Summary of Feed Carcinogenicity Study of 2-Amino-4-Chlorophenol in F344 Rats

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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 F344 Rats

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 F344/DucrlCrlj (Fischer) rats ACP-containing diets for 2 years (104 weeks). Each group of test animals consisted of either 50 male or 50 female rats. The dietary concentration of ACP was 0, 1280, 3200 or 8000 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 between any ACP -fed group of either sex and their respective controls. There was a decrease in the body weights of all the ACP-fed rats, both male and female; however, except for the 8000 ppm-fed animals, body weights recovered before the end of the experimental period. Terminal body weights of the 8000 ppm-fed males and females were suppressed to 95% and 87% of their respective controls. Slightly decreased food consumption was observed sporadically in the 8000 ppm ACP-fed females. Yellow coloration of the fur was observed in all the ACP-fed rats of both sexes. The incidence of forestomach tumor (squamous cell carcinoma and papilloma) was increased in all ACP-fed male mice. The incidence of urinary bladder tumor was increased in the 8000 ppm ACP-fed males. The incidence of squamous cell papillomas in the forestomach was increased in the 8000 ppm-fed females. In addition, the following non-neoplastic lesions were observed: the incidence of forestomach squamous cell hyperplasia was increased in the males fed 3200 and 8000 ppm APC and in females fed 8000 ppm APC; slight changes of anemic parameters including red blood cell count were noted in females fed 3200 and 8000 ppm APC; and deposition of hemosiderin in the spleen and increased spleen weights were observed in the 8000 ppm-fed females.

Conclusions

There was clear evidence of carcinogenic activity of 2-amino-4-chlorophenol in male rats. There was some evidence of carcinogenic activity of 2-amino-4-chlorophenol in female rats, based on an increased incidence of squamous cell papillomas in the forestomach.

SELECTED TABLES

TABLE C 1

BODY WEIGHT CHANGES AND

SURVIVAL ANIMAL NUMBERS: MALE

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

MEAN BODY WEIGHTS AND SURVIVAL

Week-Day on Study	Control Av. Wt.	Control No. of Surviv. <50>	1280 ppm Av. Wt.	1280 ppm % of cont. <50>	1280 ppm No. of Surviv.	3200 ppm Av. Wt.	3200 ppm % of cont. <50>	3200 ppm No. of Surviv.	8000 ppm Av. Wt.	8000 ppm % of cont. <50>	8000 ppm No. of Surviv.
0-0	129 (50)	50/50	129 (50)	100	50/50	129 (50)	100	50/50	129 (50)	100	50/50
1-7	156 (50)	50/50	156 (50)	100	50/50	156 (50)	100	50/50	152 (50)	97	50/50
2-7	186 (50)	50/50	185 (50)	99	50/50	185 (50)	99	50/50	179 (50)	96	50/50
3-7	210 (50)	50/50	206 (50)	98	50/50	207 (50)	99	50/50	200 (50)	95	50/50
4-7	229 (50)	50/50	224 (50)	98	50/50	226 (50)	99	50/50	218 (50)	95	50/50
5-7	246 (50)	50/50	239 (50)	97	50/50	242 (50)	98	50/50	234 (50)	95	50/50
6-7	259 (50)	50/50	251 (50)	97	50/50	256 (50)	99	50/50	246 (50)	95	50/50
7-7	273 (50)	50/50	265 (50)	97	50/50	269 (50)	99	50/50	259 (50)	95	50/50
8-7	285 (50)	50/50	277 (50)	97	50/50	282 (50)	99	50/50	271 (50)	95	50/50
9-7	296 (50)	50/50	286 (50)	97	50/50	293 (50)	99	50/50	282 (50)	95	50/50
10-7	305 (50)	50/50	295 (50)	97	50/50	302 (50)	99	50/50	291 (50)	95	50/50
11-7	313 (50)	50/50	303 (50)	97	50/50	311 (50)	99	50/50	298 (50)	95	50/50
12-7	318 (50)	50/50	308 (50)	97	50/50	315 (50)	99	50/50	302 (50)	95	50/50
13-7	325 (50)	50/50	314 (50)	97	50/50	320 (50)	98	50/50	307 (50)	94	50/50
14-7	333 (50)	50/50	321 (50)	96	50/50	328 (50)	98	50/50	315 (50)	95	50/50
18-7	352 (50)	50/50	343 (50)	97	50/50	351 (50)	100	50/50	338 (50)	96	50/50
22-7	368 (50)	50/50	356 (50)	97	50/50	368 (50)	100	50/50	353 (50)	96	50/50
26-7	384 (50)	50/50	371 (50)	97	50/50	384 (50)	100	50/50	368 (50)	96	50/50
30-7	394 (50)	50/50	383 (50)	97	50/50	394 (50)	100	50/50	380 (50)	96	50/50
34-7	403 (49)	49/50	391 (50)	97	50/50	405 (50)	100	50/50	389 (50)	97	50/50
38-7	413 (49)	49/50	398 (50)	96	50/50	413 (50)	100	50/50	397 (50)	96	50/50
42-7	422 (49)	49/50	410 (49)	97	49/50	424 (50)	100	50/50	406 (50)	96	50/50
46-7	430 (49)	49/50	416 (49)	97	49/50	433 (50)	101	50/50	414 (50)	96	50/50
50-7	435 (49)	49/50	423 (49)	97	49/50	438 (50)	101	50/50	420 (50)	97	50/50
54-7	440 (49)	49/50	427 (49)	97	49/50	443 (50)	101	50/50	425 (50)	97	50/50
58-7	443 (49)	49/50	431 (49)	97	49/50	447 (50)	101	50/50	430 (50)	97	50/50
62-7	446 (49)	49/50	433 (49)	97	49/50	451 (49)	101	49/50	431 (50)	97	50/50
66-7	449 (49)	49/50	437 (49)	97	49/50	455 (49)	101	49/50	432 (50)	96	50/50
70-7	451 (47)	47/50	439 (49)	97	49/50	455 (49)	101	49/50	434 (48)	96	48/50
74-7	452 (47)	47/50	441 (49)	98	49/50	457 (49)	101	49/50	435 (47)	96	47/50
78-7	452 (45)	45/50	442 (49)	98	49/50	460 (47)	102	47/50	434 (47)	96	47/50
82-7	448 (44)	44/50	440 (49)	98	49/50	457 (46)	102	46/50	433 (47)	97	47/50
86-7	444 (44)	44/50	439 (48)	99	48/50	456 (46)	103	46/50	428 (47)	96	47/50
90-7	440 (43)	43/50	437 (47)	99	47/50	453 (46)	103	46/50	422 (44)	96	44/50
94-7	431 (40)	40/50	436 (44)	101	44/50	441 (46)	102	46/50	415 (43)	96	43/50
98-7	427 (36)	36/50	422 (42)	99	42/50	441 (41)	103	41/50	412 (41)	96	41/50
102-7	414 (35)	35/50	413 (40)	100	40/50	432 (41)	104	41/50	397 (39)	96	39/50
104-7	410 (33)	33/50	414 (38)	101	38/50	423 (39)	103	39/50	390 (39)	95	39/50

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

TABLE C 2

BODY WEIGHT CHANGES AND

SURVIVAL ANIMAL NUMBERS: FEMALE

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

MEAN BODY WEIGHTS AND SURVIVAL

Week-Day on Study	Control Av. Wt.	Control No. of Surviv. <50>	1280 ppm Av. Wt.	1280 ppm % of cont. <50>	1280 ppm No. of Surviv.	3200 ppm Av. Wt.	3200 ppm % of cont. <50>	3200 ppm No. of Surviv.	8000 ppm Av. Wt.	8000 ppm % of cont. <50>	8000 ppm No. of Surviv.
0-0	100 (50)	50/50	100 (50)	100	50/50	100 (50)	100	50/50	100 (50)	100	50/50
1-7	112 (50)	50/50	111 (50)	99	50/50	111 (50)	99	50/50	109 (50)	97	50/50
2-7	122 (50)	50/50	122 (50)	100	50/50	121 (50)	99	50/50	118 (50)	97	50/50
3-7	132 (50)	50/50	131 (50)	99	50/50	130 (50)	98	50/50	126 (50)	95	50/50
4-7	139 (50)	50/50	139 (50)	100	50/50	138 (50)	99	50/50	133 (50)	96	50/50
5-7	146 (50)	50/50	145 (50)	99	50/50	144 (50)	99	50/50	139 (50)	95	50/50
6-7	151 (50)	50/50	151 (50)	100	50/50	148 (50)	98	50/50	144 (50)	95	50/50
7-7	154 (50)	50/50	154 (50)	100	50/50	153 (50)	99	50/50	147 (50)	95	50/50
8-7	158 (50)	50/50	158 (50)	100	50/50	155 (50)	98	50/50	149 (50)	94	50/50
9-7	161 (50)	50/50	161 (50)	100	50/50	159 (50)	99	50/50	153 (50)	95	50/50
10-7	165 (50)	50/50	166 (50)	101	50/50	163 (50)	99	50/50	156 (50)	95	50/50
11-7	167 (50)	50/50	168 (50)	101	50/50	166 (50)	99	50/50	158 (50)	95	50/50
12-7	169 (50)	50/50	170 (50)	101	50/50	168 (50)	99	50/50	161 (50)	95	50/50
13-7	171 (50)	50/50	172 (50)	101	50/50	170 (50)	99	50/50	163 (50)	95	50/50
14-7	173 (50)	50/50	174 (50)	101	50/50	172 (50)	99	50/50	164 (50)	95	50/50
18-7	181 (50)	50/50	182 (50)	101	50/50	179 (50)	99	50/50	169 (50)	93	50/50
22-7	186 (50)	50/50	188 (50)	101	50/50	184 (50)	99	50/50	174 (50)	94	50/50
26-7	192 (50)	50/50	192 (50)	100	50/50	189 (50)	98	50/50	178 (50)	93	50/50
30-7	196 (50)	50/50	197 (50)	101	50/50	193 (50)	98	50/50	182 (50)	93	50/50
34-7	200 (50)	50/50	201 (50)	101	50/50	196 (50)	98	50/50	186 (50)	93	50/50
38-7	207 (50)	50/50	206 (50)	100	50/50	201 (50)	97	50/50	189 (50)	91	50/50
42-7	211 (50)	50/50	211 (50)	100	50/50	206 (50)	98	50/50	194 (50)	92	50/50
46-7	215 (50)	50/50	217 (50)	101	50/50	208 (50)	97	50/50	196 (50)	91	50/50
50-7	221 (50)	50/50	221 (50)	100	50/50	212 (50)	96	50/50	200 (50)	90	50/50
54-7	227 (50)	50/50	226 (50)	100	50/50	218 (50)	96	50/50	206 (50)	91	50/50
58-7	229 (50)	50/50	232 (49)	101	49/50	222 (50)	97	50/50	210 (50)	92	50/50
62-7	236 (50)	50/50	236 (49)	100	49/50	226 (49)	96	49/50	212 (49)	90	49/50
66-7	243 (50)	50/50	246 (49)	101	49/50	234 (48)	96	48/50	219 (49)	90	49/50
70-7	250 (49)	49/50	251 (49)	100	49/50	239 (48)	96	48/50	224 (49)	90	49/50
74-7	259 (47)	47/50	260 (48)	100	48/50	246 (47)	95	47/50	230 (48)	89	48/50
78-7	267 (47)	47/50	268 (48)	100	48/50	254 (47)	95	47/50	238 (48)	89	48/50
82-7	273 (47)	47/50	272 (48)	100	48/50	257 (47)	94	47/50	241 (48)	88	48/50
86-7	277 (47)	47/50	276 (48)	100	48/50	261 (47)	94	47/50	245 (44)	88	44/50
90-7	285 (46)	46/50	282 (47)	99	47/50	267 (47)	94	47/50	251 (44)	88	44/50
94-7	288 (45)	45/50	289 (46)	100	46/50	271 (47)	94	47/50	256 (44)	89	44/50
98-7	288 (45)	45/50	292 (46)	101	46/50	273 (47)	95	47/50	256 (42)	89	42/50
102-7	293 (43)	43/50	295 (46)	101	46/50	273 (46)	93	46/50	255 (41)	87	41/50
104-7	293 (42)	42/50	294 (45)	100	45/50	273 (46)	93	46/50	254 (40)	87	40/50

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

TABLE C 3

BODY WEIGHT CHANGES: MALE

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	129± 5	156± 7	186± 8	210± 9	229± 9	246± 11	259± 11
1280 ppm	129± 5	156± 8	185± 10	206± 12	224± 13*	239± 14*	251± 15**
3200 ppm	129± 5	156± 7	185± 8	207± 8	226± 9	242± 10	256± 11
8000 ppm	129± 5	152± 8**	179± 11**	200± 12**	218± 12**	234± 13**	246± 14**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-7
Control	273± 12	285± 14	296± 15	305± 15	313± 15	318± 15	325± 16
1280 ppm	265± 17*	277± 18*	286± 18**	295± 19**	303± 19**	308± 19**	314± 20**
3200 ppm	269± 12	282± 14	293± 14	302± 14	311± 15	315± 16	320± 16
8000 ppm	259± 15**	271± 16**	282± 16**	291± 17**	298± 17**	302± 17**	307± 17**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 14-7	18-7	22-7	26-7	30-7	34-7	38-7
Control	333± 17	352± 18	368± 18	384± 20	394± 21	403± 21	413± 22
1280 ppm	321± 20**	343± 21*	356± 20**	371± 20**	383± 20*	391± 22*	398± 23**
3200 ppm	328± 16	351± 17	368± 18	384± 19	394± 22	405± 21	413± 24
8000 ppm	315± 17**	338± 16**	353± 17**	368± 18**	380± 19**	389± 19**	397± 19**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

(HAN260)

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 42-7	46-7	50-7	54-7	58-7	62-7	66-7
Control	422± 22	430± 24	435± 23	440± 23	443± 24	446± 24	449± 26
1280 ppm	410± 23*	416± 23*	423± 22*	427± 23*	431± 22*	433± 22*	437± 23
3200 ppm	424± 22	433± 23	438± 24	443± 25	447± 28	451± 26	455± 27
8000 ppm	406± 20**	414± 21**	420± 22**	425± 23**	430± 23*	431± 24**	432± 25**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

(HAN260)

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 70-7	74-7	78-7	82-7	86-7	90-7	94-7
Control	451± 25	452± 24	452± 23	448± 23	444± 33	440± 40	431± 38
1280 ppm	439± 23*	441± 24	442± 25	440± 25	439± 28	437± 33	436± 32
3200 ppm	455± 33	457± 39	460± 29	457± 30	456± 30	453± 32	441± 39
8000 ppm	434± 22**	435± 24**	434± 26**	433± 28*	428± 29*	422± 28*	415± 35

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 98-7	102-7	104-7
Control	427± 31	414± 39	410± 43
1280 ppm	422± 42	413± 48	414± 36
3200 ppm	441± 33	432± 40	423± 40
8000 ppm	412± 37	397± 34	390± 38

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

TABLE C 4

BODY WEIGHT CHANGES: FEMALE

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	100± 3	112± 4	122± 5	132± 6	139± 7	146± 7	151± 8
1280 ppm	100± 3	111± 4	122± 5	131± 5	139± 7	145± 7	151± 8
3200 ppm	100± 3	111± 4	121± 5	130± 5	138± 6	144± 7	148± 7
8000 ppm	100± 3	109± 4**	118± 6**	126± 6**	133± 7**	139± 8**	144± 9**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

(HAN260)

