Summary of Drinking Water Carcinogenicity Study of 2-Aminoethanol in F344 Rats

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Japan Bioassay Research Center

Japan Industrial Safety and Health Association

PREFACE

The tests were contracted and supported by the Ministry of Health, Labour and Welfare of Japan. The tests were conducted by Japan Bioassay Research Center (JBRC) and the report was prepared by JBRC and peer reviewed by outside expert pathologist. Complete report was submitted to Ministry of Health, Labour and Welfare of Japan on June 29, 2010.

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

Summary of Drinking Water Carcinogenicity Study of 2-Aminoethanol in F344 Rats

Purpose, materials and methods

2-Aminoethanol (CAS No. 141-43-5) is a colorless clear viscosity liquid with a melting point of 10.3°C. It is soluble in water, methanol, and acetone.

The carcinogenicity and chronic toxicity of 2-aminoethanol were examined in F344/DuCrlCrlj rats. Groups of test animals were administered 2-aminoethanol in their drinking water for 2 years (104 weeks). Each group consisted of either 50 male or 50 female rats. The drinking water concentrations of 2-aminoethanol were 0, 800, 2400 or 7200 ppm (w/w). Both sexes were administered each concentration of 2-aminoethanol. The highest dose level was chosen so as not to exceed the maximum tolerated dose (MTD), based on both growth rate and toxicity in a previous 13-week toxicity study. The identity of the 2-aminoethanol used in these experiments was confirmed by both infrared spectrometry and mass spectrometry, and it was analyzed by high performance liquid chromatography before and after its use to affirm its stability. The concentrations of 2-aminoethanol 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 temparature. 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 deep ether anesthesia. Organs and tissues were removed, weighed and examined for macroscopic lesions at necropsy. The organs and tissues were then fixed and embedded in paraffin. Five μm thick tissue sections were prepared and stained with hematoxylin and eosin and examined microscopically. Incidences of neoplastic lesions were statistically analyzed by Fisher's exact test. Any positive dose-response trends of 2-aminoethanol 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 7200 ppm 2-aminoethanol was slightly decreased, however, the decreased survival rate was not causally related to the administration of the test substance. There was no significant difference in survival rates between any other 2-aminoethanol-administered groups and their controls. Soiled fur around the genitalia and brown and red urine were observed in the 7200 ppm-administered females. Growth rates of the males and females administered 7200 ppm 2-aminoethanol were suppressed. Food consumption was decreased in the males administered 7200 ppm 2-aminoethanol throughout most of the 2-year administration period. Water consumption was decreased in the males and females administered 7200 ppm 2-aminoethanol throughout most of the 2-year administration period, and was decreased sporatically in the males administered 2400 ppm 2-aminoethanol during the 2-year administration period. Mean corpuscular volume and reticulocyte were significantly decreased in males administered 7200 ppm 2-aminoethanol. Significant decreases in total red blood cells, hematocrit, and total lymphocytes and significant increases in platelets, reticulocyte, and neutrophil leukocytes were observed in females administered 7200 ppm 2-aminoethanol.

No significant increases in the incidence of neoplastic or tumor-related lesions was found in any of the 2-aminoethanol-administered groups of either sex. Renal papillary necrosis in males and females administered 2400 and 7200 ppm 2-aminoethanol were significantly increased and urothelial hyperplasia of the pelvis was significantly increased in the females administered 7200 ppm 2-aminoethanol. Kidney weights were significantly increased in the males administered 7200 ppm 2-aminoethanol and in the females administered 2400 and 7200 ppm 2-aminoethanol. Urinary occult blood and urea nitrogen in the plasma were increased in females administered 2400 and 7200 ppm 2-aminoethanol.

Using kidney weight and renal lesions as endpoint markers, the no-observed-adverse-effect-level (NOAEL) for both males and females of 2-aminoethanol in the drinking water was 800 ppm (male: 42 mg/kg body weight per day, female: 69 mg/kg body weight per day).

Conclusions

There was no evidence for carcinogenicity of 2-aminoethanol in male or female rats.

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

Dose (ppm)		0	800	2400	7200	Peto test	Cochran-Armitage test
Number of examined animals		50 [a)]	50	50	50		
benign tumor							
skin/appendage	squamous cell papilloma	4	0	1	0		
	keratoacanthoma	6	2	2	1		
subcutis	fibroma	6	1	6	4		
pancreas	islet cell adenoma	3	5	2	4		
pituitary	adenoma	13	7	6	8		
thyroid	C-cell adenoma	12	12	8	7		
adrenal	pheochromocytoma	4	4	3	5		
testis	interstitial cell tumor	35	31	31	20 **		↓ ↓
malignant tumor							
spleen	mononuclear cell leukemia	4	2	7	0		
pancreas	islet cell adenocarcinoma	1	3	1	3		
pituitary	adenocarcinoma	1	1	2	3		

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

Dose (ppm)		0	800	2400	7200	Peto test	Cochran-Armitage test
Number of examined animals		50	50	50	50		
benign tumor							
pituitary	adenoma	12	17	16	14		
thyroid	C-cell adenoma	6	8	11	4		
adrenal	pheochromocytoma	1	1	1	3		
uterus	endometrial stromal polyp	7	5	9	5		
mammary gland	fibroadenoma	7	7	10	4		
clitoral gland	adenoma	3	3	1	2		
malignant tumor							
spleen	mononuclear cell leukemia	4	7	5	5		
adrenal	pheochromocytoma: malignant	0	0	0	1		
adrenal	pheochromocytoma (benign+malignant)	1	1	1	4	↑ [b)]	

[a)] :Numer of examined animal of pituitary is 49. [b)] :Significant in plevalence method only.

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. : 0641
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>	800 ppm Av. Wt.	800 ppm % of cont. <50>	800 ppm No. of Surviv.	2400 ppm Av. Wt.	2400 ppm % of cont. <50>	2400 ppm No. of Surviv.	7200 ppm Av. Wt.	7200 ppm % of cont. <50>	7200 ppm No. of Surviv.
0-0	121 (50)	50/50	121 (50)	100	50/50	121 (50)	100	50/50	121 (50)	100	50/50
1-7	150 (50)	50/50	149 (50)	99	50/50	149 (50)	99	50/50	141 (50)	94	50/50
2-7	181 (50)	50/50	179 (50)	99	50/50	179 (50)	99	50/50	170 (50)	94	50/50
3-7	206 (50)	50/50	204 (50)	99	50/50	205 (50)	100	50/50	194 (50)	94	50/50
4-7	225 (50)	50/50	224 (50)	100	50/50	225 (50)	100	50/50	214 (50)	95	50/50
5-7	240 (50)	50/50	239 (50)	100	50/50	241 (50)	100	50/50	229 (50)	95	50/50
6-7	253 (50)	50/50	252 (50)	100	50/50	254 (50)	100	50/50	241 (50)	95	50/50
7-7	264 (50)	50/50	263 (50)	100	50/50	265 (50)	100	50/50	252 (50)	95	50/50
8-7	274 (50)	50/50	273 (50)	100	50/50	274 (50)	100	50/50	260 (50)	95	50/50
9-7	283 (50)	50/50	282 (50)	100	50/50	282 (50)	100	50/50	266 (50)	94	50/50
10-7	290 (50)	50/50	291 (50)	100	50/50	290 (50)	100	50/50	273 (50)	94	50/50
11-7	296 (50)	50/50	299 (50)	101	50/50	299 (50)	101	50/50	279 (50)	94	50/50
12-7	303 (50)	50/50	306 (50)	101	50/50	305 (50)	101	50/50	285 (50)	94	50/50
13-7	309 (50)	50/50	312 (50)	101	50/50	312 (50)	101	50/50	290 (50)	94	50/50
14-7	315 (50)	50/50	318 (50)	101	50/50	317 (50)	101	50/50	295 (50)	94	50/50
18-7	333 (50)	50/50	336 (50)	101	50/50	334 (50)	100	50/50	309 (50)	93	50/50
22-7	347 (50)	50/50	350 (50)	101	50/50	348 (50)	100	50/50	320 (50)	92	50/50
26-7	359 (50)	50/50	362 (50)	101	50/50	360 (50)	100	50/50	329 (50)	92	50/50
30-7	372 (50)	50/50	373 (50)	100	50/50	370 (50)	99	50/50	337 (50)	91	50/50
34-7	382 (50)	50/50	385 (49)	101	49/50	380 (50)	99	50/50	345 (50)	90	50/50
38-7	390 (50)	50/50	394 (49)	101	49/50	388 (50)	99	50/50	351 (50)	90	50/50
42-7	396 (50)	50/50	401 (49)	101	49/50	394 (50)	99	50/50	356 (50)	90	50/50
46-7	404 (49)	49/50	406 (49)	100	49/50	399 (50)	99	50/50	359 (50)	89	50/50
50-7	411 (49)	49/50	411 (49)	100	49/50	405 (50)	99	50/50	363 (50)	88	50/50
54-7	417 (49)	49/50	418 (49)	100	49/50	410 (50)	98	50/50	366 (50)	88	50/50
58-7	422 (49)	49/50	424 (49)	100	49/50	416 (50)	99	50/50	369 (50)	87	50/50
62-7	430 (48)	48/50	430 (49)	100	49/50	421 (50)	98	50/50	374 (50)	87	50/50
66-7	434 (48)	48/50	435 (49)	100	49/50	426 (50)	98	50/50	377 (50)	87	50/50
70-7	438 (47)	47/50	434 (49)	99	49/50	429 (50)	98	50/50	379 (50)	87	50/50
74-7	440 (47)	47/50	434 (49)	99	49/50	433 (50)	98	50/50	379 (50)	86	50/50
78-7	443 (47)	47/50	442 (47)	100	47/50	433 (50)	98	50/50	385 (48)	87	48/50
82-7	447 (47)	47/50	446 (47)	100	47/50	436 (47)	98	47/50	385 (48)	86	48/50
86-7	440 (46)	46/50	448 (47)	102	47/50	437 (47)	99	47/50	386 (48)	88	48/50
90-7	438 (45)	45/50	448 (47)	102	47/50	439 (45)	100	45/50	383 (48)	87	48/50
94-7	435 (44)	44/50	444 (47)	102	47/50	436 (42)	100	42/50	386 (45)	89	45/50
98-7	434 (42)	42/50	441 (46)	102	46/50	435 (42)	100	42/50	386 (44)	89	44/50
102-7	428 (41)	41/50	433 (46)	101	46/50	439 (40)	103	40/50	386 (41)	90	41/50
104-7	428 (40)	40/50	426 (45)	100	45/50	431 (38)	101	38/50	387 (40)	90	40/50

