT TYPE : A1 104 SEX : MALE | [Orj:BDF1] | | ALL ANTWALS | | | | PAGE: 4 |
|---|--|--------------|-------------|-----------------|--------------|----------------|----------------|
| Group Name | Administration week-day 42-7 | week-day46-7 | 2-09 | 547 | 58-7 | 62-7 | L-99 |
| Control | 49.2 | 50.7 ± 3.8 | 51.4± 3.3 | 52.1± 3.1 | 52.1± 3.9 | 52.84 4.1 | 53.3 ± 4.0 |
| 512 ppm | 48.4± 3.5 | 49.9士 3.2 | 49.5± 3.7* | 51.2± 3.3 | 50, 9 🛨 4, 0 | 51.6 ± 4.4 | 52.1 ± 5.6 |
| 1280 ppm | 47.7± 3.9 | 49.3± 3.7 | 49.3± 4.3* | 50,6± 4.5 | 51.1± 4.3 | 52.1± 4.4 | 52.2 ± -4.5 |
| 3200 ppm | 47.6± 3.9 | 48.9± 4.1 | 49.3± 3.9* | 50.9± 3.8 | 50.6± 4.3 | 51.2 ± 5.0 | 51.7± 4.6 |
| | And the second s | | | | | | |
| Significant difference: | *: P ≤ 0.05 | # : P ≤ 0.01 | | Test of Dunnett | | | |
| (HAN260) | | | | | | | BAIS 4 |

| Tough Name Administration week day 76-7 78-7 78-7 82-7 86-7 86-7 90-7 94-7 Control 53.4± 3.8 54.4± 4.0 55.0± 4.6 53.8± 5.9 53.3± 5.9 54.4± 6.2 51.8± 7.0 512 ppm 52.9± 5.9 53.8± 6.2 54.4± 6.6 53.6± 6.7 53.4± 8.4 55.7± 6.7 56.4± 5.1* 1280 ppm 52.9± 5.9 52.9± 6.1 52.9± 6.1 52.8± 6.1 52.5± 7.7 54.0± 6.9 51.9± 8.1 3200 ppm 52.4± 5.3 53.1± 5.3 53.4± 6.8 53.2± 4.8 53.0± 6.0 53.9± 6.4 52.5± 6.2 | ANIMAL : WOUSE BEDZF1/Cr1j[Crj:BDF1] UNIT : R REPORT TYPE : A1 104 SEX : MALE | J[Cr.j:BDF1] | | DOUT WEIGHT CHANGES | (SUMMAKT) | | | PAGE : 5 |
|---|---|-----------------------|---------------|---------------------|-----------------|--------------|------|----------|
| $53.4\pm 3.8 \qquad 54.4\pm 4.0 \qquad 55.0\pm 4.6 \qquad 53.8\pm 5.9 \qquad 53.3\pm 5.9 \qquad 54.4\pm 6.2 \qquad 51.8\pm 5.9 \qquad 53.4\pm 8.4 \qquad 55.7\pm 6.7 \qquad 56.4\pm 5.9 \qquad 53.8\pm 6.1 \qquad 52.8\pm 6.1 \qquad 52.5\pm 7.7 \qquad 54.0\pm 6.9 \qquad 51.9\pm 5.2.4\pm 5.3 \qquad 53.1\pm 5.3 \qquad 53.4\pm 6.8 \qquad 53.2\pm 4.8 \qquad 53.0\pm 6.0 \qquad 53.9\pm 6.4 \qquad 52.5\pm 7.7 \qquad 53.9\pm 6.4 \qquad 52.5\pm 7.7 \qquad 53.9\pm 6.4 \qquad 52.5\pm 7.7 \qquad 53.9\pm 6.4 \qquad 52.5\pm 5.9\pm 5.2 \qquad 53.4\pm 6.8 \qquad 53.2\pm 4.8 \qquad 53.0\pm 6.0 \qquad 53.9\pm 6.4 \qquad 52.5\pm 5.2 \qquad 52.4\pm 5.3 \qquad 53.1\pm 5.3 \qquad 53.4\pm 6.8 \qquad 53.2\pm 4.8 \qquad 53.0\pm 6.0 \qquad 53.9\pm 6.4 \qquad 52.5\pm 5.2 \qquad 52.5$ | Group Name | Administratio 70-7 | on week-day | 78-7 | 82-7 | <i>L</i> -98 | Ł-06 | 94-7 |
| $52.9\pm 5.9 + 5.9 = 53.8\pm 6.2 = 54.4\pm 6.6 = 53.6\pm 6.7 = 53.4\pm 8.4 = 55.7\pm 6.7 = 56.4\pm 5.2$ $52.6\pm 4.7 = 52.9\pm 5.2 = 52.9\pm 6.1 = 52.8\pm 6.1 = 52.5\pm 7.7 = 54.0\pm 6.9 = 51.9\pm 5.2 = 52.4\pm 5.3 = 53.1\pm 5.3 = 53.4\pm 6.8 = 53.2\pm 4.8 = 53.0\pm 6.0 = 53.9\pm 6.4 = 52.5\pm 5.2 $ | Control | 53.4± 3.8 | | 55.0± 4.6 | | | | |
| 52.6 ± 4.7 52.9 ± 5.2 52.9 ± 6.1 52.8 ± 6.1 52.5 ± 7.7 54.0 ± 6.9 51.9 ± 8.4 52.4 ± 5.3 53.1 ± 5.3 53.4 ± 6.8 53.2 ± 4.8 53.0 ± 6.0 53.9 ± 6.4 52.5 ± 4.8 52.5 ± 4.8 53.0 ± 6.0 53.9 ± 6.4 52.5 ± 4.8 52.5 ± 4.8 53.0 ± 6.0 53.9 ± 6.4 52.5 ± 4.8 52.5 ± 4.8 53.0 ± 6.0 | 512 ppm | 52.9生 5.9 | | | | | | |
| 52.4 ± 5.3 53.1 ± 5.3 53.4 ± 6.8 53.2 ± 4.8 53.0 ± 6.0 53.9 ± 6.4 52.5 ± 8.9 10.00 | 1280 ppm | 52.6± 4.7 | | | | | | |
| *: P ≤ 0.05 **: P ≤ 0.01 | 3200 ppm | 52.4± 5.3 | | | | | | |
| *: P ≤ 0.05 **: P ≤ 0.01 | | | 777 | | | | | |
| | Significant difference : | | ** : P ≤ 0.01 | | Test of Dunnett | | | |

| Group Name Administration week -day $102-7$ $104-7$ Control $51.5\pm$ 7.5 $50.5\pm$ 7.9 $48.8\pm$ 8.5 512 ppm $54.9\pm$ 6.1 $55.1\pm$ 6.5* $53.0\pm$ 6.9 L280 ppm $50.4\pm$ 7.9 $49.4\pm$ 9.7 $49.3\pm$ 8.4 3200 ppm $52.5\pm$ 6.3 $52.6\pm$ 7.3 $51.7\pm$ 7.2 Significant difference: $*: P \le 0.05$ $**: P \le 0.01$ Test of Dunnett | UNIT : g REPORT TYPE : A1 104 SEX : MALE | | | | PAGE: 6 |
|---|--|------------------------|-------------------|------------|-----------------|
| $51.5\pm$ 7.5 $50.5\pm$ 7.9 $48.8\pm$ 8.5 $54.9\pm$ 6.1 $55.1\pm$ 6.5* $53.0\pm$ 6.9 $50.4\pm$ 7.9 $49.4\pm$ 9.7 $49.3\pm$ 8.4 $52.5\pm$ 6.3 $52.6\pm$ 7.3 $51.7\pm$ 7.2 $*: P \le 0.05$ **: $P \le 0.01$ | Group Name | Administration 98-7 | week-day 102-7 | 104-7 | |
| 2 ppm 54.9 ± 6.1 $55.1\pm6.5*$ 53.0 ± 6.9 6.9 0 ppm 50.4 ± 7.9 49.4 ± 9.7 49.3 ± 8.4 0 ppm 52.5 ± 6.3 52.6 ± 7.3 51.7 ± 7.2 ificant difference: *:P ≤ 0.05 **:P ≤ 0.01 | Control | 51.5士 7.5 | | | |
| 0 ppm $50.4\pm$ 7.9 $49.4\pm$ 9.7 $49.3\pm$ 8.4 0 ppm $52.5\pm$ 6.3 $52.6\pm$ 7.3 $51.7\pm$ 7.2 ificant difference: *:P \leq 0.05 **:P \leq 0.01 | 512 ppm | 54.9士 6.1 | | | |
| 0 ppm $ 52.5\pm \ 6.3 \qquad 52.6\pm \ 7.3 \qquad 51.7\pm \ 7.2 $ if icant difference ; *:P ≤ 0.05 **:P ≤ 0.01 | 1280 ppm | 50.4± 7.9 | | 49.3 ± 8.4 | |
| ificant difference ; *:P≤0.05 **:P≤0.01 | 3200 ppm | 52.5± 6.3 | | 51.7± 7.2 | |
| ificant difference : *:P≤0.05 **:P≤0.01 | | | | | |
| (HANZ60) | Significant difference: | *: P ≤ 0.05 | *★: P ≤ 0.01 | | Test of Dunnett |
| | (HAN260) | | | | BAIS4 |

TABLE C 4

BODY WEIGHT CHANGES: FEMALE

| STUDY NO. : 0580 ANUMAL : MOUSE BGDZF1/CrljfCrj:BDF1] UNIT : K REPORT TYPE : A1 104 SEX : FEMALE | [Crj:BDF1] | | BODY WEIGHT CHANGES ALL ANIMALS | (SUMMARY) | | | PAGE: 7 |
|--|---------------------|--------------------------------|---------------------------------|-----------------|-----------|----------------|------------|
| Group Name | Administrati 0-0 | Administration week-day 0-0 | 27 | 3-7 | 4-7 | 5-7 | L-9 |
| Control | 19.2± 0.8 | 20.1± 1.0 | 20.3± 1.2 | 20.9± 1.2 | 21.3± 1.2 | 22.1± 1.3 | 22.5± 1.3 |
| 512 ppm | 19.2± 0.8 | 20.1± 1.0 | 20.5 ± 1.0 | 20.9土 1.0 | 21.3± 1.1 | 22.1 ± 1.2 | 22.3± 1.3 |
| 1280 ppm | 19.2± 0.8 | 19.8士 1.0 | 20.2 ± 1.2 | 20.9± 1.4 | 21.2± 1.4 | 22.0 ± 1.4 | 22.4± 1.4 |
| 3200 ppm | 19.2 = 0.8 | 19.7± 1.1 | 20.2 ± 1.1 | 20.6± 1.1 | 21.2± 1.3 | 21.9 ± 1.3 | 22.4 ± 1.5 |
| | | | | | | | |
| Significant difference : | *:P≤0.05 | ** : P ≤ 0.01 | | Test of Dunnett | | | |
| (HAN260) | | | | | | | BAIS 4 |

| Group Name | Administration wook-day | web-day | | | | | . JAKI |
|--------------------------|-------------------------|--------------|-----------|-----------------|--------------|----------------|---------------|
| | L-L | 7-8 | L-6 | 10-7 | 11-7 | 12-7 | 13-7 |
| Control | 22.7± 1.2 | 23.6± 1.5 | 24.0± 1.7 | 24.2± 1.9 | 24.7 ± 1.9 | 24.8± 2.1 | 25.8 ± 2.3 |
| 512 ppm | 23.0 ± 1.5 | 23.7± 1.5 | 24.2± 1.6 | 24.7± 1.9 | 24.8 ± 2.2 | 25.1± 2.3 | 25.8± 2.2 |
| 1280 րրա | 22.8± 1.7 | 23.2± 1.6 | 23.6± 1.9 | 24.0± 1.8 | 24.0± 2.0 | 24.6 ± 2.1 | 25.1± 2.2 |
| 3200 ppm | 22.8± 1.5 | 23.6± 1.5 | 23.7± 1.5 | 24.1± 1.8 | 24.2± 1.9 | 24.7 ± 1.7 | 25.3± 1.9 |
| | | | | | | | |
| Significant difference ; | *: P ≤ 0.05 | ‡ : P ≤ 0.01 | | Test of Dunnett | | | |

| STUDY NO. : 0580 ANIMAL : MOUSE BGD2F1/Crlj[Crj:BDF1] UNIT : K REPORT TYPE : A1 104 SEX : FEMALE | [Crj:BDF1] | | BODY WEIGHT CHANGES ALL ANIMALS | (SUMMARY) | | | PAGE: 9 |
|--|----------------------|-----------------------------|---------------------------------|-----------------|-----------|-----------|------------|
| Group Name | Administrati 14-7 | Administration week-day14-7 | 227 | 26-7 | 30-7 | 34~7 | 38-7 |
| Control | 26.3± 2.4 | 27.5± 2.9 | 29.0± 3.4 | 31.2± 3.6 | 32.0± 4.1 | 33.4± 4.4 | 34.7± 4.3 |
| 512 ppm | 26.2± 2.3 | 27.9土 2.8 | 29.2 ± 3.0 | 31.4 ± 3.9 | 32.7± 3.9 | 33.9士 4.3 | 35.3 ± 4.4 |
| 1280 րրա | 25.6± 2.3 | 27.0± 2.9 | 28.7 ± 3.5 | 30.5± 3.8 | 31.7± 4.3 | 32.6± 4.3 | 34.4± 4.8 |
| 3200 ppm | 25.8± 2.3 | 27.2± 2.9 | 28.9± 3.6 | 30.3± 3.6 | 31.4± 3.8 | 32.4± 4.0 | 34.6± 4.8 |
| | | | | | | | |
| Significant difference : | *: P ≤ 0.05 | ** : P ≤ 0.0[| | Test of Dunnett | | | |
| (HAN260) | | | | | | | BAIS 4 |

| STOPL NO. : 0.000 ANIMAL : MOUSE B6D2F1/CrljfCrj:BDF1] UNIT : R REPORT TYPE : AI 104 SEX : FEMALE | [Crj:BDF1] | | BODY WEIGHT CHANGES ALL ANIMALS | (SUMMARY) | | | PAGE: 10 |
|---|------------------------------|---------------|---------------------------------|-----------------|----------------|---------------|-----------|
| Group Name | Administration week-day 42-7 | week~day | 2-05 | 54-7 | 28-7 | <i>L</i> -29 | L-99 |
| Control | 35.9 ± 4.6 | 37.0± 5.0 | 37.4± 5.4 | 39.0± 5.5 | 38.8± 5.6 | 39.1 ± 5.6 | 39.7± 5.2 |
| 512 ppm | 36.8± 4.4 | 37.7 ± 4.9 | 38.8士 5.1 | 40.1 ± 5.1 | 39.8± 5.5 | 40.0 ± 5.7 | 41.1± 5.7 |
| 1280 ppm | 35.4± 4.8 | 36.3± 5.0 | 36.9± 4.8 | 38.6± 5.0 | 38.6± 5.4 | 38.9± 5.6 | 39.5± 5.4 |
| 3200 ррт | 36.3± 3.9 | 37.6 ± 4.1 | 38.1± 4.2 | 39.5士 4.1 | 39.2 ± 4.5 | 39.8± 4.2 | 40.6± 4.2 |
| | | | | | | | |
| Significant difference: | *: P ≤ 0.05 | . P ≤ 0.01 | | Test of Dunnett | | | |
| (HAN260) | | | | | | | BAIS 4 |

| Group Name Administration week-day. | ANIMAL : MOUSE B6D2F1/Cr1jfCrj:BDF1] UNIT : R REPORT TYPE : A1 104 SEX : FEMALE | [Cr.j:BDF1] | | ALL ANEWALS | | | | PAGE: 11 |
|--|---|----------------------|---------------------|-------------|-----------------|-----------|---|-----------------------|
| 39. $5\pm$ 5.7 40. $0\pm$ 6.5 41. $3\pm$ 6.1 40. $1\pm$ 6.6 39. $8\pm$ 6.2 39. $9\pm$ 7.3 39. $0\pm$ 41. $3\pm$ 6.0 42. $3\pm$ 6.1 42. \pm 6.0 40. \pm 6.0 6 40. \pm | Sroup Name | Administratio 707 | on week-day 74-7 | 1-87 | L-78 | L-98 | 2-06 | <i>L</i> - F 6 |
| 41. $3\pm$ 6. 0 41. $7\pm$ 5. 9 42. $3\pm$ 6. 1 42. $5\pm$ 6. 0 42. 8± 5. 8 43. \pm 5. 8 41. $7\pm$ 6. 0 40. 8± 5. 3 41. \pm 6. 0 40. 8± 5. 3 41. \pm 6. 0 40. 8± 6. 0 40. | Control | 39.5士 5.7 | | 41.3± 6.1 | | | | 39.0± 7.6 |
| $39.7\pm$ 5.5 $40.2\pm$ 5.2 $40.6\pm$ 5.8 $39.9\pm$ 6.0 $40.8\pm$ 5.3 $41.3\pm$ 6.0 $41.4\pm$ $40.6\pm$ 4.3 $41.2\pm$ 4.7 $40.8\pm$ 4.8 $40.7\pm$ 5.1 $41.0\pm$ 5.3 $40.3\pm$ $40.3\pm$ $8:P \le 0.05$ **: $P \le 0.05$ | 512 ppm | 41.3 ± 6.0 | | | | | | |
| 40.6 ± 4.1 40.6 ± 4.3 41.2 ± 4.7 40.8 ± 4.8 40.7 ± 5.1 41.0 ± 5.3 40.3 ± 8.7 8.7 1.0 | 1280 րրտ | 39.7± 5.5 | | | | | | |
| *: P ≤ 0.05 ★: P ≤ 0.01 | 3200 ppm | 40.6± 4.1 | | 41.2± 4.7 | 40.8± 4.8 | 40.7± 5.1 | | |
| *: P ≤ 0.05 **: P ≤ 0.01 | | | | | | | AND CONTRACTOR OF THE PARTY OF | |
| | Significant difference : | *: P ≤ 0.05 | | | Test of Dunnett | | | |
| | | | | | | | | |

| ANIMAL : MOUSE B6DZFI/Crlj[Crj:BDF1] UNIT : R REPORT TYPE : AI 104 SEX : FEMALE | [Cr j:BDF1] | | ALL ANEMALS | PAGE: 12 |
|---|--------------------------------------|-------------------|---------------|----------------|
| Group Name | Administration week-day_ 98-7 102 | week-day 102-7 | 104-7 | |
| Control | 40.8 ± 5.9 | 40.5± 6.1 | 39.6± 6.1 | |
| 512 ppm | 41.6 ± 5.6 | 41.3± 5.9 | 39.1 ± 5.6 | |
| 1280 pm | 41.0± 5.2 | 41.5± 5.1 | 40.6士 4.8 | |
| 3200 ppm | 40.1± 6.0 | 38.8± 7.2 | 38.1± 7.0 | |
| | | | | |
| Significant difference : | *: P \le 0.05 | #:P≤0.01 | | Test of Dumett |
| (HAN260) | | | | BAIS 4 |

TABLE D 1

FOOD CONSUMPTION CHANGES AND

SURVIVAL ANIMAL NUMBERS: MALE

STUDY NO. : 0580
ANIMAL : MOUSE BEDZF1/Crlj[Crj:BDF1]
UNIT : g
REPORT TYPE : Al 104
SEX : MALE

| | Ş | Control | | 512 ppm | | | 1280 ppm | | | 3200 ppm | |
|----------|----------|-------------------|----------|---------------|-------------------|----------|---------------|-------------------|----------|---------------|-------------------|
| Week-Day | Av. FC. | No. of Surviv. | Av. FC. | % of cont. | No. of Surviv. | Av. FC. | % of cont. | No. of Surviv. | Av. FC. | % of cont. | No. of Surviv. |
| on Study | ~ | <20> | | <20> | | | <20> | | | <20> | |
| 11 | 4.2 (50) | | 4.1 (50) | 86 | 50/50 | 1 | 95 | 50/50 | 4.0 (50) | 95 | 50/50 |
| 27 | 3.8 (50) | | | 105 | 50/50 | 3.8 (50) | 100 | 50/50 | 4.0 (50) | 105 | 50/50 |
| 3-7 | 3.9 (50) | | 3.9 (50) | 100 | 20/20 | | 103 | 50/50 | 4.1 (50) | 105 | 50/50 |
| 4-7 | 4.0 (50) | | 3.9 (50) | 86 | 50/50 | 4.0 (50) | 100 | 50/50 | 3.9 (50) | 86 | 50/50 |
| 22 | 4.0 (50) | | 3.9 (50) | 86 | 20/20 | | 100 | 50/50 | 4.1 (50) | 103 | 50/50 |
| 2-9 | 3.9 (50) | | 4.0 (50) | 103 | 20/20 | | 100 | 20/20 | 4.1 (50) | 105 | 20/20 |
| 22 | 4.0 (50) | | 4.0 (50) | 100 | 50/50 | 0 | 100 | 50/50 | Ξ | 103 | 50/50 |
| 2-8 | 4.0 (50) | | 4.0 (50) | 100 | 50/50 | 3.9 (50) | 86 | 20/20 | 3.9 (50) | 86 | 20/20 |
| 2-6 | 4.0 (50) | | 4.1 (50) | 103 | 20/20 | 4.2 (50) | 105 | 50/50 | 4.1 (49) | 103 | 49/50 |
| 10-7 | 4.0 (50) | | 4.0 (50) | 100 | 20/20 | 4.1 (50) | 103 | 50/50 | 4.2 (49) | 105 | 49/50 |
| 11-7 | 4.1 (50) | | 3,9 (50) | 95 | 50/50 | 3.9 (50) | 95 | 50/50 | 4.1 (49) | 100 | 49/50 |
| 127 | 4.1 (50) | | 4.3 (50) | 105 | 20/20 | 4.3 (50) | 105 | 50/50 | 4.4 (49) | 107 | 49/50 |
| 137 | 4.1 (50) | | 4.3 (50) | 105 | 20/20 | 4.1 (50) | 100 | 20/20 | 4.2 (49) | 102 | 49/50 |
| 14-7 | 3.8 (50) | | 4.1 (50) | 108 | 50/50 | 4.0 (50) | 105 | 50/50 | _ | 103 | 49/50 |
| 18-7 | 4.4 (50) | | 4.3 (50) | 86 | 20/20 | 2 | 102 | 20/20 | _ | 105 | 49/50 |
| 22-7 | | | 4.1 (50) | 95 | 50/50 | _ | 98 | 50/50 | 4. (49) | 92 | 49/50 |
| 26-7 | 4.5 (50) | | 4.5 (49) | 100 | 49/50 | 60 | 96 | 50/50 | 4.3 (49) | 96 | 49/50 |
| 2-0 | | | 4.6 (49) | 100 | 49/50 | | 100 | 50/50 | 4.6 (49) | 100 | 49/50 |
| 34-7 | | | 4.5 (49) | 105 | 49/50 | _ | 102 | 20/20 | 4.4 (49) | 102 | 49/50 |
| 38-7 | _ | | 4.4 (49) | 105 | 49/20 | | 100 | 50/50 | 4.4 (49) | 105 | 49/50 |
| 42-7 | | | 4.6 (49) | 100 | 49/50 | _ | 102 | 50/50 | 4.8 (48) | 104 | 48/50 |
| 46-7 | 4.5 (48) | 48/50 | | 100 | 49/50 | D. | 100 | 20/20 | 4.3 (48) | 96 | 48/50 |
| 20-2 | 4.7 (48) | | | 96 | 49/20 | က | 91 | 20/20 | 4.6 (48) | 86 | 48/50 |
| 54-7 | 5.0 (48) | | 5.0 (49) | 100 | 49/50 | - | 96 | 20/20 | 4.9 (47) | 86 | 47/50 |
| 2-2 | 4.6 (47) | | | 100 | 49/50 | 8 | 104 | 49/20 | | 100 | 47/50 |
| 22 | _ | | | 96 | 49/20 | - | 104 | 48/50 | | 100 | 47/50 |
| 29 | ص ص | | | 100 | 48/20 | | 100 | 47/50 | _ | 106 | 47/50 |
| 20 | 5.0 (43) | | 5.0 (46) | 100 | 48/20 | _ | 100 | 46/50 | 5.0 (46) | 100 | 47/50 |
| 74-7 | 4.9 (43) | | _ | 100 | 46/50 | _ | 102 | 45/50 | _ | 100 | 47/50 |
| 78-7 | 5.4 (43) | | | 94 | 45/50 | | 93 | 45/50 | 5.3 (47) | 86 | 47/50 |
| 82-7 | 5.0 (43) | | 5.0 (44) | 100 | 45/50 | 4.8 (44) | 96 | 44/50 | 5.0 (44) | 100 | 45/50 |
| 2-98 | 4.8 (40) | 40/50 | 4.8 (44) | 100 | 45/50 | | 102 | 43/50 | _ | 106 | 45/50 |
| 2-06 | 9 | | | 92 | 43/50 | 5.4 (41) | 96 | 41/50 | 5.6 (41) | 100 | 42/50 |
| 94-7 | 5.1 (37) | 37/20 | 5.0 (40) | 86 | 40/20 | | 90 | 40/20 | 4.6 (38) | 06 | 40/20 |
| 7-86 | 4.9 (34) | • | 5.0 (37) | 102 | 38/20 | _ | 94 | 38/20 | 4.7 (35) | 96 | 38/20 |
| 7-20. | 5.3 (33) | • • | 5.4 (35) | 102 | 35/50 | | 86 | 38/20 | 5.3 (36) | 100 | 36/20 |
| 7-70 | (4.2) | 99 /50 | 1 7 (24) | 100 | 04/60 | E 1 (9E) | 100 | 00/00 | (VC) 0 H | 001 | (L) |

BAIS 4

(BI0040)