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-7
Control	154± 9	158± 10	161± 10	165± 11	167± 11	169± 11	171± 11
1280 ppm	154± 8	158± 10	161± 10	166± 10	168± 10	170± 10	172± 11
3200 ppm	153± 8	155± 9	159± 9	163± 9	166± 10	168± 10	170± 10
8000 ppm	147± 9**	149± 10**	153± 11**	156± 11**	158± 11**	161± 12**	163± 12**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 14-7	18-7	22-7	26-7	30-7	34-7	38-7
Control	173± 12	181± 12	186± 13	192± 13	196± 15	200± 15	207± 17
1280 ppm	174± 11	182± 11	188± 12	192± 13	197± 13	201± 14	206± 14
3200 ppm	172± 11	179± 11	184± 12	189± 13	193± 13	196± 14	201± 15
8000 ppm	164± 12**	169± 12**	174± 13**	178± 13**	182± 14**	186± 14**	189± 16**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 42-7	46-7	50-7	54-7	58-7	62-7	66-7
Control	211± 18	215± 18	221± 20	227± 21	229± 22	236± 24	243± 26
1280 ppm	211± 15	217± 15	221± 16	226± 17	232± 19	236± 20	246± 21
3200 ppm	206± 17	208± 17	212± 19*	218± 20	222± 22	226± 23	234± 26
8000 ppm	194± 16**	196± 18**	200± 18**	206± 19**	210± 21**	212± 21**	219± 23**

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 70-7	74-7	78-7	82-7	86-7	90-7	94-7
Control	250± 27	259± 29	267± 30	273± 30	277± 30	285± 29	288± 31
1280 ppm	251± 22	260± 24	268± 24	272± 24	276± 24	282± 26	289± 25
3200 ppm	239± 28	246± 28*	254± 29*	257± 29*	261± 30*	267± 31**	271± 31*
8000 ppm	224± 24**	230± 24**	238± 24**	241± 25**	245± 25**	251± 26**	256± 26**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

(HAN260)

BAIS 4

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 98-7	102-7	104-7
Control	288± 34	293± 31	293± 32
1280 ppm	292± 27	295± 30	294± 34
3200 ppm	273± 31*	273± 30**	273± 31*
8000 ppm	256± 24**	255± 28**	254± 32**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

TABLE D 1

FOOD CONSUMPTION CHANGES AND SURVIVAL ANIMAL NUMBERS: MALE

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

MEAN FOOD CONSUMPTION(FC) AND SURVIVAL

Week-Day on Study	Control Av. FC.	Control No. of Surviv. <50>	1280 ppm Av. FC.	1280 ppm % of cont. <50>	1280 ppm No. of Surviv.	3200 ppm Av. FC.	3200 ppm % of cont. <50>	3200 ppm No. of Surviv.	8000 ppm Av. FC.	8000 ppm % of cont. <50>	8000 ppm No. of Surviv.
1-7	13.6 (50)	50/50	13.7 (50)	101	50/50	13.8 (50)	101	50/50	13.4 (50)	99	50/50
2-7	14.1 (50)	50/50	14.3 (50)	101	50/50	14.3 (50)	101	50/50	13.7 (50)	97	50/50
3-7	15.0 (50)	50/50	14.5 (50)	97	50/50	14.8 (50)	99	50/50	14.2 (50)	95	50/50
4-7	15.0 (50)	50/50	14.5 (50)	97	50/50	14.9 (50)	99	50/50	14.7 (50)	98	50/50
5-7	14.6 (50)	50/50	14.2 (50)	97	50/50	14.6 (50)	100	50/50	14.2 (50)	97	50/50
6-7	14.7 (50)	50/50	14.2 (50)	97	50/50	14.5 (50)	99	50/50	14.2 (50)	97	50/50
7-7	14.9 (50)	50/50	14.2 (50)	95	50/50	14.4 (50)	97	50/50	14.1 (50)	95	50/50
8-7	15.2 (50)	50/50	14.7 (50)	97	50/50	14.9 (50)	98	50/50	14.6 (50)	96	50/50
9-7	15.4 (50)	50/50	14.7 (50)	95	50/50	15.0 (50)	97	50/50	14.7 (50)	95	50/50
10-7	15.4 (50)	50/50	14.5 (50)	94	50/50	14.9 (50)	97	50/50	15.1 (50)	98	50/50
11-7	15.4 (50)	50/50	14.6 (50)	95	50/50	14.9 (50)	97	50/50	14.7 (50)	95	50/50
12-7	15.3 (50)	50/50	14.5 (50)	95	50/50	15.0 (50)	98	50/50	14.8 (50)	97	50/50
13-7	15.4 (50)	50/50	14.6 (50)	95	50/50	14.8 (50)	96	50/50	14.8 (50)	96	50/50
14-7	15.4 (50)	50/50	14.7 (50)	95	50/50	15.0 (50)	97	50/50	14.8 (50)	96	50/50
18-7	15.7 (50)	50/50	15.1 (50)	96	50/50	15.0 (50)	96	50/50	15.1 (50)	96	50/50
22-7	16.2 (50)	50/50	15.6 (50)	96	50/50	15.5 (50)	96	50/50	15.5 (50)	96	50/50
26-7	16.5 (50)	50/50	16.1 (50)	98	50/50	16.0 (50)	97	50/50	16.0 (50)	97	50/50
30-7	16.0 (50)	50/50	15.7 (50)	98	50/50	15.4 (50)	96	50/50	15.7 (50)	98	50/50
34-7	16.4 (49)	49/50	15.7 (50)	96	50/50	15.7 (50)	96	50/50	15.7 (50)	96	50/50
38-7	16.4 (49)	49/50	15.8 (50)	96	50/50	16.0 (50)	98	50/50	15.7 (50)	96	50/50
42-7	16.2 (49)	49/50	15.9 (49)	98	49/50	15.7 (50)	97	50/50	15.6 (50)	96	50/50
46-7	15.9 (49)	49/50	15.3 (49)	96	49/50	15.4 (50)	97	50/50	15.3 (50)	96	50/50
50-7	15.9 (49)	49/50	15.8 (49)	99	49/50	15.5 (50)	97	50/50	15.4 (50)	97	50/50
54-7	16.3 (49)	49/50	15.8 (49)	97	49/50	15.6 (50)	96	50/50	15.7 (50)	96	50/50
58-7	15.8 (49)	49/50	15.3 (49)	97	49/50	15.1 (50)	96	50/50	15.3 (50)	97	50/50
62-7	16.7 (49)	49/50	16.3 (49)	98	49/50	16.1 (49)	96	49/50	16.1 (50)	96	50/50
66-7	16.2 (49)	49/50	16.0 (49)	99	49/50	15.9 (49)	98	49/50	15.5 (50)	96	50/50
70-7	16.4 (47)	47/50	16.2 (49)	99	49/50	15.7 (49)	96	49/50	15.8 (48)	96	48/50
74-7	16.8 (47)	47/50	16.4 (49)	98	49/50	15.8 (49)	94	49/50	16.0 (47)	95	47/50
78-7	16.7 (45)	45/50	16.8 (49)	101	49/50	16.4 (47)	98	47/50	16.5 (47)	99	47/50
82-7	16.7 (44)	44/50	16.4 (49)	98	49/50	15.9 (46)	95	46/50	16.0 (47)	96	47/50
86-7	16.4 (43)	44/50	16.2 (48)	99	48/50	15.9 (46)	97	46/50	15.9 (47)	97	47/50
90-7	16.0 (43)	43/50	15.6 (47)	98	47/50	15.4 (46)	96	46/50	15.2 (44)	95	44/50
94-7	15.6 (40)	40/50	15.0 (44)	96	44/50	14.4 (46)	92	46/50	15.3 (43)	98	43/50
98-7	15.7 (36)	36/50	15.2 (42)	97	42/50	15.2 (41)	97	41/50	14.9 (41)	95	41/50
102-7	15.2 (35)	35/50	15.3 (40)	101	40/50	15.1 (41)	99	41/50	15.3 (39)	101	39/50
104-7	15.9 (33)	33/50	15.8 (38)	99	38/50	15.4 (39)	97	39/50	15.3 (39)	96	39/50

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

TABLE D 2

FOOD CONSUMPTION CHANGES AND

SURVIVAL ANIMAL NUMBERS: FEMALE

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

MEAN FOOD CONSUMPTION(FC) AND SURVIVAL

Week-Day on Study	Control Av. FC.	Control No. of Surviv. <50>	1280 ppm Av. FC.	1280 ppm % of cont. <50>	1280 ppm No. of Surviv.	3200 ppm Av. FC.	3200 ppm % of cont. <50>	3200 ppm No. of Surviv.	8000 ppm Av. FC.	8000 ppm % of cont. <50>	8000 ppm No. of Surviv.
1-7	10.3 (50)	50/50	10.3 (50)	100	50/50	10.1 (50)	98	50/50	10.1 (50)	98	50/50
2-7	9.9 (50)	50/50	10.2 (50)	103	50/50	9.7 (50)	98	50/50	9.5 (50)	96	50/50
3-7	10.1 (50)	50/50	10.4 (50)	103	50/50	10.5 (50)	104	50/50	9.8 (50)	97	50/50
4-7	10.3 (50)	50/50	10.2 (50)	99	50/50	10.2 (50)	99	50/50	10.0 (50)	97	50/50
5-7	10.1 (50)	50/50	10.1 (50)	100	50/50	10.0 (50)	99	50/50	9.9 (50)	98	50/50
6-7	9.9 (50)	50/50	9.9 (50)	100	50/50	9.7 (50)	98	50/50	9.6 (50)	97	50/50
7-7	9.7 (50)	50/50	9.6 (50)	99	50/50	9.7 (50)	100	50/50	9.4 (50)	97	50/50
8-7	9.7 (50)	50/50	9.7 (50)	100	50/50	9.6 (50)	99	50/50	9.4 (50)	97	50/50
9-7	9.8 (50)	50/50	9.8 (50)	100	50/50	9.6 (50)	98	50/50	9.5 (50)	97	50/50
10-7	9.8 (50)	50/50	9.8 (50)	100	50/50	9.7 (50)	99	50/50	9.5 (50)	97	50/50
11-7	9.6 (50)	50/50	9.8 (50)	102	50/50	9.6 (50)	100	50/50	9.4 (50)	98	50/50
12-7	9.9 (50)	50/50	10.1 (50)	102	50/50	9.8 (50)	99	50/50	9.6 (50)	97	50/50
13-7	9.7 (50)	50/50	10.0 (50)	103	50/50	9.6 (50)	99	50/50	9.5 (50)	98	50/50
14-7	10.0 (50)	50/50	10.0 (50)	100	50/50	9.8 (50)	98	50/50	9.4 (50)	94	50/50
18-7	9.7 (50)	50/50	10.2 (50)	105	50/50	9.7 (50)	100	50/50	9.7 (50)	100	50/50
22-7	10.1 (50)	50/50	10.7 (50)	106	50/50	10.2 (50)	101	50/50	10.2 (50)	101	50/50
26-7	10.6 (50)	50/50	10.9 (50)	103	50/50	10.6 (50)	100	50/50	10.1 (50)	95	50/50
30-7	10.6 (50)	50/50	11.0 (50)	104	50/50	10.5 (50)	99	50/50	10.2 (50)	96	50/50
34-7	10.8 (50)	50/50	11.3 (50)	105	50/50	10.6 (50)	98	50/50	10.1 (50)	94	50/50
38-7	11.2 (50)	50/50	12.1 (50)	108	50/50	11.3 (50)	101	50/50	10.6 (50)	95	50/50
42-7	11.0 (50)	50/50	11.5 (50)	105	50/50	10.6 (50)	96	50/50	10.1 (50)	92	50/50
46-7	11.3 (50)	50/50	12.3 (50)	109	50/50	10.9 (50)	96	50/50	10.1 (50)	89	50/50
50-7	12.1 (50)	50/50	12.8 (50)	106	50/50	11.5 (50)	95	50/50	10.9 (50)	90	50/50
54-7	11.8 (50)	50/50	12.6 (50)	107	50/50	11.6 (50)	98	50/50	11.0 (50)	93	50/50
58-7	11.5 (50)	50/50	12.1 (49)	105	49/50	11.3 (50)	98	50/50	10.9 (50)	95	50/50
62-7	12.5 (50)	50/50	13.2 (49)	106	49/50	12.1 (49)	97	49/50	11.5 (49)	92	49/50
66-7	12.3 (50)	50/50	13.6 (49)	111	49/50	12.2 (48)	99	48/50	11.3 (49)	92	49/50
70-7	12.4 (49)	49/50	12.9 (49)	104	49/50	12.1 (48)	98	48/50	11.2 (49)	90	49/50
74-7	13.4 (47)	47/50	14.1 (48)	105	48/50	12.8 (47)	96	47/50	11.9 (48)	89	48/50
78-7	13.7 (47)	47/50	14.3 (48)	104	48/50	13.2 (47)	96	47/50	12.5 (48)	91	48/50
82-7	13.5 (47)	47/50	13.7 (48)	101	48/50	12.5 (47)	93	47/50	11.9 (48)	88	48/50
86-7	13.4 (47)	47/50	13.6 (48)	101	48/50	12.8 (47)	96	47/50	12.3 (44)	92	44/50
90-7	13.8 (46)	46/50	13.9 (47)	101	47/50	12.9 (47)	93	47/50	12.5 (44)	91	44/50
94-7	13.4 (45)	45/50	13.4 (46)	100	46/50	12.7 (47)	95	47/50	12.2 (44)	91	44/50
98-7	13.1 (45)	45/50	13.5 (46)	103	46/50	12.9 (47)	98	47/50	12.2 (42)	93	42/50
102-7	13.8 (43)	43/50	14.0 (46)	101	46/50	12.7 (46)	92	46/50	12.3 (41)	89	41/50
104-7	13.6 (42)	42/50	13.6 (45)	100	45/50	12.6 (46)	93	46/50	12.1 (40)	89	40/50

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

TABLE D 3

FOOD CONSUMPTION CHANGES: MALE

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	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	13.6± 0.7	14.1± 0.7	15.0± 0.9	15.0± 0.8	14.6± 1.0	14.7± 1.0	14.9± 1.1
1280 ppm	13.7± 0.7	14.3± 1.0	14.5± 1.0*	14.5± 0.9*	14.2± 1.0	14.2± 1.1*	14.2± 1.1**
3200 ppm	13.8± 0.7	14.3± 0.8	14.8± 0.7	14.9± 0.8	14.6± 0.8	14.5± 0.9	14.4± 0.9*
8000 ppm	13.4± 0.8	13.7± 1.0	14.2± 0.9**	14.7± 0.9	14.2± 0.9	14.2± 0.9*	14.1± 1.0**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(4)	9-7(4)	10-7(4)	11-7(4)	12-7(4)	13-7(4)	14-7(4)
Control	15.2± 1.1	15.4± 1.1	15.4± 1.3	15.4± 1.5	15.3± 1.3	15.4± 1.5	15.4± 1.4
1280 ppm	14.7± 1.3	14.7± 1.2**	14.5± 1.0**	14.6± 1.1*	14.5± 1.1**	14.6± 1.0	14.7± 1.2**
3200 ppm	14.9± 1.0	15.0± 1.0	14.9± 0.9	14.9± 1.0	15.0± 1.0	14.8± 0.9	15.0± 1.0
8000 ppm	14.6± 1.0*	14.7± 1.0**	15.1± 1.1	14.7± 1.1	14.8± 1.1	14.8± 1.2	14.8± 1.1*

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 18-7(4)	22-7(4)	26-7(4)	30-7(4)	34-7(4)	38-7(4)	42-7(4)
Control	15.7± 1.5	16.2± 1.4	16.5± 2.0	16.0± 2.0	16.4± 1.8	16.4± 1.8	16.2± 1.7
1280 ppm	15.1± 1.3*	15.6± 1.2*	16.1± 1.5	15.7± 1.3	15.7± 1.5	15.8± 2.0	15.9± 1.5
3200 ppm	15.0± 1.0*	15.5± 1.1**	16.0± 1.0	15.4± 2.3	15.7± 1.3	16.0± 1.4	15.7± 1.3
8000 ppm	15.1± 1.3*	15.5± 1.3*	16.0± 1.5	15.7± 1.5	15.7± 1.4	15.7± 1.3	15.6± 1.4

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

(HAN260)

BAIS 4

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	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	15.9± 1.9	15.9± 1.8	16.3± 1.7	15.8± 1.6	16.7± 1.5	16.2± 1.4	16.4± 1.5
1280 ppm	15.3± 1.4	15.8± 1.5	15.8± 1.6	15.3± 1.6	16.3± 1.7	16.0± 1.5	16.2± 1.7
3200 ppm	15.4± 1.2	15.5± 1.3	15.6± 1.7	15.1± 1.2	16.1± 1.3	15.9± 1.3	15.7± 1.4
8000 ppm	15.3± 1.3	15.4± 1.2	15.7± 1.1	15.3± 1.3	16.1± 1.3	15.5± 1.2	15.8± 1.5

