Summary of Inhalation Carcinogenicity Study of 2,4-Pentanedione 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 March 26, 2010.

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

Summary of Inhalation Carcinogenicity Study of 2,4-Pentanedione in F344 Rats

Purpose, materials and methods

2,4-Pentanedione (CAS No. 123-54-6) is a colorless liquid with a boiling point of 139°C (746 mmHg). It is soluble in ethanol, acetone, and water.

The carcinogenicity and chronic toxicity of 2,4-pentanedione (greater than 99.9% pure) were examined by inhalation exposure using F344/DuCrlCrlj (Fischer) rats. Groups of test animals were exposed to 2,4-pentanedione vapors at target concentrations of 0 (clean air), 100, 200 or 400 ppm (v/v) for 6 hours/day, 5 days/week for 2 years (104 weeks). Each group of test animals consisted of either 50 male or 50 female rats. Both sexes were exposed to each concentration of 2,4-pentanedione vapor. 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 2,4-pentanedione used in these experiments was confirmed by both infrared spectrometry and mass spectrometry. It was analyzed by gas chromatography before and after its use to affirm its stability. Stainless-steel inhalation exposure chambers (volume: 7.6m^3) were used throughout the 2-year exposure period. 2,4-Pentanedione vapor-air mixtures were generated by bubbling clean air through 2,4-pentanedione liquid and the mixtures delivered to the inhalation exposure chambers. Air concentrations of the 2,4-pentanedione in the inhalation exposure chambers were monitored at 15 min intervals by gas chromatography. 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 exposure period. Hematology and blood biochemistry analysis were performed 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 2,4-pentanedione 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

No significant differences in survival rates and clinical signs were found between any of the groups exposed to 2,4-pentanedione and their respective controls. The body weights of the males exposed to 200 and 400 ppm 2,4-pentanedione and females exposed to 400 ppm 2,4-pentanedione were suppressed relative to their respective controls throughout the 2-year exposure period. However, the difference in the body weights between 200 ppm-exposed males and their controls became smaller toward the end of the exposure period. The terminal body weights of the 400 ppm-exposed males and females were 90% and 88% of their respective controls. Food consumption was slightly decreased in males exposed to 200 and 400 ppm 2,4-pentanedione and in females exposed to 400 ppm 2,4-pentanedione compared with their respective controls. Mean corpuscular hemoglobin concentration was significantly increased in males exposed to 200 ppm 2,4-pentanedione and above. Plasma levela of γ-glutamyl transpeptidase was significantly increased in males exposed to 400 ppm 2,4-pentanedione. Significantly decreased plasma levels of triglyceride and significantly increased plasma levels of urea nitrogen were observed in females exposed to 400 ppm 2,4-pentanedione. There were no 2,4-pentanedione related changes in urinalysis parameters or organ weights in any of 2,4-pentanedione administered groups.

No significant increases in the incidence of neoplastic lesions were found in any of the 2,4-pentanedione-exposed groups of either sex compared with their respective controls. Non-neoplastic lesions in the nasal cavity were significantly increased in both sexes at doses of 200 ppm 2,4-pentanedione and above: squamous metaplasia of the respiratory epithelium, inflammation, hyperplasia of the transitional epithelium, and atrophy of the olfactory epithelium. Using nasal lesions as endpoint markers, the no-observed-adverse-effect-level (NOAEL) of 2,4-pentanedione, exposure by inhalation, was 100 ppm 2,4-pentanedione in both male and female rats.

Conclusions

There was no evidence for carcinogenicity of 2,4-pentanedione in male or female rats.

Incidences of selected neoplastic lesions of male rats in the 2-year inhalation carcinogenicity study of 2,4-pentanedione

Dose (ppm)		0	100	200	400	Peto test	Cochran-Armitage test
Number of examined animals		50	50	50	50		
benign tumor							
skin/appendage	keratoacanthoma	4	2	2	1		
subcutis	fibroma	8	6	3	5		
lung	bronchiolar-alveolar adenoma	3	4	3	0		
liver	hepatocellular adenoma	0	4	0	1		
pancreas	islet cell adenoma	3	2	7	2		
pituitary	adenoma	13	5	16	6		
thyroid	C-cell adenoma	3	8	9	3		
adrenal	pheochromocytoma	2	4	2	4		
testis	interstitial cell tumor	44	46	40	42		
mammary gland	fibroadenoma	0	3	0	1		
malignant tumor							
spleen	mononuclear cell leukemia	4	3	2	1		
thyroid	C-cell carcinoma	3	1	1	1		
peritoneum	mesothelioma	3	2	0	3		

Incidences of selected neoplastic lesions of female rats in the 2-year inhalation carcinogenicity study of 2,4-pentanedione

Dose (ppm)		0	100	200	400	Peto test	Cochran-Armitage test
Number of examined animals		50	50	50	50		
benign tumor							
pituitary	adenoma	21	18	19	15		
thyroid	C-cell adenoma	7	6	4	0 **		↓ ↓
adrenal	pheochromocytoma	0	1	3	2		
uterus	endometrial stromal polyp	13	3 **	12	7		
mammary gland	fibroadenoma	5	4	3	5		
malignant tumor							
spleen	mononuclear cell leukemia	2	7	0	1		

Significant difference

* : p≦0.05		** : p≦0.01		(Fisher test)
↑ : p≦0.05	increase	↑ ↑ : p≦0.01	increase	(Peto, Cochran-Armitage test)
↓ : p≦0.05	decrease	↓ ↓ : p≦0.01	decrease	(Cochran-Armitage test)

SELECTED TABLES

TABLE A

CONCENTRATIONS OF 2,4-PENTANEDIONE IN THE INHALATION CHAMBER OF THE 2-YEAR INHALATION STUDY

CONCENTRATIONS OF 2,4-PENTANEDIONE IN THE INHALATION CHAMBER OF THE 2-YEAR INHALATION STUDY

Group Name	Concentration(ppm) Mean ± S.D.
Control	0.0 ± 0.0
100 ppm	100.8 ± 0.9
200 ppm	200.9 ± 1.4
400 ppm	400.7 ± 2.3

TABLE D1

BODY WEIGHT CHANGES AND SURVIVAL ANIMAL NUMBERS : MALE

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

MEAN BODY WEIGHTS AND SURVIVAL

Week on Study	Control Av. Wt.	Control No. of Surviv. <50>	100 ppm Av. Wt.	100 ppm % of cont. <50>	100 ppm No. of Surviv.	200 ppm Av. Wt.	200 ppm % of cont. <50>	200 ppm No. of Surviv.	400 ppm Av. Wt.	400 ppm % of cont. <50>	400 ppm No. of Surviv.
0	123 (50)	50/50	123 (50)	100	50/50	123 (50)	100	50/50	123 (50)	100	50/50
1	153 (50)	50/50	152 (50)	99	50/50	150 (50)	98	50/50	143 (50)	93	50/50
2	184 (50)	50/50	185 (50)	101	50/50	184 (50)	100	50/50	178 (50)	97	50/50
3	212 (50)	50/50	211 (50)	100	50/50	209 (50)	99	50/50	199 (50)	94	50/50
4	235 (50)	50/50	232 (50)	99	50/50	230 (50)	98	50/50	217 (50)	92	50/50
5	252 (50)	50/50	250 (50)	99	50/50	246 (50)	98	50/50	231 (50)	92	50/50
6	268 (50)	50/50	265 (50)	99	50/50	261 (50)	97	50/50	243 (50)	91	50/50
7	281 (50)	50/50	279 (50)	99	50/50	272 (50)	97	50/50	255 (50)	91	50/50
8	294 (50)	50/50	293 (50)	100	50/50	284 (50)	97	50/50	267 (50)	91	50/50
9	305 (50)	50/50	303 (50)	99	50/50	295 (50)	97	50/50	276 (50)	90	50/50
10	314 (50)	50/50	311 (50)	99	50/50	302 (50)	96	50/50	283 (50)	90	50/50
11	320 (50)	50/50	317 (50)	99	50/50	308 (50)	96	50/50	287 (50)	90	50/50
12	328 (50)	50/50	324 (50)	99	50/50	315 (50)	96	50/50	294 (50)	90	50/50
13	334 (50)	50/50	330 (50)	99	50/50	321 (50)	96	50/50	302 (50)	90	50/50
14	339 (50)	50/50	335 (50)	99	50/50	326 (50)	96	50/50	305 (50)	90	50/50
18	355 (50)	50/50	350 (50)	99	50/50	341 (50)	96	50/50	321 (50)	90	50/50
22	370 (50)	50/50	364 (50)	98	50/50	356 (50)	96	50/50	334 (50)	90	50/50
26	383 (50)	50/50	375 (50)	98	50/50	368 (50)	96	50/50	347 (50)	91	50/50
30	394 (50)	50/50	385 (50)	98	50/50	378 (50)	96	50/50	354 (50)	90	50/50
34	404 (50)	50/50	395 (50)	98	50/50	389 (50)	96	50/50	364 (50)	90	50/50
38	414 (50)	50/50	403 (50)	97	50/50	398 (50)	96	50/50	371 (50)	90	50/50
42	422 (50)	50/50	416 (49)	99	49/50	405 (50)	96	50/50	376 (50)	89	50/50
46	427 (50)	50/50	420 (49)	98	49/50	409 (50)	96	50/50	379 (50)	89	50/50
50	434 (50)	50/50	425 (49)	98	49/50	411 (50)	95	50/50	384 (50)	88	50/50
54	440 (50)	50/50	431 (49)	98	49/50	418 (49)	95	49/50	389 (50)	88	50/50
58	442 (50)	50/50	435 (49)	98	49/50	419 (49)	95	49/50	390 (50)	88	50/50
62	447 (50)	50/50	439 (49)	98	49/50	423 (49)	95	49/50	395 (50)	88	50/50
66	448 (50)	50/50	441 (49)	98	49/50	425 (49)	95	49/50	399 (50)	89	50/50
70	451 (49)	49/50	443 (49)	98	49/50	426 (49)	94	49/50	400 (50)	89	50/50
74	453 (49)	49/50	445 (49)	98	49/50	428 (49)	94	49/50	402 (50)	89	50/50
78	452 (49)	49/50	445 (49)	98	49/50	427 (49)	94	49/50	399 (49)	88	49/50
82	449 (49)	49/50	443 (49)	99	49/50	430 (48)	96	48/50	398 (47)	89	47/50
86	449 (48)	48/50	442 (48)	98	48/50	430 (48)	96	48/50	402 (45)	90	45/50
90	447 (47)	47/50	439 (46)	98	46/50	430 (47)	96	47/50	400 (45)	89	45/50
94	439 (45)	45/50	428 (44)	97	44/50	414 (46)	94	46/50	387 (45)	88	45/50
98	426 (43)	43/50	419 (43)	98	43/50	410 (43)	96	43/50	382 (43)	90	43/50
102	412 (43)	43/50	413 (40)	100	40/50	406 (41)	99	41/50	375 (42)	91	42/50
104	416 (41)	41/50	413 (40)	99	40/50	406 (40)	98	40/50	374 (42)	90	42/50

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

TABLE D2

BODY WEIGHT CHANGES AND SURVIVAL ANIMAL NUMBERS : FEMALE

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

MEAN BODY WEIGHTS AND SURVIVAL

Week on Study	Control Av. Wt.	Control No. of Surviv. <50>	100 ppm Av. Wt.	100 ppm % of cont. <50>	100 ppm No. of Surviv.	200 ppm Av. Wt.	200 ppm % of cont. <50>	200 ppm No. of Surviv.	400 ppm Av. Wt.	400 ppm % of cont. <50>	400 ppm No. of Surviv.
0	99 (50)	50/50	99 (50)	100	50/50	99 (50)	100	50/50	99 (50)	100	50/50
1	113 (50)	50/50	112 (50)	99	50/50	112 (50)	99	50/50	107 (50)	95	50/50
2	127 (50)	50/50	126 (50)	99	50/50	127 (50)	100	50/50	123 (50)	97	50/50
3	138 (50)	50/50	136 (50)	99	50/50	136 (50)	99	50/50	131 (50)	95	50/50
4	147 (50)	50/50	145 (50)	99	50/50	145 (50)	99	50/50	139 (50)	95	50/50
5	155 (50)	50/50	153 (50)	99	50/50	152 (50)	98	50/50	146 (50)	94	50/50
6	161 (50)	50/50	158 (50)	98	50/50	159 (50)	99	50/50	153 (50)	95	50/50
7	166 (50)	50/50	164 (50)	99	50/50	163 (50)	98	50/50	157 (50)	95	50/50
8	171 (50)	50/50	170 (50)	99	50/50	168 (50)	98	50/50	162 (50)	95	50/50
9	175 (50)	50/50	172 (50)	98	50/50	173 (50)	99	50/50	166 (50)	95	50/50
10	179 (50)	50/50	177 (50)	99	50/50	177 (50)	99	50/50	170 (50)	95	50/50
11	182 (50)	50/50	180 (50)	99	50/50	179 (50)	98	50/50	172 (50)	95	50/50
12	186 (50)	50/50	183 (50)	98	50/50	182 (50)	98	50/50	175 (50)	94	50/50
13	188 (50)	50/50	185 (50)	98	50/50	183 (50)	97	50/50	177 (50)	94	50/50
14	191 (50)	50/50	187 (50)	98	50/50	185 (50)	97	50/50	178 (50)	93	50/50
18	197 (50)	50/50	193 (50)	98	50/50	191 (50)	97	50/50	184 (50)	93	50/50
22	201 (50)	50/50	198 (50)	99	50/50	197 (50)	98	50/50	189 (50)	94	50/50
26	208 (50)	50/50	204 (50)	98	50/50	202 (50)	97	50/50	193 (49)	93	49/50
30	211 (50)	50/50	209 (50)	99	50/50	206 (50)	98	50/50	198 (49)	94	49/50
34	218 (50)	50/50	217 (50)	100	50/50	213 (50)	98	50/50	203 (49)	93	49/50
38	223 (50)	50/50	221 (50)	99	50/50	217 (50)	97	50/50	207 (49)	93	49/50
42	227 (50)	50/50	226 (50)	100	50/50	222 (50)	98	50/50	212 (49)	93	49/50
46	231 (50)	50/50	229 (50)	99	50/50	224 (50)	97	50/50	211 (49)	91	49/50
50	235 (50)	50/50	234 (50)	100	50/50	228 (50)	97	50/50	217 (48)	92	48/50
54	239 (50)	50/50	239 (50)	100	50/50	234 (50)	98	50/50	222 (48)	93	48/50
58	243 (50)	50/50	244 (50)	100	50/50	238 (50)	98	50/50	222 (48)	91	48/50
62	251 (49)	49/50	252 (50)	100	50/50	244 (50)	97	50/50	227 (48)	90	48/50
66	254 (49)	49/50	258 (50)	102	50/50	248 (50)	98	50/50	232 (48)	91	48/50
70	262 (48)	48/50	265 (50)	101	50/50	254 (50)	97	50/50	237 (48)	90	48/50
74	266 (48)	48/50	269 (50)	101	50/50	262 (50)	98	50/50	244 (48)	92	48/50
78	270 (46)	46/50	275 (48)	102	48/50	265 (50)	98	50/50	249 (48)	92	48/50
82	271 (46)	46/50	281 (47)	104	47/50	269 (49)	99	49/50	250 (47)	92	47/50
86	277 (45)	45/50	284 (46)	103	46/50	274 (48)	99	48/50	251 (44)	91	44/50
90	281 (44)	44/50	291 (42)	104	42/50	278 (47)	99	47/50	254 (44)	90	44/50
94	277 (43)	43/50	279 (40)	101	40/50	273 (46)	99	46/50	246 (44)	89	44/50
98	282 (42)	42/50	282 (39)	100	39/50	274 (45)	97	45/50	248 (41)	88	41/50
102	283 (39)	39/50	283 (38)	100	38/50	281 (43)	99	43/50	249 (39)	88	39/50
104	284 (38)	38/50	288 (36)	101	36/50	280 (43)	99	43/50	249 (36)	88	36/50

