Summary of Drinking Water Carcinogenicity Study of 3-Aminophenol in F344 Rats

July 2012

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 July 31, 2012.

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

Summary of Drinking Water Carcinogenicity Study of 3-Aminophenol in F344 Rats

Purpose, materials and methods

3-Aminophenol (CAS No. 591-27-5) is a white to pale gray crystals and with a melting point of 122°C. It is soluble in water, alcohol, and ether.

The carcinogenicity and chronic toxicity of 3-aminophenol were examined in F344/DuCrlCrlj rats. Groups of test animals were administered 3-aminophenol in their drinking water for 2 years (104 weeks). Each group consisted of either 50 male or 50 female rats. The drinking water concentration of 3-aminophenol were 0, 625, 1250 or 2500 ppm (w/w). Both sexes were administered each concentration of 3-aminophenol. 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 3-aminophenol used in these experiments was confirmed by both infrared spectrometry and mass spectrometry. The chemical was analyzed by high performance liquid chromatography before and after use to affirm its stability. The concentrations of 3-aminophenol in the drinking water were determined by high performance liquid chromatography at the time of preparation and on the 4th day after preparation while stored at room temperature. The animals were observed daily for clinical signs and mortality. Body weight, water consumption and food consumption were measured once a week for the first 14 weeks and every 4 weeks thereafter. Animals found dead, in a moribund state, or surviving to the end of the 2-year administration period underwent complete necropsy. Urinalysis was performed near the end of the administration period. Hematology and blood biochemistry analysis were performed at the terminal necropsy: surviving animals were fasted overnight and bled under 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. Three 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 3-aminophenol 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, water consumption, 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

The survival rate of the females administered 2500 ppm 3-aminophenol was decreased, however, the decreased survival rate was not causally related to specific lesion. Brown urine was observed in the 2500 ppm-administered males and females. Soiled fur around the genitalia was observed in the 2500 ppm-administered females. Growth rates of the males and females administered 2500 ppm were suppressed throughout the 2-year administration period, and growth rates of the males and females administered 1250 ppm were suppressed in the late administration period. Food consumption was decreased in the males and females administered 2500 ppm throughout the 2-year administration period. Water consumption of males and females administered 2500 ppm and females administered 1250 ppm were suppressed throughout the 2-year administration period. Water consumption was decreased in the males administered 1250 ppm in many of the 2-year administration period.

The incidences of selected neoplastic lesions in male and female rats are presented in the tables below. The incidence of follicular adenocarcinoma in thyriod were increased in males (Peto test and Cochran-Armitage test), but the incidence is within the JBRC histrical control data. The combined incidence of follicular adenoma and adenocarcinoma in thyroid increased in males (Peto test and Cochran-Armitage test), but the incidence was not different from the JBRC histrical control data. No significant increases in the incidence of neoplastic lesions was found in any of the 3-aminophenol-administered groups of females.

In the kidney, increases of papillary necrosis and deposit of brown pigment in proximal tubule were observed in males administered 2500 ppm and females administered 1250 ppm and above. Severities of chronic progresive nephropathy (CPN) were increased in males administered 2500 ppm. Plasma urea nitrogen was increased in males administered 1250 ppm and above and females administered 2500 ppm. Occult blood in urine was increased in females administered 2500 ppm. In the nasal cavity, severity of eosinophilic change in the olfactory epithelium was increased in females administered 2500 ppm.

Using renal lesion as endpoint markers, the no-observed-adverse-effect-level (NOAEL) of 3-aminophenol in the drinking water was 625 ppm (33 mg/kg body weight per day for male and 50 mg/kg body weight per day for female).

Conclusions

The increased incidences of follicular adenocarcinomas and combined incidences of follicular adenomas and adenocarcinomas in thyroid was insufficient for the evidence of carcinogenicity in male rats. There was no evidence for carcinogenicity of 3-aminophenol in female rats.

Incidences of selected neoplastic lesions of male rats in the 2-year drinking water carcinogenicity study of 3-aminophenol

Dose (ppm)		0	625	1250	2500	Peto test	Cochran-Armitage test
Number of examined animals		50	50	50	50		
benign tumor							
skin/appendage	keratoacanthoma	3	2	4	0		
subcutis	fibroma	5	11	4	4		
lung	bronchiolar-alveolar adenoma	1	3	1	1		
pancreas	islet cell adenoma	2	6	0	5		
pituitary	adenoma	18	21	19	10		↓
thyroid	C-cell adenoma	10	7	7	8		
	follicular adenoma	1	1	2	1		
adrenal	pheochromocytoma	8	4	2 *	1 *		↓↓
testis	interstitial cell tumor	34	32	35	35		
preputial gland	adenoma	4	2	1	0		↓
Zymbal gland	Zmbal gland tumor: benign	1	0	0	2		
malignant tumor							
spleen	mononuclear cell leukemia	4	4	3	1		
pituitary	adenocarcinoma	1	0	0	0		
thyroid	C-cell carcinoma	3	1	3	2		
	follicular adenocarcinoma	0	0	1	4	↑↑	↑↑
adrenal	pheochromocytoma:malignant	1	2	2	0		
Zymbal gland	Zymbal gland tumor: malignant	0	0	0	1		
peritoneum	mesothelioma	1	2	1	4		
pituitary	adenoma＋adenocarcinoma	19	21	19	10 *		↓
thyroid	follicular adenoma＋ follicular adenocarcinoma	1	1	3	5	↑	↑
adrenal	pheochromocytoma＋ pheochromocytoma:malignant	9	6	4	1 **		↓↓
Zymbal gland	Zymbal gland tumor: benign＋ Zymbal gland tumor: malignant	1	0	0	3	↑	

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)

Incidences of selected neoplastic lesions of female rats in the 2-year drinking water carcinogenicity study of 3-aminophenol

Dose (ppm)		0	625	1250	2500	Peto test	Cochran-Armitage test
Number of examined animals		50	50	50	50 [1)]		
benign tumor							
subcutis	fibroma	1	3	1	1		
lung	bronchiolar-alveolar adenoma	3	0	1	0		
pancreas	islet cell adenoma	1	3	1	0		
pituitary	adenoma	13	11	14	9		
thyroid	C-cell adenoma	2	2	5	4		
uterus	endometrial stromal polyp	13	4 *	8	9		
mammary gland	fibroadenoma	5	8	7	6		
clitoral gland	adenoma	2	3	2	2		
malignant tumor							
spleen	mononuclear cell leukemia	4	2	4	0		
uterus	histiocytic sarcoma	1	3	1	0		

1)：Number of animals examined in pituitary is 49.

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

SELECTED TABLES (CONTINUED)

TABLE C 1

BODY WEIGHT CHANGES AND

SURVIVAL ANIMAL NUMBERS: MALE

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

MEAN BODY WEIGHTS AND SURVIVAL

Week-Day on Study	Control Av. Wt.	Control No. of Surviv. <50>	625 ppm Av. Wt.	625 ppm % of cont. <50>	625 ppm No. of Surviv.	1250 ppm Av. Wt.	1250 ppm % of cont. <50>	1250 ppm No. of Surviv.	2500 ppm Av. Wt.	2500 ppm % of cont. <50>	2500 ppm No. of Surviv.
0-0	124 (50)	50/50	124 (50)	100	50/50	124 (50)	100	50/50	124 (50)	100	50/50
1-7	155 (50)	50/50	154 (50)	99	50/50	154 (50)	99	50/50	149 (50)	96	50/50
2-7	189 (50)	50/50	187 (50)	99	50/50	187 (50)	99	50/50	180 (50)	95	50/50
3-7	217 (50)	50/50	213 (50)	98	50/50	213 (50)	98	50/50	204 (50)	94	50/50
4-7	239 (50)	50/50	236 (50)	99	50/50	235 (50)	98	50/50	225 (50)	94	50/50
5-7	255 (50)	50/50	251 (50)	98	50/50	251 (50)	98	50/50	241 (50)	95	50/50
6-7	268 (50)	50/50	264 (50)	99	50/50	264 (50)	99	50/50	252 (50)	94	50/50
7-7	281 (50)	50/50	277 (50)	99	50/50	278 (50)	99	50/50	265 (50)	94	50/50
8-7	294 (50)	50/50	290 (50)	99	50/50	291 (50)	99	50/50	277 (50)	94	50/50
9-7	304 (50)	50/50	301 (50)	99	50/50	301 (50)	99	50/50	288 (50)	95	50/50
10-7	312 (50)	50/50	310 (50)	99	50/50	310 (50)	99	50/50	295 (50)	95	50/50
11-7	320 (50)	50/50	317 (50)	99	50/50	318 (50)	99	50/50	302 (50)	94	50/50
12-7	328 (50)	50/50	324 (50)	99	50/50	325 (50)	99	50/50	308 (50)	94	50/50
13-7	333 (50)	50/50	330 (50)	99	50/50	331 (50)	99	50/50	313 (50)	94	50/50
14-7	339 (50)	50/50	336 (50)	99	50/50	337 (50)	99	50/50	318 (50)	94	50/50
18-7	353 (50)	50/50	353 (50)	100	50/50	354 (50)	100	50/50	333 (50)	94	50/50
22-7	370 (50)	50/50	370 (50)	100	50/50	370 (50)	100	50/50	347 (50)	94	50/50
26-7	380 (50)	50/50	381 (50)	100	50/50	382 (50)	101	50/50	355 (50)	93	50/50
30-7	392 (50)	50/50	394 (50)	101	50/50	396 (50)	101	50/50	368 (50)	94	50/50
34-7	402 (50)	50/50	404 (50)	100	50/50	405 (50)	101	50/50	379 (50)	94	50/50
38-7	406 (50)	50/50	407 (49)	100	49/50	409 (50)	101	50/50	382 (50)	94	50/50
42-7	415 (49)	49/50	418 (49)	101	49/50	418 (50)	101	50/50	389 (50)	94	50/50
46-7	421 (49)	49/50	423 (49)	100	49/50	425 (49)	101	49/50	395 (50)	94	50/50
50-7	426 (49)	49/50	429 (49)	101	49/50	431 (48)	101	48/50	398 (50)	93	50/50
54-7	435 (49)	49/50	438 (49)	101	49/50	439 (48)	101	48/50	404 (50)	93	50/50
58-7	441 (49)	49/50	445 (49)	101	49/50	445 (48)	101	48/50	409 (49)	93	49/50
62-7	446 (49)	49/50	451 (49)	101	49/50	448 (48)	100	48/50	413 (48)	93	48/50
66-7	450 (49)	49/50	456 (49)	101	49/50	453 (47)	101	47/50	414 (48)	92	48/50
70-7	452 (49)	49/50	457 (49)	101	49/50	455 (47)	101	47/50	415 (48)	92	48/50
74-7	455 (49)	49/50	459 (48)	101	48/50	456 (47)	100	47/50	416 (48)	91	48/50
78-7	458 (49)	49/50	459 (48)	100	48/50	459 (46)	100	46/50	415 (47)	91	47/50
82-7	459 (48)	48/50	464 (46)	101	46/50	457 (46)	100	46/50	412 (47)	90	47/50
86-7	458 (48)	48/50	461 (46)	101	46/50	450 (46)	98	46/50	406 (47)	89	47/50
90-7	454 (48)	48/50	454 (45)	100	45/50	441 (44)	97	44/50	397 (45)	87	45/50
94-7	453 (45)	45/50	444 (44)	98	44/50	435 (39)	96	39/50	393 (40)	87	40/50
98-7	452 (43)	43/50	438 (43)	97	43/50	425 (36)	94	36/50	385 (39)	85	39/50
102-7	437 (42)	42/50	425 (40)	97	40/50	418 (34)	96	34/50	377 (36)	86	36/50
104-7	436 (40)	40/50	419 (39)	96	39/50	408 (33)	94	33/50	371 (34)	85	34/50

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

TABLE C 2

BODY WEIGHT CHANGES AND

SURVIVAL ANIMAL NUMBERS: FEMALE

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

MEAN BODY WEIGHTS AND SURVIVAL

Week-Day on Study	Control Av. Wt.	Control No. of Surviv. <50>	625 ppm Av. Wt.	625 ppm % of cont. <50>	625 ppm No. of Surviv.	1250 ppm Av. Wt.	1250 ppm % of cont. <50>	1250 ppm No. of Surviv.	2500 ppm Av. Wt.	2500 ppm % of cont. <50>	2500 ppm No. of Surviv.
0-0	101 (50)	50/50	101 (50)	100	50/50	101 (50)	100	50/50	101 (50)	100	50/50
1-7	118 (50)	50/50	117 (50)	99	50/50	117 (50)	99	50/50	113 (50)	96	50/50
2-7	131 (50)	50/50	131 (50)	100	50/50	130 (50)	99	50/50	126 (50)	96	50/50
3-7	141 (50)	50/50	141 (50)	100	50/50	139 (50)	99	50/50	135 (50)	96	50/50
4-7	149 (50)	50/50	149 (50)	100	50/50	148 (50)	99	50/50	142 (50)	95	50/50
5-7	156 (50)	50/50	157 (50)	101	50/50	155 (50)	99	50/50	147 (50)	94	50/50
6-7	163 (50)	50/50	162 (50)	99	50/50	161 (50)	99	50/50	153 (50)	94	50/50
7-7	166 (50)	50/50	167 (50)	101	50/50	167 (50)	101	50/50	158 (50)	95	50/50
8-7	171 (50)	50/50	171 (50)	100	50/50	171 (50)	100	50/50	161 (50)	94	50/50
9-7	175 (50)	50/50	175 (50)	100	50/50	175 (50)	100	50/50	165 (50)	94	50/50
10-7	179 (50)	50/50	178 (50)	99	50/50	178 (50)	99	50/50	168 (50)	94	50/50
11-7	183 (50)	50/50	182 (50)	99	50/50	183 (50)	100	50/50	170 (50)	93	50/50
12-7	186 (50)	50/50	186 (50)	100	50/50	184 (50)	99	50/50	172 (50)	92	50/50
13-7	187 (50)	50/50	188 (50)	101	50/50	187 (50)	100	50/50	174 (50)	93	50/50
14-7	189 (50)	50/50	191 (50)	101	50/50	189 (50)	100	50/50	176 (50)	93	50/50
18-7	195 (50)	50/50	197 (50)	101	50/50	196 (50)	101	50/50	181 (50)	93	50/50
22-7	203 (50)	50/50	204 (50)	100	50/50	202 (50)	100	50/50	186 (50)	92	50/50
26-7	208 (50)	50/50	210 (50)	101	50/50	208 (50)	100	50/50	189 (50)	91	50/50
30-7	213 (50)	50/50	215 (50)	101	50/50	212 (50)	100	50/50	194 (50)	91	50/50
34-7	217 (50)	50/50	220 (50)	101	50/50	218 (50)	100	50/50	198 (49)	91	49/50
38-7	221 (50)	50/50	223 (50)	101	50/50	221 (50)	100	50/50	199 (49)	90	49/50
42-7	225 (50)	50/50	228 (50)	101	50/50	224 (50)	100	50/50	200 (49)	89	49/50
46-7	231 (50)	50/50	232 (50)	100	50/50	229 (50)	99	50/50	202 (49)	87	49/50
50-7	234 (50)	50/50	238 (50)	102	50/50	232 (50)	99	50/50	203 (49)	87	49/50
54-7	241 (50)	50/50	245 (50)	102	50/50	238 (50)	99	50/50	208 (48)	86	48/50
58-7	246 (49)	49/50	252 (50)	102	50/50	243 (50)	99	50/50	212 (48)	86	48/50
62-7	252 (49)	49/50	258 (50)	102	50/50	250 (50)	99	50/50	216 (47)	86	47/50
66-7	259 (49)	49/50	265 (50)	102	50/50	256 (49)	99	49/50	218 (46)	84	46/50
70-7	265 (49)	49/50	268 (49)	101	49/50	260 (48)	98	48/50	220 (46)	83	46/50
74-7	270 (49)	49/50	272 (48)	101	48/50	265 (48)	98	48/50	225 (45)	83	45/50
78-7	281 (48)	48/50	283 (47)	101	47/50	271 (48)	96	48/50	231 (43)	82	43/50
82-7	289 (47)	47/50	290 (47)	100	47/50	277 (48)	96	48/50	237 (39)	82	39/50
86-7	292 (47)	47/50	293 (47)	100	47/50	279 (47)	96	47/50	239 (39)	82	39/50
90-7	298 (47)	47/50	294 (46)	99	46/50	282 (45)	95	45/50	240 (39)	81	39/50
94-7	301 (46)	46/50	298 (43)	99	43/50	284 (45)	94	45/50	240 (37)	80	37/50
98-7	306 (44)	44/50	299 (42)	98	42/50	284 (45)	93	45/50	245 (35)	80	35/50
102-7	310 (43)	43/50	293 (41)	95	41/50	282 (44)	91	44/50	244 (35)	79	35/50
104-7	312 (43)	43/50	297 (40)	95	40/50	283 (42)	91	42/50	245 (35)	79	35/50

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

TABLE C 3

BODY WEIGHT CHANGES: MALE

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	124± 4	155± 6	189± 8	217± 9	239± 10	255± 11	268± 12
625 ppm	124± 4	154± 6	187± 8	213± 9	236± 10	251± 11	264± 12
1250 ppm	124± 4	154± 6	187± 8	213± 8	235± 8	251± 9	264± 10
2500 ppm	124± 4	149± 6**	180± 7**	204± 9**	225± 10**	241± 11**	252± 12**

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

(HAN260)

BAIS 4

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-7
Control	281± 12	294± 12	304± 13	312± 14	320± 14	328± 14	333± 13
625 ppm	277± 13	290± 14	301± 14	310± 15	317± 15	324± 16	330± 15
1250 ppm	278± 11	291± 11	301± 13	310± 14	318± 14	325± 14	331± 15
2500 ppm	265± 13**	277± 14**	288± 15**	295± 16**	302± 16**	308± 16**	313± 16**

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

(HAN260)

BAIS4

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 14-7	18-7	22-7	26-7	30-7	34-7	38-7
Control	339± 14	353± 14	370± 15	380± 17	392± 17	402± 17	406± 18
625 ppm	336± 16	353± 17	370± 18	381± 19	394± 21	404± 22	407± 23
1250 ppm	337± 16	354± 17	370± 18	382± 19	396± 20	405± 20	409± 21
2500 ppm	318± 16**	333± 19**	347± 20**	355± 21**	368± 21**	379± 20**	382± 23**

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

(HAN260)

BAIS4

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 42-7	46-7	50-7	54-7	58-7	62-7	66-7
Control	415± 20	421± 21	426± 22	435± 23	441± 23	446± 24	450± 26
625 ppm	418± 23	423± 24	429± 24	438± 26	445± 26	451± 25	456± 26
1250 ppm	418± 22	425± 25	431± 25	439± 26	445± 25	448± 29	453± 25
2500 ppm	389± 24**	395± 26**	398± 27**	404± 26**	409± 26**	413± 26**	414± 27**

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

(HAN260)

BAIS4

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 70-7	74-7	78-7	82-7	86-7	90-7	94-7
Control	452± 27	455± 26	458± 30	459± 28	458± 26	454± 29	453± 30
625 ppm	457± 28	459± 31	459± 44	464± 28	461± 29	454± 33	444± 43
1250 ppm	455± 25	456± 26	459± 25	457± 27	450± 30	441± 43	435± 43
2500 ppm	415± 27**	416± 27**	415± 26**	412± 25**	406± 27**	397± 37**	393± 36**

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

(HAN260)

BAIS4

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 98-7	102-7	104-7
Control	452± 32	437± 44	436± 45
625 ppm	438± 47	425± 49	419± 57
1250 ppm	425± 51**	418± 42*	408± 46*
2500 ppm	385± 34**	377± 30**	371± 38**

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

(HAN260)

TABLE C 4

BODY WEIGHT CHANGES: FEMALE

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0		1-7		2-7		3-7		4-7		5-7		6-7	
Control	101±	3	118±	4	131±	5	141±	6	149±	7	156±	8	163±	9
625 ppm	101±	3	117±	4	131±	4	141±	5	149±	6	157±	6	162±	7
1250 ppm	101±	3	117±	4	130±	5	139±	5	148±	6	155±	6	161±	7
2500 ppm	101±	3	113±	4**	126±	5**	135±	5**	142±	6**	147±	6**	153±	6**

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

(HAN260)

BAIS4

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-7
Control	166± 10	171± 10	175± 11	179± 11	183± 11	186± 12	187± 11
625 ppm	167± 8	171± 8	175± 8	178± 9	182± 9	186± 9	188± 9
1250 ppm	167± 8	171± 8	175± 9	178± 10	183± 10	184± 10	187± 9
2500 ppm	158± 7**	161± 8**	165± 8**	168± 9**	170± 9**	172± 9**	174± 9**

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

(HAN260)

BAIS4

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 14-7	18-7	22-7	26-7	30-7	34-7	38-7
Control	189± 11	195± 12	203± 13	208± 13	213± 14	217± 15	221± 14
625 ppm	191± 8	197± 8	204± 9	210± 9	215± 10	220± 10	223± 10
1250 ppm	189± 9	196± 10	202± 10	208± 10	212± 11	218± 11	221± 11
2500 ppm	176± 9**	181± 9**	186± 10**	189± 10**	194± 11**	198± 11**	199± 12**