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 74-7(4)	78-7(4)	82-7(4)	86-7(4)	90-7(4)	94-7(4)	98-7(4)
Control	16.8± 1.9	16.7± 1.7	16.7± 2.1	16.4± 1.8	16.0± 3.5	15.6± 2.2	15.7± 2.0
1280 ppm	16.4± 1.7	16.8± 2.0	16.4± 1.8	16.2± 1.7	15.6± 1.8	15.0± 2.0	15.2± 2.4
3200 ppm	15.8± 1.9*	16.4± 1.3	15.9± 1.3	15.9± 1.5	15.4± 1.7	14.4± 2.8	15.2± 2.1
8000 ppm	16.0± 1.5	16.5± 1.6	16.0± 1.6	15.9± 1.9	15.2± 2.3	15.3± 2.8	14.9± 1.7

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 102-7(4)	104-7(4)
Control	15.2± 3.8	15.9± 2.6
1280 ppm	15.3± 2.1	15.8± 1.8
3200 ppm	15.1± 2.3	15.4± 2.2
8000 ppm	15.3± 2.1	15.3± 1.9

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

TABLE D 4

FOOD CONSUMPTION CHANGES: FEMALE

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	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	10.3± 0.6	9.9± 0.7	10.1± 0.6	10.3± 0.7	10.1± 0.7	9.9± 0.9	9.7± 0.8
1280 ppm	10.3± 0.6	10.2± 0.6	10.4± 1.3	10.2± 0.8	10.1± 0.7	9.9± 0.9	9.6± 0.7
3200 ppm	10.1± 0.5	9.7± 0.7	10.5± 2.1	10.2± 0.6	10.0± 0.7	9.7± 0.6	9.7± 0.7
8000 ppm	10.1± 0.6	9.5± 0.7**	9.8± 0.7*	10.0± 0.9	9.9± 0.8	9.6± 0.9	9.4± 0.9

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(4)	9-7(4)	10-7(4)	11-7(4)	12-7(4)	13-7(4)	14-7(4)
Control	9.7± 0.8	9.8± 0.9	9.8± 0.9	9.6± 0.9	9.9± 1.7	9.7± 0.8	10.0± 1.3
1280 ppm	9.7± 0.7	9.8± 0.8	9.8± 0.8	9.8± 0.8	10.1± 1.1	10.0± 1.2	10.0± 0.9
3200 ppm	9.6± 0.8	9.6± 0.7	9.7± 0.7	9.6± 0.8	9.8± 0.9	9.6± 0.8	9.8± 0.9
8000 ppm	9.4± 0.8	9.5± 0.9	9.5± 0.9	9.4± 0.9	9.6± 0.8	9.5± 0.9	9.4± 1.0**

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

(HAN260)

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 18-7(4)	22-7(4)	26-7(4)	30-7(4)	34-7(4)	38-7(4)	42-7(4)
Control	9.7± 0.7	10.1± 1.1	10.6± 1.1	10.6± 1.3	10.8± 1.3	11.2± 1.6	11.0± 1.6
1280 ppm	10.2± 1.5	10.7± 1.4	10.9± 1.6	11.0± 1.6	11.3± 1.7	12.1± 2.2*	11.5± 2.1
3200 ppm	9.7± 1.1	10.2± 1.8	10.6± 1.5	10.5± 1.6	10.6± 1.4	11.3± 2.1	10.6± 1.5
8000 ppm	9.7± 1.0	10.2± 2.4	10.1± 1.0*	10.2± 1.3	10.1± 1.1**	10.6± 1.6	10.1± 1.2*

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	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	11.3± 1.7	12.1± 1.8	11.8± 1.7	11.5± 1.6	12.5± 2.0	12.3± 1.6	12.4± 1.7
1280 ppm	12.3± 2.7	12.8± 2.2	12.6± 2.4	12.1± 2.1	13.2± 2.1	13.6± 2.4*	12.9± 1.9
3200 ppm	10.9± 2.0	11.5± 1.9	11.6± 1.9	11.3± 1.8	12.1± 2.0	12.2± 2.2	12.1± 1.9
8000 ppm	10.1± 1.1**	10.9± 1.7*	11.0± 1.4*	10.9± 1.3	11.5± 1.6*	11.3± 1.5*	11.2± 1.3**

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 74-7(4)	78-7(4)	82-7(4)	86-7(4)	90-7(4)	94-7(4)	98-7(4)
Control	13.4± 1.7	13.7± 1.5	13.5± 1.6	13.4± 1.7	13.8± 2.2	13.4± 1.6	13.1± 2.5
1280 ppm	14.1± 2.1	14.3± 2.2	13.7± 2.1	13.6± 2.5	13.9± 2.7	13.4± 1.9	13.5± 1.8
3200 ppm	12.8± 2.1*	13.2± 2.2	12.5± 1.8*	12.8± 1.9	12.9± 2.0*	12.7± 1.9	12.9± 2.0
8000 ppm	11.9± 1.1**	12.5± 1.4**	11.9± 1.6**	12.3± 1.1**	12.5± 1.3**	12.2± 1.6**	12.2± 1.3**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

(HAN260)

BAIS 4

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 102-7(4)	104-7(4)
Control	13.8± 1.9	13.6± 1.9
1280 ppm	14.0± 2.2	13.6± 2.4
3200 ppm	12.7± 2.1*	12.6± 2.4
8000 ppm	12.3± 1.5**	12.1± 2.0**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

TABLE E 1

CHEMICAL INTAKE CHANGES: MALE

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g／kg／d a y
REPORT TYPE : A1 104
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2	3	4	5	6	7
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
1280 ppm	0.113± 0.003	0.099± 0.003	0.090± 0.003	0.083± 0.003	0.076± 0.003	0.072± 0.003	0.069± 0.003
3200 ppm	0.282± 0.009	0.247± 0.009	0.228± 0.007	0.211± 0.007	0.192± 0.007	0.181± 0.007	0.171± 0.007
8000 ppm	0.706± 0.025	0.615± 0.021	0.570± 0.020	0.538± 0.022	0.488± 0.017	0.462± 0.023	0.437± 0.020

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g／kg／d a y
REPORT TYPE : A1 104
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8	9	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
1280 ppm	0.068± 0.004	0.066± 0.003	0.063± 0.003	0.062± 0.003	0.061± 0.003	0.060± 0.003	0.058± 0.004
3200 ppm	0.169± 0.007	0.163± 0.007	0.158± 0.007	0.153± 0.007	0.152± 0.007	0.148± 0.008	0.146± 0.008
8000 ppm	0.431± 0.015	0.418± 0.016	0.415± 0.020	0.394± 0.021	0.391± 0.021	0.384± 0.021	0.376± 0.020

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g／kg／d a y
REPORT TYPE : A1 104
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 18	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
1280 ppm	0.056± 0.004	0.056± 0.004	0.056± 0.005	0.053± 0.004	0.052± 0.005	0.051± 0.006	0.050± 0.004
3200 ppm	0.137± 0.006	0.134± 0.007	0.133± 0.006	0.124± 0.017	0.124± 0.009	0.124± 0.014	0.118± 0.009
8000 ppm	0.357± 0.027	0.350± 0.023	0.348± 0.029	0.331± 0.028	0.323± 0.027	0.317± 0.027	0.307± 0.026

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g／kg／d a y
REPORT TYPE : A1 104
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 46	50	54	58	62	66	70
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
1280 ppm	0.047± 0.004	0.048± 0.005	0.047± 0.005	0.045± 0.005	0.048± 0.005	0.047± 0.004	0.047± 0.005
3200 ppm	0.114± 0.007	0.113± 0.008	0.112± 0.011	0.108± 0.007	0.114± 0.009	0.112± 0.007	0.111± 0.008
8000 ppm	0.296± 0.024	0.294± 0.023	0.296± 0.021	0.285± 0.025	0.300± 0.026	0.288± 0.024	0.292± 0.033

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g／kg／d a y
REPORT TYPE : A1 104
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 74	78	82	86	90	94	98
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
1280 ppm	0.048± 0.005	0.049± 0.006	0.048± 0.005	0.047± 0.005	0.046± 0.005	0.044± 0.006	0.046± 0.006
3200 ppm	0.111± 0.011	0.114± 0.010	0.112± 0.007	0.112± 0.011	0.109± 0.011	0.104± 0.018	0.110± 0.014
8000 ppm	0.295± 0.031	0.304± 0.034	0.297± 0.036	0.298± 0.038	0.289± 0.047	0.298± 0.083	0.292± 0.039

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g／kg／d a y
REPORT TYPE : A1 104
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 102	104
Control	0.000± 0.000	0.000± 0.000
1280 ppm	0.048± 0.009	0.049± 0.006
3200 ppm	0.112± 0.016	0.117± 0.015
8000 ppm	0.309± 0.045	0.317± 0.043

TABLE E 2

CHEMICAL INTAKE CHANGES: FEMALE

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g／kg／d a y
REPORT TYPE : A1 104
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2	3	4	5	6	7
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
1280 ppm	0.118± 0.005	0.107± 0.006	0.102± 0.013	0.094± 0.005	0.089± 0.004	0.085± 0.006	0.080± 0.004
3200 ppm	0.291± 0.011	0.257± 0.012	0.258± 0.055	0.236± 0.009	0.221± 0.008	0.209± 0.008	0.203± 0.009
8000 ppm	0.742± 0.032	0.648± 0.035	0.624± 0.033	0.603± 0.035	0.565± 0.028	0.536± 0.030	0.514± 0.027

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g／kg／d a y
REPORT TYPE : A1 104
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8	9	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
1280 ppm	0.079± 0.004	0.078± 0.003	0.076± 0.003	0.074± 0.004	0.076± 0.008	0.075± 0.007	0.074± 0.004
3200 ppm	0.197± 0.010	0.193± 0.009	0.189± 0.009	0.185± 0.010	0.186± 0.012	0.180± 0.011	0.182± 0.012
8000 ppm	0.505± 0.022	0.498± 0.025	0.489± 0.027	0.477± 0.024	0.475± 0.022	0.465± 0.028	0.457± 0.026

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g／kg／d a y
REPORT TYPE : A1 104
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 18	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
1280 ppm	0.072± 0.008	0.073± 0.009	0.073± 0.009	0.072± 0.008	0.072± 0.009	0.075± 0.012	0.070± 0.011
3200 ppm	0.174± 0.015	0.177± 0.026	0.179± 0.021	0.174± 0.021	0.173± 0.016	0.180± 0.029	0.165± 0.018
8000 ppm	0.457± 0.035	0.467± 0.101	0.452± 0.031	0.448± 0.048	0.434± 0.034	0.451± 0.061	0.417± 0.040

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g／kg／d a y
REPORT TYPE : A1 104
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 46	50	54	58	62	66	70
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
1280 ppm	0.072± 0.015	0.074± 0.011	0.071± 0.011	0.067± 0.010	0.071± 0.010	0.071± 0.013	0.066± 0.009
3200 ppm	0.168± 0.027	0.173± 0.024	0.169± 0.022	0.163± 0.020	0.172± 0.025	0.166± 0.025	0.163± 0.022
8000 ppm	0.414± 0.033	0.438± 0.066	0.427± 0.041	0.418± 0.052	0.436± 0.054	0.413± 0.047	0.403± 0.051

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g／kg／d a y
REPORT TYPE : A1 104
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 74	78	82	86	90	94	98
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
1280 ppm	0.070± 0.008	0.068± 0.009	0.064± 0.010	0.063± 0.011	0.063± 0.012	0.060± 0.009	0.060± 0.008
3200 ppm	0.167± 0.025	0.168± 0.025	0.156± 0.022	0.157± 0.021	0.155± 0.022	0.151± 0.022	0.152± 0.023
8000 ppm	0.416± 0.049	0.422± 0.057	0.398± 0.056	0.405± 0.049	0.402± 0.046	0.384± 0.051	0.383± 0.046

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g／kg／d a y
REPORT TYPE : A1 104
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 102	104
Control	0.000± 0.000	0.000± 0.000
1280 ppm	0.061± 0.009	0.059± 0.010
3200 ppm	0.150± 0.026	0.148± 0.027
8000 ppm	0.387± 0.047	0.383± 0.064

TABLE F 1

HEMATOLOGY: MALE

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	33	7.56± 1.25	12.9± 2.4	35.9± 5.4	47.9± 4.9	17.1± 1.6	35.7± 1.8	951± 217
1280 ppm	38	8.14± 1.14*	13.8± 2.4	38.0± 5.2	46.8± 2.4	16.9± 1.4	36.1± 2.0	976± 285
3200 ppm	39	8.43± 0.74**	14.5± 1.2**	39.7± 2.9**	47.1± 1.5	17.2± 0.7	36.6± 0.7	887± 131
8000 ppm	38	7.88± 0.89	13.4± 1.9	37.2± 4.1	47.4± 3.0	17.1± 1.7	35.9± 1.7	1018± 224

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

(HCL070)

BA1S 4

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	RETICULOCYTE %	
Control	33	5.6±	4.9
1280 ppm	38	4.0±	2.7*
3200 ppm	39	3.4±	1.0**
8000 ppm	38	4.7±	2.2

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHER
Control	33	9.83± 13.41	0± 1	45± 12	1± 1	0± 0	5± 2	40± 11	8± 22
1280 ppm	38	9.26± 13.09	1± 1	51± 11	2± 2	0± 0	6± 2	38± 10	3± 15
3200 ppm	39	6.62± 1.85	0± 0	49± 7	2± 1	0± 0	6± 2*	42± 7	1± 1
8000 ppm	38	8.02± 1.59**	0± 1	51± 9	2± 1	0± 0	5± 2	41± 9	1± 2

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

(HCL070)

TABLE F 2

HEMATOLOGY: FEMALE

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$		HEMOGLOBIN g/dℓ		HEMATOCRIT %		MCV f ℓ		MCH p g		MCHC g/dℓ		PLATELET $10^3/\mu\ell$	
Control	42	8.03±	0.78	15.0±	1.6	40.0±	3.6	49.9±	1.6	18.7±	0.7	37.4±	1.1	671±	146
1280 ppm	44	7.81±	0.92	14.6±	1.8	39.4±	4.1	50.6±	2.3	18.8±	0.9	37.1±	1.4	694±	163
3200 ppm	46	7.91±	0.66*	14.9±	1.2	40.2±	2.8	50.9±	1.6**	18.8±	0.4	37.0±	0.8**	748±	181**
8000 ppm	39	7.62±	0.31**	14.5±	0.5**	39.3±	1.4**	51.5±	0.9**	19.0±	0.3*	36.8±	0.3**	771±	83**

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

(HCL070)

BA1S4

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	RETICULOCYTE %	
Control	42	3.0±	1.7
1280 ppm	44	4.1±	5.2
3200 ppm	46	3.6±	2.4**
8000 ppm	39	4.2±	0.5**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHER
Control	42	3.09± 1.48	1± 1	43± 11	2± 1	0± 0	5± 2	48± 11	1± 3
1280 ppm	44	3.34± 1.81	1± 1	43± 11	1± 1	0± 0	5± 2	47± 13	3± 13
3200 ppm	46	3.27± 1.85	1± 1	41± 11	2± 1	0± 0	5± 2	52± 10	1± 1
8000 ppm	39	3.39± 1.58	1± 1	37± 10	2± 1	0± 0	5± 2	55± 9*	1± 4

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

TABLE G 1

BIOCHEMISTRY: MALE

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	TOTAL PROTEIN g／dℓ	ALBUMIN g／dℓ	A/G RATIO	T-BILIRUBIN mg／dℓ	GLUCOSE mg／dℓ	T-CHOLESTEROL mg／dℓ	TRIGLYCERIDE mg／dℓ
Control	33	6.7± 0.4	2.7± 0.2	0.7± 0.1	0.19± 0.14	144± 20	195± 79	106± 82
1280 ppm	38	6.7± 0.4	2.8± 0.3	0.7± 0.1	0.15± 0.03	145± 17	181± 52	97± 42
3200 ppm	39	6.8± 0.4	2.8± 0.2	0.7± 0.1	0.16± 0.03	147± 21	201± 55	109± 52
8000 ppm	38	6.6± 0.3	2.8± 0.2	0.7± 0.1	0.15± 0.03	149± 17	219± 85	140± 100