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

TABLE C 2

BODY WEIGHT CHANGES AND

SURVIVAL ANIMAL NUMBERS: FEMALE

STUDY NO. : 0641
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>	800 ppm Av. Wt.	800 ppm % of cont. <50>	800 ppm No. of Surviv.	2400 ppm Av. Wt.	2400 ppm % of cont. <50>	2400 ppm No. of Surviv.	7200 ppm Av. Wt.	7200 ppm % of cont. <50>	7200 ppm No. of Surviv.
0-0	100 (50)	50/50	100 (50)	100	50/50	100 (50)	100	50/50	100 (50)	100	50/50
1-7	116 (50)	50/50	115 (50)	99	50/50	115 (50)	99	50/50	110 (50)	95	50/50
2-7	128 (50)	50/50	127 (50)	99	50/50	128 (50)	100	50/50	123 (50)	96	50/50
3-7	137 (50)	50/50	135 (50)	99	50/50	135 (50)	99	50/50	132 (50)	96	50/50
4-7	145 (50)	50/50	143 (50)	99	50/50	144 (50)	99	50/50	138 (50)	95	50/50
5-7	150 (50)	50/50	149 (50)	99	50/50	149 (50)	99	50/50	144 (50)	96	50/50
6-7	155 (50)	50/50	154 (50)	99	50/50	155 (50)	100	50/50	148 (50)	95	50/50
7-7	160 (50)	50/50	158 (50)	99	50/50	159 (50)	99	50/50	152 (50)	95	50/50
8-7	164 (50)	50/50	162 (50)	99	50/50	163 (50)	99	50/50	156 (50)	95	50/50
9-7	167 (50)	50/50	165 (50)	99	50/50	166 (50)	99	50/50	159 (50)	95	50/50
10-7	171 (50)	50/50	168 (50)	98	50/50	170 (50)	99	50/50	162 (50)	95	50/50
11-7	173 (50)	50/50	172 (50)	99	50/50	173 (50)	100	50/50	165 (50)	95	50/50
12-7	177 (50)	50/50	176 (50)	99	50/50	176 (50)	99	50/50	167 (50)	94	50/50
13-7	178 (50)	50/50	177 (50)	99	50/50	178 (50)	100	50/50	169 (50)	95	50/50
14-7	180 (50)	50/50	179 (50)	99	50/50	180 (50)	100	50/50	170 (50)	94	50/50
18-7	186 (50)	50/50	187 (50)	101	50/50	188 (50)	101	50/50	176 (50)	95	50/50
22-7	191 (50)	50/50	192 (50)	101	50/50	193 (50)	101	50/50	180 (50)	94	50/50
26-7	196 (50)	50/50	197 (50)	101	50/50	199 (50)	102	50/50	185 (50)	94	50/50
30-7	202 (50)	50/50	203 (50)	100	50/50	205 (50)	101	50/50	189 (50)	94	50/50
34-7	207 (50)	50/50	210 (50)	101	50/50	210 (50)	101	50/50	192 (50)	93	50/50
38-7	210 (50)	50/50	213 (50)	101	50/50	213 (50)	101	50/50	195 (49)	93	49/50
42-7	215 (50)	50/50	218 (50)	101	50/50	219 (50)	102	50/50	199 (49)	93	49/50
46-7	218 (50)	50/50	221 (50)	101	50/50	222 (50)	102	50/50	201 (49)	92	49/50
50-7	224 (50)	50/50	226 (50)	101	50/50	226 (50)	101	50/50	203 (49)	91	49/50
54-7	227 (50)	50/50	230 (50)	101	50/50	230 (50)	101	50/50	207 (49)	91	49/50
58-7	231 (50)	50/50	234 (50)	101	50/50	234 (50)	101	50/50	209 (49)	90	49/50
62-7	238 (50)	50/50	241 (50)	101	50/50	243 (50)	102	50/50	212 (49)	89	49/50
66-7	244 (50)	50/50	247 (49)	101	49/50	249 (50)	102	50/50	217 (47)	89	47/50
70-7	250 (50)	50/50	253 (49)	101	49/50	254 (50)	102	50/50	219 (47)	88	47/50
74-7	255 (50)	50/50	258 (49)	101	49/50	259 (50)	102	50/50	222 (46)	87	46/50
78-7	261 (50)	50/50	264 (48)	101	48/50	264 (50)	101	50/50	223 (44)	85	44/50
82-7	265 (49)	49/50	270 (46)	102	46/50	270 (50)	102	50/50	224 (44)	85	44/50
86-7	267 (49)	49/50	273 (44)	102	44/50	275 (50)	103	50/50	227 (42)	85	42/50
90-7	273 (48)	48/50	280 (43)	103	43/50	274 (49)	100	49/50	232 (38)	85	38/50
94-7	278 (46)	46/50	284 (43)	102	43/50	281 (48)	101	48/50	230 (38)	83	38/50
98-7	279 (44)	44/50	284 (42)	102	42/50	283 (46)	101	46/50	227 (36)	81	36/50
102-7	280 (40)	40/50	285 (39)	102	39/50	284 (44)	101	44/50	222 (35)	79	35/50
104-7	280 (38)	38/50	281 (38)	100	38/50	283 (42)	101	42/50	221 (33)	79	33/50

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

TABLE C 3

BODY WEIGHT CHANGES: MALE

STUDY NO. : 0641
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	121± 5	150± 7	181± 9	206± 11	225± 12	240± 13	253± 14
800 ppm	121± 5	149± 7	179± 11	204± 12	224± 14	239± 14	252± 16
2400 ppm	121± 5	149± 7	179± 10	205± 11	225± 12	241± 13	254± 14
7200 ppm	121± 5	141± 7**	170± 10**	194± 12**	214± 12**	229± 13**	241± 13**

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

STUDY NO. : 0641
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	264± 15	274± 16	283± 16	290± 16	296± 18	303± 18	309± 18
800 ppm	263± 17	273± 18	282± 17	291± 18	299± 18	306± 18	312± 18
2400 ppm	265± 15	274± 15	282± 16	290± 16	299± 16	305± 17	312± 17
7200 ppm	252± 13**	260± 14**	266± 14**	273± 15**	279± 16**	285± 16**	290± 16**

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

STUDY NO. : 0641
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	315± 19	333± 19	347± 21	359± 21	372± 22	382± 24	390± 26
800 ppm	318± 17	336± 17	350± 18	362± 19	373± 19	385± 20	394± 20
2400 ppm	317± 17	334± 18	348± 19	360± 21	370± 21	380± 22	388± 23
7200 ppm	295± 16**	309± 17**	320± 19**	329± 20**	337± 22**	345± 23**	351± 24**

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

STUDY NO. : 0641
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	396± 27	404± 24	411± 23	417± 23	422± 23	430± 23	434± 26
800 ppm	401± 21	406± 22	411± 24	418± 23	424± 23	430± 24	435± 24
2400 ppm	394± 24	399± 25	405± 26	410± 26	416± 27	421± 27	426± 28
7200 ppm	356± 25**	359± 27**	363± 29**	366± 28**	369± 31**	374± 29**	377± 31**

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

STUDY NO. : 0641
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	438± 23	440± 24	443± 28	447± 46	440± 31	438± 35	435± 32
800 ppm	434± 30	434± 38	442± 26	446± 27	448± 26	448± 27	444± 27
2400 ppm	429± 28	433± 28	433± 29	436± 28	437± 34	439± 27	436± 29
7200 ppm	379± 30**	379± 42**	385± 29**	385± 31**	386± 34**	383± 41**	386± 40**

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

STUDY NO. : 0641
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	434± 31	428± 41	428± 42
800 ppm	441± 29	433± 32	426± 40
2400 ppm	435± 50	439± 82	431± 26
7200 ppm	386± 49**	386± 61**	387± 59**

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

TABLE C 4

BODY WEIGHT CHANGES: FEMALE

STUDY NO. : 0641
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	100± 4	116± 5	128± 6	137± 6	145± 7	150± 7	155± 8
800 ppm	100± 4	115± 4	127± 5	135± 6	143± 6	149± 7	154± 7
2400 ppm	100± 4	115± 4	128± 4	135± 5	144± 6	149± 7	155± 6
7200 ppm	100± 4	110± 5**	123± 5**	132± 6**	138± 7**	144± 7**	148± 7**

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

STUDY NO. : 0641
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	160± 8	164± 8	167± 9	171± 9	173± 10	177± 10	178± 10
800 ppm	158± 8	162± 8	165± 8	168± 8	172± 9	176± 9	177± 9
2400 ppm	159± 7	163± 8	166± 8	170± 9	173± 9	176± 9	178± 10
7200 ppm	152± 8**	156± 9**	159± 9**	162± 9**	165± 10**	167± 9**	169± 10**

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

STUDY NO. : 0641
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	180± 10	186± 10	191± 11	196± 11	202± 13	207± 12	210± 13
800 ppm	179± 9	187± 10	192± 10	197± 10	203± 11	210± 13	213± 12
2400 ppm	180± 10	188± 10	193± 11	199± 11	205± 12	210± 12	213± 13
7200 ppm	170± 10**	176± 10**	180± 10**	185± 11**	189± 10**	192± 12**	195± 12**

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

(HAN260) BAIS 4

STUDY NO. : 0641
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	215± 13	218± 14	224± 15	227± 15	231± 15	238± 18	244± 20
800 ppm	218± 13	221± 14	226± 15	230± 16	234± 17	241± 18	247± 20
2400 ppm	219± 14	222± 14	226± 14	230± 15	234± 16	243± 18	249± 18
7200 ppm	199± 12**	201± 13**	203± 15**	207± 15**	209± 16**	212± 18**	217± 19**

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

STUDY NO. : 0641
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 70-7	74-7	78-7	82-7	86-7	90-7	94-7
Control	250± 20	255± 21	261± 21	265± 22	267± 25	273± 26	278± 27
800 ppm	253± 22	258± 23	264± 23	270± 23	273± 24	280± 24	284± 23
2400 ppm	254± 21	259± 22	264± 26	270± 30	275± 29	274± 28	281± 26
7200 ppm	219± 20**	222± 23**	223± 24**	224± 26**	227± 25**	232± 23**	230± 23**

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

STUDY NO. : 0641
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	279± 29	280± 31	280± 31
800 ppm	284± 21	285± 24	281± 29
2400 ppm	283± 28	284± 28	283± 30
7200 ppm	227± 22**	222± 27**	221± 25**

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

TABLE D 1

FOOD CONSUMPTION CHANGES AND SURVIVAL ANIMAL NUMBERS: MALE

STUDY NO. : 0641
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>	800 ppm Av. FC.	800 ppm % of cont. <50>	800 ppm No. of Surviv.	2400 ppm Av. FC.	2400 ppm % of cont. <50>	2400 ppm No. of Surviv.	7200 ppm Av. FC.	7200 ppm % of cont. <50>	7200 ppm No. of Surviv.
1-7	13.3 (50)	50/50	13.3 (50)	100	50/50	13.4 (50)	101	50/50	11.8 (50)	89	50/50
2-7	15.0 (50)	50/50	15.1 (50)	101	50/50	14.7 (50)	98	50/50	13.6 (50)	91	50/50
3-7	15.7 (50)	50/50	15.5 (50)	99	50/50	15.5 (50)	99	50/50	14.2 (50)	90	50/50
4-7	16.0 (50)	50/50	15.7 (50)	98	50/50	15.6 (50)	98	50/50	14.4 (50)	90	50/50
5-7	15.6 (50)	50/50	15.6 (50)	100	50/50	15.6 (50)	100	50/50	14.5 (50)	93	50/50
6-7	15.1 (50)	50/50	15.1 (50)	100	50/50	15.2 (50)	101	50/50	14.2 (50)	94	50/50
7-7	14.9 (50)	50/50	15.0 (50)	101	50/50	14.9 (50)	100	50/50	14.0 (50)	94	50/50
8-7	15.4 (50)	50/50	15.7 (50)	102	50/50	15.3 (50)	99	50/50	14.1 (50)	92	50/50
9-7	14.9 (50)	50/50	15.4 (50)	103	50/50	15.0 (50)	101	50/50	13.6 (50)	91	50/50
10-7	15.1 (50)	50/50	15.4 (50)	102	50/50	15.5 (50)	103	50/50	14.0 (50)	93	50/50
11-7	14.4 (50)	50/50	14.7 (50)	102	50/50	14.7 (50)	102	50/50	13.6 (50)	94	50/50
12-7	14.5 (50)	50/50	14.7 (50)	101	50/50	14.7 (50)	101	50/50	13.6 (50)	94	50/50
13-7	14.5 (50)	50/50	14.6 (50)	101	50/50	14.4 (50)	99	50/50	13.4 (50)	92	50/50
14-7	14.7 (50)	50/50	14.7 (50)	100	50/50	14.6 (50)	99	50/50	13.6 (50)	93	50/50
18-7	14.5 (50)	50/50	14.6 (50)	101	50/50	14.3 (50)	99	50/50	13.2 (50)	91	50/50
22-7	14.8 (49)	50/50	14.8 (50)	100	50/50	14.8 (50)	100	50/50	13.5 (50)	91	50/50
26-7	15.0 (50)	50/50	15.1 (50)	101	50/50	14.8 (50)	99	50/50	13.3 (50)	89	50/50
30-7	14.8 (50)	50/50	14.8 (50)	100	50/50	14.6 (50)	99	50/50	13.3 (50)	90	50/50
34-7	15.0 (50)	50/50	15.1 (49)	101	49/50	14.9 (50)	99	50/50	13.6 (50)	91	50/50
38-7	15.3 (50)	50/50	15.3 (49)	100	49/50	15.2 (50)	99	50/50	13.7 (50)	90	50/50
42-7	15.4 (50)	50/50	15.5 (49)	101	49/50	15.3 (50)	99	50/50	13.9 (50)	90	50/50
46-7	15.8 (49)	49/50	15.8 (49)	100	49/50	15.5 (50)	98	50/50	14.2 (50)	90	50/50
50-7	16.1 (49)	49/50	15.9 (49)	99	49/50	15.7 (50)	98	50/50	14.1 (50)	88	50/50
54-7	15.6 (49)	49/50	15.7 (49)	101	49/50	15.4 (50)	99	50/50	14.1 (50)	90	50/50
58-7	15.8 (49)	49/50	15.9 (49)	101	49/50	15.6 (50)	99	50/50	14.2 (50)	90	50/50
62-7	15.9 (48)	48/50	15.8 (49)	99	49/50	15.3 (50)	96	50/50	14.2 (50)	89	50/50
66-7	16.2 (48)	48/50	16.1 (49)	99	49/50	15.8 (50)	98	50/50	14.8 (50)	91	50/50
70-7	16.4 (47)	47/50	15.8 (49)	96	49/50	15.8 (50)	96	50/50	14.8 (50)	90	50/50
74-7	16.2 (47)	47/50	15.9 (49)	98	49/50	15.9 (50)	98	50/50	14.6 (50)	90	50/50
78-7	16.7 (47)	47/50	16.4 (47)	98	47/50	16.0 (50)	96	50/50	14.6 (48)	87	48/50
82-7	16.4 (47)	47/50	16.2 (47)	99	47/50	15.8 (47)	96	47/50	14.4 (48)	88	48/50
86-7	16.5 (46)	46/50	16.3 (47)	99	47/50	15.8 (47)	96	47/50	14.4 (48)	87	48/50
90-7	16.2 (45)	45/50	16.1 (47)	99	47/50	15.6 (45)	96	45/50	14.3 (48)	88	48/50
94-7	16.6 (44)	44/50	15.8 (47)	95	47/50	15.9 (42)	96	42/50	14.6 (45)	88	45/50
98-7	16.2 (41)	42/50	15.9 (46)	98	46/50	15.5 (42)	96	42/50	14.7 (44)	91	44/50
102-7	15.6 (41)	41/50	15.1 (46)	97	46/50	15.2 (39)	97	40/50	14.3 (41)	92	41/50
104-7	15.6 (39)	40/50	15.1 (45)	97	45/50	15.5 (38)	99	38/50	14.3 (40)	92	40/50