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

(HAN260)

BAIS4

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 42-7	46-7	50-7	54-7	58-7	62-7	66-7
Control	225± 16	231± 16	234± 17	241± 19	246± 19	252± 20	259± 23
625 ppm	228± 11	232± 12	238± 14	245± 16	252± 18	258± 19	265± 21
1250 ppm	224± 12	229± 13	232± 14	238± 15	243± 17	250± 19	256± 19
2500 ppm	200± 12**	202± 14**	203± 16**	208± 15**	212± 17**	216± 18**	218± 21**

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

(HAN260)

BAIS4

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 70-7	74-7	78-7	82-7	86-7	90-7	94-7
Control	265± 24	270± 26	281± 22	289± 22	292± 22	298± 21	301± 23
625 ppm	268± 20	272± 22	283± 21	290± 23	293± 29	294± 32	298± 33
1250 ppm	260± 19	265± 21	271± 22	277± 23*	279± 22*	282± 20**	284± 20**
2500 ppm	220± 23**	225± 26**	231± 25**	237± 22**	239± 23**	240± 25**	240± 27**

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

(HAN260)

BAIS4

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 98-7		102-7		104-7	
Control	306±	26	310±	32	312±	38
625 ppm	299±	41	293±	27*	297±	26
1250 ppm	284±	22**	282±	22**	283±	22**
2500 ppm	245±	26**	244±	30**	245±	34**

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

TABLE D 1

FOOD CONSUMPTION CHANGES AND SURVIVAL ANIMAL NUMBERS: MALE

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

MEAN FOOD CONSUMPTION(FC) AND SURVIVAL

Week-Day on Study	Control Av. FC.	Control No. of Surviv. <50>	625 ppm Av. FC.	625 ppm % of cont. <50>	625 ppm No. of Surviv.	1250 ppm Av. FC.	1250 ppm % of cont. <50>	1250 ppm No. of Surviv.	2500 ppm Av. FC.	2500 ppm % of cont. <50>	2500 ppm No. of Surviv.
1-7	13.6 (50)	50/50	13.7 (50)	101	50/50	13.9 (50)	102	50/50	13.0 (50)	96	50/50
2-7	15.4 (50)	50/50	15.4 (50)	100	50/50	15.2 (50)	99	50/50	14.5 (50)	94	50/50
3-7	16.3 (50)	50/50	16.0 (50)	98	50/50	16.0 (50)	98	50/50	15.0 (50)	92	50/50
4-7	16.4 (50)	50/50	16.2 (50)	99	50/50	16.1 (50)	98	50/50	15.3 (50)	93	50/50
5-7	16.3 (50)	50/50	16.2 (50)	99	50/50	15.9 (50)	98	50/50	15.3 (50)	94	50/50
6-7	15.8 (50)	50/50	15.6 (50)	99	50/50	15.7 (50)	99	50/50	15.2 (50)	96	50/50
7-7	15.5 (50)	50/50	15.4 (50)	99	50/50	15.4 (50)	99	50/50	14.9 (50)	96	50/50
8-7	15.9 (50)	50/50	15.8 (50)	99	50/50	15.8 (50)	99	50/50	15.2 (50)	96	50/50
9-7	15.8 (50)	50/50	15.9 (50)	101	50/50	16.0 (50)	101	50/50	15.5 (50)	98	50/50
10-7	15.7 (50)	50/50	15.7 (50)	100	50/50	16.0 (50)	102	50/50	15.2 (50)	97	50/50
11-7	15.3 (50)	50/50	15.4 (50)	101	50/50	15.4 (50)	101	50/50	14.8 (50)	97	50/50
12-7	15.6 (50)	50/50	15.4 (50)	99	50/50	15.5 (50)	99	50/50	15.2 (50)	97	50/50
13-7	15.6 (50)	50/50	15.4 (50)	99	50/50	15.4 (50)	99	50/50	14.6 (50)	94	50/50
14-7	15.4 (50)	50/50	15.4 (50)	100	50/50	15.4 (50)	100	50/50	14.8 (50)	96	50/50
18-7	15.0 (50)	50/50	15.0 (50)	100	50/50	15.1 (50)	101	50/50	14.4 (50)	96	50/50
22-7	15.7 (50)	50/50	15.8 (50)	101	50/50	15.9 (50)	101	50/50	14.9 (50)	95	50/50
26-7	16.0 (50)	50/50	15.9 (50)	99	50/50	16.0 (50)	100	50/50	15.0 (50)	94	50/50
30-7	15.7 (50)	50/50	16.1 (50)	103	50/50	16.3 (50)	104	50/50	14.9 (50)	95	50/50
34-7	15.7 (50)	50/50	15.8 (50)	101	50/50	16.1 (50)	103	50/50	15.4 (50)	98	50/50
38-7	15.8 (50)	50/50	15.8 (49)	100	49/50	16.1 (50)	102	50/50	15.5 (50)	98	50/50
42-7	16.1 (49)	49/50	16.3 (49)	101	49/50	16.2 (50)	101	50/50	15.5 (50)	96	50/50
46-7	16.1 (49)	49/50	16.2 (49)	101	49/50	16.2 (49)	101	49/50	15.6 (50)	97	50/50
50-7	16.1 (49)	49/50	16.3 (49)	101	49/50	16.5 (48)	102	48/50	15.8 (50)	98	50/50
54-7	16.8 (49)	49/50	17.2 (49)	102	49/50	17.0 (48)	101	48/50	16.2 (50)	96	50/50
58-7	16.8 (49)	49/50	17.1 (49)	102	49/50	17.1 (48)	102	48/50	16.2 (49)	96	49/50
62-7	16.7 (49)	49/50	17.0 (49)	102	49/50	16.7 (48)	100	48/50	16.1 (48)	96	48/50
66-7	16.4 (49)	49/50	16.8 (49)	102	49/50	16.8 (47)	102	47/50	15.9 (48)	97	48/50
70-7	16.2 (49)	49/50	16.6 (49)	102	49/50	16.6 (47)	102	47/50	15.5 (48)	96	48/50
74-7	16.6 (49)	49/50	16.6 (48)	100	48/50	16.6 (47)	100	47/50	15.5 (48)	93	48/50
78-7	16.1 (49)	49/50	16.2 (48)	101	48/50	16.1 (46)	100	46/50	15.0 (47)	93	47/50
82-7	16.1 (48)	48/50	16.4 (46)	102	46/50	16.0 (46)	99	46/50	14.9 (47)	93	47/50
86-7	16.3 (48)	48/50	16.1 (46)	99	46/50	15.7 (46)	96	46/50	15.0 (47)	92	47/50
90-7	16.0 (48)	48/50	16.0 (45)	100	45/50	15.7 (44)	98	44/50	14.8 (44)	93	45/50
94-7	16.2 (45)	45/50	15.9 (44)	98	44/50	15.3 (39)	94	39/50	14.7 (40)	91	40/50
98-7	16.7 (43)	43/50	16.1 (43)	96	43/50	15.5 (36)	93	36/50	14.3 (39)	86	39/50
102-7	15.9 (41)	42/50	15.2 (40)	96	40/50	15.6 (34)	98	34/50	14.4 (36)	91	36/50
104-7	15.8 (40)	40/50	15.5 (39)	98	39/50	15.6 (33)	99	33/50	14.3 (34)	91	34/50

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

TABLE D 2

FOOD CONSUMPTION CHANGES AND SURVIVAL ANIMAL NUMBERS: FEMALE

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

MEAN FOOD CONSUMPTION(FC) AND SURVIVAL

Week-Day on Study	Control Av. FC.	Control No. of Surviv. <50>	625 ppm Av. FC.	625 ppm % of cont. <50>	625 ppm No. of Surviv.	1250 ppm Av. FC.	1250 ppm % of cont. <50>	1250 ppm No. of Surviv.	2500 ppm Av. FC.	2500 ppm % of cont. <50>	2500 ppm No. of Surviv.
1-7	11.0 (50)	50/50	10.9 (50)	99	50/50	10.9 (50)	99	50/50	10.0 (50)	91	50/50
2-7	11.1 (50)	50/50	11.2 (50)	101	50/50	10.9 (50)	98	50/50	10.4 (50)	94	50/50
3-7	11.0 (50)	50/50	11.1 (50)	101	50/50	10.9 (50)	99	50/50	10.2 (50)	93	50/50
4-7	11.0 (50)	50/50	11.2 (50)	102	50/50	11.0 (50)	100	50/50	10.2 (50)	93	50/50
5-7	10.9 (50)	50/50	11.0 (50)	101	50/50	10.9 (50)	100	50/50	10.0 (50)	92	50/50
6-7	10.8 (50)	50/50	10.7 (50)	99	50/50	10.7 (50)	99	50/50	9.8 (50)	91	50/50
7-7	10.4 (50)	50/50	10.5 (50)	101	50/50	10.5 (50)	101	50/50	9.7 (50)	93	50/50
8-7	10.6 (50)	50/50	10.5 (50)	99	50/50	10.4 (50)	98	50/50	9.7 (50)	92	50/50
9-7	10.7 (50)	50/50	10.6 (50)	99	50/50	10.4 (50)	97	50/50	9.6 (50)	90	50/50
10-7	10.6 (50)	50/50	10.7 (50)	101	50/50	10.5 (50)	99	50/50	9.7 (50)	92	50/50
11-7	10.7 (50)	50/50	10.7 (50)	100	50/50	10.6 (50)	99	50/50	9.4 (50)	88	50/50
12-7	10.6 (50)	50/50	10.9 (50)	103	50/50	10.4 (50)	98	50/50	9.7 (50)	92	50/50
13-7	10.5 (50)	50/50	10.7 (50)	102	50/50	10.4 (50)	99	50/50	9.5 (50)	90	50/50
14-7	10.7 (50)	50/50	11.0 (50)	103	50/50	10.6 (50)	99	50/50	9.8 (50)	92	50/50
18-7	10.7 (50)	50/50	10.9 (50)	102	50/50	10.4 (50)	97	50/50	9.5 (50)	89	50/50
22-7	10.7 (50)	50/50	11.0 (50)	103	50/50	10.5 (50)	98	50/50	9.5 (50)	89	50/50
26-7	11.0 (50)	50/50	11.1 (50)	101	50/50	10.9 (50)	99	50/50	9.8 (50)	89	50/50
30-7	10.7 (50)	50/50	11.1 (50)	104	50/50	10.7 (50)	100	50/50	9.6 (50)	90	50/50
34-7	10.8 (50)	50/50	11.0 (50)	102	50/50	10.9 (50)	101	50/50	9.8 (49)	91	49/50
38-7	10.8 (50)	50/50	11.1 (50)	103	50/50	10.8 (50)	100	50/50	9.7 (49)	90	49/50
42-7	11.0 (50)	50/50	11.4 (50)	104	50/50	11.0 (50)	100	50/50	10.0 (49)	91	49/50
46-7	11.4 (50)	50/50	11.4 (50)	100	50/50	11.3 (50)	99	50/50	10.1 (49)	89	49/50
50-7	11.1 (50)	50/50	11.7 (50)	105	50/50	11.1 (50)	100	50/50	10.1 (49)	91	49/50
54-7	11.6 (50)	50/50	12.0 (50)	103	50/50	11.6 (50)	100	50/50	10.5 (48)	91	48/50
58-7	11.7 (49)	49/50	12.0 (50)	103	50/50	11.6 (50)	99	50/50	10.6 (48)	91	48/50
62-7	12.0 (49)	49/50	12.2 (50)	102	50/50	12.0 (50)	100	50/50	10.6 (47)	88	47/50
66-7	12.0 (49)	49/50	12.1 (50)	101	50/50	11.6 (49)	97	49/50	10.5 (46)	88	46/50
70-7	11.7 (49)	49/50	11.8 (49)	101	49/50	11.7 (48)	100	48/50	10.6 (46)	91	46/50
74-7	12.1 (49)	49/50	12.1 (48)	100	48/50	12.1 (48)	100	48/50	10.7 (45)	88	45/50
78-7	12.3 (48)	48/50	12.5 (47)	102	47/50	11.9 (48)	97	48/50	10.8 (43)	88	43/50
82-7	12.5 (47)	47/50	12.3 (47)	98	47/50	11.9 (48)	95	48/50	10.9 (39)	87	39/50
86-7	12.2 (47)	47/50	12.2 (47)	100	47/50	11.8 (47)	97	47/50	10.9 (39)	89	39/50
90-7	12.4 (47)	47/50	12.1 (46)	98	46/50	11.9 (45)	96	45/50	10.9 (39)	88	39/50
94-7	12.6 (46)	46/50	12.6 (43)	100	43/50	12.3 (45)	98	45/50	11.1 (37)	88	37/50
98-7	13.0 (44)	44/50	12.5 (41)	96	42/50	12.1 (45)	93	45/50	11.3 (35)	87	35/50
102-7	13.2 (42)	43/50	12.8 (41)	97	41/50	12.0 (44)	91	44/50	11.4 (35)	86	35/50
104-7	12.8 (42)	43/50	12.7 (40)	99	40/50	11.8 (42)	92	42/50	11.4 (35)	89	35/50

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

TABLE D 3

FOOD CONSUMPTION CHANGES: MALE

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 1-7 (7)	2-7 (7)	3-7 (7)	4-7 (7)	5-7 (7)	6-7 (7)	7-7 (7)
Control	13.6± 0.7	15.4± 0.8	16.3± 0.8	16.4± 0.8	16.3± 0.8	15.8± 0.9	15.5± 0.9
625 ppm	13.7± 0.7	15.4± 0.9	16.0± 0.9	16.2± 0.8	16.2± 0.8	15.6± 0.9	15.4± 0.9
1250 ppm	13.9± 0.7	15.2± 0.8	16.0± 0.7	16.1± 0.6	15.9± 0.7*	15.7± 0.8	15.4± 0.8
2500 ppm	13.0± 0.8**	14.5± 0.8**	15.0± 0.9**	15.3± 0.8**	15.3± 0.8**	15.2± 0.7**	14.9± 0.8**

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

(HAN260)

BAIS4

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 8-7 (7)	9-7 (7)	10-7 (7)	11-7 (7)	12-7 (7)	13-7 (7)	14-7 (7)
Control	15.9± 0.9	15.8± 0.9	15.7± 0.8	15.3± 0.8	15.6± 0.8	15.6± 0.7	15.4± 0.7
625 ppm	15.8± 1.0	15.9± 0.9	15.7± 0.9	15.4± 0.9	15.4± 0.8	15.4± 0.7	15.4± 0.7
1250 ppm	15.8± 0.8	16.0± 0.8	16.0± 0.8	15.4± 0.8	15.5± 0.8	15.4± 0.7	15.4± 0.9
2500 ppm	15.2± 0.9**	15.5± 0.9	15.2± 0.9**	14.8± 0.9**	15.2± 0.8	14.6± 0.7**	14.8± 0.8**

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

(HAN260)

BAIS4

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 18-7 (7)	22-7 (7)	26-7 (7)	30-7 (7)	34-7 (7)	38-7 (7)	42-7 (7)
Control	15.0± 0.7	15.7± 0.8	16.0± 0.9	15.7± 0.9	15.7± 0.7	15.8± 0.9	16.1± 0.9
625 ppm	15.0± 0.7	15.8± 0.9	15.9± 0.9	16.1± 0.9	15.8± 0.9	15.8± 0.8	16.3± 0.8
1250 ppm	15.1± 0.9	15.9± 0.8	16.0± 0.9	16.3± 0.8**	16.1± 1.0	16.1± 0.9	16.2± 1.1
2500 ppm	14.4± 0.8**	14.9± 0.8**	15.0± 0.9**	14.9± 0.9**	15.4± 0.8	15.5± 1.0	15.5± 1.0**

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

(HAN260)

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 46-7(7)	50-7(7)	54-7(7)	58-7(7)	62-7(7)	66-7(7)	70-7(7)
Control	16.1± 0.9	16.1± 1.0	16.8± 0.9	16.8± 1.0	16.7± 0.9	16.4± 1.0	16.2± 1.1
625 ppm	16.2± 1.0	16.3± 0.9	17.2± 0.9	17.1± 1.0	17.0± 0.8	16.8± 0.9	16.6± 1.0
1250 ppm	16.2± 1.0	16.5± 1.0	17.0± 0.9	17.1± 1.0	16.7± 2.0	16.8± 1.0	16.6± 1.1
2500 ppm	15.6± 1.0	15.8± 0.9	16.2± 0.9**	16.2± 1.0**	16.1± 1.0*	15.9± 1.0*	15.5± 1.1*

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

(HAN260)

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 74-7 (7)	78-7 (7)	82-7 (7)	86-7 (7)	90-7 (7)	94-7 (7)	98-7 (7)
Control	16.6± 1.0	16.1± 2.1	16.1± 1.4	16.3± 1.1	16.0± 1.5	16.2± 1.6	16.7± 1.2
625 ppm	16.6± 1.5	16.2± 1.9	16.4± 1.2	16.1± 1.4	16.0± 2.5	15.9± 1.7	16.1± 2.6
1250 ppm	16.6± 1.0	16.1± 1.0	16.0± 1.2	15.7± 1.9	15.7± 1.9	15.3± 2.3*	15.5± 2.4**
2500 ppm	15.5± 1.2**	15.0± 0.9**	14.9± 1.0**	15.0± 1.3**	14.8± 1.7**	14.7± 1.2**	14.3± 3.1**

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

(HAN260)

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 102-7 (7)	104-7 (7)
Control	15.9± 2.0	15.8± 2.5
625 ppm	15.2± 2.5	15.5± 2.2
1250 ppm	15.6± 1.5	15.6± 1.4
2500 ppm	14.4± 1.4**	14.3± 2.2**

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

(HAN260)

BAIS4

TABLE D 4

FOOD CONSUMPTION CHANGES: FEMALE

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 1-7 (7)	2-7 (7)	3-7 (7)	4-7 (7)	5-7 (7)	6-7 (7)	7-7 (7)
Control	11.0± 0.5	11.1± 0.6	11.0± 0.8	11.0± 0.7	10.9± 0.8	10.8± 0.8	10.4± 0.9
625 ppm	10.9± 0.7	11.2± 0.6	11.1± 0.7	11.2± 0.6	11.0± 0.6	10.7± 0.6	10.5± 0.7
1250 ppm	10.9± 0.5	10.9± 0.6	10.9± 0.6	11.0± 0.7	10.9± 0.7	10.7± 0.6	10.5± 0.7
2500 ppm	10.0± 0.5**	10.4± 0.6**	10.2± 0.6**	10.2± 0.6**	10.0± 0.6**	9.8± 0.6**	9.7± 0.6**

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

(HAN260)

BAIS4

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 8-7 (7)	9-7 (7)	10-7 (7)	11-7 (7)	12-7 (7)	13-7 (7)	14-7 (7)
Control	10.6± 0.9	10.7± 0.8	10.6± 0.8	10.7± 0.7	10.6± 0.8	10.5± 0.7	10.7± 0.8
625 ppm	10.5± 0.7	10.6± 0.6	10.7± 0.6	10.7± 0.7	10.9± 0.6	10.7± 0.6	11.0± 0.6*
1250 ppm	10.4± 0.7	10.4± 0.7	10.5± 0.7	10.6± 0.8	10.4± 0.6	10.4± 0.6	10.6± 0.6
2500 ppm	9.7± 0.6**	9.6± 0.8**	9.7± 0.7**	9.4± 0.6**	9.7± 0.7**	9.5± 0.6**	9.8± 0.6**

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

(HAN260)

BAIS4

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 18-7(7)	22-7(7)	26-7(7)	30-7(7)	34-7(7)	38-7(7)	42-7(7)
Control	10.7± 0.8	10.7± 0.8	11.0± 0.8	10.7± 0.8	10.8± 0.7	10.8± 0.7	11.0± 0.8
625 ppm	10.9± 0.6	11.0± 0.7	11.1± 0.6	11.1± 0.6*	11.0± 0.5	11.1± 0.6	11.4± 0.6*
1250 ppm	10.4± 0.6*	10.5± 0.6	10.9± 0.6	10.7± 0.6	10.9± 0.6	10.8± 0.6	11.0± 0.7
2500 ppm	9.5± 0.6**	9.5± 0.7**	9.8± 0.6**	9.6± 0.6**	9.8± 0.6**	9.7± 0.7**	10.0± 0.6**

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

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 46-7 (7)	50-7 (7)	54-7 (7)	58-7 (7)	62-7 (7)	66-7 (7)	70-7 (7)
Control	11.4± 0.7	11.1± 0.9	11.6± 1.1	11.7± 0.8	12.0± 1.0	12.0± 1.0	11.7± 0.9
625 ppm	11.4± 0.8	11.7± 0.8**	12.0± 0.9	12.0± 0.9	12.2± 1.0	12.1± 1.0	11.8± 1.1
1250 ppm	11.3± 0.8	11.1± 0.6	11.6± 0.7	11.6± 0.8	12.0± 0.9	11.6± 0.7	11.7± 1.2
2500 ppm	10.1± 0.6**	10.1± 0.8**	10.5± 0.7**	10.6± 0.9**	10.6± 0.9**	10.5± 1.0**	10.6± 1.1**

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

(HAN260)