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

(HCL074)

BAIS 4

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : AI

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dl	AST IU/l	ALT IU/l	LDH IU/l	ALP IU/l	G-GTP IU/l	CK IU/l
Control	33	284± 113	95± 85	40± 28	149± 87	188± 80	6± 5	126± 42
1280 ppm	38	261± 69	79± 24	34± 13	141± 45	196± 56	6± 3	117± 55
3200 ppm	39	286± 83	80± 83	32± 13	132± 50	170± 60	8± 5	112± 47
8000 ppm	38	308± 113	73± 28	32± 13	126± 35	196± 186	14± 7**	114± 54

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	UREA NITROGEN mg/dl	CREATININE mg/dl	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dl	INORGANIC PHOSPHORUS mg/dl
Control	33	19.4± 4.7	0.6± 0.1	143± 1	3.8± 0.5	106± 1	10.7± 0.4	4.3± 0.5
1280 ppm	38	18.7± 3.3	0.6± 0.1	143± 1	3.9± 0.3	106± 2	10.6± 0.3	4.3± 0.4
3200 ppm	39	19.8± 3.4	0.6± 0.1	142± 1	3.9± 0.3	106± 2	10.7± 0.4	4.2± 0.6
8000 ppm	38	25.0± 20.8*	0.7± 0.3	142± 1	4.1± 0.2**	105± 2	10.6± 0.6	5.0± 3.0*

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

TABLE G 2

BIOCHEMISTRY: FEMALE

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	TOTAL PROTEIN g/dℓ	ALBUMIN g/dℓ	A/G RATIO	T-BILIRUBIN mg/dℓ	GLUCOSE mg/dℓ	T-CHOLESTEROL mg/dℓ	TRIGLYCERIDE mg/dℓ
Control	42	6.9± 0.5	3.6± 0.4	1.1± 0.1	0.14± 0.04	143± 14	132± 44	87± 77
1280 ppm	44	6.9± 0.5	3.6± 0.4	1.1± 0.1	0.14± 0.03	143± 21	130± 32	71± 53
3200 ppm	46	7.0± 0.4	3.6± 0.2	1.1± 0.1	0.13± 0.02	146± 14	130± 28	58± 53
8000 ppm	39	7.1± 0.3	3.8± 0.3**	1.1± 0.1*	0.14± 0.02	145± 26	136± 23	54± 28

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dℓ	AST IU/ℓ	ALT IU/ℓ	LDH IU/ℓ	ALP IU/ℓ	G-GTP IU/ℓ	CK IU/ℓ
Control	42	243± 78	114± 89	48± 22	181± 67	118± 68	2± 2	87± 23
1280 ppm	44	239± 57	113± 53	47± 24	201± 105	106± 59	2± 1	102± 94
3200 ppm	46	239± 55	104± 40	42± 17	185± 76	116± 107	2± 1	84± 28
8000 ppm	39	252± 37	93± 36	41± 19	157± 67	93± 26	4± 6**	79± 17

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

(HCL074)

BA1S4

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	UREA NITROGEN mg/dl	CREATININE mg/dl	SODIUM mEq/l	POTASSIUM mEq/l	CHLORIDE mEq/l	CALCIUM mg/dl	INORGANIC PHOSPHORUS mg/dl
Control	42	19.1± 17.5	0.6± 0.6	142± 1	3.7± 0.5	104± 2	10.7± 0.6	4.4± 2.2
1280 ppm	44	16.7± 5.3	0.5± 0.1	142± 2	3.7± 0.4	105± 2	10.6± 0.5	3.9± 0.8
3200 ppm	46	16.4± 2.5	0.5± 0.1	142± 1	3.7± 0.4	105± 2	10.6± 0.4	4.0± 0.8
8000 ppm	39	16.4± 2.0	0.5± 0.1	142± 2	3.7± 0.4	104± 1	10.6± 0.3	3.9± 0.7

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

(HCL074)

BA1S4

TABLE H 1

URINALYSIS: MALE

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Bilirubin −	+	2+	3+	CHI
Control	33	0	5	3	11	11	3	0		0	0	0	0	20	13		33	0	0	0	0	0		30	3	0	0	0	0		32	0	0	1	
1280 ppm	38	0	1	5	11	15	6	0		0	0	0	0	23	15		38	0	0	0	0	0		33	5	0	0	0	0		38	0	0	0	
3200 ppm	39	0	1	4	5	14	15	0	*	0	0	0	0	26	13		39	0	0	0	0	0		35	4	0	0	0	0		39	0	0	0	
8000 ppm	39	0	3	1	15	17	3	0		0	0	0	1	23	15		39	0	0	0	0	0		36	3	0	0	0	0		39	0	0	0	

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

(HCL101)

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	Occult blood — ± + 2+ 3+	CHI	Urobilinogen ± + 2+ 3+ 4+	CHI
Control	33	33 0 0 0 0		33 0 0 0 0	
1280 ppm	38	38 0 0 0 0		38 0 0 0 0	
3200 ppm	39	37 0 1 0 1		39 0 0 0 0	
8000 ppm	39	36 0 0 1 2		39 0 0 0 0	

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

(HCL101)

TABLE H 2

URINALYSIS: FEMALE

STUDY NO. : 0579 URINALYSIS
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Bilirubin −	+	2+	3+	CHI
Control	43	0	2	1	9	16	12	3		0	0	2	8	23	10		43	0	0	0	0	0		11	32	0	0	0	0		43	0	0	0	
1280 ppm	45	0	2	9	13	6	13	2	*	0	0	4	11	14	16		45	0	0	0	0	0		14	31	0	0	0	0		45	0	0	0	
3200 ppm	46	0	1	2	2	9	28	4	*	0	1	3	12	19	11		46	0	0	0	0	0		16	30	0	0	0	0		45	1	0	0	
8000 ppm	40	0	4	4	8	12	9	3		0	0	1	8	18	13		40	0	0	0	0	0		18	22	0	0	0	0		40	0	0	0	

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

STUDY NO. : 0579 URINALYSIS
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

Group Name	NO. of Animals	Occult blood — ± + 2+ 3+	CHI	Urobilinogen ± + 2+ 3+ 4+	CHI
Control	43	39 0 1 0 3		43 0 0 0 0	
1280 ppm	45	44 0 0 1 0		45 0 0 0 0	
3200 ppm	46	45 1 0 0 0		46 0 0 0 0	
8000 ppm	40	39 0 0 0 1		40 0 0 0 0	

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

TABLE J 1

ORGAN WEIGHT, ABSOLUTE: MALE

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	Body Weight	ADRENALS	TESTES	HEART	LUNGS	KIDNEYS
Control	33	390± 43	0.102± 0.157	3.452± 2.157	1.248± 0.110	1.524± 0.583	2.967± 0.282
1280 ppm	38	394± 35	0.179± 0.583	3.045± 1.294	1.261± 0.075	1.427± 0.196	2.966± 0.312
3200 ppm	39	403± 38	0.077± 0.023	3.062± 1.076	1.273± 0.080	1.395± 0.119	3.139± 0.370*
8000 ppm	39	371± 38	0.072± 0.020*	3.227± 1.331	1.280± 0.131	1.373± 0.125	3.348± 0.555**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	SPLEEN		LIVER		BRAIN	
Control	33	1.457±	1.472	11.842±	1.793	2.063±	0.057
1280 ppm	38	1.071±	0.322	11.400±	1.518	2.077±	0.045
3200 ppm	39	1.040±	0.185	11.756±	1.364	2.082±	0.048
8000 ppm	39	1.125±	0.143	11.590±	1.395	2.072±	0.046

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

(HCL040)

TABLE J 2

ORGAN WEIGHT, ABSOLUTE: FEMALE

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	Body Weight	ADRENALS	OVARIES	HEART	LUNGS	KIDNEYS
Control	42	277± 33	0.076± 0.010	0.183± 0.295	0.905± 0.083	0.953± 0.066	1.841± 0.165
1280 ppm	45	280± 32	0.073± 0.010	0.361± 1.084	0.885± 0.076	0.950± 0.130	1.854± 0.183
3200 ppm	46	259± 31*	0.096± 0.182**	0.187± 0.307	0.869± 0.079	0.925± 0.071	1.812± 0.156
8000 ppm	40	240± 31**	0.069± 0.007**	0.151± 0.137	0.866± 0.055	0.939± 0.166	1.834± 0.186

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

(HCL040)

BAIS 4

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	SPLEEN	LIVER	BRAIN
Control	42	0.629± 0.302	6.952± 1.077	1.879± 0.042
1280 ppm	45	0.644± 0.433	6.828± 1.047	1.881± 0.051
3200 ppm	46	0.559± 0.107	6.341± 0.779**	1.881± 0.044
8000 ppm	40	0.702± 0.147**	6.502± 0.812	1.866± 0.057

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

TABLE K 1

ORGAN WEIGHT, RELATIVE: MALE

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	Body Weight (g)	ADRENALS	TESTES	HEART	LUNGS	KIDNEYS
Control	33	390± 43	0.027± 0.041	0.883± 0.539	0.323± 0.036	0.395± 0.156	0.773± 0.140
1280 ppm	38	394± 35	0.046± 0.153	0.775± 0.337	0.322± 0.033	0.364± 0.054	0.759± 0.119
3200 ppm	39	403± 38	0.019± 0.006	0.760± 0.263	0.319± 0.037	0.351± 0.068*	0.783± 0.093
8000 ppm	39	371± 38	0.020± 0.007	0.861± 0.337	0.350± 0.059	0.379± 0.097	0.927± 0.282**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

(HCL042)

BAIS 4

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	SPLEEN	LIVER	BRAIN
Control	33	0.376± 0.385	3.055± 0.455	0.536± 0.064
1280 ppm	38	0.275± 0.086	2.907± 0.413	0.531± 0.048
3200 ppm	39	0.259± 0.043*	2.926± 0.310	0.522± 0.057
8000 ppm	39	0.305± 0.034	3.150± 0.408	0.567± 0.082*

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

TABLE K 2

ORGAN WEIGHT, RELATIVE: FEMALE

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	Body Weight (g)	ADRENALS	OVARIES	HEART	LUNGS	KIDNEYS
Control	42	277± 33	0.028± 0.005	0.065± 0.095	0.332± 0.056	0.349± 0.050	0.674± 0.097
1280 ppm	45	280± 32	0.026± 0.004	0.123± 0.366	0.319± 0.035	0.341± 0.040	0.668± 0.076
3200 ppm	46	259± 31*	0.040± 0.087	0.071± 0.101	0.339± 0.040	0.362± 0.049	0.708± 0.090*
8000 ppm	40	240± 31**	0.029± 0.006	0.064± 0.060	0.365± 0.041**	0.399± 0.107**	0.778± 0.153**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	SPLEEN	LIVER	BRAIN
Control	42	0.233± 0.122	2.532± 0.415	0.691± 0.101
1280 ppm	45	0.231± 0.143	2.455± 0.356	0.680± 0.074
3200 ppm	46	0.219± 0.050	2.457± 0.196	0.738± 0.100**
8000 ppm	40	0.294± 0.053**	2.739± 0.427**	0.791± 0.116**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

(HCL042)

TABLE L 1

HISTOPATHOLOGICAL FINDINGS:

NON-NEOPLASTIC LESIONS:MALE: ALL ANIMALS

Organ	Findings	Group Name	Control				1280 ppm				3200 ppm				8000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Integumentary system/appandage}																		
skin/app			<50>				<50>				<50>				<50>			
	mineralization		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	inflammation		0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	squamous cell hyperplasia		0	0	0	0	0	1	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)
	epidermal cyst		0	0	0	0	0	1	0	0	0	1	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)
	sebaceous hyperplasia		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)
	ulcer:squamous epithelium		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
subcutis			<50>				<50>				<50>				<50>			
	hemorrhage		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	fibrosis:focal		0	1	0	0	0	1	0	0	0	2	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(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

Organ	Findings	Group Name	Control				1280 ppm				3200 ppm				8000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}																		
nasal cavit			<50>				<50>				<50>				<50>			
	thrombus		0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	eosinophilic change:olfactory epithelium		14	5	0	0	16	5	0	0	12	3	0	0	9	6	0	0
			(28)	(10)	(0)	(0)	(32)	(10)	(0)	(0)	(24)	(6)	(0)	(0)	(18)	(12)	(0)	(0)
	eosinophilic change:respiratory epithelium		1	0	0	0	5	0	0	0	2	0	0	0	2	0	0	0
			(2)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	inflammation:foreign body		15	0	0	0	16	4	0	0	19	2	0	0	12	0	0	0
			(30)	(0)	(0)	(0)	(32)	(8)	(0)	(0)	(38)	(4)	(0)	(0)	(24)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		2	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	respiratory metaplasia:gland		8	0	0	0	7	0	0	0	6	0	0	0	9	0	0	0
			(16)	(0)	(0)	(0)	(14)	(0)	(0)	(0)	(12)	(0)	(0)	(0)	(18)	(0)	(0)	(0)
lung			<50>				<50>				<50>				<50>			
	congestion		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)
	edema		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1 (%)	Control 50 2 (%)	Control 50 3 (%)	Control 50 4 (%)	1280 ppm 50 1 (%)	1280 ppm 50 2 (%)	1280 ppm 50 3 (%)	1280 ppm 50 4 (%)	3200 ppm 50 1 (%)	3200 ppm 50 2 (%)	3200 ppm 50 3 (%)	3200 ppm 50 4 (%)	8000 ppm 50 1 (%)	8000 ppm 50 2 (%)	8000 ppm 50 3 (%)	8000 ppm 50 4 (%)
{Respiratory system}																		
lung		<50>																
	inflammatory infiltration		1 (2)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	bronchiolar-alveolar cell hyperplasia		0 (0)	2 (4)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)
{Hematopoietic system}																		
bone marrow		<50>																
	granulation		3 (6)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	increased hematopoiesis		7 (14)	0 (0)	0 (0)	0 (0)	6 (12)	0 (0)	0 (0)	0 (0)	8 (16)	0 (0)	0 (0)	0 (0)	9 (18)	0 (0)	0 (0)	0 (0)
lymph node		<50>																
	lymphadenitis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)
spleen		<50>																
	congestion		0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (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

Organ	Findings	Group Name	Control				1280 ppm				3200 ppm				8000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}																		
spleen			<50>				<50>				<50>				<50>			
	necrosis:focal		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	deposit of hemosiderin		7	1	0	0	4	3	0	0	6	3	0	0	6	1	0	0
			(14)	(2)	(0)	(0)	(8)	(6)	(0)	(0)	(12)	(6)	(0)	(0)	(12)	(2)	(0)	(0)
	fibrosis:focal		0	0	0	0	0	1	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	extramedullary hematopoiesis		3	0	0	0	2	4	0	0	1	4	0	0	5	1	1	0
			(6)	(0)	(0)	(0)	(4)	(8)	(0)	(0)	(2)	(8)	(0)	(0)	(10)	(2)	(2)	(0)
	engorgement of erythrocyte		0	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
{Circulatory system}																		
heart			<50>				<50>				<50>				<50>			
	thrombus		0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)
	myocardial fibrosis		21	0	0	0	20	2	0	0	18	0	0	0	19	1	0	0
			(42)	(0)	(0)	(0)	(40)	(4)	(0)	(0)	(36)	(0)	(0)	(0)	(38)	(2)	(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