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

TABLE D 2

FOOD CONSUMPTION CHANGES AND SURVIVAL ANIMAL NUMBERS: FEMALE

STUDY NO. : 0641
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>	800 ppm Av. FC.	800 ppm % of cont. <50>	800 ppm No. of Surviv.	2400 ppm Av. FC.	2400 ppm % of cont. <50>	2400 ppm No. of Surviv.	7200 ppm Av. FC.	7200 ppm % of cont. <50>	7200 ppm No. of Surviv.
1-7	10.5 (50)	50/50	10.6 (50)	101	50/50	10.4 (50)	99	50/50	9.1 (50)	87	50/50
2-7	10.7 (50)	50/50	10.7 (50)	100	50/50	10.6 (50)	99	50/50	10.0 (49)	93	50/50
3-7	10.5 (50)	50/50	10.5 (50)	100	50/50	10.3 (50)	98	50/50	9.8 (50)	93	50/50
4-7	10.6 (50)	50/50	10.6 (50)	100	50/50	10.5 (50)	99	50/50	9.6 (50)	91	50/50
5-7	10.3 (50)	50/50	10.3 (50)	100	50/50	10.2 (50)	99	50/50	9.4 (50)	91	50/50
6-7	10.1 (50)	50/50	10.0 (50)	99	50/50	9.9 (50)	98	50/50	9.2 (50)	91	50/50
7-7	10.0 (50)	50/50	10.0 (50)	100	50/50	9.9 (50)	99	50/50	9.2 (50)	92	50/50
8-7	10.1 (50)	50/50	10.1 (50)	100	50/50	9.9 (50)	98	50/50	9.2 (50)	91	50/50
9-7	9.9 (50)	50/50	9.9 (50)	100	50/50	9.9 (50)	100	50/50	9.0 (50)	91	50/50
10-7	10.0 (50)	50/50	10.0 (50)	100	50/50	9.8 (50)	98	50/50	9.1 (50)	91	50/50
11-7	9.9 (50)	50/50	10.0 (50)	101	50/50	9.9 (50)	100	50/50	9.0 (50)	91	50/50
12-7	10.1 (50)	50/50	10.2 (50)	101	50/50	10.0 (50)	99	50/50	9.1 (50)	90	50/50
13-7	9.9 (50)	50/50	10.1 (50)	102	50/50	9.9 (50)	100	50/50	9.0 (50)	91	50/50
14-7	10.1 (50)	50/50	10.4 (50)	103	50/50	10.1 (50)	100	50/50	9.2 (50)	91	50/50
18-7	9.9 (50)	50/50	10.2 (50)	103	50/50	10.0 (50)	101	50/50	9.0 (50)	91	50/50
22-7	10.3 (50)	50/50	10.4 (50)	101	50/50	10.2 (50)	99	50/50	9.2 (50)	89	50/50
26-7	9.9 (50)	50/50	10.1 (50)	102	50/50	10.0 (50)	101	50/50	9.1 (50)	92	50/50
30-7	10.1 (50)	50/50	10.3 (50)	102	50/50	10.3 (50)	102	50/50	9.2 (50)	91	50/50
34-7	10.3 (50)	50/50	10.4 (50)	101	50/50	10.3 (50)	100	50/50	9.2 (50)	89	50/50
38-7	10.3 (50)	50/50	10.4 (50)	101	50/50	10.4 (50)	101	50/50	9.4 (49)	91	49/50
42-7	10.5 (50)	50/50	10.7 (50)	102	50/50	10.6 (50)	101	50/50	9.8 (49)	93	49/50
46-7	10.6 (50)	50/50	10.8 (50)	102	50/50	10.7 (50)	101	50/50	9.7 (49)	92	49/50
50-7	10.8 (50)	50/50	11.0 (50)	102	50/50	10.9 (50)	101	50/50	9.9 (49)	92	49/50
54-7	11.0 (50)	50/50	11.1 (50)	101	50/50	11.3 (50)	103	50/50	10.1 (49)	92	49/50
58-7	11.1 (50)	50/50	11.0 (50)	99	50/50	10.9 (50)	98	50/50	10.0 (49)	90	49/50
62-7	11.3 (50)	50/50	11.5 (50)	102	50/50	11.3 (50)	100	50/50	10.1 (49)	89	49/50
66-7	11.5 (50)	50/50	11.4 (49)	99	49/50	11.4 (50)	99	50/50	10.3 (47)	90	47/50
70-7	11.7 (50)	50/50	11.9 (49)	102	49/50	11.3 (50)	97	50/50	10.6 (47)	91	47/50
74-7	11.6 (50)	50/50	11.8 (49)	102	49/50	11.5 (50)	99	50/50	10.6 (46)	91	46/50
78-7	12.0 (50)	50/50	12.2 (48)	102	48/50	11.9 (50)	99	50/50	10.5 (44)	88	44/50
82-7	11.8 (49)	49/50	12.0 (46)	102	46/50	11.9 (50)	101	50/50	10.4 (44)	88	44/50
86-7	11.5 (49)	49/50	11.6 (44)	101	44/50	11.9 (50)	103	50/50	10.4 (42)	90	42/50
90-7	11.8 (48)	48/50	12.1 (43)	103	43/50	11.6 (49)	98	49/50	10.8 (38)	92	38/50
94-7	12.1 (46)	46/50	12.7 (43)	105	43/50	12.4 (48)	102	48/50	10.5 (38)	87	38/50
98-7	12.1 (44)	44/50	12.3 (42)	102	42/50	12.0 (46)	99	46/50	10.8 (36)	89	36/50
102-7	12.1 (40)	40/50	12.1 (39)	100	39/50	11.8 (44)	98	44/50	10.5 (35)	87	35/50
104-7	11.8 (38)	38/50	11.7 (38)	99	38/50	11.7 (42)	99	42/50	10.5 (33)	89	33/50

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

TABLE D 3

FOOD CONSUMPTION CHANGES: MALE

STUDY NO. : 0641
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	13.3± 0.8	15.0± 0.9	15.7± 1.1	16.0± 0.9	15.6± 0.8	15.1± 1.0	14.9± 1.0
800 ppm	13.3± 0.8	15.1± 1.3	15.5± 1.2	15.7± 1.1	15.6± 1.0	15.1± 1.0	15.0± 1.0
2400 ppm	13.4± 0.8	14.7± 1.0	15.5± 1.0	15.6± 1.1	15.6± 1.0	15.2± 1.1	14.9± 1.1
7200 ppm	11.8± 0.7**	13.6± 1.0**	14.2± 1.1**	14.4± 1.0**	14.5± 0.8**	14.2± 0.9**	14.0± 0.9**

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

STUDY NO. : 0641
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	15.4± 1.1	14.9± 1.1	15.1± 1.2	14.4± 1.1	14.5± 1.0	14.5± 0.9	14.7± 0.9
800 ppm	15.7± 1.2	15.4± 1.2	15.4± 1.2	14.7± 1.0	14.7± 1.0	14.6± 0.9	14.7± 0.9
2400 ppm	15.3± 1.1	15.0± 1.1	15.5± 1.0	14.7± 1.0	14.7± 0.9	14.4± 0.9	14.6± 1.0
7200 ppm	14.1± 1.0**	13.6± 1.0**	14.0± 1.0**	13.6± 1.0**	13.6± 1.0**	13.4± 1.0**	13.6± 0.9**

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

STUDY NO. : 0641
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	14.5± 0.9	14.8± 1.0	15.0± 0.9	14.8± 0.9	15.0± 1.1	15.3± 1.0	15.4± 1.0
800 ppm	14.6± 0.8	14.8± 1.0	15.1± 1.0	14.8± 0.9	15.1± 0.9	15.3± 0.9	15.5± 0.9
2400 ppm	14.3± 1.1	14.8± 1.0	14.8± 1.1	14.6± 0.9	14.9± 1.0	15.2± 0.9	15.3± 1.1
7200 ppm	13.2± 1.0**	13.5± 1.0**	13.3± 1.1**	13.3± 0.9**	13.6± 1.0**	13.7± 1.0**	13.9± 1.1**

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

STUDY NO. : 0641
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	15.8± 0.9	16.1± 0.8	15.6± 0.8	15.8± 1.3	15.9± 0.9	16.2± 1.3	16.4± 0.9
800 ppm	15.8± 1.0	15.9± 1.1	15.7± 0.9	15.9± 0.9	15.8± 1.0	16.1± 1.0	15.8± 2.1*
2400 ppm	15.5± 1.1	15.7± 1.1*	15.4± 1.0	15.6± 1.0	15.3± 1.0*	15.8± 1.0	15.8± 1.1*
7200 ppm	14.2± 1.0**	14.1± 1.6**	14.1± 1.1**	14.2± 1.2**	14.2± 1.1**	14.8± 1.1**	14.8± 1.1**

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

STUDY NO. : 0641
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	16.2± 1.0	16.7± 1.1	16.4± 1.5	16.5± 1.4	16.2± 1.6	16.6± 2.0	16.2± 1.3
800 ppm	15.9± 1.4	16.4± 1.0	16.2± 1.0	16.3± 0.8	16.1± 1.1	15.8± 2.4	15.9± 1.3
2400 ppm	15.9± 1.1	16.0± 2.4	15.8± 1.3	15.8± 2.2	15.6± 1.6	15.9± 1.3	15.5± 2.2
7200 ppm	14.6± 1.4**	14.6± 1.2**	14.4± 1.2**	14.4± 1.4**	14.3± 1.8**	14.6± 1.2**	14.7± 1.4**

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

STUDY NO. : 0641
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	15.6± 2.7	15.6± 2.1
800 ppm	15.1± 1.8	15.1± 2.2
2400 ppm	15.2± 1.4	15.5± 1.3
7200 ppm	14.3± 1.6**	14.3± 1.8**

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

TABLE D 4

FOOD CONSUMPTION CHANGES: FEMALE

STUDY NO. : 0641
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	10.5± 0.7	10.7± 0.6	10.5± 0.7	10.6± 0.6	10.3± 0.6	10.1± 0.7	10.0± 0.6
800 ppm	10.6± 0.6	10.7± 0.6	10.5± 0.7	10.6± 0.6	10.3± 0.7	10.0± 0.6	10.0± 0.7
2400 ppm	10.4± 0.5	10.6± 0.6	10.3± 0.5	10.5± 0.7	10.2± 0.8	9.9± 0.6	9.9± 0.7
7200 ppm	9.1± 0.6**	10.0± 0.6**	9.8± 0.6**	9.6± 0.7**	9.4± 0.6**	9.2± 0.7**	9.2± 0.7**