TABLE D 2

FOOD CONSUMPTION CHANGES AND

SURVIVAL ANIMAL NUMBERS: FEMALE

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STUDY NO. : 0580
ANIMAL : MOUSE BED2F1/Crij[Crij:BDF1]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

| | 5 | Contro] | | 512 ppm | | | 1280 ppm | | | 3200 ppm | | |
|----------|-----------|-------------------|----------|---------------|-------------------|----------|---------------|-------------------|-----------|----------|------------------|---|
| Week-Day | Av. FC. | No. of Surviv. | Av. FC. | % of cont. | No. of Surviv. | Av. FC. | % of cont. | No. of Surviv. | Av. FC. | % of | No. of Surviv | |
| on Study | ~ | 20> | | <20> | | | <20> | | | (20) | | |
| 1-7 | 3.8 (50) | 20/20 | 3.8 (50) | 100 | 20/20 | _ | 76 | 50/50 | 3.8 (50) | 100 | 50/50 | *************************************** |
| 2-7 | 2 | 20/20 | _ | 103 | 20/20 | 3.4 (50) | 26 | 20/20 | 3.5 (50) | 100 | 50/50 | |
| 3-7 | 3.6 (50) | 20/20 | 3.6 (50) | 100 | 20/20 | _ | 103 | 20/20 | 3.5 (50) | 26 | 50/50 | |
| 4-7 | 4 | 20/20 | 2 | 103 | 20/20 | 4 | 100 | 50/50 | 3.4 (50) | 100 | 50/50 | |
| 2-2 | 9 | 20/20 | 3.5 (50) | 26 | 50/50 | ŝ | 67 | 50/50 | 3.5 (50) | 97 | 50/50 | |
| 2-9 | ~ | 20/20 | 3.8 (50) | 103 | 20/20 | ·~ | 100 | 20/20 | _ | 100 | 50/50 | |
| 2-2 | n. | 20/20 | 3.7 (50) | 106 | 20/20 | ~ | 106 | 20/20 | _ | 103 | 50/50 | |
| 2-8 | 3.8 (50) | 20/20 | 3.8 (50) | 100 | 20/20 | 8 | 100 | 20/20 | 3.9 (50) | 103 | 50/50 | |
| 2-6 | 3, 9 (50) | 20/20 | 4.1 (50) | 105 | 20/20 | 0 | 103 | 20/20 | 3.8 (50) | 26 | 50/50 | |
| 10-7 | 3.7 (50) | 20/20 | 4.0 (50) | 108 | 20/20 | 20 | 103 | 20/20 | 3.8 (50) | 103 | 50/50 | |
| 11-7 | 3.9 (50) | 20/20 | 3.9 (49) | 100 | 20/20 | ∞ | 26 | 20/20 | 3.8 (50) | 26 | 50/50 | |
| 12-7 | 4.0 (50) | 20/20 | 4.1 (50) | 103 | 50/50 | _ | 103 | 20/20 | 4.0 (50) | 100 | 50/20 | |
| 13-7 | 4.1 (50) | 20/20 | 4.1 (50) | 100 | 50/50 | 4.3 (50) | 105 | 20/20 | 4.0 (50) | 86 | 50/50 | |
| 14-7 | 4.0 (50) | 20/20 | 4.0 (50) | 100 | 50/50 | 4.0 (50) | 100 | 20/20 | 3.8 (50) | 95 | 50/50 | |
| 18-7 | 4.3 (50) | 50/50 | 4.3 (50) | 100 | 50/50 | 2 | 105 | 20/20 | 4.3 (50) | 001 | 50/50 | |
| 227 | 4.4 (50) | 20/20 | 4.5 (50) | 102 | 20/20 | _ | 105 | 20/20 | 4.5 (49) | 102 | 49/50 | |
| 2-92 | 4.6 (50) | 20/20 | 4.5 (50) | 88 | 20/20 | _ | 86 | 20/20 | _ | 93 | 49/50 | |
| 30-7 | _ | 20/20 | 4.9 (50) | 100 | 20/20 | 5.1 (50) | 104 | 20/20 | _ | 86 | 49/50 | |
| 34-7 | 4.5 (49) | 50/50 | 4.8 (50) | 107 | 20/20 | _ | 109 | 20/20 | 4.3 (49) | 96 | 49/50 | |
| 38-7 | ص ص | 20/20 | 4.3 (50) | 96 | 20/20 | 9 | 102 | 20/20 | 4.7 (49) | 104 | 49/50 | |
| 42-7 | 5.2 (50) | 20/20 | 5.4 (50) | 104 | 20/20 | ກ | 102 | 20/20 | 5.2 (48) | 100 | 48/50 | |
| 46-7 | _ | 20/20 | 4.7 (50) | 86 | 20/20 | 9 | 96 | 20/20 | 4.9 (48) | 102 | 48/50 | |
| 2-09 | 4.8 (49) | 20/20 | 4.8 (49) | 100 | 20/20 | 9 | 96 | 20/20 | 4.8 (46) | 100 | 48/50 | |
| 54-7 | က | 20/20 | 5.4 (50) | 102 | 20/20 | 5.5 (50) | 104 | 20/20 | 5.3 (48) | 100 | 48/50 | |
| 58-7 | 5, 3 (50) | 50/50 | 5.1 (49) | 96 | 49/50 | 0 | 94 | 20/20 | 4.8 (48) | 91 | 48/50 | |
| 627 | _ | 20/20 | 4.7 (48) | 100 | 48/50 | 4.7 (49) | 100 | 49/50 | _ | 111 | 48/50 | |
| 299 | 5.2 (48) | 49/50 | 5.4 (47) | 104 | 47/50 | ~ | 100 | 49/50 | _ | 102 | 48/50 | |
| 7-07 | 4.9 (48) | 49/50 | 4.8 (47) | 86 | 47/50 | ∞ | 86 | 49/50 | 5.2 (47) | 106 | 47/50 | |
| 74-7 | 5.2 (48) | 49/50 | 5.5 (47) | 106 | 47/50 | 2 | 100 | 48/50 | _ | 100 | 47/50 | |
| 78-7 | 5.2 (47) | 48/50 | 5.6 (45) | 108 | 46/50 | 4 | 104 | 47/50 | _ | 102 | 46/50 | |
| 827 | 5.2 (47) | 48/50 | 5.8 (44) | 112 | 44/50 | Ċ: | 94 | 47/50 | | 100 | 44/50 | |
| 2-98 | 1.5 (46) | 47/50 | 5.2 (42) | 116 | 43/50 | œ | 107 | 44/50 | 5.1 (40) | 113 | 41/50 | |
| 2-06 | 5.3 (44) | 45/50 | ,_ | 106 | 41/50 | co | 104 | 10/20 | | 109 | 38/50 | |
| 94-7 | 4.9 (39) | 41/50 | - | 104 | 39/20 | ro - | 112 | 36/20 | - | 110 | 36/50 | |
| 98-7 | 5.3 (36) | 36/20 | 5.3 (34) | 100 | 34/50 | 8 | 100 | 33/20 | 5.5 (34) | 104 | 34/50 | |
| 102-7 | _ | 34/50 | 6.2 (28) | 111 | 29/20 | 5.9 (28) | 105 | 30/20 | 6.0 (29) | 107 | 30/50 | |
| 104-7 | 4.6 (32) | 34/50 | 4.8 (27) | 104 | 28/50 | 4 | 117 | 28/50 | 5, 4 (28) | 117 | 30/50 | |

BAIS 4

(BI0040)

TABLE D 3

FOOD CONSUMPTION CHANGES: MALE

| SEA . MALE Groun Name | 1 deministration | deninietration wook-day(offortivo) | | | | | |
|--------------------------|------------------|------------------------------------|-----------|-----------------|---------------|-------------|------------------|
| | 1-7 (4) | 2-7(4) | 3~7 (4) | 4-7(4) | 5-7 (4) | 6-7 (4) | 7-7(4) |
| Control | 4. 2± 0.5 | 3.8± 0.5 | 3.9± 0.5 | 4.0 ± 0.5 | 4.0± 0.5 | 3.9± 0.4 | 4.0 ± 0.5 |
| 512 ppm | 4.1 = 0.4 | 4.0 ± 0.5 | 3.9 ± 0.5 | 3.9 ± 0.6 | 3.9 ± 0.5 | 4.0 ± 0.5 | 4.0 ± 0.6 |
| 1280 թթա | 4.0± 0.5 | 3.8± 0.6 | 4.0± 0.5 | 4.0 ± 0.5 | 4.0± 0.5 | 3.9± 0.4 | 4.0± 0.6 |
| 3200 ppm | 4.0 + 0.7 | 4.0 ± 0.7 | 4.1 ± 0.6 | 3.9± 0.7 | 4.1± 0.6 | 4.1± 0.6 | 4. 1± 0.6 |
| | | | | | | | |
| Significant difference ; | * : P \le 0.05 * | # : P ≤ 0.01 | | Test of Dunnett | | | |

| SEX : MALE | A Line | N | A CONTRACTOR OF THE CONTRACTOR | | | | |
|--------------------------|----------------|---------------------------------|--|-----------------|-----------|-----------|-----------|
| roup round | 8-7 (4) | ween day (ellective) 9-7 (4) | 10-7(4) | 11-7(4) | 12-7 (4) | 13-7 (4) | 14-7 (4) |
| Control | 4.0± 0.4 | 4.0 = 0.4 | 4.0 ± 0.6 | 4.1± 0.6 | 4.1+ 0.4 | 4.1 ± 0.4 | 3.8 ± 0.6 |
| 512 ppm | 4.0-1-0.5 | 4. 1± 0.4 | 4.0 ± 0.6 | 3.9± 0.7 | 4.3 ± 0.4 | 4.3 ± 0.5 | 4.1 ± 0.6 |
| 1280 ppm | 3.9± 0.7 | 4.2 ± 0.4 | 4.1± 0.4 | 3.9± 0.5 | 4.3± 0.5 | 4.1 0.5 | 4.0± 0.6 |
| 3200 ppm | 3.9± 0.8 | 4.1± 0.5 | 4. 2± 0.6 | 4.1± 0.6 | 4.4± 0.6 | 4.2± 0.4 | 3.9± 0.7 |
| | | | | | | | |
| Significant difference ; | * : P ≤ 0.05 * | . P ≤ 0.01 | | Test of Dunnett | | | |

| STUDY NO. : 0580 ANIMAL : MOUSE DEDZF1/Cr1j[Crj:BDF1] UNIT : R REPORT TYPE : A1 104 SEX : MALE | [Cr.j:BDF1] | 75. IA | FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS | JES (SUMMARY) | | | PAGE | PAGE: 3 |
|--|---------------------------|------------------------------------|--|-----------------|--|-----------|----------|---------|
| Group Name | Administration 18-7(4) | Administration week-day(effective) | 26-7 (4) | 30-7(4) | 34-7(4) | 38-7(4) | 42-7 (4) | |
| Control | 4.4± 0.5 | 4.3± 0.7 | 4.5± 0.6 | 4.6士 0.5 | 4.3± 0.8 | 4.2± 0.7 | 4.6± 0.4 | |
| 512 ppm | 4.3 ± 0.4 | 4.1 | 4.5± 0.5 | 4.6 ± 0.6 | 4.5 - 0.5 | 4.4 ± 0.5 | 4.6± 0.5 | |
| 1280 ppm | 4.5± 0.5 | 4.1± 0.7 | 4.3± 0.5 | 4.6 = 0.4 | 4.4± 0.7 | 4.2± 0.8 | 4.7± 0.5 | |
| 3200 ppm | 4. 6± 0.4 | 4.1 ± 0.7 | 4.3± 0.6 | 4.6 ± 0.5 | 4.4± 0.8 | 4.4 + 0.7 | 4.8± 0.5 | |
| | | | | | | | | |
| Significant difference ; | *: P ≤ 0.05 | ‡ : P ≤ 0.01 | | Test of Dunnett | Tangang and the same of the sa | | | |

| ONII REPORT TYPE : AI 104 SEX : MALE | | | | | | | PAGE : | 4 |
|--|---------------------------|--|-------------|-----------------|-----------|---------------|-------------|---|
| Group Name | Administration 46-7(4) | Administration week-day(effective)_46-7(4) 50-7(4) | 54-7(4) | 58-7(4) | 62-7(4) | 66-7(4) | 70-7 (4) | |
| Control | 4.5 ± 0.7 | 4.7 ± 0.6 | 5.0± 0.7 | 4.6± 0.9 | 4.7± 1.0 | 4.9士 0.7 | 5.0± 1.0 | |
| 512 ppm | 4.5 ± 0.5 | 4.5 ± 0.9 | 5.0 ± 0.7 | 4.6 ± 0.7 | 4.5 - 1.0 | 4.9 ± 0.9 | 5.0 1 0.6 | |
| 1280 ppm | 4.5± 0.6 | 4.3± 0.9* | 4.8 + 0.9 | 4.8± 0.7 | 4.9 ± 0.8 | 4.9+ 0.8 | 5.0 ± 0.9 | |
| 3200 ррш | 4.3 ± 0.8 | 4.6± 0.8 | 4.9十 0.5 | 4.6± 1.0 | 4.7 ± 1.1 | 5.2 ± 1.0 | 5.0 ± 0.8 | |
| | | | | | | | | |
| Significant difference; ★:P≦0.05 | | ‡ : P ≤ 0.01 | | Test of Dunnett | | | | |
| | | | | | | | | |

PAGE: 5 4.9 ± 1.4 5.0 ± 0.9 4.6 ± 1.1 4.7 ± 1.2 98-7(4) 5.1 ± 1.0 5.0 ± 1.0 4.6 ± 1.2 4.6 ± 1.3 94-7(4) 5.6 ± 0.9 5.3± 1.0 5.4 ± 1.1 5.6 ± 1.1 90-7(4) 4.8 ± 1.4 4.8± 1.2 4.9 ± 1.0 5.1 ± 1.3 86-7(4) FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS 5.0± 1.0 4.8 ± 1.0 5.0 ± 1.1 5.0 ± 1.3 82-7(4) 0.8 5.4 ± 0.7 5.0 ± 0.8 5.3 ± 0.9 5.1± 4.9 ± 0.7 4.9 ± 0.8 5.0 ± 1.1 4.9 ± 1.1 STUDY NO. : 0580
ANIMAL : MOUSE BEDZF1/Cr1j[Crj:BDF1]
UNIT : R
REPORT TYPE : A1 104
SEX : MALE 512 ppm 1280 ррш 3200 ppm Control Group Name

Test of Dunnett

★: P ≤ 0.01

Significant difference : $*:P \le 0.05$

(HAN260)

PAGE: 6 FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS 4.7± 1.6 4.7 ± 1.5 5.1 ± 1.3 5.0 ± 1.2 5.3 ± 1.2 5.4 ± 1.2 5.2 ± 1.2 5.3 ± 1.4 STUDY NO. : 0580
ANIMAL : MOUSE BGDZF1/Cr1j[Crj:BDF1]
UNIT : R
REPORT TYPE : A1 104
SEX : MALE 512 ppm 1280 ppm 3200 ppm Control Group Name

Test of Dunnett

★: P ≤ 0.01

Significant difference : $*:P \leq 0.05$

(HAN260)

TABLE D 4

FOOD CONSUMPTION CHANGES: FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS STUDY NO.: 0580
ANIMAL : MOUSE BGDZF1/Cr1j[Crj:BDF1]
UNIT : K
REPORT TYPE : A1 104
SEX : FEMALE

PAGE: 7

| Group Name | Administration | Administration week day (effective) | | | | | |
|--------------------------|----------------|-------------------------------------|-----------|-----------------|-------------|-------------|-----------|
| | 1-7 (4) | 2-7(4) | 3-7(4) | 4-7(4) | 5-7(4) | 6-7 (4) | 7-7 (4) |
| Control | 3.8± 0.6 | 3.5± 0.5 | 3.6± 0.6 | 3.4± 0.6 | 3.6± 0.6 | 3.7 ± 0.6 | 3.5± 0.5 |
| 512 ppm | 3.8 ± 0.6 | 3.6土 0.5 | 3.6 4 0.6 | 3.5 - 0.5 | 3.5± 0.4 | 3.8 ± 0.5 | 3.7 ± 0.6 |
| 1280 ppm | 3.7± 0.5 | 3.4± 0.6 | 3.7 ± 0.6 | 3.4 ± 0.5 | 3.5± 0.6 | 3.7± 0.5 | 3.7 ± 0.5 |
| 3200 ppm | 3.8± 0.6 | 3.5± 0.6 | 3.5± 0.6 | 3.4± 0.5 | 3.5 ± 0.4 | 3.7 ± 0.5 | 3.6 + 0.5 |
| | | | | | | | |
| Significant difference ; | *: P ≤ 0.05 | * : P & 0.01 | | Test of Dunnett | | | |

| STUDY NO. : 0580 ANIMAL : MOUSE BGDZP1/Cr1j[Crj:BDF1] UNIT : R REPORT TYPE : A1 104 SEX : FEMALE | j(Crj:BDF1] | FOA | FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS | SS (SUMMARY) | | | | PAGE : |
|--|--------------------------|--|--|--------------|-----------|-------------|-----------|--------|
| Group Name | Administration 8-7(4) | Administration week-day(effective) 8-7(4) | 10-7(4) | 11-7(4) | 12-7 (4) | 13-7 (4) | 14-7(4) | |
| Control. | 3.8± 0.7 | 3.9 ± 0.6 | 3.7 ± 0.7 | 3.9± 0.6 | 4.0 ± 0.6 | 4.1± 0.7 | 4.0 ± 0.8 | |
| 512 ppm | 3,8 ± 0,5 | 4.1 ± 0.5 | 4.0 ± 0.6 | 3.94 0.6 | 4.1 ± 0.7 | 4.1 ± 0.7 | 4.0 ± 0.6 | |
| 1280 թյա | 3.8± 0.7 | 4.0 ± 0.7 | 3.8 ± 0.6 | 3.8± 0.7 | 4.1± 0.8 | 4.3 1.0 | 4.0 ± 0.9 | |
| 3200 ppm | 3.9± 0.5 | 3.8± 0.4 | 3.8± 0.6 | 3.8± 0.5 | 4.0 ± 0.6 | 4.0 ± 0.6 | 3.8 ± 0.6 | |
| | | | | | | | | |

Test of Dunnett

| STUDY NO. : 0580 ANIMAL : MOUSE BGDZF1/Cr1jfCrj:BDF1] UNIT : R REPORT TYPE : A1 104 SEX : FEMALE | Cr.j:BDF1.] | F00 ALI | FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS | ES (SUMMARY) | | | PAGE: |
|--|---------------------------|------------------------------------|--|-----------------|-----------|---------------|----------|
| Group Name | Administration 18-7(4) | Administration week-day(effective) | 26-7 (4) | 30-7(4) | 34-7 (4) | 38-7 (4) | |
| Control | 4.3± 0.7 | 4.4± 1.0 | 4.64 1.0 | 4.9 ± 0.9 | 4.5± 1.0 | 4, 5 ± L. I | 5.2± 1.0 |
| 512 ppm | 4.31 0.7 | 4.5 ± 0.7 | 4.5± 1.0 | 4.9± 1.0 | 4.8± 1.0 | 4.3± 0.9 | 5.4± 1.0 |
| 1280 ppm | 4.5± 1.0 | 4.6± 1.1 | 4.5± 1.2 | 5.1± 1.1 | 4.9 + 1.2 | 4.6± 1.3 | 5.3+ 1.2 |
| 3200 ppm | 4.3± 0.9 | 4.5± 0.9 | 4.3 ± 0.8 | 4.8± 0.9 | 4.3± 0.8 | 4.7 ± 1.1 | 5.2± 1.1 |
| | | | | | | | |
| Significant difference ; | *: P ≤ 0.05 | **: P ≤ 0.0[| ************************************** | Test of Dunnett | | | |

| STUDY NO.: 0580 ANIMAL: MOUSE BEDZFL/CrljfCrj:BDF1] UNIT: R REPORT TYPE: A1 104 SEX: FEMALE | Cr.j:BDF1] | FOG | FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS | ES (SUMMARY) | | | PAGE: 10 |
|---|---------------------------|------------------------------------|--|-----------------|--|-------------|-----------|
| Group Name | Administration 46-7(4) | Administration week-day(effective) | 54-7(4) | 58-7(4) | 62-7(4) | 66-7(4) | 70-7 (4) |
| Control | 4.8± 1.2 | 4.8± 1.2 | 5.3士 1.2 | 5.3土 1.5 | 4.7± 1.2 | 5.2± 1.1 | 4.9+ 1.3 |
| 512 ppm | 4.7 ± 1.1 | 4.8 ± 1.0 | 5.4± 0.9 | 5.1 ± 1.3 | 4.7 - 1.0 | 5.4生 1.1 | 4.8± 1.3 |
| 1280 ppm | 4.6± 1.2 | 4.6± 1.3 | 5.5 = 1.3 | 5.0+ 1.4 | 4.7 ± 1.3 | 5.2 \pm 1.2 | 4.8 + 1.4 |
| 3200 ppm | 4.9± 1.1 | 4.8± 1.0 | 5.3± 1.0 | 4.8± 1.3 | 5.2 ± 1.0 | 5.3± 1.1 | 5.2± 1.1 |
| | | | | | | | |
| Significant difference : | * : P ≤ 0.05 | * : P ≤ 0.01 | | Test of Dunnett | | | |
| (HAN260) | | | AND | | A STORE OF THE STO | | BAIS 4 |

| REPORT TYPE : A1 104 SEX : FEMALE | | | | | | | PAGE: 11 |
|--------------------------------------|------------------------|------------------------------------|-----------|----------|---------------|---------------|---------------|
| | Administration 74-7(4) | Administration week-day(effective) | 82-7(4) | 86-7(4) | 90-7 (4) | 94-7 (4) | 98-7(4) |
| | 5.2± 1.4 | 5.2+ 1.2 | 5.2± 1.3 | 4.5± 1.6 | 5.3土 1.5 | 4.9± 1.8 | 5.3± 1.5 |
| | 5.5士 1.4 | 5.6± 1.0 | 5.8 ± 1.3 | 5.2 1.2 | 5.6± 1.1 | 5.1 ± 1.6 | 5.3 ± 1.1 |
| | 5.2± 1.3 | 5.4± 1.2 | 4.9± 1.4 | 4.8 1.4 | 5.5 ± 1.4 | 5.5+ 1.5 | 5.3± 1.5 |
| | 5.2 ± 1.4 | 5.3士 1.2 | 5.2 ± 1.3 | 5.1± 1.7 | 5.8 ± 1.2 | 5.4 ± 1.4 | 5.5± 1.6 |

BAIS 4 Test of Dunnett **★**: P ≤ 0.01 Significant difference : * : P \leq 0.05 (HAN260)

| 512 ppm 6.2± 1.2 4.8± 1.3 1280 ppm 5.9± 1.5 5.4± 1.2 3200 ppm 6.0± 1.5 5.4± 1.3* | |
|--|----------------|
| Significant difference: *:PS005 \$:PS001 | Test of humott |

TABLE E 1

CHEMICAL INTAKE CHANGES: MALE

| PAGE: 1 | | | | | | |
|---|------------------------------|---------------|-------------------|------------------|-------------------|--|
| PA | 7 | 0,000± 0.000 | 0.068 = 0.010 | 0.171 ± 0.024 | 0.437 ± 0.066 | |
| | 9 | 0.000 ± 0.000 | 0.069 ± 0.008 | 0.171 ± 0.017 | 0.453 ± 0.061 | |
| | 5 | 0.000 ± 0.000 | 0.070± 0.007 | 0.179± 0.023 | 0.457 ± 0.066 | |
| (SUMMARY) | 4 | 0.000 ± 0.000 | 0.071 ± 0.009 | 0.182± 0.025 | 0.459± 0.069 | |
| CHEMICAL INTAKE CHANGES ALL ANIMALS | 3 | 0.000土 0.000 | 0.074 ± 0.008 | 0.189± 0.025 | 0.490 ± 0.070 | |
| ਲੋ ਚ | (weeks) | 0.000 年 0.000 | 0.079 ± 0.009 | 0.189 ± 0.027 | 0.495士 0.082 | |
| Crlj[Crj:BDF1] v | Administration (weeks)_ l | 0.000 ± 0.000 | 0.083 ⊕ 0.008 | 0.204 ± 0.023 | 0.515± 0.076 | |
| STUDY NO. : 0580 ANIMAL : MOUSE BGDZF1/Cr1j[Crj:BDF1] UNIT : g / kg / d a y REPORT TYPE : A1 104 SEX : MALE | Group Name | Control | 512 ppm | 1280 րթա | 3200 ppm | |

| STUDY NO.: 0580 ANIMAL: MOUSE BEDZF1/CrijfCrj:EDF1] UNIT: R / kg / d a y REPORT TYPE: A1 104 SEX: MALE | rj:BDF1] | O 4 | CHEMICAL INTAKE CHANGES (SUMMARY) ALL ANIMALS | (SUMMARY) | | | PAGE: 2 |
|--|-------------------------|------------------|--|-----------------|-------------------|-----------------|------------------|
| Group Name | Administration (weeks)9 | (#eeks) | 10 | 11 | 12 | 13 | 14 |
| Control | 0.000 ≠ 0.000 | 0.000 ± 0.000 | 0.000 ± 0.000 | 0.000 ± 0.000 | 0.000 ± 0.000 | 0.000 ± 0.000 | 0.000± 0.000 |
| 512 ppm | 0.067± 0.008 | 0.066 ± 0.007 | 0.064上 0.009 | 0.062 = 0.010 | 0.065 = 0.007 | 0.064± 0.008 | 0.059 ± 0.008 |
| 1280 ppm | 0.163 = 0.027 | 0.169 ± 0.018 | 0.164± 0.017 | 0.153± 0.021 | 0.162± 0.017 | 0.153 ± 0.019 | 0.145± 0.021 |
| 3200 ppm | 0.413 ± 0.070 | 0.425± 0.053 | 0. 420 ± 0. 056 | 0.410 ± 0.059 | 0.423 ± 0.058 | 0.395 ± 0.039 | 0.362 ± 0.065 |
| | | | | | | | |

BA1S 4

| STUDY NO. : 0580 ANTMAL : MOUSE BGDZF1/Crlj[Crj:BDF1] UNIT : R / kg / d a y REPORT TYPE : A1 104 SEX : MALE | rj:BDF1] | ਹ ਝ | CHEMICAL INTAKE CHANGES (SUMMARY) ALL ANIMALS | (SUMMARY) | | | PAGE: 3 |
|---|------------------------|---------------|--|---------------|-------------------|---------------|--------------|
| Group Name | Administration (weeks) | (weeks) 22 | 26 | 30 | 34 | 388 | 42 |
| Control | 0.000± 0.000 | 0.000 ± 0.000 | 0.000± 0.000 | 0.000 + 0.000 | 0.000 ± 0.000 | 0.000 ± 0.000 | 0.000± 0.000 |
| 512 ppm | 0.059± 0.006 | 0.053 ± 0.007 | 0.055± 0.007 | 0.053 ± 0.007 | 0,050± 0,006 | 0.048 ± 0.006 | 0.049± 0.007 |
| 1280 ppm | 0.152± 0.017 | 0.134± 0.022 | 0.133 ± 0.017 | 0.135 ± 0.014 | 0.126± 0.020 | 0.117± 0.022 | 0.127± 0.015 |
| 3200 ppm | 0.390± 0.042 | 0.338± 0.052 | 0.332 ± 0.045 | 0.348± 0.057 | 0.321 ± 0.055 | 0.309± 0.048 | 0.323± 0.050 |
| | | | | | | | |

| PAGE: 4 | | 0.000 ± 0.000 | ⊕ 0.006 | + 0.024 | + 0.060 | |
|---|------------------------------|---------------|---------------|------------------|-------------------|--|
| | 70 | 0.000 | 0.048± | 0.122± | 0.306± | |
| | 99 | 0.000 ± 0.000 | 0.048士 0.007 | 0.122 ± 0.021 | 0.323 ± 0.078 | |
| | 62 | 0.000 ± 0.000 | 0.045 ± 0.009 | 0.120± 0.021 | 0.296± 0.072 | |
| (SUMMARY) | 58 | 0.000 ± 0.000 | 0.046士 0.008 | 0.120± 0.018 | 0.293土 0.058 | |
| CHEMICAL INTAKE CHANGES (SUMMARY) ALL ANIMALS | 54 | 0.000± 0.000 | 0.050 ± 0.008 | 0.122± 0.023 | 0.308± 0.043 | |
| A. C. | (weeks) 50 | 0.000 ± 0.000 | 0.047 ± 0.009 | 0.112 ± 0.020 | 0.300土 0.049 | |
| -1.j[Cr.j:BBF1.] | Administration (weeks) 46 50 | 0.000 ≠ 0.000 | 0.046 ± 0.005 | 0.118 ± 0.019 | 0.285 ± 0.051 | |
| STUDY NO.: 0580 ANIMAL: MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT: R/kg/day REPORT TYPE: A1 104 SEX: MALE | Group Name | Control | 512 ppm | 1280 ppm | 3200 ppm | |

| STUDY NO.: 0580 ANIMAL: MOUSE BGDZF1/Cr1j[Crj:BDF1] UNIT: R/kg/day REPORT TYPE: A1 104 SEX: MALE |]:BDF1] | | CHEMICAL INTAKE CHANGES (SUMMARY) ALL ANDMALS | (SUMMARY) | | | PAGE: 5 |
|--|---------------------------|-------------------|---|-----------------|-----------------|-----------------|--------------|
| Group Name | Administration (weeks) 74 | (weeks) 78 | 88 | 98 | 06 | 94 | 86 |
| Control | 0.000 幸 0.000 | 0.000 ± 0.000 | 0.000± 0.000 | 0.000 ± 0.000 | 0.000 ± 0.000 | 0.000 ± 0.000 | 0.000± 0.000 |
| 512 ppm | 0.047 ± 0.007 | 0.048 ± 0.007 | 0.048± 0.012 | 0.047 ± 0.012 | 0.048 ± 0.008 | 0.046 ± 0.009 | 0.046⊥ 0.009 |
| 1280 րրա | 0.122 ± 0.025 | 0.122 ± 0.022 | 0.117± 0.025 | 0.122 ± 0.027 | 0.130 ± 0.039 | 0.113± 0.031 | 0.117± 0.034 |
| 3200 ppm | 0.295± 0.068 | 0.322 ± 0.053 | 0, 298 ± 0, 068 | 0.305± 0.079 | 0.334± 0.071 | 0.278 ± 0.079 | 0.288± 0.079 |

| CHEMICAL INTAKE CHANGES (SUMMARY) ALL ANIMALS PAGE: 6 | Administration (weeks) 102 | $0.000\pm 0.000 \pm 0.000 \pm 0.000$ | $0.051\pm \ 0.012$ $0.046\pm \ 0.016$ | $0.141\pm\ 0.047$ $0.138\pm\ 0.050$ | 0.328 ± 0.092 0.320 ± 0.118 | |
|--|-------------------------------|--------------------------------------|---------------------------------------|-------------------------------------|-----------------------------------|--|
| 2c j: BDF1] | Administration 102 | 0.000 ± 0.000 | 0.051 ± 0.012 | 0.141± 0.047 | 0.328 ± 0.092 | |
| STUDY NO. : 0580 ANIMAL : MOUSE BEDZF1/Crlj[Crj:BDF1] UNIT : K / Kg / d a y REPORT TYPE : A1 104 SEX : MALE | Group Name | Control | 512 ppm | 1280 ppm | 3200 ppm | |