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

TABLE D3

BODY WEIGHT CHANGES : MALE

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 0	1	2	3	4	5	6
Control	123± 5	153± 8	184± 9	212± 10	235± 11	252± 11	268± 12
100 ppm	123± 5	152± 7	185± 8	211± 9	232± 10	250± 10	265± 11
200 ppm	123± 5	150± 8	184± 10	209± 10	230± 10*	246± 11*	261± 11**
400 ppm	123± 5	143± 6**	178± 7**	199± 8**	217± 9**	231± 9**	243± 10**

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

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 7	8	9	10	11	12	13
Control	281± 12	294± 13	305± 14	314± 14	320± 14	328± 15	334± 15
100 ppm	279± 12	293± 12	303± 13	311± 13	317± 14	324± 15	330± 15
200 ppm	272± 12**	284± 13**	295± 13**	302± 14**	308± 15**	315± 15**	321± 15**
400 ppm	255± 11**	267± 12**	276± 12**	283± 13**	287± 13**	294± 13**	302± 13**

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

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 14	18	22	26	30	34	38
Control	339± 15	355± 17	370± 18	383± 19	394± 19	404± 22	414± 23
100 ppm	335± 16	350± 17	364± 22	375± 28	385± 33	395± 37	403± 41
200 ppm	326± 15**	341± 16**	356± 17**	368± 18**	378± 18**	389± 19**	398± 21**
400 ppm	305± 14**	321± 16**	334± 17**	347± 19**	354± 19**	364± 20**	371± 21**

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

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 42	46	50	54	58	62	66
Control	422± 23	427± 24	434± 23	440± 24	442± 24	447± 24	448± 23
100 ppm	416± 19	420± 19	425± 18	431± 18	435± 18	439± 19	441± 21
200 ppm	405± 21**	409± 22**	411± 23**	418± 24**	419± 26**	423± 28**	425± 25**
400 ppm	376± 21**	379± 21**	384± 22**	389± 22**	390± 23**	395± 24**	399± 23**

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

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 70	74	78	82	86	90	94
Control	451± 23	453± 22	452± 23	449± 26	449± 23	447± 26	439± 36
100 ppm	443± 23	445± 22	445± 22	443± 25	442± 23	439± 25	428± 35
200 ppm	426± 30**	428± 36**	427± 40**	430± 27**	430± 27**	430± 25**	414± 42**
400 ppm	400± 27**	402± 32**	399± 29**	398± 32**	402± 19**	400± 20**	387± 23**

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

(HAN260)

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 98		102		104	
Control	426±	30	412±	45	416±	50
100 ppm	419±	44	413±	45	413±	52
200 ppm	410±	36**	406±	46	406±	50
400 ppm	382±	18**	375±	16**	374±	20**

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

(HAN260)

TABLE D4

BODY WEIGHT CHANGES : FEMALE

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 0	1	2	3	4	5	6
Control	99± 3	113± 4	127± 5	138± 6	147± 6	155± 7	161± 7
100 ppm	99± 3	112± 5	126± 5	136± 5	145± 6	153± 6	158± 7
200 ppm	99± 3	112± 5	127± 6	136± 6	145± 7	152± 8	159± 8
400 ppm	99± 3	107± 4**	123± 6**	131± 5**	139± 6**	146± 6**	153± 6**

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

(HAN260)

BAIS 4

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 7	8	9	10	11	12	13
Control	166± 8	171± 8	175± 9	179± 10	182± 9	186± 10	188± 10
100 ppm	164± 7	170± 8	172± 8	177± 8	180± 8	183± 8	185± 8
200 ppm	163± 9	168± 9	173± 10	177± 10	179± 9	182± 10*	183± 9*
400 ppm	157± 7**	162± 8**	166± 8**	170± 8**	172± 8**	175± 8**	177± 8**

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

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 14	18	22	26	30	34	38
Control	191± 10	197± 11	201± 12	208± 11	211± 12	218± 12	223± 13
100 ppm	187± 9	193± 10	198± 11	204± 12	209± 12	217± 13	221± 13
200 ppm	185± 10*	191± 11*	197± 11	202± 12*	206± 11	213± 12	217± 13*
400 ppm	178± 9**	184± 9**	189± 9**	193± 10**	198± 11**	203± 12**	207± 12**

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

(HAN260)

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 42	46	50	54	58	62	66
Control	227± 14	231± 15	235± 15	239± 16	243± 16	251± 18	254± 19
100 ppm	226± 13	229± 13	234± 15	239± 15	244± 16	252± 17	258± 18
200 ppm	222± 13	224± 15*	228± 15	234± 15	238± 17	244± 18	248± 20
400 ppm	212± 12**	211± 14**	217± 13**	222± 14**	222± 14**	227± 15**	232± 16**

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

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 70	74	78	82	86	90	94
Control	262± 20	266± 21	270± 22	271± 25	277± 24	281± 27	277± 30
100 ppm	265± 20	269± 21	275± 25	281± 26	284± 37	291± 47	279± 27
200 ppm	254± 21	262± 21	265± 22	269± 22	274± 22	278± 21	273± 22
400 ppm	237± 16**	244± 17**	249± 19**	250± 27**	251± 16**	254± 16**	246± 16**

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

(HAN260)

BAIS 4

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 98	102	104
Control	282± 31	283± 31	284± 34
100 ppm	282± 31	283± 31	288± 24
200 ppm	274± 29	281± 23	280± 23
400 ppm	248± 18**	249± 21**	249± 19**

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

TABLE E1

FOOD CONSUMPTION CHANGES AND SURVIVAL ANIMAL NUMBERS : MALE

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

MEAN FOOD CONSUMPTION(FC) AND SURVIVAL

Week on Study	Control Av. FC.	Control No. of Surviv. <50>	100 ppm Av. FC.	100 ppm % of cont. <50>	100 ppm No. of Surviv.	200 ppm Av. FC.	200 ppm % of cont. <50>	200 ppm No. of Surviv.	400 ppm Av. FC.	400 ppm % of cont. <50>	400 ppm No. of Surviv.
1	14.5 (50)	50/50	14.4 (50)	99	50/50	14.1 (50)	97	50/50	13.1 (50)	90	50/50
2	16.2 (50)	50/50	16.5 (50)	102	50/50	16.3 (50)	101	50/50	15.5 (50)	96	50/50
3	16.7 (50)	50/50	16.9 (50)	101	50/50	16.4 (50)	98	50/50	15.0 (50)	90	50/50
4	17.1 (50)	50/50	16.8 (50)	98	50/50	16.5 (50)	96	50/50	15.1 (50)	88	50/50
5	17.3 (50)	50/50	17.2 (50)	99	50/50	16.7 (50)	97	50/50	15.7 (50)	91	50/50
6	16.9 (50)	50/50	16.7 (50)	99	50/50	16.5 (50)	98	50/50	15.4 (50)	91	50/50
7	17.4 (50)	50/50	17.3 (50)	99	50/50	16.7 (50)	96	50/50	16.0 (50)	92	50/50
8	17.1 (50)	50/50	17.0 (50)	99	50/50	16.4 (50)	96	50/50	15.9 (50)	93	50/50
9	17.6 (50)	50/50	17.1 (50)	97	50/50	17.0 (50)	97	50/50	15.9 (50)	90	50/50
10	17.0 (50)	50/50	16.5 (47)	97	50/50	16.2 (50)	95	50/50	15.5 (50)	91	50/50
11	17.0 (50)	50/50	16.7 (50)	98	50/50	16.5 (50)	97	50/50	15.6 (50)	92	50/50
12	16.4 (50)	50/50	16.2 (50)	99	50/50	15.8 (45)	96	50/50	15.1 (50)	92	50/50
13	16.7 (50)	50/50	16.4 (50)	98	50/50	16.1 (50)	96	50/50	15.5 (50)	93	50/50
14	16.2 (50)	50/50	15.8 (50)	98	50/50	15.2 (50)	94	50/50	14.8 (50)	91	50/50
18	16.4 (50)	50/50	16.3 (50)	99	50/50	15.6 (50)	95	50/50	15.3 (50)	93	50/50
22	16.6 (50)	50/50	16.7 (50)	101	50/50	16.0 (50)	96	50/50	15.5 (50)	93	50/50
26	16.2 (50)	50/50	16.2 (50)	100	50/50	15.9 (50)	98	50/50	15.2 (50)	94	50/50
30	16.5 (50)	50/50	16.5 (50)	100	50/50	16.2 (50)	98	50/50	15.4 (50)	93	50/50
34	16.6 (50)	50/50	16.5 (50)	99	50/50	16.3 (50)	98	50/50	15.8 (50)	95	50/50
38	17.3 (50)	50/50	16.8 (50)	97	50/50	16.6 (50)	96	50/50	15.9 (50)	92	50/50
42	17.2 (50)	50/50	17.0 (49)	99	49/50	16.4 (50)	95	50/50	15.9 (50)	92	50/50
46	16.9 (50)	50/50	16.7 (49)	99	49/50	16.4 (50)	97	50/50	15.7 (50)	93	50/50
50	17.0 (50)	50/50	17.1 (49)	101	49/50	16.4 (50)	96	50/50	15.9 (50)	94	50/50
54	17.0 (50)	50/50	16.9 (49)	99	49/50	16.7 (49)	98	49/50	16.1 (50)	95	50/50
58	17.0 (50)	50/50	17.2 (49)	101	49/50	16.4 (49)	96	49/50	15.9 (50)	94	50/50
62	17.3 (50)	50/50	17.2 (49)	99	49/50	16.6 (49)	96	49/50	16.0 (50)	92	50/50
66	17.0 (50)	50/50	17.0 (49)	100	49/50	16.8 (49)	99	49/50	16.1 (50)	95	50/50
70	17.1 (49)	49/50	17.0 (49)	99	49/50	16.5 (48)	96	49/50	15.8 (50)	92	50/50
74	17.2 (49)	49/50	16.9 (49)	98	49/50	16.6 (49)	97	49/50	15.8 (50)	92	50/50
78	16.8 (49)	49/50	17.0 (49)	101	49/50	16.5 (49)	98	49/50	16.0 (49)	95	49/50
82	16.6 (49)	49/50	16.6 (49)	100	49/50	16.4 (48)	99	48/50	15.4 (47)	93	47/50
86	16.9 (48)	48/50	16.8 (48)	99	48/50	16.5 (48)	98	48/50	15.9 (45)	94	45/50
90	17.3 (47)	47/50	17.1 (46)	99	46/50	16.5 (47)	95	47/50	16.3 (45)	94	45/50
94	17.0 (45)	45/50	16.7 (44)	98	44/50	15.9 (46)	94	46/50	15.1 (45)	89	45/50
98	16.2 (43)	43/50	15.7 (43)	97	43/50	15.7 (43)	97	43/50	15.4 (43)	95	43/50
102	16.6 (43)	43/50	16.4 (40)	99	40/50	16.9 (41)	102	41/50	15.6 (42)	94	42/50
104	16.4 (41)	41/50	16.5 (40)	101	40/50	16.8 (40)	102	40/50	15.5 (42)	95	42/50

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

TABLE E2

FOOD CONSUMPTION CHANGES AND SURVIVAL ANIMAL NUMBERS : FEMALE

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

MEAN FOOD CONSUMPTION(FC) AND SURVIVAL

Week on Study	Control Av. FC.	Control No. of Surviv. <50>	100 ppm Av. FC.	100 ppm % of cont. <50>	100 ppm No. of Surviv.	200 ppm Av. FC.	200 ppm % of cont. <50>	200 ppm No. of Surviv.	400 ppm Av. FC.	400 ppm % of cont. <50>	400 ppm No. of Surviv.
1	10.9 (50)	50/50	10.7 (50)	98	50/50	10.6 (50)	97	50/50	10.0 (50)	92	50/50
2	12.1 (50)	50/50	11.8 (50)	98	50/50	12.1 (50)	100	50/50	11.8 (50)	98	50/50
3	11.4 (50)	50/50	11.2 (50)	98	50/50	11.3 (50)	99	50/50	10.4 (50)	91	50/50
4	11.7 (50)	50/50	11.2 (50)	96	50/50	11.3 (50)	97	50/50	10.5 (50)	90	50/50
5	11.7 (50)	50/50	11.6 (50)	99	50/50	11.3 (50)	97	50/50	11.0 (50)	94	50/50
6	11.7 (50)	50/50	11.3 (50)	97	50/50	11.6 (50)	99	50/50	10.8 (50)	92	50/50
7	11.3 (50)	50/50	11.1 (50)	98	50/50	11.1 (50)	98	50/50	10.8 (50)	96	50/50
8	11.4 (50)	50/50	11.4 (50)	100	50/50	11.1 (50)	97	50/50	11.0 (50)	96	50/50
9	11.4 (50)	50/50	11.0 (50)	96	50/50	10.9 (50)	96	50/50	10.6 (50)	93	50/50
10	11.4 (50)	50/50	11.0 (50)	96	50/50	11.2 (50)	98	50/50	10.7 (50)	94	50/50
11	11.3 (50)	50/50	11.1 (50)	98	50/50	10.7 (50)	95	50/50	10.5 (50)	93	50/50
12	11.6 (50)	50/50	10.8 (50)	93	50/50	10.6 (50)	91	50/50	10.4 (50)	90	50/50
13	11.2 (50)	50/50	11.0 (50)	98	50/50	10.7 (50)	96	50/50	10.4 (50)	93	50/50
14	11.6 (50)	50/50	10.6 (50)	91	50/50	10.5 (50)	91	50/50	10.1 (50)	87	50/50
18	10.8 (50)	50/50	10.8 (50)	100	50/50	10.5 (50)	97	50/50	10.3 (50)	95	50/50
22	11.1 (50)	50/50	10.9 (50)	98	50/50	10.6 (50)	95	50/50	10.5 (50)	95	50/50
26	10.8 (50)	50/50	10.9 (50)	101	50/50	10.5 (50)	97	50/50	10.2 (49)	94	49/50
30	11.1 (50)	50/50	11.0 (50)	99	50/50	10.8 (50)	97	50/50	10.8 (49)	97	49/50
34	11.4 (50)	50/50	11.5 (50)	101	50/50	11.1 (50)	97	50/50	10.8 (49)	95	49/50
38	11.9 (50)	50/50	11.5 (50)	97	50/50	11.0 (50)	92	50/50	11.2 (49)	94	49/50
42	11.6 (50)	50/50	11.8 (50)	102	50/50	11.3 (50)	97	50/50	11.0 (49)	95	49/50
46	11.7 (50)	50/50	11.5 (50)	98	50/50	11.3 (50)	97	50/50	10.8 (49)	92	49/50
50	11.9 (50)	50/50	11.7 (50)	98	50/50	11.4 (50)	96	50/50	11.3 (48)	95	48/50
54	11.4 (50)	50/50	11.3 (50)	99	50/50	11.3 (50)	99	50/50	11.6 (48)	102	48/50
58	11.7 (50)	50/50	12.0 (50)	103	50/50	11.5 (50)	98	50/50	10.8 (48)	92	48/50
62	12.3 (49)	49/50	12.3 (50)	100	50/50	11.7 (50)	95	50/50	11.2 (48)	91	48/50
66	11.7 (49)	49/50	12.2 (50)	104	50/50	11.8 (50)	101	50/50	11.7 (48)	100	48/50
70	12.3 (48)	48/50	12.5 (50)	102	50/50	11.8 (50)	96	50/50	11.7 (48)	95	48/50
74	12.2 (48)	48/50	12.2 (50)	100	50/50	12.1 (50)	99	50/50	11.6 (48)	95	48/50
78	12.1 (46)	46/50	12.3 (48)	102	48/50	11.8 (50)	98	50/50	11.6 (48)	96	48/50
82	12.1 (46)	46/50	12.2 (47)	101	47/50	12.0 (49)	99	49/50	11.2 (47)	93	47/50
86	12.4 (45)	45/50	12.5 (46)	101	46/50	12.4 (48)	100	48/50	11.4 (44)	92	44/50
90	13.1 (44)	44/50	13.1 (41)	100	42/50	12.7 (47)	97	47/50	12.0 (44)	92	44/50
94	12.1 (43)	43/50	12.0 (40)	99	40/50	11.6 (46)	96	46/50	10.6 (44)	88	44/50
98	13.4 (42)	42/50	13.4 (39)	100	39/50	12.6 (45)	94	45/50	11.9 (41)	89	41/50
102	13.1 (39)	39/50	13.2 (38)	101	38/50	13.0 (43)	99	43/50	11.6 (39)	89	39/50
104	13.2 (38)	38/50	13.1 (36)	99	36/50	12.4 (43)	94	43/50	11.6 (36)	88	36/50