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

STUDY NO. : 0641
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	10.1± 0.7	9.9± 0.7	10.0± 0.7	9.9± 0.7	10.1± 0.7	9.9± 0.7	10.1± 0.7
800 ppm	10.1± 0.7	9.9± 0.6	10.0± 0.6	10.0± 0.7	10.2± 0.7	10.1± 0.6	10.4± 0.7
2400 ppm	9.9± 0.7	9.9± 0.7	9.8± 0.7	9.9± 0.7	10.0± 0.7	9.9± 0.7	10.1± 0.6
7200 ppm	9.2± 0.6**	9.0± 0.7**	9.1± 0.7**	9.0± 0.7**	9.1± 0.6**	9.0± 0.6**	9.2± 0.6**

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

STUDY NO. : 0641
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	9.9± 0.7	10.3± 0.6	9.9± 0.6	10.1± 0.7	10.3± 0.5	10.3± 0.5	10.5± 0.6
800 ppm	10.2± 0.6	10.4± 0.7	10.1± 0.6	10.3± 0.6	10.4± 0.7	10.4± 0.6	10.7± 0.8
2400 ppm	10.0± 0.7	10.2± 0.7	10.0± 0.6	10.3± 0.6	10.3± 0.8	10.4± 0.8	10.6± 0.7
7200 ppm	9.0± 0.6**	9.2± 0.5**	9.1± 0.6**	9.2± 0.5**	9.2± 0.5**	9.4± 0.6**	9.8± 0.8**

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

STUDY NO. : 0641
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	10.6± 0.7	10.8± 0.8	11.0± 0.7	11.1± 0.6	11.3± 0.9	11.5± 0.9	11.7± 1.1
800 ppm	10.8± 0.7	11.0± 0.8	11.1± 0.9	11.0± 0.9	11.5± 0.9	11.4± 1.0	11.9± 1.1
2400 ppm	10.7± 0.7	10.9± 0.8	11.3± 2.6	10.9± 0.9	11.3± 0.9	11.4± 0.8	11.3± 1.0
7200 ppm	9.7± 0.8**	9.9± 0.9**	10.1± 0.8**	10.0± 0.7**	10.1± 0.9**	10.3± 0.8**	10.6± 0.9**

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

(HAN260)

STUDY NO. : 0641
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	11.6± 0.8	12.0± 0.9	11.8± 1.0	11.5± 1.1	11.8± 1.1	12.1± 1.9	12.1± 1.8
800 ppm	11.8± 1.2	12.2± 1.2	12.0± 1.1	11.6± 1.9	12.1± 1.1	12.7± 1.5	12.3± 1.6
2400 ppm	11.5± 0.8	11.9± 1.0	11.9± 1.3	11.9± 2.1	11.6± 1.2	12.4± 1.0	12.0± 1.5
7200 ppm	10.6± 1.0**	10.5± 1.2**	10.4± 1.6**	10.4± 1.1**	10.8± 1.1**	10.5± 1.5**	10.8± 1.2**

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

STUDY NO. : 0641
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	12.1± 1.3	11.8± 1.2
800 ppm	12.1± 1.6	11.7± 1.9
2400 ppm	11.8± 1.1	11.7± 1.0
7200 ppm	10.5± 2.0**	10.5± 1.4**

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

TABLE E 1

WATER CONSUMPTION CHANGES AND SURVIVAL ANIMAL NUMBERS: MALE

STUDY NO. : 0641
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>	800 ppm Av. WC.	800 ppm % of cont. <50>	800 ppm No. of Surviv.	2400 ppm Av. WC.	2400 ppm % of cont. <50>	2400 ppm No. of Surviv.	7200 ppm Av. WC.	7200 ppm % of cont. <50>	7200 ppm No. of Surviv.
1-7	16.3 (50)	50/50	15.6 (50)	96	50/50	14.6 (50)	90	50/50	13.1 (50)	80	50/50
2-7	17.5 (50)	50/50	16.9 (50)	97	50/50	15.7 (50)	90	50/50	13.4 (50)	77	50/50
3-7	18.0 (50)	50/50	17.6 (49)	98	50/50	16.3 (50)	91	50/50	13.0 (49)	72	50/50
4-7	17.9 (50)	50/50	18.4 (50)	103	50/50	16.2 (50)	91	50/50	12.8 (50)	72	50/50
5-7	17.8 (49)	50/50	17.7 (50)	99	50/50	16.2 (50)	91	50/50	12.9 (50)	72	50/50
6-7	17.5 (50)	50/50	17.5 (49)	100	50/50	16.7 (50)	95	50/50	12.6 (50)	72	50/50
7-7	17.1 (50)	50/50	18.1 (48)	106	50/50	16.5 (50)	96	50/50	12.8 (50)	75	50/50
8-7	16.8 (50)	50/50	18.7 (47)	111	50/50	16.6 (50)	99	50/50	12.7 (50)	76	50/50
9-7	17.0 (50)	50/50	18.1 (49)	106	50/50	17.3 (49)	102	50/50	13.1 (50)	77	50/50
10-7	17.2 (50)	50/50	17.5 (49)	102	50/50	17.2 (49)	100	50/50	13.3 (50)	77	50/50
11-7	17.2 (50)	50/50	16.8 (50)	98	50/50	16.6 (50)	97	50/50	12.5 (50)	73	50/50
12-7	17.5 (50)	50/50	17.1 (48)	98	50/50	15.9 (50)	91	50/50	12.0 (50)	69	50/50
13-7	16.7 (50)	50/50	16.7 (49)	100	50/50	15.4 (49)	92	50/50	11.6 (50)	69	50/50
14-7	17.1 (50)	50/50	16.8 (49)	98	50/50	15.4 (50)	90	50/50	12.5 (50)	73	50/50
18-7	16.0 (50)	50/50	16.3 (50)	102	50/50	15.0 (50)	94	50/50	11.3 (50)	71	50/50
22-7	15.8 (50)	50/50	16.1 (50)	102	50/50	14.9 (50)	94	50/50	11.4 (50)	72	50/50
26-7	16.1 (50)	50/50	16.5 (50)	102	50/50	15.5 (50)	96	50/50	12.4 (50)	77	50/50
30-7	15.7 (50)	50/50	16.3 (50)	104	50/50	15.0 (50)	96	50/50	12.5 (50)	80	50/50
34-7	16.0 (50)	50/50	16.4 (49)	103	49/50	15.2 (50)	95	50/50	12.3 (50)	77	50/50
38-7	16.1 (50)	50/50	16.1 (49)	100	49/50	15.3 (50)	95	50/50	12.2 (50)	76	50/50
42-7	16.1 (50)	50/50	16.7 (49)	104	49/50	15.4 (50)	96	50/50	12.6 (50)	78	50/50
46-7	16.5 (49)	49/50	16.7 (49)	101	49/50	15.6 (50)	95	50/50	13.0 (50)	79	50/50
50-7	16.4 (49)	49/50	17.1 (49)	104	49/50	15.9 (50)	97	50/50	13.0 (50)	79	50/50
54-7	16.3 (49)	49/50	16.6 (49)	102	49/50	15.8 (50)	97	50/50	12.9 (50)	79	50/50
58-7	16.4 (49)	49/50	16.6 (49)	101	49/50	15.8 (50)	96	50/50	13.0 (50)	79	50/50
62-7	17.0 (48)	48/50	16.9 (49)	99	49/50	15.9 (50)	94	50/50	13.1 (50)	77	50/50
66-7	16.8 (48)	48/50	16.7 (49)	99	49/50	15.9 (50)	95	50/50	13.6 (50)	81	50/50
70-7	17.5 (47)	47/50	16.8 (49)	96	49/50	16.1 (50)	92	50/50	14.0 (50)	80	50/50
74-7	17.5 (47)	47/50	16.7 (49)	95	49/50	16.4 (50)	94	50/50	14.1 (50)	81	50/50
78-7	18.0 (46)	47/50	17.7 (47)	98	47/50	16.5 (50)	92	50/50	14.9 (48)	83	48/50
82-7	18.4 (46)	47/50	17.3 (47)	94	47/50	16.4 (47)	89	47/50	14.2 (48)	77	48/50
86-7	18.5 (44)	46/50	18.0 (47)	97	47/50	16.5 (47)	89	47/50	13.9 (48)	75	48/50
90-7	18.4 (42)	45/50	17.7 (47)	96	47/50	16.9 (45)	92	45/50	14.4 (48)	78	48/50
94-7	18.3 (39)	44/50	18.5 (47)	101	47/50	17.2 (41)	94	42/50	14.7 (45)	80	45/50
98-7	18.7 (37)	42/50	18.8 (46)	101	46/50	18.2 (41)	97	42/50	15.1 (44)	81	44/50
102-7	19.0 (37)	41/50	19.2 (45)	101	46/50	18.4 (38)	97	40/50	15.0 (41)	79	41/50
104-7	20.0 (36)	40/50	18.7 (41)	94	45/50	18.8 (37)	94	38/50	15.3 (40)	77	40/50

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

TABLE E 2

WATER CONSUMPTION CHANGES AND SURVIVAL ANIMAL NUMBERS: FEMALE

STUDY NO. : 0641
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>	800 ppm Av. WC.	800 ppm % of cont. <50>	800 ppm No. of Surviv.	2400 ppm Av. WC.	2400 ppm % of cont. <50>	2400 ppm No. of Surviv.	7200 ppm Av. WC.	7200 ppm % of cont. <50>	7200 ppm No. of Surviv.
1-7	15.4 (49)	50/50	15.7 (48)	102	50/50	13.9 (50)	90	50/50	10.8 (50)	70	50/50
2-7	15.9 (49)	50/50	18.0 (48)	113	50/50	14.1 (50)	89	50/50	10.3 (50)	65	50/50
3-7	16.0 (47)	50/50	15.9 (38)	99	50/50	14.5 (44)	91	50/50	10.7 (50)	67	50/50
4-7	15.6 (45)	50/50	16.7 (36)	107	50/50	15.6 (47)	100	50/50	10.3 (50)	66	50/50
5-7	18.0 (48)	50/50	18.0 (39)	100	50/50	16.3 (48)	91	50/50	10.1 (50)	56	50/50
6-7	16.1 (44)	50/50	17.3 (36)	107	50/50	16.2 (44)	101	50/50	9.9 (50)	61	50/50
7-7	15.9 (44)	50/50	18.0 (31)	113	50/50	15.5 (37)	97	50/50	10.6 (49)	67	50/50
8-7	16.6 (43)	50/50	16.5 (30)	99	50/50	15.0 (38)	90	50/50	10.0 (50)	60	50/50
9-7	16.5 (47)	50/50	18.5 (33)	112	50/50	16.1 (44)	98	50/50	9.6 (50)	58	50/50
10-7	16.4 (47)	50/50	17.6 (39)	107	50/50	14.6 (41)	89	50/50	9.5 (50)	58	50/50
11-7	16.5 (42)	50/50	18.2 (40)	110	50/50	15.6 (41)	95	50/50	9.4 (49)	57	50/50
12-7	15.9 (43)	50/50	18.7 (34)	118	50/50	14.6 (43)	92	50/50	9.6 (50)	60	50/50
13-7	16.4 (46)	50/50	18.4 (34)	112	50/50	16.0 (39)	98	50/50	9.8 (50)	60	50/50
14-7	16.3 (43)	50/50	18.0 (29)	110	50/50	15.2 (39)	93	50/50	9.7 (49)	60	50/50
18-7	17.2 (46)	50/50	16.7 (27)	97	50/50	15.4 (39)	90	50/50	10.4 (50)	60	50/50
22-7	16.8 (44)	50/50	18.6 (42)	111	50/50	16.4 (43)	98	50/50	10.3 (50)	61	50/50
26-7	17.0 (47)	50/50	18.5 (40)	109	50/50	16.5 (44)	97	50/50	10.7 (48)	63	50/50
30-7	16.5 (47)	50/50	18.4 (40)	112	50/50	15.6 (38)	95	50/50	10.5 (50)	64	50/50
34-7	16.7 (48)	50/50	17.3 (44)	104	50/50	15.1 (43)	90	50/50	10.5 (48)	63	50/50
38-7	16.2 (47)	50/50	17.9 (45)	110	50/50	15.4 (43)	95	50/50	10.8 (49)	67	49/50
42-7	15.9 (49)	50/50	18.3 (44)	115	50/50	16.0 (44)	101	50/50	11.1 (49)	70	49/50
46-7	15.7 (49)	50/50	16.0 (45)	102	50/50	16.7 (46)	106	50/50	10.8 (48)	69	49/50
50-7	15.1 (49)	50/50	16.6 (44)	110	50/50	17.0 (43)	113	50/50	11.8 (49)	78	49/50
54-7	15.3 (49)	50/50	15.5 (45)	101	50/50	15.2 (44)	99	50/50	11.4 (48)	75	49/50
58-7	14.7 (50)	50/50	15.2 (49)	103	50/50	14.9 (47)	101	50/50	11.1 (49)	76	49/50
62-7	14.7 (50)	50/50	16.4 (49)	112	50/50	14.3 (47)	97	50/50	11.3 (48)	77	49/50
66-7	14.7 (49)	50/50	16.6 (46)	113	49/50	14.2 (47)	97	50/50	11.2 (47)	76	47/50
70-7	14.7 (50)	50/50	15.5 (47)	105	49/50	14.1 (47)	96	50/50	12.4 (47)	84	47/50
74-7	14.4 (50)	50/50	15.5 (47)	108	49/50	14.8 (48)	103	50/50	12.4 (46)	86	46/50
78-7	14.6 (50)	50/50	16.3 (46)	112	48/50	14.5 (48)	99	50/50	12.5 (44)	86	44/50
82 7	14.3 (48)	49/50	15.6 (46)	109	46/50	14.3 (49)	100	50/50	12.9 (43)	90	44/50
86-7	15.0 (47)	49/50	15.8 (42)	105	44/50	15.4 (48)	103	50/50	13.2 (42)	88	42/50
90-7	14.9 (46)	48/50	15.3 (43)	103	43/50	14.4 (49)	97	49/50	13.8 (38)	93	38/50
94-7	15.5 (45)	46/50	15.6 (41)	101	43/50	14.8 (47)	95	48/50	15.3 (37)	99	38/50
98-7	16.1 (44)	44/50	16.4 (41)	102	42/50	15.3 (45)	95	46/50	16.8 (36)	104	36/50
102-7	16.7 (40)	40/50	16.4 (34)	98	39/50	16.4 (44)	98	44/50	17.1 (35)	102	35/50
104-7	16.8 (38)	38/50	16.4 (36)	98	38/50	15.9 (42)	95	42/50	18.4 (31)	110	33/50