Organ	Findings	Group Name	Control				1280 ppm				3200 ppm				8000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
tooth			<50>				<50>				<50>				<50>			
	dysplasia		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
tongue			<50>				<50>				<50>				<50>			
	inflammatory infiltration		0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)
	squamous cell hyperplasia		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
	arteritis		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
stomach			<50>				<50>				<50>				<50>			
	erosion:forestomach		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	ulcer:forestomach		5	0	0	0	0	1	0	0 *	3	0	0	0	2	1	0	0
			(10)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(6)	(0)	(0)	(0)	(4)	(2)	(0)	(0)
	hyperplasia:forestomach		1	3	0	0	2	1	0	0	10	4	0	0 *	13	24	8	0 **
			(2)	(6)	(0)	(0)	(4)	(2)	(0)	(0)	(20)	(8)	(0)	(0)	(26)	(48)	(16)	(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

Organ	Findings	Group Name	Control				1280 ppm				3200 ppm				8000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
stomach			<50>				<50>				<50>				<50>			
	erosion:glandular stomach		6	0	0	0	0	0	0	0 *	4	0	0	0	1	0	0	0
			(12)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	ulcer:glandular stomach		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia:glandular stomach		1	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:glandular stomach		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)
liver			<50>				<50>				<50>				<50>			
	herniation		7	0	0	0	7	0	0	0	7	0	0	0	5	0	0	0
			(14)	(0)	(0)	(0)	(14)	(0)	(0)	(0)	(14)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	peliosis-like lesion		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	necrosis:central		1	0	1	0	0	2	0	0	1	1	1	0	1	2	0	0
			(2)	(0)	(2)	(0)	(0)	(4)	(0)	(0)	(2)	(2)	(2)	(0)	(2)	(4)	(0)	(0)
	necrosis:focal		1	0	0	0	1	1	0	0	0	0	0	0	0	1	0	0
			(2)	(0)	(0)	(0)	(2)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)

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(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				1280 ppm				3200 ppm				8000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
liver			<50>				<50>				<50>				<50>			
	fatty change		0	1	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		2	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	clear cell focus		7	1	0	0	6	0	0	0	5	1	0	0	7	1	0	0
			(14)	(2)	(0)	(0)	(12)	(0)	(0)	(0)	(10)	(2)	(0)	(0)	(14)	(2)	(0)	(0)
	acidophilic cell focus		3	1	0	0	2	0	0	0	3	0	0	0	1	0	0	0
			(6)	(2)	(0)	(0)	(4)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	basophilic cell focus		3	0	0	0	2	0	0	0	1	0	0	0	5	0	0	0
			(6)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	spongiosis hepatis		2	0	0	0	2	0	0	0	0	1	0	0	3	1	0	0
			(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(6)	(2)	(0)	(0)
	bile duct hyperplasia		7	41	0	0	7	42	0	0	6	43	0	0	24	24	0	0 **
			(14)	(82)	(0)	(0)	(14)	(84)	(0)	(0)	(12)	(86)	(0)	(0)	(48)	(48)	(0)	(0)
	hepatocellular hypertrophy:central		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)

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(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				1280 ppm				3200 ppm				8000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
liver			<50>				<50>				<50>				<50>			
	focal fatty change		0	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(2)	(0)	(0)
bile duct			<50>				<50>				<50>				<50>			
	duct ectasia		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
pancreas			<50>				<50>				<50>				<50>			
	atrophy		19	5	0	0	18	2	0	0	13	3	0	0	23	1	0	0
			(38)	(10)	(0)	(0)	(36)	(4)	(0)	(0)	(26)	(6)	(0)	(0)	(46)	(2)	(0)	(0)
	arteritis		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	islet cell hyperplasia		1	0	0	0	0	0	0	0	1	1	0	0	0	1	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(2)	(0)	(0)	(0)	(2)	(0)	(0)
{Urinary system}																		
kidney			<50>				<50>				<50>				<50>			
	chronic nephropathy		14	20	10	0	16	24	8	0	9	24	15	0	9	22	14	1
			(28)	(40)	(20)	(0)	(32)	(48)	(16)	(0)	(18)	(48)	(30)	(0)	(18)	(44)	(28)	(2)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
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(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1	Control 50 2	Control 50 3	Control 50 4	1280 ppm 50 1	1280 ppm 50 2	1280 ppm 50 3	1280 ppm 50 4	3200 ppm 50 1	3200 ppm 50 2	3200 ppm 50 3	3200 ppm 50 4	8000 ppm 50 1	8000 ppm 50 2	8000 ppm 50 3	8000 ppm 50 4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}																		
kidney			<50>				<50>				<50>				<50>			
	mineralization:pelvis		1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:cortex		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	urothelial hyperplasia:pelvis		0	1	0	0	0	0	0	0	1	0	1	0	1	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(2)	(0)	(2)	(0)	(0)	(0)
	atypical tubule hyperplasia		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
urin bladd			<50>				<50>				<50>				<50>			
	inflammatory polyp		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
	nodular hyperplasia:transitional epithelium		0	0	0	0	0	1	0	0	0	0	0	0	1	1	0	0
			(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(2)	(0)	(0)
{Endocrine system}																		
pituitary			<50>				<50>				<50>				<50>			
	cyst		0	1	0	0	2	1	0	0	0	2	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(4)	(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				1280 ppm				3200 ppm				8000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Endocrine system}																		
pituitary			<50>				<50>				<50>				<50>			
	hyperplasia		8	7	0	0	5	7	0	0	12	3	0	0	6	9	0	0
			(16)	(14)	(0)	(0)	(10)	(14)	(0)	(0)	(24)	(6)	(0)	(0)	(12)	(18)	(0)	(0)
	Rathke pouch		1	0	0	0	1	0	0	0	2	0	0	0	1	0	0	0
			(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	aberrant craniopharyngeal tissue		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thyroid			<50>				<50>				<50>				<50>			
	ultimibranchial body remanet		1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	follicular hyperplasia		1	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	C-cell hyperplasia		9	3	0	0	8	3	0	0	15	2	0	0	15	4	0	0
			(18)	(6)	(0)	(0)	(16)	(6)	(0)	(0)	(30)	(4)	(0)	(0)	(30)	(8)	(0)	(0)
adrenal			<50>				<50>				<50>				<50>			
	necrosis		0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				1280 ppm				3200 ppm				8000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Endocrine system}																		
adrenal			<50>				<50>				<50>				<50>			
	hyperplasia:cortical cell		0	2	0	0	0	0	0	0	0	2	0	0	0	0	0	0
			(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia:medulla		2	1	0	0	2	2	0	0	2	2	0	0	2	3	0	0
			(4)	(2)	(0)	(0)	(4)	(4)	(0)	(0)	(4)	(4)	(0)	(0)	(4)	(6)	(0)	(0)
	focal fatty change:cortex		1	0	0	0	1	0	0	0	2	0	0	0	1	0	0	0
			(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
{Reproductive system}																		
testis			<50>				<50>				<50>				<50>			
	mineralization		2	2	0	0	0	0	0	0	4	0	0	0	1	0	0	0
			(4)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	arteritis		5	3	0	0	4	1	0	0	9	0	0	0	4	3	0	0
			(10)	(6)	(0)	(0)	(8)	(2)	(0)	(0)	(18)	(0)	(0)	(0)	(8)	(6)	(0)	(0)
	interstitial cell hyperplasia		11	0	0	0	12	0	0	0	6	2	0	0	15	1	0	0
			(22)	(0)	(0)	(0)	(24)	(0)	(0)	(0)	(12)	(4)	(0)	(0)	(30)	(2)	(0)	(0)
epididymis			<50>				<50>				<50>				<50>			
	arteritis		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50				1280 ppm 50				3200 ppm 50				8000 ppm 50			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Reproductive system}																		
epididymis		<50>																
	spermatogenic granuloma		0 (0)	1 (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)
prostate		<50>																
	inflammation		0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hyperplasia		6 (12)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	6 (12)	1 (2)	0 (0)	0 (0)	6 (12)	0 (0)	0 (0)	0 (0)
mammary gl		<50>																
	galactocele		0 (0)	1 (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)
{Special sense organs/appendage}																		
eye		<50>																
	cataract		10 (20)	0 (0)	0 (0)	0 (0)	7 (14)	0 (0)	0 (0)	0 (0)	6 (12)	0 (0)	0 (0)	0 (0)	13 (26)	0 (0)	0 (0)	0 (0)
	retinal atrophy		13 (26)	7 (14)	0 (0)	0 (0)	2 (4)	4 (8)	2 (4)	0 (0) **	1 (2)	2 (4)	2 (4)	0 (0) **	2 (4)	8 (16)	3 (6)	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

Organ	Findings	Group Name	Control				1280 ppm				3200 ppm				8000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Special sense organs/appendage}																		
eye			<50>				<50>				<50>				<50>			
	keratitis		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
	squamous cell metaplasia:cornea		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
nasolacr d			<50>				<50>				<50>				<50>			
	inflammation		1	0	0	0	2	0	0	0	1	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Musculoskeletal system}																		
muscle			<50>				<50>				<50>				<50>			
	atrophy		0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0
			(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)
bone			<50>				<50>				<50>				<50>			
	osteosclerosis		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Body cavities}																		
mediastinum			<50>				<50>				<50>				<50>			
	hemorrhage		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(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

Organ	Findings	Group Name	Control				1280 ppm				3200 ppm				8000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Body cavities}																		
retroperit			<50>				<50>				<50>				<50>			
	cyst		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(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

TABLE L 4

HISTOPATHOLOGICAL FINDINGS: NON-NEOPLASTIC

LESIONS: FEMALE: ALL ANIMALS

Organ	Findings	Group Name	Control				1280 ppm				3200 ppm				8000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Integumentary system/appandage}																		
skin/app			<50>				<50>				<50>				<50>			
	squamous cell hyperplasia		0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
	scab		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	epidermal cyst		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Respiratory system}																		
nasal cavit			<50>				<50>				<50>				<50>			
	thrombus		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	goblet cell hyperplasia		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
	eosinophilic change:olfactory epithelium		8	32	2	0	12	33	2	0	13	30	1	0	18	18	1	0 *
			(16)	(64)	(4)	(0)	(24)	(66)	(4)	(0)	(26)	(60)	(2)	(0)	(36)	(36)	(2)	(0)
	eosinophilic change:respiratory epithelium		16	0	0	0	16	0	0	0	14	0	0	0	4	0	0	0 **
			(32)	(0)	(0)	(0)	(32)	(0)	(0)	(0)	(28)	(0)	(0)	(0)	(8)	(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

Organ	Findings	Group Name	Control				1280 ppm				3200 ppm				8000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}																		
nasal cavit			<50>				<50>				<50>				<50>			
	inflammation:foreign body		0	0	0	0	4	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	respiratory metaplasia:gland		8	0	0	0	5	0	0	0	9	0	0	0	6	0	0	0
			(16)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(18)	(0)	(0)	(0)	(12)	(0)	(0)	(0)
lung			<50>				<50>				<50>				<50>			
	congestion		0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
	edema		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	accumulation of foamy cells		1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	bronchiolar-alveolar cell hyperplasia		1	0	0	0	1	0	0	0	1	0	0	0	2	0	0	0
			(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	inflammation:foreign body		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
{Hematopoietic system}																		
bone marrow			<50>				<50>				<50>				<50>			
	granulation		5	0	0	0	1	2	0	0	6	1	0	0	2	2	0	0
			(10)	(0)	(0)	(0)	(2)	(4)	(0)	(0)	(12)	(2)	(0)	(0)	(4)	(4)	(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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50				1280 ppm 50				3200 ppm 50				8000 ppm 50			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Hematopoietic system}																		
bone marrow			<50>				<50>				<50>				<50>			
	increased hematopoiesis		4 (8)	0 (0)	0 (0)	0 (0)	6 (12)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)
spleen			<50>				<50>				<50>				<50>			
	congestion		0 (0)	1 (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)
	deposit of hemosiderin		21 (42)	13 (26)	0 (0)	0 (0)	24 (48)	15 (30)	0 (0)	0 (0)	23 (46)	20 (40)	0 (0)	0 (0)	24 (48)	20 (40)	0 (0)	0 * (0)
	extramedullary hematopoiesis		10 (20)	1 (2)	0 (0)	0 (0)	14 (28)	4 (8)	0 (0)	0 (0)	9 (18)	2 (4)	0 (0)	0 (0)	13 (26)	6 (12)	0 (0)	0 (0)
	engorgement of erythrocyte		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)
{Circulatory system}																		
heart			<50>				<50>				<50>				<50>			
	myocardial fibrosis		9 (18)	0 (0)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)	6 (12)	0 (0)	0 (0)	0 (0)	7 (14)	0 (0)	0 (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

Organ	Findings	Group Name	Control				1280 ppm				3200 ppm				8000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
tongue			<50>				<50>				<50>				<50>			
	arteritis		2	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
			(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
stomach			<50>				<50>				<50>				<50>			
	ulcer:forestomach		0	1	0	0	1	0	0	0	1	0	0	0	1	2	0	0
			(0)	(2)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(4)	(0)	(0)
	hyperplasia:forestomach		2	0	0	0	1	1	0	0	5	4	0	0	16	24	0	0 **
			(4)	(0)	(0)	(0)	(2)	(2)	(0)	(0)	(10)	(8)	(0)	(0)	(32)	(48)	(0)	(0)
	erosion:glandular stomach		1	0	0	0	1	0	0	0	1	0	0	0	1	0	0	0
			(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	hyperplasia:glandular stomach		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:glandular stomach		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
liver			<50>				<50>				<50>				<50>			
	herniation		6	0	0	0	8	0	0	0	7	0	0	0	9	0	0	0
			(12)	(0)	(0)	(0)	(16)	(0)	(0)	(0)	(14)	(0)	(0)	(0)	(18)	(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

Organ	Findings	Group Name	Control				1280 ppm				3200 ppm				8000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
liver			<50>				<50>				<50>				<50>			
	peliosis-like lesion		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:focal		1	0	0	0	2	0	0	0	0	0	0	0	2	0	0	0
			(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	fatty change		0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		13	1	1	0	10	1	0	0	11	0	0	0	7	0	0	0
			(26)	(2)	(2)	(0)	(20)	(2)	(0)	(0)	(22)	(0)	(0)	(0)	(14)	(0)	(0)	(0)
	clear cell focus		2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	basophilic cell focus		25	0	0	0	28	0	0	0	20	3	0	0	23	1	0	0
			(50)	(0)	(0)	(0)	(56)	(0)	(0)	(0)	(40)	(6)	(0)	(0)	(46)	(2)	(0)	(0)
	bile duct hyperplasia		18	0	0	0	11	1	0	0	10	0	0	0	5	2	0	0 **
			(36)	(0)	(0)	(0)	(22)	(2)	(0)	(0)	(20)	(0)	(0)	(0)	(10)	(4)	(0)	(0)
	focal fatty change		1	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			(2)	(0)	(0)	(0)	(2)	(0)	(0)	(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 ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				1280 ppm				3200 ppm				8000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
pancreas			<50>				<50>				<50>				<50>			
	atrophy		1	1	0	0	4	2	0	0	3	1	0	0	3	2	0	0
			(2)	(2)	(0)	(0)	(8)	(4)	(0)	(0)	(6)	(2)	(0)	(0)	(6)	(4)	(0)	(0)
	islet cell hyperplasia		1	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(2)	(0)	(0)
{Urinary system}																		
kidney			<50>				<50>				<50>				<50>			
	cyst		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	chronic nephropathy		28	5	0	1	29	4	1	0	30	5	0	0	29	6	1	0
			(56)	(10)	(0)	(2)	(58)	(8)	(2)	(0)	(60)	(10)	(0)	(0)	(58)	(12)	(2)	(0)
	dilatation:tubular lumen		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	atypical tubule hyperplasia		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	dilated pelvis		0	1	0	0	0	0	0	0	0	1	0	0	0	1	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(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