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

TABLE E3

FOOD CONSUMPTION CHANGES : MALE

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 1	2	3	4	5	6	7
Control	14.5± 0.8	16.2± 1.1	16.7± 1.0	17.1± 1.1	17.3± 1.0	16.9± 1.0	17.4± 1.0
100 ppm	14.4± 0.7	16.5± 1.0	16.9± 0.8	16.8± 0.9	17.2± 0.9	16.7± 0.9	17.3± 1.0
200 ppm	14.1± 0.9	16.3± 1.2	16.4± 1.0	16.5± 1.1*	16.7± 0.9**	16.5± 1.0	16.7± 0.9**
400 ppm	13.1± 0.7**	15.5± 1.1**	15.0± 0.8**	15.1± 1.0**	15.7± 0.9**	15.4± 0.9**	16.0± 0.8**

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

(HAN260)

BAIS 4

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 8	9	10	11	12	13	14
Control	17.1± 1.0	17.6± 0.9	17.0± 1.0	17.0± 0.9	16.4± 1.0	16.7± 0.9	16.2± 0.8
100 ppm	17.0± 1.0	17.1± 0.9*	16.5± 0.9*	16.7± 1.0	16.2± 1.0	16.4± 0.9	15.8± 0.9
200 ppm	16.4± 1.0**	17.0± 1.0**	16.2± 0.9**	16.5± 1.0*	15.8± 0.9**	16.1± 1.0**	15.2± 1.1**
400 ppm	15.9± 0.8**	15.9± 0.8**	15.5± 0.9**	15.6± 0.9**	15.1± 1.0**	15.5± 0.8**	14.8± 0.9**

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

(HAN260)

BAIS 4

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 18	22	26	30	34	38	42
Control	16.4± 1.1	16.6± 1.1	16.2± 0.9	16.5± 1.0	16.6± 1.0	17.3± 1.1	17.2± 1.1
100 ppm	16.3± 1.3	16.7± 1.9	16.2± 1.0	16.5± 1.0	16.5± 1.0	16.8± 1.0	17.0± 0.8
200 ppm	15.6± 0.8**	16.0± 1.0*	15.9± 1.0	16.2± 0.9	16.3± 1.0	16.6± 1.1**	16.4± 1.1**
400 ppm	15.3± 1.0**	15.5± 1.1**	15.2± 1.0**	15.4± 1.2**	15.8± 1.0**	15.9± 1.0**	15.9± 1.0**

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

(HAN260)

BAIS 4

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 46	50	54	58	62	66	70
Control	16.9± 1.0	17.0± 0.8	17.0± 1.0	17.0± 1.1	17.3± 0.9	17.0± 1.0	17.1± 1.0
100 ppm	16.7± 1.0	17.1± 0.8	16.9± 0.9	17.2± 1.6	17.2± 0.8	17.0± 0.9	17.0± 1.1
200 ppm	16.4± 0.9*	16.4± 0.9**	16.7± 0.9	16.4± 1.0*	16.6± 0.9**	16.8± 1.4	16.5± 0.9*
400 ppm	15.7± 1.0**	15.9± 1.1**	16.1± 0.9**	15.9± 1.0**	16.0± 1.2**	16.1± 0.9**	15.8± 1.1**

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

(HAN260)

BAIS 4

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 74	78	82	86	90	94	98
Control	17.2± 0.8	16.8± 1.3	16.6± 1.1	16.9± 1.5	17.3± 1.4	17.0± 2.0	16.2± 1.7
100 ppm	16.9± 0.8	17.0± 0.9	16.6± 1.7	16.8± 1.1	17.1± 1.2	16.7± 1.4	15.7± 1.9
200 ppm	16.6± 1.2*	16.5± 1.0	16.4± 1.0	16.5± 1.0	16.5± 1.9*	15.9± 1.8**	15.7± 2.2
400 ppm	15.8± 1.3**	16.0± 1.4**	15.4± 1.5**	15.9± 1.3**	16.3± 1.7**	15.1± 1.3**	15.4± 1.2

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

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 102	104
Control	16.6± 3.2	16.4± 2.9
100 ppm	16.4± 2.7	16.5± 1.7
200 ppm	16.9± 1.8	16.8± 2.0
400 ppm	15.6± 1.1**	15.5± 1.7**

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

(HAN260)

TABLE E4

FOOD CONSUMPTION CHANGES : FEMALE

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 1	2	3	4	5	6	7
Control	10.9± 0.6	12.1± 1.1	11.4± 0.8	11.7± 1.2	11.7± 0.7	11.7± 1.1	11.3± 1.1
100 ppm	10.7± 0.5	11.8± 0.8	11.2± 0.7	11.2± 0.8*	11.6± 0.8	11.3± 1.0*	11.1± 0.9
200 ppm	10.6± 0.5*	12.1± 1.1	11.3± 0.8	11.3± 0.9	11.3± 0.7*	11.6± 1.0	11.1± 0.8
400 ppm	10.0± 0.5**	11.8± 1.0	10.4± 0.7**	10.5± 0.7**	11.0± 0.8**	10.8± 0.8**	10.8± 0.8**

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

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 8	9	10	11	12	13	14
Control	11.4± 1.1	11.4± 1.0	11.4± 1.1	11.3± 0.8	11.6± 1.1	11.2± 0.9	11.6± 1.3
100 ppm	11.4± 1.1	11.0± 0.8	11.0± 0.9	11.1± 0.7	10.8± 0.9**	11.0± 0.6	10.6± 0.8**
200 ppm	11.1± 1.2	10.9± 0.8**	11.2± 1.1	10.7± 0.8**	10.6± 0.9**	10.7± 0.7**	10.5± 0.9**
400 ppm	11.0± 1.0	10.6± 0.8**	10.7± 1.1**	10.5± 0.8**	10.4± 0.8**	10.4± 0.9**	10.1± 1.1**

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

(HAN260)

BAIS 4

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 18	22	26	30	34	38	42
Control	10.8± 1.2	11.1± 1.2	10.8± 0.7	11.1± 1.1	11.4± 1.0	11.9± 1.1	11.6± 1.2
100 ppm	10.8± 0.9	10.9± 1.0	10.9± 1.0	11.0± 0.9	11.5± 0.9	11.5± 1.1	11.8± 1.0
200 ppm	10.5± 0.9	10.6± 0.9	10.5± 0.9	10.8± 0.8	11.1± 0.9	11.0± 0.8**	11.3± 1.0
400 ppm	10.3± 1.0	10.5± 1.0*	10.2± 0.7**	10.8± 1.1	10.8± 0.9**	11.2± 1.0**	11.0± 1.0*

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

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 46	50	54	58	62	66	70
Control	11.7± 0.9	11.9± 1.1	11.4± 1.0	11.7± 1.0	12.3± 1.1	11.7± 1.2	12.3± 1.1
100 ppm	11.5± 1.0	11.7± 0.7	11.3± 1.1	12.0± 0.9	12.3± 1.0	12.2± 1.0	12.5± 1.1
200 ppm	11.3± 1.1	11.4± 0.7*	11.3± 0.8	11.5± 0.8	11.7± 0.8**	11.8± 1.2	11.8± 0.9*
400 ppm	10.8± 0.7**	11.3± 1.0**	11.6± 1.5	10.8± 0.8**	11.2± 0.9**	11.7± 1.2	11.7± 0.8**

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

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 74	78	82	86	90	94	98
Control	12.2± 1.2	12.1± 1.0	12.1± 1.1	12.4± 1.2	13.1± 1.7	12.1± 1.6	13.4± 1.4
100 ppm	12.2± 0.8	12.3± 1.8	12.2± 1.3	12.5± 2.2	13.1± 1.0	12.0± 1.1	13.4± 1.4
200 ppm	12.1± 0.9	11.8± 1.0	12.0± 1.0	12.4± 1.1	12.7± 1.2	11.6± 1.2	12.6± 2.2
400 ppm	11.6± 0.9**	11.6± 1.2*	11.2± 0.9**	11.4± 0.8**	12.0± 1.0**	10.6± 1.0**	11.9± 1.6**

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

(HAN260)

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 102	104
Control	13.1± 1.7	13.2± 1.1
100 ppm	13.2± 1.5	13.1± 1.3
200 ppm	13.0± 1.3	12.4± 1.2*
400 ppm	11.6± 1.2**	11.6± 1.2**

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

(HAN260)

TABLE F1

HEMATOLOGY : MALE

STUDY NO. : 0675
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 fℓ	MCH pg	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	40	7.59± 1.26	12.7± 2.5	36.2± 6.1	47.7± 3.1	16.7± 1.6	34.9± 1.7	1170± 413
100 ppm	39	7.78± 1.43	13.0± 2.6	37.0± 6.0	48.3± 6.3	16.8± 2.3	34.8± 2.0	1101± 421
200 ppm	39	7.99± 0.99	13.6± 1.9	37.9± 4.5	47.5± 2.0	17.0± 1.1	35.7± 1.2*	1048± 288
400 ppm	42	8.05± 1.26	13.6± 2.6	38.2± 6.0	47.5± 2.8	16.9± 1.5	35.4± 1.8*	1078± 319

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

(HCL070)

BAIS 4

STUDY NO. : 0675
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	40	5.0± 2.7
100 ppm	39	5.5± 5.6
200 ppm	39	3.9± 1.7
400 ppm	42	4.7± 2.6

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

(HCL070)

BAIS 4

STUDY NO. : 0675
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 (%) NEUTRO		LYMPHO		MONO		EOSINO		BASO		OTHER	
Control	40	6.57±	2.28	50±	9	41±	8	6±	2	1±	1	0±	0	2±	1
100 ppm	39	6.83±	1.88	48±	7	43±	6	6±	1	1±	1	0±	0	1±	1
200 ppm	39	11.45±	20.74	50±	11	39±	12	6±	1	1±	1	0±	0	4±	14
400 ppm	42	10.34±	20.57	50±	11	40±	10	5±	2	1±	0*	0±	1	4±	14

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

(HCL070)

BAIS 4

TABLE F2

HEMATOLOGY : FEMALE

STUDY NO. : 0675
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 $10^5/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV fℓ	MCH pg	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	37	7.80± 1.28	14.5± 2.0	39.1± 4.7	50.9± 5.6	18.8± 1.6	37.0± 1.5	728± 168
100 ppm	36	8.04± 0.66	14.9± 1.2	39.9± 2.9	49.7± 2.0	18.6± 0.7	37.4± 0.7	688± 108
200 ppm	42	8.13± 0.56	15.0± 1.0	40.0± 2.6	49.2± 1.4	18.5± 0.7	37.5± 0.8	725± 137
400 ppm	36	8.09± 0.75	15.2± 1.1	40.6± 2.4	50.5± 3.8	18.8± 1.0	37.3± 0.8	765± 169

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

(HCL070)

BAIS 4

STUDY NO. : 0675
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	37	4.0± 5.6
100 ppm	36	2.6± 1.4
200 ppm	42	2.6± 1.6
400 ppm	36	3.3± 3.9

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

(HCL070)

BAIS 4

STUDY NO. : 0675
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 (%) NEUTRO		LYMPHO		MONO		EOSINO		BASO		OTHER	
Control	37	4.49±	5.41	38±	11	53±	12	5±	2	2±	1	0±	0	1±	1
100 ppm	36	4.01±	2.88	38±	9	52±	10	5±	2	2±	1	0±	1	2±	5
200 ppm	42	3.88±	1.75	39±	7	52±	7	5±	2	2±	1	0±	0	1±	1
400 ppm	36	3.24±	0.98	42±	7	51±	7	5±	1	2±	1	0±	0	1±	0

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

(HCL070)

BAIS 4

TABLE G1

BIOCHEMISTRY : MALE

STUDY NO. : 0675
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	40	6.8± 0.4	2.8± 0.3	0.7± 0.1	0.14± 0.03	147± 30	192± 52	131± 88
100 ppm	39	6.8± 0.4	2.9± 0.2	0.7± 0.1	0.48± 2.06	160± 19	186± 66	140± 99
200 ppm	40	6.8± 0.3	2.8± 0.3	0.7± 0.1	0.14± 0.03	152± 25	194± 76	139± 94
400 ppm	42	6.8± 0.3	2.8± 0.2	0.7± 0.1	0.16± 0.04	155± 15	193± 64	135± 92

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

(HCL074)

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE 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	40	279± 69	91± 88	37± 19	140± 44	335± 131	8± 10	111± 45
100 ppm	39	272± 86	116± 251	40± 42	148± 90	351± 175	8± 5	108± 31
200 ppm	40	275± 96	78± 26	35± 12	155± 149	321± 81	7± 4	113± 52
400 ppm	42	274± 84	73± 27	34± 9	157± 150	332± 58	9± 4**	108± 40

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

(HCL074)

BAIS 4

STUDY NO. : 0675
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	40	21.1± 7.3	0.6± 0.1	142± 1	3.8± 0.4	106± 2	10.5± 0.6	4.3± 1.0
100 ppm	39	20.6± 5.8	0.6± 0.2	143± 2	3.8± 0.3	106± 2	10.4± 0.5	4.4± 0.9
200 ppm	40	20.6± 6.0	0.6± 0.1	142± 1	3.7± 0.5	106± 2	10.5± 0.4	4.3± 0.8
400 ppm	42	20.1± 3.9	0.6± 0.1	142± 1	3.9± 0.3	106± 2	10.4± 0.4	4.5± 0.6

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

(HCL074)

TABLE G2

BIOCHEMISTRY : FEMALE

STUDY NO. : 0675
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	38	7.2± 0.5	3.6± 0.3	1.0± 0.1	0.15± 0.20	142± 21	156± 41	123± 101
100 ppm	36	7.3± 0.4	3.5± 0.3	1.0± 0.1	0.15± 0.08	140± 15	165± 49	142± 115
200 ppm	42	7.2± 0.4	3.5± 0.3	0.9± 0.1	0.13± 0.02	142± 14	161± 49	107± 88
400 ppm	36	7.2± 0.4	3.6± 0.3	1.0± 0.1	0.13± 0.01	144± 15	155± 39	63± 58**

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

(HCL074)

BAIS4

STUDY NO. : 0675
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	38	290± 74	118± 59	51± 35	155± 71	189± 65	2± 1	96± 22
100 ppm	36	299± 87	192± 256	64± 45	167± 119	238± 169	3± 3	102± 68
200 ppm	42	286± 83	134± 90	59± 28	147± 49	221± 84	3± 2	91± 21
400 ppm	36	275± 68	108± 42	52± 23	138± 50	185± 55	3± 1	91± 25

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

(HCL074)