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

TABLE E 3

WATER CONSUMPTION CHANGES: MALE

STUDY NO. : 0641
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	16.3± 1.6	17.5± 1.4	18.0± 1.8	17.9± 1.5	17.8± 1.7	17.5± 1.9	17.1± 1.8
800 ppm	15.6± 1.0	16.9± 1.8*	17.6± 2.3	18.4± 3.9	17.7± 2.5	17.5± 3.0	18.1± 2.4*
2400 ppm	14.6± 1.0**	15.7± 1.2**	16.3± 1.2**	16.2± 1.6**	16.2± 1.6**	16.7± 3.3**	16.5± 2.3*
7200 ppm	13.1± 4.5**	13.4± 2.1**	13.0± 1.2**	12.8± 1.0**	12.9± 1.1**	12.6± 0.9**	12.8± 1.1**

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

STUDY NO. : 0641
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	16.8± 1.4	17.0± 1.8	17.2± 2.0	17.2± 2.3	17.5± 2.3	16.7± 1.8	17.1± 2.5
800 ppm	18.7± 2.1**	18.1± 2.1**	17.5± 2.7	16.8± 2.0	17.1± 3.0	16.7± 2.6	16.8± 3.0
2400 ppm	16.6± 2.0	17.3± 2.1	17.2± 1.4	16.6± 2.4	15.9± 2.5**	15.4± 1.5**	15.4± 2.2**
7200 ppm	12.7± 1.1**	13.1± 1.3**	13.3± 1.2**	12.5± 1.1**	12.0± 1.2**	11.6± 0.9**	12.5± 2.2**

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

STUDY NO. : 0641
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	16.0± 1.4	15.8± 1.4	16.1± 1.0	15.7± 1.2	16.0± 1.3	16.1± 1.3	16.1± 1.3
800 ppm	16.3± 2.1	16.1± 2.4	16.5± 1.7	16.3± 1.7	16.4± 1.5	16.1± 1.4	16.7± 1.4**
2400 ppm	15.0± 1.4**	14.9± 1.5**	15.5± 1.2**	15.0± 1.1**	15.2± 0.9**	15.3± 1.0**	15.4± 0.9**
7200 ppm	11.3± 1.1**	11.4± 0.9**	12.4± 1.1**	12.5± 1.1**	12.3± 0.9**	12.2± 0.9**	12.6± 1.1**

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

STUDY NO. : 0641
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	16.5± 1.2	16.4± 1.2	16.3± 1.0	16.4± 1.5	17.0± 1.3	16.8± 2.0	17.5± 2.0
800 ppm	16.7± 1.4	17.1± 2.7*	16.6± 1.3	16.6± 1.2	16.9± 1.4	16.7± 1.4	16.8± 2.1
2400 ppm	15.6± 1.3**	15.9± 1.0	15.8± 1.2	15.8± 1.0**	15.9± 1.3**	15.9± 1.1**	16.1± 1.3**
7200 ppm	13.0± 1.0**	13.0± 1.2**	12.9± 1.3**	13.0± 1.2**	13.1± 1.3**	13.6± 1.5**	14.0± 1.5**

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

STUDY NO. : 0641
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	17.5± 2.3	18.0± 2.3	18.4± 3.0	18.5± 3.3	18.4± 3.3	18.3± 4.1	18.7± 3.6
800 ppm	16.7± 2.0	17.7± 1.5	17.3± 1.5	18.0± 1.9	17.7± 2.2	18.5± 3.5	18.8± 3.2
2400 ppm	16.4± 1.3*	16.5± 2.4**	16.4± 1.8**	16.5± 2.1**	16.9± 2.2	17.2± 2.4	18.2± 3.0
7200 ppm	14.1± 1.4**	14.9± 1.7**	14.2± 1.5**	13.9± 2.0**	14.4± 2.2**	14.7± 2.0**	15.1± 2.8**

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

STUDY NO. : 0641
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) 102-7(3)	104-7(3)
Control	19.0± 3.7	20.0± 4.3
800 ppm	19.2± 3.4	18.7± 3.9
2400 ppm	18.4± 2.9	18.8± 3.4
7200 ppm	15.0± 2.9**	15.3± 2.8**

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

TABLE E 4

WATER CONSUMPTION CHANGES: FEMALE

STUDY NO. : 0641
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) 1-7(3)	2-7(3)	3-7(3)	4-7(3)	5-7(3)	6-7(3)	7-7(3)
Control	15.4± 3.4	15.9± 4.2	16.0± 2.7	15.6± 2.7	18.0± 7.6	16.1± 4.0	15.9± 4.1
800 ppm	15.7± 4.2	18.0± 7.6	15.9± 3.4	16.7± 4.6	18.0± 6.9	17.3± 5.4	18.0± 5.3
2400 ppm	13.9± 4.0**	14.1± 4.5**	14.5± 4.4**	15.6± 4.1	16.3± 6.5*	16.2± 5.9*	15.5± 4.7
7200 ppm	10.8± 1.0**	10.3± 0.8**	10.7± 2.6**	10.3± 2.3**	10.1± 1.2**	9.9± 1.0**	10.6± 2.3**

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

STUDY NO. : 0641
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	16.6± 4.8	16.5± 7.1	16.4± 4.4	16.5± 4.6	15.9± 3.8	16.4± 4.5	16.3± 4.8
800 ppm	16.5± 4.9	18.5± 7.4	17.6± 5.8	18.2± 5.1	18.7± 5.5	18.4± 5.3	18.0± 5.0
2400 ppm	15.0± 4.1	16.1± 5.2	14.6± 3.9*	15.6± 4.9	14.6± 4.3*	16.0± 5.6	15.2± 4.8
7200 ppm	10.0± 3.2**	9.6± 1.3**	9.5± 2.0**	9.4± 1.5**	9.6± 3.0**	9.8± 2.6**	9.7± 3.3**

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

STUDY NO. : 0641
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	17.2± 4.8	16.8± 4.8	17.0± 4.7	16.5± 4.6	16.7± 4.0	16.2± 4.0	15.9± 3.5
800 ppm	16.7± 4.9	18.6± 5.4	18.5± 5.2	18.4± 4.7	17.3± 4.6	17.9± 4.9	18.3± 4.8*
2400 ppm	15.4± 4.3	16.4± 5.4	16.5± 5.1	15.6± 4.2	15.1± 3.6*	15.4± 4.2	16.0± 4.9
7200 ppm	10.4± 3.0**	10.3± 3.8**	10.7± 3.0**	10.5± 2.5**	10.5± 2.2**	10.8± 2.7**	11.1± 2.8**

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

STUDY NO. : 0641
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	15.7± 3.6	15.1± 3.2	15.3± 4.0	14.7± 2.9	14.7± 2.8	14.7± 2.8	14.7± 2.8
800 ppm	16.0± 3.3	16.6± 4.0	15.5± 3.7	15.2± 3.6	16.4± 4.4	16.6± 4.6	15.5± 3.2
2400 ppm	16.7± 4.7	17.0± 5.5	15.2± 4.6	14.9± 4.5	14.3± 4.0	14.2± 3.5	14.1± 3.4
7200 ppm	10.8± 1.9**	11.8± 3.6**	11.4± 3.1**	11.1± 2.7**	11.3± 2.5**	11.2± 2.3**	12.4± 2.8**

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

STUDY NO. : 0641
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	14.4± 3.0	14.6± 3.0	14.3± 2.1	15.0± 2.5	14.9± 2.5	15.5± 3.8	16.1± 4.4
800 ppm	15.5± 4.1	16.3± 4.4	15.6± 4.2	15.8± 5.5	15.3± 3.6	15.6± 3.6	16.4± 3.9
2400 ppm	14.8± 3.5	14.5± 3.3	14.3± 3.3	15.4± 5.8	14.4± 4.3*	14.8± 3.5	15.3± 3.8
7200 ppm	12.4± 2.9**	12.5± 3.4**	12.9± 3.3*	13.2± 2.4**	13.8± 2.8*	15.3± 2.6	16.8± 3.7

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

STUDY NO. : 0641
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	16.7± 3.8	16.8± 3.9
800 ppm	16.4± 3.8	16.4± 3.8
2400 ppm	16.4± 4.9	15.9± 3.6
7200 ppm	17.1± 3.9	18.4± 3.3

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

TABLE F 1

CHEMICAL INTAKE CHANGES: MALE

STUDY NO. : 0641
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : mg／kg／d a y
REPORT TYPE : A1 104
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1		2		3		4		5		6		7	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
800 ppm	84±	4	76±	6	69±	8	66±	14	59±	9	56±	11	55±	7
2400 ppm	235±	10	210±	11	192±	11	172±	14	162±	12	158±	27	150±	17
7200 ppm	667±	243	567±	77	483±	31	432±	24	405±	25	375±	21	365±	24

STUDY NO. : 0641
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : mg／kg／d a y
REPORT TYPE : A1 104
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8		9		10		11		12		13		14	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
800 ppm	55±	6	52±	6	48±	8	45±	6	45±	10	43±	7	43±	9
2400 ppm	146±	14	147±	15	143±	10	134±	17	125±	16	119±	8	117±	14
7200 ppm	352±	26	353±	28	349±	27	323±	21	304±	24	289±	21	306±	53

STUDY NO. : 0641
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : mg／kg／d a y
REPORT TYPE : A1 104
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 18		22		26		30		34		38		42	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
800 ppm	39±	5	37±	6	37±	4	35±	4	34±	3	33±	2	33±	3
2400 ppm	108±	7	102±	8	103±	6	97±	6	96±	4	95±	5	94±	4
7200 ppm	264±	22	258±	18	273±	23	267±	22	257±	15	250±	16	256±	21

STUDY NO. : 0641
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
800 ppm	33±	2	33±	5	32±	2	31±	2	32±	2	31±	2	31±	3
2400 ppm	94±	6	94±	5	93±	6	91±	5	91±	6	89±	5	90±	6
7200 ppm	261±	16	258±	19	254±	29	255±	23	253±	23	260±	27	268±	41

STUDY NO. : 0641
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
800 ppm	31±	3	32±	2	31±	2	32±	3	32±	3	33±	6	34±	5
2400 ppm	91±	5	91±	13	90±	7	90±	8	92±	10	95±	13	101±	18
7200 ppm	272±	48	279±	33	265±	30	260±	41	274±	52	280±	70	291±	108