TABLE E 2

CHEMICAL INTAKE CHANGES: FEMALE

| PAGE: 7 | | 0.000 | 0.012 | 0.027 | 0.066 | |
|--|------------------------|---------------|-----------------|--------------|------------|--|
| | 7 | 0.000± | 0.083土(| 0.209± | 0.500± 0 | |
| | | 0.000 | 0.011 | 0.031 | 0,059 | |
| | 9 | 0.000+ | 0.088± | 0.214± | 0.534± | |
| | | 0.000 | 0.010 | 0.033 | 0.058 | |
| | 2 | 0.000 ≠ 0.000 | 0.082 | 0.204± 0.033 | 0.505土 | |
| | | 0.000 | 0.012 | 0.031 | 0.071 | |
| (SUMMARY) | 4 | 0.000 ∓ | 0.083± | 0.204± 0.031 | 0.514± | |
| E CHANGES | | 0.000 | 0.014 | 0.037 | 0.081 | |
| CHEMICAL INTAKE CHANGES ALL ANIMALS | 3 | 0.000 ⊞ | 0.089 ± | $0.224\pm$ | 0.547± | |
| | | 0.000 | 0.013 | 0.030 | 0.090 | |
| | Administration (weeks) | € 000 + | 0.090 ⊡ | 0.213士 | 0.554± | |
| | istration | 0,000 | 0.015 | 0.024 | 0.094 | |
| STUDY NO. : 0580 ANIMAL : MOUSE BEDZFI/Crlj[Crj:BDF1] UNIT : g /kg / d a y REFORT TYPE : A1 104 SEX : FEMALE | Admini 1 | 0.000 + 0.000 | 0.096 ± 0.015 | 0.238± 0.024 | $0.624\pm$ | |
| STUDY NO. : 0580 ANIMAL : MOUSE F UNIT : g / kg, REPORT TYPE : A1 10 SEX : FEMALE | Group Name | Control | 512 ppm | 1280 րբա | 3200 ppm | |

| CHEMICAL INTAKE CHANGES (SUMMARY) ALL ANTMALS PAGE: 8 | Administration (weeks) 8 10 11 12 13 14 | $0.000 \qquad 0.000 \pm 0.000 \qquad 0.00$ | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | $0.038 \qquad 0.215 \pm \hspace{0.05in} 0.037 \qquad 0.205 \pm \hspace{0.05in} 0.032 \qquad 0.204 \pm \hspace{0.05in} 0.040 \qquad 0.212 \pm \hspace{0.05in} 0.039 \qquad 0.218 \pm \hspace{0.05in} 0.050 \qquad 0.199 \pm \hspace{0.05in} 0.043$ | 0.060 0.510 ± 0.050 0.508 ± 0.059 0.501 ± 0.059 0.520 ± 0.065 0.512 ± 0.068 0.476 ± 0.065 |
|--|---|--|--|---|---|
| CHEMIC ALL AN | weeks) | 0.000 | 0.011 | 0.037 | 0.050 |
| Or j: BDF1] | Administration (v | 0.000± 0.000 | 0.082 ± 0.011 | 0.212 ± 0.038 | 0.529 ± 0.060 |
| STUDY NO.: 0580 ANIMAL : MOUSE BGDZFI/CrjjfCrj;BDF1] UNIT : g / kg / d a y REPORT TYPE : A1 104 SEX : FEMALE | Group Name | Control | 512 ppm | 1280 բթա | 3200 ppm |

| STUDY NO. : 0580 ANIMAL : MOUSE BGDZF1/Crij[Crj:BDF1] UNIT : g / kg / d a y REPORT TYPE : Al 104 SEX : FEMALE |]:B0F1] | | CHEMICAL INTAKE CHANGES (SUMMARY) ALL ANIMALS | (SUMMARY) | | | PAGE: 9 |
|--|------------------------|------------------|---|---------------|-----------------|---------------|-------------------|
| Group Name | Administration (weeks) | (weeks) 22 | 26 | 30 | 34 | 38 | 42 |
| Control | 0.000 = 0.000 | 0.000 ± 0.000 | 0.000± 0.000 | 0.000 ± 0.000 | 0.000 ± 0.000 | 0.000 ± 0.000 | 0.000 ± 0.000 |
| 512 ppm | 0.079 ± 0.013 | 0.079 ± 0.013 | 0.073 土 0.013 | 0.077± 0.014 | 0.072 ± 0.012 | 0.063± 0.013 | 0.076± 0.013 |
| 1280 րրա | 0.213 = 0.046 | 0.204 ± 0.045 | 0.191± 0.045 | 0.209± 0.049 | 0.192± 0.044 | 0.170 ± 0.041 | 0.194士 0.041 |
| 3200 ppm | 0.503 ± 0.082 | 0.499 ± 0.083 | 0.452士 0.080 | 0.492± 0.073 | 0.431± 0.094 | 0.433 ± 0.080 | 0.459 ± 0.081 |
| | | | | | | | |

| STUDY NO.: 0580 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1] UNIT : R / kg / d a y REPORT TYPE : A1 104 SEX : FEMALE | cj:BDF1] | | CHEMICAL INTAKE CHANGES ALL ANIMALS | (SUMMARY) | | | PAGE: 10 |
|--|------------------------|-------------------|--|-------------------|------------------|-------------------|------------------|
| Group Name | Administration (weeks) | (weeks) 50 | 54 | 58 | 62 | 99 | 70 |
| Contro] | 0.000± 0.000 | 0.000 ± 0.000 | 0.000 ± 0.000 | 0.000 ± 0.000 | 0.000 ± 0.000 | 0.000 ± 0.000 | 0.000± 0.000 |
| 512 ppm | 0.063 ± 0.013 | 0.064 ± 0.013 | 0.069± 0.013 | 0.066 ± 0.015 | 0.060 ± 0.012 | 0.068 ± 0.013 | 0, 060 ± 0, 016 |
| 1280 ppm | 0.163 ± 0.040 | 0.162± 0.044 | 0.182 ± 0.045 | 0.167 ± 0.041 | 0.157 ± 0.037 | 0.172 ± 0.039 | 0.157± 0.042 |
| 3200 ppm | 0.421 ± 0.087 | 0.411± 0.078 | 0.429 ± 0.061 | 0.389± 0.084 | 0.415± 0.067 | 0.419 ± 0.069 | 0.413 ± 0.080 |
| | | | | | | | |

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(HAN300)

| PAGE: 11 | 86 | 0.000± 0.000 | 0.065 ± 0.016 | 0.166± 0.043 | 0.441 = 0.111 |
|---|------------------------|---------------|-------------------|-----------------|-------------------|
| | 94 | 0.000 ± 0.000 | 0.064生 0.020 | 0.175 ± 0.050 | 0.433± 0.101 |
| | 06 | 0.000 ± 0.000 | 0.068± 0.016 | 0.171 = 0.040 | 0.457 ± 0.097 |
| (SUMMARY) | 86 | 0.000 ± 0.000 | 0.062± 0.014 | 0.152士 0.041 | 0,404± 0,125 |
| CHEMICAL INTAKE CHANGES ALL ANTMALS | 82 | 0.000 ± 0.000 | 0.071± 0.019 | 0.159± 0.042 | 0.407 ± 0.093 |
| CHI ALJ | (Weeks) 78 | 0.000 ± 0.000 | 0.069 ± 0.015 | 0.173± 0.037 | 0.411 0.094 |
| [Cr.j:B0F1] | Administration (weeks) | 0.000 ± 0.000 | 0.068± 0.016 | 0.167 ± 0.036 | 0.411 ± 0.100 |
| STUDY NO. : 0580 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] UNIT : R/Kg/day REPORT TYPE : A1 104 SEX : FEMALE | Group Name | Control | 512 ppm | 1280 ppm | 3200 ppm |

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(HAN300)

| PAGE : 12 | | | | | |
|---|------------------------|--------------|---------------|---------------|------------------|
| CHEMICAL INTAKE CHANGES (SUMMARY) ALL ANLWALS | | 0.000 | 0.020 | 0.040 | 0.115 |
| | (weeks) | 0.000± | 0.064土 | 0.173± | 0.464土 |
| STUDY NO. : 0580 ANIMAL : MOUSE BGDZF1/Cr1j[Crj:BDF1] UNIT : g / kg / d a y REPORT TYPE : A1 104 SEX : FEMALE | Administration (weeks) | 0.000± 0.000 | 0.078 ± 0.017 | 0.183 ± 0.050 | 0.498 ± 0.103 |
| STUDY NO. : 0580 ANIMAL : MOUSE UNIT : g/k REPORT TYPE : A1 SEX : FEMALE | Group Name | Control. | 512 ppm | 1280 ppm | 3200 ррш |

TABLE F 1

HEMATOLOGY: MALE

| REPORT TYPE : A1 NO. of RED BLOOD CELL HEMOGLOBIN No. of RED BLOOD CELL HEMOGLOBIN Animals 10 6 / μ e g / d e 33 9.73 \pm 1.52 13.8 \pm 1.9 34 9.57 \pm 0.96 14.0 \pm 1.3 35 9.23 \pm 1.44 13.4 \pm 2.0 35 9.39 \pm 1.56 13.6 \pm 2.1 | HEMATOLOGY (SUMMARY) ALL ANIMALS (105W) PAGE : | HEMATOCRIT MCV MCH NCHC PLATELET % f 2 D g g /d ℓ 103/ $\mu\ell$ | $40.8\pm$ 4.9 $42.2\pm$ 2.5 $14.3\pm$ 0.8 $33.9\pm$ 1.1 $1530\pm$ 441 | $41.0\pm$ 3.8 $42.9\pm$ 2.2 $14.6\pm$ 0.8 $34.1\pm$ 0.9 $1660\pm$ 341 | $39.3\pm$ 5.3 $42.9\pm$ 3.5 $14.5\pm$ 1.0 $33.9\pm$ 1.3 $1601\pm$ 429 | $40.1\pm$ 5.1 $43.3\pm$ 4.0 $14.5\pm$ 0.7 $33.7\pm$ 1.9 $1667\pm$ 348 | |
|---|--|---|---|---|---|---|--|
| E B6D2F1/Cr1j(Cr.j:BDF1] 1 RBPORT TYPE : Λ1 NO. of RBD BLOOD CELL Animals 106/με 33 9.73± 1.52 34 9.57± 0.96 35 9.23± 1.44 35 9.39± 1.56 | HEMATOLOGY (SUN ALL ANIMALS (10 | NI | 1.9 | 1.3 | 2.0 | 2.1 | |
| E B6D2F1/Cr1j[Crj: NO. of Animals 33 9 34 9 35 9 | BDF1] : A1 | | L. 52 | 0.96 | 1. 44 | 1. 56 | |
| 1.0 : 0580 1.1 : MOUSI IRE. TIME : MALE Name Name Name 1280 ppm 1280 | STUDY NO. : 0580 ANIMAL : MOUSE BGDZF1/CrljfCrj:1 MEASURE. TIME : 1 SEX : MALE REPORT TYPE | | æ | 34 | 35 | 35 | TA A A A A A A A A A A A A A A A A A A |

(HCL070)

| SEX : MALE REPORT TYPE : A1 PAGE : 2 Group Name No. of Factority | STUDY NO.: 0580 ANIMAL: MOUSE MEASIBE TIME: 1 | 0 SE B6D2F1/Crl _] | j[Crj:BDF1] | HEMATOLOGY (SUMMARY) ALL ANIMALS (1054) | |
|--|---|---------------------------------|----------------|---|-----------------|
| RETICULOCYTE % 3.3± 3.5 2.5± 1.0 3.5± 3.5 4.2± 7.6 * : P ≤ 0.05 ** : P ≤ 0.01 Test of Dunnett | SEX : MALE | REPORT | TYPE : A1 | | |
| titrol 33 3.3± 3.5 2 ppm 34 2.5± 1.0 9 ppm 35 3.5± 3.5 9 ppm 35 4.2± 7.6 [ficant difference : *: P ≤ 0.05 **: P ≤ 0.01] Test of Dunett | Group Name | NO. of Animals | RETICULOCYTE % | | |
| 2 ppm 34 2.5± 1.0) ppm 35 3.5± 3.5) ppm 35 4.2± 7.6) figurat difference; *:P ≤ 0.05 **:P ≤ 0.01 Test of Dunnett | Сонтго | £ | | | |
|) ppm 35 $3.5\pm$ 3.5 $1.2\pm$ 1.0 | 512 ppm | 34 | | | |
| D ppm 35 4.2± 7.6 Great difference : *: P ≤ 0.05 **: P ≤ 0.01 Test of Dunnett | 1280 ppm | 35 | | | |
| lficant difference ; *: P ≤ 0.05 **: P ≤ 0.01 Test of Dunnett | 3200 ppm | 35 | | | |
| | Significant | difference ; | * : P ≤ 0.05 | ** : P ≤ 0.01 | Test of Dunnett |
| | (HCL070) | | | | BAIS A |

| Animals 10 d / MS MSEG (%) EOSINO EASINO EASINO </th <th>STUDY NO. : 0584 ANIMAL : MOUS MEASURE. TIME : SEX : MALE</th> <th>STUDY NO. : 0580 ANTHAL : MOUSE BEDZEL/Crlj[Crj:BDFL] MEASURE. TIME : 1 SEX : MALE REPORT TYPE : A1</th> <th>FI/Crj:BDF1] REPORT TYPE : A1</th> <th></th> <th>HEMATOLOGY (SUMMARY) ALL ANIMALS (105W)</th> <th>(105W)</th> <th></th> <th></th> <th></th> <th></th> <th></th> <th></th> <th></th> <th></th> <th>PAGE :</th> <th>·· ເລ</th> | STUDY NO. : 0584 ANIMAL : MOUS MEASURE. TIME : SEX : MALE | STUDY NO. : 0580 ANTHAL : MOUSE BEDZEL/Crlj[Crj:BDFL] MEASURE. TIME : 1 SEX : MALE REPORT TYPE : A1 | FI/Crj:BDF1] REPORT TYPE : A1 | | HEMATOLOGY (SUMMARY) ALL ANIMALS (105W) | (105W) | | | | | | | | | PAGE : | ·· ເລ |
|---|--|---|----------------------------------|-----------------------|---|--------|---------|------------|-----------------|---|----------|--|-----------------|---|---------|--|
| 33 3.84± 3.68 1± 1 27± 10 2± 1 0± 0 4± 2 63± 34 4.19± 3.97 1± 1 25± 12 2± 1 0± 0 4 0 4± 2 65± 35 5.26± 10.39 1± 2 29± 15 3± 2 0± 0 5 0± 0 3± 2 60± 35 3.70± 1.74 1± 1 25± 13 2± 1 0± 0 5 3± 2 68± | Group Name | NO. of Animals | ΨBC 1 0³∕μβ | Differentia N-BAND | WBC N-SEG | E08 | SINO | | BASO | | MONO | | CYMPHO | 000000000000000000000000000000000000000 | OTHER | The second secon |
| 34 4.19± 3.97 1± 1 25± 12 2± 1 0± 0 4± 2 65± 35 5.26± 10.39 1± 2 29± 15 3± 2 0± 0 5 0± 0 35 3.70± 1.74 1± 1 25± 13 2± 1 0± 0 5 3± 2 60± | Control | 33 | 3.84± 3.68 | 1 +1 | | 0 | +1 | _ | + 1 | 0 | 4= | .7 | €3± | 12 | 57 † | 2 |
| 35 5.26 \pm 10.39 1 \pm 2 29 \pm 15 3 \pm 2 0 \pm 0 3 \pm 2 60 \pm 35 3.70 \pm 1.74 1 \pm 1 25 \pm 13 2 \pm 1 0 \pm 0 35 5 68 \pm | 512 ppm | 34 | | 1 + | | 23 | 2 ÷ | _ | 0 | 0 | <u>+</u> | 69 | 65 <u>- </u> | 16 | 3.± | 13 |
| 35 3.70 ± 1.74 1 ± 1 25 ± 13 2 ± 1 0 ± 0 0 ± 2 $68\pm$ | 1280 ppm | 35 | | | | 10 | ÷ | 23 | 1 ~0 | 0 | 3+ | 63 | + 09 | 18 | 4 | 16 |
| | 3200 ppm | 35 | | 1+ | | m | 5+ | - - | ∓0 | 0 | 3+ | 63 | ∓89 | 15 | 1+ | 67 |
| Significant difference; $*: P \le 0.05$ **: $P \le 0.01$ Test of Dunnett | Significant | difference; | * : P ≤ 0.05 | ★ : P ≤ 0.01 | | | Test of | Dunnett | | | | With a should district 1 and a second second | | | | |

TABLE F 2

HEMATOLOGY: FEMALE

| STUDY NO.: 0580 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] MMASNER TYME: 1 SEX : FEMALE | 3 BGD2F1/Cr1j L REPORT 1 | F1/Cr13[Cr3:BDF1] REPORT TYPE : A1 | | ALL | HEMATOLOGY (SUMMARY) ALL ANIMALS (1054) | MARY) 15W) | | | | | | | | |
|---|--------------------------------|--|----------------------|------|--|---------------|-----------------|------|------------|-----|-----------------|--|---|---|
| Group Name | NO. of Animals | RED BLOOD CELL 1 OF / MR | HEMOCLOBIN g / dl | OBIN | HEMATOCRIT | 117 | MCV f & | | MCH p.g | | MCHC g / dl? | | PLATELET 1 0³/μβ | PAGE: 4 |
| Control | 34 | 9.11 = 1.50 | 13.5± | 2.0 | 39.9∓ | 4. 4 | 44.3± | 4.2 | 14.9± | 0.8 | 33.9± | 1. 6 | 1051 | 351 |
| 512 ppm | 88 | 9. 66 ± 0.88 | 14.41 | 1.2 | 41.5± | 2.7 | 43.1± | 2.1 | 14.9± | 0.5 | 34.6± | 0.9 | 1030 ± | 302 |
| 1280 ppm | 58 | 9.66± 0.76 | 14.3. | 1.1 | 41.1# | 2.7 | 42.7± | J. 4 | 14.8 | 0.4 | 34.8± | 0.8** | 1173± | 156 |
| 3200 ppm | 59 | 9.44 ± 0.64 | 14.0± | 1.0 | 40.8± | 8 | 43.2± | 1.4 | 14.9± | 0.4 | 34.4± | 9.0 | 1138± | 298 |
| Significant o | lifference; | Significant difference ; * $*$: P \leq 0.05 | ** : P ≤ 0.01 | 01 | | Te | Test of Dunnett | ett | | | | No. 11. Company of the Company of th | SIS SISTANA LANGARANA SALAMAN ALAKA SALAMAN | *************************************** |

| 1 | | (IIO) CTURE WAYER TO TO | |
|--|----------------|-------------------------|-----------------|
| | RT TYPE : A1 | | PAGE : |
| Group Name NO. of Animals | RETICULOCYTE % | | |
| Control 34 | 5.2 ± 6.3 | | |
| 512 ppm 28 | 3.2 ± 2.8 | | |
| 1280 ppm 28 | $2.6\pm$ 1.0 | | |
| 3200 ppm 29 | 3.6 ± 1.8 | | |
| Significant difference ; * : P \leq 0.05 | ; *:P≤0.05 | ** : P ≤ 0.01 Tes | Test of Dunnett |

| NO. Anin oul 3 opm 2 opm 2 opm 2 cant differ | ANTMAL : MOUSE BEDZFI/Crij(Crj;BDF1) MEASURE, TIME : 1 SEX : FEMALF | USE BODZFI/CF. : 1 REPORT | REPORT TYPE : A1 | | | ALL AINIMALS (105W) | (10011) | | | | | | | | | ŝ | |
|--|---|---------------------------------|--------------------|------------------|-----------|---|--|--------|-----------|--|--|----------|----|----------------|----|---|--|
| | Group Name | .0N | WBC | Difi | ferential | WBC (% | | | | Annual of the second se | | | | | | rau | |
| $5.11\pm 6.94 \qquad 1.1 + 1 \qquad 2.5 \pm 15 \qquad 1.1 + 1 \qquad 0.1 + 1 \qquad $ | TO PROPERTY AND A STATE OF THE | Animals | 1 0³/µl | N-BAND | | N-SEG | | EOSINO | | BASO | | MONO | | LYMPIJO | | OTHER | 071070000000710071000000 |
| | Control | 34 | | +1 | - | 722+ | 15 | +1 | ~ | †1 0 | 0 | 4 | 67 | + 1 | 61 | + 1 | 14 |
| 3.55 \pm 2.29 1 \pm 1 1 22 \pm 7 2 \pm 2 0 \pm 0 4 4 2 69 \pm 10 2 \pm 2.83 \pm 1.41 2 \pm 1 30 \pm 18 2 \pm 1 0 \pm 0 4 4 2 59 \pm 20 3 \pm 8 : P \leq 0.05 ** : P \leq 0.01 Test of Dumett | 512 ppm | 28 | 27.20 ± 127.52 | +1 | | 21 🛨 | 10 | 2 + | | - - 0 | 0 | 4 == | 64 | ∓89 | 17 | 4-1- | 19 |
| 2.83 \pm 1.41 $2\pm$ 1 30 \pm 18 $2\pm$ 1 0 \pm 0 4 \pm 2 59 \pm 20 3 \pm * : P \leq 0.05 ** : P \leq 0.01 Test of Dunnett | 1280 ppm | 87 | | + | | $22\pm$ | 7 | +1 | 2) | +0 | 0 | 4+ | 63 | +69 | 10 | + 2 | 7 |
| * : P ≤ 0.05 | 3200 ppm | 59 | | 5 ++ | | 30十 | 18 | 5+2 | yerd | +0 | 0 | 4. +I | 63 | 29 + | 20 | # | 9 |
| | Significant | difference; | | ‡ ∴ P ≤ (|), 01 | 7 ALCO 1 | AT AN THE GALLAN STEIN COMMENT OF THE STEIN STEI | Test (| of Dunnet | 1. | FOR PASSED THE STREET, | | | | | 10 mm m m m m m m m m m m m m m m m m m | A CONTRACTOR OF THE REAL PROPERTY OF THE PROPERTY OF THE PROPERTY OF THE |

TABLE G 1

BIOCHEMISTRY: MALE

| STUDY NO. : 0580 ANIMAL : MOUSE BGDZF1/Cr1j[Crj:BDF1] MEASURE. TIME : 1 SEX : MALE REPORT TYPE : A1 | SE BGDZF1/Cr1j[1 REPORT T | F1/Crlj[Crj:BDF1] KEPORT TYPE : A1 | | | B10 ALL | BIOCHEMISTRY (SUMMARY) ALL ANIMALS (105W) | (SUMMARY) (05W) | | | | | | | | PAGE: 1 |
|---|--|---------------------------------------|--------|-------------------|------------|--|--------------------|------------------|----------------------|--------------------|----|------------------------|--------|-----------------------|---------|
| Group Name | NO. of Animals | TOTAL PROTEIN g/d2 | ROTEIN | ALBUMIN g / d& | | A/G RAT10 | 10 | T-BILIK ng/de | T-BILIRUBIN mg/de | GLUCOSE GLUCOSE | | T-CHOLESTEROL mg/dl | STEROL | TRIGLYCERIDE mg/dl | ERIDE |
| Control | 83 83 | 5.6∄ | 8.0 | 2.7± | 0.5 | F. 0.+ | 0.2 | 0.14± | 0.05 | 178∓ | 49 | 125± | 57 | 37± | 73 |
| 512 ppm | 33 | 5. 4 ⊞ | 0.8 | 2.7 -1- | 0.4 | 1.0土 | 0.1 | 0.13± | 0.03 | ∓661 | 36 | 128± | 65 | ∓09 | 22* |
| 1280 ppm | 35 | 5,7± | 1.2 | 2.7± | 0.4 | 1.0 ± | 0.3 | 0.15+ | 0.07 | 177± | 57 | 125 ± | 110 | 38+ | 20 |
| 3200 ppm | 35 | 5.5 | 6.0 | 2.8 | 0.5 | 1.0± | 0.2 | 0.15± | 0.08 | +1881 | 47 | 140 ± | 83 | 49士 | 61 |
| Significant (HCL074) | Significant difference; *: P ≤ 0.05 .074) | ∀∥ * | | ** : P S 0.01 | | | | Test of Dunnett | mnett | | | | | | BAIS 4 |

| ANTMAL : MOUSE BGD2F1/Cr15[Crj:BDF1] MEASURE, TIME : 1 | BGD2F1/Cr1j | [Crj:BDF1] | | | ALL | ALL ANIMALS (105W) | 05W) | | | | | | | | |
|---|-------------------|---|------|---------------------|-------|--------------------|------|-----------------|------|----------------|--|------------------|---|------------|--------|
| SEX : MALE | | REPORT TYPE : A1 | | | | | | | | | | | | | PAGE : |
| Group Name | NO. of Animals | PHOSPHOLIPID mg/dl | TPID | AST I U Z | 7 | ALT I U / g | 2 | LDH I U / g | 2 | ALP I U / g | ğ | G-GTP 1 U / g | | CK IU/2 | 6 |
| Control | 33 | 208± | 83 | 平669 | 3131 | ∓172 | 1033 | ∓168I | 8013 | T67 | 119 | +! | 1 | 56土 | 35 |
| 512 ppm | 33 | 218± | 91 | 115± | 509 | 4- 29 | 106* | 495 ± | 335 | 153 ± | 122 | ÷l | - | ∓09 | 13 |
| 1280 ppm | 35 | 506± | 144 | | 66 | £29 | 96 | 473.± | 291 | ±621 | 33 | +1 | 1 | €3 + | 49 |
| 3200 ppm | 35 | 229± | 96 | 102± | 254** | 114± | 443* | 1578± | 7106 | 151 | 001 | +0 | - | ∓08 | 184 |
| Significant difference; *: P ≤ 0.05 | fference ; | * : P \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \\ \ | 05 | ‡ : P ≤ 0.01 | | | | Test of Dunnett | nett | | ************************************** | | | | |

| STUDY NO. : 0580 ANTMAL : MOUSE BGDZF1/Crlj[Crj:BDF1] MEASNEE. TIME : 1 |) E B6D2F1/Cr1j[1 | [Cr.j:BDF1] | | | | BIOCHEMISTRY (SUMMARY) ALL ANIMALS (105W) | (SUMMAR' | (.k | | | | | | |
|---|--------------------------|-------------|------------------------|--------------------|----------|--|-----------|----------------------|---------|-------------------|-----|------------------|----------------------|---------|
| SEX : MALE | REPORT 1 | TYPE : AI | | | | | | | | | | | | PAGE: 3 |
| Group Name | NO. of Animals | UREA NI | UREA NITROGEN mg/dl | SODIUM m Eq / J | R | POTASSIUM m Eq∕2 | SIUM 2 | CHLORIDE m Eq / & | 8 3(| CALCIUM Fig/dl | ¥ | INORGAN mg/de | INORGANIC PHOSPHORUS | |
| Control | 89 | 20.0∓ | 3.7 | 153± | - | 4. 2. + | 0.4 | ±021 | 89 | 9.3 | 0.6 | 6.4± | 1.1 | |
| 512 ppm | 34 | 23.1± | 11.4 | T23 T | 2 | 4.3± | 0.5 | 上121 | 2 | 9.1. | 0.6 | 6.5± | 1.0 | |
| 1280 ppm | 35 | 26.4 | 15.0** | 153 ± | က | 4.4 | 9.0 | $120\pm$ | 4 | 9.5+ | 9.0 | 年9.9 | 1. 3 | |
| 3200 ppm | 35 | 26.2± | 19.9* | 153± | 73 | 4.4 | 9.0 | 120± | 4 | 9. 1+1 | 9.0 | 6.4± | 1.0 | |
| Significant | Significant difference ; | *:P≤0.05 | 3.05 | # : P ≤ 0.0 | 01 | 07730A300A400A400A0000000000000000000000 | | Test of Dunnett | nett | | | | | |
| (HCL074) | | | | | | | | | | | | | | BAIS 4 |