BAIS 4

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 74-7 (7)	78-7 (7)	82-7 (7)	86-7 (7)	90-7 (7)	94-7 (7)	98-7 (7)
Control	12.1± 1.0	12.3± 1.0	12.5± 1.0	12.2± 1.0	12.4± 1.0	12.6± 1.2	13.0± 1.3
625 ppm	12.1± 1.3	12.5± 1.0	12.3± 1.0	12.2± 1.4	12.1± 2.5	12.6± 1.6	12.5± 1.0
1250 ppm	12.1± 1.0	11.9± 0.9*	11.9± 0.9*	11.8± 0.9	11.9± 1.1	12.3± 0.9	12.1± 1.8*
2500 ppm	10.7± 1.2**	10.8± 0.8**	10.9± 0.7**	10.9± 0.8**	10.9± 1.0**	11.1± 0.9**	11.3± 1.0**

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

(HAN260)

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 102-7 (7)	104-7 (7)
Control	13.2± 1.3	12.8± 1.6
625 ppm	12.8± 1.3	12.7± 1.1
1250 ppm	12.0± 1.7**	11.8± 1.6*
2500 ppm	11.4± 1.2**	11.4± 1.3**

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

(HAN260)

TABLE E 1

WATER CONSUMPTION CHANGES AND

SURVIVAL ANIMAL NUMBERS: MALE

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

MEAN WATER CONSUMPTION(WC) AND SURVIVAL

Week-Day on Study	Control Av. WC.	Control No. of Surviv. <50>	625 ppm Av. WC.	625 ppm % of cont. <50>	625 ppm No. of Surviv.	1250 ppm Av. WC.	1250 ppm % of cont. <50>	1250 ppm No. of Surviv.	2500 ppm Av. WC.	2500 ppm % of cont. <50>	2500 ppm No. of Surviv.
1-7	17.5 (50)	50/50	17.0 (50)	97	50/50	16.3 (50)	93	50/50	13.8 (49)	79	50/50
2-7	19.4 (50)	50/50	18.6 (50)	96	50/50	17.7 (50)	91	50/50	14.6 (50)	75	50/50
3-7	20.4 (48)	50/50	19.3 (49)	95	50/50	18.6 (50)	91	50/50	14.8 (50)	73	50/50
4-7	20.0 (50)	50/50	18.8 (50)	94	50/50	18.0 (50)	90	50/50	14.7 (50)	74	50/50
5-7	20.0 (49)	50/50	19.0 (50)	95	50/50	18.2 (49)	91	50/50	15.3 (50)	77	50/50
6-7	19.6 (49)	50/50	18.3 (49)	93	50/50	18.1 (50)	92	50/50	15.2 (50)	78	50/50
7-7	19.0 (49)	50/50	18.3 (50)	96	50/50	17.6 (50)	93	50/50	14.6 (50)	77	50/50
8-7	18.5 (49)	50/50	17.9 (50)	97	50/50	17.3 (50)	94	50/50	14.3 (50)	77	50/50
9-7	18.5 (49)	50/50	18.0 (50)	97	50/50	17.2 (50)	93	50/50	14.5 (50)	78	50/50
10-7	19.0 (50)	50/50	17.8 (50)	94	50/50	17.1 (50)	90	50/50	14.2 (50)	75	50/50
11-7	18.3 (50)	50/50	17.2 (50)	94	50/50	16.5 (50)	90	50/50	13.9 (50)	76	50/50
12-7	18.0 (50)	50/50	17.0 (50)	94	50/50	16.1 (50)	89	50/50	13.6 (50)	76	50/50
13-7	18.2 (50)	50/50	16.9 (50)	93	50/50	16.2 (50)	89	50/50	13.6 (50)	75	50/50
14-7	17.6 (49)	50/50	16.9 (50)	96	50/50	16.0 (50)	91	50/50	13.4 (50)	76	50/50
18-7	17.2 (50)	50/50	16.7 (50)	97	50/50	16.1 (50)	94	50/50	13.6 (50)	79	50/50
22-7	17.4 (50)	50/50	16.7 (50)	96	50/50	15.9 (50)	91	50/50	13.5 (50)	78	50/50
26-7	17.0 (50)	50/50	16.3 (50)	96	50/50	15.5 (50)	91	50/50	13.2 (50)	78	50/50
30-7	16.9 (50)	50/50	16.7 (50)	99	50/50	15.8 (50)	93	50/50	13.8 (50)	82	50/50
34-7	16.9 (50)	50/50	16.4 (50)	97	50/50	15.6 (50)	92	50/50	13.8 (50)	82	50/50
38-7	16.7 (50)	50/50	16.3 (49)	98	49/50	15.6 (50)	93	50/50	13.9 (50)	83	50/50
42-7	16.6 (49)	49/50	16.4 (49)	99	49/50	15.5 (49)	93	50/50	13.6 (50)	82	50/50
46-7	16.9 (49)	49/50	16.6 (49)	98	49/50	15.9 (49)	94	49/50	14.0 (50)	83	50/50
50-7	17.2 (49)	49/50	16.7 (49)	97	49/50	16.0 (48)	93	48/50	14.0 (50)	81	50/50
54-7	17.4 (49)	49/50	17.0 (49)	98	49/50	16.2 (48)	93	48/50	14.2 (50)	82	50/50
58-7	17.1 (49)	49/50	16.5 (49)	96	49/50	15.8 (48)	92	48/50	13.6 (49)	80	49/50
62-7	16.8 (49)	49/50	16.7 (48)	99	49/50	15.6 (48)	93	48/50	13.6 (48)	81	48/50
66-7	17.1 (49)	49/50	17.4 (49)	102	49/50	16.4 (47)	96	47/50	14.5 (48)	85	48/50
70-7	17.0 (49)	49/50	17.1 (49)	101	49/50	16.5 (46)	97	47/50	14.4 (48)	85	48/50
74-7	18.2 (49)	49/50	17.5 (48)	96	48/50	16.8 (46)	92	47/50	14.8 (48)	81	48/50
78-7	17.8 (49)	49/50	17.7 (48)	99	48/50	16.9 (46)	95	46/50	15.3 (47)	86	47/50
82-7	18.7 (48)	48/50	18.9 (46)	101	46/50	17.8 (46)	95	46/50	15.4 (45)	82	47/50
86-7	19.4 (48)	48/50	19.7 (46)	102	46/50	18.2 (46)	94	46/50	16.9 (47)	87	47/50
90-7	19.3 (47)	48/50	18.5 (41)	96	45/50	17.7 (42)	92	44/50	15.6 (45)	81	45/50
94-7	19.9 (44)	45/50	19.8 (40)	99	44/50	19.3 (38)	97	39/50	16.0 (38)	80	40/50
98-7	19.9 (43)	43/50	22.0 (42)	111	43/50	20.4 (36)	103	36/50	16.4 (39)	82	39/50
102-7	19.1 (39)	42/50	19.8 (30)	104	40/50	19.4 (30)	102	34/50	17.3 (36)	91	36/50
104-7	18.9 (36)	40/50	20.6 (33)	109	39/50	18.7 (28)	99	33/50	17.4 (34)	92	34/50

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

(BI0040)

TABLE E 2

WATER CONSUMPTION CHANGES AND SURVIVAL ANIMAL NUMBERS: FEMALE

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

MEAN WATER CONSUMPTION(WC) AND SURVIVAL

Week-Day on Study	Control Av. WC.	Control No. of Surviv. <50>	625 ppm Av. WC.	625 ppm % of cont. <50>	625 ppm No. of Surviv.	1250 ppm Av. WC.	1250 ppm % of cont. <50>	1250 ppm No. of Surviv.	2500 ppm Av. WC.	2500 ppm % of cont. <50>	2500 ppm No. of Surviv.
1-7	15.5 (49)	50/50	15.1 (49)	97	50/50	14.2 (49)	92	50/50	11.2 (50)	72	50/50
2-7	17.2 (46)	50/50	16.1 (47)	94	50/50	14.6 (47)	85	50/50	10.9 (50)	63	50/50
3-7	18.6 (49)	50/50	18.3 (49)	98	50/50	15.9 (49)	85	50/50	10.9 (50)	59	50/50
4-7	16.9 (47)	50/50	16.7 (46)	99	50/50	14.9 (48)	88	50/50	10.3 (50)	61	50/50
5-7	17.2 (46)	50/50	17.6 (47)	102	50/50	14.0 (48)	81	50/50	10.5 (50)	61	50/50
6-7	17.8 (44)	50/50	16.8 (44)	94	50/50	14.2 (48)	80	50/50	10.5 (50)	59	50/50
7-7	18.4 (45)	50/50	16.9 (42)	92	50/50	14.0 (48)	76	50/50	10.1 (50)	55	50/50
8-7	17.8 (42)	50/50	16.6 (44)	93	50/50	14.0 (50)	79	50/50	10.0 (50)	56	50/50
9-7	18.0 (45)	50/50	17.0 (45)	94	50/50	14.2 (50)	79	50/50	9.5 (50)	53	50/50
10-7	18.7 (47)	50/50	16.4 (41)	88	50/50	13.4 (49)	72	50/50	9.5 (50)	51	50/50
11-7	18.9 (45)	50/50	16.8 (45)	89	50/50	13.7 (48)	72	50/50	9.5 (50)	50	50/50
12-7	17.7 (44)	50/50	16.8 (41)	95	50/50	13.8 (49)	78	50/50	9.7 (50)	55	50/50
13-7	17.6 (45)	50/50	15.9 (40)	90	50/50	13.6 (50)	77	50/50	9.4 (50)	53	50/50
14-7	18.9 (42)	50/50	17.3 (44)	92	50/50	14.0 (49)	74	50/50	9.7 (50)	51	50/50
18-7	19.7 (41)	50/50	18.1 (39)	92	50/50	14.0 (48)	71	50/50	9.8 (50)	50	50/50
22-7	19.9 (44)	50/50	17.7 (41)	89	50/50	14.4 (47)	72	50/50	9.9 (50)	50	50/50
26-7	19.3 (45)	50/50	18.2 (40)	94	50/50	14.8 (46)	77	50/50	10.0 (50)	52	50/50
30-7	18.1 (48)	50/50	17.0 (42)	94	50/50	14.4 (48)	80	50/50	9.7 (50)	54	50/50
34-7	17.7 (48)	50/50	17.0 (45)	96	50/50	14.3 (48)	81	50/50	10.1 (49)	57	49/50
38-7	17.3 (47)	50/50	16.1 (45)	93	50/50	13.3 (48)	77	50/50	10.1 (49)	58	49/50
42-7	16.8 (47)	50/50	16.4 (45)	98	50/50	14.5 (49)	86	50/50	10.4 (49)	62	49/50
46-7	17.1 (48)	50/50	17.2 (45)	101	50/50	14.7 (48)	86	50/50	10.7 (49)	63	49/50
50-7	15.5 (48)	50/50	16.1 (46)	104	50/50	14.1 (48)	91	50/50	10.9 (49)	70	49/50
54-7	15.1 (50)	50/50	15.5 (49)	103	50/50	13.7 (50)	91	50/50	10.8 (48)	72	48/50
58-7	15.3 (47)	49/50	15.7 (47)	103	50/50	13.4 (49)	88	50/50	11.5 (48)	75	48/50
62-7	15.6 (48)	49/50	16.4 (48)	105	50/50	13.7 (50)	88	50/50	10.9 (47)	70	47/50
66-7	15.4 (49)	49/50	15.6 (49)	101	50/50	13.2 (48)	86	49/50	11.4 (46)	74	46/50
70-7	14.9 (49)	49/50	14.5 (49)	97	49/50	12.9 (48)	87	48/50	11.6 (46)	78	46/50
74-7	15.7 (49)	49/50	14.6 (48)	93	48/50	13.4 (48)	85	48/50	11.9 (45)	76	45/50
78-7	15.6 (48)	48/50	15.9 (47)	102	47/50	13.6 (48)	87	48/50	12.1 (43)	78	43/50
82-7	16.4 (47)	47/50	16.7 (46)	102	47/50	14.8 (48)	90	48/50	12.9 (39)	79	39/50
86-7	17.5 (46)	47/50	16.2 (46)	93	47/50	15.0 (47)	86	47/50	13.5 (39)	77	39/50
90-7	16.5 (47)	47/50	15.5 (45)	94	46/50	14.3 (45)	87	45/50	13.1 (39)	79	39/50
94-7	16.4 (45)	46/50	16.3 (42)	99	43/50	15.2 (44)	93	45/50	13.1 (37)	80	37/50
98-7	17.4 (43)	44/50	17.0 (42)	98	42/50	15.5 (44)	89	45/50	13.2 (35)	76	35/50
102-7	17.9 (41)	43/50	17.5 (41)	98	41/50	15.5 (43)	87	44/50	13.6 (35)	76	35/50
104-7	17.1 (40)	43/50	17.4 (40)	102	40/50	15.6 (41)	91	42/50	13.7 (35)	80	35/50

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

TABLE E 3

WATER CONSUMPTION CHANGES: MALE

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 1-7 (3)	2-7 (3)	3-7 (3)	4-7 (3)	5-7 (3)	6-7 (3)	7-7 (3)
Control	17.5± 1.2	19.4± 1.9	20.4± 1.5	20.0± 1.8	20.0± 1.5	19.6± 2.0	19.0± 1.6
625 ppm	17.0± 1.1	18.6± 1.4	19.3± 1.8**	18.8± 1.4**	19.0± 1.4**	18.3± 1.2**	18.3± 1.7**
1250 ppm	16.3± 1.3**	17.7± 1.3**	18.6± 1.7**	18.0± 1.2**	18.2± 1.2**	18.1± 2.1**	17.6± 1.4**
2500 ppm	13.8± 1.0**	14.6± 1.4**	14.8± 1.0**	14.7± 0.9**	15.3± 0.9**	15.2± 1.0**	14.6± 1.1**

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

(HAN260)

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 8-7 (3)	9-7 (3)	10-7 (3)	11-7 (3)	12-7 (3)	13-7 (3)	14-7 (3)
Control	18.5± 1.4	18.5± 1.5	19.0± 1.8	18.3± 1.7	18.0± 1.9	18.2± 1.4	17.6± 1.7
625 ppm	17.9± 1.3	18.0± 1.5	17.8± 1.1**	17.2± 1.2**	17.0± 1.1**	16.9± 1.1**	16.9± 1.0
1250 ppm	17.3± 1.6**	17.2± 1.4**	17.1± 1.2**	16.5± 1.1**	16.1± 1.1**	16.2± 1.0**	16.0± 1.1**
2500 ppm	14.3± 1.0**	14.5± 0.7**	14.2± 0.9**	13.9± 0.9**	13.6± 0.8**	13.6± 0.8**	13.4± 0.9**

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

(HAN260)

BAIS4

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 18-7 (3)	22-7 (3)	26-7 (3)	30-7 (3)	34-7 (3)	38-7 (3)	42-7 (3)
Control	17.2± 1.4	17.4± 1.7	17.0± 2.1	16.9± 1.6	16.9± 1.2	16.7± 1.0	16.6± 1.1
625 ppm	16.7± 1.1	16.7± 1.2	16.3± 0.9	16.7± 1.3	16.4± 1.1*	16.3± 1.4*	16.4± 1.2
1250 ppm	16.1± 1.0**	15.9± 1.0**	15.5± 1.0**	15.8± 0.9**	15.6± 0.9**	15.6± 1.0**	15.5± 1.0**
2500 ppm	13.6± 0.9**	13.5± 0.8**	13.2± 0.9**	13.8± 1.0**	13.8± 0.8**	13.9± 0.9**	13.6± 0.9**

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

(HAN260)

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 46-7 (3)	50-7 (3)	54-7 (3)	58-7 (3)	62-7 (3)	66-7 (3)	70-7 (3)
Control	16.9± 1.2	17.2± 1.3	17.4± 1.2	17.1± 1.3	16.8± 1.3	17.1± 1.4	17.0± 1.5
625 ppm	16.6± 1.1	16.7± 1.2	17.0± 1.4	16.5± 1.6	16.7± 1.6	17.4± 1.6	17.1± 1.8
1250 ppm	15.9± 1.1**	16.0± 1.0**	16.2± 1.5**	15.8± 1.4**	15.6± 2.2**	16.4± 1.3	16.5± 1.7
2500 ppm	14.0± 1.1**	14.0± 1.0**	14.2± 1.1**	13.6± 1.2**	13.6± 1.1**	14.5± 1.5**	14.4± 1.8**

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

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 74-7 (3)	78-7 (3)	82-7 (3)	86-7 (3)	90-7 (3)	94-7 (3)	98-7 (3)
Control	18.2± 1.7	17.8± 2.5	18.7± 2.7	19.4± 2.6	19.3± 3.3	19.9± 3.8	19.9± 4.5
625 ppm	17.5± 2.6	17.7± 2.8	18.9± 3.3	19.7± 4.3	18.5± 4.0	19.8± 4.2	22.0± 7.8
1250 ppm	16.8± 1.3**	16.9± 1.8*	17.8± 2.3	18.2± 2.9	17.7± 3.0	19.3± 4.0	20.4± 6.2
2500 ppm	14.8± 2.4**	15.3± 2.5**	15.4± 2.0**	16.9± 4.7**	15.6± 3.8**	16.0± 2.3**	16.4± 5.9**

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

(HAN260)

BAIS4

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration 102-7(3)	week-day(effective) 104-7(3)
Control	19.1± 4.9	18.9± 4.1
625 ppm	19.8± 4.3	20.6± 4.5
1250 ppm	19.4± 4.0	18.7± 3.2
2500 ppm	17.3± 3.9	17.4± 4.8

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

(HAN260)

BAIS4

TABLE E 4

WATER CONSUMPTION CHANGES: FEMALE

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration 1-7 (3)	week-day (effective) 2-7 (3)	3-7 (3)	4-7 (3)	5-7 (3)	6-7 (3)	7-7 (3)
Control	15.5± 1.6	17.2± 3.0	18.6± 5.9	16.9± 3.0	17.2± 3.1	17.8± 4.0	18.4± 4.7
625 ppm	15.1± 1.3	16.1± 2.2	18.3± 6.1	16.7± 4.2	17.6± 4.1	16.8± 3.8	16.9± 4.1
1250 ppm	14.2± 1.2**	14.6± 2.2**	15.9± 5.2**	14.9± 3.8**	14.0± 1.8**	14.2± 2.2**	14.0± 2.5**
2500 ppm	11.2± 1.0**	10.9± 0.7**	10.9± 0.8**	10.3± 0.9**	10.5± 1.1**	10.5± 1.0**	10.1± 1.5**

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

(HAN260)

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 8-7 (3)	9-7 (3)	10-7 (3)	11-7 (3)	12-7 (3)	13-7 (3)	14-7 (3)
Control	17.8± 3.8	18.0± 4.1	18.7± 4.0	18.9± 4.6	17.7± 3.7	17.6± 3.5	18.9± 4.2
625 ppm	16.6± 3.7	17.0± 4.6	16.4± 3.3**	16.8± 3.7	16.8± 3.9	15.9± 3.5*	17.3± 3.9
1250 ppm	14.0± 3.2**	14.2± 4.3**	13.4± 2.0**	13.7± 2.9**	13.8± 3.3**	13.6± 3.4**	14.0± 3.3**
2500 ppm	10.0± 2.4**	9.5± 1.3**	9.5± 1.9**	9.5± 1.4**	9.7± 1.3**	9.4± 0.9**	9.7± 1.3**

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

(HAN260)

BAIS4

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 18-7 (3)	22-7 (3)	26-7 (3)	30-7 (3)	34-7 (3)	38-7 (3)	42-7 (3)
Control	19.7± 4.6	19.9± 4.6	19.3± 4.1	18.1± 4.4	17.7± 4.4	17.3± 4.5	16.8± 3.3
625 ppm	18.1± 4.9	17.7± 4.4*	18.2± 5.3	17.0± 4.6	17.0± 4.5	16.1± 4.3	16.4± 3.9
1250 ppm	14.0± 3.0**	14.4± 3.8**	14.8± 3.7**	14.4± 3.7**	14.3± 3.7**	13.3± 2.4**	14.5± 3.6**
2500 ppm	9.8± 1.1**	9.9± 1.0**	10.0± 1.2**	9.7± 1.0**	10.1± 0.9**	10.1± 1.0**	10.4± 1.2**

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

(HAN260)

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 46-7 (3)	50-7 (3)	54-7 (3)	58-7 (3)	62-7 (3)	66-7 (3)	70-7 (3)
Control	17.1± 3.4	15.5± 3.6	15.1± 2.8	15.3± 3.1	15.6± 3.2	15.4± 2.8	14.9± 2.5
625 ppm	17.2± 4.5	16.1± 4.2	15.5± 3.5	15.7± 3.8	16.4± 4.3	15.6± 4.4	14.5± 3.3
1250 ppm	14.7± 3.9**	14.1± 3.5**	13.7± 3.1**	13.4± 2.4**	13.7± 3.2**	13.2± 1.9**	12.9± 1.5**
2500 ppm	10.7± 1.1**	10.9± 1.9**	10.8± 1.6**	11.5± 1.9**	10.9± 1.2**	11.4± 1.4**	11.6± 1.9**

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

(HAN260)