BAIS 4

STUDY NO. : 0675
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	38	17.3± 2.4	0.6± 0.1	141± 2	3.3± 0.3	103± 3	10.6± 0.5	4.0± 0.8
100 ppm	36	17.4± 1.8	0.6± 0.1	141± 1	3.4± 0.4	104± 2	10.7± 0.4	4.0± 0.7
200 ppm	42	17.4± 1.9	0.6± 0.1	140± 1	3.4± 0.4	104± 2	10.6± 0.4	3.9± 0.7
400 ppm	36	19.2± 1.8**	0.6± 0.1	140± 1	3.5± 0.4	104± 2	10.5± 0.4	4.1± 0.7

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

(HCL074)

BAIS 4

TABLE H1

URINALYSIS : MALE

STUDY NO. : 0675
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	43	0	1	3	3	15	21	0		0	0	0	3	24	16		43	0	0	0	0	0		42	1	0	0	0	0		42	1	0	0	
100 ppm	43	0	1	4	7	17	14	0		0	0	0	1	27	15		43	0	0	0	0	0		41	2	0	0	0	0		40	2	0	1	
200 ppm	42	0	0	1	7	22	12	0		0	0	1	3	25	13		42	0	0	0	0	0		40	2	0	0	0	0		42	0	0	0	
400 ppm	42	0	0	1	5	14	22	0		0	0	0	4	20	18		42	0	0	0	0	0		39	3	0	0	0	0		42	0	0	0	

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

(HCL101)

BAIS 4

STUDY NO. : 0675
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	43	43	0	0	0	0		43	0	0	0	0	
100 ppm	43	39	1	0	3	0		43	0	0	0	0	
200 ppm	42	42	0	0	0	0		42	0	0	0	0	
400 ppm	42	38	1	1	1	1		42	0	0	0	0	

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

(HCL101)

BAIS 4

TABLE H2

URINALYSIS : FEMALE

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE 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	41	0	3	2	4	11	13	8		0	1	6	11	20	3		41	0	0	0	0	0		36	5	0	0	0	0		41	0	0	0	
100 ppm	39	0	0	2	6	17	8	6		0	0	1	9	26	3		39	0	0	0	0	0		32	7	0	0	0	0		39	0	0	0	
200 ppm	44	0	0	1	12	14	8	9		0	1	4	12	21	6		44	0	0	0	0	0		42	1	1	0	0	0		44	0	0	0	
400 ppm	41	0	0	3	7	11	11	9		0	1	6	11	17	6		41	0	0	0	0	0		32	6	3	0	0	0		41	0	0	0	

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

(HCL101)

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	Occult blood −	±	+	2+	3+	CHI	Urobilinogen ±	+	2+	3+	4+	CHI
Control	41	41	0	0	0	0		41	0	0	0	0	
100 ppm	39	36	0	0	1	2		39	0	0	0	0	
200 ppm	44	42	0	0	0	2		44	0	0	0	0	
400 ppm	41	39	0	1	1	0		41	0	0	0	0	

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

(HCL101)

TABLE J1

ORGAN WEIGHT, ABSOLUTE : MALE

STUDY NO. : 0675
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	41	391± 52	0.115± 0.243	3.608± 1.279	1.228± 0.116	1.378± 0.120	2.765± 0.348
100 ppm	39	390± 54	0.091± 0.115	3.517± 1.402	1.245± 0.112	1.416± 0.244	2.860± 0.401
200 ppm	40	381± 51	0.073± 0.014	3.101± 1.306	1.209± 0.104	1.363± 0.115	2.799± 0.350
400 ppm	42	352± 19**	0.079± 0.059*	3.673± 1.362	1.184± 0.080	1.339± 0.179**	2.730± 0.243

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

(HCL040)

STUDY NO. : 0675
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	41	1.052± 0.463	11.071± 2.073	2.093± 0.060
100 ppm	39	1.328± 1.926	11.407± 1.609	2.108± 0.063
200 ppm	40	1.028± 0.371	11.114± 1.844	2.091± 0.046
400 ppm	42	1.138± 0.843	10.576± 1.088	2.061± 0.045*

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

(HCL040)

TABLE J2

ORGAN WEIGHT, ABSOLUTE : FEMALE

STUDY NO. : 0675
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	38	263± 33	0.089± 0.076	0.142± 0.141	0.889± 0.077	0.970± 0.131	1.875± 0.165
100 ppm	36	269± 23	0.072± 0.009	0.123± 0.032	0.894± 0.074	0.965± 0.111	1.876± 0.169
200 ppm	42	262± 21	0.071± 0.010**	0.178± 0.443	0.869± 0.052	0.939± 0.057	1.851± 0.196
400 ppm	36	234± 18**	0.073± 0.017**	0.136± 0.151	0.843± 0.066*	0.926± 0.060	1.773± 0.132*

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

(HCL040)

STUDY NO. : 0675
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	38	0.771±	1.049	6.844±	1.014	1.908±	0.037
100 ppm	36	0.749±	0.673	7.089±	1.214	1.889±	0.048
200 ppm	42	0.567±	0.153	6.896±	0.911	1.889±	0.041
400 ppm	36	0.523±	0.089	6.162±	0.545**	1.863±	0.037**

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

(HCL040)

BAIS 4

TABLE K1

ORGAN WEIGHT, RELATIVE : MALE

STUDY NO. : 0675
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	41	391± 52	0.030± 0.064	0.917± 0.304	0.319± 0.046	0.358± 0.053	0.723± 0.166
100 ppm	39	390± 54	0.024± 0.032	0.907± 0.351	0.325± 0.050	0.372± 0.099	0.748± 0.157
200 ppm	40	381± 51	0.019± 0.004	0.819± 0.341	0.321± 0.039	0.364± 0.060	0.745± 0.119
400 ppm	42	352± 19**	0.023± 0.017	1.043± 0.382	0.338± 0.026**	0.383± 0.065*	0.778± 0.073**

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

(HCL042)

BAIS 4

STUDY NO. : 0675
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	41	0.272± 0.126	2.856± 0.548	0.545± 0.080
100 ppm	39	0.362± 0.603	2.966± 0.555	0.549± 0.063
200 ppm	40	0.274± 0.104	2.929± 0.404	0.558± 0.072
400 ppm	42	0.331± 0.290	3.014± 0.323*	0.588± 0.033**

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

(HCL042)

BAIS 4

TABLE K2

ORGAN WEIGHT, RELATIVE : FEMALE

STUDY NO. : 0675
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	38	263± 33	0.035± 0.032	0.055± 0.058	0.343± 0.053	0.377± 0.083	0.726± 0.118
100 ppm	36	269± 23	0.027± 0.003	0.046± 0.012	0.333± 0.027	0.360± 0.047	0.700± 0.070
200 ppm	42	262± 21	0.027± 0.004	0.068± 0.167	0.333± 0.025	0.360± 0.035	0.709± 0.088
400 ppm	36	234± 18**	0.031± 0.008	0.058± 0.063**	0.362± 0.029**	0.398± 0.035**	0.762± 0.066**

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

(HCL042)

BAIS 4

STUDY NO. : 0675
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	38	0.311± 0.479	2.628± 0.414	0.739± 0.104
100 ppm	36	0.280± 0.256	2.639± 0.431	0.706± 0.058
200 ppm	42	0.217± 0.061	2.633± 0.314	0.725± 0.060
400 ppm	36	0.225± 0.038	2.645± 0.215	0.803± 0.067**

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

(HCL042)

TABLE L1

HISTOPATHOLOGICAL FINDINGS :

NON-NEOPLASTIC LESIONS : MALE

ALL ANIMALS

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50				100 ppm 50				200 ppm 50				400 ppm 50			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Integumentary system/appandage]																		
skin/app																		
	epidermal cyst		<50>				<50>				<50>				<50>			
			0 (0)	0 (0)	0 (0)	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)
[Respiratory system]																		
nasal cavit																		
	thrombus		<50>				<50>				<50>				<50>			
			2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	mineralization		38 (76)	0 (0)	0 (0)	0 (0)	43 (86)	0 (0)	0 (0)	0 (0)	41 (82)	0 (0)	0 (0)	0 (0)	39 (78)	1 (2)	0 (0)	0 (0)
	eosinophilic change:olfactory epithelium		36 (72)	11 (22)	0 (0)	0 (0)	44 (88)	3 (6)	0 (0)	0 (0)	41 (82)	2 (4)	0 (0)	0 * (0)	41 (82)	1 (2)	0 (0)	0 ** (0)
	eosinophilic change:respiratory epithelium		12 (24)	0 (0)	0 (0)	0 (0)	16 (32)	0 (0)	0 (0)	0 (0)	11 (22)	0 (0)	0 (0)	0 (0)	10 (20)	0 (0)	0 (0)	0 (0)
	inflammation:foreign body		10 (20)	0 (0)	0 (0)	0 (0)	18 (36)	2 (4)	0 (0)	0 (0)	14 (28)	1 (2)	0 (0)	0 (0)	10 (20)	2 (4)	0 (0)	0 (0)
	inflammation:respiratory epithelium		3 (6)	1 (2)	0 (0)	0 (0)	7 (14)	2 (4)	0 (0)	0 (0)	14 (28)	2 (4)	0 (0)	0 ** (0)	22 (44)	2 (4)	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				100 ppm 50				200 ppm 50				400 ppm 50			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Respiratory system}																		
nasal cavit			<50>				<50>				<50>				<50>			
	respiratory metaplasia:olfactory epithelium		15 (30)	0 (0)	0 (0)	0 (0)	13 (26)	0 (0)	0 (0)	0 (0)	16 (32)	0 (0)	0 (0)	0 (0)	17 (34)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:gland		50 (100)	0 (0)	0 (0)	0 (0)	48 (96)	0 (0)	0 (0)	0 (0)	50 (100)	0 (0)	0 (0)	0 (0)	49 (98)	0 (0)	0 (0)	0 (0)
	squamous cell metaplasia:respiratory epithelium		2 (4)	0 (0)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	20 (40)	0 (0)	0 (0)	0 ** (0)	37 (74)	1 (2)	0 (0)	0 ** (0)
	hyperplasia:transitional epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	7 (14)	0 (0)	0 (0)	0 * (0)
	atrophy:olfactory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	21 (42)	0 (0)	0 (0)	0 ** (0)
nasopharynx			<50>				<50>				<50>				<50>			
	inflammation		0 (0)	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)	0 (0)
larynx			<50>				<50>				<50>				<50>			
	inflammation		1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (6)	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				100 ppm 50				200 ppm 50				400 ppm 50			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Respiratory system}																		
larynx			<50>				<50>				<50>				<50>			
	inflammation:foreign body		0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)
lung			<50>				<50>				<50>				<50>			
	hemorrhage		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	edema		2 (4)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
	inflammatory infiltration		6 (12)	2 (4)	0 (0)	0 (0)	3 (6)	2 (4)	0 (0)	0 (0)	4 (8)	1 (2)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)
	fibrosis:focal		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)	0 (0)
	accumulation of foamy cells		4 (8)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
	bronchiolar-alveolar cell hyperplasia		1 (2)	0 (0)	1 (2)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	2 (4)	1 (2)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)
	inflammation:foreign body		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (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				100 ppm 50				200 ppm 50				400 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>			
	congestion		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	deposit of hemosiderin		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)	0 (0)
	granulation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	increased hematopoiesis		6 (12)	0 (0)	0 (0)	0 (0)	6 (12)	0 (0)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)	8 (16)	0 (0)	0 (0)	0 (0)
	decreased hematopoiesis		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)	0 (0)	0 (0)	0 (0)
spleen			<50>				<50>				<50>				<50>			
	congestion		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	fatty change		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)	0 (0)
	deposit of hemosiderin		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)	1 (2)	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 (%)	2 (%)	3 (%)	4 (%)	100 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)	200 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)	400 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)
{Hematopoietic system}																		
spleen																		
	fibrosis:focal		<50>				<50>				<50>				<50>			
			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)
	extramedullary hematopoiesis		9	2	1	0	3	2	2	0	3	3	2	0	9	3	3	0
			(18)	(4)	(2)	(0)	(6)	(4)	(4)	(0)	(6)	(6)	(4)	(0)	(18)	(6)	(6)	(0)
	lymph-follicular 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)
{Circulatory system}																		
heart																		
	thrombus		<50>				<50>				<50>				<50>			
			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)
	myocardial fibrosis		14	2	0	0	10	1	0	0	8	0	0	0	13	0	0	0
			(28)	(4)	(0)	(0)	(20)	(2)	(0)	(0)	(16)	(0)	(0)	(0)	(26)	(0)	(0)	(0)
{Digestive system}																		
stomach																		
	ulcer:forestomach		<50>				<50>				<50>				<50>			
			2	2	1	0	1	1	3	0	0	0	1	0	1	0	0	0
			(4)	(4)	(2)	(0)	(2)	(2)	(6)	(0)	(0)	(0)	(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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50				100 ppm 50				200 ppm 50				400 ppm 50			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Digestive system}																		
stomach			<50>				<50>				<50>				<50>			
	hyperplasia:forestomach		1 (2)	2 (4)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	1 (2)	2 (4)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)
	erosion:glandular stomach		3 (6)	1 (2)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)
	ulcer:glandular stomach		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)	0 (0)
	hyperplasia:glandular stomach		0 (0)	0 (0)	0 (0)	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)
	mineralization:glandular stomach		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)	0 (0)
liver			<50>				<50>				<50>				<50>			
	herniation		4 (8)	0 (0)	0 (0)	0 (0)	7 (14)	0 (0)	0 (0)	0 (0)	6 (12)	0 (0)	0 (0)	0 (0)	12 (24)	0 (0)	0 (0)	0 (0)
	necrosis:central		0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)
	fatty change:peripheral		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)