TABLE G 2

BIOCHEMISTRY: FEMALE

| Group Name NO. of TO | THE CHILL WATER | | ALL ANIMALS (105W) | | | | PAGE : |
|--|-----------------------|---------------------|--------------------|----------------------|------------------|------------------------|-----------------------|
| | TOTAL PROTEIN g/dl | ALBUMIN g / dê | A/G RAT10 | T-BILIRUBIN mg/dl | mg/de GLUCOSE | T-CHOLESTEROL mg/dl | TRIGLYCERIDE mg/dl |
| Control 34 4.5 | 4.9 ± 0.6 | 2.5士 0.3 | 1.1± 0.2 | 0.14土 0.05 | 137 ± 40 | 73± 23 | 31± 14 |
| 512 ppm 28 4.9 | 4.9± 0.4 | 2.6 - 0.2 | 1.1± 0.1 | 0.14 ± 0.05 | 144± 29 | 71 ± 18 | 91 ∓ 1E |
| 1280 ppm 28 5.(| 5.0 ± 0.6 | 2.6士 0.4 | 1.1± 0.2 | 0.13± 0.02 | 142± 29 | 80± 34 | 30± 14 |
| 3200 ppm 30 5.2 | 5.2士 0.5 | 2.7± 0.3 | 1.1 ± 0.1 | 0.13 ± 0.03 | 145± 37 | 92 ± 40 | 37± 23 |
| Significant difference ; * : P \leq 0.05 | ≤ 0.05 | * : P ≤ 0.01 | | Test of Dunnett | | | |

| ANNWAL : MOUSE BGDZF1/Cr1jfCrj:BDF1] MEKSURE. TIME : 1 SEX : FEWALE REPORT TYPE : A1 | E BODZFI/CFIJI 1 REPORT T | ZFI/CFIJICFJ:BBFI] REPORT TYPE : AI | | | | | | | | | | | | | PAGE : |
|--|-------------------------------------|--|----------------------------|----------------|---------------------------------------|-------------|--|-----------------|------|----------------|--|------------------|--|---|--------|
| Group Name | NO. of Animals | PHOSPHOLIPID mg/d2 | TP10 | AST 1 U / 2 | | ALT IU/2 | TOTAL TRANSPORTATION OF THE PROPERTY OF THE PR | LDH I U / & | 8 | ALP I U / & | e | G-GTP I U / R | | CK IU/l | õ |
| Control | 34 | 128± | 36 | ∓621 | 346 | 74± | 160 | 711± | 1367 | 224+ | 86 | # 1 | -1 | 126± | 249 |
| 512 ppm | 88 | 于081 | 32 | ∓911 | 66 | 58 <u>+</u> | 20 | 437± | 476 | 212 ± | 63 | Ħ | | ∓99 | 50 |
| 1280 ррт | 88 | 138# | 51 | 84± | 23 | 36+ | 15 | 353 ± | 183 | 198+ | 78 | +1 | П | 127± | 252 |
| 3200 ppm | 30 | 155 🛨 | 3 6 * | $101 \pm$ | 72 | 41+ | 31 | 449土 | 409 | 181± | 75 | 11 | - | ₩28 | 127 |
| Significant o | Significant difference; *: P ≤ 0.05 | * : P \le 0. | VIII (Lake by Assemilaneau | * : P ≤ 0.01 | · · · · · · · · · · · · · · · · · · · | | PTYTO PARAMETERS IN THE PARAMETERS IN | Test of Dunnett | nett | | APPROXITATION AND AND AND AND AND AND AND AND AND AN | | THE PROPERTY OF THE PARTY OF TH | *************************************** | |

| Tough Name No. of Animals UNEAN ITROGEN SODIUM PUTASSIUM CHLORIDE CALCIUM INDRGANIC PROSTHORUS Control 34 20.7± 19.9 153± 1 4.3± 0.8 122± 2 9.0± 0.6 6.3± 2.0 512 ppm 28 15.8± 3.3 152± 2 4.0± 0.3 122± 2 8.9± 0.4 5.8± 0.8 1280 ppm 28 18.0± 10.4 152± 2 4.0± 0.4 122± 3 9.0± 0.6 6.5± 1.0 3200 ppm 30 20.8± 17.5 152± 2 4.2± 0.4 121± 2 9.3± 0.9 6.5± 1.3 Significant difference; *:P ≤ 0.05 **:P ≤ 0.01 **:P ≤ 0.01 | STUDY NO. : 0580 ANIMAL : MOUSE BGDZFL/Crlj[Crj:BDF1] MEASURE. TIME : 1 SEX : FEMALE REPORT TYPE : A1 |) SE BGDZF1/Cr1 1 REPORT | FI/Crlj[Crj:BDFL] REPORT TYPE : Al | | BIO | BIOCHEMISTRY (SUMMARY) ALL ANIMALS (105W) | SUMMARY) JSW) | | | | | | | PAGE: |
|--|---|-----------------------------------|---------------------------------------|------------------|--|--|------------------|----------------------|--|------------------|---|--------------------|----------------|-------|
| | Group Name | NO. of Animals | UREA NITROGEN mg/d2 | SODIUM m Eq / | | POTASSIC mÉq / & | JM | CHLORIDE m Eq / 2 | | CALCIUA mg/d2 | | INORGAI mg / d£ | VIC PHOSPHORUS | |
| 15.8± 3.3 152± 2 4.0± 0.3 122± 2 8.9± 0.4 5.8± 18.0± 10.4 152± 3 9.0± 0.4 6.1± 20.8± 17.5 152± 2 4.2± 0.4 121± 2 9.3± 0.9 6.5± *: P ≤ 0.05 **: P ≤ 0.01 Test of Dumett Test of Dumett | Control | 34 | | | - | 4.3+ | 8.0 | 122 ± | 57 | €0.6 | 0.6 | 6.3土 | 2.0 | |
| $18.0\pm$ 10.4 $152\pm$ 1 $4.1\pm$ 0.4 $122\pm$ 3 $9.0\pm$ 0.4 $6.1\pm$ $20.8\pm$ 17.5 $152\pm$ 2 $4.2\pm$ 0.4 $121\pm$ 2 $9.3\pm$ 0.9 $6.5\pm$ *: P \leq 0.05 **: P \leq 0.01 | 512 ppm | 88 | | | 63 | 4.0土 | 0.3 | 122 🕂 | 83 | 8.9± | 0.4 | 5.8∄ | 0.8 | |
| $20.8\pm~17.5$ $152\pm~2$ $4.2\pm~0.4$ $121\pm~2$ $9.3\pm~0.9$ $6.5\pm$ *: P ≤ 0.05 **: P ≤ 0.05 | 1280 ppm | 82 | | | | 4.1± | 0.4 | 122 ± | က | €0.6 | 0.4 | 6.1± | 1.0 | |
| *:P \ 0.05 | 3200 ppm | 30 | | | 2 | 4.2+ | 0.4 | 121 ± | 23 | 9.3± | 6.0 | 6.5± | 1.3 | |
| | Significant | difference; | | * : P ≤ 0.01 | THE REAL PROPERTY OF THE PROPE | *************************************** | | est of Dunne | ************************************** | | 979999999999999999999999999999999999999 | | | |

TABLE H 1

URINALYSIS: MALE

| SEX : MALE | REPORT TYPE : A1 | TYPE : A. | _ | | | | | | | | | | | PAGE : |
|-------------|--------------------------|-------------|--------------|--------|---------------------|------------------|--------|-----|-----------------------------|--------------------|---------|--------------------------------|-------------------------|--------|
| Group Name | NO. of Animals | рН 5.0 (| 6.0 6 | 3.5 7. | 6.0 6.5 7.0 7.5 8.0 | 5 8. | 0 8.5 | CHI | Protein — ± + 2+ 3+ 4+ CIII | Glucose + 2+3+4+ | 4+ CIII | Ketone body ± + 2+3+4+ CIII | Occult blood - ± + 2+3+ | CIII |
| Control | 33 | 0 | 8 - | 15 | 7 3 | 0 | 0 | | 0 3 24 6 0 0 | 33 0 0 0 0 | 0 | 21 6 6 0 0 0 | 27 0 1 0 5 | |
| 512 ppm | 35 | 0 | 7 | 17 1. | .3 | 0 | 0 | | 0 124 7 0 0 | 35 0 0 0 0 | 0 | 21 9 5 0 0 0 | 31 0 1 0 3 | |
| 1280 ppm | 36 | 0 | 8 | 11 % | 8 | 0 4 | - | | 0 621 7 2 0 | 36 0 0 0 0 | 0 | 17 10 9 0 0 0 | 34 0 0 0 2 | |
| 3200 ppm | 36 | 0 | 3 | 15 1 | 11 5 | 59 | 0 | | 0 12 18 6 0 0 * | 36 0 0 0 0 | 0 | 21 9 6 0 0 0 | 31 0 0 0 5 | |
| Significant | Significant difference ; | | * : P ≤ 0.05 | . 05 | # | √II * | ≥ 0.01 | | Tes | Test of CHI SQUARE | | | | |

| GIII | EX : MALE | REPORT | MEANDER. 1 REPORT TYPE : A1 | PAGE : |
|------|----------------|-------------------|---------------------------------|--------------------|
| | | NO. of Animals | Urobilinogen ± + 2+3+4+ CIII | |
| | - | \$ | | |
| | CONTROL | ÷ | 33 0 0 0 | |
| | 512 ppm | 35 | 35 0 0 0 0 | |
| | 1280 ррт | 36 | 36 0 0 0 0 | |
| | 3200 ppm | 36 | 36 0 0 0 0 | |
| | Significant di | ifference ; | * : P ≤ 0.05 ** : P ≤ 0.01 | Test of CHI SQUARE |

TABLE H 2

URINALYSIS: FEMALE

URINALYSIS

STUDY NO. : 0580
ANIMAL : MOUSE BEDZFI/Crij[Crj:BDF1]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1 REPORT TYPE : A1

| | | | | | | | | | | | | | | | | . 7007 |
|-------------|--------------------------|-----------|---------------|------------------------------|-----------------------------|-------|---------------|----------|--------------------------|---------|-------------------------|------|-------------------------------|------|--------------------------|--------|
| Group Name | NO. of Animals | рН 5.0 | 6.0 | 6.5 | 5.0 6.0 6.5 7.0 7.5 8.0 8.5 | 7.5 8 | 8.0 8 | 8.5 CIII | Protein - ± + 2+ 3+ 4+ C | CIII | Glucose - + 2+3+4+ CIII | | Ketone body - ± + 2+ 3+ 4+ | CIII | Occult blood - ± + 2+ 3+ | GII |
| Control | 34 | 0 | 4 10 | 0.1 | cs | 7 | 9 | ¢2 | 0 3 15 14 2 0 | , | 34 0 0 0 0 0 | 23 | 2 25 6 1 0 0 | | 28 1 0 0 5 | |
| 512 ppm | 53 | 0 | - | 9 | 12 | ~ | 4 | 23 | 0 2 18 8 1 0 | | 29 0 0 0 0 0 | 3 20 | 0 0 0 9 0 | | 26 1 0 1 1 | |
| 1280 ppm | 38 | 0 | 0 | ဘ | 4 | 6 | 4 | m | 0 3 18 6 1 0 | 24 | 28 0 0 0 0 0 | 3 19 | 94200 | | 22 1 0 2 3 | |
| 3200 ppm | 30 | 0 | 0 | Ţ. | 6 | 7 | ဘ | 1 | 1 4 18 6 1 0 | çı | 30 0 0 0 0 0 | 5 57 | 2 24 3 1 0 0 | | 29 0 0 0 1 | |
| Significant | Significant difference ; | | *: P \le 0.05 | 0.05 | * | * | ** : P ≤ 0.01 |), 01 | | lest of | Test of CH1 SQUARE | | | | | |
| (IICL101) | | | | TO DESCRIPTION OF THE PERSON | | | | | | | | | | | | |

| Group Name NO. of Urobilings | | PAGE : |
|--------------------------------------|--------------------------------|--------------------|
| Animals | Urobilinogen ± + 2+3+4+ CII | |
| Control 34 34 0 0 0 | 0 0 | |
| 512 ppm 29 29 0 0 (| 0 0 | |
| 1280 ppm 28 28 0 0 (| 0 0 | |
| 3200 ppm 30 30 0 0 0 0 | 0 0 | |
| Significant difference ; *: P ≦ 0.05 | 0.05 ** : P ≤ 0.01 | Test of CHI SQUARE |

TABLE J 1

ORGAN WEIGHT, ABSOLUTE: MALE

ORGAN WEIGHT:ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (105W)

STUDY NO. : 0580
ANIMAL : MOUSE BEDZF1/Cr1j[Crj:BDF1]
REPORT TYPE : A1
SEX : MALE
UNIT: g

| Choung Money | g ON | 1 - M - 1 - U | | 0.111 | THE CHIEF | | | | | | | | |
|--|--------------------------|-------------------|---------------|----------|------------|--------|---|----------|--|---|--|--------|--|
| oroup Name | Animals | body Weight | | ADKENALS | TESTES | λ3 | IIEART | | LUNGS | S | KIDNEYS | YS | |
| THE COMMENTS OF THE CONTRACT O | | | | | | | *************************************** | | Addition and the control of the cont | 70.170.70.470.180.1888.1888.1888.1888.1888.1888.188 | o jeloklabi okia sasa mama sasa mama saja gaja | | |
| Control | 33 | 45.5± 8.2 | 0.010 = | 0.001 | $0.222\pm$ | 0.028 | 0.220± | 0.025 | 0.207± | 0.050 | $0.640\pm$ | 0. 167 | |
| 512 ppm | 34 | 49.8± 7.1 | 0.010 ± | 0.001 | 0. 222 ± | 0. 030 | 0. 215 ± | 0.020 | 0.213± | 0.070 | 0.665± | 0.373 | |
| 1280 բրա | 36 | 45.8± 8.8 | ⊕0.010∓ | 0.002 | 0. 222 ± | 0.029 | 0.219± | 0.025 | 0.211± | 0.059 | 0.724± | 0.479 | |
| 3200 ppm | 35 | 48.5± 7.2 | $0.012\pm$ | 0.012 | 0.225土 | 0.033 | 0. 222 ± | 0.021 | 0.242± | 0.147 | 0.653± | 0.137 | |
| Significant | Significant difference ; | *: P \square 0.05 | ** : P ≤ 0.01 | | | Test | Test of Dunnett | 2000-000 | | | A COLUMN A SER BEN'N A SER | | |

(IICL040)

ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (105W)

STUDY NO. : 0580
ANIMAL : MOUSE BGDZF1/Crlj[Crj:BDF1]
REPORT TYPE : A1
SEX : MALE
UNIT: g

| Group Name | NO. of Animals | SPLEEN | ien ien | LIVER | es es | BRAIN | NJ |
|-------------|--------------------------|--------------|---------|--|--|---|-----------------|
| | | | | THE CARACTER CONTRACTOR OF THE CONTRACTOR CO | *************************************** | *************************************** | |
| Control | 33 | 0.126± 0.113 | 0.113 | ∓628.1 | 0.576 | $0.449\pm$ | 0.014 |
| 512 ppm | 34 | 0.161± | 0.325 | 1.857 ± | 0.728 | 0. 453 ± | 0.019 |
| 1280 ppm | 36 | 0.168± | 0. 194 | 1.799+ | 0.687 | 0.451± | 0.017 |
| 3200 ppm | 35 | 0.094土 | 0.054 | 1. 782± | 0.537 | 0.449± | 0.019 |
| Significant | Significant difference ; | *: P ≤ 0.05 | 1000 | * : P ≤ 0.01 | AND THE PROPERTY OF THE PROPER | | Test of Dunnett |

(IICL040)

TABLE J 2

ORGAN WEIGHT, ABSOLUTE: FEMALE

| . 25 VC | LAGE | | | | | |
|---|-------------------|---------------|-------------------|-------------------|-------------------|--|
| | KIDNEYS | 0.558± 0.642 | 0.432 ± 0.057 | 0.472 ± 0.225 | 0.471 ± 0.153 | |
| | PUNGS | 0.198 ± 0.042 | 0.189 ± 0.054 | 0.181 ± 0.013 | 0.224 ± 0.204 | African i fanns men men men men en menget trigjege trigge graf district district men en men en men |
| | IIEART | 0.170± 0.024 | 0.176± 0.031 | 0.176± 0.025 | 0.167 ± 0.020 | |
| ORCAN WEIGHT:ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (1059) | OVARIES | 0.106± 0.211 | 0.055土 0.157 | 0.057 ± 0.147 | 0.067± 0.210 | |
| ORGAN WE SURVIVAL | ADRENALS | 0.014 = 0.003 | 0.013 ± 0.001 | 0.014 = 0.002 | 0.014 ± 0.004 | |
| :BDF1] | Body Weight | 36.4± 6.3 | 35.9± 5.4 | 37.4± 4.7 | 35.1 ± 6.8 | |
| STUDY NO. : 0580 ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1] REPORT TYPE : A1 SEX : FEMALE UNIT: g | NO. of Animals | 34 | 78 | 28 | 30 | THE RESIDENCE OF THE PERSON OF |
| STUDY NO. : 0580 ANIMAL : MOUSE REPORT TYPE : A1 SEX : FEMALE UNIT: g | Group Name | Control | 512 ppm | 1280 թբա | 3200 ppm | |

(IICI,040)

BAIS 4

Test of Dunnett

★: P ≤ 0.01

Significant difference ; * : P \leq 0.05

PAGE: 4

ORGAN WEIGHT:ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (105W) 0.0130.015 0.013 0.468 ± 0.019 BRAIN $0.467\pm$ $0.468\pm$ $0.467\pm$ 1.404 ± 0.425 0.2620.235 0.291 LIVER $1.368\pm$ $1.412\pm$ 1.403 ± 0.188 0.081 0.232 ± 0.307 0.178 ± 0.247 SPLEEN $0.167\pm$ 0.138± STUDY NO. : 0580
ANIMAL : MOUSE BGDZF1/Cr1j[Crj:BDF1]
REPORT TYPE : A1
SEX : FEMALE
UNIT: g NO. of Animals 34 28 28 30 1280 руш 512 ppm 3200 ppm Control Group Name

(HCL,040)

BAIS 4

Test of Dunnett

★ : P ≤ 0.01

Significant difference ; * : P \leq 0.05

TABLE K 1

ORGAN WEIGHT, RELATIVE: MALE

ORGAN WEIGHT:RELATIVE (SUMMARY) SURVIVAL ANIMALS (105W)

STUDY NO. : 0580
ANIMAL : MOUSE BGDZF1/Cr1j[Crj:BDF1]
REPORT TYPE : A1
SEX : MALE
UNIT: %

| | (8) | | 541541 | HEAKI | LUNGS | KIDNEYS |
|----------------------|--------|---------------|---------------|-----------------|-----------------|-----------------|
| Control 33 45.5± 8.2 | 8. 2 | 0.023 ± 0.006 | 0.507土 0.119 | 0.498± 0.097 | 0.473 ± 0.144 | 1. 441 + 0. 385 |
| 512 ppm 34 49.8上 | 7.1 | 0.020 ± 0.004 | 0.454 土 0.080 | 0,441 ± 0.074** | 0. 443 ± 0. 203 | 1.330 ± 0.576* |
| 1280 ppm 36 45.8土 | & & | 0.024 | 0.501士 0.115 | 0.498 ± 0.127 | 0. 477 ± 0. 151 | 1 660 + 1 221 |
| 3200 ppm 35 48.5± | 7.2 | 0.030 ± 0.050 | 0.476 ± 0.108 | 0.468± 0.088 | 0.554± 0.601 | 1. 392± 0. 450 |

(IICI,042)

ORGAN WEIGHT: RELATIVE (SUMMARY) SURVIVAL ANIMALS (105W)

STUDY NO. : 0580
ANIMAL : MOUSE BGDZF1/Cr1j[Crj:BDF1]
REPORT TYPE : A1
SEX : MALE
UNIT: %

PAGE: 2

| Group Name | NO. of Animals | SPLEEN | LIVER | BRAIN |
|-------------|-------------------------|-------------------|-------------------|-------------------|
| Control | 33 | 0.299土 0.279 | 4.323± 1.775 | L. 024± 0. 223 |
| 512 ppm | 34 | 0.331± 0.688 | $3.883\pm\ 2.140$ | $0.928\pm\ 0.140$ |
| 1280 ppm | 36 | $0.391\pm\ 0.437$ | $4.149\pm\ 2.229$ | 1.025 \pm 0.216 |
| 3200 ppm | 35 | 0.209士 0.147 | $3.878\pm\ 1.871$ | 0.952± 0.182 |
| Significant | Significant difference; | *:P≤0.05 | ** : P ≤ 0.01 | Test of Dunnett |

(HCL042)

TABLE K 2

ORGAN WEIGHT, RELATIVE: FEMALE

ORCAN WEIGHT: RELATIVE (SUMMARY) SURVIVAL ANIMALS (105W)

PAGE: 3

 1.282 ± 0.669 1.400 ± 0.598 1.505 \pm 1.331 1. 228 ± 0.227 KIDNEYS 0.553 ± 0.101 0.548 ± 0.248 0.491 ± 0.073 0.752 ± 1.176 LUNGS 0.477 ± 0.085 0.475 ± 0.075 0.490 ± 0.100 0.499 ± 0.111 HEART 0.211 ± 0.696 0.296 ± 0.607 0.163 ± 0.476 0.151 ± 0.382 OVARIES 0.039 ± 0.008 0.041 ± 0.016 0.037 ± 0.007 0.038 ± 0.007 ADRENALS **★**: P ≤ 0.01 Body Weight (g) 36.4 ± 6.3 5.4 37.4士 4.7 35.1 ± 6.8 Significant difference ; \star : P \leq 0.05 $35.9 \pm$ STUDY NO. : 0580
ANIMAL : MOUSE B6D2F1/Cr1j[Crj:BDF1]
REPORT TYPE : A1
SEX : FEMALE
UNIT: % No. of Animals 34 28 82 30 512 ррт 3200 ppm Control 1280 ррт Group Name

(IICL042)

BAIS 4

Test of Dunnett

ORGAN WEIGHT: RELATIVE (SUMMARY) SURVIVAL ANIMALS (105W)

STUDY NO. : 0580
ANIMAL : MOUSE BGDZF1/Cr1j[Crj:BDF1]
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

| Group Name | NO. of Animals | SPLEEN | LIVER | BRAIN | 600000 |
|-------------|-------------------|-------------------------------------|---------------------|-------------------|--|
| Control | 34 | 0.625± 0.765 | 3.873 ± 0.929 | 1. 325 ± 0. 244 | |
| 512 ppm | 82 | 0.506土 0.655 | 4.005 ± 1.022 | 1. 333 ± 0. 214 | |
| 1280 ppm | 78 | 0.371 ± 0.214 | $3.665\pm\ 0.503$ | 1. 268 ± 0. 182 | |
| 3200 ppm | 30 | 0.487 ± 0.546 | 4.094 ± 0.831 | $1.391\pm\ 0.324$ | |
| Significant | difference; | Significant difference; *:P≤0.05 *# | ‡ : P ≤ 0.01 | Test of Pumett | THE PROPERTY AND A STATE OF TH |

TABLE L 1

HISTOPATHOLOGICAL FINDINGS:

NON-NEOPLASTIC LESIONS: MALE: ALL ANIMALS

| Organ Findings [Integumentary system/appandage] skin/app ulcer squamous cell hy | Group Name No. of Animals on Study Grade | | | | |
|---|---|--|--|---|--|
| sutary s | 1655 | Control 50 1 2 3 4 (%) (%) (%) (%) | 512 ppm 50 1 2 3 4 (%) (%) (%) | 1280 ppm 50 3 4 (%) (%) (%) (%) | 3200 ppm 50 1 2 3 4 (%) (%) (%) (%) |
| | (арындақс) | | | | |
| nomenbs | | <50> 0 1 0 0 (0) (2) (0) (0) | (0)(0)(0)(0) 0 0 0 0 0 0 0 0 | <pre></pre> | (50) 0 1 0 (0) (2) (0) (|
| | squamous cell hyperplasia | | (0)(0)(0)(0) | 0 1 0 0 (0) (0) (0) | 0 0 0 0 |
| scab | | 0 1 0 0 (0) (0) (0) (0) | (0)(2)(0) | 0 2 0 0 (0) (4) (0) (0) | 0 0 0 0 |
| ерідея | epidermal cyst | | (0)(0)(0)(0) | 1 0 0 0 (2) (2) (3) (4) (5) | 0 0 0 0 |
| duct ec | duct ectasia:sebaceous gland | | | | 1 0 0 (2) (3) (4) (4) |
| subcutis thrombus | sn | <50> 0 1 0 0 (0) (2) (0) (0) | (6) (0) (0) (0) 0 0 0 0 0 0 (0) | <pre></pre> | <00> (0) (0) (0) (0) (0) (0) (0) (0) (0) (0) |
| [Respiratory system] | | | | | |
| nasal cavit mineral | mineralization | <pre></pre> | <pre></pre> | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 | <50> 1 0 0 0 (2) (0) (0) (0) |
| Grade 1: Slight <a> a : Number of ar b | 2: Moderate 3: Marked of animals examined at the site of animals with lesion 1:00 *: P ≤ 0.05 ***: P ≤ 0.01 | 4 : Severe Test of Cli Square | | | |

| SEX : MAL | : MALE | | | | | | | | | PAGE |
|--|--|--|----------------------------|------------------------|---------------------|-------------------------------|---|-------------------------------|-------------------|-------------------------------------|
| Organ | Findings | Group Name No. of Animals on Study Grade | %) (%) (%) | Control 50 3 4 (%) (%) | (%) | 512 ppm 50 3 4 (%) (%) | (%) (%) | 1280 ppm 50 3 4 (%) (%) | (%) | 3200 ppm 50 2 3 4 (%) (%) (%) |
| (Respiratory system) | ys.tcm) | | | | | | | | | |
| nasal cavit | inflammation | | (50) 0 1 (0) (2) (| 0 (0) | 0 0 | <50> 0 1 0 0) (2) (0) | (8) (8) (8) (8) (8) (8) (8) (8) (8) (8) | (50) (0) (0) | 0) (0) | <50> 0 0 0 0) (0) (0) |
| | eosinophilic change:olfactory epithelium | רחשו | 30 2 (60) (4) | 1 0 (2) (0) | 27 7 (54) (14) | (0) (0) (| 27 10 (54) (20) | (0) (0) | 26 2 (52) (4 | 2 0 0 4) (0) (0) |
| | eosinophilic change:respiratory epithelium | lium | 12 14 (24) (28) (| 1 0 (2) (0) | 30 3 | (0)(0)(| 25 6 (50) (12) | *0 0 | 14 1 (28) (2 | 1 0 0 2) (0) (0) |
| | inflammation respiratory epithelium | | 0 (0) | (0) (0) | 0 1 (0) (2) | 0 0 0 | (0)(0) | (0) (0) | 0) (0) | (0) (0) (0 |
| | respiratory metaplasia:olfactory epithelium | lelium | 23 3 (46) (46) (| (0) (0) | 27 3 (54) (6) | (0) (0) (| 17 4 (34) (8) | (0) (0) | 18 1 (36) (2 | 1 0 0 2) (0) (0) |
| | respiratory metaplasia:gland | | 21 8 (42) (42) (42) | 3 0 (9) | 28 14 (56) (28) | *0 0 (0) (| 20 16 (40) (32) | (0) (0) | 26 6 (52) (12) | (0)(0)() |
| | squamous cell metaplasia:respiratory epithelium | pithelium | 0 (0) | (0) (0) | (0) (0) | (0) (0) (| (0) (0) | 0 (0) | 1 0 (2) (0) | (0) (0) (0 |
| | epithelial Ayperplasia:transitional cell type | ll type | 0 0 0 | (0) (0) | 1 0 (2) (0) | (0) (0) (| (0) (0) | (0) (0) | 0) (0) | (0) (0) (0 |
| Grade 1 : Slight <a> a : Number b b : Number c : c : c : b a c : c : c : b a c : c : c : c : b a c : c : c : c : c : b a c : c : c : c : c : b a c : c : c : c : c : b a c : c : c : c : c : b a c : c : c : c : c : b a c : c : c : c : c : c : c : b c : c : c : c : c : c : c : b c : c : c : c : c : c : c : c : c : c | 2: Moderate of animals examined at the of animals with lesion Figo | Marked | 4 : Severe | | | | | MICROSOM PROMOS MARKET LANG. | | |

| Organ Findings. [Respiratory system] nasal cavit necrosis | | | | | | | | | |
|---|---|--|----------------------------|------------------|---------------------------------------|----------|---|--|-----------------|
| y sys | | Group Name No. of Animals on Study Grade | Con 50 1 2 6) (%) | trol 3 4 (%) (%) | 512 ppm 50 1 2 3 (%) (%) (%) | 4 (%) | 1280 ppm 50 4 (%) (%) (%) (%) | 3200 ppm 50 1 2 3 (%) (%) (%) | ppm 3 4 (%) (%) |
| | | | | | | | | | |
| | necrosis:olfactory epithelium | | <00> (50> (50) () | 0 0 | (0) (0) (0) 0 0 0 (0) (0) | 0 (0 | <550> 0 0 0 0 0 0 0 0 0 0 0 0 | (50) 0 1 ((0) (2) ((| 0 0 0 |
| nasopharynx eosino | eosinophilic change | | <50> 1 0 (2) (0) (| 1 0 2) (0) | <250> 1 0 0 (2) (0) (0) | 0 (0) | <pre></pre> | (20) (0) (0) (0) (0) | (0) (0 0 0 |
| inflam | inflammation | | 1 0 (2) (0) (| 0 0 | (0) (0) (0) | 0 0 | | 0 0 0 | (0) (0 |
| lung hemorrhage | rhage | | (50> 1 0 (2) (0) (| (0) (0 0 0 | (50) 0 1 0 (0) (2) (0) | 0 (0) | <00 (0) (0) (0) (0) (0) (0) (0) (0) (0) (| (20) (0) (0) | 0 0 |
| едеша | | | 1 0 (2) (0) (| 0 0 | 0 0 0 | 0 0 | (0)(0)(0)(0)(0) | 0 0 0 | 0 (0) |
| inflam | inflammatory infiltration | | 1 0 (2) (0) (| 0 0 | 0 0 0 | 0 0) | 1 1 0 0 (2) (2) (0) (0) | 1 0 (| 0 (0) |
| l ympho | lymphocytic infiltration | | 2 0 (1) (0) (| 0 0 | 2 0 0 (1) (0) (0) | 0 (0) | 2 0 0 0 (4) (4) (6) (6) (6) | 0 0 0 | 0 0 |
| Grade 1 : Slight (a > a : Number b b : Number (c) c : b / a * | 2: Moderate of animals examined at the of animals with lesion 100 | 3 : Marked 4 Site | : Severe | | | | | | |