Organ	Findings	Group Name	Control				1280 ppm				3200 ppm				8000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Endocrine system}																		
pituitary			<50>				<50>				<50>				<50>			
	angiectasis		1	0	0	0	1	0	0	0	1	1	0	0	0	1	0	0
			(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(2)	(0)	(0)	(0)	(2)	(0)	(0)
	cyst		1	0	0	0	2	2	0	0	2	1	0	0	2	0	0	0
			(2)	(0)	(0)	(0)	(4)	(4)	(0)	(0)	(4)	(2)	(0)	(0)	(4)	(0)	(0)	(0)
	hyperplasia		8	4	0	0	12	9	0	0	6	8	0	0	7	9	0	0
			(16)	(8)	(0)	(0)	(24)	(18)	(0)	(0)	(12)	(16)	(0)	(0)	(14)	(18)	(0)	(0)
	Rathke pouch		2	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
thyroid			<50>				<50>				<50>				<50>			
	C-cell hyperplasia		15	4	0	0	9	2	0	0	8	5	0	0	10	4	0	0
			(30)	(8)	(0)	(0)	(18)	(4)	(0)	(0)	(16)	(10)	(0)	(0)	(20)	(8)	(0)	(0)
adrenal			<50>				<50>				<50>				<50>			
	peliosis-like lesion		1	1	0	0	1	0	0	0	1	0	0	0	0	1	0	0
			(2)	(2)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(2)	(0)	(0)
	necrosis:focal		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(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

Organ	Findings	Group Name	Control				1280 ppm				3200 ppm				8000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Endocrine system}																		
adrenal			<50>				<50>				<50>				<50>			
	hyperplasia:medulla		0	0	0	0	2	0	0	0	2	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	focal fatty change:cortex		2	0	0	0	3	0	0	0	0	0	0	0	2	1	0	0
			(4)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(2)	(0)	(0)
{Reproductive system}																		
ovary			<50>				<50>				<50>				<50>			
	cyst		1	2	0	0	1	1	0	0	0	1	0	0	2	0	0	0
			(2)	(4)	(0)	(0)	(2)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(4)	(0)	(0)	(0)
uterus			<50>				<50>				<50>				<50>			
	dilatation		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)
	decidual change		0	2	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	cystic endometrial hyperplasia		1	0	0	0	3	0	0	0	3	0	0	0	0	1	0	0
			(2)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(2)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
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Organ	Findings	Group Name	Control				1280 ppm				3200 ppm				8000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Reproductive system}																		
mammary gl			<50>				<50>				<50>				<50>			
	galactocele		0	2	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
{Special sense organs/appendage}																		
eye			<50>				<50>				<50>				<50>			
	cataract		4	0	0	0	3	0	0	0	6	0	0	0	3	0	0	0
			(8)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(12)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
	retinal atrophy		27	4	1	0	11	4	0	0 **	6	0	5	0 **	15	3	1	0
			(54)	(8)	(2)	(0)	(22)	(8)	(0)	(0)	(12)	(0)	(10)	(0)	(30)	(6)	(2)	(0)
	iritis		0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
Harder gl			<50>				<50>				<50>				<50>			
	lymphocytic infiltration		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
nasolacr d			<50>				<50>				<50>				<50>			
	inflammation		5	3	0	0	3	1	0	0	7	2	0	0	2	1	0	0
			(10)	(6)	(0)	(0)	(6)	(2)	(0)	(0)	(14)	(4)	(0)	(0)	(4)	(2)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
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Organ	Findings	Group Name	Control				1280 ppm				3200 ppm				8000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Musculoskeletal system}																		
bone			<50>				<50>				<50>				<50>			
	osteosclerosis		7	4	0	0	4	4	1	0	1	2	1	0	1	0	0	0 **
			(14)	(8)	(0)	(0)	(8)	(8)	(2)	(0)	(2)	(4)	(2)	(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 ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

TABLE O 1

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS: MALE

Group Name	Control	1280 ppm	3200 ppm	8000 ppm
	SITE : subcutis TUMOR : fibroma			
Tumor rate				
Overall rates(a)	9/50(18.0)	6/50(12.0)	7/50(14.0)	3/50(6.0)
Adjusted rates(b)	24.24	13.16	13.04	2.56
Terminal rates(c)	8/33(24.2)	5/38(13.2)	5/39(12.8)	1/39(2.6)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.2448			
Prevalence method(d)	P = 0.9951			
Combined analysis(d)	P = 0.9699			
Cochran-Armitage test(e)	P = 0.0924			
Fisher Exact test(e)		P = 0.2883	P = 0.3929	P = 0.0606
	SITE : subcutis TUMOR : fibroma,fibrosarcoma			
Tumor rate				
Overall rates(a)	9/50(18.0)	6/50(12.0)	8/50(16.0)	3/50(6.0)
Adjusted rates(b)	24.24	13.16	13.33	2.56
Terminal rates(c)	8/33(24.2)	5/38(13.2)	5/39(12.8)	1/39(2.6)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.2632			
Prevalence method(d)	P = 0.9950			
Combined analysis(d)	P = 0.9667			
Cochran-Armitage test(e)	P = 0.0991			
Fisher Exact test(e)		P = 0.2883	P = 0.5000	P = 0.0606
	SITE : lung TUMOR : bronchiolar-alveolar adenoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	3/50(6.0)	0/50(0.0)	1/50(2.0)
Adjusted rates(b)	3.03	7.89	0.0	2.56
Terminal rates(c)	1/33(3.0)	3/38(7.9)	0/39(0.0)	1/39(2.6)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P = 0.7281			
Combined analysis(d)	P = --------			
Cochran-Armitage test(e)	P = 0.5752			
Fisher Exact test(e)		P = 0.3087	P = 0.5000	P = 0.7525

Group Name	Control	1280 ppm	3200 ppm	8000 ppm
	SITE : spleen			
	TUMOR : mononuclear cell leukemia			
Tumor rate				
Overall rates(a)	9/50(18.0)	3/50(6.0)	0/50(0.0)	1/50(2.0)
Adjusted rates(b)	18.18	2.63	0.0	0.0
Terminal rates(c)	6/33(18.2)	1/38(2.6)	0/39(0.0)	0/39(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8721			
Prevalence method(d)	P = 0.9997			
Combined analysis(d)	P = 0.9992			
Cochran-Armitage test(e)	P = 0.0067**			
Fisher Exact test(e)		P = 0.0606	P = 0.0013**	P = 0.0078**
	SITE : stomach			
	TUMOR : squamous cell papilloma			
Tumor rate				
Overall rates(a)	0/50(0.0)	2/50(4.0)	11/50(22.0)	39/50(78.0)
Adjusted rates(b)	0.0	5.26	23.08	92.31
Terminal rates(c)	0/33(0.0)	2/38(5.3)	9/39(23.1)	36/39(92.3)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P < 0.0001**?			
Combined analysis(d)	P = -------			
Cochran-Armitage test(e)	P < 0.0001**			
Fisher Exact test(e)		P = 0.2475	P = 0.0003**	P < 0.0001**
	SITE : stomach			
	TUMOR : squamous cell carcinoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	0/50(0.0)	0/50(0.0)	12/50(24.0)
Adjusted rates(b)	0.0	0.0	0.0	27.27
Terminal rates(c)	0/33(0.0)	0/38(0.0)	0/39(0.0)	9/39(23.1)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P < 0.0001**?			
Combined analysis(d)	P = -------			
Cochran-Armitage test(e)	P < 0.0001**			
Fisher Exact test(e)		P = N.C.	P = N.C.	P = 0.0001**

Group Name	Control	1280 ppm	3200 ppm	8000 ppm
	SITE : stomach			
	TUMOR : squamous cell papilloma, squamous cell carcinoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	2/50(4.0)	11/50(22.0)	43/50(86.0)
Adjusted rates(b)	0.0	5.26	23.08	95.12
Terminal rates(c)	0/33(0.0)	2/38(5.3)	9/39(23.1)	37/39(94.9)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P < 0.0001**?			
Combined analysis(d)	P = ----------			
Cochran-Armitage test(e)	P < 0.0001**			
Fisher Exact test(e)		P = 0.2475	P = 0.0003**	P < 0.0001**
	SITE : liver			
	TUMOR : hepatocellular adenoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	4/50(8.0)	1/50(2.0)	3/50(6.0)
Adjusted rates(b)	3.03	9.76	2.56	7.69
Terminal rates(c)	1/33(3.0)	2/38(5.3)	1/39(2.6)	3/39(7.7)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P = 0.3278			
Combined analysis(d)	P = ----------			
Cochran-Armitage test(e)	P = 0.6341			
Fisher Exact test(e)		P = 0.1811	P = 0.7525	P = 0.3087
	SITE : liver			
	TUMOR : hepatocellular adenoma, hepatocellular carcinoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	4/50(8.0)	3/50(6.0)	3/50(6.0)
Adjusted rates(b)	3.03	9.76	7.69	7.69
Terminal rates(c)	1/33(3.0)	2/38(5.3)	3/39(7.7)	3/39(7.7)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P = 0.3401			
Combined analysis(d)	P = ----------			
Cochran-Armitage test(e)	P = 0.6534			
Fisher Exact test(e)		P = 0.1811	P = 0.3087	P = 0.3087

Group Name	Control	1280 ppm	3200 ppm	8000 ppm
	SITE : pancreas			
	TUMOR : islet cell adenoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	4/50(8.0)	6/50(12.0)	3/50(6.0)
Adjusted rates(b)	6.06	9.09	14.63	7.69
Terminal rates(c)	2/33(6.1)	3/38(7.9)	5/39(12.8)	3/39(7.7)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P = 0.4782			
Combined analysis(d)	P = -------			
Cochran-Armitage test(e)	P = 0.8932			
Fisher Exact test(e)		P = 0.3389	P = 0.1343	P = 0.5000
	SITE : pancreas			
	TUMOR : islet cell adenoma, islet cell adenocarcinoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	4/50(8.0)	6/50(12.0)	3/50(6.0)
Adjusted rates(b)	6.06	9.09	14.63	7.69
Terminal rates(c)	2/33(6.1)	3/38(7.9)	5/39(12.8)	3/39(7.7)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P = 0.4782			
Combined analysis(d)	P = -------			
Cochran-Armitage test(e)	P = 0.8932			
Fisher Exact test(e)		P = 0.3389	P = 0.1343	P = 0.5000
	SITE : urinary bladder			
	TUMOR : transitional cell carcinoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	0/50(0.0)	0/50(0.0)	7/50(14.0)
Adjusted rates(b)	0.0	0.0	0.0	17.95
Terminal rates(c)	0/33(0.0)	0/38(0.0)	0/39(0.0)	7/39(17.9)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P < 0.0001**			
Combined analysis(d)	P = -------			
Cochran-Armitage test(e)	P < 0.0001**			
Fisher Exact test(e)		P = N.C.	P = N.C.	P = 0.0062**

Group Name	Control	1280 ppm	3200 ppm	8000 ppm
	SITE : urinary bladder			
	TUMOR : transitional cell papilloma, transitional cell carcinoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	0/50(0.0)	1/50(2.0)	7/50(14.0)
Adjusted rates(b)	0.0	0.0	2.56	17.95
Terminal rates(c)	0/33(0.0)	0/38(0.0)	1/39(2.6)	7/39(17.9)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P < 0.0001**			
Combined analysis(d)	P = --------			
Cochran-Armitage test(e)	P < 0.0001**			
Fisher Exact test(e)		P = N.C.	P = 0.5000	P = 0.0062**
	SITE : pituitary gland			
	TUMOR : adenoma			
Tumor rate				
Overall rates(a)	13/50(26.0)	10/50(20.0)	12/50(24.0)	6/50(12.0)
Adjusted rates(b)	23.53	13.16	20.93	10.26
Terminal rates(c)	7/33(21.2)	5/38(13.2)	8/39(20.5)	4/39(10.3)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.9135			
Prevalence method(d)	P = 0.8906			
Combined analysis(d)	P = 0.9669			
Cochran-Armitage test(e)	P = 0.0979			
Fisher Exact test(e)		P = 0.3176	P = 0.5000	P = 0.0624
	SITE : thyroid			
	TUMOR : C-cell adenoma			
Tumor rate				
Overall rates(a)	8/50(16.0)	7/50(14.0)	3/50(6.0)	2/50(4.0)
Adjusted rates(b)	21.62	18.42	6.52	5.13
Terminal rates(c)	7/33(21.2)	7/38(18.4)	2/39(5.1)	2/39(5.1)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P = 0.9933			
Combined analysis(d)	P = --------			
Cochran-Armitage test(e)	P = 0.0308*			
Fisher Exact test(e)		P = 0.5000	P = 0.0999	P = 0.0458*

Group Name	Control	1280 ppm	3200 ppm	8000 ppm
	SITE : thyroid TUMOR : C-cell carcinoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	3/50(6.0)	2/50(4.0)	4/50(8.0)
Adjusted rates(b)	3.03	5.26	5.13	10.26
Terminal rates(c)	1/33(3.0)	2/38(5.3)	2/39(5.1)	4/39(10.3)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5587			
Prevalence method(d)	P = 0.1009			
Combined analysis(d)	P = 0.1512			
Cochran-Armitage test(e)	P = 0.2385			
Fisher Exact test(e)		P = 0.3087	P = 0.5000	P = 0.1811
	SITE : thyroid TUMOR : C-cell adenoma, C-cell carcinoma			
Tumor rate				
Overall rates(a)	9/50(18.0)	10/50(20.0)	5/50(10.0)	6/50(12.0)
Adjusted rates(b)	24.32	23.68	10.87	15.38
Terminal rates(c)	8/33(24.2)	9/38(23.7)	4/39(10.3)	6/39(15.4)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5587			
Prevalence method(d)	P = 0.8895			
Combined analysis(d)	P = 0.9074			
Cochran-Armitage test(e)	P = 0.2736			
Fisher Exact test(e)		P = 0.5000	P = 0.1940	P = 0.2883
	SITE : adrenal gland TUMOR : pheochromocytoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	8/50(16.0)	5/50(10.0)	4/50(8.0)
Adjusted rates(b)	2.56	21.05	12.82	10.26
Terminal rates(c)	0/33(0.0)	8/38(21.1)	5/39(12.8)	4/39(10.3)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P = 0.4903			
Combined analysis(d)	P = ----------			
Cochran-Armitage test(e)	P = 0.8657			
Fisher Exact test(e)		P = 0.0154*	P = 0.1022	P = 0.1811

Group Name	Control	1280 ppm	3200 ppm	8000 ppm
	SITE : adrenal gland			
	TUMOR : pheochromocytoma, pheochromocytoma:malignant			
Tumor rate				
Overall rates(a)	2/50(4.0)	9/50(18.0)	5/50(10.0)	4/50(8.0)
Adjusted rates(b)	5.13	23.68	12.82	10.26
Terminal rates(c)	1/33(3.0)	9/38(23.7)	5/39(12.8)	4/39(10.3)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P = 0.6512			
Combined analysis(d)	P = --------			
Cochran-Armitage test(e)	P = 0.8232			
Fisher Exact test(e)		P = 0.0256*	P = 0.2180	P = 0.3389
	SITE : testis			
	TUMOR : interstitial cell tumor			
Tumor rate				
Overall rates(a)	30/50(60.0)	38/50(76.0)	35/50(70.0)	35/50(70.0)
Adjusted rates(b)	72.73	89.74	78.05	82.05
Terminal rates(c)	24/33(72.7)	34/38(89.5)	30/39(76.9)	32/39(82.1)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P = 0.4721			
Combined analysis(d)	P = --------			
Cochran-Armitage test(e)	P = 0.6121			
Fisher Exact test(e)		P = 0.0664	P = 0.2009	P = 0.2009
	SITE : mammary gland			
	TUMOR : fibroadenoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	0/50(0.0)	1/50(2.0)	3/50(6.0)
Adjusted rates(b)	6.06	0.0	2.56	7.14
Terminal rates(c)	2/33(6.1)	0/38(0.0)	1/39(2.6)	2/39(5.1)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P = 0.1495			
Combined analysis(d)	P = --------			
Cochran-Armitage test(e)	P = 0.2474			
Fisher Exact test(e)		P = 0.2475	P = 0.5000	P = 0.5000

Group Name	Control	1280 ppm	3200 ppm	8000 ppm
	SITE : preputial/clitoral gland			
	TUMOR : adenoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	4/50(8.0)	1/50(2.0)	3/50(6.0)
Adjusted rates(b)	0.0	10.53	0.0	7.14
Terminal rates(c)	0/33(0.0)	4/38(10.5)	0/39(0.0)	2/39(5.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3846			
Prevalence method(d)	P = 0.2064			
Combined analysis(d)	P = 0.2175			
Cochran-Armitage test(e)	P = 0.3822			
Fisher Exact test(e)		P = 0.0587	P = 0.5000	P = 0.1212
	SITE : peritoneum			
	TUMOR : mesothelioma			
Tumor rate				
Overall rates(a)	1/50(2.0)	2/50(4.0)	3/50(6.0)	4/50(8.0)
Adjusted rates(b)	3.03	5.26	2.56	5.13
Terminal rates(c)	1/33(3.0)	2/38(5.3)	1/39(2.6)	2/39(5.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0706			
Prevalence method(d)	P = 0.3694			
Combined analysis(d)	P = 0.1142			
Cochran-Armitage test(e)	P = 0.1665			
Fisher Exact test(e)		P = 0.5000	P = 0.3087	P = 0.1811

(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 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 ; * : $P \leqq 0.05$ ** : $P \leqq 0.01$
N.C. :Statistical value cannot be calculated and was not significant.