STUDY NO. : 0641
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
800 ppm	35±	6	35±	7
2400 ppm	105±	27	104±	17
7200 ppm	287±	92	288±	66

TABLE F 2

CHEMICAL INTAKE CHANGES: FEMALE

STUDY NO. : 0641
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) 1		2		3		4		5		6		7	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
800 ppm	109±	29	114±	49	93±	19	94±	27	98±	40	90±	28	91±	29
2400 ppm	290±	79	264±	83	259±	83	261±	72	263±	107	251±	90	234±	69
7200 ppm	706±	68	606±	34	583±	133	537±	108	508±	53	480±	41	499±	105

STUDY NO. : 0641
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
800 ppm	82±	26	90±	37	84±	28	85±	25	86±	27	83±	24	80±	22
2400 ppm	222±	60	233±	75	206±	55	215±	65	199±	59	215±	76	201±	62
7200 ppm	462±	141	437±	57	422±	84	413±	61	413±	124	419±	108	411±	136

STUDY NO. : 0641
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
800 ppm	73±	21	78±	23	75±	20	72±	18	66±	17	68±	18	68±	18
2400 ppm	197±	58	207±	71	200±	63	183±	49	174±	42	175±	48	176±	56
7200 ppm	424±	122	414±	149	420±	123	398±	92	394±	82	399±	95	402±	94

STUDY NO. : 0641
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) 46		50		54		58		62		66		70	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
800 ppm	58±	12	59±	15	54±	14	52±	13	55±	16	54±	15	49±	10
2400 ppm	181±	51	181±	59	159±	50	153±	47	142±	40	139±	37	134±	35
7200 ppm	387±	61	419±	129	398±	110	385±	90	386±	91	374±	78	412±	107

STUDY NO. : 0641
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
800 ppm	48±	13	50±	14	46±	12	46±	14	44±	10	44±	9	46±	10
2400 ppm	138±	37	133±	33	128±	33	136±	60	130±	59	129±	42	132±	47
7200 ppm	412±	133	408±	125	423±	128	427±	111	436±	121	485±	109	536±	125

STUDY NO. : 0641
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
800 ppm	47±	12	47±	11
2400 ppm	142±	57	138±	45
7200 ppm	561±	150	610±	143

TABLE G 1

HEMATOLOGY: MALE

STUDY NO. : 0641
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	40	7.81± 1.36	13.6± 2.7	38.8± 6.1	50.0± 2.7	17.4± 1.3	34.9± 2.1	1041± 288
800 ppm	45	8.18± 1.45	14.4± 2.5	40.6± 6.0	50.5± 6.7	17.8± 2.2	35.3± 1.6	1019± 334
2400 ppm	38	8.46± 1.00	14.8± 2.0	41.6± 4.6	49.2± 1.8	17.4± 1.0	35.4± 1.4	962± 264
7200 ppm	40	8.39± 1.00	14.7± 1.9	40.8± 4.4	48.7± 2.0**	17.5± 0.9	35.9± 1.4	901± 244

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

STUDY NO. : 0641
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	RETICULOCYTE %	
Control	40	5.5±	4.8
800 ppm	45	5.0±	5.4
2400 ppm	38	4.0±	2.3
7200 ppm	40	3.2±	1.9**

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

STUDY NO. : 0641
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 $10^3/\mu l$		Differential WBC (%) NEUTRO		LYMPHO		MONO		EOSINO		BASO		OTHER	
Control	40	8.84±	6.07	49±	10	42±	10	6±	2	1±	1	0±	0	1±	1
800 ppm	45	6.74±	1.85	47±	7	45±	7	6±	1	2±	1	0±	0	1±	1
2400 ppm	38	6.91±	1.38	46±	8	46±	9	5±	1	2±	1	0±	0	1±	0
7200 ppm	40	6.29±	1.72	46±	7	46±	7	5±	1	2±	1	0±	0	1±	0**

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

(HCL070)

TABLE G 2

HEMATOLOGY: FEMALE

STUDY NO. : 0641
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	37	7.84± 1.31	14.9± 2.5	40.5± 5.7	52.2± 4.3	19.0± 1.2	36.6± 1.7	782± 252
800 ppm	38	7.80± 1.53	14.8± 2.4	40.1± 5.8	53.2± 10.0	19.4± 2.5	36.7± 1.5	709± 180
2400 ppm	42	7.66± 1.10	14.4± 2.0	39.1± 4.8	51.4± 3.0	18.8± 1.1	36.6± 1.1	815± 202
7200 ppm	33	7.17± 0.94**	13.6± 1.6	37.0± 3.9*	51.9± 2.7	19.0± 0.9	36.7± 1.2	886± 134**

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

(HCL070)

STUDY NO. : 0641
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	RETICULOCYTE %	
Control	37	4.7±	7.8
800 ppm	38	4.8±	7.7
2400 ppm	42	4.0±	3.7
7200 ppm	33	4.1±	2.0**

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

STUDY NO. : 0641
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$		Differential WBC (%) NEUTRO		LYMPHO		MONO		EOSINO		BASO		OTHER	
Control	37	4.42±	3.21	41±	13	51±	13	5±	1	2±	1	0±	0	1±	1
800 ppm	38	7.14±	10.00	37±	14	48±	17	5±	2	2±	1	0±	1	8±	24
2400 ppm	42	4.87±	3.68	40±	13	52±	13	5±	2	2±	1	0±	0	1±	1
7200 ppm	33	3.84±	3.18	50±	12*	42±	12*	6±	1	2±	1	0±	0	1±	0

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

(HCL070)

BAIS 4

TABLE H 1

BIOCHEMISTRY: MALE

STUDY NO. : 0641
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	TOTAL PROTEIN g/dl	ALBUMIN g/dl	A/G RATIO	T-BILIRUBIN mg/dl	GLUCOSE mg/dl	T-CHOLESTEROL mg/dl	TRIGLYCERIDE mg/dl
Control	40	6.7± 0.5	2.8± 0.3	0.7± 0.1	0.18± 0.10	154± 28	195± 47	148± 121
800 ppm	45	6.6± 0.4	2.9± 0.3	0.8± 0.1	0.14± 0.03**	160± 21	149± 47**	104± 61
2400 ppm	38	6.7± 0.3	2.9± 0.2	0.8± 0.1	0.14± 0.03*	159± 18	127± 27**	79± 39**
7200 ppm	40	6.5± 0.6**	3.0± 0.3	0.9± 0.1**	0.15± 0.04	147± 27	123± 37**	65± 53**

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

(HCL074)

BAIS 4

STUDY NO. : 0641
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	PHOSPHOLIPID mg／dℓ	AST IU／ℓ	ALT IU／ℓ	LDH IU／ℓ	ALP IU／ℓ	G-GTP IU／ℓ	CK IU／ℓ
Control	40	284± 73	106± 74	42± 22	181± 54	267± 205	7± 3	120± 73
800 ppm	45	223± 68**	106± 43	48± 20	219± 68**	170± 45**	3± 1**	108± 31
2400 ppm	38	190± 36**	116± 35**	56± 21*	209± 50	188± 43**	3± 1**	109± 25
7200 ppm	40	186± 60**	137± 88**	61± 26**	240± 205*	190± 89**	3± 3**	135± 215

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

STUDY NO. : 0641
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	UREA NITROGEN mg/dℓ	CREATININE mg/dℓ	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dℓ	INORGANIC PHOSPHORUS mg/dℓ
Control	40	20.3± 8.2	0.7± 0.2	142± 2	3.5± 0.2	105± 2	10.6± 0.5	4.2± 0.9
800 ppm	45	19.2± 4.1	0.6± 0.1	143± 1	3.6± 0.3	105± 2	10.4± 0.4	4.1± 0.5
2400 ppm	38	18.0± 2.4	0.6± 0.1	143± 1	3.6± 0.3	105± 1	10.3± 0.2**	4.1± 0.5
7200 ppm	40	19.9± 9.9	0.6± 0.1**	143± 2	3.5± 0.4	104± 2	10.3± 0.5**	4.1± 1.0

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

TABLE H 2

BIOCHEMISTRY: FEMALE

STUDY NO. : 0641
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	TOTAL PROTEIN g／dℓ		ALBUMIN g／dℓ		A/G RATIO		T-BILIRUBIN mg／dℓ		GLUCOSE mg／dℓ		T-CHOLESTEROL mg／dℓ		TRIGLYCERIDE mg／dℓ	
Control	38	6.9±	0.4	3.5±	0.3	1.0±	0.2	0.16±	0.13	151±	16	135±	49	106±	119
800 ppm	38	6.9±	0.4	3.5±	0.3	1.0±	0.1	0.40±	1.27**	146±	18	129±	26	109±	107
2400 ppm	42	6.9±	0.6	3.4±	0.3	1.0±	0.2	0.15±	0.04	147±	17	119±	25	66±	39
7200 ppm	33	6.5±	0.6**	3.4±	0.4	1.1±	0.2	0.13±	0.02	139±	23	119±	45**	58±	34*

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

STUDY NO. : 0641
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dl	AST IU/l	ALT IU/l	LDH IU/l	ALP IU/l	G-GTP IU/l	CK IU/l
Control	38	245± 77	140± 115	56± 32	253± 268	136± 121	2± 1	100± 36
800 ppm	38	241± 70	229± 242**	77± 42**	389± 728**	169± 159	3± 2	104± 37
2400 ppm	42	219± 45	168± 84**	61± 25*	262± 92*	131± 50	2± 1	110± 82
7200 ppm	33	218± 49*	147± 55	44± 13	239± 80	188± 372	2± 3**	110± 63

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

(HCL074)

STUDY NO. : 0641
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	UREA NITROGEN mg/dℓ	CREATININE mg/dℓ	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dℓ	INORGANIC PHOSPHORUS mg/dℓ
Control	38	17.1± 2.9	0.6± 0.1	141± 1	3.6± 0.3	104± 2	10.5± 0.3	3.9± 0.7
800 ppm	38	16.9± 2.1	0.5± 0.1	141± 2	3.6± 0.4	104± 2	10.5± 0.4	3.8± 0.7
2400 ppm	42	17.6± 6.9	0.5± 0.1	141± 1	3.6± 0.4	104± 2	10.4± 0.3	4.0± 1.2
7200 ppm	33	27.0± 15.9**	0.6± 0.1	141± 3	3.8± 0.4	104± 2	10.5± 0.4	4.7± 1.3**

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

TABLE I 1

URINALYSIS: MALE

STUDY NO. : 0641 URINALYSIS
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Bilirubin −	+	2+	3+	CHI
Control	40	0	3	1	9	14	10	0		0	0	0	1	29	10		40	0	0	0	0	0		37	3	0	0	0	0		39	1	0	0	
800 ppm	45	0	0	3	6	23	12	1		0	0	0	0	34	11		45	0	0	0	0	0		43	2	0	0	0	0		44	1	0	0	
2400 ppm	38	0	0	1	9	16	12	0		0	0	0	0	27	11		38	0	0	0	0	0		32	6	0	0	0	0		38	0	0	0	
7200 ppm	40	0	3	4	6	15	12	0		0	0	0	1	27	12		40	0	0	0	0	0		30	10	0	0	0	0	*	40	0	0	0	

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

(HCL101) BATS 4

STUDY NO. : 0641 URINALYSIS
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

Group Name	NO. of Animals	Occult blood −	±	+	2+	3+	CHI	Urobilinogen ±	+	2+	3+	4+	CHI
Control	40	36	1	0	1	2		40	0	0	0	0	
800 ppm	45	44	0	0	0	1		45	0	0	0	0	
2400 ppm	38	37	0	1	0	0		38	0	0	0	0	
7200 ppm	40	28	1	2	3	6		40	0	0	0	0	

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

TABLE I 2

URINALYSIS: FEMALE

STUDY NO. : 0641
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	38	0	1	5	6	16	9	1		0	1	1	10	18	8		38	0	0	0	0	0		17	21	0	0	0	0		38	0	0	0	
800 ppm	38	0	2	4	8	8	14	2		0	0	3	7	18	10		38	0	0	0	0	0		12	25	1	0	0	0		36	1	0	1	
2400 ppm	43	0	2	11	9	11	10	0		0	0	2	8	19	14		43	0	0	0	0	0		10	32	0	1	0	0		43	0	0	0	
7200 ppm	33	0	6	9	6	5	4	3	*	0	0	0	0	11	22	**	33	0	0	0	0	0		17	16	0	0	0	0		33	0	0	0	

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

STUDY NO. : 0641 URINALYSIS
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