7 0 0 (14) (14) (10) (10) (10) 1 0 0 ((2) ((3) (0 0 0 0 1 0 0 (2) (2) (0) (0 0 0 0 e **%** 3200 ppm 50 0 0 2 (%) 00 0 (0) - 8 5 0 0 0 (10) (10) (0) 4 8 (0) (0) (0) (0) (0)(0)(0)(0) (0)(6)(0)(0) (2) (0) (0) 3 1280 ppm 50 2 8 -|89 HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W) 4 % (0)(0)(0)(0)(0) 2 0 0 0 (4) (0) (0) (0) 0 0 0 6 (0) (0) (0) (0) (2) (0) (0) (0) 0 (0 1 0 0 (2) (2) (0) ((%) (%) 512 ppm 50 0 1 0 (0) (0) (0) 1 88 4 8 5 0 0 0 (10) (10) (10) (10) 00 0 0 0 0 0 0 0 00 00 0 1 0 (0) (2) (0) (_ 2 0 0 (4) (4) (0) (1 2 3 (%) (%) (%) Control 50 (0) (0) (0) Test of Chi Square 4 : Severe Group Name No. of Animals on Study Grade 3 : Marked ** : P ≤ 0.01 i : Slight 2 : Moderate 3 : Ma a : Number of animals examined at the site b : Number of animals with lesion c : b / a * 100 bronchiolar-alveolar cell hyperplasia Significant difference; *: P ≤ 0.05 accumulation of foamy cells : MOUSE B6D2F1/Crij[Crj:BDF1] inflammatory infiltration granulopolesis:increased mastcell hyperplasia myelofibrosis Findings [Hematopoietic system] (Respiratory system) REPORT TYPE : A1 SEX : MALE STUDY NO. : 0580 роне шаггож lymph node Grade (a) b (c) Organ lung

BA1S4

PAGE: 4

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| ANIMAL : MOUSE BEDZF1/Crij[Crj:BDF1] REPORT TYPE : Al SEX : MALE | ALL ANIMALS (0-105W) | | <u>.</u> | PAGE : |
|--|---|---|--|--|
| OrganFindings | Group Name Control No. of Animals on Study 50 Grade | 512 ppm 50 1 2 3 4 (%) (%) (%) | 1280 ppm 50 1 2 3 4 (%) (%) (%) (%) | 3200 ppm 50 1 2 3 4 (%) (%) (%) (%) |
| (Hematopoietic system) | | | | |
| spleen atrophy | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 | <50> 1 0 0 0 (2) (0) (0) (0) | (6) (6) (6) (6) 0 0 0 0 0 0 0 0 | (0) (0) (0) (0) (0) (0) |
| congestion | | | 1 0 0 0 0 (2) (3) (4) (6) | (0)(0)(0)(0) |
| angiectasis | 1 0 0 0 (2) (3) (4) (6) (6) | | (0)(0)(0)(0)(0) | |
| deposit of hemosiderin | 1 0 0 0 (2) (3) (4) (5) (6) | (2) (0) (0) (0) | | 1 0 0 0 (2) (3) (4) (6) |
| deposit of melanin | 1 0 0 0 (2) (2) (3) (4) (5) | 2 0 0 0 (4) (4) (6) (6) (6) | (2)(0)(0)(0) | 1 0 0 0 (0) (0) (0) |
| extramedullary hematopoiesis | 10 13 6 0 (20) (26) (12) (0) | 19 9 2 0 (38) (18) (4) (0) | 12 9 6 0 (24) (18) (12) (0) | 16 11 5 0 (32) (22) (10) (0) |
| follicular hyperplasia | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | 3 0 0 0 0 (0) (0) | 2 0 0 0 (4) (4) (6) (6) (6) | 2 1 0 0 (4) (2) (0) (0) |
| (Circulatory system) | | | | |
| heart mineralization | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 | (50) 2 0 0 (4)(0)(0)(0) | <pre></pre> | <50> 1 0 0 (2) (0) (0) (0) |
| Grade 1 : Slight 2 : Moderate 3 : N | 3: Marked 4: Severe re site P < 0.01 Test of Chi Senare | | | |

| Organ Findings | Group Name No. of Animals on Study Grade | | | | |
|--|--|---|--|-------------------------------------|---|
| datory sys | | Control 50 1 2 3 4 (%) (%) (%) (%) | 512 ppm 50 512 ppm 50 60 60 60 60 60 60 60 60 60 60 60 60 60 | 1280 ppm 50 1 2 3 4 (%) (%) (%) | 3200 ppm 50 3 4 (%) (%) (%) (%) |
| | | | | | |
| , co | inflammatory infiltxation | <00 (0) (0) (0) 0 0 0 0 0 0 0 0 0 0 0 0 0 | <pre></pre> | (0)(0)(0)(0) 0 0 0 0 0 0 0 0 | (0)(0)(0)(0) 0 0 0 0 0 0 0 0 0 0 0 0 |
| 2007 | | (0)(0)(0)(0)(0) | (0)(0)(0)(0)(0) | (0)(0)(0)(0)(0) | 1 0 0 0 0 (0) (0) (0) |
| myocarditis | | | (0)(0)(0)(0)(0) | (0)(0)(0)(0)(0) | 1 0 0 0 (2) (3) (4) (6) |
| arteritis | | 0 1 0 0 (0) (0) (0) (0) | 1 0 0 0 (2) (3) (4) (5) | | |
| (Digestive system) | | | | | |
| oral cavity ulcer | | (0)(0)(0)(0) 0 0 0 0 0 0 0 0 | <pre></pre> | <pre></pre> | <pre></pre> |
| tooth dysplasia | | <50> 3 1 0 0 (6) (2) (0) (0) | <50> 3 2 0 (6) (4) (0) (0) | <50> 7 3 0 0 (14) (6) (0) (0) | <50> 2 3 0 0 (4) (6) (0) (0) |
| Grade 1 : Slight <a> a : Number of an b b : Number of an (c) c : b / a * 100 | 2 : Moderate 3 : Marked timals examined at the site timals with lesion | 4 : Severe | | | |

(HPT150)

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W)

| KEPOKI IYPE : AI SEX : MAL | : A1 : MALE | | | | | PA | PAGE: |
|-------------------------------|--|--|--|---|--|--|-------|
| Organ | Findings | Group Name No. of Animals on Study Grade | Control 50 4 4 (%) (%) (%) (%) (%) (%) | 512 ppm 50 1 2 3 4 (%) (%) (%) (%) | 1280 ppm 50 3 4 (%) (%) (%) (%) | 3200 ppm 50 1 2 3 (%) (%) (%) | 4 8 |
| (Digestive system) | ystem) | | | | | | |
| rooth | odontogenic cyst | | <50> <50> (0) (0) (2) (0) (0) (2) (0) (0) (2) (2) (2) (2) (2) (2) (2) (2) (2) (2 | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 | <00 | <50> 0 0 0 (0) (0) (0) | 0 0 |
| tongue | arteritis | | <50> 1 0 0 0 (2) (0) (0) (0) | <50> 2 0 0 0 (4) (0) (0) (0) | <00) (0) (0) (0) 0 0 0 0 0 0 0 0 0 0 | <00) (0) (0) (0) 0 0 0 0 <000> | 0 0 |
| salivary gl | atrophy:focal | | (0) (0) (0) (0) (0) (0) (0) (0) (0) (0) | <50> 1 0 0 0 (2) (0) (0) (0) | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 0 0 0 0 | <50> (0) (0) (0) (0) (0) (0) (0) (0) (0) (0) | 0 0 |
| | lymphocytic infiltration | | 1 0 0 0 (2) (3) (4) (6) (6) | 1 0 0 0 (0) (0) | | 2 0 0 (4) (4) (6) (6) | 0 0 |
| | granulation | | | 1 0 0 0 (2) (3) (3) (4) | (0)(0)(0)(0)(0) | $\begin{pmatrix} 1 & 1 & 0 \\ (2) & (2) & (0) & ($ | 0 0 |
| | Xairliograiuloma | | (0)(0)(0)(0) | 0 1 1 0 (0) (2) (2) (0) | 1 0 0 0 (2) (3) (4) (5) | 0 0 0 | 0 6 |
| stomach | ulcer:forestomach | | <50> 1 0 0 0 (2) (0) (0) (0) | (0) (0) (0) (0) 0 0 0 0 0 (0) (0) | <50> 1 0 1 0 (2) (0) (2) (0) | <50> 3 0 0 (6) (0) (0) (| 0 6 |
| Grade < a > b | 1 : Slight 2 : Moderate 3 :) a : Number of animals examined at the site b : Number of animals with lesion | 3 : Marked due site | 4 : Severe | | | | |

| STUDY NO. : 0580 ANIMAL : MOUS REPORT TYPE : A1 SEX : MALE | : 0580 : MOUSE B&D2F1/Cr1;[Cr.j:EDF1] : A1 : MALE | HISTOPATHOLOGICAL FINDINGS :N ALL ANIMALS (0-105W) | HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W) | | PAGE : |
|--|--|---|--|--|--|
| Огвап | Findings | Group Name Control No. of Animals on Study 50 Grade (%) (%) (%) (%) (%) | 512 ppm 50 1 2 3 4 (%) (%) (%) (%) | 1280 ppm 50 1 2 3 4 (%) (%) (%) (%) | 3200 ppm 50 1 2 3 4 (%) (%) (%) (%) |
| {Digestive system} | (ens) | | | | |
| stomach | hyperplasia:forestomach | <00> (0) (0) (0) (0) (0) (0) | <50> <50> (50> (4) (0) (0) (0) | <pre></pre> | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ |
| | erosion∶glandular stomach | 5 0 0 0 (10) (10) (10) (10) (10) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | 4 1 0 0 (8) (8) (8) (9) (10) | 3 0 0 0 0 0 0 0 |
| | ulcer:glandular stomach | 1 0 0 0 (2) (2) (0) (0) | | (2) (2) (0) (0) | |
| | hyperplasia:glandular stomach | 15 0 0 0 (30) (30) (30) (30) (30) (30) (30 | 13 0 0 0 (26) (26) (30) (30) | 10 0 0 0 (20) (20) (30) (30) | 7 0 0 0 0 (14) (14) (14) (15) (15) |
| | degeneration:glandular stomach | 2 0 0 0 (4) (7) (6) (7) | (0)(0)(0)(0)(0) | | |
| large intes | inflammation | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 | (0)(0)(0)(0) 0 0 0 0 0 0 0 0 | <50> 0 0 1 0 (0) (0) (2) (0) | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 |
| liver | anglectasis | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 0 0 0 0 | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 0 0 0 0 | (0) (0) (0) (0) 0 0 0 0 0 <05> | <50> 1 0 0 0 (2) (0) (0) (0) |

BAIS4

Test of Chi Square

Grade 1 : Slight 2 : Moderate 3 : Marked \langle a \rangle a : Number of animals examined at the site b : Number of animals with lesion (c) c : b / a * 100 Significant difference ; * : P \leq 0.05 **: P \leq 0.01 .

4 : Severe

| STUDY NO. : 058 ANIMAL : MOU REPORT TYPE : AI SEX : MAL | : 0580 : MOUSE B6D2F1/Cr1;[Cr;:BDF1] :: A1 | HISTOPATHOLOGICAL FINDLNGS ALL ANIMALS (0-105W) | HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W) | | PAGE: 9 |
|---|--|---|---|-------------------------------------|--|
| Organ | Findings | Group Name Control No. of Animals on Study 50 Grade 1 2 3 4 (%) (%) (%) (%) | 512 ppm 50 1 2 3 4 (%) (%) (%) | 1280 ppm 50 1 2 3 4 (%) (%) (%) (%) | 3200 ppm 50 |
| (Digestive system) | system) | | | | |
| liver | necrosis:focal | (0) (0) (0) (0) (0) | (50) 0 1 0 0 (0) (2) (0) (0) | <50> <50> (0) (2) (0) (0) | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 |
| | fatty change:central | | | (0) (0) (0) (0) | 0 1 0 0 (0) (0) (0) |
| | inflammatory infiltration | | (0)(0)(0)(0)(0) | 2 0 0 0 (4) (4) (6) (6) (6) | |
| | granulation | | (0) (0) (0) (0) (0) | (2) (0) (0) (0) | $\begin{pmatrix} 1 & 1 & 0 & 0 \\ (2) & (2) & (0) & (0) \end{pmatrix}$ |
| | inflammatory cell nest | 5 0 0 0 (10) (10) (10) (10) | 3 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 | 4 0 0 0 0 (8) (8) (9) (9) (9) | 2 0 0 0 (4) (4) (6) (6) |
| | clear cell focus | 1 0 0 0 (2) (3) (0) (0) | 1 0 3 0 (2) (3) (6) (6) (7) | (0) (2) (0) (0) | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ |
| | acidophilic cell focus | 2 2 1 0 (4)(4)(2)(0) | 1 3 0 0 (2) (3) (6) (0) (0) | 2 1 1 0 (4) (2) (2) (0) | 4 0 1 0 (8) (8) (9) (5) (9) |
| | basophilic cell focus | (2) (2) (0) (0) | 0 0 1 0 (0) (0) (0) | 1 0 0 0 (2) (3) (3) (4) | 1 0 0 0 (2) (3) (4) (6) (6) |
| Grade <a>b b co) Significant | Grade 1: Slight 2: Moderate 3: 1 < a > a : Number of animals examined at the site b : Number of animals with lesion (c) c: b / a * 100 | 3: Marked 4: Severe he site P ≤ 0.01 Test of Chi Square | | | |
| (HPT150) | | | | | BAIS4 |

HISTOPATHOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

| SEX : MALE | : MALE | *************************************** | | | | | | PAGE | נצו |
|--|--|---|--------------------------------|----------------|---|-------------------------|-------------------------------|--|------|
| Organ | Findings | Group Name No. of Animals on Study Grade (9 | Control 1 2 3 (%) (%) | 3 4 | 512 ppm 50 1 2 3 4 (%) (%) (%) (%) | 1 (%) (%) | 1280 ppm 50 3 4 60 (%) (%) | 3200 ppm 50 1 2 3 (%) (%) (%) | 4 % |
| (Digestive system) | system) | | | | | | | | |
| Liver | biliary cyst | | <50> 1 0 C (2) (0) (0 | (0) (0 0 0 | (0)(0)(0)(0) 0 0 0 0 0 0 0 0 | 2 0 (4) (0) | <50> 0 0 0 0) (0) (0) | (250) (0) (0) (0) (0) | 0 0 |
| pancreas | islet cell hyperplasia | | (50) 4 0 C (8) (0) (0 | 0 (0) | <50> 1 0 0 0 (2) (0) (0) (0) | <5 7 0 (14) (0) | (50) (0) (0) (0) | (0) (0) (9) (3 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 | 0 (0 |
| (Urinary system) | (stem) | | | | | | | | |
| kidney | atrophy | | <50> 0 0 1 (0) (0) (2 | 1 0 2) (0) | (0) (0) (0) (0) 0 0 0 0 0 0 0 | (0) (0) (0) (0) | <50> 0 0 0 0) (0) | <050 | 0 0 |
| | cyst | Č | 0) (0) (0) | 0 0 | 1 0 0 0 (2) (3) (3) (3) | (0) (0) | (0) (0) | 1 0 0 (2) (0) (| 00 |
| | hyaline droplet | | | 0 (0 | 2 0 0 0 (4) (4) (6) (6) | 1 0 (2) (0) | (0) (0) | 1 1 0 (2) (2) (0) (| 00 |
| | deposit of hemosiderin | | 1 0 0 ((2) (0) (0 | 0 0 | | 1 0 (2) (0) | (0) (0) | 1 0 0 () () (| 0 0 |
| Grade 1 : Slight < a > a : Number b b : Number (c) c : b / a * | 2 : Moderate of animals examined at of animals with lesion | farked 4 | : Severe | | | | | | |

| SEX : MALE | | | | | | | | | | | | | | | | | | PAGE |
|--|---|--|----------------|------------|-----------------|------|--------|------------------------------|---|--------|--------|--------|--------------------|--|---|----------------|---------------------|------|
| Organ Find | findings | Group Name No. of Animals on Study Grade | on Study | 2 8 | Control 50 3 | 4 8 | 1 3 | 2/ % | 512 ppm 50 3 | 4 8 | 4/8 | | 1280 ppm 50 3 | 4 (5) | 1 (2) | | 3200 ppm 50 | mc 4 |
| ry system | | | | | | | | | | (2) | | | | (8) | 8 | | | |
| kidney Lympi | lymphocytic infiltration | | 1 (2) | ° - 6 - |) (0) 0 (0) | 0 (0 | 3 (9) | (6 (0 (0) | (50) | 0) | 1 (2) | 0 > | <50> 0 0 (0) | 0 0) | 1 2 | 1 0 2) (0) | <50> 0) (0) | 00 |
| scar | | | 1 (2) | 0 0 | 0 (0) | 0 (0 | 0 0 | 0 0 | 0 (6) | 0 (0) | 0) | 0 0 | 0 0 | 0 0) | 1 2 | 1 0 2) (0) | (0) (| 0 0 |
| infl | inflammatory polyp | | 0 0 | 1 (2) | 0 (0) | 0 (0 | 0 (0 | 1 (2) | 1 (2) | 0 (0) | 0) | 1 (2) | 1 (2) | 0 (0) | 0 0) | 0 (0 | (0) (| 0 0 |
| ossi | ossi fication | | 0) | 0 0 | 0 (0) | 0 (0 | (2) | o ô | 06 | 0 (0) | 0) | 0 0 | 0 0 | 0 0) | 1 (2 | 1 0 2) (0) | (0) (| 0 0 |
| hydr | hydronephrosis | | .2 .2 .4 | 0 0 | 3 (9 (| 0 (0 | 1 (2) | 0 0) | | 0) | 1 (2) | 1 (2) | 2 (4 | 0) | 0 0 | . 1 | 2 (4) | 0 0 |
| papi | papillary necrosis | | 0) | 0 0 | 0 (0) | 0 (0 | 1 (2) | (2) | 0 0 | 0) | 0) | 0) | 0 0 | 0) | 0 0 | 0 0 | 0 0 0 | 00 |
| шіле | mineralization:cortex | | 0) | 0 0 | 0 (0) | 0 (0 | 1 (2) | o ô | 0 0 | 0 (0) | 1 (2) | 0 0 | 0 0 | 0) | - 2 | 1 0 2) (0) | (0) | 0 0 |
| ego.i | regeneration:proximal tubule | | 0 0) | 0 0 | 0 (0) | 0 (0 | 0 0 | o ô | 0 0 | 0 (0) | 1 (2) | 0 0 | 0 0 | (O) | 0) | 0 0 | 0 0 0 | 00 |
| Grade 1 : Slight (a > b : Number b : Number (c) c:b/a* | 2 : Moderate of animals examined of animals with lesi | Marked | 4 : Severe | 90 | | | | VI (100A) Label (n. da. sana | 00000 T TO T | | | | | MATERIAL PROPERTY OF THE PROPE | ARREST CONTRACTOR OF THE ARREST CONTRACTOR OF | | | |

PAGE: 12 4 % 0 0 0 0 (0 (0 0 0 0 (0 3200 ppm 50 0 2 0) (0 4) ლ § 00 000 1 1 2) (2) 25 62 00) 0 0) 0 0 000 0 0) 0 0 1 % 0 0 o (i) 4 8 00 00 0 0 0 0 0 0 0 1280 ppm 50 1 4 2) (8) + 0 0 0 e 8 ~ §€ 2) (0 0 - 8 HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105#) 4 % 0 0 00 00 0 (0) 0 0 0 0 0 $\overline{}$ 512 ppm 50 e 86 1 0 0 (2) (2) (3) 00 0 (0) (0) 0 0 0 0 1 0 (2) (3) (62 63 (%) (%) 00 4 8 00 00 00 00 00 0 1 3 (0) (2) (6) ($\overline{}$ 0 0 0 0 1 0 0 (2) (0) (J Control 50 2 3 (%) 0 0 00 (0) (0) (0) (0) 0 0 0 **<49>** 3 0 (0) Test of Chi Square 4 : Severe Group Name No. of Animals on Study Grade 3 : Marked ** : $P \leq 0.01$ 1: Slight 2: Moderate 3: Me a: Number of animals examined at the site b: Number of animals with lesion c: b/a*100 * : P ≤ 0.05 : MOUSE B6D2F1/Cr1;[Cr;:BDF1] inflammatory infiltration inflammation inflammation hyperplasia Significant difference ; dilatation Findings ANIMAL : MOUSE REPORT TYPE : AI SEX : MALE cyst : 0580 (Endocrine system) (Urinary system) STUDY NO. urin bladd pituitary urethra Organ

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| (4) | |
|---|--|
| ATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMA IMALS (0-105W) | |
| 0580 MOUSE B6D2F1/Cr1j[Crj:BDF1] ALL ANL MALE | |
| STUDY NO. : 0580 ANIMAL : MOUSE J REPORT TYPE : A1 SEX : MALE | |

| Organ | Findings | Group Name Control No. of Animals on Study 50 Grade (%) (%) (%) (%) | 512 ppm 50 1 2 3 4 (%) (%) (%) | 1280 ppm 50 4 (%) (%) (%) (%) | 3200 ppm 50 1 2 3 4 (%) (%) (%) |
|--------------------|-----------------------------------|---|---|--|--|
| (Endocrine system) | stem) | | | | |
| pituítary | Rathke pouch | <49> 2 0 0 (4) (0) (0) (0) | <49> 2 0 0 (4) (0) (0) (0) | <pre></pre> | <49> (49> (2) (0) (0) (0) |
| thyroid | cyst | <50> 2 0 0 0 (4) (0) (0) (0) | (0)(0)(0)(0) | <50> 4 0 0 0 (8) (0) (0) (0) | <pre></pre> |
| | focal follicular cell hyperplasia | | | (0)(0)(0)(0)(0) | 0 1 0 0 0 (0) (0) (0) |
| paratkyroid | cyst | <50> 1 0 0 0 (2) (0) (0) (0) | <pre><50> 1 0 0 0 (2) (0) (0) (0)</pre> | (50) 1 0 0 0 (2) (0) (0) (0) | <50> 0 0 0 0 (0) (0) (0) |
| adrenal | spindle-cell hyperplasia | <50> 28 4 0 0 (56) (8) (0) (0) | <pre></pre> | <pre></pre> | <pre></pre> |
| | hyperplasia:cortical cell | | 2 0 0 0 0 (4) (4) (6) (6) | (0)(0)(0)(0)(0) | 1 0 0 0 (0) (0) |
| | hyperplasia:medulla | 0 0 0 0 | (0)(0)(0)(0) | 1 0 0 0 0 (2) (3) (0) (0) (0) | |

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

<a> a : Number of animals examined at the site

b b : Number of animals with lesion

(c) c : b / a * 100

Significant difference ; *: P ≤ 0.05 **: P ≤ 0.01 Test of Chi Square

(IIPT150)

13 (26) ((000 0 (0 0 0 5 (10) (- 8 (22) (0) (0) (0) 00 o ô 00 00 4 8 0 0 0 0 0 0 0 0 0 0 0 0 0 0 (0) (2) (0) (3(%) 1280 ppm 50 2 (%) 2 (4)) 0 0 --| <u>S</u> HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105#) 4 8 00 00 00 00 00 00 2) (0) (0 0 (0) 1 0 0 2) (0) (0) (3 0 0 6 512 ppm 50 e 8 0 (0 0 (0 0 0 0 0 2 8 13 (26) () 0 0 0 0 - 8 0 0 0 4 8 (0)(0)(0)(0)(0) 00 00 06 Control 50 2 3 (%) (%) 1 0 0 (2) (0) (0) 0 0 0 0 (0)(0)(0) 2) (2) (~ € Group Name
No. of Animals on Study
Grade : 0580 : MOUSE B6D2F1/Cr1;[Cr;:BDF1] inflammatory infiltration spermatogenic granuloma mineralization granulation hemorrhage Findings (Reproductive system) REPORT TYPE : A1 SEX : MALE STUDY NO. ANIMAL epididymis semin ves testis Organ

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3200 ppm 50

| Grade | 1 : Slight | 1 : Slight 2 : Moderate | 3 : Marked | , pe | 4 : Severe | |
|------------|----------------|--|--------------|---|--------------------|-------|
| < a > | a : Number o | a : Number of animals examined at the site | at the site | | | |
| ā | b : Number o | b : Number of animals with lesion | tion | | | |
| (°) | c:b/a*100 | 100 | | | | |
| Significan | t difference ; | ignificant difference ; *: $P \le 0.05$ **: $P \le 0.01$ | **: P ≤ 0.01 | Test of | Test of Chi Square | |
| | | | | *************************************** | | |
| (IIPT150) | | | | | | BAIS4 |

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2 0 0 (1) (0) (0) (

mineralization

| STUDY NO. : 0580 ANIMAL : MOUSE B6D2F1/Cx1;[Cr.j:BDF1] REPORT TYPE : A1 SEX : MALE | -1;[Cr.j:BDF1] | HISTOPATHOLOGICAL FINDINGS : ALL ANIMALS (0-105W) | HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W) | | PAGE: 15 |
|--|---|---|---|--|--|
| Organ Findings | Group Name No. of Ania Grade | Group Name Control No. of Animals on Study 50 Grade (%) (%) (%) (%) (%) | 512 ppm 50 1 2 3 4 (%) (%) (%) (%) | 1280 ppm 50 1 2 3 4 (%) (%) (%) | 3200 ppm 50 |
| {Reproductive system} mammary gl duct ectasia | | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 | (50) (0) (0) (0) (0) (0) | <50> (0) (0) (0) (0) (0) | (0) (0) (0) (0) |
| {Nervous system} brain mineralization | = | (50) 12 0 0 0 (24) (0) (0) (0) | (50) (0) (0) (0) (0) (0) (0) | <550> 6 0 0 0 (12) (0) (0) (0) | <50> 12 0 0 0 (24) (0) (0) (0) |
| (Special sense organs/appendage) eye keratitis | (n8 | (50) 0 0 1 0 (0) (0) (2) (0) | (0)(0)(0)(0) 0 0 0 0 0 0 0 0 | <00 (0) (0) (0) (0) (0) | <50> 1 0 0 0 (2) (0) (0) (0) |
| Harder gl hyperplasia | | <50> 1 0 0 0 (2) (0) (0) (0) | <50> 1 0 0 0 (2) (0) (0) (0) | <50> 1 0 0 0 (2) (0) (0) (0) | <50> 0 1 0 0 (0) (2) (0) (0) |
| (Musculoskeletal system) bone osteosclerosis | v | (0) (0) (0) (0) 0 0 0 0 (0) (0) (0) | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 | <50> 0 0 0 0 (0) (0) (0) (0) | (50) 1 0 0 0 (2) (0) (0) (0) |
| Grade 1: Slight <a> a : Number of a b : Number of a c : b / a * 100 Significant difference : * | 1: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 fference; *:P ≤ 0.05 **:P ≤ 0.01 Te | 4 : Severe Test of Chi Square | | | |
| (Hr.11307) | | | | | BAIS4 |