BAIS4

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 74-7 (3)	78-7 (3)	82-7 (3)	86-7 (3)	90-7 (3)	94-7 (3)	98-7 (3)
Control	15.7± 2.5	15.6± 2.8	16.4± 2.7	17.5± 3.8	16.5± 3.0	16.4± 2.8	17.4± 3.6
625 ppm	14.6± 3.1*	15.9± 3.6	16.7± 3.8	16.2± 3.7	15.5± 3.5	16.3± 3.2	17.0± 3.9
1250 ppm	13.4± 1.6**	13.6± 1.9**	14.8± 2.7**	15.0± 2.4**	14.3± 2.4**	15.2± 3.4*	15.5± 3.3*
2500 ppm	11.9± 1.7**	12.1± 1.4**	12.9± 1.6**	13.5± 1.6**	13.1± 2.5**	13.1± 2.1**	13.2± 2.1**

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

(HAN260)

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day (effective) 102-7 (3)	104-7 (3)
Control	17.9± 3.9	17.1± 3.2
625 ppm	17.5± 4.3	17.4± 3.8
1250 ppm	15.5± 3.0**	15.6± 3.1
2500 ppm	13.6± 2.9**	13.7± 3.0**

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

TABLE F 1

CHEMICAL INTAKE CHANGES: MALE

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : mg／kg／day
REPORT TYPE : A1 104
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1		2		3		4		5		6		7	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
625 ppm	69±	4	62±	4	57±	5	50±	3	47±	3	43±	3	41±	3
1250 ppm	133±	9	118±	7	109±	9	96±	6	91±	6	86±	11	79±	6
2500 ppm	230±	14	202±	19	181±	10	163±	7	159±	7	150±	7	138±	8

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : mg／kg／day
REPORT TYPE : A1 104
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8		9		10		11		12		13		14	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
625 ppm	39±	2	37±	3	36±	2	34±	2	33±	2	32±	2	32±	2
1250 ppm	74±	6	72±	6	69±	5	65±	4	62±	4	61±	3	59±	3
2500 ppm	129±	7	126±	6	121±	7	115±	7	111±	6	109±	6	105±	6

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : mg／kg／day
REPORT TYPE : A1 104
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 18		22		26		30		34		38		42	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
625 ppm	30±	2	28±	2	27±	1	27±	2	25±	2	25±	2	25±	2
1250 ppm	57±	4	54±	3	51±	3	50±	3	48±	2	48±	2	46±	3
2500 ppm	102±	6	98±	5	93±	5	94±	6	91±	5	91±	4	87±	5

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : mg／kg／day
REPORT TYPE : A1 104
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 46		50		54		58		62		66		70	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
625 ppm	24±	2	24±	2	24±	2	23±	2	23±	2	24±	2	23±	2
1250 ppm	47±	3	46±	3	46±	4	44±	4	44±	6	45±	3	45±	5
2500 ppm	89±	5	88±	6	88±	6	83±	5	82±	5	88±	7	87±	10

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : mg／kg／day
REPORT TYPE : A1 104
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 74		78		82		86		90		94		98	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
625 ppm	24±	3	24±	3	25±	4	27±	5	26±	5	28±	7	31±	11
1250 ppm	46±	4	46±	4	49±	6	51±	8	50±	8	56±	15	62±	27
2500 ppm	89±	13	92±	15	94±	13	105±	35	98±	28	101±	16	106±	40

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : mg／kg／day
REPORT TYPE : A1 104
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 102		104	
Control	0±	0	0±	0
625 ppm	29±	9	31±	11
1250 ppm	59±	19	59±	19
2500 ppm	116±	30	118±	35

TABLE F 2

CHEMICAL INTAKE CHANGES: FEMALE

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : mg／kg／day
REPORT TYPE : A1 104
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1		2		3		4		5		6		7	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
625 ppm	80±	6	76±	9	81±	26	70±	17	70±	17	65±	15	63±	15
1250 ppm	152±	11	141±	19	143±	47	126±	33	113±	12	110±	18	105±	17
2500 ppm	248±	19	217±	11	203±	13	182±	13	177±	17	172±	15	160±	20

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : mg/kg/day
REPORT TYPE : A1 104
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8		9		10		11		12		13		14	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
625 ppm	61±	14	61±	16	58±	12	58±	12	57±	13	53±	11	56±	13
1250 ppm	103±	25	102±	30	94±	14	93±	18	94±	23	91±	22	92±	21
2500 ppm	154±	35	143±	16	141±	26	139±	19	141±	18	135±	11	137±	17

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : mg／kg／day
REPORT TYPE : A1 104
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 18		22		26		30		34		38		42	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
625 ppm	57±	16	55±	14	54±	16	50±	15	49±	14	45±	13	45±	11
1250 ppm	90±	18	89±	24	90±	23	85±	21	82±	21	75±	13	81±	20
2500 ppm	135±	14	133±	11	133±	13	126±	10	128±	9	128±	11	130±	12

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : mg／kg／day
REPORT TYPE : A1 104
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 46		50		54		58		62		66		70	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
625 ppm	46±	13	42±	11	39±	9	39±	10	40±	10	37±	11	34±	8
1250 ppm	80±	21	76±	18	72±	17	69±	14	69±	19	64±	10	63±	9
2500 ppm	133±	11	136±	32	130±	24	136±	27	127±	15	132±	19	133±	29

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : mg／kg／day
REPORT TYPE : A1 104
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 74		78		82		86		90		94		98	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
625 ppm	34±	6	35±	9	36±	8	35±	8	33±	8	34±	7	36±	9
1250 ppm	63±	9	63±	10	67±	13	68±	12	64±	12	67±	17	68±	17
2500 ppm	134±	24	132±	22	137±	21	142±	23	138±	30	138±	28	136±	27

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : mg／kg／d a y
REPORT TYPE : A1 104
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 102		104	
Control	0±	0	0±	0
625 ppm	38±	11	37±	9
1250 ppm	69±	15	69±	16
2500 ppm	140±	30	142±	34

(HAN300)

BAIS 5

TABLE G 1

HEMATOLOGY: MALE

STUDY NO. : 0711
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	39	7.71± 1.78	12.8± 2.9	38.5± 7.2	51.6± 10.5	16.9± 2.6	32.9± 2.1	944± 355
625 ppm	37	7.88± 1.35	13.1± 2.3	39.2± 5.8	50.0± 3.0	16.6± 1.1	33.2± 1.3	958± 331
1250 ppm	32	8.25± 1.07	13.7± 1.9	40.7± 5.1	49.3± 2.3	16.6± 1.1	33.6± 1.1	959± 257
2500 ppm	34	8.17± 1.79	13.6± 2.9	40.5± 7.7	50.0± 3.5	16.7± 1.1	33.4± 1.2	970± 420

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

(HCL070)

BAIS4

STUDY NO. : 0711
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 %	METHEMOGLOBIN %
Control	39	7.0± 10.4	0.8± 0.5
625 ppm	37	4.7± 3.6	0.8± 0.5
1250 ppm	32	3.5± 1.7	0.7± 0.3
2500 ppm	34	4.4± 3.0	0.8± 0.2

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

(HCL070)

BAIS 4

STUDY NO. : 0711
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	39	10.23± 13.79	47± 13	46± 13	5± 1	1± 1	0± 1	2± 1
625 ppm	37	6.25± 1.83	50± 10	42± 9	5± 1	2± 1	0± 0	2± 1
1250 ppm	32	5.98± 1.93	50± 6	42± 6	5± 1	1± 1	0± 0	2± 1
2500 ppm	34	6.66± 1.77	49± 9	43± 9	5± 2	2± 1	0± 0	2± 1

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

(HCL070)

BAIS4

TABLE G 2

HEMATOLOGY: FEMALE

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV fℓ	MCH pg	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	43	8.20± 0.87	14.8± 1.5	42.4± 3.6	51.9± 2.8	18.0± 1.0	34.8± 1.2	698± 138
625 ppm	40	8.21± 0.91	14.7± 1.5	42.4± 3.8	51.9± 2.9	18.0± 0.8	34.7± 0.9	711± 179
1250 ppm	42	7.97± 1.17	14.4± 2.2	41.5± 5.2	52.3± 3.1	18.0± 1.2	34.5± 1.9	687± 152
2500 ppm	35	8.31± 0.56	14.8± 0.9	42.6± 2.5	51.3± 1.1	17.9± 0.5	34.8± 0.5	724± 92

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

(HCL070)

BAIS 4

STUDY NO. : 0711
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 %	METHEMOGLOBIN %
Control	43	3.0± 2.0	0.6± 0.2
625 ppm	40	3.6± 4.0	0.7± 0.3
1250 ppm	42	4.3± 6.0	0.7± 0.3
2500 ppm	35	2.8± 1.0	0.7± 0.2

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

(HCL070)

BAIS4

STUDY NO. : 0711
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	43	3.87±	2.68	43±	10	50±	11	5±	1	2±	1	0±	0	1±	1
625 ppm	40	3.17±	1.06	42±	9	51±	9	4±	1	2±	1	0±	0	1±	1
1250 ppm	42	4.33±	6.39	44±	11	49±	10	4±	1**	2±	1	0±	0	2±	3**
2500 ppm	35	3.25±	1.69	42±	8	48±	10	6±	3**	2±	1	0±	0	2±	3*

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

(HCL070)

BAIS 4

TABLE H 1

BIOCHEMISTRY: MALE

STUDY NO. : 0711
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	39	6.8± 0.5	2.9± 0.3	0.7± 0.2	1.15± 5.72	138± 25	182± 51	131± 83
625 ppm	37	6.7± 0.3	2.8± 0.2	0.7± 0.1	0.15± 0.06	140± 27	190± 69	140± 130
1250 ppm	32	6.9± 0.3	2.8± 0.3	0.7± 0.1	0.14± 0.04	141± 24	204± 67	155± 102
2500 ppm	34	6.7± 0.4	2.8± 0.3	0.7± 0.1	0.15± 0.04	142± 16	199± 65	132± 81

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

(HCL074)

BAIS 5

STUDY NO. : 0711
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 U/L	ALT U/L	LDH U/L	ALP U/L	G-GTP U/L	CK U/L
Control	39	265± 62	122± 179	40± 20	159± 219	384± 214	8± 6	111± 100
625 ppm	37	277± 95	85± 47	38± 13	103± 30	311± 84	7± 4	95± 21
1250 ppm	32	289± 95	104± 190	49± 86	112± 40	301± 95	9± 6	103± 43
2500 ppm	34	280± 88	78± 25	36± 10	100± 28	338± 81	13± 7**	94± 21

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

(HCL074)

BAIS 5

STUDY NO. : 0711
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	39	19.5± 4.5	0.6± 0.1	142± 2	3.8± 0.3	106± 2	10.7± 0.3	4.0± 0.7
625 ppm	37	23.6± 12.0	0.8± 0.4	142± 1	3.7± 0.3	106± 2	10.8± 0.7	4.3± 1.2
1250 ppm	32	24.0± 7.7**	0.7± 0.3	142± 1	3.7± 0.4	106± 1	10.9± 0.5	4.1± 0.8
2500 ppm	34	24.6± 6.4**	0.7± 0.1	142± 2	3.7± 0.3	106± 2	10.6± 0.5	4.0± 0.5

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

(HCL074)

BAIS 5

TABLE H 2

BIOCHEMISTRY: FEMALE

STUDY NO. : 0711
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	43	7.1± 0.5	3.6± 0.4	1.0± 0.1	0.12± 0.02	142± 17	151± 51	125± 126
625 ppm	40	7.2± 0.4	3.7± 0.3	1.0± 0.1	0.13± 0.05	141± 14	151± 36	95± 46
1250 ppm	42	7.1± 0.4	3.6± 0.3	1.0± 0.1	0.13± 0.07	140± 15	142± 46	93± 54
2500 ppm	35	7.1± 0.4	3.6± 0.3	1.0± 0.1	0.13± 0.01**	142± 12	147± 35	77± 55**

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

(HCL074)

BAIS 5

STUDY NO. : 0711
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 U/L	ALT U/L	LDH U/L	ALP U/L	G-GTP U/L	CK U/L
Control	43	269± 82	112± 58	46± 21	134± 56	200± 150	2± 1	80± 23
625 ppm	40	268± 51	143± 89	56± 30	158± 73	194± 111	2± 2	80± 16
1250 ppm	42	255± 69	131± 87	49± 22	152± 78	244± 421	3± 3	83± 21
2500 ppm	35	258± 52	104± 38	44± 12	122± 50	204± 79	3± 3	82± 14

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

(HCL074)

BAIS 5

STUDY NO. : 0711
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	43	17.5± 2.9	0.6± 0.1	141± 2	3.5± 0.3	104± 2	10.8± 0.3	3.8± 0.8
625 ppm	40	17.1± 1.9	0.6± 0.1	141± 2	3.4± 0.4	104± 2	10.8± 0.4	3.5± 0.7
1250 ppm	42	16.8± 1.9	0.6± 0.1	141± 2	3.5± 0.4	104± 2	10.7± 0.4	3.6± 0.7
2500 ppm	35	18.9± 3.0**	0.5± 0.1	141± 2	3.4± 0.4	104± 2	10.7± 0.4	3.8± 0.5

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

(HCL074)

BAIS 5

TABLE I 1

URINALYSIS: MALE

STUDY NO. : 0711
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	41	0	2	4	10	12	10	3		0	0	0	1	11	29		41	0	0	0	0	0		33	8	0	0	0	0		39	0	0	2	
625 ppm	39	0	1	4	8	12	10	4		0	0	1	0	11	27		39	0	0	0	0	0		35	3	1	0	0	0		39	0	0	0	
1250 ppm	34	0	0	5	5	7	13	4		0	0	0	0	6	28		34	0	0	0	0	0		28	6	0	0	0	0		34	0	0	0	
2500 ppm	34	0	0	3	11	8	12	0		0	0	0	0	4	30		34	0	0	0	0	0		27	7	0	0	0	0		34	0	0	0	

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

(HCL101)

BAIS5

STUDY NO. : 0711
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	41	37	1	1	2	0		40	0	1	0	0	
625 ppm	39	38	0	0	0	1		39	0	0	0	0	
1250 ppm	34	34	0	0	0	0		34	0	0	0	0	
2500 ppm	34	34	0	0	0	0		34	0	0	0	0	

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

(HCL101)

BAIS5

TABLE I 2

URINALYSIS: FEMALE

STUDY NO. : 0711
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	43	0	0	0	10	13	15	5		0	0	0	9	28	6		43	0	0	0	0	0		25	18	0	0	0	0		43	0	0	0	
625 ppm	40	0	0	1	3	9	17	10		0	0	0	12	25	3		40	0	0	0	0	0		21	19	0	0	0	0		40	0	0	0	
1250 ppm	43	0	2	1	6	9	14	11		0	0	1	10	28	4		43	0	0	0	0	0		21	21	0	0	1	0		43	0	0	0	
2500 ppm	35	0	1	0	6	12	12	4		0	0	0	2	30	3		35	0	0	0	0	0		18	16	1	0	0	0		35	0	0	0	

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

(HCL101)

STUDY NO. : 0711
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	43	42	1	0	0	0		43	0	0	0	0	
625 ppm	40	40	0	0	0	0		40	0	0	0	0	
1250 ppm	43	41	1	1	0	0		43	0	0	0	0	
2500 ppm	35	30	0	0	0	5	*	35	0	0	0	0	

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

(HCL101)

BAIS5

TABLE K 1

ORGAN WEIGHT, ABSOLUTE: MALE

STUDY NO. : 0711
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	39	413± 36	0.080± 0.022	2.755± 1.170	1.280± 0.099	1.492± 0.284	2.807± 0.250
625 ppm	37	400± 49	0.103± 0.133	2.607± 1.149	1.255± 0.113	1.427± 0.119	2.902± 0.502
1250 ppm	32	384± 45*	0.073± 0.015	3.252± 1.448	1.217± 0.117	1.402± 0.092	2.906± 0.329
2500 ppm	34	348± 38**	0.068± 0.015**	2.967± 1.262	1.138± 0.132**	1.326± 0.077**	2.747± 0.229

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

(HCL040)

BAIS 5

STUDY NO. : 0711
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	39	2.763±	7.157	12.103±	2.716	2.127±	0.041
625 ppm	37	1.226±	0.993	11.866±	1.773	2.113±	0.048
1250 ppm	32	1.115±	0.438	11.557±	1.608	2.111±	0.047
2500 ppm	34	0.969±	0.172	10.717±	1.039*	2.109±	0.050

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

(HCL040)

BAIS5

TABLE K 2

ORGAN WEIGHT, ABSOLUTE: FEMALE

STUDY NO. : 0711
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	43	293± 38	0.074± 0.013	0.193± 0.223	0.942± 0.115	1.036± 0.118	1.922± 0.266
625 ppm	40	278± 25	0.071± 0.010	0.171± 0.100	0.916± 0.066	1.000± 0.070	1.923± 0.180
1250 ppm	42	266± 22**	0.071± 0.009	0.159± 0.063	0.888± 0.081*	1.005± 0.127	1.927± 0.152
2500 ppm	35	233± 34**	0.065± 0.012**	0.165± 0.165	0.829± 0.051**	0.943± 0.062**	1.974± 0.127

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

(HCL040)

BAIS 5

STUDY NO. : 0711
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	43	0.729±	0.470	7.536±	1.487	1.938±	0.065
625 ppm	40	0.659±	0.282	7.116±	1.125	1.921±	0.041
1250 ppm	42	1.132±	2.114	6.997±	0.848	1.920±	0.046
2500 ppm	35	0.519±	0.078**	6.593±	1.309**	1.910±	0.041

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

(HCL040)

BAIS5

TABLE L 1

ORGAN WEIGHT, RELATIVE: MALE

STUDY NO. : 0711
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	39	413± 36	0.019± 0.005	0.677± 0.299	0.312± 0.034	0.365± 0.088	0.686± 0.088
625 ppm	37	400± 49	0.027± 0.038	0.655± 0.294	0.317± 0.036	0.362± 0.047	0.743± 0.200
1250 ppm	32	384± 45*	0.020± 0.006	0.842± 0.347	0.321± 0.043	0.372± 0.062	0.774± 0.174**
2500 ppm	34	348± 38**	0.020± 0.005	0.842± 0.342	0.330± 0.049	0.384± 0.041**	0.796± 0.097**

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

(HCL042)

BAIS 5

STUDY NO. : 0711
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	39	0.692± 1.828	2.940± 0.665	0.520± 0.050
625 ppm	37	0.303± 0.217	2.993± 0.475	0.537± 0.065
1250 ppm	32	0.290± 0.107	3.024± 0.339*	0.560± 0.087**
2500 ppm	34	0.280± 0.050	3.098± 0.357**	0.614± 0.083**

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

(HCL042)

BAIS 5

TABLE L 2

ORGAN WEIGHT, RELATIVE: FEMALE

STUDY NO. : 0711
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	43	293± 38	0.025± 0.004	0.066± 0.073	0.325± 0.045	0.358± 0.054	0.663± 0.098
625 ppm	40	278± 25	0.026± 0.005	0.062± 0.038	0.331± 0.030	0.362± 0.038	0.698± 0.116
1250 ppm	42	266± 22**	0.027± 0.004	0.060± 0.025	0.337± 0.051	0.380± 0.062	0.729± 0.078**
2500 ppm	35	233± 34**	0.028± 0.007*	0.073± 0.078	0.363± 0.054**	0.412± 0.056**	0.861± 0.109**

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

(HCL042)

BAIS5

STUDY NO. : 0711
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	43	0.252± 0.163	2.585± 0.463	0.671± 0.077
625 ppm	40	0.236± 0.095	2.561± 0.350	0.696± 0.073
1250 ppm	42	0.441± 0.853	2.644± 0.361	0.726± 0.063**
2500 ppm	35	0.226± 0.040	2.835± 0.309*	0.836± 0.109**

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

(HCL042)

TABLE M 1

HISTOPATHOLOGICAL FINDINGS:

NON-NEOPLASTIC LESIONS:

MALE: ALL ANIMALS

STUDY NO. : 0711
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 1+ (%)	Control 50 2+ (%)	Control 50 3+ (%)	Control 50 4+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
{Integumentary system/appandage}																		
skin/app		<50>																
	epidermal cyst		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)
	sebaceous 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)	0 (0)	1 (2)	0 (0)	0 (0)
subcutis		<50>																
	inflammation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)
	fibrosis		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)
	epidermal cyst		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)
{Respiratory system}																		
nasal cavit		<50>																
	thrombus		2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	4 (8)	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 1+ (%)	Control 50 2+ (%)	Control 50 3+ (%)	Control 50 4+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
{Respiratory system}																		
nasal cavit			<50>				<50>				<50>				<50>			
	mineralization		35 (70)	0 (0)	0 (0)	0 (0)	42 (84)	0 (0)	0 (0)	0 (0)	35 (70)	0 (0)	0 (0)	0 (0)	43 (86)	0 (0)	0 (0)	0 (0)
	eosinophilic change:olfactory epithelium		41 (82)	5 (10)	1 (2)	0 (0)	38 (76)	4 (8)	0 (0)	0 (0)	36 (72)	3 (6)	0 (0)	0 (0)	40 (80)	7 (14)	0 (0)	0 (0)
	eosinophilic change:respiratory epithelium		3 (6)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
	inflammation:foreign body		16 (32)	2 (4)	0 (0)	0 (0)	22 (44)	3 (6)	0 (0)	0 (0)	11 (22)	6 (12)	0 (0)	0 (0)	15 (30)	3 (6)	0 (0)	0 (0)
	inflammation:respiratory epithelium		9 (18)	1 (2)	0 (0)	0 (0)	10 (20)	0 (0)	0 (0)	0 (0)	12 (24)	0 (0)	0 (0)	0 (0)	6 (12)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:olfactory epithelium		5 (10)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:gland		41 (82)	0 (0)	0 (0)	0 (0)	38 (76)	0 (0)	0 (0)	0 (0)	40 (80)	0 (0)	0 (0)	0 (0)	38 (76)	0 (0)	0 (0)	0 (0)
	squamous cell metaplasia:transitional epithelium		0 (0)	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)