Group Name	NO. of Animals	Occult blood −	±	+	2+	3+	CHI	Urobilinogen ±	+	2+	3+	4+	CHI
Control	38	38	0	0	0	0		38	0	0	0	0	
800 ppm	38	35	0	1	0	2		37	1	0	0	0	
2400 ppm	43	35	1	0	4	3	*	43	0	0	0	0	
7200 ppm	33	5	1	0	0	27	**	33	0	0	0	0	

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

TABLE K 1

ORGAN WEIGHT, ABSOLUTE: MALE

STUDY NO. : 0641
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	40	401± 45	0.076± 0.019	2.832± 0.974	1.239± 0.097	1.404± 0.183	2.864± 0.579
800 ppm	45	402± 38	0.106± 0.222	2.715± 1.097	1.238± 0.097	1.367± 0.146	2.740± 0.312
2400 ppm	38	406± 26	0.085± 0.096	2.763± 0.839	1.228± 0.092	1.345± 0.110	2.675± 0.172
7200 ppm	40	369± 60**	0.079± 0.073	2.142± 0.935**	1.152± 0.107**	1.245± 0.090**	2.714± 0.282

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

(HCL040)

BAIS 4

STUDY NO. : 0641
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	40	1.158±	0.552	11.774±	1.703	2.104±	0.054
800 ppm	45	0.933±	0.403**	10.539±	1.113**	2.105±	0.041
2400 ppm	38	0.885±	0.282**	10.166±	0.914**	2.108±	0.038
7200 ppm	40	0.680±	0.113**	9.046±	1.367**	2.078±	0.037*

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

TABLE K 2

ORGAN WEIGHT, ABSOLUTE: FEMALE

STUDY NO. : 0641
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	Body Weight	ADRENALS	OVARIES	HEART	LUNGS	KIDNEYS
Control	38	263± 31	0.069± 0.007	0.129± 0.021	0.886± 0.089	0.976± 0.172	1.819± 0.163
800 ppm	38	264± 30	0.070± 0.007	0.142± 0.097	0.903± 0.076	1.065± 0.442	1.864± 0.165
2400 ppm	42	267± 29	0.072± 0.008	0.163± 0.231	0.890± 0.068	0.977± 0.078	1.952± 0.155**
7200 ppm	33	207± 25**	0.076± 0.041	0.119± 0.022	0.783± 0.083**	0.881± 0.056**	2.078± 0.244**

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

STUDY NO. : 0641
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	SPLEEN		LIVER		BRAIN	
Control	38	0.759±	0.901	6.814±	1.095	1.925±	0.041
800 ppm	38	1.236±	2.217	7.237±	1.153	1.913±	0.049
2400 ppm	42	0.666±	0.293	7.161±	1.116	1.921±	0.046
7200 ppm	33	0.478±	0.232**	5.858±	0.676**	1.869±	0.037**

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

TABLE L 1

ORGAN WEIGHT, RELATIVE: MALE

STUDY NO. : 0641
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	40	401± 45	0.019± 0.006	0.710± 0.244	0.312± 0.041	0.354± 0.061	0.731± 0.238
800 ppm	45	402± 38	0.027± 0.057	0.673± 0.257	0.311± 0.044	0.345± 0.075	0.690± 0.129
2400 ppm	38	406± 26	0.021± 0.024	0.684± 0.228	0.303± 0.022	0.332± 0.031	0.660± 0.039
7200 ppm	40	369± 60**	0.022± 0.020	0.591± 0.261	0.317± 0.035	0.344± 0.045	0.751± 0.125*

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

(HCL042)

BAIS 4

STUDY NO. : 0641
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	40	0.291± 0.139	2.960± 0.501	0.531± 0.058
800 ppm	45	0.240± 0.156**	2.647± 0.433**	0.529± 0.057
2400 ppm	38	0.219± 0.072**	2.508± 0.199**	0.521± 0.031
7200 ppm	40	0.188± 0.033**	2.485± 0.400**	0.576± 0.081**

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

TABLE L 2

ORGAN WEIGHT, RELATIVE: FEMALE

STUDY NO. : 0641
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	Body Weight (g)	ADRENALS	OVARIES	HEART	LUNGS	KIDNEYS
Control	38	263± 31	0.027± 0.005	0.049± 0.007	0.340± 0.032	0.376± 0.069	0.703± 0.117
800 ppm	38	264± 30	0.027± 0.004	0.054± 0.035	0.345± 0.043	0.411± 0.191	0.714± 0.113
2400 ppm	42	267± 29	0.027± 0.005	0.059± 0.074	0.337± 0.039	0.371± 0.053	0.740± 0.100**
7200 ppm	33	207± 25**	0.038± 0.020**	0.057± 0.008**	0.382± 0.046**	0.433± 0.063**	1.028± 0.268**

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

(HCL042)

STUDY NO. : 0641
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	SPLEEN	LIVER	BRAIN
Control	38	0.289± 0.325	2.608± 0.376	0.745± 0.109
800 ppm	38	0.505± 0.978	2.759± 0.468	0.734± 0.092
2400 ppm	42	0.255± 0.121	2.707± 0.458	0.730± 0.089
7200 ppm	33	0.235± 0.129	2.854± 0.328	0.919± 0.133**

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

TABLE M 1

HISTOPATHOLOGICAL FINDINGS:

NON-NEOPLASTIC LESIONS:

MALE: ALL ANIMALS

STUDY NO. : 0641
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 (%)	800 ppm 50 1 (%)	800 ppm 50 2 (%)	800 ppm 50 3 (%)	800 ppm 50 4 (%)	2400 ppm 50 1 (%)	2400 ppm 50 2 (%)	2400 ppm 50 3 (%)	2400 ppm 50 4 (%)	7200 ppm 50 1 (%)	7200 ppm 50 2 (%)	7200 ppm 50 3 (%)	7200 ppm 50 4 (%)
{Integumentary system/appandage}																		
skin/app		<50>																
	mineralization		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)
	fibrosis:focal		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)
	scab		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
subcutis		<50>																
	cyst		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)
	inflammation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	abscess		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)
	fibrosis		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)
{Respiratory system}																		
nasal cavit		<50>																
	thrombus		1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1 (%)	Control 50 2 (%)	Control 50 3 (%)	Control 50 4 (%)	800 ppm 50 1 (%)	800 ppm 50 2 (%)	800 ppm 50 3 (%)	800 ppm 50 4 (%)	2400 ppm 50 1 (%)	2400 ppm 50 2 (%)	2400 ppm 50 3 (%)	2400 ppm 50 4 (%)	7200 ppm 50 1 (%)	7200 ppm 50 2 (%)	7200 ppm 50 3 (%)	7200 ppm 50 4 (%)
{Respiratory system}																		
nasal cavit			<50>				<50>				<50>				<50>			
	mineralization		28	0	0	0	25	1	0	0	32	0	0	0	25	0	0	0
			(56)	(0)	(0)	(0)	(50)	(2)	(0)	(0)	(64)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
	eosinophilic change:olfactory epithelium		38	7	0	0	42	5	0	0	37	9	0	0	34	13	0	0
			(76)	(14)	(0)	(0)	(84)	(10)	(0)	(0)	(74)	(18)	(0)	(0)	(68)	(26)	(0)	(0)
	eosinophilic change:respiratory epithelium		11	0	0	0	17	0	0	0	19	0	0	0	17	0	0	0
			(22)	(0)	(0)	(0)	(34)	(0)	(0)	(0)	(38)	(0)	(0)	(0)	(34)	(0)	(0)	(0)
	inflammation:foreign body		15	0	0	0	15	0	0	0	16	0	0	0	14	0	0	0
			(30)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(32)	(0)	(0)	(0)	(28)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		12	0	0	0	7	0	0	0	6	1	0	0	10	0	0	0
			(24)	(0)	(0)	(0)	(14)	(0)	(0)	(0)	(12)	(2)	(0)	(0)	(20)	(0)	(0)	(0)
	respiratory metaplasia:gland		50	0	0	0	50	0	0	0	48	0	0	0	47	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(96)	(0)	(0)	(0)	(94)	(0)	(0)	(0)
	squamous cell metaplasia:respiratory epithelium		6	1	0	0	2	0	0	0	1	1	0	0	4	0	0	0
			(12)	(2)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(2)	(0)	(0)	(8)	(0)	(0)	(0)
larynx			<50>				<50>				<50>				<50>			
	inflammation		2	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				800 ppm				2400 ppm				7200 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}																		
lung			<50>				<50>				<50>				<50>			
	congestion		2	1	0	0	0	0	0	0	0	0	0	0	2	0	0	0
			(4)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	inflammatory infiltration		1	0	0	0	2	0	0	0	1	1	0	0	1	0	0	0
			(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(2)	(0)	(0)	(2)	(0)	(0)	(0)
	accumulation of foamy cells		2	0	0	0	1	0	0	0	1	0	0	0	1	0	0	0
			(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	bronchiolar-alveolar cell hyperplasia		4	2	0	0	2	0	0	0	1	0	0	0	1	0	0	0
			(8)	(4)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	inflammation:foreign body		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
{Hematopoietic system}																		
bone marrow			<50>				<50>				<50>				<50>			
	granulation		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)
	increased hematopoiesis		9	2	0	0	4	2	0	0	4	0	0	0	3	0	0	0
			(18)	(4)	(0)	(0)	(8)	(4)	(0)	(0)	(8)	(0)	(0)	(0)	(6)	(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				800 ppm				2400 ppm				7200 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>			
	decreased hematopoiesis		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)
spleen			<50>				<50>				<50>				<50>			
	congestion		2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	deposit of hemosiderin		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)
	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)
	fibrosis:focal		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)
	extramedullary hematopoiesis		12	5	0	0	13	1	0	0	11	2	0	0	7	1	0	0
			(24)	(10)	(0)	(0)	(26)	(2)	(0)	(0)	(22)	(4)	(0)	(0)	(14)	(2)	(0)	(0)
{Circulatory system}																		
heart			<50>				<50>				<50>				<50>			
	thrombus		0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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				800 ppm				2400 ppm				7200 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>			
	necrosis:focal		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization		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)
	myocardial fibrosis		15	1	0	0	14	0	0	0	19	1	0	0	15	1	0	0
			(30)	(2)	(0)	(0)	(28)	(0)	(0)	(0)	(38)	(2)	(0)	(0)	(30)	(2)	(0)	(0)
artery/aort			<50>				<50>				<50>				<50>			
	mineralization		0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
{Digestive system}																		
tongue			<50>				<50>				<50>				<50>			
	squamous cell hyperplasia		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)
stomach			<50>				<50>				<50>				<50>			
	erosion:forestomach		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)	(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 (%)	800 ppm 50 1 (%)	800 ppm 50 2 (%)	800 ppm 50 3 (%)	800 ppm 50 4 (%)	2400 ppm 50 1 (%)	2400 ppm 50 2 (%)	2400 ppm 50 3 (%)	2400 ppm 50 4 (%)	7200 ppm 50 1 (%)	7200 ppm 50 2 (%)	7200 ppm 50 3 (%)	7200 ppm 50 4 (%)
{Digestive system}																		
stomach		<50>	0	0	1	0	0	1	0	0	0	0	1	0	1	0	0	0
	ulcer:forestomach		(0)	(0)	(2)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(2)	(0)	(2)	(0)	(0)	(0)
	hyperplasia:forestomach		1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	erosion:glandular stomach		5	2	0	0	1	0	0	0	5	0	0	0	2	0	0	0
			(10)	(4)	(0)	(0)	(2)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	ulcer:glandular stomach		1	0	0	0	1	1	0	0	2	1	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(2)	(2)	(0)	(0)	(4)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia:glandular stomach		1	0	0	0	1	0	0	0	1	0	0	0	1	0	0	0
			(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	mineralization:glandular stomach		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)
small intes		<50>	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	ulcer		(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	erosion		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)

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				800 ppm				2400 ppm				7200 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>			
	necrosis		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)
large intes			<50>				<50>				<50>				<50>			
	mineralization		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)
liver			<50>				<50>				<50>				<50>			
	herniation		3	0	0	0	5	0	0	0	6	0	0	0	3	0	0	0
			(6)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(12)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
	necrosis:central		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)
	necrosis:focal		1	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	fatty change:peripheral		0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)
	cyst		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)