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				100 ppm 50				200 ppm 50				400 ppm 50			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Digestive system}																		
liver			<50>				<50>				<50>				<50>			
	granulation		37 (74)	1 (2)	0 (0)	0 (0)	41 (82)	0 (0)	0 (0)	0 (0)	42 (84)	0 (0)	0 (0)	0 (0)	33 (66)	0 (0)	0 (0)	0 (0)
	increased extramedullary hematopoiesis		1 (2)	0 (0)	0 (0)	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)
	clear cell focus		4 (8)	1 (2)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	3 (6)	1 (2)	1 (2)	0 (0)	3 (6)	1 (2)	0 (0)	0 (0)
	acidophilic cell focus		11 (22)	3 (6)	0 (0)	0 (0)	12 (24)	4 (8)	0 (0)	0 (0)	7 (14)	5 (10)	0 (0)	0 (0)	6 (12)	4 (8)	1 (2)	0 (0)
	basophilic cell focus		5 (10)	1 (2)	0 (0)	0 (0)	2 (4)	1 (2)	0 (0)	0 (0)	3 (6)	1 (2)	0 (0)	0 (0)	6 (12)	2 (4)	0 (0)	0 (0)
	spongiosis hepatis		5 (10)	0 (0)	0 (0)	0 (0)	7 (14)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)
	bile duct hyperplasia		6 (12)	44 (88)	0 (0)	0 (0)	4 (8)	45 (90)	0 (0)	0 (0)	9 (18)	40 (80)	0 (0)	0 (0)	10 (20)	38 (76)	0 (0)	0 (0)
pancreas			<50>				<50>				<50>				<50>			
	atrophy		10 (20)	2 (4)	0 (0)	0 (0)	7 (14)	1 (2)	0 (0)	0 (0)	7 (14)	1 (2)	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 / No. of Animals on Study / Grade	Control 50				100 ppm 50				200 ppm 50				400 ppm 50			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Digestive system}																		
pancreas	islet cell hyperplasia		<50>				<50>				<50>				<50>			
			4 (8)	2 (4)	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)	0 * (0)
{Urinary system}																		
kidney	necrosis:focal		<50>				<50>				<50>				<50>			
			0 (0)	0 (0)	0 (0)	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)
	hyaline droplet		3 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	1 (2)	0 (0)	1 (2)	0 (0)
	chronic nephropathy		22 (44)	21 (42)	5 (10)	0 (0)	17 (34)	22 (44)	7 (14)	2 (4)	19 (38)	25 (50)	5 (10)	0 (0)	21 (42)	22 (44)	5 (10)	1 (2)
	mineralization:cortex		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)	0 (0)
	urothelial hyperplasia:pelvis		1 (2)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
urin bladd	dilatation		<50>				<50>				<50>				<50>			
			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)	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				100 ppm 50				200 ppm 50				400 ppm 50			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Urinary system}																		
urin bladd																		
	papillomatosis	<50>	0 (0)	0 (0)	1 (2)	0 (0)	<50> 0 (0)	0 (0)	0 (0)	0 (0)	<50> 0 (0)	0 (0)	1 (2)	0 (0)	<50> 0 (0)	0 (0)	0 (0)	0 (0)
{Endocrine system}																		
pituitary																		
	angiectasis	<50>	0 (0)	0 (0)	0 (0)	0 (0)	<50> 1 (2)	0 (0)	0 (0)	0 (0)	<50> 0 (0)	0 (0)	0 (0)	0 (0)	<50> 0 (0)	0 (0)	0 (0)	0 (0)
	cyst		1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hyperplasia		18 (36)	5 (10)	0 (0)	0 (0)	9 (18)	9 (18)	2 (4)	0 (0)	8 (16)	5 (10)	3 (6)	0 (0)	19 (38)	2 (4)	1 (2)	0 (0)
	Rathke pouch		2 (4)	0 (0)	0 (0)	0 (0)	6 (12)	0 (0)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)
thyroid																		
	follicular hyperplasia	<50>	1 (2)	0 (0)	0 (0)	0 (0)	<50> 2 (4)	0 (0)	0 (0)	0 (0)	<50> 0 (0)	0 (0)	0 (0)	0 (0)	<50> 0 (0)	1 (2)	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				100 ppm 50				200 ppm 50				400 ppm 50			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Endocrine system}																		
thyroid			<50>				<50>				<50>				<50>			
	C-cell hyperplasia		8 (16)	1 (2)	2 (4)	0 (0)	12 (24)	3 (6)	1 (2)	0 (0)	12 (24)	0 (0)	1 (2)	0 (0)	6 (12)	3 (6)	1 (2)	0 (0)
	cystic thyroid follicle		0 (0)	0 (0)	0 (0)	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)
parathyroid			<50>				<50>				<50>				<50>			
	hyperplasia		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)
adrenal			<50>				<50>				<50>				<50>			
	thrombus		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	cyst		0 (0)	0 (0)	0 (0)	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)
	hyperplasia:cortical cell		0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hyperplasia:medulla		3 (6)	3 (6)	0 (0)	0 (0)	2 (4)	3 (6)	0 (0)	0 (0)	0 (0)	4 (8)	1 (2)	0 (0)	0 (0)	2 (4)	2 (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				100 ppm 50				200 ppm 50				400 ppm 50			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Endocrine system}																		
adrenal																		
	focal fatty change:cortex		3	0	0	0	1	0	0	0	3	0	0	0	0	0	0	0
			(6)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
		<50>					<50>				<50>				<50>			
{Reproductive system}																		
testis																		
	mineralization		1	0	0	0	0	0	0	0	1	0	0	0	3	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
	interstitial cell hyperplasia		3	0	0	0	0	1	0	0	6	0	0	0	2	0	0	0
			(6)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(12)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
		<50>					<50>				<50>				<50>			
semin ves																		
	inflammation		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)
	hyperplasia		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)
		<50>					<50>				<50>				<50>			
prostate																		
	inflammation		9	3	0	0	10	1	0	0	7	0	0	0	5	1	1	0
			(18)	(6)	(0)	(0)	(20)	(2)	(0)	(0)	(14)	(0)	(0)	(0)	(10)	(2)	(2)	(0)
		<50>					<50>				<50>				<50>			

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 / No. of Animals on Study / Grade	Control 50 1	2	3	4	100 ppm 50 1	2	3	4	200 ppm 50 1	2	3	4	400 ppm 50 1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Reproductive system}																		
prostate			<50>				<50>				<50>				<50>			
	hyperplasia		10	0	0	0	9	0	0	0	11	3	0	0	5	0	0	0
			(20)	(0)	(0)	(0)	(18)	(0)	(0)	(0)	(22)	(6)	(0)	(0)	(10)	(0)	(0)	(0)
{Nervous system}																		
spinal cord			<50>				<50>				<50>				<50>			
	gliosis		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)
{Special sense organs/appendage}																		
eye			<50>				<50>				<50>				<50>			
	cataract		1	2	0	0	1	0	0	0	2	0	0	0	0	0	0	0
			(2)	(4)	(0)	(0)	(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	retinal atrophy		1	0	3	0	1	0	0	0	0	0	2	0	0	0	0	0
			(2)	(0)	(6)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)
	keratitis		3	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(6)	(0)	(0)	(0)	(0)	(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 / No. of Animals on Study / Grade	Control 50				100 ppm 50				200 ppm 50				400 ppm 50			
			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>			
	iritis		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)
	ulcer:cornea		1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)
Harder gl			<50>				<50>				<50>				<50>			
	inflammation		3	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(6)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	epidermal cyst		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)
{Musculoskeletal system}																		
bone			<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)
	osteosclerosis		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)

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 L4

HISTOPATHOLOGICAL FINDINGS :

NON-NEOPLASTIC LESIONS : FEMALE

ALL ANIMALS

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50				100 ppm 50				200 ppm 50				400 ppm 50			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Integumentary system/appandage}																		
skin/app	inflammation	<a>	<50>				<50>				<50>				<50>			
		b	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(c)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
subcutis	abscess	<a>	<50>				<50>				<50>				<50>			
		b	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
		(c)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Respiratory system}																		
nasal cavit	adhesion	<a>	<50>				<50>				<50>				<50>			
		b	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
		(c)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	thrombus	b	2	0	0	0	3	0	0	0	0	0	0	0	1	0	0	0
		(c)	(4)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	mineralization	b	29	0	0	0	28	0	0	0	34	0	0	0	37	0	0	0
		(c)	(58)	(0)	(0)	(0)	(56)	(0)	(0)	(0)	(68)	(0)	(0)	(0)	(74)	(0)	(0)	(0)
	eosinophilic change:olfactory epithelium	b	13	35	2	0	16	33	1	0	18	30	0	0	37	8	0	0 **
		(c)	(26)	(70)	(4)	(0)	(32)	(66)	(2)	(0)	(36)	(60)	(0)	(0)	(74)	(16)	(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				100 ppm 50				200 ppm 50				400 ppm 50			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Respiratory system}																		
nasal cavit			<50>				<50>				<50>				<50>			
	eosinophilic change:respiratory epithelium		40	3	0	0	41	0	0	0	28	0	0	0 **	17	0	0	0 **
			(80)	(6)	(0)	(0)	(82)	(0)	(0)	(0)	(56)	(0)	(0)	(0)	(34)	(0)	(0)	(0)
	inflammation:foreign body		2	0	0	0	0	0	0	0	3	1	0	0	3	0	0	0
			(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(2)	(0)	(0)	(6)	(0)	(0)	(0)
	inflammation:respiratory epithelium		5	0	0	0	9	0	0	0	14	1	0	0 *	27	0	0	0 **
			(10)	(0)	(0)	(0)	(18)	(0)	(0)	(0)	(28)	(2)	(0)	(0)	(54)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		1	0	0	0	5	0	0	0	2	1	0	0	2	1	0	0
			(2)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(4)	(2)	(0)	(0)	(4)	(2)	(0)	(0)
	respiratory metaplasia:gland		48	0	0	0	50	0	0	0	49	0	0	0	45	1	0	0
			(96)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(98)	(0)	(0)	(0)	(90)	(2)	(0)	(0)
	desquamation:olfactory epithelium		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)
	squamous cell metaplasia:respiratory epithelium		5	0	0	0	6	0	0	0	17	0	0	0 **	39	4	0	0 **
			(10)	(0)	(0)	(0)	(12)	(0)	(0)	(0)	(34)	(0)	(0)	(0)	(78)	(8)	(0)	(0)
	hyperplasia:transitional epithelium		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)	(4)	(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				100 ppm 50				200 ppm 50				400 ppm 50			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Respiratory system}																		
nasal cavit			<50>				<50>				<50>				<50>			
	atrophy:olfactory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	20 (40)	0 (0)	0 (0)	0 (0) **
larynx			<50>				<50>				<50>				<50>			
	inflammation		9 (18)	0 (0)	0 (0)	0 (0)	14 (28)	0 (0)	0 (0)	0 (0)	11 (22)	0 (0)	0 (0)	0 (0)	7 (14)	0 (0)	0 (0)	0 (0)
	inflammation:foreign body		2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
lung			<50>				<50>				<50>				<50>			
	hemorrhage		0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	edema		4 (8)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	inflammatory infiltration		4 (8)	0 (0)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	accumulation of foamy cells		2 (4)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	1 (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				100 ppm 50				200 ppm 50				400 ppm 50			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Respiratory system}																		
lung			<50>				<50>				<50>				<50>			
	bronchiolar-alveolar cell hyperplasia		2 (4)	1 (2)	0 (0)	0 (0)	2 (4)	1 (2)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)
{Hematopoietic system}																		
bone marrow			<50>				<50>				<50>				<50>			
	deposit of hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	granulation		0 (0)	1 (2)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	increased hematopoiesis		9 (18)	0 (0)	0 (0)	0 (0)	6 (12)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)
	myelofibrosis		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)	0 (0)	0 (0)	0 (0)
spleen			<50>				<50>				<50>				<50>			
	congestion		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)	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				100 ppm 50				200 ppm 50				400 ppm 50			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Hematopoietic system}																		
spleen			<50>				<50>				<50>				<50>			
	deposit of hemosiderin		11 (22)	0 (0)	0 (0)	0 (0)	7 (14)	0 (0)	0 (0)	0 (0)	8 (16)	0 (0)	0 (0)	0 (0)	15 (30)	0 (0)	0 (0)	0 (0)
	inflammation		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)	0 (0)	0 (0)	0 (0)
	fibrosis:focal		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)	0 (0)
	extramedullary hematopoiesis		10 (20)	4 (8)	3 (6)	0 (0)	12 (24)	2 (4)	2 (4)	0 (0)	18 (36)	1 (2)	0 (0)	0 (0)	16 (32)	2 (4)	2 (4)	0 (0)
{Circulatory system}																		
heart			<50>				<50>				<50>				<50>			
	thrombus		1 (2)	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)	0 (0)
	myocardial fibrosis		6 (12)	1 (2)	0 (0)	0 (0)	10 (20)	1 (2)	0 (0)	0 (0)	7 (14)	0 (0)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)
	arteritis		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)	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 (%)	2 (%)	3 (%)	4 (%)	100 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)	200 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)	400 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)
{Digestive system}																		
stomach																		
	ulcer:forestomach		<50>				<50>				<50>				<50>			
			2 (4)	0 (0)	1 (2)	0 (0)	1 (2)	1 (2)	3 (6)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	4 (8)	1 (2)	0 (0)	0 (0)
	hyperplasia:forestomach		1 (2)	0 (0)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	1 (2)	0 (0)	3 (6)	1 (2)	1 (2)	0 (0)
	erosion:glandular stomach		1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	ulcer:glandular stomach		1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)
	mineralization:glandular stomach		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
large intes																		
	dilatation		<50>				<50>				<50>				<50>			
			0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)
	squamous cell metaplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
liver																		
	herniation		<50>				<50>				<50>				<50>			
			7 (14)	0 (0)	0 (0)	0 (0)	7 (14)	0 (0)	0 (0)	0 (0)	10 (20)	0 (0)	0 (0)	0 (0)	14 (28)	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 (%)	100 ppm 50 1 (%)	100 ppm 50 2 (%)	100 ppm 50 3 (%)	100 ppm 50 4 (%)	200 ppm 50 1 (%)	200 ppm 50 2 (%)	200 ppm 50 3 (%)	200 ppm 50 4 (%)	400 ppm 50 1 (%)	400 ppm 50 2 (%)	400 ppm 50 3 (%)	400 ppm 50 4 (%)
{Digestive system}																		
liver			<50>				<50>				<50>				<50>			
	peliosis-like lesion		0 (0)	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)	0 (0)
	necrosis:central		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	necrosis:focal		2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	fatty change:central		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)
	fatty change:peripheral		0 (0)	0 (0)	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)
	mineralization		0 (0)	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)	0 (0)
	degeneration:central		0 (0)	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)
	inflammatory infiltration		0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	1 (2)	0 (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
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				100 ppm 50				200 ppm 50				400 ppm 50			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Digestive system}																		
liver			<50>				<50>				<50>				<50>			
	lymphocytic infiltration		0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	granulation		16 (32)	1 (2)	0 (0)	0 (0)	15 (30)	1 (2)	0 (0)	0 (0)	19 (38)	6 (12)	1 (2)	0 (0)	18 (36)	3 (6)	0 (0)	0 (0)
	scar		0 (0)	0 (0)	0 (0)	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)
	increased extramedullary hematopoiesis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	clear cell focus		0 (0)	0 (0)	0 (0)	0 (0)	3 (6)	1 (2)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	3 (6)	1 (2)	0 (0)	0 (0)
	acidophilic cell focus		2 (4)	0 (0)	0 (0)	0 (0)	2 (4)	2 (4)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	2 (4)	0 (0)	0 (0)
	basophilic cell focus		15 (30)	1 (2)	0 (0)	0 (0)	9 (18)	2 (4)	0 (0)	0 (0)	17 (34)	0 (0)	1 (2)	0 (0)	20 (40)	1 (2)	0 (0)	0 (0)
	bile duct hyperplasia		6 (12)	0 (0)	0 (0)	0 (0)	15 (30)	0 (0)	0 (0)	0 * (0)	6 (12)	0 (0)	1 (2)	0 (0)	5 (10)	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				100 ppm 50				200 ppm 50				400 ppm 50			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Digestive system}																		
pancreas			<50>				<50>				<50>				<50>			
	atrophy		2 (4)	0 (0)	0 (0)	0 (0)	2 (4)	1 (2)	0 (0)	0 (0)	6 (12)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)
	islet cell hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	1 (2)	0 (0)	0 (0)
{Urinary system}																		
kidney			<50>				<50>				<50>				<50>			
	necrosis:focal		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)	0 (0)	0 (0)	0 (0)
	hyaline droplet		0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	1 (2)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	chronic nephropathy		19 (38)	11 (22)	0 (0)	0 (0)	18 (36)	7 (14)	3 (6)	0 (0)	23 (46)	9 (18)	0 (0)	0 (0)	15 (30)	9 (18)	0 (0)	1 (2)
	mineralization:cortex		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)	0 (0)
	urothelial hyperplasia:pelvis		1 (2)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	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 / No. of Animals on Study / Grade	Control 50				100 ppm 50				200 ppm 50				400 ppm 50			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Urinary system}																		
kidney			<50>				<50>				<50>				<50>			
	atypical tubule hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
urin bladd			<50>				<50>				<50>				<50>			
	dilatation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
{Endocrine system}																		
pituitary			<50>				<50>				<50>				<50>			
	angiectasis		1 (2)	0 (0)	0 (0)	0 (0)	7 (14)	0 (0)	0 (0)	0 (0)	2 (4)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)
	hemorrhage		0 (0)	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)	0 (0)
	cyst		14 (28)	0 (0)	0 (0)	0 (0)	15 (30)	0 (0)	0 (0)	0 (0)	10 (20)	0 (0)	0 (0)	0 (0)	13 (26)	1 (2)	0 (0)	0 (0)
	hyperplasia		7 (14)	2 (4)	4 (8)	0 (0)	8 (16)	2 (4)	4 (8)	0 (0)	5 (10)	4 (8)	5 (10)	0 (0)	4 (8)	3 (6)	1 (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				100 ppm 50				200 ppm 50				400 ppm 50			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Endocrine system}																		
pituitary			<50>				<50>				<50>				<50>			
	Rathke pouch		1 (2)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
thyroid			<50>				<50>				<50>				<50>			
	inflammatory infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	ultimobranchial body remanet		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	follicular hyperplasia		1 (2)	0 (0)	0 (0)	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)
	C-cell hyperplasia		3 (6)	2 (4)	1 (2)	0 (0)	3 (6)	2 (4)	0 (0)	0 (0)	7 (14)	0 (0)	0 (0)	0 (0)	7 (14)	0 (0)	0 (0)	0 (0)
adrenal			<50>				<50>				<50>				<50>			
	peliosis-like lesion		2 (4)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	increased extramedullary hematopoiesis		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)	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				100 ppm 50				200 ppm 50				400 ppm 50			
			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 (0)	1 (2)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)
	hyperplasia:medulla		0 (0)	0 (0)	1 (2)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
	focal fatty change:cortex		4 (8)	2 (4)	0 (0)	0 (0)	7 (14)	0 (0)	1 (2)	0 (0)	5 (10)	2 (4)	0 (0)	0 (0)	6 (12)	1 (2)	0 (0)	0 (0)
	necrosis:cortex		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)	0 (0)	0 (0)	0 (0)
{Reproductive system}																		
ovary			<50>				<50>				<50>				<50>			
	cyst		1 (2)	0 (0)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	mesothelial hyperplasia		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)	0 (0)
uterus			<50>				<50>				<50>				<50>			
	cystic endometrial hyperplasia		6 (12)	0 (0)	0 (0)	0 (0)	9 (18)	0 (0)	0 (0)	0 (0)	5 (10)	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 / No. of Animals on Study / Grade	Control 50				100 ppm 50				200 ppm 50				400 ppm 50			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Reproductive system}																		
vagina			<50>				<50>				<50>				<50>			
	cyst		0 (0)	0 (0)	0 (0)	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)
mammary gl			<50>				<50>				<50>				<50>			
	hyperplasia		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)
	galactocele		0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
{Nervous system}																		
brain			<50>				<50>				<50>				<50>			
	vacuolic change		0 (0)	0 (0)	0 (0)	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)
{Special sense organs/appendage}																		
eye			<50>				<50>				<50>				<50>			
	cataract		1 (2)	1 (2)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	1 (2)	2 (4)	0 (0)	0 (0)	2 (4)	1 (2)	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				100 ppm 50				200 ppm 50				400 ppm 50			
			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>			
	retinal atrophy		0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	1 (2)	2 (4)	1 (2)	0 (0)	0 (0)	1 (2)	2 (4)	0 (0)
	keratitis		3 (6)	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)
	ulcer:cornea		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)
Harder gl			<50>				<50>				<50>				<50>			
	degeneration		0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
	inflammation		1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
{Musculoskeletal system}																		
muscle			<50>				<50>				<50>				<50>			
	mineralization		0 (0)	0 (0)	0 (0)	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)