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W) STUDY NO. : 0580
ANIMAL : MOUSE BEDZFI/Crlj[Crj:BDFl]
REPORT TYPE : A1
SEX : MALE

PAGE : 16

| Ory infiltration (2) (3) (3) (3) (3) (4) (6) (6) (7) (8) (8) (8) (8) (8) (8) (8) (8) (8) (8 | | | Group Name No. of Animals on Study Grade | Control 50 3 4 | | mqq s | mdd . |
|--|---|---|--|-----------------------------------|---------------------------------------|--|---|
| Inflammatory infiltration | Organ | Findings. | (%) | (%) | | (%) | 389 |
| Inflammatory infiltration | (Body cavitiv | (รก | | | | | |
| Second S | pleura | inflammatory infiltration | 0 0 | <50> (0) (0) (0) (0) | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 | | (50) 0 1 0 (0) (2) (0) (0) |
| Strict | peritoneum | peritonitis | (O) | <50> (0) (0) (0) (0) | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 | _ | (0) (0) (0) (0) 0 0 0 0 0 000 0000 |
| 1: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100 c: | mesenterium | hemorrhage | 0 | (0) (0) (0) 0 0 0 0 (0) (0) | (0)(0)(0)(0) | (50) 1 0 0 0 (2) (0) (0) (0) | (0)(0)(0)(0) 0 0 0 0 0 0 0 0 0 0 0 0 |
| | Grade <a>ca> b (cc) Significant of | 2: Moderate f animals examined f animals with lesi 100 *: P \$ 0.05 | arked 01 | | | | |

TABLE L 4

HISTOPATHOLOGICAL FINDINGS: NON-NEOPLASTIC

LESIONS: FEMALE: ALL ANIMALS

| STUDY NO. : 058 ANLMAL : MOU REPORT TYPE : A1 SEX : FEM | : 0580 : MOUSE B6DZF1/Crlj[Crj:BDF1] : A1 : FEMALE | HISTOPATH ALL ANIMA | OCCCAL FIN | OLINGS : NC | HISTOPATBOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105%) | | PAGE : 17 | 2 |
|---|--|---|--|-------------|---|--|--|---|
| Organ | Findings | Group Name No. of Animals on Study Grade (%) | Control 50 2 3 (%) (%) | 4 (%) | 512 ppm 50 1 2 3 4 (%) (%) (%) | 1280 ppm 50 1280 ppm 50 1280 ppm 50 12 3 4 168 ppm 68 18 18 18 18 18 18 18 18 18 18 18 18 18 | 3200 ppm 50 (%) (%) (%) | 1 |
| {Integumental | [Integumentary system/appandage] | | | | | | | |
| skin/app | ulcer | 60 | <50> 1 0 (2) (0) (| 0 (0) | (0) (0) (0) (0) 0 0 0 0 <05> | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 | |
| | inflammation | 1 (2) (| 0 (0) | (O) | | (0)(0)(0)(0) | (0)(0)(0)(0) | |
| | scab | 1 (2) (| 0 (0) | 0 (0) | (0)(0)(0)(0)(0) | (0)(0)(0)(0) | 1 0 0 0 (2) (2) (3) (4) (5) | |
| | epidermal cyst | (2) (| 0 (0) | 0 (0) | | | (0)(0)(0)(0) | |
| (Respiratory system) | system) | | | | | | | |
| nasal cavit | mineralization | 60) | <20> (0) (0) (0) (0) (0) (0) (0) (0 | (O) | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 | (0) (0) (0) (0) 0 0 0 0 <09> | <50> 1 0 0 0 (2) (0) (0) (0) | |
| | inflammation | 0 0 | 0 (0) | 0 (0) | 1 0 0 0 (2) (3) (4) (5) | (0)(0)(0)(0) | (0) (0) (0) (0) | |
| | eosinophilic change:olfactory epithelium | 23 (46) | 5 0 (10) (0) (| (O) | 18 1 0 0 (36) (36) (2) (0) (0) | 23 2 0 0 (46) (46) (4) (0) (0) | 16 0 0 0 ** (32) (0) (0) (0) | |
| Grade <a>> b | Grade 1 : Slight 2 : Moderate 3 : h < a > a : Number of animals examined at the site b : Number of animals with lesion (c) c : b / a * 100 Significant difference ; * : $\Gamma \le 0.05$ ** : $\Gamma \le 0.05$ | 3 : Marked 4 : Severe ne site P ≤ 0.01 Test of Chi Square | | | | | | , |
| (IIPT150) | | | | | | | BAIS4 | |

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUBMARY) ALL ANIMALS (0-105#)

STUDY NO. : 0580
ANIMAL : MOUSE BGDZF1/Cr1,i[Cr;:BDF1]
ALL ANIMALS
REPORT TYPE : A1
SEX : FEMALE

| | Group Name No. of Animals on Study | | 512 ppm 50 | 1280 ppm 50 | 3200 ppm 50 |
|----------------------|--|-----------------------------------|---------------------------------------|--|---|
| Organ | Findings | (%) (%) (%) (%) | (%) (%) (%) (%) | (%) (%) (%) (%) | (%) (%) (%) (%) |
| (Respiratory system) | system} | | | | |
| nasal cavit | eosinophilic change:respiratory epithelium | <pre></pre> | <pre></pre> | <50> 19 17 3 0 (38) (34) (6) (0) | <50> 18 13 1 0 * (36) (26) (2) (0) |
| | respiratory metaplasia:olfactory epithelium | 13 2 0 0 (26) (4) (0) (0) | 10 0 0 0 (20) (20) (0) (0) | 8 1 0 0 (16) (2) (0) (0) | 13 1 0 0 (26) (20) (00) |
| | respiratory metaplasia:gland | 35 9 0 0 (70) (70) (18) (0) (0) | 34 9 0 0 (68) (18) (0) (0) | 40 5 0 0 (80) (80) (80) (80) | 36 5 0 0 (72) (10) (0) (0) |
| | squamous cell metaplasia:respiratory epithelium | 2 0 0 0 (4) (4) (6) (6) (6) | 1 0 0 0 0 (2) (2) (3) (4) | | |
| | ulcer:respiratory epithelium | 1 0 0 0 (2) (2) (3) (4) (4) | 1 0 0 0 (2) (2) (3) (4) | | |
| паѕорһагупх | eosinophilic change | <50> 3 0 0 0 (6) (0) (0) | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 | <pre></pre> | (0) (0) (0) (0) 3 0 0 0 (0) (0) (0) |
| lung | lymphocytic infiltration | (50) (2) (0) (0) (0) | \$ 0 (0) (0) (0) (0) (0) | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 0 0 0 | (50) 1 0 0 0 (2) (0) (0) (0) |
| Grade < a > b | 1: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with lesion | 4 : Severe | | | |

| Organ Findings (Ruspiratory system) lung accumulation bone marrow augiectasis | Findings ctum) accumulation of foamy cells bronchiolar-alveolar cell hyperplasia ystem) | Group Name Control No. of Animals on Study 50 Grade (%) (%) (%) (%) 7 0 0 (14) (0) (0) (0) | 3 4 (%) (%) | 512 ppm | | VXXX |
|---|--|---|----------------|--|---|--|
| y sys | ion of foamy cells ur-alveolar cell hyperplasia | (50) (0) (0) | | 1 2 3 4 (%) (%) (%) | 1280 ppm 50 4 (%) (%) (%) (%) | 200 ppm 50 1 2 3 4 (%) (%) (%) |
| tic s | ion of foamy cells r-alveolar cell hyperplasia | <50> 0 (0) | | | | |
| tic s | u-alveolar cell hyperplasia | | (0) (0 | <50> 12 0 0 (24) (0) (0) (0) | <50> 4 0 0 (8) (0) (0) (0) | <pre></pre> |
| tic s | | 3 0 (9) (9) | 0 0 | | 3 0 0 0 (6) (7) (8) (8) (8) | |
| | | | | | | |
| | ²³ | (90 (0) (0) (0) (0) (0) (0) (0) (| 0 0 | (50) 1 0 0 0 (2) (0) (0) (0) | (0)(0)(0)(0) 0 0 0 0 0 0 0 0 0 0 | (20) (0) (0) (0) (0) (0) (0) (0) (0) (0) (|
| granulation | щ | 0 0 0 | (O) (O O O | | 1 0 0 0 (2) (2) (3) (4) (4) | 1 0 0 0 (2) (3) (4) (5) |
| increased b | increased hematopoiesis | 0 0 | 0 0 | (0)(0)(0)(0) | (0)(0)(0)(0) | (2) (0) (0) (0) |
| myelofibrosis | sis | 1 1 (2) (2) (| (0) (0 0 0 | (2) (0) (0) (0) | | |
| splcen deposit of | deposit of hemosiderin | <50> 5 0 (10) (0) (| (0) (0 0 0 | <pre></pre> | <50> 4 0 0 0 (8) (0) (0) (0) | (50) 11 0 0 0 (22) (0) (0) (0) |
| Grade 1: Slight <a> a : Number of an b : Number of an c : b / a * 100 Significant difference ; * | 2: Moderate imals examined at the imals with lesion : P \leq 0.05 **: P | 3: Marked 4: Severe site ≤ 0.01 Test of Chi Square | | | | |

| ANIMAL : MOU REPORT TYPE : AI SEX : FEN | : MOUSE BEDZF1/Cr1,[Cr.j:BDF1] PE: A1 : FEMALE | | ALL ANIMAL | S (0-105W) | | ALL ANIMALS (0-105W) | : | | | | | | _ | PAGE: 20 |
|---|--|--|------------|------------------------|-----------|--|-------------------------------|---|-----------------------|---------------------------|------|---------------------|----------------------------------|----------|
| Organ | Findings | Group Name No. of Animals on Study Grade | s on Study | Control 50 3 (%) (%) | 4 (%) | 1 (%) (%) | 512 ppm 50 3 4 | • | 12 1 2 (%) (%) | 280 ppm 50 3 (%) | (%) | 1 (%) | 3200 ppm 50 2 3 (%) (%) | 4 (%) |
| (Hematopoi | (Hematopoietic system) | | | | | | | | | | | | | |
| spleen | deposit of melanin | | 1 (2) (| <50> 0 0 0 0 | 0 (0) | 1 0 (2) (2) (0) | <50> 0 0 0 0) (0) (0) | _ | (5) 1 0 2) (0) |) (0 0 00 | 0 0 | 0 0 | <50> 0 0 0) (0) | 0 0 |
| | extramedullary hematopoiesis | | 7 (14) (| 5 2 (10) (4) | o (o) | 11 2 (22) (4) | (0) (0) | J | 14 3 28) (6) | 6 (12) (| 0 (0 | 13 6 (26) (12) | 3 (9) | 0) |
| | follicular hyperplasia | | 0 0 | 1 0 2) (0) | 0 (0) | 0 3 (0) | (0) (0) | Ü | 1 1 2) (2) | 1 (2) (| 0 (0 |) (0 0 | 0 1 0) (2) | 0 (0 |
| Circulato | (Circulatory system) | | | | | | | | | | | | | |
| heart | thrombus | | 0 0 | <50> 1 0 2) (0) | 0 (6 | , 1 0 (2) (3) (4) | <50> 0 0 0 0) (0) (0) | J | (5) (1) (2) (3) | 0 0 0 | 0 (0 | 0 0 | <50> 1 0 2) (0) | 0 0 |
| | mineralization | | 0 0 | 0 0 | 0 (0) | (0) (0) | (0) (0) | Ü | 1 0 2) (0) | 0 (0) | o (o | 0 0 | 0 (0 | 0 0 |
| | inflammatory infiltration | | 0 (0) | (0) (0 0 0 | 0 (0) | (0) (0) | (0) (0) (| Ü | 0 0 | 0 (0) | 0 (0 | 1 (2) (| 0 0 | ° 6 |
| | arteritis | | 0 (0) | 0 0 | 0 (0) | (0) (0) | (0)(0) | _ | 1 0 2) (0) | 0 (0) | 0 (0 | 1 (2) (| 0 0 | 0 (0 |
| Grade (a > b (c) Significan | Grade 1: Slight 2: Moderate 3:) <a> a : Number of animals examined at the site b : Number of animals with lesion (c) c: b / a * 100 Similicant difference : *: P ≤ 0.05 **: P ≤ 0. | farked 01 1 | 4 : Severe | | | ************************************** | | | | | | | | |

| (SUMMARY) | |
|--------------------|---------------------|
| LESIONS | |
| : NON-NEOPLASTIC 1 | |
| FINDINGS | (M) |
| HISTOPATHOLOGICAL | ALL ANTHALS (0-105) |
| | |
| | |
| | |
| | Ξ |

| REPORT TYPE SEX | : A1 : FEMALE | | | | PAGE : |
|---|---|---|---|--|--|
| Organ | Findings | Group Name Control No. of Animals on Study 50 Grade 1 2 3 4 (%) (%) (%) (%) | 512 ppm 50 1 2 3 4 (%) (%) (%) (%) | 1280 ppm 50 1 2 3 4 (%) (%) (%) | 3200 ppm 50 1 2 3 4 (%) (%) (%) |
| (Digostive system) | ystem) | | | | |
| oral cavity | thrombus | (0) (0) (0) (0) 0 0 0 0 <05> | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 0 0 0 0 | <50> 0 0 1 0 (0) (0) (2) (0) |
| tooth | dysplasia | <50> 2 0 0 0 (4) (0) (0) (0) | <50> 0 2 0 (0) (4) (0) (0) | <50> 3 0 0 0 (6) (0) (0) | <550> 0 0 0 0 (0) (0) (0) |
| tongue | inflammation | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 | <50> 1 0 0 0 (2) (0) (0) (0) | <50> (0) (0) (0) (0) (0) (0) (0) (0) (0) (0) | <pre></pre> |
| salivary gl | lymphocytic infiltration | <50> 4 0 0 0 (8) (0) (0) (0) | 3 0 0 0 0 0 0 (0 0) (0 0) (0 0) | <50> 4 0 0 0 (8) (0) (0) (0) | <50> 4 0 0 0 (8) (0) (0) (0) |
| stomach | ulcer:forestomach | <50> 2 0 0 0 (4) (0) (0) (0) | (50) 1 0 0 0 (2) (0) (0) (0) | <50> (0) (0) (0) (0) (0) | <50> 1 0 0 0 (2) (0) (0) (0) |
| | hyperplasia:forestomach | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | 3 0 0 0 0 0 0 0 0 | (0) (0) (0) (0) (0) | 1 0 0 0 (2) (3) (4) |
| | erosion:glandular stomach | 3 1 0 0 (6) (7) (10) (10) | 8 0 0 0 0 0 (16) (16) (16) | 1 0 0 0 (2) (3) (4) (5) | 3 0 0 0 0 (0) (0) (0) |
| Grade <a>><a>><ba>b<ba>(c)</ba></ba> <a>Significant | Grade 1: Slight 2: Moderate 3: N < a > a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 c: b / a * 100 c: b / a * 100 c: c: b / a * 100 c: c: b / a * 100 c: c: c: b / a * 100 c: c: c: b / a * 100 c: c: c: b / a * c: c: b / a * c: c: c: b / a * c: | 3 : Marked 4 : Severe the site . P < 0.01 Tack of Chi Samme | | | |

| SEX : FEM | : FEMALE | | | | | PAGE : |
|--------------------|---|--|--|---|--|--|
| Organ | Findings | Group Name No. of Animals on Study Grade | Control y 50 1 2 3 4 (%) (%) (%) (%) | 512 ppm 50 1 2 3 4 (%) (%) (%) | 1280 ppm 50 4 (%) (%) (%) (%) | 3200 ppm 50 1 2 3 4 (%) (%) (%) |
| (Digestive system) | ys (cm) | | | | | |
| stomach | ulcer:glandular stomach | | <pre></pre> | <00 (0) (0) (0 | <pre></pre> | <50> 1 0 0 0 (2) (0) (0) (0) |
| | hyperplasia:glandular stomach | 1 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 3 | 13 0 0 0 26) (0) (0) (0) | 6 0 0 0 (12) (12) (13) (13) (13) (14) | 4 0 0 0 * (8) (8) (9) | 6 0 0 0 (12) (12) (13) (13) (13) (14) |
| small intes | lymphocytic infiltration | | <pre><20></pre> <pre>(0) (0) (0) (0)</pre> | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 | <pre></pre> | <50> 1 0 0 0 (2) (0) (0) (0) |
| liver | angiectasis | | 3 (50) 3 0 0 0 6) (0) (0) (0) | <50> 2 0 0 0 (4) (0) (0) (0) | <50> 1 0 0 0 (2) (0) (0) (0) | <50> 0 2 0 (0) (4) (0) (0) |
| | necrosis:centra] | | 2) (0) (0) (0) | | | |
| | necrosis:focal | Č | 0 0 0 0 0 | | (0)(0)(2)(0) | 0 0 0 0 0 |
| | inflammatory infiltration | J | 2) (0) (0) (0) | | | 0 0 0 0 0 |
| Grade < a > b | 1: Slight 2: Moderate 3: 9 a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 | 3 : Marked 4 : Severe | /ere | | | |

| STUDY NO. ANLMAL REPORT TYPE SEX | : 0580 : MOUSE B6D2F1/Cr1;[Cr.j:BDF1] ; : A1 : FEMALE | ALL 1 | HISTOPATHOLOGICAL FINDINGS ALL ANIMALS (0-105W) | HISTOPATHOLOGICAL FINDINGS :NOW-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105%) | | PAGE : |
|----------------------------------|--|---------------------------------------|--|--|--|--|
| | | Group Name No. of Animals on Study | Control y 50 | 512 ppm 50 | 1280 ppm 50 | 3200 ppm |
| Organ | Findings. | Grade | (%) | (%) (%) (%) (%) | (%) (%) (%) (%) | $\begin{array}{c ccccccccccccccccccccccccccccccccccc$ |
| (Digestive system) | system) | | | | | |
| liver | lymphocytic infiltration | Č | <50> 1 0 0 0 2) (0) (0) (0) | (0) (0) (0) (0) 0 0 0 0 <05> | <50> 0 0 0 0 (0) (0) (0) (0) | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 |
| | granulation | 7 3 3 | 11 1 0 0 22) (2) (0) (0) | 16 1 0 0 (32) (2) (0) (0) | 20 1 0 0 (40) (2) (0) (0) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |
| | inflammatory cell nest | | 4 0 0 0 8) (0) (0) (0) | | (2) (0) (0) (0) | $\begin{pmatrix} 1 & 0 & 0 & 0 \\ 2 & (0) & (0) & (0) \end{pmatrix}$ |
| | extramedullary homatopojesis | Č | 2) (0) (0) (0) | (0) (0) (0) (0) | 3 0 0 0 (0) (9) (9) | (2) (0) (0) (0) |
| | clear cell focus | | (0) (0) (0) (0 0 0 | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ | (0) (0) (0) (0) (0) | |
| | acidophilic cell focus | | 1 1 2 0 2) (2) (4) (0) | 1 1 4 0 (2) (2) (8) (0) | 1 2 3 0 (2) (4) (6) (0) | $ \begin{array}{cccccccccccccccccccccccccccccccccccc$ |
| | basophilic cell focus | | (0)(0)(0)(0)(0 | | 2 0 0 0 (4) (4) (6) (6) (6) | 1 0 0 0 () () () () |
| | biliary cyst | Č | (0) (0) (0) (0 0 0 | 1 0 0 0 (2) (2) (3) (4) (4) | (0) (0) (0) (0) (0) | (2) (0) (0) (0) |
| Grade < a > b (c) Significant | Grade 1: Slight 2: Moderate 3: N < a > a : Number of animals examined at the site b : Number of animals with lesion (c) c: b / a * 100 Significant difference ; *: $P \le 0.05$ **: $P \le 0.05$ | farked 4: | Severe i Square | | | |
| (IIPT150) | | | | | | BAIS |

PAGE: 23

| STUDY NO. : 058 ANIMAL : MOU REPORT TYPE : A1 SEX : FEM | : 0580 : MOUSE BEDZFI/Crlj[Crj:BDF1] : Al : FEWALE | HISTOPATHOLOGICAL FINDINGS :1 ALL ANIMALS (0-105#) | HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105#) | (A | PAGE |
|---|--|--|--|--|--|
| Organ | Group No. of Grade Findings | Group Name Control No. of Animals on Study 50 Grade 1 2 3 4 (%) (%) (%) (%) | 512 ppm 50 1 2 3 4 (%) (%) (%) | 1280 ppm 50 1 2 3 4 (%) (%) (%) | 3200 ppm 50 1 2 3 4 (%) (%) (%) (%) |
| (Digestive system) | (m) sks(rem) | | | | |
| liver | mineralization:central | (0) (0) (0) (0) 0 0 0 0 (0) (0) (0) | <50> 1 0 0 0 (2) (0) (0) (0) | <00 (0) (0) (0) (0) (0) (0) (0) (| (0)(0)(0)(0) |
| | hyperplasia:Ito-cell | | | | 0 1 0 0 (0) (0) (0) (0) |
| gall bladd | hyperplasia | <pre></pre> | (0)(0)(0)(0) | <20\$ (0) (0) (0) (0) (0) (0) | <50> 0 1 0 0 (0) (2) (0) (0) |
| pancreas | lymphocytic infiltration | (0)(0)(0)(0) 0 0 0 0 0 0 0 0 | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 | <50> 1 0 0 0 (2) (0) (0) (0) | <50> (0) (0) (0) (0) |
| | islet cell hyperplasia | | | | 2 0 0 0 (4) (4) (6) (6) (6) |
| (Urinary system) | stem) | | | | |
| kidney | cyst | <50> 0 1 0 0 (0) (2) (0) (0) | (0)(0)(0)(0) | <pre></pre> | (0)(0)(0)(0) |
| Grade <a>b b (c) Significant | Grade 1: Slight 2: Moderate 3: Marked $\langle a \rangle$ a : Number of animals examined at the site b : Number of animals with lesion (c) c: b / a * 100 Significant difference; *: P \leq 0.05 **: P \leq 0.01 | ted 4 : Severe Test of Chi Square | | | |
| (IIPT150) | | | | | |

| Group Nan No. of Ar Grade frade frade frade framyloid framyloid ic infiltration ory polyp ory polyp ic infiltration ory militration ory mil | ANLMAL REPORT TYPE SEX | : NOUSE BGD2F1/Cr1,[Crj:BDF1] : FEMALE | | יורד זוואדאשערבט (במסש) (אפטר | , | | | | | | | | | | | PAGE: |
|--|------------------------------|---|--------------------------------------|-------------------------------|--------------------------------|---------------|---|--|---------------|-------|------------------------|---------------|---------------|---------------|---------------------------|-------|
| Payline Grouplet | gan | Findings | Group Name No. of Animal Grade | s on Study (%) | Contro 50 2 3 (%) (%) | 1 | (%) | 512 p 50 2 (%) (9 | | 1 (%) | 1280 50 2 (%) | | | (4) | 3200 ppi 50 3) (%) | |
| Modeline droplet | rinary s | :Asrcm) | | | | | | | | | | | | | | |
| deposit of ampleid (0) (0) (0) (0) (0) (0) (0) (0 | dney | hyaline droplet | | 3 | <50> 3 6) (| $\overline{}$ | 1 (3) | | _ | 8 | 4 8 | $\overline{}$ | Ç | | <50> 5) (10) | |
| inflammatory infiltration (0) (0) (0) (0) (0) (0) (0) (0 | | deposit of amyloid | | 0 0 | 0 0 | $\overline{}$ | 0 | \smile | \smile | 0 0 | 0 0 | \smile | C | \smile | \smile | |
| Jymphocytic infiltration 8 | | inflammatory infiltration | | 0 0 | 。 0 0 | $\overline{}$ | 0 0 | ~ | $\overline{}$ | 00 | - 3 | \smile | J | $\overline{}$ | $\overline{}$ | |
| scar inflammatory polyp inflammatory polyp ossification 1 | | lymphocytic infiltration | | | \$\tag{2}\$ | \smile | 9 | \smile | \smile | | 0 0 | \smile | $\overline{}$ | $\overline{}$ | $\overline{}$ | |
| inflammatory polyp (2) (4) (0) (0) (2) (0) (1) (0) (2) (0) (2) (0) (2) (0) (4) (0) (6) (6) (6) (6) (6) (6) (6) (6) (6) (6 | | scar | | 2) | 0 6 | $\overline{}$ | 06 | $\overline{}$ | $\overline{}$ | 0 0 | 00 | $\overline{}$ | J | \smile | <u> </u> | |
| 1 0 0 0 0 0 0 0 0 0 | | inflammatory polyp | | 2 1 | 2 (4) (| \smile | 2 (4) | <u> </u> | <u> </u> | 1 3 | 0 0 | ~ | J | _ | _ | |
| lydronephrosis | | ossification | | 23 |) 0 0 | $\overline{}$ | 23 | \smile | $\overline{}$ | 0 0 | 0 6 | $\overline{}$ | <u> </u> | $\overline{}$ | J | |
| 1 : Slight 2 : Moderate 3 : Marked a : Number of animals examined at the site b : Number of animals with lesion c : b / a * 100 | | lydronephrosis | | 0 0 | 2 4) (| \smile | 1 (5) | $\overline{}$ | $\overline{}$ | 0 0 | 0 0 | \smile | \sim | $\overline{}$ | | |
| | ade a > b | 2 : Moderate of animals examined of animals with lesi | farked | 4 : Severe | | | enne enne en | 70 100 100 100 100 100 100 100 100 100 1 | | | | | | | | |

| Organ Findings. [Urinary system] | | | | | | | . 7007 |
|---|---|--|----------------------------|------------------------|---|---|--|
| ry system) | SS | Group Name No. of Animals on Study Grade | 1 2 %) (%) | Control 50 3 4 (%) (%) | 512 ppm 50 1 2 3 4 (%) (%) (%) (%) | 1280 ppm 50 1 2 3 4 (%) (%) (%) (%) (%) | 3200 ppm 50 1 2 3 4 (%) (%) (%) (%) |
| | | | | | | | |
| | regeneration:proximal tubule | Ç | (00) (0) | (0) (0 0 0 | (0) (0) (0) (0) 0 0 0 0 (0) (0) (0) | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 | (50) 0 0 1 0 (0) (0) (2) (0) |
| urin bladd dilatation | ion | J | <50> 1 1 (2) (2) (| (0) (0 0 0 | (50) 1 0 0 0 (2) (0) (0) (0) | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 | (0)(0)(0)(0) |
| inflamm | inflammatory infiltration | J | 1 0 (2) (-0) (- | (0) (0 0 0 | (0)(0)(0)(0)(0) | (0)(0)(0)(0)(0) | (0)(0)(0)(0)(0) |
| 1 ymphoc; | lymphocytic infiltration | Ü | 0 0 0 | 0 0 | 1 0 0 0 (2) (2) (3) (4) (4) | 1 0 0 0 (2) (3) (3) (4) | (0) (0) (0) (0) |
| (Endocrine system) | | | | | | | |
| pituitary angiectasis | asis | | (0) (0) (0) (0) | (0) (0 0 0 | (50) 1 0 0 0 (2) (0) (0) (0) | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 | (50) 1 0 0 0 (2) (0) (0) (0) |
| cyst | | | 0 (0) | (0) (0 0 0 | (0)(0)(0)(0) | 1 0 0 0 (2) (3) (6) (6) | 2 0 0 0 (4) (4) (6) (6) |
| Grade 1 : Slight (a 2) a : Number b b : Number (c) c : b / a * | 2: Moderate of animals examined at the of animals with lesion 100 | Narked 4 | : Severe | | | | |

| HISTOPATHOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMM) | N-NEOPLASTIC LESIONS | (SUMMARY) |
|--|----------------------|-----------|
| ALL ANIMALS (0-105W) | | |

| HISTOPATHOLOCICAL FINITNGS : NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W) | PAGE: 27 | Group Name Control 512 ppm 1280 ppm 3200 ppm 3200 ppm No. of Animals on Study 50 |
|---|--------------|--|
| : MOUSE BED2F1/Cr1j[Crj:BDF1] TYPE : Al | SEX : FEMALE | Group Name No. of Animals on Study |

| | | oroup name Control No. of Animals on Study 50 | 512 ppm 50 | 1280 ppm 50 | 3200 ppm |
|--------------------|------------------------------|--|---|--|--|
| Organ | Findings | Grade 1 2 3 4 (%) (%) (%) (%) | 1 2 3 4 (%) (%) (%) (%) | (%) (%) (%) (%) | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ |
| {Endocrine system} | (ketem) | | | | |
| pituitary | hyperplasia | (50) 9 5 3 0 (18) (10) (6) (0) | <pre></pre> | <50> 8 4 4 0 (16) (8) (8) (0) | <50> 7 6 4 0 (14) (12) (8) (0) |
| | Rathke pouch | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | | (0) (0) (0) (0) (0) 0 0 0 | |
| thyrold | cyst | <pre></pre> | (0) (0) (0) (0) 0 0 0 0 0 000 | <50> 2 0 0 0 (4) (0) (0) (0) | (6) (0) (0) (0) (0) (0) (0) (0) |
| | lymphocytic infiltration | | 1 0 0 0 0 (2) (2) (3) (4) | (0) (0) (0) (0) (0) 0 | |
| parathyroid | cyst | (0)(0)(0)(0) 0 0 0 0 0 0 0 0 0 0 | (50) 1 0 0 0 (2) (0) (0) (0) | <50> 1 0 0 0 (2) (0) (0) (0) | (0)(0)(0)(0) 0 0 0 0 0 0 0 0 0 0 0 0 |
| adrenal | fatty change | <50> 0 0 1 0 (0) (0) (2) (0) | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 | (0)(0)(0)(0) 0 0 0 0 0 0 0 0 | (0)(0)(0)(0) 0 0 0 0 0 0 0 0 0 0 0 0 |
| | extramedullary hematopoiesis | | 0 0 0 0 0 | (2) (0) (0) (0) | |