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+ (%)	625 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)	1250 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)	2500 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)
{Respiratory system}																		
larynx		<50>	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
	ulcer		(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	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)
	inflammation		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	hyperplasia:epithelium		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	inflammation:foreign body		1	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
trachea		<50>	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
	inflammation:foreign body		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
lung		<50>	3	0	0	0	2	0	0	0	2	0	0	0	1	0	0	0
	congestion		(6)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(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

STUDY NO. : 0711
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 1+ (%)	Control 50 2+ (%)	Control 50 3+ (%)	Control 50 4+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
{Respiratory system}																		
lung			<50>				<50>				<50>				<50>			
	hemorrhage		3 (6)	1 (2)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	3 (6)	2 (4)	0 (0)	0 (0)	4 (8)	1 (2)	0 (0)	0 (0)
	inflammatory infiltration		3 (6)	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)
	ossification		0 (0)	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)
	accumulation of foamy cells		2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)
	bronchiolar-alveolar cell hyperplasia		5 (10)	0 (0)	1 (2)	0 (0)	5 (10)	1 (2)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)
	uremic pneumonitis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
{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)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1+ (%)	Control 50 2+ (%)	Control 50 3+ (%)	Control 50 4+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
{Hematopoietic system}																		
bone marrow		<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)	1 (2)	0 (0)	0 (0)
	inflammatory infiltration		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		1 (2)	0 (0)	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)
	increased hematopoiesis		7 (14)	7 (14)	3 (6)	0 (0)	9 (18)	5 (10)	1 (2)	0 (0)	14 (28)	4 (8)	0 (0)	0 (0)	8 (16)	5 (10)	2 (4)	0 (0)
lymph node		<50>					<50>				<50>				<50>			
	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)
	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)
	inflammatory infiltration		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)
spleen		<50>					<50>				<50>				<50>			
	congestion		1 (2)	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)

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+ (%)	625 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)	1250 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)	2500 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)
[Hematopoietic system]																		
spleen		<50>																
	deposit of hemosiderin		12	0	0	0	5	0	0	0	13	1	0	0	12	2	0	0
			(24)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(26)	(2)	(0)	(0)	(24)	(4)	(0)	(0)
	inflammatory infiltration		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	fibrosis:focal		0	0	0	0	1	2	0	0	1	1	1	0	0	0	0	0
			(0)	(0)	(0)	(0)	(2)	(4)	(0)	(0)	(2)	(2)	(2)	(0)	(0)	(0)	(0)	(0)
	extramedullary hematopoiesis		21	3	1	0	21	1	0	0	15	4	1	0	16	1	0	0
			(42)	(6)	(2)	(0)	(42)	(2)	(0)	(0)	(30)	(8)	(2)	(0)	(32)	(2)	(0)	(0)
[Circulatory system]																		
heart		<50>																
	thrombus		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization		0	0	0	0	1	1	0	0	0	0	0	0	0	0	1	0
			(0)	(0)	(0)	(0)	(2)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)
	myocardial fibrosis		17	1	0	0	21	2	0	0	24	2	0	0	21	1	0	0
			(34)	(2)	(0)	(0)	(42)	(4)	(0)	(0)	(48)	(4)	(0)	(0)	(42)	(2)	(0)	(0)

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

Organ	Findings	Group Name	Control				625 ppm				1250 ppm				2500 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+ (%)
{Circulatory system}																		
heart			<50>				<50>				<50>				<50>			
	myocarditis		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)
artery/aort			<50>				<50>				<50>				<50>			
	mineralization		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)
{Digestive system}																		
oral cavity			<50>				<50>				<50>				<50>			
	squamous cell hyperplasia		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)
tongue			<50>				<50>				<50>				<50>			
	mineralization		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)
	lymphocytic infiltration		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	arteritis		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)	(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				625 ppm				1250 ppm				2500 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)
{Digestive system}																		
salivary gl			<50>				<50>				<50>				<50>			
	inflammation		0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
stomach			<50>				<50>				<50>				<50>			
	ulcer:forestomach		3	2	0	0	0	1	1	0	1	1	2	0	3	2	2	0
			(6)	(4)	(0)	(0)	(0)	(2)	(2)	(0)	(2)	(2)	(4)	(0)	(6)	(4)	(4)	(0)
	hyperplasia:forestomach		0	0	0	0	4	0	0	0	0	0	0	0	3	2	0	0
			(0)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(4)	(0)	(0)
	erosion:glandular stomach		5	0	0	0	6	0	0	0	5	0	0	0	5	0	0	0
			(10)	(0)	(0)	(0)	(12)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	ulcer:glandular stomach		2	0	0	0	3	0	0	0	1	0	0	0	0	0	0	0
			(4)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:glandular stomach		0	0	0	0	0	1	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)
small intes			<50>				<50>				<50>				<50>			
	ulcer		0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(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+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
{Digestive system}																		
small intes		<50>																
	erosion		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)
large intes		<50>																
	ulcer		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)
liver		<50>																
	herniation		5 (10)	0 (0)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	7 (14)	0 (0)	0 (0)	0 (0)
	necrosis:central		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)	0 (0)	0 (0)	0 (0)
	necrosis:focal		0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
	fatty change:central		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	fatty change:peripheral		0 (0)	1 (2)	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				625 ppm				1250 ppm				2500 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)
{Digestive system}																		
liver			<50>				<50>				<50>				<50>			
	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)
	inflammatory infiltration		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)
	granulation		39 (78)	1 (2)	0 (0)	0 (0)	37 (74)	1 (2)	0 (0)	0 (0)	41 (82)	0 (0)	0 (0)	0 (0)	42 (84)	1 (2)	0 (0)	0 (0)
	inflammatory cell nest		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)
	extramedullary hematopoiesis		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)
	clear cell focus		0 (0)	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)
	acidophilic cell focus		18 (36)	1 (2)	0 (0)	0 (0)	19 (38)	0 (0)	0 (0)	0 (0)	14 (28)	1 (2)	0 (0)	0 (0)	12 (24)	0 (0)	0 (0)	0 (0)
	basophilic cell focus		3 (6)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	0 (0)	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 1+ (%)	Control 50 2+ (%)	Control 50 3+ (%)	Control 50 4+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
{Digestive system}																		
liver			<50>				<50>				<50>				<50>			
	spongiosis hepatis		7 (14)	0 (0)	0 (0)	0 (0)	6 (12)	0 (0)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 * (0)
	bile duct hyperplasia		48 (96)	0 (0)	0 (0)	0 (0)	49 (98)	0 (0)	0 (0)	0 (0)	47 (94)	0 (0)	0 (0)	0 (0)	49 (98)	0 (0)	0 (0)	0 (0)
	cholangiofibrosis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	biliary cyst		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)
	focal fatty change		2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)
pancreas			<50>				<50>				<50>				<50>			
	atrophy		8 (16)	1 (2)	0 (0)	0 (0)	10 (20)	0 (0)	0 (0)	0 (0)	8 (16)	0 (0)	0 (0)	0 (0)	4 (8)	2 (4)	0 (0)	0 (0)
	inflammatory infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	arteritis		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)

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+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
{Digestive system}																		
pancreas		<50>																
	basophilic cell focus		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)
	islet cell hyperplasia		1 (2)	0 (0)	0 (0)	0 (0)	3 (6)	1 (2)	0 (0)	0 (0)	3 (6)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
{Urinary system}																		
kidney		<50>																
	hyaline droplet		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)
	eosinophilic body		1 (2)	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)
	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)
	scar		0 (0)	1 (2)	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)
	chronic nephropathy		27 (54)	11 (22)	10 (20)	0 (0)	19 (38)	16 (32)	9 (18)	3 (6)	14 (28)	17 (34)	14 (28)	1 (2)	12 (24)	20 (40)	12 (24)	3 * (6)

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+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
{Urinary system}																		
kidney		<50>																
	papillary necrosis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)	19 (38)	0 (0)	0 (0)	0 ** (0)
	mineralization:papilla		0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	mineralization:pelvis		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)
	mineralization:cortex		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)	0 (0)	0 (0)
	urothelial hyperplasia:pelvis		0 (0)	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)
	dilated pelvis		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)
	deposit of brown pigment		0 (0)	0 (0)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	27 (54)	0 (0)	0 (0)	0 ** (0)
urin bladd		<50>																
	dilatation		0 (0)	0 (0)	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)

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				625 ppm				1250 ppm				2500 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+ (%)
{Urinary system}																		
urin bladd			<50>				<50>				<50>				<50>			
	hemorrhage		0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
	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)
	papillary and/or nodular hyperplasia		0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Endocrine system}																		
pituitary			<50>				<50>				<50>				<50>			
	atrophy		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)
	angiectasis		2	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)
	cyst		4	1	0	0	0	0	0	0	4	0	0	0	1	0	0	0
			(8)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	hyperplasia		9	1	0	0	9	5	0	0	4	4	1	0	7	2	0	0
			(18)	(2)	(0)	(0)	(18)	(10)	(0)	(0)	(8)	(8)	(2)	(0)	(14)	(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 1+ (%)	Control 50 2+ (%)	Control 50 3+ (%)	Control 50 4+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
{Endocrine system}																		
pituitary		<50>																
	Rathke pouch		2 (4)	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)
	aberrant craniopharyngeal tissue		0 (0)	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)
thyroid		<50>																
	ultimobranchial body remanet		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)
	follicular hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	C-cell hyperplasia		9 (18)	7 (14)	0 (0)	0 (0)	9 (18)	3 (6)	1 (2)	0 (0)	11 (22)	4 (8)	0 (0)	0 (0)	5 (10)	5 (10)	0 (0)	0 (0)
	cystic thyroid follicle		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
parathyroid		<50>																
	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)

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+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
(Endocrine system)																		
adrenal			<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)
	lymphocytic infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	hyperplasia:medulla		1 (2)	1 (2)	0 (0)	0 (0)	2 (4)	2 (4)	0 (0)	0 (0)	3 (6)	2 (4)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	focal fatty change:cortex		4 (8)	0 (0)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
(Reproductive system)																		
testis			<50>				<50>				<50>				<50>			
	mineralization		0 (0)	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)
	interstitial cell hyperplasia		21 (42)	0 (0)	0 (0)	0 (0)	21 (42)	1 (2)	0 (0)	0 (0)	12 (24)	0 (0)	0 (0)	0 (0)	14 (28)	0 (0)	0 (0)	0 (0)
semin ves			<50>				<50>				<50>				<50>			
	inflammation		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 / No. of Animals on Study / Grade	Control 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)	625 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)	1250 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)	2500 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)
{Reproductive system}																		
prostate			<50>				<50>				<50>				<50>			
	hemorrhage		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)
	inflammation		9	2	0	0	9	2	0	0	12	1	0	0	8	1	0	0
			(18)	(4)	(0)	(0)	(18)	(4)	(0)	(0)	(24)	(2)	(0)	(0)	(16)	(2)	(0)	(0)
	hyperplasia		9	1	0	0	7	0	1	0	11	0	0	0	8	1	0	0
			(18)	(2)	(0)	(0)	(14)	(0)	(2)	(0)	(22)	(0)	(0)	(0)	(16)	(2)	(0)	(0)
mammary gl			<50>				<50>				<50>				<50>			
	galactocele		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)
{Nervous system}																		
brain			<50>				<50>				<50>				<50>			
	hemorrhage		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)
spinal cord			<50>				<50>				<50>				<50>			
	hemorrhage		2	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)

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+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
{Special sense organs/appendage}																		
eye		<50>																
	inflammatory infiltration		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)
	cataract		0 (0)	3 (6)	3 (6)	0 (0)	2 (4)	2 (4)	3 (6)	0 (0)	1 (2)	6 (12)	1 (2)	0 (0)	2 (4)	0 (0)	2 (4)	0 (0)
	retinal atrophy		7 (14)	6 (12)	4 (8)	0 (0)	3 (6)	2 (4)	5 (10)	0 (0)	5 (10)	3 (6)	6 (12)	0 (0)	10 (20)	3 (6)	3 (6)	0 (0)
	keratitis		1 (2)	0 (0)	1 (2)	0 (0)	4 (8)	3 (6)	0 (0)	0 (0)	4 (8)	1 (2)	0 (0)	0 (0)	2 (4)	1 (2)	0 (0)	0 (0)
	iritis		2 (4)	0 (0)	1 (2)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)
Harder gl		<50>																
	lymphocytic infiltration		1 (2)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)
	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)
{Musculoskeletal system}																		
muscle		<50>																
	atrophy		0 (0)	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)

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				625 ppm				1250 ppm				2500 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}																		
muscle																		
	mineralization		<50>				<50>				<50>				<50>			
			0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
bone																		
	fracture		<50>				<50>				<50>				<50>			
			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)
	osteosclerosis		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)
{Body cavities}																		
peritoneum																		
	inflammation		<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)

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 M 4

HISTOPATHOLOGICAL FINDINGS:

NON-NEOPLASTIC LESIONS:

FEMALE: ALL ANIMALS

Organ	Findings	Group Name	Control				625 ppm				1250 ppm				2500 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)
{Integumentary system/appandage}																		
subcutis			<50>				<50>				<50>				<50>			
	phlegmone		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)
	fibrosis		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)
{Respiratory system}																		
nasal cavit			<50>				<50>				<50>				<50>			
	thrombus		1	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	mineralization		29	0	0	0	28	0	0	0	31	0	0	0	21	0	0	0
			(58)	(0)	(0)	(0)	(56)	(0)	(0)	(0)	(62)	(0)	(0)	(0)	(42)	(0)	(0)	(0)
	rhinitis		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)
	eosinophilic change:olfactory epithelium		6	32	10	0	16	29	4	0	9	36	4	0	2	20	23	0 *
			(12)	(64)	(20)	(0)	(32)	(58)	(8)	(0)	(18)	(72)	(8)	(0)	(4)	(40)	(46)	(0)
	eosinophilic change:respiratory epithelium		12	0	0	0	9	0	0	0	5	0	0	0	20	0	0	0
			(24)	(0)	(0)	(0)	(18)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(40)	(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+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
{Respiratory system}																		
nasal cavit		<50>																
	inflammation:foreign body		6 (12)	2 (4)	0 (0)	0 (0)	2 (4)	2 (4)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	3 (6)	2 (4)	0 (0)	0 (0)
	inflammation:respiratory epithelium		11 (22)	0 (0)	0 (0)	0 (0)	8 (16)	1 (2)	0 (0)	0 (0)	8 (16)	0 (0)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:olfactory epithelium		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)
	respiratory metaplasia:gland		48 (96)	0 (0)	0 (0)	0 (0)	50 (100)	0 (0)	0 (0)	0 (0)	48 (96)	0 (0)	0 (0)	0 (0)	46 (92)	0 (0)	0 (0)	0 (0)
	squamous cell metaplasia:transitional epithelium		0 (0)	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)
nasopharynx		<50>																
	inflammation:foreign body		1 (2)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)
larynx		<50>																
	inflammation		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)

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+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
(Respiratory system)																		
larynx		<50>																
	inflammation:foreign body		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
lung		<50>																
	congestion		1 (2)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)
	hemorrhage		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)
	inflammatory infiltration		3 (6)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	accumulation of foamy cells		4 (8)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)
	bronchiolar-alveolar cell hyperplasia		2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)
	uremic pneumonitis		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)
(Hematopoietic system)																		
bone marrow		<50>																
	hemorrhage		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)	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				625 ppm				1250 ppm				2500 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)
(Hematopoietic system)																		
bone marrow			<50>				<50>				<50>				<50>			
	granulation		3	0	0	0	1	0	0	0	0	1	0	0	3	0	0	0
			(6)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(6)	(0)	(0)	(0)
	increased hematopoiesis		5	4	3	0	7	10	1	0	3	0	7	0	9	4	1	0
			(10)	(8)	(6)	(0)	(14)	(20)	(2)	(0)	(6)	(0)	(14)	(0)	(18)	(8)	(2)	(0)
thymus			<50>				<50>				<50>				<50>			
	inflammatory infiltration		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
spleen			<50>				<50>				<50>				<50>			
	congestion		0	0	0	0	2	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	deposit of hemosiderin		16	0	0	0	17	0	0	0	18	0	0	0	21	0	0	0
			(32)	(0)	(0)	(0)	(34)	(0)	(0)	(0)	(36)	(0)	(0)	(0)	(42)	(0)	(0)	(0)
	fibrosis:focal		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)
	focal lymphoid hyperplasia		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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				625 ppm				1250 ppm				2500 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)
(Hematopoietic system)																		
spleen			<50>				<50>				<50>				<50>			
	extramedullary hematopoiesis		16	4	0	0	22	4	2	0	16	4	1	0	19	4	1	0
			(32)	(8)	(0)	(0)	(44)	(8)	(4)	(0)	(32)	(8)	(2)	(0)	(38)	(8)	(2)	(0)
(Circulatory system)																		
heart			<50>				<50>				<50>				<50>			
	thrombus		1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
			(2)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	inflammatory infiltration		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	lymphocytic 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)
	myocardial fibrosis		20	0	0	0	24	0	0	0	15	0	0	0	22	0	0	0
			(40)	(0)	(0)	(0)	(48)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(44)	(0)	(0)	(0)
(Digestive system)																		
tongue			<50>				<50>				<50>				<50>			
	thrombus		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1+ (%)	Control 50 2+ (%)	Control 50 3+ (%)	Control 50 4+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
(Digestive system)																		
tongue			<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)	2 (4)	0 (0)	0 (0)	0 (0)
	lymphocytic infiltration		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
	arteritis		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)
stomach			<50>				<50>				<50>				<50>			
	epidermal cyst		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)
	ulcer:forestomach		1 (2)	1 (2)	0 (0)	0 (0)	1 (2)	1 (2)	1 (2)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hyperplasia:forestomach		0 (0)	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)
	erosion:glandular stomach		5 (10)	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)
	ulcer:glandular stomach		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	2 (4)	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	Control				625 ppm				1250 ppm				2500 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)
{Digestive system}																		
small intes			<50>				<50>				<50>				<50>			
	inflammatory infiltration		0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
large intes			<50>				<50>				<50>				<50>			
	diverticula		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
liver			<50>				<50>				<50>				<50>			
	herniation		6	0	0	0	8	0	0	0	7	0	0	0	4	0	0	0
			(12)	(0)	(0)	(0)	(16)	(0)	(0)	(0)	(14)	(0)	(0)	(0)	(8)	(0)	(0)	(0)
	angiectasis		0	0	0	0	4	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:central		0	1	0	0	1	0	0	0	0	1	0	0	2	0	0	0
			(0)	(2)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(4)	(0)	(0)	(0)
	necrosis:focal		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	fatty change:central		1	1	0	0	1	0	0	0	0	1	0	0	0	0	0	0
			(2)	(2)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)	625 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)	1250 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)	2500 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)
{Digestive system}																		
liver			<50>				<50>				<50>				<50>			
	fatty change:peripheral		2	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	deposit of hemosiderin		2	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization		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)
	inflammatory infiltration		1	0	0	0	2	0	0	0	1	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	lymphocytic infiltration		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	granulation		26	0	0	0	37	1	0	0 *	32	1	0	0	33	0	0	0
			(52)	(0)	(0)	(0)	(74)	(2)	(0)	(0)	(64)	(2)	(0)	(0)	(66)	(0)	(0)	(0)
	inflammatory cell nest		10	0	0	0	0	1	0	0 **	1	0	0	0 *	6	0	0	0
			(20)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(2)	(0)	(0)	(0)	(12)	(0)	(0)	(0)
	extramedullary hematopoiesis		0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(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+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
{Digestive system}																		
liver			<50>				<50>				<50>				<50>			
	acidophilic cell focus		8 (16)	0 (0)	0 (0)	0 (0)	6 (12)	3 (6)	0 (0)	0 (0)	9 (18)	1 (2)	0 (0)	0 (0)	5 (10)	2 (4)	0 (0)	0 (0)
	basophilic cell focus		38 (76)	1 (2)	0 (0)	0 (0)	36 (72)	0 (0)	0 (0)	0 (0)	36 (72)	0 (0)	0 (0)	0 (0)	32 (64)	1 (2)	0 (0)	0 (0)
	spongiosis hepatis		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)
	bile duct hyperplasia		26 (52)	0 (0)	0 (0)	0 (0)	31 (62)	0 (0)	0 (0)	0 (0)	23 (46)	0 (0)	0 (0)	0 (0)	18 (36)	0 (0)	0 (0)	0 (0)
	cholangiofibrosis		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)
	focal fatty change		2 (4)	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)
pancreas			<50>				<50>				<50>				<50>			
	atrophy		0 (0)	1 (2)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	3 (6)	1 (2)	0 (0)	0 (0)
	islet cell hyperplasia		2 (4)	1 (2)	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)