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				100 ppm				200 ppm				400 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		2	2	0	0	3	1	1	0	4	1	1	0	1	2	0	0
			(4)	(4)	(0)	(0)	(6)	(2)	(2)	(0)	(8)	(2)	(2)	(0)	(2)	(4)	(0)	(0)
{Body cavities}																		
peritoneum			<50>				<50>				<50>				<50>			
	inflammatory infiltration		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)
	peritonitis		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 O1

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS : MALE

Group Name	Control	100 ppm	200 ppm	400 ppm
	SITE : skin/appendage			
	TUMOR : keratoacanthoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	2/50(4.0)	2/50(4.0)	1/50(2.0)
Adjusted rates(b)	9.76	5.00	4.26	2.38
Terminal rates(c)	4/41(9.8)	2/40(5.0)	1/40(2.5)	1/42(2.4)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.9034			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.1848			
Fisher Exact test(e)		P = 0.3389	P = 0.3389	P = 0.1811
	SITE : subcutis			
	TUMOR : fibroma			
Tumor rate				
Overall rates(a)	8/50(16.0)	6/50(12.0)	3/50(6.0)	5/50(10.0)
Adjusted rates(b)	17.07	11.63	6.67	10.87
Terminal rates(c)	7/41(17.1)	4/40(10.0)	2/40(5.0)	4/42(9.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8798			
Prevalence method(d)	P = 0.7255			
Combined analysis(d)	P = 0.8299			
Cochran-Armitage test(e)	P = 0.3206			
Fisher Exact test(e)		P = 0.3871	P = 0.0999	P = 0.2768
	SITE : lung			
	TUMOR : bronchiolar-alveolar adenoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	4/50(8.0)	3/50(6.0)	0/50(0.0)
Adjusted rates(b)	7.32	10.00	7.50	0.0
Terminal rates(c)	3/41(7.3)	4/40(10.0)	3/40(7.5)	0/42(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.9567			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0999			
Fisher Exact test(e)		P = 0.5000	P = 0.6611	P = 0.1212

Group Name	Control	100 ppm	200 ppm	400 ppm
	SITE : lung			
	TUMOR : bronchiolar-alveolar adenoma, bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	5/50(10.0)	4/50(8.0)	3/50(6.0)	0/50(0.0)
Adjusted rates(b)	12.20	10.00	7.50	0.0
Terminal rates(c)	5/41(12.2)	4/40(10.0)	3/40(7.5)	0/42(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.9908			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0268*			
Fisher Exact test(e)		P = 0.5000	P = 0.3575	P = 0.0281*
	SITE : spleen			
	TUMOR : mononuclear cell leukemia			
Tumor rate				
Overall rates(a)	4/50(8.0)	3/50(6.0)	2/50(4.0)	1/50(2.0)
Adjusted rates(b)	2.44	2.50	2.50	2.38
Terminal rates(c)	1/41(2.4)	1/40(2.5)	1/40(2.5)	1/42(2.4)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.9694			
Prevalence method(d)	P = 0.4932			
Combined analysis(d)	P = 0.9198			
Cochran-Armitage test(e)	P = 0.1539			
Fisher Exact test(e)		P = 0.5000	P = 0.3389	P = 0.1811
	SITE : liver			
	TUMOR : hepatocellular adenoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	4/50(8.0)	0/50(0.0)	1/50(2.0)
Adjusted rates(b)	0.0	10.00	0.0	2.22
Terminal rates(c)	0/41(0.0)	4/40(10.0)	0/40(0.0)	0/42(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.5767			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.8183			
Fisher Exact test(e)		P = 0.0587	P = N.C.	P = 0.5000

Group Name	Control	100 ppm	200 ppm	400 ppm
	SITE : pancreas			
	TUMOR : islet cell adenoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	2/50(4.0)	7/50(14.0)	2/50(4.0)
Adjusted rates(b)	7.32	5.00	16.28	4.76
Terminal rates(c)	3/41(7.3)	2/40(5.0)	6/40(15.0)	2/42(4.8)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.5300			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.9254			
Fisher Exact test(e)		P = 0.5000	P = 0.1589	P = 0.5000
	SITE : pancreas			
	TUMOR : islet cell adenoma, islet cell adenocarcinoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	2/50(4.0)	7/50(14.0)	2/50(4.0)
Adjusted rates(b)	9.76	5.00	16.28	4.76
Terminal rates(c)	4/41(9.8)	2/40(5.0)	6/40(15.0)	2/42(4.8)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.6522			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.6830			
Fisher Exact test(e)		P = 0.3389	P = 0.2623	P = 0.3389
	SITE : pituitary gland			
	TUMOR : adenoma			
Tumor rate				
Overall rates(a)	13/50(26.0)	5/50(10.0)	16/50(32.0)	6/50(12.0)
Adjusted rates(b)	29.27	10.00	35.00	11.11
Terminal rates(c)	12/41(29.3)	4/40(10.0)	14/40(35.0)	4/42(9.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4521			
Prevalence method(d)	P = 0.8900			
Combined analysis(d)	P = 0.8634			
Cochran-Armitage test(e)	P = 0.2821			
Fisher Exact test(e)		P = 0.0332*	P = 0.3299	P = 0.0624

Group Name	Control	100 ppm	200 ppm	400 ppm
	SITE : pituitary gland			
	TUMOR : adenoma, adenocarcinoma			
Tumor rate				
Overall rates(a)	13/50(26.0)	5/50(10.0)	16/50(32.0)	6/50(12.0)
Adjusted rates(b)	29.27	10.00	35.00	11.11
Terminal rates(c)	12/41(29.3)	4/40(10.0)	14/40(35.0)	4/42(9.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4521			
Prevalence method(d)	P = 0.8900			
Combined analysis(d)	P = 0.8634			
Cochran-Armitage test(e)	P = 0.2821			
Fisher Exact test(e)		P = 0.0332*	P = 0.3299	P = 0.0624
	SITE : thyroid			
	TUMOR : C-cell adenoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	8/50(16.0)	9/50(18.0)	3/50(6.0)
Adjusted rates(b)	7.32	17.50	20.00	7.14
Terminal rates(c)	3/41(7.3)	7/40(17.5)	8/40(20.0)	3/42(7.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3948			
Prevalence method(d)	P = 0.6421			
Combined analysis(d)	P = 0.6233			
Cochran-Armitage test(e)	P = 0.7360			
Fisher Exact test(e)		P = 0.0999	P = 0.0606	P = 0.6611
	SITE : thyroid			
	TUMOR : C-cell carcinoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	1/50(2.0)	1/50(2.0)	1/50(2.0)
Adjusted rates(b)	4.76	0.0	2.50	0.0
Terminal rates(c)	1/41(2.4)	0/40(0.0)	1/40(2.5)	0/42(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5139			
Prevalence method(d)	P = 0.8995			
Combined analysis(d)	P = 0.8273			
Cochran-Armitage test(e)	P = 0.3266			
Fisher Exact test(e)		P = 0.3087	P = 0.3087	P = 0.3087

Group Name	Control	100 ppm	200 ppm	400 ppm
	SITE : thyroid			
	TUMOR : C-cell adenoma, C-cell carcinoma			
Tumor rate				
Overall rates(a)	6/50(12.0)	9/50(18.0)	10/50(20.0)	4/50(8.0)
Adjusted rates(b)	11.90	17.50	22.50	7.14
Terminal rates(c)	4/41(9.8)	7/40(17.5)	9/40(22.5)	3/42(7.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4785			
Prevalence method(d)	P = 0.7874			
Combined analysis(d)	P = 0.7662			
Cochran-Armitage test(e)	P = 0.4349			
Fisher Exact test(e)		P = 0.2883	P = 0.2070	P = 0.3703
	SITE : adrenal gland			
	TUMOR : pheochromocytoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	4/50(8.0)	2/50(4.0)	4/50(8.0)
Adjusted rates(b)	4.88	10.00	5.00	9.52
Terminal rates(c)	2/41(4.9)	4/40(10.0)	2/40(5.0)	4/42(9.5)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.2859			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.5459			
Fisher Exact test(e)		P = 0.3389	P = 0.6913	P = 0.3389
	SITE : adrenal gland			
	TUMOR : pheochromocytoma, pheochromocytoma:malignant			
Tumor rate				
Overall rates(a)	4/50(8.0)	5/50(10.0)	2/50(4.0)	4/50(8.0)
Adjusted rates(b)	7.32	12.50	5.00	9.52
Terminal rates(c)	3/41(7.3)	5/40(12.5)	2/40(5.0)	4/42(9.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.9139 ?			
Prevalence method(d)	P = 0.4740			
Combined analysis(d)	P = 0.5966			
Cochran-Armitage test(e)	P = 0.8205			
Fisher Exact test(e)		P = 0.5000	P = 0.3389	P = 0.6425

Group Name	Control	100 ppm	200 ppm	400 ppm
	SITE : testis			
	TUMOR : interstitial cell tumor			
Tumor rate				
Overall rates(a)	44/50(88.0)	46/50(92.0)	40/50(80.0)	42/50(84.0)
Adjusted rates(b)	95.56	97.62	88.37	93.02
Terminal rates(c)	39/41(95.1)	39/40(97.5)	35/40(87.5)	39/42(92.9)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.8073			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.3348			
Fisher Exact test(e)		P = 0.3703	P = 0.2070	P = 0.3871
	SITE : mammary gland			
	TUMOR : fibroadenoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	3/50(6.0)	0/50(0.0)	1/50(2.0)
Adjusted rates(b)	0.0	6.52	0.0	2.38
Terminal rates(c)	0/41(0.0)	1/40(2.5)	0/40(0.0)	1/42(2.4)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.4770			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 1.0000			
Fisher Exact test(e)		P = 0.1212	P = N.C.	P = 0.5000
	SITE : mammary gland			
	TUMOR : adenoma, fibroadenoma, adenocarcinoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	3/50(6.0)	0/50(0.0)	1/50(2.0)
Adjusted rates(b)	0.0	6.52	0.0	2.38
Terminal rates(c)	0/41(0.0)	1/40(2.5)	0/40(0.0)	1/42(2.4)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.4770			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 1.0000			
Fisher Exact test(e)		P = 0.1212	P = N.C.	P = 0.5000

Group Name	Control	100 ppm	200 ppm	400 ppm
SITE : peritoneum				
TUMOR : mesothelioma				
Tumor rate				
Overall rates(a)	3/50(6.0)	2/50(4.0)	0/50(0.0)	3/50(6.0)
Adjusted rates(b)	7.32	5.00	0.0	7.14
Terminal rates(c)	3/41(7.3)	2/40(5.0)	0/40(0.0)	3/42(7.1)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.5030			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 1.0000			
Fisher Exact test(e)		P = 0.5000	P = 0.1212	P = 0.6611

(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 O2

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS : FEMALE

Group Name	Control	100 ppm	200 ppm	400 ppm
	SITE : spleen			
	TUMOR : mononuclear cell leukemia			
Tumor rate				
Overall rates(a)	2/50(4.0)	7/50(14.0)	0/50(0.0)	1/50(2.0)
Adjusted rates(b)	2.63	13.89	0.0	0.0
Terminal rates(c)	1/38(2.6)	5/36(13.9)	0/43(0.0)	0/36(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.6189			
Prevalence method(d)	P = 0.9453			
Combined analysis(d)	P = 0.9247			
Cochran-Armitage test(e)	P = 0.1539			
Fisher Exact test(e)		P = 0.0798	P = 0.2475	P = 0.5000
	SITE : pituitary gland			
	TUMOR : adenoma			
Tumor rate				
Overall rates(a)	21/50(42.0)	18/50(36.0)	19/50(38.0)	15/50(30.0)
Adjusted rates(b)	43.59	38.89	34.88	29.73
Terminal rates(c)	16/38(42.1)	14/36(38.9)	15/43(34.9)	10/36(27.8)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5041			
Prevalence method(d)	P = 0.8953			
Combined analysis(d)	P = 0.8551			
Cochran-Armitage test(e)	P = 0.2433			
Fisher Exact test(e)		P = 0.3410	P = 0.4192	P = 0.1488
	SITE : pituitary gland			
	TUMOR : adenoma, adenocarcinoma			
Tumor rate				
Overall rates(a)	21/50(42.0)	18/50(36.0)	19/50(38.0)	17/50(34.0)
Adjusted rates(b)	43.59	38.89	34.88	29.73
Terminal rates(c)	16/38(42.1)	14/36(38.9)	15/43(34.9)	10/36(27.8)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.2436			
Prevalence method(d)	P = 0.8953			
Combined analysis(d)	P = 0.7322			
Cochran-Armitage test(e)	P = 0.4740			
Fisher Exact test(e)		P = 0.3410	P = 0.4192	P = 0.2684