Grade 1: Slight 2: Moderate 3: Marked 4: Severe (a > a: Number of animals examined at the site b b: Number of animals with lesion (c) c: b/a*100 Significant difference: *: P \leq 0.05 **: P \leq 0.01 Test of Chi Square (HPT150)

| (SUMMARY) | |
|--|--------------------------|
| HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMM | |
| GICAL FINDINGS : | (10) |
| HISTOPATHOLOGICAL | make of constitution the |
| | |
| | |

| REPORT TYPE : AI SEX : FEM | . MOOSE BODGEL/OFLICE, BUFIL : FAIL | ALL ANIMALS (U-1050) | | | PAGE: 28 |
|---|--|--|---|--|--|
| Organ | Findings | Group Name Control No. of Animals on Study 50 Grade 1 2 3 4 (%) (%) (%) (%) | 512 ppm 50 1 2 3 4 (%) (%) (%) | 1280 ppm 50 4 (%) (%) (%) | 3200 ppm 50 1 2 3 4 (%) (%) (%) (%) |
| (Endocrine system) | ;ys.tem} | | | | |
| adrenal | spindle-cell hyperplasia | $\langle 50 \rangle$ 34 13 0 0 (68) (26) (0) (0) | <pre></pre> | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ | <50> 40 9 0 (80) (18) (0) (0) |
| | hyperplasia:cortical cell | | (0)(0)(0)(0)(0) | 1 0 0 0 (2) (2) (3) (4) (4) | (0)(0)(0)(0) |
| | focal fatty change:cortex | 1 0 0 0 () () () () () | 2 1 0 0 (4) (5) (6) (6) | (0)(0)(0)(0) | 2 0 0 0 (4) (4) (6) (6) |
| (Reproductive system) | 'o system) | | | | |
| ovary | angiectasis | (0)(0)(0)(0) 0 0 0 0 0 0 0 0 0 0 0 0 | (0) (0) (0) (0) (0) | <00 (0) (0) (0) (0) (0) | $\begin{array}{cccccccccccccccccccccccccccccccccccc$ |
| | thrombus | 0 0 1 0 (0) (0) (2) (0) | | | 0 0 1 0 (0) (0) (0) |
| | cyst | 3 1 0 0 (6) (2) (0) (0) | 0 0 1 0 (0) (0) (0) | 3 0 2 0 (6) (6) (4) (0) | 0 1 0 0 (0) (0) (0) |
| | lymphocytic infiltration | 1 0 0 0 (2) (3) (4) (6) (6) (6) | (0)(0)(0)(0)(0) | | |
| Grade <a>b <a>c <a>c<!--</td--><td>Grade 1: Slight 2: Moderate 3:) <a>a> Number of animals examined at the site b b: Number of animals with lesion c c b a * 100 c Significant difference; * : P \leq 0.05 **: P \leq 0.</td><td>3 : Marked 4 : Severe e site ≥ 0.01 Test of Chi Square</td><td></td><td></td><td></td> | Grade 1: Slight 2: Moderate 3:) <a>a> Number of animals examined at the site b b: Number of animals with lesion c c b a * 100 c Significant difference; * : P \leq 0.05 **: P \leq 0. | 3 : Marked 4 : Severe e site ≥ 0.01 Test of Chi Square | | | |

| STUDY NO. : 058 ANIMAL : MOU REPORT TYPE : AI SEX : FEM | : 0580 : MOUSE B6D2F1/Cr1;[Cr;:BDF1] : A1 : FEMALE | HISTOPATH ALL ANIMO | HISTOPATHOLOGICAL FIND ALL ANIMALS (0-105%) | INGS : NON | HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-105W) | (SUMMARY) | | PAGE : 29 |
|--|---|--|--|------------|---|-----------|---|--|
| | | Group Name | Control | | 512 ppm | | 1280 ppm | 3200 ррт |
| Organ | Findings | Grade (%) | | (%) | | 4 (% | 50 (%) (%) (%) (%) | 50 1 2 3 4 (%) (%) (%) |
| (Reproductive system) | system) | | | | | | | |
| ulerus | stromal hyperplasia | 0 0 | (0) (0) (0) (0) (0) | 0 (0 | <pre> (0) (0) (0) (0) (0) </pre> | 0 (6 | <00 (0) (0) (0) (0) (0) (0) (0) (0) (0) (| <50> 1 0 0 0 (2) (0) (0) (0) |
| | cystic endometrial hyperplasia | 28 (56) (| 0 0 0 | 0 (0 | 32 1 0 (64) (2) (0) (| 0 0 | 29 0 0 0 0 (58) (69) (69) | 29 0 0 0 (58) (58) (60) (60) |
| (Nervous system) | .em) | | | | | | | |
| brain | mineralization | 5 (10) (| <50> 0 0 (0) (0) (| 0 (0 | <50> 10 0 0 (20) (0) (0) (| 0 0 | \$ 0 (0) (0) (0) (0) (0) | (50) 4 0 0 0 (8) (0) (0) (0) |
| (Special sens | (Special sense organs/appendage) | | | | | | | |
| еуе | keratitis | 2 (7) (7) | <50> 0 0 0) (0) (| 0 (0 | <50> 0 1 0 (0) (2) (0) (| 0 (0 | <pre></pre> | (20) (0) (0) (0) (0) (0) |
| | degeneration:cornea |) (0) | 1 0 2) (0) (| 0 (0 | 2 0 0 (4) (0) (0) (| 0 (0 | | (2) (0) (0) (0) |
| Grade 1: Slight <a> a : Number b b : Number (c) c : b / a * Significant difference ; | 1: Slight 2: Moderate 3::) a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 hifference; *:P ≤ 0.05 **:P ≤ 0. | 3 : Marked 4 : Severe site ≤ 0.01 Test of Chi Square | | | | | | |
| (HPT150) | | | | | | | | BAIS4 |

| STUDY NO. : 058C ANIMAL : MOUS REPORT TYPE : AI SEX : FEM. | : 0580 : WOUSE BEDZF1/Crlj[Crj:EDF1] : A1 : FEMALE | HISTOPATHOLOGICAL FINDINGS : ALL ANIMALS (0-105W) | HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0-1054) | | PAGE: 30 |
|---|---|--|--|--|--|
| Organ | Findings | Group Name Control No. of Animals on Study 50 Grade 1 2 3 4 (%) (%) (%) (%) | 512 ppm 50 1 2 3 4 (%) (%) (%) (%) | 1280 ppm 50 | . 3200 ppm 50 (%) (%) (%) |
| (Special sense | (Special sense organs/appendage) | | | | |
| eye | mineralization:cornea | <50> 0 0 0 0 0 0 0 0 0 0 0 0 | (0) (0) (0) (0) 0 0 0 0 0 <005> | <50> 2 0 0 0 (4) (0) (0) (0) | <pre></pre> |
| Harder gl | hyperplasia | <50> 0 0 0 0 0 0 0 0 0 0 0 0 | (50) 2 0 0 0 (4) (0) (0) (0) | <00 | (0) (0) (0) (0) 0 0 0 0 0 0 0 0 0 |
| (Musculoskeletal system) | tal system) | | | | |
| muscle | mineralization | <50> 1 0 0 0 (2) (0) (0) (0) | (0) (0) (0) (0) 0 0 0 0 0 0 0 | <50> 0 0 0 0 (0) (0) (0) (0) | (0) (0) (0) (0) 0 0 0 0 <05> |
| attoq | osteosclerosis | <50> 0 0 0 0 0 0 0 0 0 0 0 | (0) (0) (0) (0) 0 0 0 0 <05> | <50> 0 0 0 0 (0) (0) (0) | (50) 1 0 0 0 (2) (0) (0) (0) |
| Grade 1: Slight (a > a : Number b b : Number (c) c: b/a* Significant difference: (HPT150) | 2: Moderate of animals examined at the of animals with lesion : 100 *: P ≤ 0.05 **: P | 3: Marked 4: Severe site ≤ 0.01 Test of Chi Square | | | BAIS1 |

TABLE O 1

NEOPLASTIC LESIONS-INCIDENCE AND

STATISTICAL ANALYSIS: MALE

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|---------------|---|
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| STTE 1u | Control | 512 ppm | a. 1980 | | |
|---|--|--|----------------|-------------|--|
| SITE : TUMOR : 3/50(3/33(1) P = 0.81 | | • | mdd oost | 3200 ppm | |
| 3/50(3/33(p = p = 1) | : lung : bronchiolar-alveolar adenoma | EU | | | |
| d d d | | | | | |
| <u> </u> | 3/50(6.0) | 6/50 (12.0) | 2/50(4.0) | 2/50 (4.0) | |
| | 9. 09 | 13.04 | | 5.00 | |
| method(d) i method(d) analysis(d) | 9. 1) | 4/34(11.8) | 2/36(5.6) | 1/35(2.9) | |
| (F) (F) | | | | | |
| | *** | | | | |
| | 596 | | | | |
| | **** | | | | |
| Cochran-Armitage test(e) P = 0.3226 | 226 | | | | |
| Fisher Exact test(e) | | P = 0.2435 | P = 0.5000 | P = 0.5000 | |
| SITE : | : lung | value of | | | |
| | | Iloina | | | |
| Overall rates(a) 6/50(12.0) | 12.0) | 4/50(8.0) | 8/50(16.0) | 7/50(-14,0) | |
| | 17.65 | 11.76 | 16.67 | 20.00 | |
| 5/33(| 15.2) | 4/34 (11.8) | 6/36(16.7) | 7/35(20.0) | |
| Statistical analysis | | | | | |
| | | | | | |
| | 556 | | | | |
| | 959 | | | | |
| Ь | 046 | | | | |
| Cochran-Armitage test(e) $P = 0.5395$ | 395 | | | | |
| Fisher Exact test(e) | | P = 0.3703 | P = 0.3871 | P = 0.5000 | |
| | | | | | |
| TUMOR : | | bronchiolar—alveolar adenoma, bronchiolar—alveolar carcinoma | | | |
| Overall rates(a) 9/50(18.0) | (8.0) | 9/50(18.0) | 10/50 (20, 0) | 9/50(-18-0) | |
| | 26. 47 | 20.59 | 22.22 | 22.86 | |
| 8/33(| 24.2) | 7/34(20 6) | 8/36(22 9) | 8/35(22 0) | |
| is | ì | | | | |
| Peto test | | | | | |
| Standard method(d) $P = 0.4556$ | 556 | | | | |
| Prevalence method(d) $P = 0.5620$ | 620 | | | | |
| | 009 | | | | |
| itage test(e) | 296 | | | | |
| | | P = 0.6024 | P = 0.5000 | P = 0.6024 | |

| Group Name | Control | 512 ppm | 1280 ppm | 3200 ppm | |
|--|---|---|-------------------------|------------|--|
| | SITE : lung TUMOR : bronchiolar-alveolar ade | : lung : bronchiolar-alveolar adenoma, bronchiolar-alveolar carcinoma, squamous cell carcinoma | squamous cell carcinoma | | The state of the s |
| Tumor rate | | | | | |
| Overall rates(a) | 9/50(18.0) | 9/50(18.0) | 11/50(22.0) | 9/50(18.0) | |
| Adjusted rates(b) | 26.47 | 20.59 | 25.00 | 22.86 | |
| Terminal rates(c) | 8/33(24.2) | 7/34(20.6) | 9/36(25.0) | 8/35(22.9) | |
| Statistical analysis Peto test | | | | | |
| Standard method(d) | P = 0.4556 | | | | |
| Prevalence method(d) | P = 0.5610 | | | | |
| Combined analysis(d) | P = 0.5591 | | | | |
| Cochran-Armitage test(e) | P = 0.9924 | | | | |
| Fisher Exact test(e) | | P = 0,6024 | P = 0.4016 | P = 0.6024 | |
| | SITE : lymph node TUMOR : malignant lymphoma | | | | ANTICLE THE RESIDENCE OF THE STREET OF THE S |
| [umor rate | | | | | |
| Overall rates(a) | 3/50(6.0) | 6/50 (12.0) | 8/50(16.0) | 2/50(4.0) | |
| Adjusted rates(b) | 9. 09 | 5.88 | 22. 22 | | |
| Terminal rates(c) Statistical analysis Peto test | 3/33(9.1) | 2/34(5.9) | 8/36(22.2) | 1/35(2.9) | |
| Standard method(d) | P = 0.6351 | | | | |
| Prevalence method(d) | P = 0.7743 | | | | |
| Combined analysis(d) | P = 0,8057 | | | | |
| Cochran-Armitage test(e) | P = 0.4275 | | | | |
| Fisher Exact test(e) | | P = 0.2435 | P = 0.0999 | P = 0.5000 | |
| | SITE : spleen TIMOR · hemonaicearcome | | | | |
| Tumor rate | | | | | |
| Overall rates(a) | 4/50(8.0) | 2/50(4.0) | 0/50(0.0) | 1/50(2.0) | |
| Adjusted rates(b) | 8.89 | 0.0 | 0.0 | 0.0 | |
| Terminal rates(c) | 1/33(3.0) | 0/34(0.0) | 0/36(0.0) | 0/35(0.0) | |
| Peto test | | | | | |
| Standard method(d) | P = 0.4010 | | | | |
| Prevalence method(d) | P = 0.9962 | | | | |
| Combined analysis(d) | P = 0.9335 | | | | |
| Cochran-Armitage test(e) | P = 0.1532 | ; | | | |
| Fisher Exact test(e) | | 0 3330 | D = 0 0587 | 1011 | |

| Group Name | Control | 512 ppm | 1280 ppm | 3200 ppm | |
|--|---|------------------------|---------------------------------------|---------------|--|
| | SITE : spleen TUMOR : hemangioma,hemangiosarcoma | | | | A C TANDON BY THE TANDAN AND A STATE AND A |
| Tumor rate | A /50 (0 0) | | , , , , , , , , , , , , , , , , , , , | | |
| Adjusted rates(b) | 8.89 | 3/30(0.0) 2.86 | 2/50(4.0) 4.26 | 1/50(2.0) | |
| Terminal rates(c) Statistical analysis | 1/33(3.0) | 0/31(0.0) | 1/36(2.8) | 0/35(0.0) | |
| Peto test Standard method(d) | P = 0.4010 | | | | |
| Prevalence method(d) | P = 0.9755 | | | | |
| Combined analysis(d) | P = 0.9246 P = 0.1665 | | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = 0.3389 | P = 0.1811 | |
| | SITE : stomach THMOP : conseque cell masillame | | | | |
| Tumor rate | | | | | |
| Overall rates(a) | 0/50(0.0) | 4/50(8.0) | 3/50 (6.0) | 6/50(12.0) | |
| Adjusted rates(b) | | 8.51 | 8.33 | 13, 95 | |
| Terminal rates(c) Statistical analysis | 0/33(0.0) | 2/34(5.9) | 3/36(8.3) | 3/35(8.6) | |
| Peto test | | | | | |
| Standard method(d) | р = | | | | |
| Prevalence method(d) | F = 0.02/3* | | | | |
| Cochran-Armitage test(e) | P = 0.0365* | | | | |
| Fisher Exact test(e) | | P = 0.0587 | P = 0.1212 | P = 0.0133* | |
| | SITE : liver | | | | |
| · | TUMOR : hepatocellular adenoma | | | | |
| lumor rate | (0.00.707) 81 | () 0 / 0 1/ 0 1 | () () () () () () | | |
| Overall rates(a) Adjusted rates(h) | 14/ 50 (26. 0) | 13/501 Z6. 0/ 31 43 | 13/50(20.0) | 19/50(38. 0) | |
| Terminal rates(c) | 11/33 (33.3) | 10/34(29.4) | 12/36 (33.3) | 15/35 (42.9) | |
| Statistical analysis | | | | | |
| Standard method(d) | P = 0.2429 | | | | |
| Prevalence method(d) | P = 0.1761 | | | | |
| Combined analysis(d) | P = 0.1335 | | | | |
| Cochran-Armitage test(e) Fisher Exact test(e) | P = 0.1820 | P = 0.5000 | 0.5000 | 926] O = d | |
| | | | | | |

| . MALE | | | | | PAGE: 4 |
|--|---|-------------------|---|-------------------|--|
| Group Name | Control | 512 ppm | 1280 ppm | 3200 ppm | |
| | SITE : liver TUMOR : histiocytic sarcoma | | | | The same of the sa |
| Tumor rate Overall rates(a) | 0/50(0.0) | 3/50(6.0) | 0/50(0.0) | 2/50(4.0) | |
| Adjusted rates(b) Terminal rates(c) | 0.0 0/33(0.0) | 0.0 0/34(0.0) | 0.0 0/36(0.0) | 0.0 0/35(0.0) | |
| Statistical analysis Peto test | | | | | |
| Standard method(d) | P = 0.2791 | | | | |
| rrevalence method(d) Combined analysis(d) | r = P = 0.2791 | | | | |
| Cochran-Armitage test(e) Fisher Exact test(e) | P = 0.5274 | P = 0.1212 | P = N. C. | P = 0, 2475 | |
| | SITE : liver TUMOR : hemangiosarcoma | | | | |
| [umor rate | | | | | |
| Overall rates(a) | 5/50(10.0) | 3/50(6.0) | 0/50(0.0) | 1/50(2.0) | |
| Adjusted rates(b) | 15, 15 | 4.35 | 0.0 | 2.86 | |
| lerminal rates(c) Statistical analysis | 5/33(-15.2) | 1/34(2.9) | 0/36(0.0) | 1/35(2.9) | |
| Peto test | | | | | |
| Standard method(d) Prevalence method(d) | F = 0.5516 P = 0.9518 | | | | |
| Combined analysis(d) | P = 0.9781 | | | | |
| Cochran-Armitage test(e) | P = 0.0683 | | | | |
| Fisher Exact test(e) | | P = 0.3575 | P = 0.0281* | P = 0.1022 | |
| | | | | | |
| limor rate | TUMOR : hepatocellular carcinoma | a | | | |
| Overall rates(a) | 20/50 (40.0) | 7/50 (14.0) | 7/50(14.0) | 8/50(16.0) | |
| Adjusted rates(b) | 42. 42 | 18.92 | 11.11 | 15.38 | |
| Terminal rates(c) Statistical analysis | 14/33(42.4) | 6/34(17.6) | 4/36(11.1) | 5/35(14.3) | |
| Peto test | | | | | |
| Standard method(d) | P = 0.8323 P = 0.0234 | | | | |
| Combined analysis(d) | $\Gamma = 0.9144$ P = 0.9859 | | | | |
| Cochran-Armitage test(e) | P = 0.0415* | | 111111111111111111111111111111111111111 | | |
| Fisher Exact test(e) | | 1' = 0, 0031** | ** S | **/ 4 | |

| STUDY No. : 0580 ANIMAL : MOUSE BEDZFL/Crlj[Crj:BDF1] SEX : MALE | zlj[Crj:BDFl] | NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS | ISTICAL AMLYSIS | PAGE | |
|--|--|---|-----------------|-----------------|---|
| Group Name | Control | 512 ppm | 1280 ppm | 3200 mdd | |
| | SITE : liver TUMOR : hemanciona.hemanciosarcoma | ntiosarcoma | | | |
| Tumor rate | | | | | |
| Overall rates(a) | 6/50(12.0) | 4/50(8.0) | 1/50(2.0) | 1/50 (2.0) | |
| Adjusted rates(b) | 16.67 | 6.52 | 2.70 | 2.86 | |
| Terminal rates(c) Statistical analysis | 5/33(-15.2) | 2/34(5.9) | 0/36(0.0) | 1/35(2.9) | |
| Peto test | | | | | |
| Standard method(d) | P = 0.5616 | | | | |
| Prevalence method(d) | P = 0.9855 | | | | |
| Combined analysis(d) | P = 0.9890 | | | | |
| Cochran-Armitage test(e) | P = 0.0385* | | | | |
| Fisher Exact test(e) | | P = 0.3703 | P = 0.0559 | P = 0.0559 | |
| | The state of the s | | | | - CONTRACTOR OF CASE CASE CASE CASE CASE CASE CASE CASE |
| | SITE : liver | | | | |
| Timor vato | NUMOR : hepatocellular | IUMOR : hepatocellular adenoma,hepatocellular carcinoma | | | |
| Overall rates(a) | 28/50(56.0) | 17/50(34 0) | 18/50(36.0) | 03/20(46.0) | |
| Adjusted rates(b) | 58.82 | 41.67 | 70 CO 100 CO | 40, 50 (40, 0) | |
| Terminal rates(c) | 19/33(57.6) | 13/34 (38.2) | 14/36(38.9) | 10. 37 | |
| Statistical analysis | | | | | |
| Peto test | | | | | |
| Standard method(d) | P = 0.6439 | | | | |
| Prevalence method(d) | P = 0.6382 | | | | |
| Combined analysis(d) | P = 0.6942 | | | | |
| Cochran-Armitage test(e) | P = 0.8157 | | | | |
| Fisher Exact test(e) | | P = 0, 0219* | P = 0.0352* | P = 0.2119 | |
| (IIPT360A) | | | | | RATSA |

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

STUDY No. : 0580
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
SEX : MALE

| | | | | | . 700 r |
|--------------------------------|---|--|-------------|--------------------|---------|
| Group Name | Control | 512 ppm | 1280 ppm | 3200 mdd | |
| | SITE : liver TUMOR : hepatocellular aden | SITE : liver TUMOR : hepatocellular adenoma, hepatocellular carcinoma, hepatoblastoma | | | |
| Tumor rate Overall rates(a) | 29/50(58.0) | 18/50(36.0) | (0 36 0) | 94/50(40 0) | |
| Adjusted rates(b) | 58.82 | 44, 44 | 38.89 | 73, 30 (43. 0) | |
| Terminal rates(c) | 19/33(57.6) | 14/34(41.2) | 14/36(38.9) | 17/35(48 6) | |
| Statistical analysis | | | | (6 10.1) 0.0 (1.1 | |
| Peto test | | | | | |
| Standard method(d) | P = 0.5872 | | | | |
| Prevalence method(d) | P = 0.6446 | | | | |
| Combined analysis(d) | P = 0.6717 | | | | |
| Cochran-Armitage test(e) | P = 0.8135 | | | | |
| Fisher Exact test(e) | | P = 0,0223* | P = 0.0223* | P = 0.2115 | |
| (IIPT360A) | | | | | BATCA |
| | | | | | FCIPO |

(a): Number of tumor-bearing animals/number of animals examined at the site.
(b): Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.
(c): Observed tumor incidence at terminal kill.
(d): Beneath the control incidence are the P-values associated with the trend test.
Standard method : Death analysis

Combined analysis: Death analysis + Incidental tumor test Prevalence method : Incidental tumor test

(e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.
?: The conditional probabilities of the largest and smallest possible out comes can not estimated or this P-value is beyond the estimated P-value.
-----: There is no data which should be statistical analysis.
Significant difference; * : P ≤ 0.05 **: P ≤ 0.01
N.C. Statistical value cannot be calculated and was not significant.

BAIS4 6/50(12. 0) 8. 57 3/35(8. 6) 2/50(4.0) 2.86 1/35(2.9) 3200 ppm P = 0.0559P = 0.50003/50(6.0) 5.56 2/36(5.6) 8/50(16.0) 22.22 8/36(22.2) 1280 ppm P = 0.0999P = 0.3087NEOPLASTIC LESIONS-INCLDENCE AND STATISTICAL ANALYSIS 512 ppm 5/50(10.0) 2.94 1/34(2.9) 6/50(12.0) 5.88 2/31(5.9) P = 0.1022P = 0.2435SITE : ALL SITE TUMOR : histiocytic sarcoma SITE : ALL SITE TUMOR : malignant lymphoma 1/50(2.0) 0.0 0/33(0.0) 3/50 (6.0) 9.09 3/33 (9.1) Control P = 0.3363 P = 0.0504 P = 0.0873 P = 0.1286 P = 0. 6351 P = 0. 7743 P = 0. 8057 P = 0. 4275
 STUDY No.
 : 0580

 ANIMAL
 : MOUSE B6D2F1/Cr1jfCrj:BDF1]

 SEX
 : MALE
 Standard method (d)
Prevalence method (d)
Combined analysis(d)
Cochran-Armitage test(e)
Fisher Exact test(e) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e) Standard method(d) Prevalence method(d) Adjusted rates(b) Terminal rates(c) Statistical analysis Group Name Statistical analysis Tumor rate Overall rates(a) Adjusted rates(b) Terminal rates(c) Tumor rate Overall rates(a) Peto test Peto test (HPT360A)

| STITE ALL SITE ALL SITE ALL SITE TUMOR hemanglosarcoma 1280 ppm 3200 ppm | STUDY No. : 0580 ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1] SEX : MALE | rlj[Crj:BDFt] | NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS | TSTICAL ANALYSIS | | PAGE: 2 |
|---|--|-------------------------|---|------------------|-------------------|---------|
| SITE : ALL SITE TUMOR : hemangiosarcoma 9/50(18.0) 2.91 6/33(18.2) 1/34(2.9) 0/50(0.0) 0.0 6/33(0.0) 1/34(2.9) 0/36(0.0) 1/34(2.9) 0/36(0.0) 0/36(0.0) 0/36(0.0) 1/34(2.9) 0/36(0.0) 0/36(0.0) 0/36(0.0) 0/36(0.0) 0/36(0.0) | ıp Name | Control | 512 ppm | 1280 ppm | 3200 ppm | |
| TUMOR : hemanglosarcoma $9/50$ (8. 0) $0/50$ (0. 0) $0/50$ (0. 0) $0/50$ (0. 0) $0/50$ (0. 0) $0/30$ (0. | | SITE : ALL SITE | | | | |
| 9/50(18.0) 	 4/50(8.0) 	 0/50(0.0) 	 0/50(0.0) 	 0/50(0.0) 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 	 0.0 | | TUMOR : hemangiosarcoma | | | | |
| 9/50(18.0) 4/50(8.0) 0/50(0.0) 2.94 0/50(0.0) 2.94 0.0 6/33(18.2) 1/34(2.9) 0/36(0.0) 1/34(2.9) 0/36(0.0) 1/34(2.9) 0/36(0.0) 1/34(2.9) 0/36(0.0) 1/34(2.9) 0/36(0.0) 1/34(2.9) 0/36(0.0) 1/34(2.9) 0/36(0.0) | | | | | | |
| 20.00 | s(a) | 9/50(18.0) | 4/50(8.0) | 0/50(0.0) | 2/50(4 0) | |
| b | es (b) | 20.00 | 2.94 | 0.0 | 16:1 \ 22./T | |
| P = 0.5266 P = 0.9884 P = 0.9984 P = 0.9930 P = 0.0233* P = 0.1168 | es(c) | 6/33(18.2) | | 0/38 (0.0) | 1/35(2.00 | |
| P = 0.5266 P = 0.9984 P = 0.9930 p = 0.0233* P = 0.0013** | nalysis | | | | (c : 2) (c : 4) | |
| P = 0, 5266 P = 0, 9984 P = 0, 9930 P = 0, 0233* P = 0, 02168 P = 0, 0013** | | | | | | |
| P = 0.9984 P = 0.9930 P = 0.0233* $P = 0.1168$ $P = 0.0013**$ | thod(d) | P = 0.5266 | | | | |
| P = 0.9930 $P = 0.0233*$ $P = 0.1168$ $P = 0.0013**$ | method(d) | P = 0.9984 | | | | |
| P = 0.0233* P = 0.1168 P = 0.0013** | alysis(d) | P = 0.9930 | | | | |
| P = 0, 1168 P = 0, 0013** | Cochran-Armitage test(e) | P = 0.0233* | | | | |
| | Fisher Exact test(e) | | P = 0.1168 | P = 0.0013** | P = 0.0256* | |
| | | | | | | |

(a): Number of tumor-bearing animals/number of animals examined at the site.
(b): Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.
(c): Observed tumor incidence at terminal kill.
(d): Beneath the control incidence are the P-values associated with the trend test.