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+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
(Urinary system)																		
kidney			<50>				<50>				<50>				<50>			
	hyaline droplet		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	deposit of hemosiderin		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)
	inflammatory infiltration		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)
	scar		1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)
	chronic nephropathy		13 (26)	5 (10)	1 (2)	0 (0)	22 (44)	2 (4)	0 (0)	1 (2)	19 (38)	6 (12)	0 (0)	1 (2)	15 (30)	5 (10)	0 (0)	0 (0)
	papillary necrosis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	10 (20)	0 (0)	0 (0)	0 (0) **	25 (50)	7 (14)	2 (4)	0 (0) **
	mineralization:cortico-medullary junction		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)
	mineralization:papilla		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	4 (8)	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+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
{Urinary system}																		
kidney		<50>					<50>				<50>				<50>			
	mineralization:pelvis		2 (4)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	urothelial hyperplasia:pelvis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (6)	2 (4)	0 (0)	0 (0)
	dilated pelvis		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)	0 (0)	0 (0)	0 (0)
	dilatation:collecting tubule		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)
	deposit of brown pigment		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	11 (22)	0 (0)	0 (0)	0 ** (0)	41 (82)	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)	2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)
	hemorrhage		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)
	papillary and/or nodular 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)	2 (4)	0 (0)	0 (0)	0 (0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1+ (%)	Control 50 2+ (%)	Control 50 3+ (%)	Control 50 4+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
(Endocrine system)																		
pituitary			<50>				<50>				<50>				<49>			
	angiectasis		2 (4)	0 (0)	0 (0)	0 (0)	2 (4)	1 (2)	0 (0)	0 (0)	0 (0)	4 (8)	0 (0)	0 * (0)	1 (2)	1 (2)	0 (0)	0 (0)
	cyst		12 (24)	4 (8)	0 (0)	0 (0)	17 (34)	4 (8)	0 (0)	0 (0)	15 (30)	6 (12)	1 (2)	0 (0)	12 (24)	4 (8)	0 (0)	0 (0)
	hyperplasia		5 (10)	5 (10)	3 (6)	0 (0)	9 (18)	7 (14)	5 (10)	0 (0)	12 (24)	5 (10)	1 (2)	0 (0)	5 (10)	9 (18)	1 (2)	0 (0)
	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>			
	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)	0 (0)	0 (0)	0 (0)	0 (0)
	C-cell hyperplasia		8 (16)	5 (10)	0 (0)	0 (0)	9 (18)	4 (8)	0 (0)	0 (0)	8 (16)	2 (4)	3 (6)	0 (0)	3 (6)	0 (0)	0 (0)	0 * (0)
	cystic thyroid follicle		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	1 (2)	0 (0)	0 (0)
adrenal			<50>				<50>				<50>				<50>			
	angiectasis		1 (2)	0 (0)	0 (0)	0 (0)	2 (4)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	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 1+ (%)	Control 50 2+ (%)	Control 50 3+ (%)	Control 50 4+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
[Endocrine system]																		
adrenal			<50>				<50>				<50>				<50>			
	necrosis:zonal		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)
	inflammatory infiltration		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)
	hyperplasia:cortical cell		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	hyperplasia:medulla		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)	1 (2)	0 (0)	0 (0)
	focal fatty change:cortex		5 (10)	1 (2)	0 (0)	0 (0)	10 (20)	2 (4)	0 (0)	0 (0)	8 (16)	2 (4)	1 (2)	0 (0)	2 (4)	2 (4)	0 (0)	0 (0)
[Reproductive system]																		
ovary			<50>				<50>				<50>				<50>			
	cyst		0 (0)	2 (4)	0 (0)	0 (0)	1 (2)	3 (6)	0 (0)	0 (0)	1 (2)	2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)
uterus			<50>				<50>				<50>				<50>			
	dilatation		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	Control				625 ppm				1250 ppm				2500 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)	1+ (%)	2+ (%)	3+ (%)	4+ (%)
{Reproductive system}																		
uterus			<50>				<50>				<50>				<50>			
	cystic endometrial hyperplasia		19	1	0	0	25	0	0	0	27	0	0	0	24	0	0	0
			(38)	(2)	(0)	(0)	(50)	(0)	(0)	(0)	(54)	(0)	(0)	(0)	(48)	(0)	(0)	(0)
vagina			<50>				<50>				<50>				<50>			
	dilatation		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)
mammary gl			<50>				<50>				<50>				<50>			
	granulation		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)
{Nervous system}																		
brain			<50>				<50>				<50>				<50>			
	deformity		1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
	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)
spinal cord			<50>				<50>				<50>				<50>			
	hemorrhage		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)

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+ (%)	625 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)	1250 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)	2500 ppm 50 1+ (%)	2+ (%)	3+ (%)	4+ (%)
(Special sense organs/appendage)																		
eye		<50>	1	0	2	0	3	2	0	0	1	2	1	0	1	3	0	0
	cataract		(2)	(0)	(4)	(0)	(6)	(4)	(0)	(0)	(2)	(4)	(2)	(0)	(2)	(6)	(0)	(0)
	retinal atrophy		13	11	3	0	11	8	2	0	7	4	3	0 *	15	8	2	0
			(26)	(22)	(6)	(0)	(22)	(16)	(4)	(0)	(14)	(8)	(6)	(0)	(30)	(16)	(4)	(0)
	keratitis		2	0	0	0	3	0	0	0	2	2	0	0	0	0	0	0
			(4)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(4)	(4)	(0)	(0)	(0)	(0)	(0)	(0)
	iritis		0	0	0	0	2	1	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(4)	(2)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:cornea		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)
Harder gl		<50>	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
	degeneration		(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	lymphocytic infiltration		4	0	0	0	2	1	0	0	1	1	0	0	2	0	0	0
			(8)	(0)	(0)	(0)	(4)	(2)	(0)	(0)	(2)	(2)	(0)	(0)	(4)	(0)	(0)	(0)
nasolacr d		<50>	1	0	0	0	3	0	0	0	0	1	0	0	0	0	0	0
	inflammation		(2)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1+ (%)	Control 50 2+ (%)	Control 50 3+ (%)	Control 50 4+ (%)	625 ppm 50 1+ (%)	625 ppm 50 2+ (%)	625 ppm 50 3+ (%)	625 ppm 50 4+ (%)	1250 ppm 50 1+ (%)	1250 ppm 50 2+ (%)	1250 ppm 50 3+ (%)	1250 ppm 50 4+ (%)	2500 ppm 50 1+ (%)	2500 ppm 50 2+ (%)	2500 ppm 50 3+ (%)	2500 ppm 50 4+ (%)
(Musculoskeletal system)																		
muscle		<50>																
	mineralization		0 (0)	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)
	degeneration		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)
bone		<50>																
	osteosclerosis		0 (0)	1 (2)	0 (0)	0 (0)	2 (4)	1 (2)	0 (0)	0 (0)	3 (6)	1 (2)	1 (2)	0 (0)	1 (2)	1 (2)	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

TABLE P 1

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS: MALE

Group Name	Control	625 ppm	1250 ppm	2500 ppm
	SITE : skin/appendage			
	TUMOR : keratoacanthoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	2/50(4.0)	4/50(8.0)	0/50(0.0)
Adjusted rates(b)	7.50	5.13	11.11	0.0
Terminal rates(c)	3/40(7.5)	2/39(5.1)	3/33(9.1)	0/34(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.8823			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.1848			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.1212
	SITE : subcutis			
	TUMOR : fibroma			
Tumor rate				
Overall rates(a)	5/50(10.0)	11/50(22.0)	4/50(8.0)	4/50(8.0)
Adjusted rates(b)	12.50	24.39	10.26	8.82
Terminal rates(c)	5/40(12.5)	9/39(23.1)	3/33(9.1)	3/34(8.8)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.2282			
Prevalence method(d)	P = 0.8456			
Combined analysis(d)	P = 0.7633			
Cochran-Armitage test(e)	P = 0.3031			
Fisher Exact test(e)		P = 0.0857	P = 0.5000	P = 0.5000
	SITE : lung			
	TUMOR : bronchiolar-alveolar adenoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	3/50(6.0)	1/50(2.0)	1/50(2.0)
Adjusted rates(b)	2.50	7.69	3.03	2.94
Terminal rates(c)	1/40(2.5)	3/39(7.7)	1/33(3.0)	1/34(2.9)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.5834			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.6742			
Fisher Exact test(e)		P = 0.3087	P = 0.7525	P = 0.7525

Group Name	Control	625 ppm	1250 ppm	2500 ppm
	SITE : lung			
	TUMOR : bronchiolar-alveolar adenoma, bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	3/50(6.0)	1/50(2.0)	1/50(2.0)
Adjusted rates(b)	5.00	7.69	3.03	2.94
Terminal rates(c)	2/40(5.0)	3/39(7.7)	1/33(3.0)	1/34(2.9)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.9034 ?			
Prevalence method(d)	P = 0.7370			
Combined analysis(d)	P = 0.8444			
Cochran-Armitage test(e)	P = 0.2225			
Fisher Exact test(e)		P = 0.6611	P = 0.3087	P = 0.3087
	SITE : spleen			
	TUMOR : mononuclear cell leukemia			
Tumor rate				
Overall rates(a)	4/50(8.0)	4/50(8.0)	3/50(6.0)	1/50(2.0)
Adjusted rates(b)	7.50	2.56	0.0	0.0
Terminal rates(c)	3/40(7.5)	1/39(2.6)	0/33(0.0)	0/34(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5447			
Prevalence method(d)	P = 0.9852			
Combined analysis(d)	P = 0.8888			
Cochran-Armitage test(e)	P = 0.1588			
Fisher Exact test(e)		P = 0.6425	P = 0.5000	P = 0.1811
	SITE : pancreas			
	TUMOR : islet cell adenoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	6/50(12.0)	0/50(0.0)	5/50(10.0)
Adjusted rates(b)	5.00	15.38	0.0	14.71
Terminal rates(c)	2/40(5.0)	6/39(15.4)	0/33(0.0)	5/34(14.7)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.1873			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.5285			
Fisher Exact test(e)		P = 0.1343	P = 0.2475	P = 0.2180

Group Name	Control	625 ppm	1250 ppm	2500 ppm
	SITE : pancreas TUMOR : islet cell adenoma, islet cell adenocarcinoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	8/50(16.0)	1/50(2.0)	5/50(10.0)
Adjusted rates(b)	10.00	20.51	0.0	14.71
Terminal rates(c)	4/40(10.0)	8/39(20.5)	0/33(0.0)	5/34(14.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3944			
Prevalence method(d)	P = 0.4968			
Combined analysis(d)	P = 0.4783			
Cochran-Armitage test(e)	P = 0.8021			
Fisher Exact test(e)		P = 0.1783	P = 0.1811	P = 0.5000
	SITE : pancreas TUMOR : islet cell adenoma, mixed acinar-islet cell adenoma, islet cell adenocarcinoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	9/50(18.0)	1/50(2.0)	5/50(10.0)
Adjusted rates(b)	10.00	21.43	0.0	14.71
Terminal rates(c)	4/40(10.0)	8/39(20.5)	0/33(0.0)	5/34(14.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3944			
Prevalence method(d)	P = 0.5579			
Combined analysis(d)	P = 0.5382			
Cochran-Armitage test(e)	P = 0.7137			
Fisher Exact test(e)		P = 0.1168	P = 0.1811	P = 0.5000
	SITE : pituitary gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	18/50(36.0)	21/50(42.0)	19/50(38.0)	10/50(20.0)
Adjusted rates(b)	35.71	42.50	45.71	17.65
Terminal rates(c)	13/40(32.5)	16/39(41.0)	14/33(42.4)	6/34(17.6)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1922			
Prevalence method(d)	P = 0.9858			
Combined analysis(d)	P = 0.9280			
Cochran-Armitage test(e)	P = 0.0435*			
Fisher Exact test(e)		P = 0.3410	P = 0.5000	P = 0.0591

Group Name	Control	625 ppm	1250 ppm	2500 ppm
	SITE : pituitary gland TUMOR : adenoma, adenocarcinoma			
Tumor rate				
Overall rates(a)	19/50(38.0)	21/50(42.0)	19/50(38.0)	10/50(20.0)
Adjusted rates(b)	38.10	42.50	45.71	17.65
Terminal rates(c)	14/40(35.0)	16/39(41.0)	14/33(42.4)	6/34(17.6)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1922			
Prevalence method(d)	P = 0.9911			
Combined analysis(d)	P = 0.9470			
Cochran-Armitage test(e)	P = 0.0287*			
Fisher Exact test(e)		P = 0.4192	P = 0.5815	P = 0.0385*
	SITE : thyroid TUMOR : C-cell adenoma			
Tumor rate				
Overall rates(a)	10/50(20.0)	7/50(14.0)	7/50(14.0)	8/50(16.0)
Adjusted rates(b)	22.50	17.95	15.15	18.60
Terminal rates(c)	9/40(22.5)	7/39(17.9)	5/33(15.2)	5/34(14.7)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3793			
Prevalence method(d)	P = 0.6130			
Combined analysis(d)	P = 0.5942			
Cochran-Armitage test(e)	P = 0.6956			
Fisher Exact test(e)		P = 0.2977	P = 0.2977	P = 0.3976
	SITE : thyroid TUMOR : C-cell carcinoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	1/50(2.0)	3/50(6.0)	2/50(4.0)
Adjusted rates(b)	7.32	2.56	8.11	2.94
Terminal rates(c)	2/40(5.0)	1/39(2.6)	2/33(6.1)	1/34(2.9)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1080			
Prevalence method(d)	P = 0.7233			
Combined analysis(d)	P = 0.5149			
Cochran-Armitage test(e)	P = 0.8627			
Fisher Exact test(e)		P = 0.3087	P = 0.6611	P = 0.5000

Group Name	Control	625 ppm	1250 ppm	2500 ppm
	SITE : thyroid TUMOR : follicular adenocarcinoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	0/50(0.0)	1/50(2.0)	4/50(8.0)
Adjusted rates(b)	0.0	0.0	2.63	11.76
Terminal rates(c)	0/40(0.0)	0/39(0.0)	0/33(0.0)	4/34(11.8)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.0021**			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0046**			
Fisher Exact test(e)		P = N.C.	P = 0.5000	P = 0.0587
	SITE : thyroid TUMOR : C-cell adenoma, C-cell carcinoma			
Tumor rate				
Overall rates(a)	13/50(26.0)	8/50(16.0)	10/50(20.0)	10/50(20.0)
Adjusted rates(b)	29.27	20.51	22.22	20.93
Terminal rates(c)	11/40(27.5)	8/39(20.5)	7/33(21.2)	6/34(17.6)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1296			
Prevalence method(d)	P = 0.7274			
Combined analysis(d)	P = 0.6089			
Cochran-Armitage test(e)	P = 0.6570			
Fisher Exact test(e)		P = 0.1631	P = 0.3176	P = 0.3176
	SITE : thyroid TUMOR : follicular adenoma, follicular adenocarcinoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	1/50(2.0)	3/50(6.0)	5/50(10.0)
Adjusted rates(b)	2.50	2.56	6.38	13.51
Terminal rates(c)	1/40(2.5)	1/39(2.6)	1/33(3.0)	4/34(11.8)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.0185*			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0372*			
Fisher Exact test(e)		P = 0.7525	P = 0.3087	P = 0.1022

Group Name	Control	625 ppm	1250 ppm	2500 ppm
	SITE : adrenal gland TUMOR : pheochromocytoma			
Tumor rate				
Overall rates(a)	8/50(16.0)	4/50(8.0)	2/50(4.0)	1/50(2.0)
Adjusted rates(b)	20.00	9.52	6.06	2.94
Terminal rates(c)	8/40(20.0)	3/39(7.7)	2/33(6.1)	1/34(2.9)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.9939			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0097**			
Fisher Exact test(e)		P = 0.1783	P = 0.0458*	P = 0.0154*
	SITE : adrenal gland TUMOR : pheochromocytoma, pheochromocytoma:malignant			
Tumor rate				
Overall rates(a)	9/50(18.0)	6/50(12.0)	4/50(8.0)	1/50(2.0)
Adjusted rates(b)	22.50	14.29	6.06	2.94
Terminal rates(c)	9/40(22.5)	5/39(12.8)	2/33(6.1)	1/34(2.9)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3806			
Prevalence method(d)	P = 0.9979			
Combined analysis(d)	P = 0.9948			
Cochran-Armitage test(e)	P = 0.0067**			
Fisher Exact test(e)		P = 0.2883	P = 0.1168	P = 0.0078**
	SITE : testis TUMOR : interstitial cell tumor			
Tumor rate				
Overall rates(a)	34/50(68.0)	32/50(64.0)	35/50(70.0)	35/50(70.0)
Adjusted rates(b)	75.00	76.92	82.35	86.49
Terminal rates(c)	30/40(75.0)	30/39(76.9)	27/33(81.8)	29/34(85.3)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.1003			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.6818			
Fisher Exact test(e)		P = 0.4165	P = 0.5000	P = 0.5000

Group Name	Control	625 ppm	1250 ppm	2500 ppm
	SITE : preputial/clitoral gland			
	TUMOR : adenoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	2/50(4.0)	1/50(2.0)	0/50(0.0)
Adjusted rates(b)	7.50	5.13	2.13	0.0
Terminal rates(c)	3/40(7.5)	2/39(5.1)	0/33(0.0)	0/34(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.9095 ?			
Prevalence method(d)	P = 0.9687			
Combined analysis(d)	P = 0.9872			
Cochran-Armitage test(e)	P = 0.0319*			
Fisher Exact test(e)		P = 0.3389	P = 0.1811	P = 0.0587
	SITE : Zymbal gland			
	TUMOR : Zmbal gland tumor:benign , Zymbal gland tumor:malignant			
Tumor rate				
Overall rates(a)	1/50(2.0)	0/50(0.0)	0/50(0.0)	3/50(6.0)
Adjusted rates(b)	2.50	0.0	0.0	0.0
Terminal rates(c)	1/40(2.5)	0/39(0.0)	0/33(0.0)	0/34(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0041**?			
Prevalence method(d)	P = 0.9078 ?			
Combined analysis(d)	P = 0.0475*			
Cochran-Armitage test(e)	P = 0.0877			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.3087

Group Name	Control	625 ppm	1250 ppm	2500 ppm
	SITE : peritoneum TUMOR : mesothelioma			
Tumor rate				
Overall rates(a)	1/50(2.0)	2/50(4.0)	1/50(2.0)	4/50(8.0)
Adjusted rates(b)	2.50	5.13	0.0	8.82
Terminal rates(c)	1/40(2.5)	2/39(5.1)	0/33(0.0)	3/34(8.8)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1315			
Prevalence method(d)	P = 0.1307			
Combined analysis(d)	P = 0.0588			
Cochran-Armitage test(e)	P = 0.1432			
Fisher Exact test(e)		P = 0.5000	P = 0.7525	P = 0.1811

(HPT360A)

BAIS5

(a) : Number of tumor-bearing animals/number of animals examined at the site.
(b) : Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.
(c) : Observed tumor incidence at terminal kill.
(d) : Beneath the control incidence are the P-values associated with the trend test.
Standard method : Death analysis
Prevalence method : Incidental tumor test
Combined analysis : Death analysis + Incidental tumor test
(e) : The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.
? : The conditional probabilities of the largest and smallest possible out comes can not estimated or this P-value is beyond the estimated P-value.
------ : There is no data which should be statistical analysis.
Significant difference ; * : $P \leqq 0.05$ ** : $P \leqq 0.01$
N.C. :Statistical value cannot be calculated and was not significant.