Group Name	Control	100 ppm	200 ppm	400 ppm
	SITE : thyroid			
	TUMOR : C-cell adenoma			
Tumor rate				
Overall rates(a)	7/50(14.0)	6/50(12.0)	4/50(8.0)	0/50(0.0)
Adjusted rates(b)	18.42	13.95	9.30	0.0
Terminal rates(c)	7/38(18.4)	5/36(13.9)	4/43(9.3)	0/36(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.9982			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0069**			
Fisher Exact test(e)		P = 0.5000	P = 0.2623	P = 0.0062**
	SITE : thyroid			
	TUMOR : C-cell adenoma,C-cell carcinoma			
Tumor rate				
Overall rates(a)	9/50(18.0)	7/50(14.0)	4/50(8.0)	1/50(2.0)
Adjusted rates(b)	23.68	16.67	9.30	2.78
Terminal rates(c)	9/38(23.7)	6/36(16.7)	4/43(9.3)	1/36(2.8)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.9985			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0056**			
Fisher Exact test(e)		P = 0.3929	P = 0.1168	P = 0.0078**
	SITE : adrenal gland			
	TUMOR : pheochromocytoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	1/50(2.0)	3/50(6.0)	2/50(4.0)
Adjusted rates(b)	0.0	2.78	6.98	5.56
Terminal rates(c)	0/38(0.0)	1/36(2.8)	3/43(7.0)	2/36(5.6)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.1018			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.2072			
Fisher Exact test(e)		P = 0.5000	P = 0.1212	P = 0.2475

Group Name	Control	100 ppm	200 ppm	400 ppm
	SITE : adrenal gland			
	TUMOR : pheochromocytoma, pheochromocytoma:malignant			
Tumor rate				
Overall rates(a)	1/50(2.0)	1/50(2.0)	3/50(6.0)	3/50(6.0)
Adjusted rates(b)	2.63	2.78	6.98	8.33
Terminal rates(c)	1/38(2.6)	1/36(2.8)	3/43(7.0)	3/36(8.3)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.1068			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.2225			
Fisher Exact test(e)		P = 0.7525	P = 0.3087	P = 0.3087
	SITE : uterus			
	TUMOR : endometrial stromal polyp			
Tumor rate				
Overall rates(a)	13/50(26.0)	3/50(6.0)	12/50(24.0)	7/50(14.0)
Adjusted rates(b)	28.95	8.33	27.91	16.67
Terminal rates(c)	11/38(28.9)	3/36(8.3)	12/43(27.9)	6/36(16.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.9104 ?			
Prevalence method(d)	P = 0.7048			
Combined analysis(d)	P = 0.7751			
Cochran-Armitage test(e)	P = 0.4316			
Fisher Exact test(e)		P = 0.0061**	P = 0.5000	P = 0.1054
	SITE : mammary gland			
	TUMOR : fibroadenoma			
Tumor rate				
Overall rates(a)	5/50(10.0)	4/50(8.0)	3/50(6.0)	5/50(10.0)
Adjusted rates(b)	13.16	4.26	6.98	7.14
Terminal rates(c)	5/38(13.2)	1/36(2.8)	3/43(7.0)	1/36(2.8)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1652			
Prevalence method(d)	P = 0.7003			
Combined analysis(d)	P = 0.4832			
Cochran-Armitage test(e)	P = 0.9658			
Fisher Exact test(e)		P = 0.5000	P = 0.3575	P = 0.6297

STUDY No. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
SEX : FEMALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

Group Name	Control	100 ppm	200 ppm	400 ppm
SITE : mammary gland				
TUMOR : adenoma, fibroadenoma, adenocarcinoma				
Tumor rate				
Overall rates(a)	6/50(12.0)	4/50(8.0)	5/50(10.0)	7/50(14.0)
Adjusted rates(b)	13.16	2.78	11.63	11.90
Terminal rates(c)	5/38(13.2)	1/36(2.8)	5/43(11.6)	3/36(8.3)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4431			
Prevalence method(d)	P = 0.3175			
Combined analysis(d)	P = 0.3213			
Cochran-Armitage test(e)	P = 0.5928			
Fisher Exact test(e)		P = 0.3703	P = 0.5000	P = 0.5000

(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 Q1

CAUSE OF DEATH : MALE

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
SEX : MALE

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

Group Name	Control	100 ppm	200 ppm	400 ppm
Number of Dead and Moribund Animal	9	10	10	8
no microscop confirm	0	1	2	0
pneumonia	0	1	0	0
urinary retention	0	0	1	0
tumor d:leukemia	3	2	1	0
tumor d:skin/app	0	0	0	1
tumor d:subcutis	1	1	0	2
tumor d:liver	0	0	0	1
tumor d:kidney	0	0	2	0
tumor d:pituitary	1	1	2	1
tumor d:thyroid	1	1	1	1
tumor d:adrenal	1	0	0	0
tumor d:brain	0	1	0	0
tumor d:spinal cord	1	0	0	0
tumor d:Zymbal gl	1	0	0	2
tumor d:bone	0	1	0	0
tumor d:retroperit	0	1	1	0

(BIO120)

BAIS4

TABLE Q2

CAUSE OF DEATH : FEMALE

STUDY NO. : 0675
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
SEX : FEMALE

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

Group Name	Control	100 ppm	200 ppm	400 ppm
Number of Dead and Moribund Animal	12	14	7	14
no microscop confirm	2	2	1	2
peritonitis	0	1	0	0
tumor d:leukemia	0	2	0	1
tumor d:lymph node	0	0	0	1
tumor d:stomach	1	0	0	0
tumor d:small intes	0	0	0	1
tumor d:pituitary	4	4	4	6
tumor d:uterus	2	0	1	1
tumor d:mammary gl	1	3	0	2
tumor d:prep/cli gl	0	1	0	0
tumor d:brain	0	1	0	0
tumor d:periph nerv	0	0	1	0
tumor d:Zymbal gl	1	0	0	0
tumor d:muscle	1	0	0	0

(BIO120)