Standard method : Death analysis

Prevalence method : Incidental tumor test

Combined analysis: Death analysis + Incidental tumor test

(e): The Cochran Armitage and Fisher exact test compare directly the overall incidence rates.

?: The Cochran Armitage and Fisher exact test compare directly the overall incidence rates.

?: The conditional probabilities of the largest and smallest possible out comes can not estimated or this P-value is beyond the estimated P-value.

-----: There is no data which should be statistical analysis.

Significant difference; *: P ≤ 0.05 **: P ≤ 0.01

N.C.:Statistical value cannot be calculated and was not significant.

TABLE O 2

NEOPLASTIC LESIONS-INCIDENCE AND

STATISTICAL ANALYSIS: FEMALE

| STSV IANA |
|---------------------------------|
| NP STATISTICAL |
| NEOPLASTIC LESIONS-INCIDENCE AN |
| |

| Group Name | Control | 512 ppm | 1280 ppm | 3200 ppm | |
|-----------------------------------|---|---|------------|-------------|--|
| | SITE : lung TUMOR : bronchiolar-alveolar carcinoma | r carcinoma | | | |
| Tumor rate | | | | | |
| Overall rates(a) | 2/50(4.0) | 1/50(2.0) | 2/50(4.0) | 4/50 (8.0) | |
| Adjusted rates(b) | 2.94 | | | 13.33 | |
| Terminal rates(c) | 1/31(2.9) | 1/28(3.6) | 1/28(3.6) | 1/30(13.3) | |
| otatisticai analysis Peto test | | | | | |
| Standard method(d) | P = 1,0000 ? | | | | |
| Prevalence method(d) | | | | | |
| Combined analysis(d) | P = 0.0842 | | | | |
| Cochran-Armitage test(e) | P = 0.1929 | | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = 0.6913 | P = 0.3389 | |
| , | SITE : lung TUMOR : bronchiolar—alveola | : lung : bronchiolar-alveolar adenoma,bronchiolar-alveolar carcinoma | | | |
| lumor rate | | | | | |
| Overall rates(a) | 4/50(8.0) | 2/50(4.0) | 2/50(4.0) | 5/50(10.0) | |
| Adjusted rates(b) | 8.82 | 4.00 | 6.25 | 16.67 | |
| lerminal rates(c) | 3/34(8.8) | 1/28(3.6) | 1/28(3.6) | 5/30 (16.7) | |
| Statistical analysis Peto test | | | | | |
| Standard mothod(d) | P = 1 0000 9 | | | | |
| Demonstration (d) | | | | | |
| Frevalence method(d) | F = 0.1080 | | | | |
| Combined analysis(d) | P = 0.1809 | | | | |
| Cochran-Armitage test(e) | P = 0.4279 | | | | |
| Fisher Exact test(e) | | P = 0.3389 | P = 0.3389 | P = 0.5000 | |
| | | | | | |
| | TUMOR : malignant lymphoma | | | | |
| Tumor rate | | | | | |
| Overall rates(a) | 12/50(24.0) | 16/50 (32.0) | 7/50(14.0) | 7/50(14.0) | |
| Adjusted rates(b) | 14.71 | 14. 29 | 0.0 | 13. 33 | |
| Terminal rates(c) | 5/34(14.7) | 4/28 (14.3) | 0/28(0.0) | 4/30(13.3) | |
| Statistical analysis | | | | | |
| reto test | 0 - 0 0469 | | | | |
| Standard method(d) | F = 0.9462 | | | | |
| Frevalence method(d) | F = 0.5803 | | | | |
| Combined analysis(d) | F = 0.9280 | | | | |
| Cochran-Armitage test(e) | P = 0.0662 | | | | |
| Fisher Exact test(e) | | (4), 9(1, 1) == (1 | 0 = 0 | | |

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| SITIS TUMC P P P P P | Control : spleen | | | | |
|---|---------------------------|-------------|-------------|-------------|--------------------------|
| SITIE TUMC TUMC TUMC TUMC TUMC TUMC TUMC TUMC | | 512 ppm | 1280 ppm | 3200 ppm | |
|)) | ٠. | | | | |
| P P P P P P P P P P P P P P P P P P P | | | | | |
| 1) 3) st (e) | 1/50(2.0) | 1/50(2.0) | 3/50(6.0) | 0/50(0.0) | |
| J) J) st (e) | 2.94 | 3, 23 | 7.32 | 0.0 | |
| J) J) st (e) | 54(-2.9) | 0/28(0.0) | 2/28(7.1) | 0/30(0.0) | |
| | | | | | |
| | | | | | |
| | P = 0.6950 | | | | |
| | *** | | | | |
| Fisher Exact test(e) | P = 0. 4818 | P = 0.7525 | P = 0.3087 | P = 0.5000 | |
| ETIS. | | | | | |
| TUMOR Timor rate | : squamous cell papilloma | | | | |
| Tps (2) | 50(0 0) | 1/50(20) | | | |
| _ | 0.0 | 2.70 | 1/30/1 2.0/ | 3/30(6.0) | |
| | 0/34(0 0) | (0 0) 86/0 | (0 0) 86/0 | 9.08 | |
| is | | | | | |
| Feto test Standard mathad(d) | | | | | |
| | #02G0 O | | | | |
| revalence method (d) $\Gamma = 0$ Combined analysis (d) $\Gamma = 0$ | 0.0273* | | | | |
| (e) P = | 0.0549 | | | | |
| • | | P = 0.5000 | P = 0.5000 | P = 0.1212 | |
| SITE | : liver | | | | V000001-1-0016-0-1-1-1-1 |
| TUMOR | TUMOR : hemangioma | | | | |
| | | | | | |
| | 2/50(4.0) | 1/50(2.0) | 2/50(4.0) | 4/50(8.0) | |
| | 5.88 | 3.57 | 5.13 | 13, 33 | |
| ates(c) analysis | 7,54(5.9) | 1/28(3.0) | 1/28(3.6) | 4/30(-13.3) | |
| | | | | | |
| ቷ የ | | | | | |
| Frevalence method (d) $I' = 0$ | = 0.0872 = | | | | |
| (3) | P = 1030 | | | | |
| | | P = 0.5000 | P = 0.6913 | P = 0.3389 | |

| | | | | | rage . |
|--|--|-------------|------------|-------------|--|
| Group Name | Control | 512 ppm | 1280 ppm | 3200 ppm | |
| | SITE : liver TUMOR : hepatocellular adenoma | o | | | And the second s |
| Tumor rate | | | | | |
| Overall rates(a) | 5/50(10.0) | 6/50(12.0) | 4/50(8.0) | 3/50(6.0) | |
| Adjusted rates(b) | 14.71 | 21. 43 | 11.11 | 10.00 | |
| Terminal rates(c) Statistical analysis | 5/34(14.7) | 6/28(21.4) | 3/28(10.7) | 3/30(10.0) | |
| Peto test | | | | | |
| Standard method(d) | b = d | | | | |
| Prevalence method(d) | P = 0.7948 | | | | |
| Combined analysis(d) | d | | | | |
| Cocuran-Armitage test(e) Fisher Exact test(e) | r = 0.3463 | P = 0.5000 | P = 0,5000 | P = 0.3575 | |
| | | | | | |
| | SITE : liver | | | | |
| fumor rate | TUMOR : hemanglosarcoma | | | | |
| Overall rates(a) | 4/50(8.0) | 3/50 (6.0) | 0/20(0 0) | 0/20(0 0) | |
| Adjusted rates(b) | 11.76 | 6.45 | 0.0 | 0.0 | |
| Terminal rates(c) | 4/34(11.8) | 1/28(3.6) | 0/28(0.0) | 0/30(0.0) | |
| Statistical analysis | | | | | |
| reto test | 5 | | | | |
| Standard method(d) | V = 0.5483 $V = 0.0046$ | | | | |
| Tevalence method(d) | D = 0 9950 | | | | |
| Cochran-Armitage test(e) | D = 0.9500 | | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = 0.0587 | P = 0.0587 | |
| | CTTT | | | | |
| | TUMOR : hepatocellular carcinoma | oma | | | |
| Tumor rate | | | | | |
| Overall rates(a) | 0/50(0.0) | 3/50(6.0) | 1/50(2.0) | 1/50 (2.0) | |
| Adjusted rates(b) | 0.0 | | 3.13 | | |
| Terminal rates(c) | 0/34(0.0) | 2/28(7.1) | 0/28(0.0) | 0/30(0.0) | |
| Statistical analysis | | | | | |
| reto test Standard mothod(d) | | | | | |
| Destrations mathod(d) | D = 0.4950 | | | | |
| Combined analysis(d) | D = | | | | |
| Cochran-Armitage test(e) | P = 0.9335 | | | | |
| | | 4 | | | |

| SITE : liver Tumor rate Group Name Control SITE : liver Tumor rate G50 (12.0) Adjusted rates(a) G50 (12.0) Adjusted rates(b) G50 (12.0) G | 512 ppm | | |
|--|-------------|----------------------|-------------|
| at (e) (e) (e) (f) (f) (f) (f) (f) (f) (f) (f) (f) (f | | 1280 ppm | 3200 ppm |
| st (e) | | | |
| (e) (e) (e) (f) (f) (f) (f) (f) (f) (f) (f) (f) (f | | | |
| (a) (b) (c) (c) (d) (d) (d) (d) (d) (d) (d) (d) (d) (d | | 2/50(-4.0) | 4/50(8.0) |
| 11) (a) (b) (c) (d) (d) (d) (e) (e) (e) (e) (f) (f) (f) (f) (f) (f) (f) (f) (f) (f | | 1/28(3.6) | 4/30 (13.3) |
| at (e) (e) (e) (f) (f) (f) (f) (f) (f) (f) (f) (f) (f | | | |
| a) (a) (b) (c) (d) (d) (d) (e) (e) | | | |
| 1) 1) 1) 1) 1) 1) 1) | | | |
| 1) 11) 13 st(e) 10) | 0.3703 | P = 0.1343 | P = 0.3703 |
| 1) 14) 15) 16) | | | |
| 5/50 (10.0) 14.71 5/34 (14.7) P = 19 | r carcinoma | | |
| 11. 71 5/34 (11.7) 13. | 50(16.0) | 5/50(10.0) | 4/50(8.0) |
| 5/34(14.7) P = 1) | 25.81 | 13.89 | 11.76 |
| D = 1) | 28 (25.0) | 3/28(10.7) | 3/30(10.0) |
| P = | | | |
| 1) | | | |
| Str(e) P = | | | |
| SITE : pituitary gland TUMOR : adenoma 2/50(4.0) 0/34(0.0) | | | |
| SITE : pituitary gland TUMOR : adenoma 2/50(4.0) 0.34(0.0) | 0.2768 | P = 0.6297 | 0008 0 = d |
| SITE : pituitary gland TUMOR : adenoma 2/50(4.0) 0.0 0/34(0.0) | | | |
| TUMOK : adenoma 2/50(4.0) 0.0 0/34(0.0) | | | |
| 2/50(4.0) 0.0 0/34(0.0) | | | |
| 0,0000 | 50(14 0) | 5/50/ 10 0) | (0 61 /05/9 |
| 0/34(0.0) | 17.86 | 5/50/ 10.0/ 19 E0 | 0/30(15.0) |
| | 28(17.9) | 3/28 (10.7) | 6/30(20.0) |
| Peto test | | | |
| | | | |
| Standard method(d) $P = 0.9012$ | | | |
| Trevalence method (d) $F = 0.042/4$ Combined analysis (d) $P = 0.1649$ | | | |
| (e) | | | |
| | 0.0709 | 0010 | |

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

| SEA . FEMALE | | | | | PAGE: 11 |
|--|--|----------------------|--------------------|----------------|----------|
| Group Name | Control | 512 ppm | 1280 ppm | 3200 ppm | |
| | SITE : uterus TUMOR : histiocytic sarcoma | | | | 000000 |
| Tumor rate Overall rates(a) | 12/50(24 0) | 7/50(14 0) | (0 /0 / 01/01 | | |
| Adjusted rates(h) | 17.65 | 7.14 | 7, 14 | 13/50 (26. 0) | |
| Terminal rates(c) Statistical analysis Peto test | 6/34(-176) | 2/28(7.1) | 2/28(7.1) | 3/30(10.0) | |
| Standard method(d) | P = 0.0484* | | | | |
| Prevalence method(d) | P = 0, 7898 | | | | |
| Combined analysis(d) | P = 0.1667 | | | | |
| Cocnran-Armilage test(e) Fisher Exact test(e) | V = 0.4290 | P = 0.1540 | P = 0.5924 | P = 0,5000 | |
| | SITE : Harderian gland TUMOR : adenoma | | | | |
| Tumor rate | | | | | |
| Overall rates(a) | 0/50(0.0) | 1/50(2.0) | 4/50(8.0) | 2/50(4.0) | |
| Adjusted rates(U) Terminal rates(C) | 0.0 0/31(0.0) | 3. 57 1/28(3. 6) | 9, 30 2/28 (7, 1) | 5.71 | |
| Statistical analysis | | | | | |
| sto test Standard method(d) | P = | | | | |
| Prevalence method(d) | P = 0.1228 | | | | |
| Combined analysis(d) | P = | | | | |
| Cochran-Arwitage test(e) | P = 0.2968 | | | | |
| Fisher Exact test(e) | | P = 0.5000 | P = 0.0587 | P = 0.2475 | |

⁽a): Number of tumor-bearing animals/number of animals examined at the site.
(b): Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.
(c): Observed tumor incidence at terminal kill.
(d): Beneath the control incidence are the P-values associated with the trend test.

Prevalence method : Incidental tumor test Standard method : Death analysis

BAIS4 17/50 (34. 0) 10. 00 3/30 (10. 0) 7/50 (14. 0) 13. 33 4/30 (13. 3) 3200 ppm P = 0.3329P = 0.154012/50(24. 0) 7. 14 2/28(7. 1) 7/50(14.0) 0.0 0/28(0.0) 1280 ppm P = 0.4100P = 0.1540NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS 9/50(18. 0) 14. 29 4/28(14. 3) 16/50 (32. 0) 14. 29 4/28 (14. 3) 512 ppm P = 0.1710P = 0.2522SITE : ALL SITE TUMOR : histiocytic sarcoma SITE : ALL SITE TUMOR : malignant lymphoma 14/50 (28.0) 20.59 7/34 (20.6) 12/50 (24. 0) 14. 71 5/34 (14. 7) P = 0.0076** P = 0.9033 P = 0.0837 P = 0.2091 Control P = 0.9462 P = 0.5803 P = 0.9286 P = 0.0662 STUDY No. : 0580
ANIMAL : MOUSE BGD2F1/CrljfCrj:BDF1]
SEX : FEMALE Standard method(d)
Prevalence method(d)
Combined analysis(d)
Cochran-Armitage test(e)
Fisher Exact test(e) Combined analysis(d) Cochran-Armitage test(e) Fisher Exact test(e) Standard method(d) Prevalence method(d) Tumor rate
Overall rates(a)
Adjusted rates(b)
Terminal rates(c)
Statistical analysis Group Name Statistical analysis Terminal rates(c) Overall rates(a) Adjusted rates(b) Peto test Peto test Tumor rate (IIPT360A)

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

| TOWN TO THE PARTY OF THE PARTY | | | | | PAGE: 4 |
|---|-------------------------|------------|------------|---|---|
| Group Name | Control | 512 ppm | 1280 ppm | 3200 ppm | |
| 0 | מהוא אווי אוויא | | | THE REPORT OF THE PARTY OF THE | *************************************** |
| , L | TUMOR : hemangiosarcoma | | | | |
| | ı | | | | |
| Overall rates(a) | 5/50(10.0) | 3/50(6.0) | 1/50(2.0) | 0/20(0 0) | |
| Adjusted rates(b) | 14.71 | 6. 45 | 2.44 | 0.0 | |
| Terminal rates(c) | 5/34(14.7) | 1/28(3.6) | 0/28(0.0) | 0/30(0.0) | |
| Statistical analysis Peto test | | | | | |
| Standard method(d) | P = 0.5483 | | | | |
| Prevalence method(d) | P = 0.9934 | | | | |
| Combined analysis(d) | P = 0.9945 | | | | |
| Cochran-Armitage test(e) | P = 0.0182* | | | | |
| Fisher Exact test(e) | | P = 0.3575 | P = 0.1022 | P = 0.0281* | |

(a): Number of tumor-bearing animals/number of animals examined at the site.
(b): Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.
(c): Observed tumor incidence at terminal kill.
(d): Beneath the control incidence are the P-values associated with the trend tust.
Standard method : Death analysis
Prevalence method : Incidental tumor test

Combined analysis : Death analysis + Incidental tumor test

TABLE Q 1

HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER: $B6D2F1/Crlj \ MALE \ MICE$

TABLE Q1 HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER: B6D2F1/Crlj MALE MICE

| Organs | No. of animals | No. of animals bearing tumor | Incidence | Min Max. |
|---------------------------------|----------------|------------------------------|-----------|----------|
| Tumors | examined | | (%) | (%) |
| Stomach Squamous cell papilloma | 1946 | 5 | 0.3 | 0 - 2 |

39 carcinogenicity studies examined in Japan Bioassay Research Center were used.

Study No.: 0044, 0060, 0062, 0064, 0066, 0068, 0096, 0105, 0116, 0140, 0159, 0163, 0190, 0206,

 $0211,\,0225,\,0243,\,0268,\,0270,\,0279,\,0285,\,0297,\,0319,\,0329,\,0343,\,0348,\,0366,\,0372,\,0343,\,0348,\,0366,\,0372,\,0366$

 $0402,\,0406,\,0418,\,0422,\,0438,\,0449,\,0458,\,0462,\,0498,\,0515,\,0561$

TABLE Q 2

HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER: $B6D2F1/Crlj \; FEMALE \; MICE$

TABLE Q2 HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER: B6D2F1/Crlj FEMALE MICE

| Organs Tumors | No. of animals examined | No. of animals bearing tumor | Incidence (%) | Min Max. (%) |
|--|----------------------------|------------------------------|------------------|-----------------|
| Stomach Squamous cell papilloma | 1947 | 8 | 0.4 | 0-6 V |
| Lung Bronchiolar-alveolar carcinoma | 1947 | 55 | 2.8 | 0 - 8 V |
| Pituitary gland Adenoma | 1938 | 277 | 14.3 | 2 - 34 V |
| Uterus Histiocytic sarcoma | 1947 | 401 | 20.6 | 10 - 32 🗸 |
| All organ Histiocytic sarcoma | 1947 | 456 | 23.4 | 12 - 36 🗸 |

39 carcinogenicity studies examined in Japan Bioassay Research Center were used.

Study No.:

0044, 0060, 0062, 0064, 0066, 0068, 0096, 0105, 0116, 0140, 0159, 0163, 0190, 0206, 0211, 0225, 0243, 0268, 0270, 0279, 0285, 0297, 0319, 0329, 0343, 0348, 0366, 0372,

 $0402,\,0406,\,0418,\,0422,\,0438,\,0449,\,0458,\,0462,\,0498,\,0515,\,0561$

TABLE R

CAUSE OF DEATH OF MICE IN THE 2-YEAR FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

| STUDY NO. : 0580 ANIMAL : MOUSE BEDZI | : 0580 : MOUSE B6D2F1/Crl;[Crj:BDF1] | | | COUSE OF DEATH (SUMMARY) (0-105W) | |
|---------------------------------------|---|---------|----------|-----------------------------------|---|
| SEX : MALE | | | | PA | PAGE: 1 |
| Group Name | Control | 512 ppm | 1280 ppm | 3200 ppm | |
| Number of Dead and Moribund Animal | 17 | 16 | 14 | 15 | |
| no microscop confirm | 0 | 0 | | 2 | Milydd commence consequence or consequence or |
| digestive sy les | 0 | 1 | 0 | 0 | |
| urinary retention | 4 | 1 | 4 | ຄ | |
| arteritis | | 0 | 0 | 0 | |
| tooth lesion | 0 | 0 | | 0 | |
| hydronephrosis | 2 | 0 | 0 | | |
| peritonitis | 0 | 0 | 1 | 0 | |
| tumor dileukemia | 0 | 4 | 0 | | |
| tumor d:subcutis | 1 | 1 | | 0 | |
| tumor d:lung | 0 | 0 | 2 | 0 | |
| tumor d:lymph node | 1 | 0 | 0 | 0 | |
| tumor d:spleen | 0 | 2 | 0 | - | |
| tumor d:liver | 80 | 5 | က | 2 | |
| tumor d:epididymis | 0 | 0 | | 0 | |
| tumor diperiph nerv | 0 | 1 | 0 | | |
| tumor d:Harder gl | 0 | 1 | 0 | 0 | |
| (B10120) | | | | | BAIS4 |

| SEX : FEMALE SEX | . 0580 : MOUSE B6D2F1/Cr1,[Cr.j:BDF1] : FEMALE | | J (| COUSE OF DEATH (SUMMARY) (0-105W) | 3E: 2 |
|---------------------------------------|--|---------|----------|------------------------------------|---|
| Group Name | Control | 512 ppm | 1280 ppm | 3200 ppm | |
| Number of Dead and Moribund Animal | 16 | 22 | 22 | 20 | |
| no microscop confirm | 0 | 0 | | 0 | |
| cardiovascular les | 0 | 0 | 0 | T-1 | |
| renal lesion | 0 | 0 | - | 0 | |
| thrombosis | 0 | 0 | 0 | _ | |
| tooth lesion | 0 | _ | 0 | 0 | |
| hydronephrosis | 0 | 0 | П | 0 | |
| tumor d:leukemia | 2 | 12 | 7 | n | |
| tumor d:lung | | 0 | 0 | 0 | |
| tumor displeen | _ | 0 | 0 | N | |
| tumor d:liver | 0 | | 0 | W | |
| tumor d:pituitary | 2 | 1 | 1 | 0 | |
| tumor d:ovary | 0 | 1 | 0 | | |
| tumor diuterus | S | D. | 11 | 10 | |
| tumor d:bone | 0 | 1 | 0 | 0 | |
| (BI0120) | | | | BAYS | BATS4 |
| | | | | | × 1 4 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 1 |

FIGURES

FIGURE 1 SURVIVAL ANIMAL RATE OF MALE MICE IN THE 2-YEAR FEED STUDY OF 2-AMINO-4-CHLOROPHENOL SURVIVAL ANIMAL RATE OF FEMALE MICE IN THE 2-YEAR FEED FIGURE 2 STUDY OF 2-AMINO-4-CHLOROPHENOL BODY WEIGHT CHANGES OF MALE MICE IN THE 2-YEAR FEED FIGURE 3 STUDY OF 2-AMINO-4-CHLOROPHENOL BODY WEIGHT CHANGES OF FEMALE MICE IN THE 2-YEAR FEED FIGURE 4 STUDY OF 2-AMINO-4-CHLOROPHENOL FIGURE 5 FOOD CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR FEED STUDY OF 2-AMINO-4-CHLOROPHENOL FOOD CONSUMPTION CHANGES OF FEMALE MICE IN THE FIGURE 6 2-YEAR FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

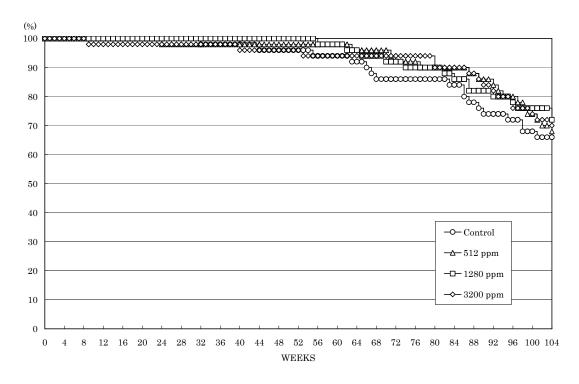


FIGURE 1 SURVIVAL ANIMAL RATE OF MALE MICE IN THE 2-YEAR FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

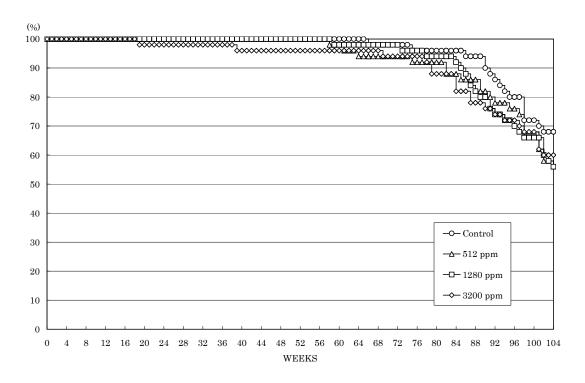


FIGURE 2 SURVIVAL ANIMAL RATE OF FEMALE MICE IN THE 2-YEAR FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

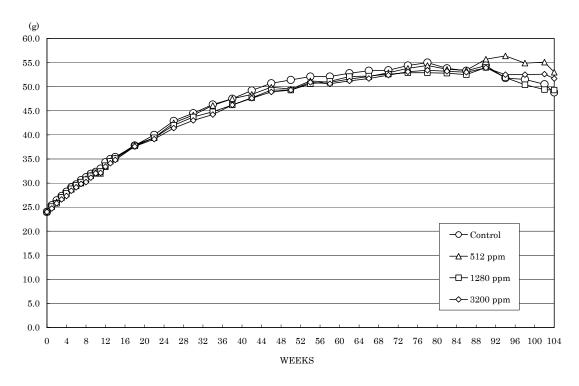


FIGURE 3 BODY WEIGHT CHANGES OF MALE MICE IN THE 2-YEAR FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

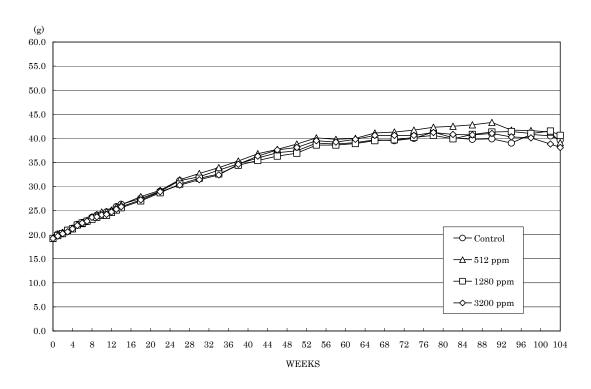


FIGURE 4 BODY WEIGHT CHANGES OF FEMALE MICE IN THE 2-YEAR FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

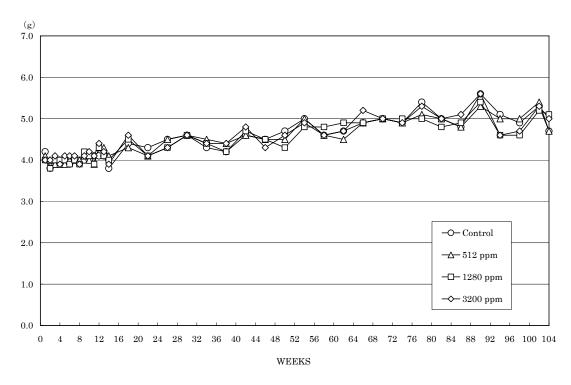


FIGURE 5 FOOD CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

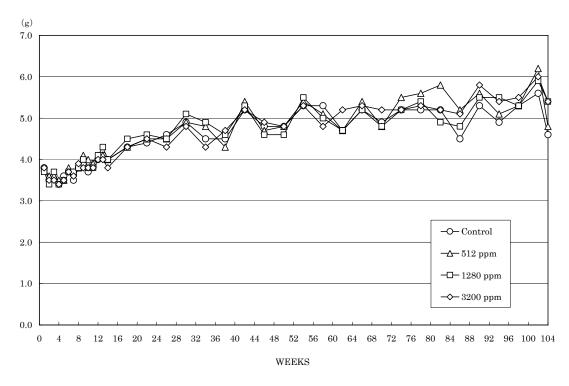


FIGURE 6 FOOD CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR FEED STUDY OF 2-AMINO-4-CHLOROPHENOL



Photograph 1

Forestomach: Squamous cell papilloma

Mouse, Male, 1280 ppm, Animal No. 0580-1236 (H&E)