TABLE P 2

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS: FEMALE

Group Name	Control	625 ppm	1250 ppm	2500 ppm
	SITE : subcutis TUMOR : fibroma			
Tumor rate				
Overall rates(a)	1/50(2.0)	3/50(6.0)	1/50(2.0)	1/50(2.0)
Adjusted rates(b)	2.33	2.50	2.38	2.86
Terminal rates(c)	1/43(2.3)	1/40(2.5)	1/42(2.4)	1/35(2.9)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.7085			
Prevalence method(d)	P = 0.4282			
Combined analysis(d)	P = 0.5895			
Cochran-Armitage test(e)	P = 0.6742			
Fisher Exact test(e)		P = 0.3087	P = 0.7525	P = 0.7525
	SITE : subcutis TUMOR : fibroma, fibrosarcoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	3/50(6.0)	1/50(2.0)	2/50(4.0)
Adjusted rates(b)	2.33	2.50	2.38	2.86
Terminal rates(c)	1/43(2.3)	1/40(2.5)	1/42(2.4)	1/35(2.9)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3357			
Prevalence method(d)	P = 0.4282			
Combined analysis(d)	P = 0.3485			
Cochran-Armitage test(e)	P = 0.8453			
Fisher Exact test(e)		P = 0.3087	P = 0.7525	P = 0.5000
	SITE : lung TUMOR : bronchiolar-alveolar adenoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	0/50(0.0)	1/50(2.0)	0/50(0.0)
Adjusted rates(b)	6.98	0.0	2.38	0.0
Terminal rates(c)	3/43(7.0)	0/40(0.0)	1/42(2.4)	0/35(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.9570			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0877			
Fisher Exact test(e)		P = 0.1212	P = 0.3087	P = 0.1212

Group Name	Control	625 ppm	1250 ppm	2500 ppm
	SITE : spleen TUMOR : mononuclear cell leukemia			
Tumor rate				
Overall rates(a)	4/50(8.0)	2/50(4.0)	4/50(8.0)	0/50(0.0)
Adjusted rates(b)	2.33	2.50	7.14	0.0
Terminal rates(c)	1/43(2.3)	1/40(2.5)	3/42(7.1)	0/35(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.9576			
Prevalence method(d)	P = 0.6341			
Combined analysis(d)	P = 0.9277			
Cochran-Armitage test(e)	P = 0.0999			
Fisher Exact test(e)		P = 0.3389	P = 0.6425	P = 0.0587
	SITE : pancreas TUMOR : islet cell adenoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	3/50(6.0)	1/50(2.0)	0/50(0.0)
Adjusted rates(b)	2.33	7.32	2.38	0.0
Terminal rates(c)	1/43(2.3)	2/40(5.0)	1/42(2.4)	0/35(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.8439			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.2508			
Fisher Exact test(e)		P = 0.3087	P = 0.7525	P = 0.5000
	SITE : pancreas TUMOR : islet cell adenoma, islet cell adenocarcinoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	3/50(6.0)	1/50(2.0)	0/50(0.0)
Adjusted rates(b)	4.65	7.32	2.38	0.0
Terminal rates(c)	2/43(4.7)	2/40(5.0)	1/42(2.4)	0/35(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.9274			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.1232			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.2475

Group Name	Control	625 ppm	1250 ppm	2500 ppm
	SITE : pituitary gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	13/50(26.0)	11/50(22.0)	14/50(28.0)	9/49(18.4)
Adjusted rates(b)	27.27	23.26	25.58	22.86
Terminal rates(c)	11/43(25.6)	9/40(22.5)	10/42(23.8)	8/35(22.9)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3993			
Prevalence method(d)	P = 0.6245			
Combined analysis(d)	P = 0.5836			
Cochran-Armitage test(e)	P = 0.4468			
Fisher Exact test(e)		P = 0.4076	P = 0.5000	P = 0.2513
	SITE : pituitary gland TUMOR : adenoma, adenocarcinoma			
Tumor rate				
Overall rates(a)	15/50(30.0)	13/50(26.0)	15/50(30.0)	9/49(18.4)
Adjusted rates(b)	29.55	26.19	26.09	22.86
Terminal rates(c)	12/43(27.9)	10/40(25.0)	10/42(23.8)	8/35(22.9)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.6045			
Prevalence method(d)	P = 0.7328			
Combined analysis(d)	P = 0.7552			
Cochran-Armitage test(e)	P = 0.2116			
Fisher Exact test(e)		P = 0.4120	P = 0.5862	P = 0.1322
	SITE : thyroid TUMOR : C-cell adenoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	2/50(4.0)	5/50(10.0)	4/50(8.0)
Adjusted rates(b)	4.65	5.00	11.90	11.43
Terminal rates(c)	2/43(4.7)	2/40(5.0)	5/42(11.9)	4/35(11.4)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.0988			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.3086			
Fisher Exact test(e)		P = 0.6913	P = 0.2180	P = 0.3389

Group Name	Control	625 ppm	1250 ppm	2500 ppm
	SITE : thyroid TUMOR : C-cell adenoma, C-cell carcinoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	2/50(4.0)	5/50(10.0)	5/50(10.0)
Adjusted rates(b)	9.30	5.00	11.90	11.43
Terminal rates(c)	4/43(9.3)	2/40(5.0)	5/42(11.9)	4/35(11.4)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.0858 ?			
Prevalence method(d)	P = 0.2689			
Combined analysis(d)	P = 0.1571			
Cochran-Armitage test(e)	P = 0.4809			
Fisher Exact test(e)		P = 0.3389	P = 0.5000	P = 0.5000
	SITE : uterus TUMOR : endometrial stromal polyp			
Tumor rate				
Overall rates(a)	13/50(26.0)	4/50(8.0)	8/50(16.0)	9/50(18.0)
Adjusted rates(b)	29.55	10.00	16.00	20.00
Terminal rates(c)	12/43(27.9)	4/40(10.0)	6/42(14.3)	7/35(20.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.5902			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.6560			
Fisher Exact test(e)		P = 0.0155*	P = 0.1631	P = 0.2348
	SITE : uterus TUMOR : endometrial stromal sarcoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	3/50(6.0)	1/50(2.0)	0/50(0.0)
Adjusted rates(b)	2.33	0.0	0.0	0.0
Terminal rates(c)	1/43(2.3)	0/40(0.0)	0/42(0.0)	0/35(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.6948			
Prevalence method(d)	P = 0.9006 ?			
Combined analysis(d)	P = 0.8414			
Cochran-Armitage test(e)	P = 0.2508			
Fisher Exact test(e)		P = 0.3087	P = 0.7525	P = 0.5000

Group Name	Control	625 ppm	1250 ppm	2500 ppm
	SITE : mammary gland TUMOR : fibroadenoma			
Tumor rate				
Overall rates(a)	5/50(10.0)	8/50(16.0)	7/50(14.0)	6/50(12.0)
Adjusted rates(b)	11.63	17.50	16.67	17.14
Terminal rates(c)	5/43(11.6)	7/40(17.5)	7/42(16.7)	6/35(17.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5644			
Prevalence method(d)	P = 0.2842			
Combined analysis(d)	P = 0.3211			
Cochran-Armitage test(e)	P = 0.9433			
Fisher Exact test(e)		P = 0.2768	P = 0.3798	P = 0.5000
	SITE : mammary gland TUMOR : adenoma, fibroadenoma, adenocarcinoma			
Tumor rate				
Overall rates(a)	7/50(14.0)	10/50(20.0)	7/50(14.0)	6/50(12.0)
Adjusted rates(b)	16.28	20.00	16.67	17.14
Terminal rates(c)	7/43(16.3)	8/40(20.0)	7/42(16.7)	6/35(17.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.7004			
Prevalence method(d)	P = 0.5066			
Combined analysis(d)	P = 0.5768			
Cochran-Armitage test(e)	P = 0.5468			
Fisher Exact test(e)		P = 0.2977	P = 0.6129	P = 0.5000

Group Name	Control	625 ppm	1250 ppm	2500 ppm
	SITE : preputial/clitoral gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	3/50(6.0)	2/50(4.0)	2/50(4.0)
Adjusted rates(b)	2.33	7.50	2.38	0.0
Terminal rates(c)	1/43(2.3)	3/40(7.5)	1/42(2.4)	0/35(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1450			
Prevalence method(d)	P = 0.8415			
Combined analysis(d)	P = 0.4928			
Cochran-Armitage test(e)	P = 0.8627			
Fisher Exact test(e)		P = 0.5000	P = 0.6913	P = 0.6913

(HPT360A)

BAIS5

(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 R

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

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

Organs Tumors	No. of animals examined	No. of animals bearing tumor	Incidence (%)	Min. - Max. (%)
Thyroid	2841			
follicular adenoma[1)]		27	1.0	0 - 4
follicular adenocarcinoma[2)]		38	1.3	0 - 8
1) + 2)		65	2.3	0 - 8
Zymbal gland	2848			
Zymbal gland tumor: benign[1)]		10	0.4	0 - 4
Zymbal gland tumor: malignant[2)]		16	0.6	0 - 4
1) + 2)		26	0.9	0 - 4

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

Study No. : 0043, 0059, 0061, 0063, 0065, 0067, 0095, 0104, 0115, 0130, 0141, 0158, 0162, 0189, 0205, 0210, 0224, 0242, 0246, 0267, 0269, 0278, 0284, 0288, 0294, 0296, 0318, 0328, 0342, 0347, 0365, 0371, 0396, 0399, 0401, 0407, 0417, 0421, 0437, 0448, 0457, 0461, 0497, 0535, 0560, 0579, 0581, 0610, 0612, 0641, 0667, 0675, 0684, 0686, 0691, 0704, 0731

TABLE S 1

CAUSE OF DEATH: MALE

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
SEX : MALE

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

Group Name	Control	625 ppm	1250 ppm	2500 ppm
Number of Dead and Moribund Animal	10	11	17	16
urinary sy les	0	0	1	0
renal lesion	0	1	0	0
urinary retention	1	1	0	0
chronic nephropathy	0	0	1	2
tumor d:leukemia	1	3	3	1
tumor d:subcutis	1	1	0	1
tumor d:nasal cavit	0	1	0	0
tumor d:lung	1	0	0	0
tumor d:oral cavity	0	0	0	1
tumor d:pancreas	0	0	1	0
tumor d:kidney	0	0	1	0
tumor d:pituitary	2	3	3	4
tumor d:thyroid	0	0	1	1
tumor d:adrenal	0	0	2	0
tumor d:prep/cli gl	1	0	0	0
tumor d:brain	1	0	0	1
tumor d:spinal cord	0	1	0	0
tumor d:Harder gl	1	0	0	0
tumor d:Zymbal gl	0	0	0	3
tumor d:bone	1	0	1	0
tumor d:pleura	0	0	2	0
tumor d:mediastinum	0	0	0	1
tumor d:peritoneum	0	0	1	1

TABLE S 2

CAUSE OF DEATH: FEMALE

STUDY NO. : 0711
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
SEX : FEMALE

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

Group Name	Control	625 ppm	1250 ppm	2500 ppm
Number of Dead and Moribund Animal	7	10	8	15
no microscop confirm	0	0	1	3
respiratory sy les	0	0	0	1
renal lesion	0	0	0	4
tumor d:leukemia	3	1	1	0
tumor d:subcutis	0	2	0	1
tumor d:oral cavity	0	0	1	0
tumor d:liver	0	0	0	1
tumor d:pituitary	2	2	3	1
tumor d:thyroid	0	0	0	1
tumor d:ovary	1	0	0	0
tumor d:uterus	0	3	1	0
tumor d:mammary gl	0	2	0	0
tumor d:prep/cli gl	1	0	1	2
tumor d:brain	0	0	0	1

FIGURES

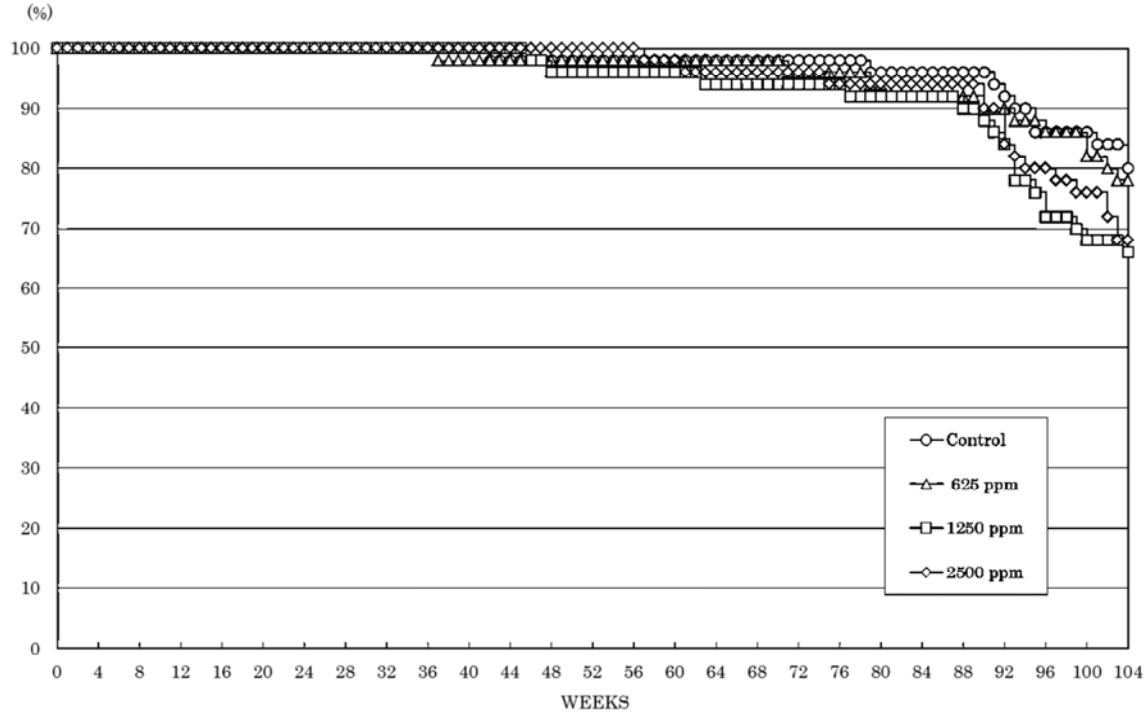


FIGURE 1 SURVIVAL ANIMAL RATE OF MALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL

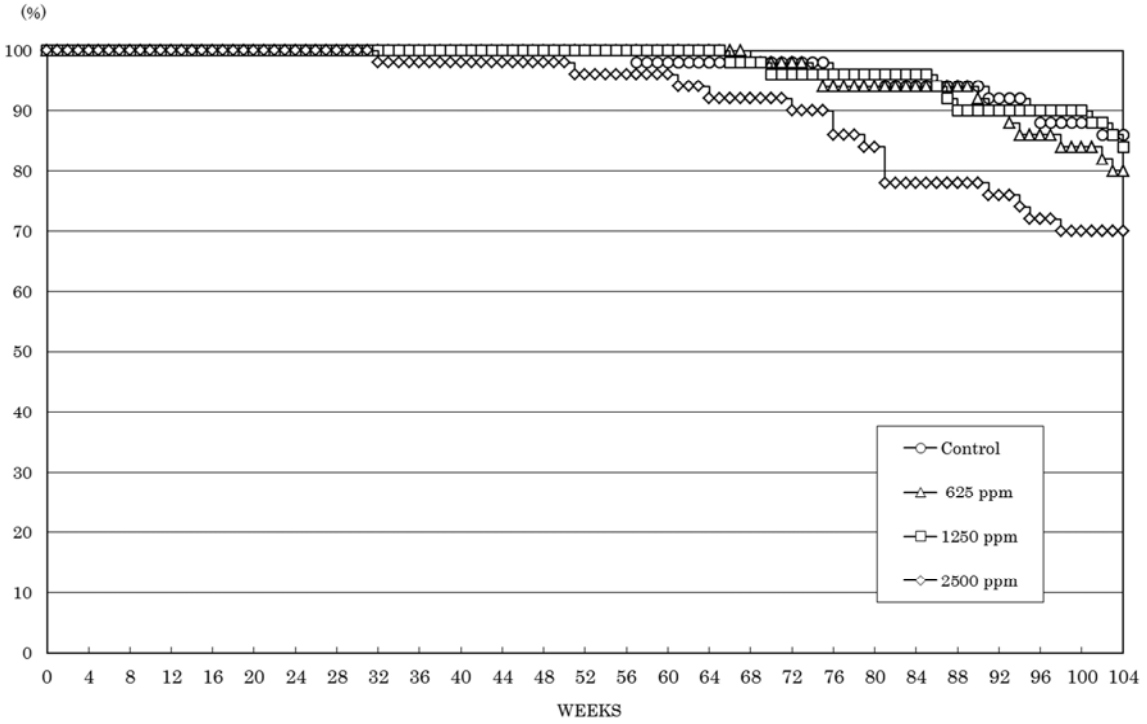


FIGURE 2 SURVIVAL ANIMAL RATE OF FEMALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL

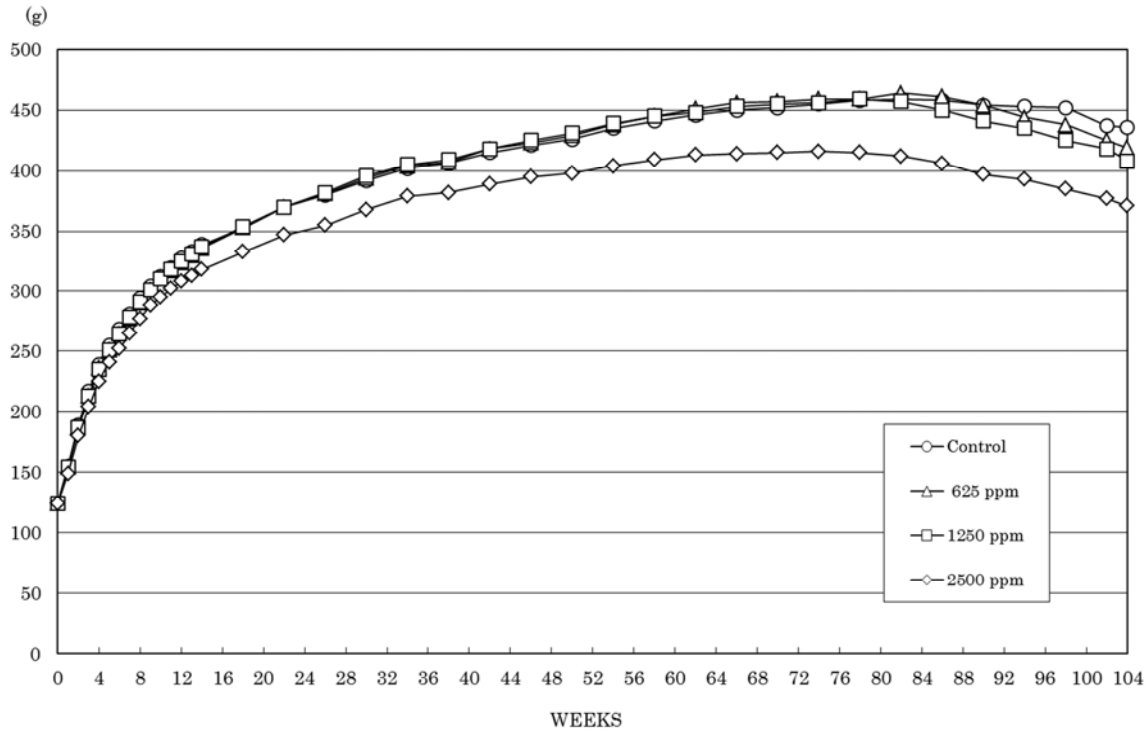


FIGURE 3 BODY WEIGHT CHANGES OF MALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL

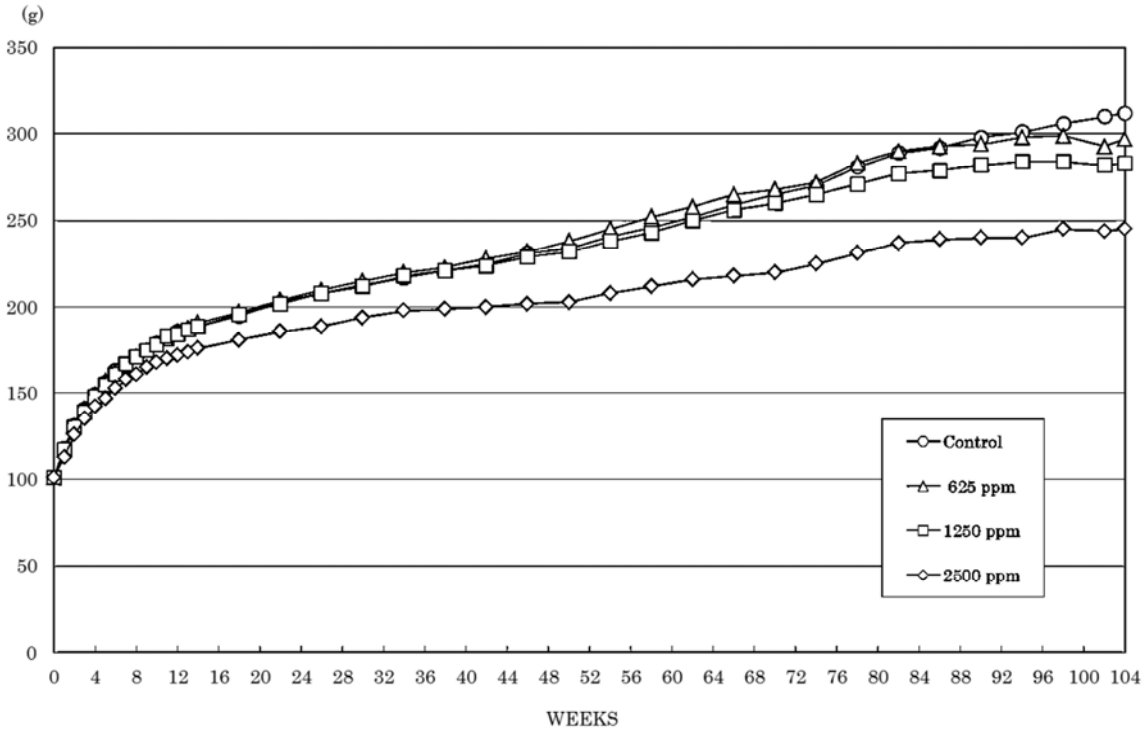


FIGURE 4 BODY WEIGHT CHANGES OF FEMALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL

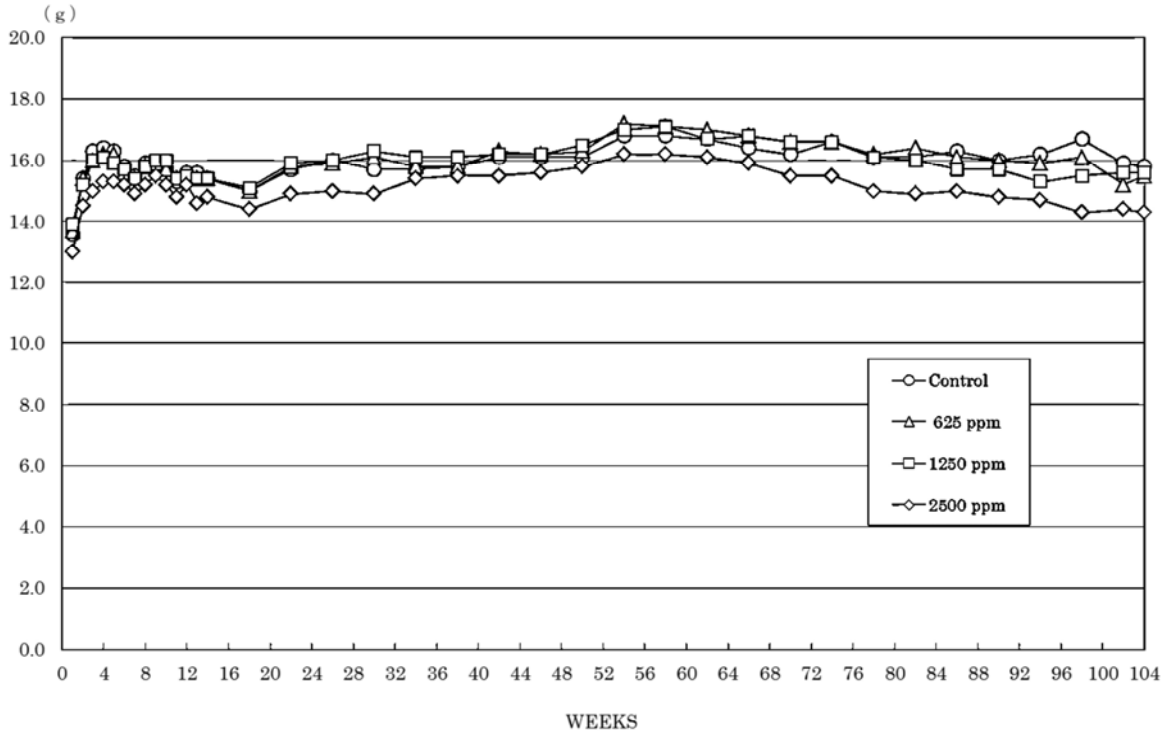


FIGURE 5 FOOD CONSUMPTION CHANGES OF MALE RATS IN THE 2-YEAR DRINKING WATER STUDY 3-AMINOPHENOL

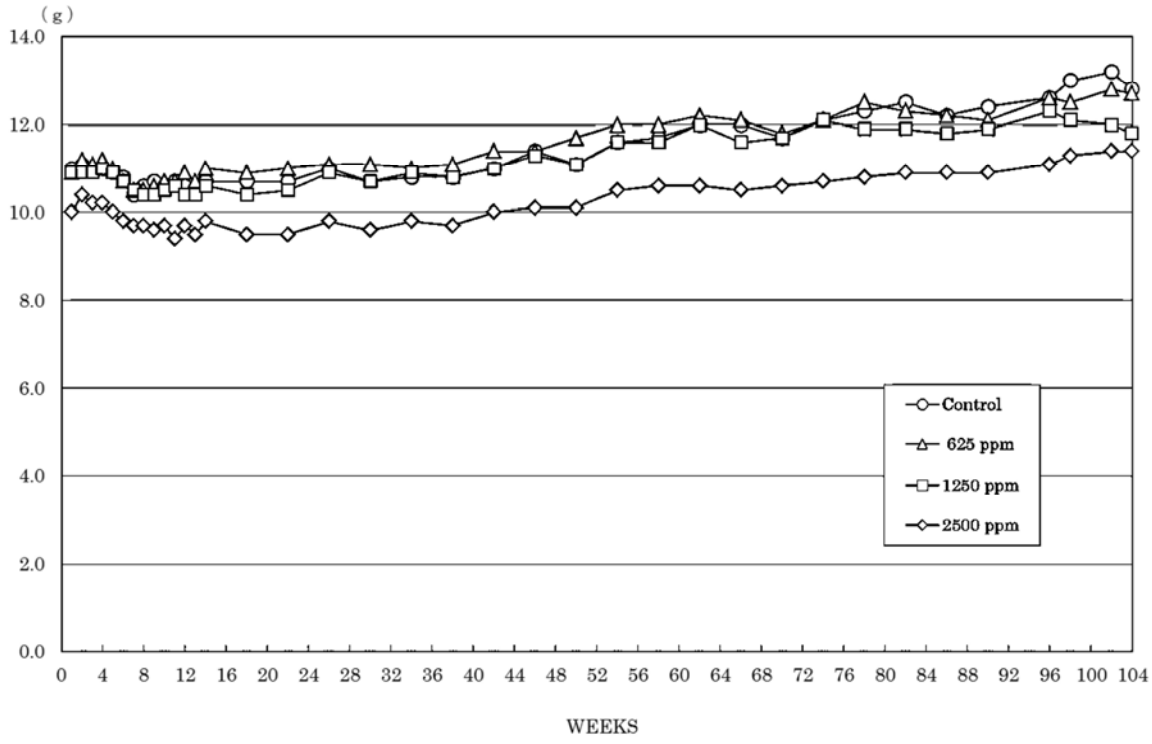


FIGURE 6 FOOD CONSUMPTION CHANGES OF FEMALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL

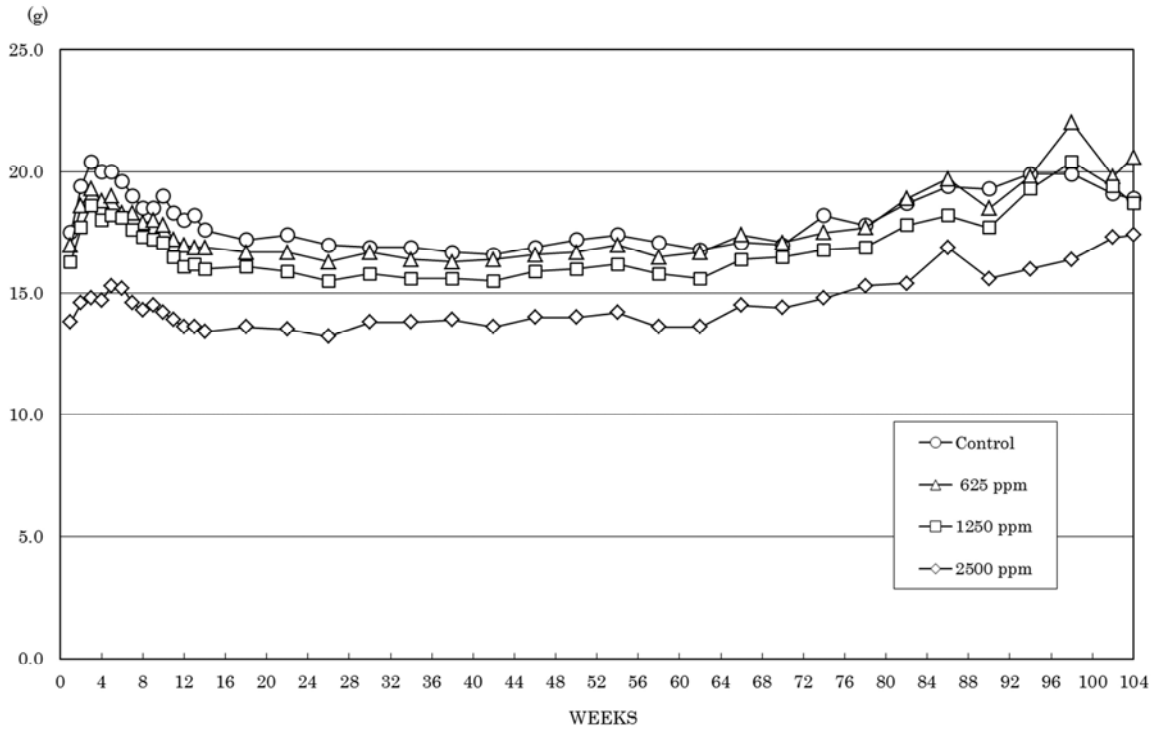


FIGURE 7 WATER CONSUMPTION CHANGES OF MALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL

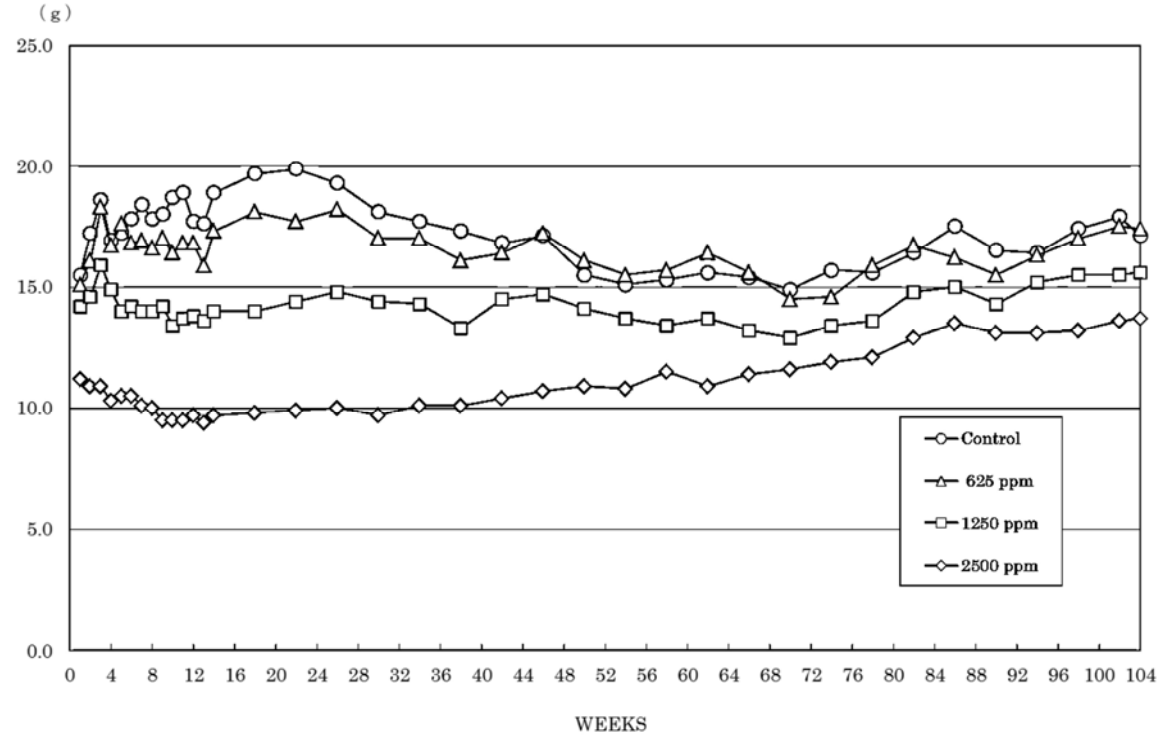
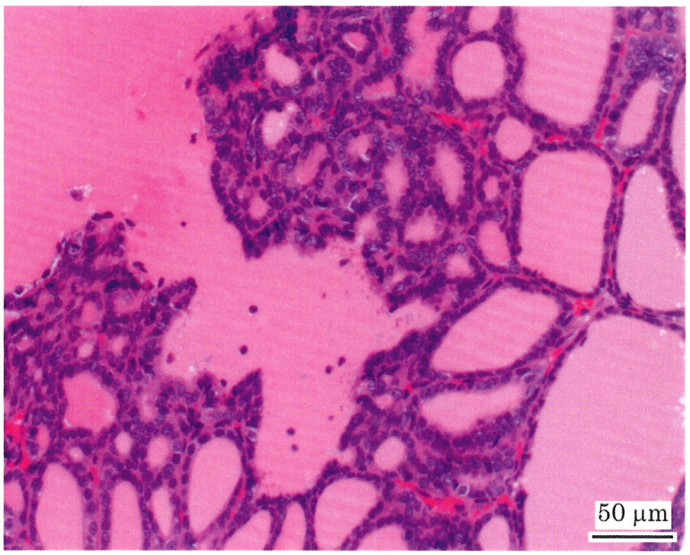
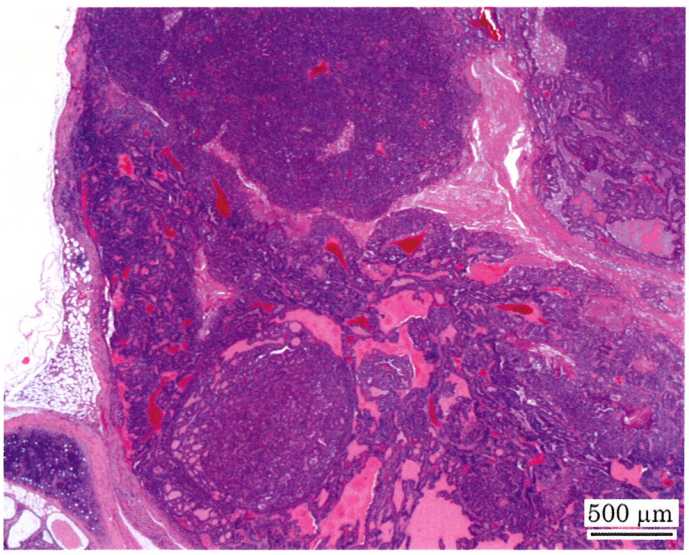


FIGURE 8 WATER CONSUMPTION CHANGES OF FEMALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF 3-AMINOPHENOL

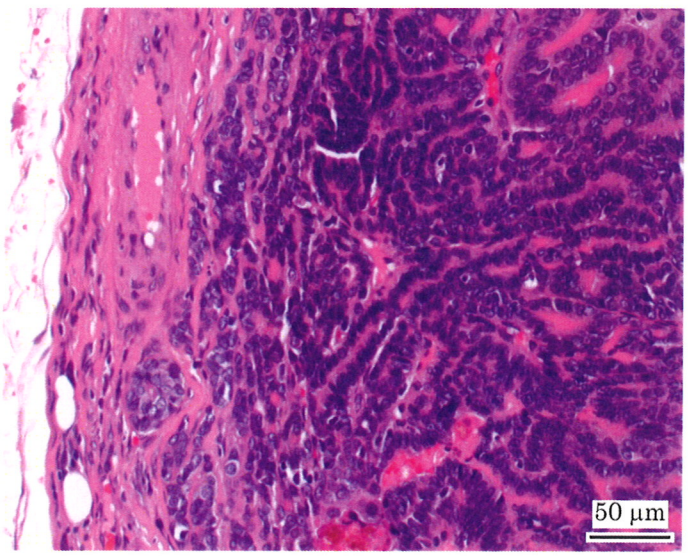
Photograph 1
Thyroid: Follicular adenoma
Rat, Male, 1250 ppm, Animal No. 0711-1230 (H&E)



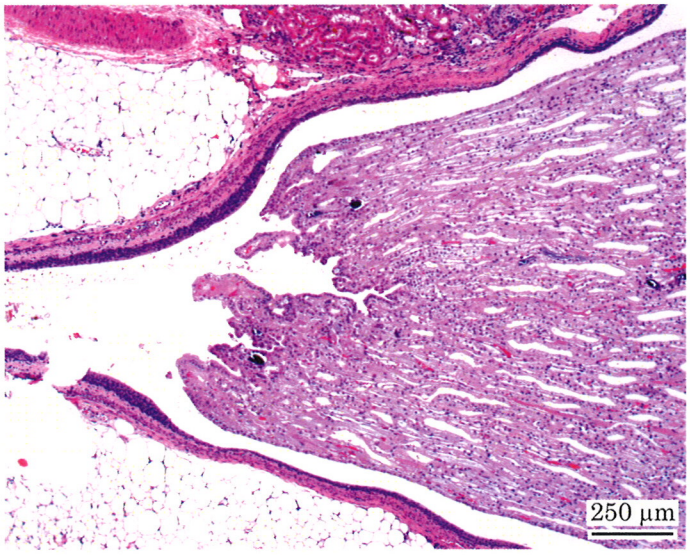
Photograph 2
Thyroid: Follicular adenoma
Rat, Male, 1250 ppm, Animal No. 0711-1230 (H&E)



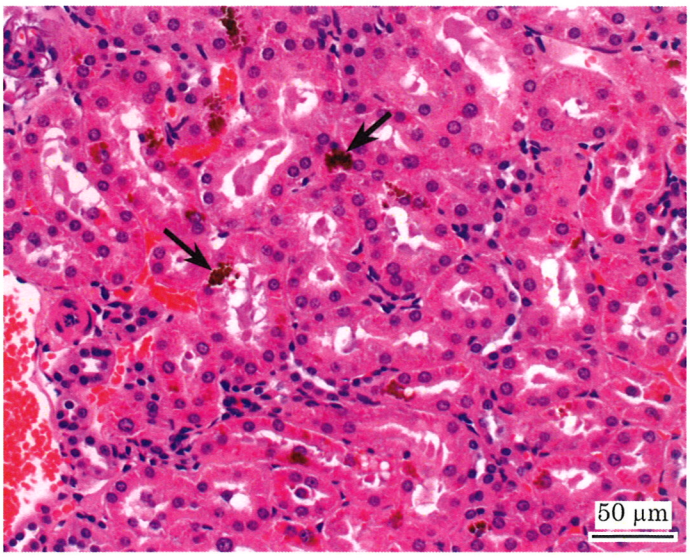
Photograph 3
Thyroid: Follicular adenocarcinoma
Rat, Male, 2500 ppm, Animal No. 0711-1328 (H&E)



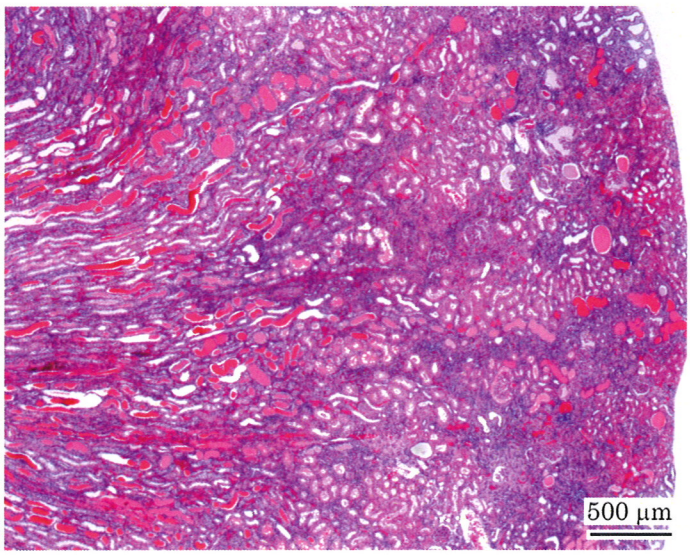
Photograph 4
Thyroid: Follicular adenocarcinoma
Rat, Male, 2500 ppm, Animal No. 0711-1328(H&E)



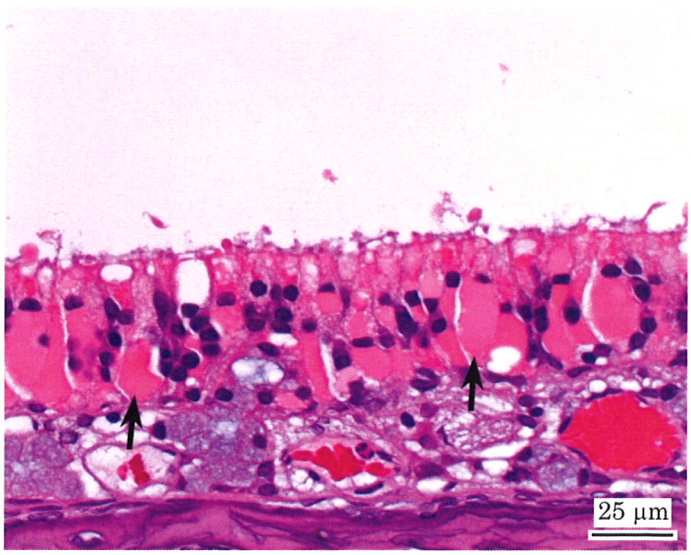
Photograph 5
Kidney: Papillary necrosis
Rat, Female, 2500 ppm, Animal No. 0711-2348 (H&E)



Photograph 6
Kidney: Deposit of brown pigment (Arrows)
Rat, Female, 2500 ppm, Animal No. 0711-2314 (H&E)



Photograph 7
Kidney: Chronic nephropathy
Rat, Male, 2500 ppm, Animal No. 0711-1331 (H&E)



Photograph 8
Nasal cavity: Eosinophilic change: olfactory epithelium (Arrows)
Rat, Female, 2500 ppm, Animal No. 0711-2302 (H&E)