TABLE O 2

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS: FEMALE

Group Name	Control	1280 ppm	3200 ppm	8000 ppm
SITE : spleen				
TUMOR : mononuclear cell leukemia				
Tumor rate				
Overall rates(a)	6/50(12.0)	2/50(4.0)	0/50(0.0)	1/50(2.0)
Adjusted rates(b)	6.98	2.22	0.0	0.0
Terminal rates(c)	2/42(4.8)	1/45(2.2)	0/46(0.0)	0/40(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8073			
Prevalence method(d)	P = 0.9867			
Combined analysis(d)	P = 0.9804			
Cochran-Armitage test(e)	P = 0.0492*			
Fisher Exact test(e)		P = 0.1343	P = 0.0133*	P = 0.0559
SITE : stomach				
TUMOR : squamous cell papilloma				
Tumor rate				
Overall rates(a)	1/50(2.0)	1/50(2.0)	1/50(2.0)	25/50(50.0)
Adjusted rates(b)	2.38	2.22	2.17	58.54
Terminal rates(c)	1/42(2.4)	1/45(2.2)	1/46(2.2)	23/40(57.5)
Statistical analysis				
Peto test				
Standard method(d)	P = --------			
Prevalence method(d)	P < 0.0001**?			
Combined analysis(d)	P = --------			
Cochran-Armitage test(e)	P < 0.0001**			
Fisher Exact test(e)		P = 0.7525	P = 0.7525	P < 0.0001**
SITE : stomach				
TUMOR : squamous cell papilloma, squamous cell carcinoma				
Tumor rate				
Overall rates(a)	1/50(2.0)	1/50(2.0)	1/50(2.0)	25/50(50.0)
Adjusted rates(b)	2.38	2.22	2.17	58.54
Terminal rates(c)	1/42(2.4)	1/45(2.2)	1/46(2.2)	23/40(57.5)
Statistical analysis				
Peto test				
Standard method(d)	P = --------			
Prevalence method(d)	P < 0.0001**?			
Combined analysis(d)	P = --------			
Cochran-Armitage test(e)	P < 0.0001**			
Fisher Exact test(e)		P = 0.7525	P = 0.7525	P < 0.0001**

Group Name	Control	1280 ppm	3200 ppm	8000 ppm
	SITE : pituitary gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	9/50(18.0)	7/50(14.0)	10/50(20.0)	10/50(20.0)
Adjusted rates(b)	14.29	13.33	19.15	20.00
Terminal rates(c)	6/42(14.3)	6/45(13.3)	8/46(17.4)	8/40(20.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5167			
Prevalence method(d)	P = 0.2217			
Combined analysis(d)	P = 0.2627			
Cochran-Armitage test(e)	P = 0.6008			
Fisher Exact test(e)		P = 0.3929	P = 0.5000	P = 0.5000
	SITE : pituitary gland TUMOR : adenoma, adenocarcinoma			
Tumor rate				
Overall rates(a)	9/50(18.0)	7/50(14.0)	10/50(20.0)	11/50(22.0)
Adjusted rates(b)	14.29	13.33	19.15	20.00
Terminal rates(c)	6/42(14.3)	6/45(13.3)	8/46(17.4)	8/40(20.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3048			
Prevalence method(d)	P = 0.2217			
Combined analysis(d)	P = 0.1830			
Cochran-Armitage test(e)	P = 0.4178			
Fisher Exact test(e)		P = 0.3929	P = 0.5000	P = 0.4016
	SITE : thyroid TUMOR : C-cell adenoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	5/50(10.0)	2/50(4.0)	4/50(8.0)
Adjusted rates(b)	2.38	11.11	4.35	10.00
Terminal rates(c)	1/42(2.4)	5/45(11.1)	2/46(4.3)	4/40(10.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P = 0.1986			
Combined analysis(d)	P = --------			
Cochran-Armitage test(e)	P = 0.4708			
Fisher Exact test(e)		P = 0.1022	P = 0.5000	P = 0.1811

Group Name	Control	1280 ppm	3200 ppm	8000 ppm
	SITE : thyroid			
	TUMOR : C-cell adenoma, C-cell carcinoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	7/50(14.0)	3/50(6.0)	4/50(8.0)
Adjusted rates(b)	4.55	15.56	6.52	10.00
Terminal rates(c)	1/42(2.4)	7/45(15.6)	3/46(6.5)	4/40(10.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P = 0.4107			
Combined analysis(d)	P = --------			
Cochran-Armitage test(e)	P = 0.9562			
Fisher Exact test(e)		P = 0.0798	P = 0.5000	P = 0.3389
	SITE : uterus			
	TUMOR : endometrial stromal polyp			
Tumor rate				
Overall rates(a)	7/50(14.0)	6/50(12.0)	3/50(6.0)	4/50(8.0)
Adjusted rates(b)	14.58	13.33	4.35	9.76
Terminal rates(c)	6/42(14.3)	6/45(13.3)	2/46(4.3)	3/40(7.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3857			
Prevalence method(d)	P = 0.8391			
Combined analysis(d)	P = 0.8300			
Cochran-Armitage test(e)	P = 0.3089			
Fisher Exact test(e)		P = 0.5000	P = 0.1589	P = 0.2623
	SITE : mammary gland			
	TUMOR : fibroadenoma			
Tumor rate				
Overall rates(a)	7/50(14.0)	6/50(12.0)	7/50(14.0)	3/50(6.0)
Adjusted rates(b)	14.29	13.33	14.89	4.26
Terminal rates(c)	6/42(14.3)	6/45(13.3)	6/46(13.0)	1/40(2.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3207			
Prevalence method(d)	P = 0.9290			
Combined analysis(d)	P = 0.8944			
Cochran-Armitage test(e)	P = 0.1972			
Fisher Exact test(e)		P = 0.5000	P = 0.6129	P = 0.1589

Group Name	Control	1280 ppm	3200 ppm	8000 ppm
	SITE : mammary gland			
	TUMOR : adenoma, fibroadenoma			
Tumor rate				
Overall rates(a)	7/50(14.0)	6/50(12.0)	7/50(14.0)	4/50(8.0)
Adjusted rates(b)	14.29	13.33	14.89	6.38
Terminal rates(c)	6/42(14.3)	6/45(13.3)	6/46(13.0)	2/40(5.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3207			
Prevalence method(d)	P = 0.8510			
Combined analysis(d)	P = 0.8036			
Cochran-Armitage test(e)	P = 0.3594			
Fisher Exact test(e)		P = 0.5000	P = 0.6129	P = 0.2623
	SITE : mammary gland			
	TUMOR : adenoma, fibroadenoma, adenocarcinoma			
Tumor rate				
Overall rates(a)	7/50(14.0)	7/50(14.0)	7/50(14.0)	4/50(8.0)
Adjusted rates(b)	14.29	15.56	14.89	6.38
Terminal rates(c)	6/42(14.3)	7/45(15.6)	6/46(13.0)	2/40(5.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3207			
Prevalence method(d)	P = 0.8760			
Combined analysis(d)	P = 0.8332			
Cochran-Armitage test(e)	P = 0.3030			
Fisher Exact test(e)		P = 0.6129	P = 0.6129	P = 0.2623

(HPT360A)

BAIS4

(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 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 Q 1

HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER:

F344/DuCrlCrlj MALE RATS

TABLE Q1 HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER : F344/DuCrlCrlj MALE RATS

Organs Tumors	No. of animals examined	No. of animals bearing tumor	Incidence (%)	Min. - Max. (%)
Stomach	2249			
Squamous cell papilloma 1)		5	0.2	0 - 2
Squamous cell carcinoma 2)		4	0.2	0 - 2
1)+2)		9	0.4	0 - 2
Urine bladdar	2249			
Transitional cell papilloma		11	0.5	0 - 4
Transitional cell carcinoma		0	0.0	0 - 0
Spleen	2249			
Mononuclear cell leukemia		264	11.7	2 - 22
Thyroid	2243			
C-cell adenoma		317	14.1	2 - 30
Adrenal	2249			
Pheochromocytoma		258	11.5	0 - 40
Pheochromocytoma:malignant		37	1.6	0 - 8

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

Study No. : 0043, 0059, 0061, 0063, 0065, 0067, 0095, 0104, 0115, 0130, 0141, 0158, 0162, 0189, 0205, 0210, 0224, 0242, 0246, 0267, 0269, 0278, 0284, 0288, 0294, 0296, 0318, 0328, 0342, 0347, 0365, 0371, 0396, 0399, 0401, 0407, 0417, 0421, 0437, 0448, 0457, 0461, 0497, 0535, 0560

TABLE Q 2

HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER: F344/DuCrlCrlj FEMALE RATS

TABLE Q2 HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER : F344/DuCrlCrlj FEMALE RATS

Organs Tumors	No. of animals examined	No. of animals bearing tumor	Incidence (%)	Min. - Max. (%)
Stomach	2097			
Squamous cell papilloma		5	0.2	0 - 2
Squamous cell carcinoma		0	0.0	0 - 0
Spleen	2097			
Mononuclear cell leukemia		267	12.7	2 - 26

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

Study No. : 0043, 0059, 0061, 0063, 0065, 0067, 0095, 0104, 0115, 0130, 0141, 0158, 0162, 0189, 0205, 0210, 0224, 0242, 0246, 0267, 0269, 0278, 0284, 0296, 0303, 0318, 0328, 0342, 0347, 0365, 0371, 0399, 0401, 0417, 0421, 0437, 0448, 0457, 0461, 0497, 0535, 0560

TABLE R

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

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
SEX : MALE

COUSE OF DEATH (SUMMARY)
(0-105W)

Group Name	Control	1280 ppm	3200 ppm	8000 ppm
Number of Dead and Moribund Animal	17	12	11	11
no microscop confirm	3	2	1	2
cardiovascular les	0	0	0	1
adrenal lesion	1	0	0	0
tumor d:leukemia	3	2	0	1
tumor d:subcutis	1	1	2	2
tumor d:tongue	0	0	1	0
tumor d:pituitary	5	5	3	2
tumor d:thyroid	0	1	0	0
tumor d:prep/cli gl	0	0	1	0
tumor d:spinal cord	1	0	0	0
tumor d:Zymbal gl	2	0	0	0
tumor d:bone	0	0	0	1
tumor d:vertebra	1	0	0	0
tumor d:peritoneum	0	1	2	2
tumor d:retroperit	0	0	1	0

STUDY NO. : 0579
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
SEX : FEMALE

COUSE OF DEATH (SUMMARY)
(0-105W)

Group Name	Control	1280 ppm	3200 ppm	8000 ppm
Number of Dead and Moribund Animal	8	5	4	10
no microscop confirm	0	1	0	0
tumor d:leukemia	4	1	0	1
tumor d:subcutis	0	0	0	1
tumor d:kidney	0	0	1	0
tumor d:pituitary	3	1	1	3
tumor d:uterus	0	1	2	3
tumor d:mammary gl	1	0	0	1
tumor d:brain	0	1	0	1