BAIS4

FIGURES

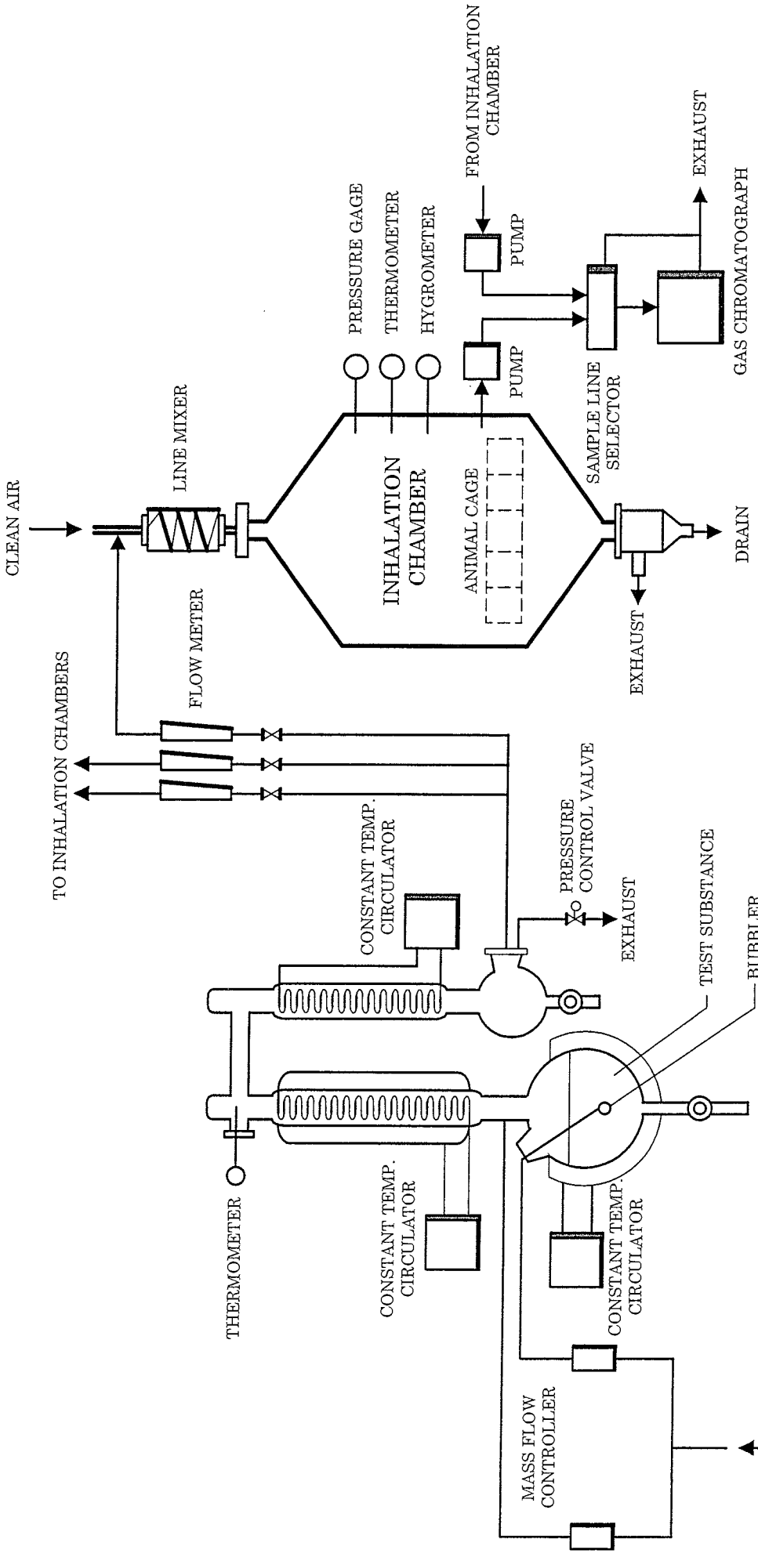


FIGURE 1 2,4-PENTANEDIONE VAPOR GENERATION SYSTEM AND INHALATION SYSTEM

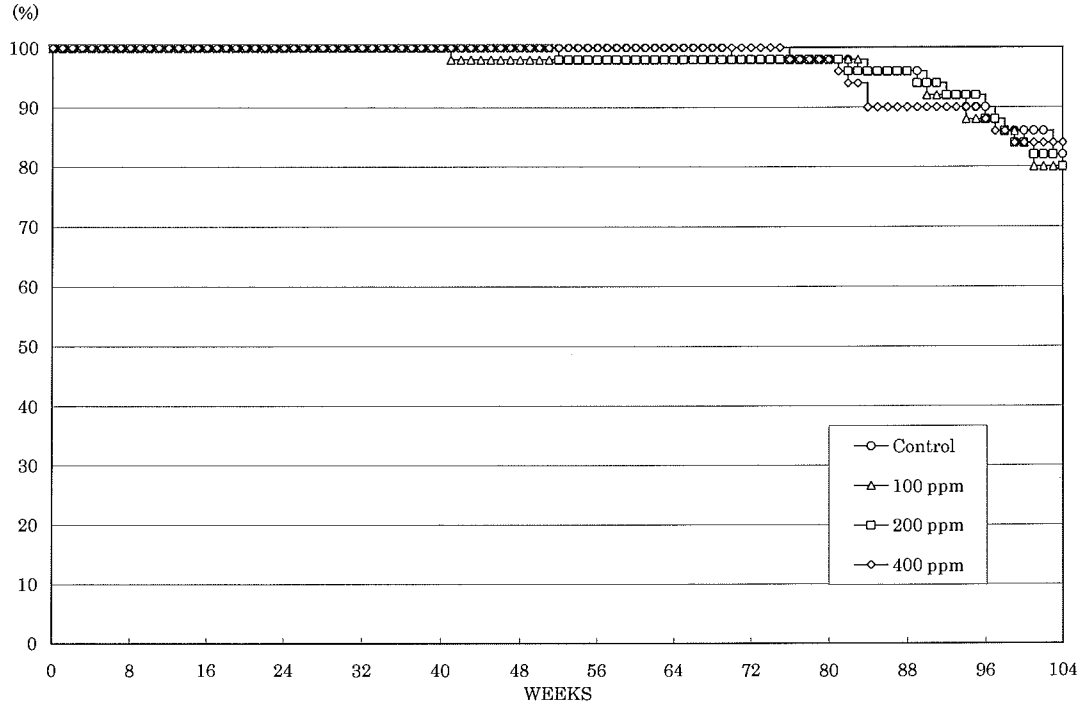


FIGURE 2 SURVIVAL ANIMAL RATE OF MALE RATS IN THE 2-YEAR INHALATION STUDY OF 2,4-PENTANEDIONE

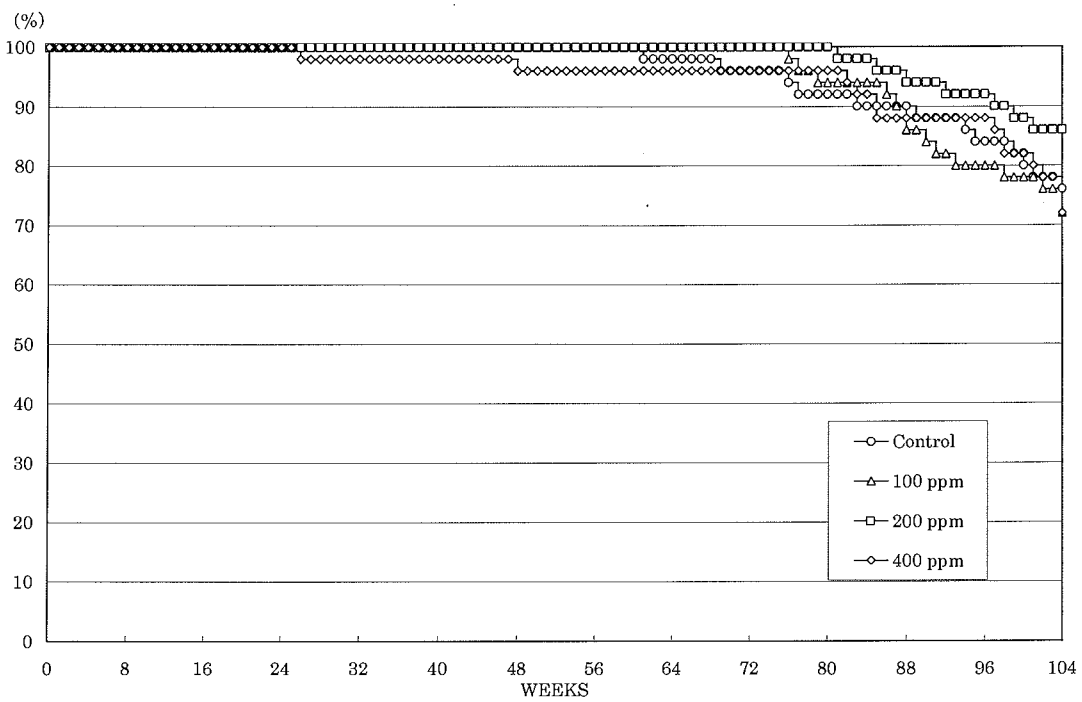


FIGURE 3 SURVIVAL ANIMAL RATE OF FEMALE RATS IN THE 2-YEAR INHALATION STUDY OF 2,4-PENTANEDIONE

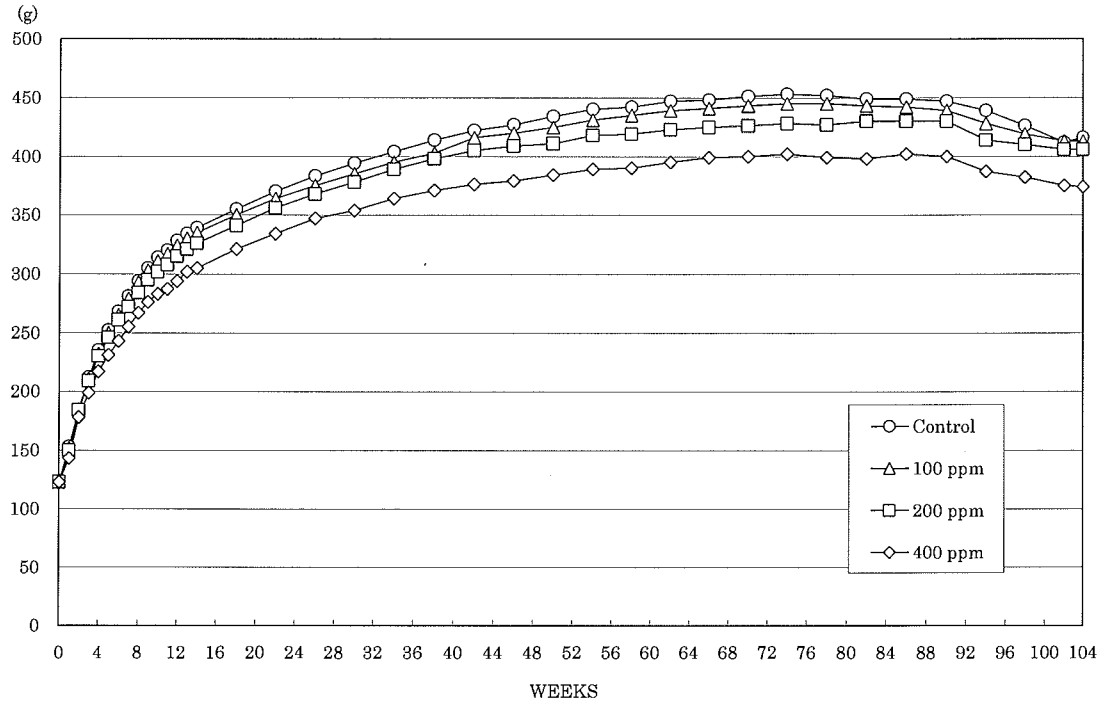


FIGURE 4 BODY WEIGHT CHANGES OF MALE RATS IN THE 2-YEAR INHALATION STUDY OF 2,4-PENTANEDIONE

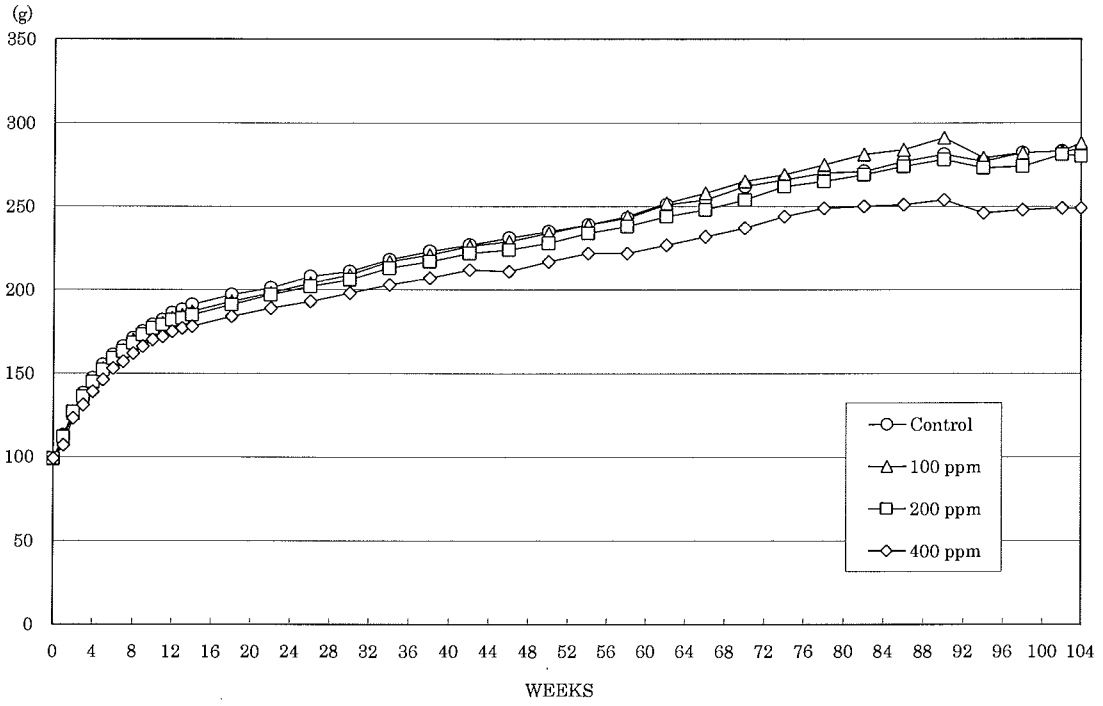


FIGURE 5 BODY WEIGHT CHANGES OF FEMALE RATS IN THE 2-YEAR INHALATION STUDY OF 2,4-PENTANEDIONE

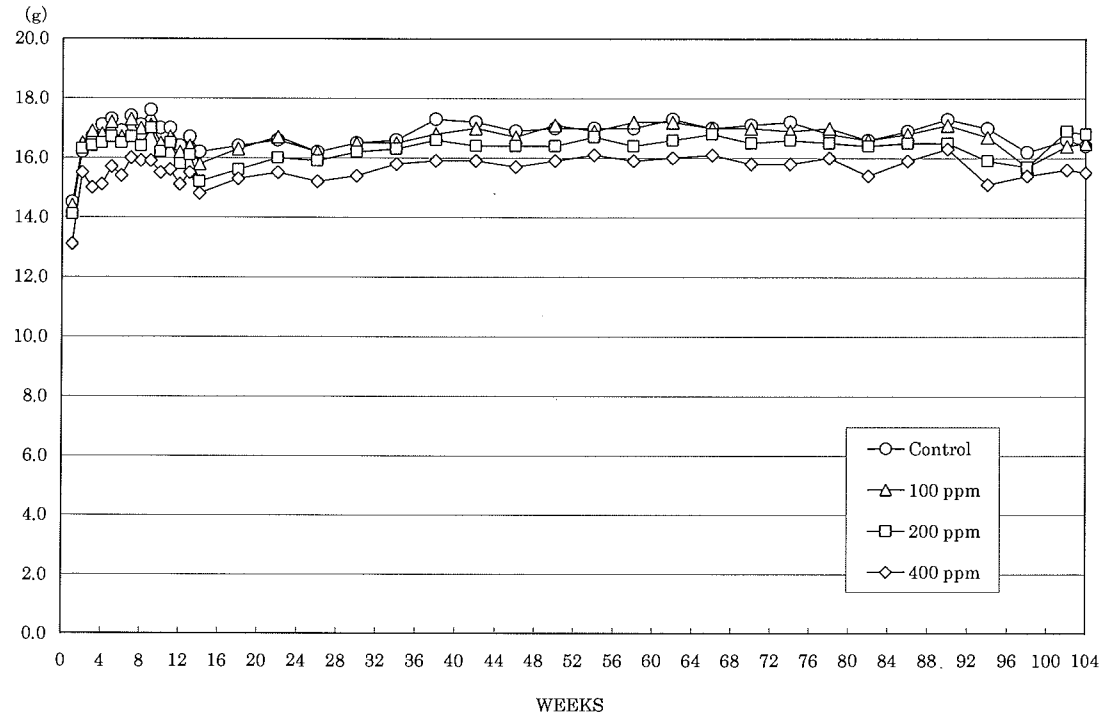


FIGURE 6 FOOD CONSUMPTION CHANGES OF MALE RATS IN THE 2-YEAR INHALATION STUDY OF 2,4-PENTANEDIONE

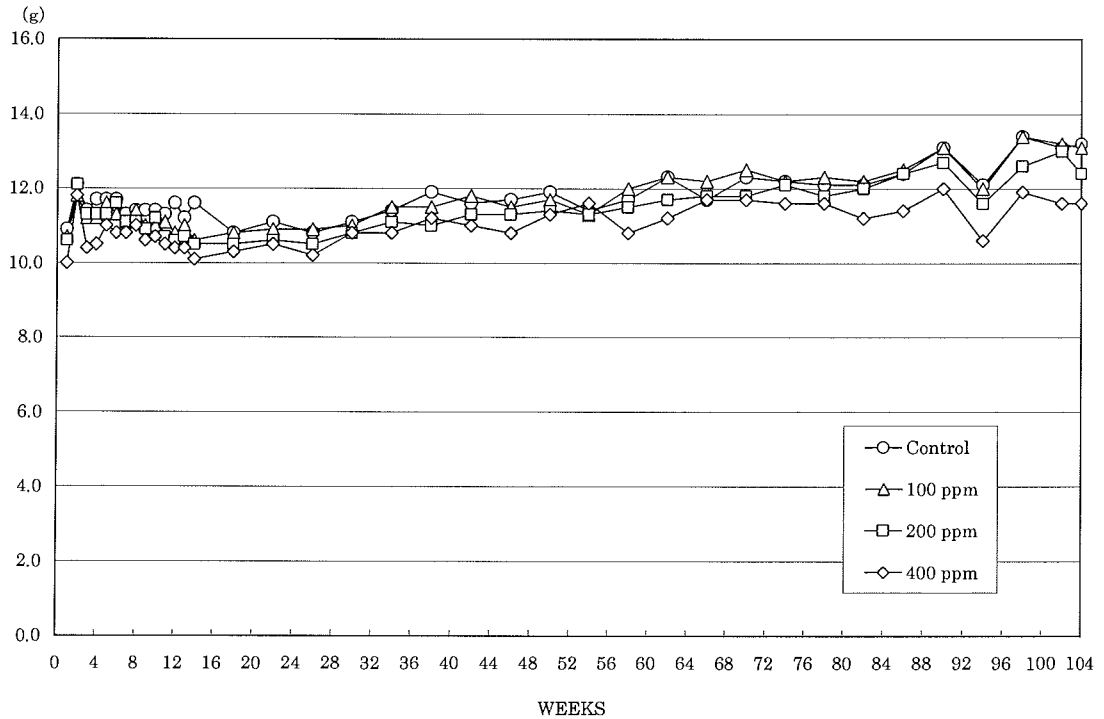
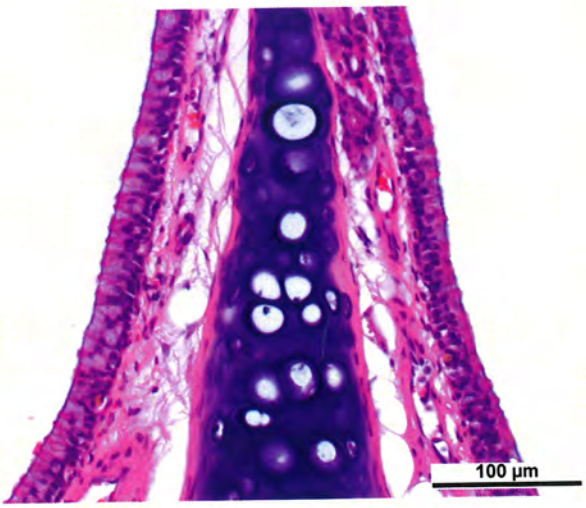
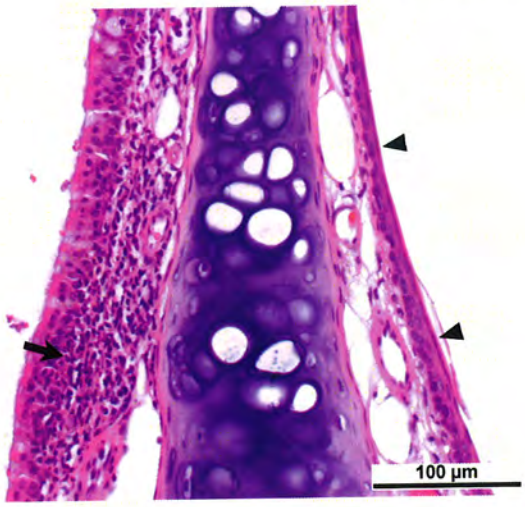


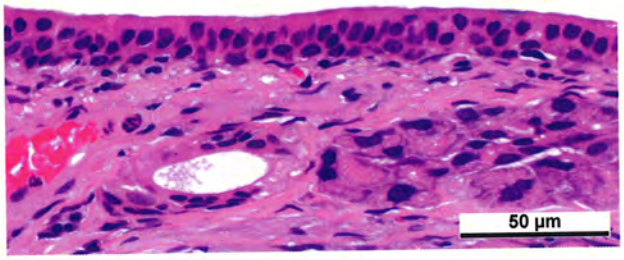
FIGURE 7 FOOD CONSUMPTION CHANGES OF FEMALE RATS IN THE 2-YEAR INHALATION STUDY OF 2,4-PENTANEDIONE



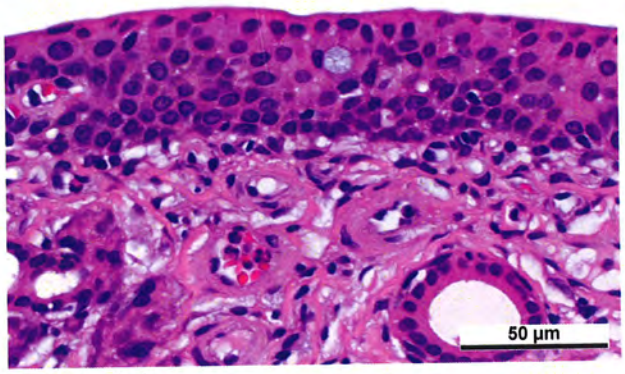
Photograph 1
Nasal cavity (Level 1): Normal (respiratory epithelium)
Rat, Female, Control, Animal No. 0675-2035 (H&E)



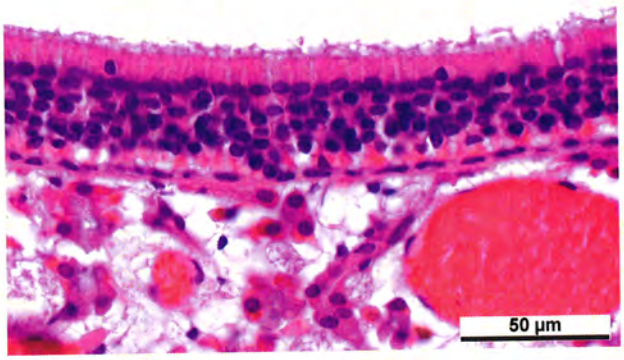
Phograph 2
Nasal cavity (Level 1): Squamous metaplasia (arrowheads) of the respiratory epithelium and inflammation (arrow)
Rat, Female, 400 ppm, Animal No. 0675-2303 (H&E)



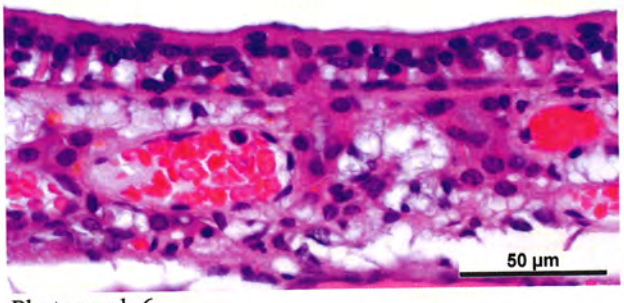
Photograph 3
Nasal cavity (Level 1): Normal (transitional epithelium)
Rat, Male, Control, Animal No. 0675-1003 (H&E)



Photograph 4
Nasal cavity (Level 1): Hyperplasia of the transitional epithelium
Rat, Male, 400 ppm, Animal No. 0675-1320 (H&E)



Photograph 5
Nasal cavity (Level 2): Normal (olfactory epithelium)
Rat, Female, Control, Animal No. 0675-2030 (H&E)



Photograph 6
Nasal cavity (Level 2): Atrophy of the olfactory epithelium
Rat, Female, 400 ppm, Animal No. 0675-2307 (H&E)