FIGURES

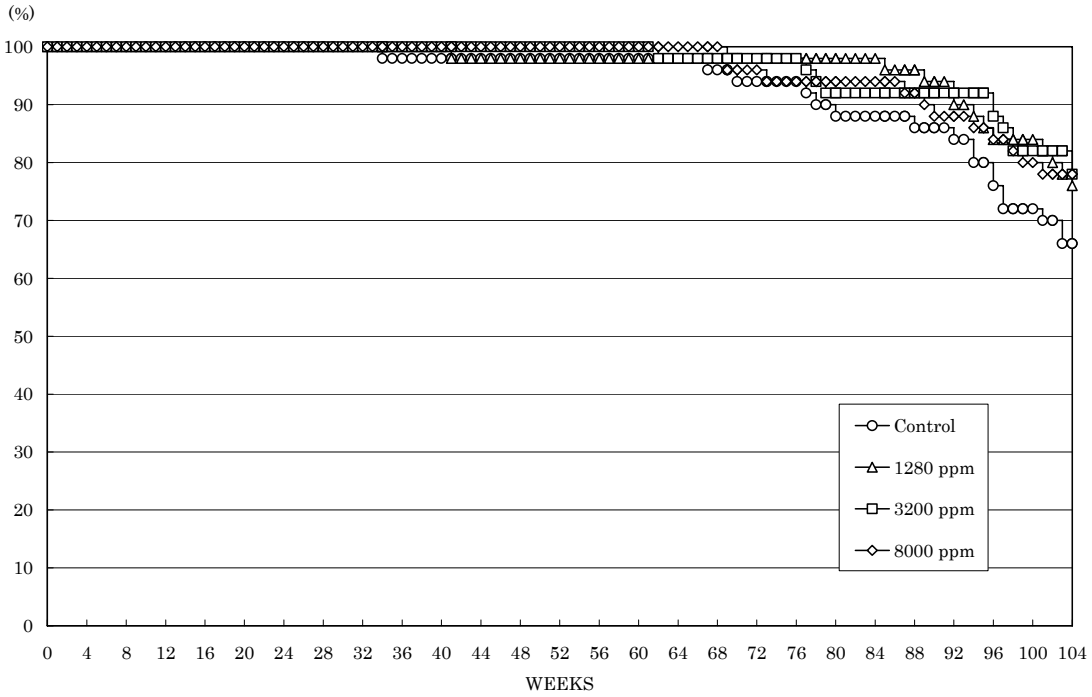


FIGURE 1 SURVIVAL ANIMAL RATE OF MALE RATS IN THE 2-YEAR FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

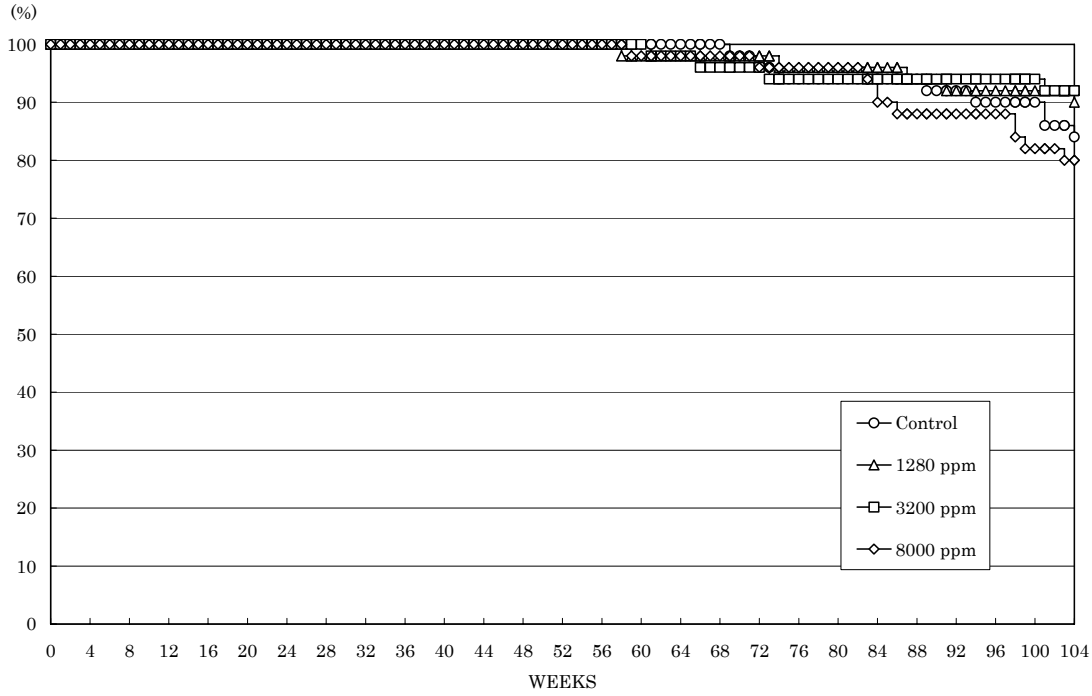


FIGURE 2 SURVIVAL ANIMAL RATE OF FEMALE RATS THE 2-YEAR FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

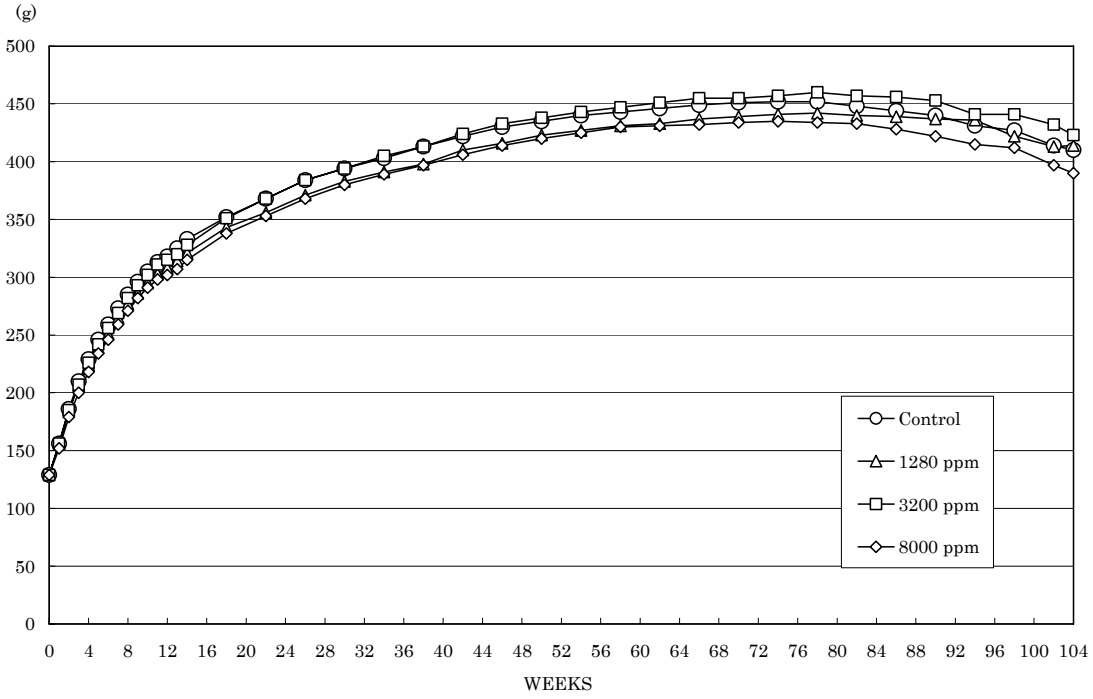


FIGURE 3 BODY WEIGHT CHANGES OF MALE RATS IN THE 2-YEAR FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

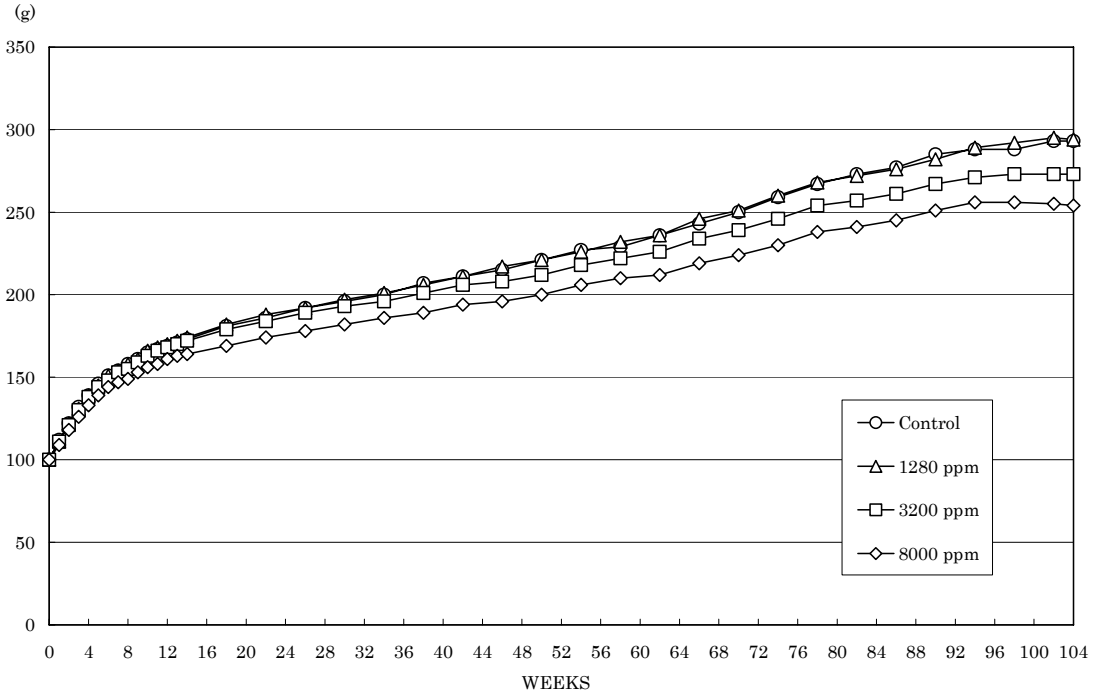


FIGURE 4 BODY WEIGHT CHANGES OF FEMALE RATS IN THE 2-YEAR FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

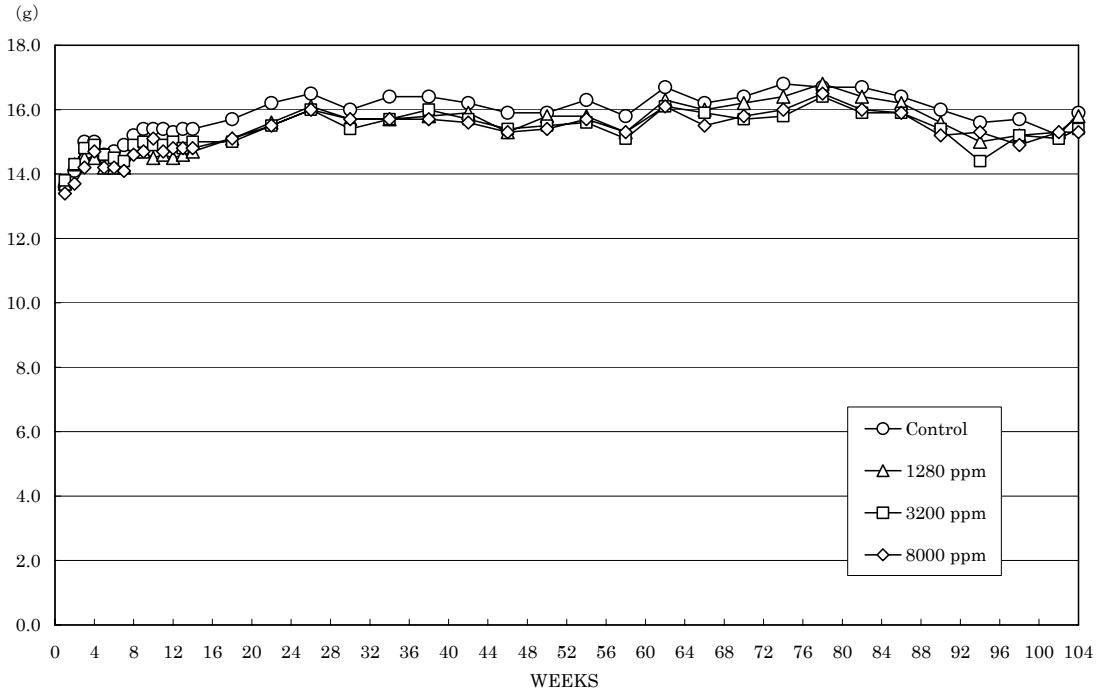


FIGURE 5 FOOD CONSUMPTION CHANGES OF MALE RATS IN THE 2-YEAR FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

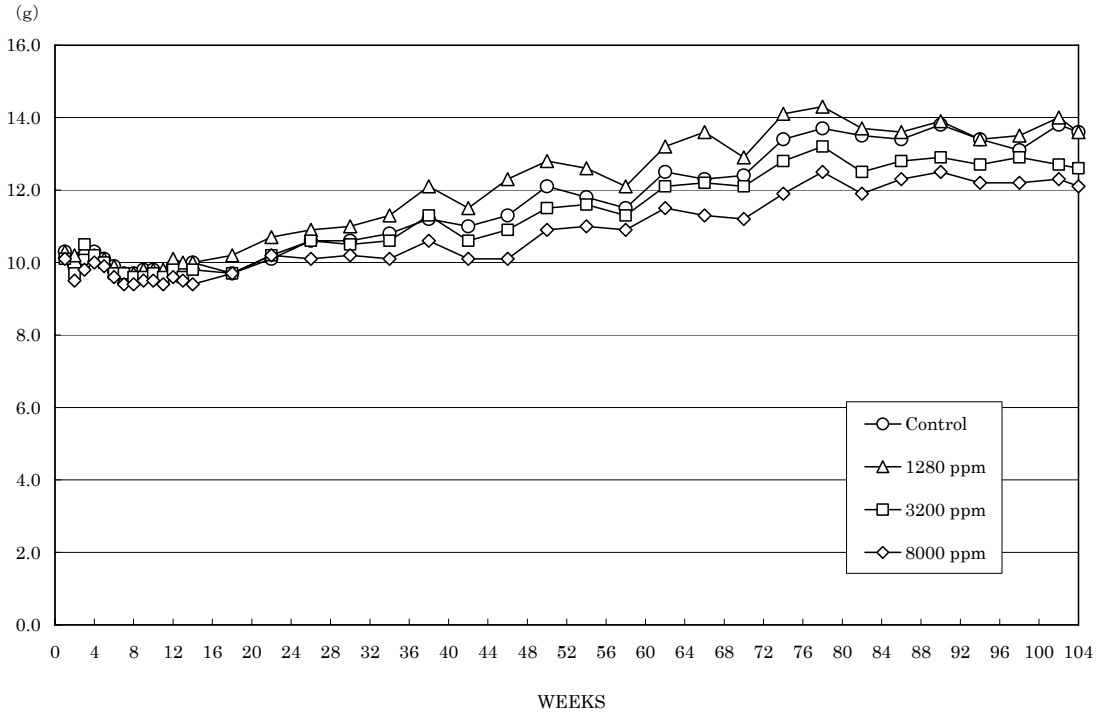
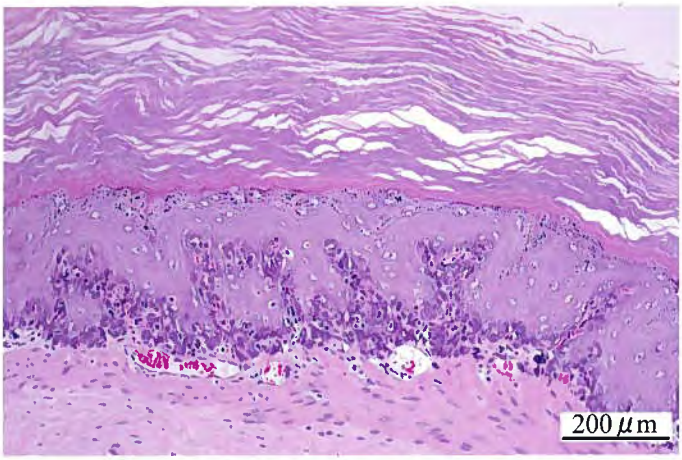


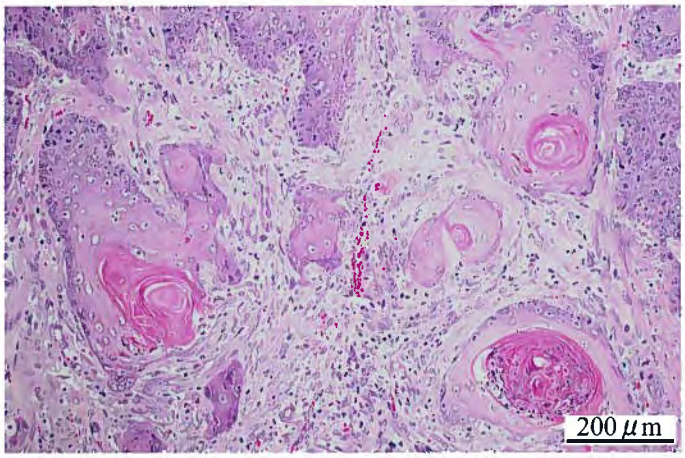
FIGURE 6 FOOD CONSUMPTION CHANGES OF FEMALE RATS IN THE 2-YEAR FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

Photograph 1
Forestomach: nodule (arrows)
Rat, Male, 8000 ppm, Animal No. 0579-1304

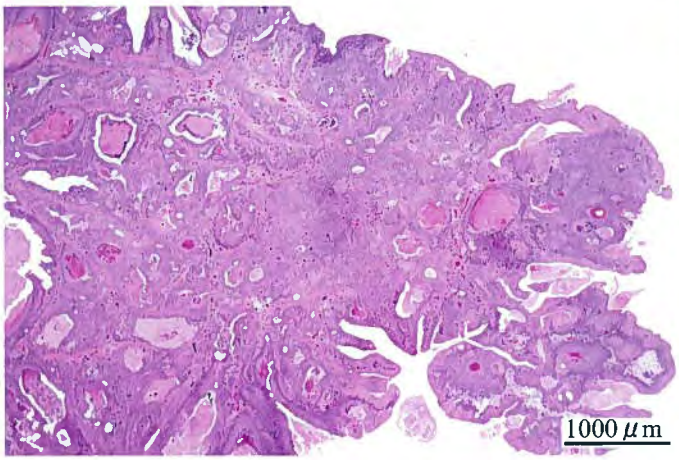


Photograph 2
Forestomach: Squamous cell hyperplasia
Rat, Male, 8000 ppm, Animal No. 0579-1340 (H&E)

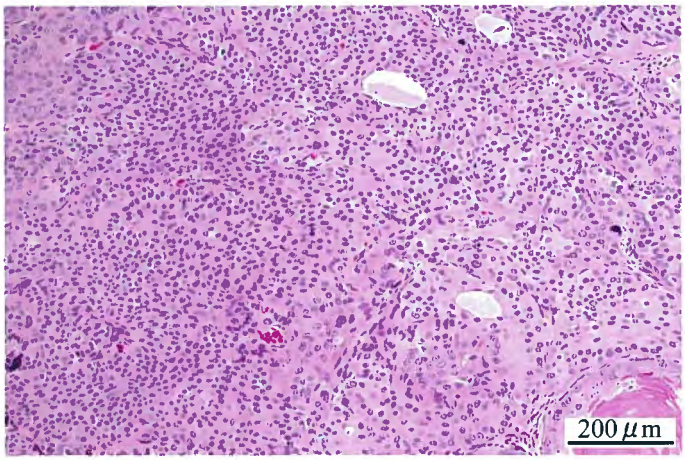
Photograph 3
Forestomash: Squamous cell papilloma
Rat, Male, 8000 ppm, Animal No. 0579-1336 (H&E)



Photograph 4
Forestomash: Squamous cell carcinoma
Rat, Male, 8000 ppm, Animal No. 0579-1344 (H&E)



Photograph 5
Urinary bladder: Transitional cell carcinoma
Rat, Male, 8000 ppm, Animal No. 0579-1329 (H&E)



Photograph 6
Higher magnification of photograph 5
Urinary bladder: Transitional cell carcinoma
Rat, Male, 8000 ppm, Animal No. 0579-1329 (H&E)