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				800 ppm				2400 ppm				7200 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>			
	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)
	inflammatory cell nest		38	1	0	0	45	0	0	0	41	0	0	0	41	0	0	0
			(76)	(2)	(0)	(0)	(90)	(0)	(0)	(0)	(82)	(0)	(0)	(0)	(82)	(0)	(0)	(0)
	extramedullary hematopoiesis		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)
	acidophilic cell focus		16	2	0	0	10	1	0	0	12	1	0	0	6	0	0	0 *
			(32)	(4)	(0)	(0)	(20)	(2)	(0)	(0)	(24)	(2)	(0)	(0)	(12)	(0)	(0)	(0)
	basophilic cell focus		4	0	0	0	7	0	0	0	9	0	0	0	5	0	0	0
			(8)	(0)	(0)	(0)	(14)	(0)	(0)	(0)	(18)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	spongiosis hepatis		2	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	bile duct hyperplasia		44	0	0	0	47	0	0	0	45	0	0	0	48	0	0	0
			(88)	(0)	(0)	(0)	(94)	(0)	(0)	(0)	(90)	(0)	(0)	(0)	(96)	(0)	(0)	(0)
	bile ductular proliferation		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)

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				800 ppm				2400 ppm				7200 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>			
	cholangiofibrosis		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)
	focal fatty change		0	0	0	0	1	0	0	0	2	1	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(4)	(2)	(0)	(0)	(2)	(0)	(0)	(0)
pancreas			<50>				<50>				<50>				<50>			
	atrophy:focal		3	1	0	0	3	0	0	0	6	1	0	0	5	1	0	0
			(6)	(2)	(0)	(0)	(6)	(0)	(0)	(0)	(12)	(2)	(0)	(0)	(10)	(2)	(0)	(0)
	islet cell hyperplasia		1	1	0	0	0	0	0	0	2	0	0	0	2	0	0	0
			(2)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
{Urinary system}																		
kidney			<50>				<50>				<50>				<50>			
	cyst		0	0	0	0	2	0	0	0	0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	hyaline droplet		0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)

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				800 ppm				2400 ppm				7200 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}																		
kidney			<50>				<50>				<50>				<50>			
	scar		0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	chronic nephropathy		9	21	11	3	21	15	9	0	28	12	2	0 **	24	7	3	0 **
			(18)	(42)	(22)	(6)	(42)	(30)	(18)	(0)	(56)	(24)	(4)	(0)	(48)	(14)	(6)	(0)
	papillary necrosis		0	0	0	0	0	0	0	0	7	0	0	0 *	37	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(14)	(0)	(0)	(0)	(74)	(0)	(0)	(0)
	mineralization:papilla		0	0	0	0	0	0	0	0	1	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	mineralization:pelvis		2	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	dilatation:tubular lumen		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)
	urothelial hyperplasia:pelvis		2	0	0	0	1	0	0	0	1	1	0	0	0	0	0	0
			(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
	inflammation:papilla		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)

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				800 ppm				2400 ppm				7200 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>			
	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)
	transitional cell hyperplasia		0	1	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
{Endocrine system}																		
pituitary			<49>				<50>				<50>				<50>			
	angiectasis		0	0	0	0	0	0	0	0	1	1	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(2)	(0)	(0)	(4)	(0)	(0)	(0)
	cyst		4	0	0	0	3	1	0	0	3	0	0	0	6	0	0	0
			(8)	(0)	(0)	(0)	(6)	(2)	(0)	(0)	(6)	(0)	(0)	(0)	(12)	(0)	(0)	(0)
	hyperplasia		12	9	2	0	14	8	0	0	12	9	3	0	13	4	2	0
			(24)	(18)	(4)	(0)	(28)	(16)	(0)	(0)	(24)	(18)	(6)	(0)	(26)	(8)	(4)	(0)
	Rathke pouch		2	0	0	0	2	1	0	0	0	0	0	0	3	0	0	0
			(4)	(0)	(0)	(0)	(4)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
	aberrant craniopharyngeal tissue		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	Control				800 ppm				2400 ppm				7200 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Endocrine system)																		
thyroid			<50>				<50>				<50>				<50>			
	ultimobranchial body remanet		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)
	C-cell hyperplasia		8	0	0	0	6	2	0	0	3	2	1	0	5	3	2	0
			(16)	(0)	(0)	(0)	(12)	(4)	(0)	(0)	(6)	(4)	(2)	(0)	(10)	(6)	(4)	(0)
	cystic thyroid follicle		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)
parathyroid			<50>				<50>				<50>				<50>			
	hyperplasia		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
adrenal			<50>				<50>				<50>				<50>			
	cyst		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)
	osseous metaplasia		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)
	hyperplasia:cortical cell		3	0	0	0	2	0	0	0	1	1	0	0	2	1	0	0
			(6)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(2)	(0)	(0)	(4)	(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				800 ppm				2400 ppm				7200 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Endocrine system}																		
adrenal			<50>				<50>				<50>				<50>			
	hyperplasia:medulla		3	3	0	0	2	1	0	0	2	2	0	0	1	3	1	0
			(6)	(6)	(0)	(0)	(4)	(2)	(0)	(0)	(4)	(4)	(0)	(0)	(2)	(6)	(2)	(0)
	focal fatty change:cortex		1	1	0	0	2	0	0	0	3	0	0	0	4	1	0	0
			(2)	(2)	(0)	(0)	(4)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(8)	(2)	(0)	(0)
{Reproductive system}																		
testis			<50>				<50>				<50>				<50>			
	mineralization		0	0	0	0	2	0	0	0	2	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
	inflammatory infiltration		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)
	arteritis		3	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0
			(6)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	interstitial cell hyperplasia		8	0	0	0	5	0	0	0	9	0	0	0	11	0	0	0
			(16)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(18)	(0)	(0)	(0)	(22)	(0)	(0)	(0)
prostate			<50>				<50>				<50>				<50>			
	inflammation		6	0	0	0	2	0	0	0	1	0	0	0	4	0	0	0
			(12)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(8)	(0)	(0)	(0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1 (%)	Control 50 2 (%)	Control 50 3 (%)	Control 50 4 (%)	800 ppm 50 1 (%)	800 ppm 50 2 (%)	800 ppm 50 3 (%)	800 ppm 50 4 (%)	2400 ppm 50 1 (%)	2400 ppm 50 2 (%)	2400 ppm 50 3 (%)	2400 ppm 50 4 (%)	7200 ppm 50 1 (%)	7200 ppm 50 2 (%)	7200 ppm 50 3 (%)	7200 ppm 50 4 (%)
{Reproductive system}																		
prostate		<50>																
	hyperplasia		7 (14)	1 (2)	0 (0)	0 (0)	6 (12)	0 (0)	0 (0)	0 (0)	4 (8)	1 (2)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
mammary gl		<50>																
	galactocele		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)
{Nervous system}																		
brain		<50>																
	hemorrhage		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)
spinal cord		<50>																
	hemorrhage		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)
{Special sense organs/appendage}																		
eye		<50>																
	cataract		8 (16)	1 (2)	0 (0)	0 (0)	6 (12)	0 (0)	0 (0)	0 (0)	3 (6)	1 (2)	0 (0)	0 (0)	4 (8)	3 (6)	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				800 ppm				2400 ppm				7200 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Special sense organs/appendage}																		
eye			<50>				<50>				<50>				<50>			
	retinal atrophy		10	4	6	0	4	4	6	0	1	2	4	0 *	10	4	8	0
			(20)	(8)	(12)	(0)	(8)	(8)	(12)	(0)	(2)	(4)	(8)	(0)	(20)	(8)	(16)	(0)
	keratitis		2	3	0	0	3	1	0	0	3	2	0	0	2	3	0	0
			(4)	(6)	(0)	(0)	(6)	(2)	(0)	(0)	(6)	(4)	(0)	(0)	(4)	(6)	(0)	(0)
	iritis		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)
	degeneration:optic nerve		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)
Harder gl			<50>				<50>				<50>				<50>			
	degeneration		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	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)
	hyperplasia		1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Musculoskeletal system}																		
muscle			<50>				<50>				<50>				<50>			
	mineralization		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				800 ppm				2400 ppm				7200 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Musculoskeletal system}																		
bone			<50>				<50>				<50>				<50>			
	osteosclerosis		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)
{Body cavities}																		
peritoneum			<50>				<50>				<50>				<50>			
	inflammatory infiltration		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)

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				800 ppm				2400 ppm				7200 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Integumentary system/appandage}																		
skin/app			<50>				<50>				<50>				<50>			
	ulcer		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)
	scab		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
{Respiratory system}																		
nasal cavit			<50>				<50>				<50>				<50>			
	thrombus		2	0	0	0	0	0	0	0	3	0	0	0	3	0	0	0
			(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
	mineralization		24	0	0	0	24	0	0	0	18	0	0	0	19	0	0	0
			(48)	(0)	(0)	(0)	(48)	(0)	(0)	(0)	(36)	(0)	(0)	(0)	(38)	(0)	(0)	(0)
	eosinophilic change:olfactory epithelium		18	30	2	0	10	39	1	0	10	34	6	0	11	31	6	0
			(36)	(60)	(4)	(0)	(20)	(78)	(2)	(0)	(20)	(68)	(12)	(0)	(22)	(62)	(12)	(0)
	eosinophilic change:respiratory epithelium		36	0	0	0	39	0	0	0	37	1	0	0	26	0	0	0
			(72)	(0)	(0)	(0)	(78)	(0)	(0)	(0)	(74)	(2)	(0)	(0)	(52)	(0)	(0)	(0)
	inflammation:foreign body		6	0	0	0	5	0	0	0	2	0	0	0	1	0	0	0
			(12)	(0)	(0)	(0)	(10)	(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
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(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				800 ppm				2400 ppm				7200 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}																		
nasal cavit			<50>				<50>				<50>				<50>			
	respiratory metaplasia:olfactory epithelium		2	0	0	0	2	0	0	0	2	0	0	0	6	0	0	0
			(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(12)	(0)	(0)	(0)
	respiratory metaplasia:gland		49	0	0	0	50	0	0	0	49	0	0	0	49	0	0	0
			(98)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(98)	(0)	(0)	(0)	(98)	(0)	(0)	(0)
	squamous cell metaplasia:respiratory epithelium		5	0	0	0	1	0	0	0	0	0	0	0	2	0	0	0
			(10)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
lung			<50>				<50>				<50>				<50>			
	congestion		4	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(8)	(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	0	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	accumulation of foamy cells		1	0	0	0	1	0	0	0	1	0	0	0	2	0	0	0
			(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	bronchiolar-alveolar cell hyperplasia		0	2	0	0	1	1	0	0	0	1	0	0	1	0	0	0
			(0)	(4)	(0)	(0)	(2)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(2)	(0)	(0)	(0)
{Hematopoietic system}																		
bone marrow			<50>				<50>				<50>				<50>			
	granulation		1	0	0	0	3	0	0	0	3	1	1	0	1	0	0	0
			(2)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(6)	(2)	(2)	(0)	(2)	(0)	(0)	(0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1 (%)	Control 50 2 (%)	Control 50 3 (%)	Control 50 4 (%)	800 ppm 50 1 (%)	800 ppm 50 2 (%)	800 ppm 50 3 (%)	800 ppm 50 4 (%)	2400 ppm 50 1 (%)	2400 ppm 50 2 (%)	2400 ppm 50 3 (%)	2400 ppm 50 4 (%)	7200 ppm 50 1 (%)	7200 ppm 50 2 (%)	7200 ppm 50 3 (%)	7200 ppm 50 4 (%)
{Hematopoietic system}																		
bone marrow		<50>																
	increased hematopoiesis		6 (12)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)	7 (14)	0 (0)	0 (0)	0 (0)
	decreased hematopoiesis		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)
spleen		<50>																
	congestion		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)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
	extramedullary hematopoiesis		17 (34)	3 (6)	2 (4)	0 (0)	14 (28)	1 (2)	2 (4)	0 (0)	16 (32)	2 (4)	1 (2)	0 (0)	16 (32)	5 (10)	1 (2)	0 (0)
{Circulatory system}																		
heart		<50>																
	thrombus		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	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				800 ppm				2400 ppm				7200 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>			
	myocardial fibrosis		5	0	0	0	8	0	0	0	5	0	0	0	7	0	0	0
			(10)	(0)	(0)	(0)	(16)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(14)	(0)	(0)	(0)
{Digestive system}																		
oral cavity			<50>				<50>				<50>				<50>			
	inflammatory infiltration		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	squamous cell hyperplasia		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)
tongue			<50>				<50>				<50>				<50>			
	ulcer		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	squamous cell hyperplasia		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
stomach			<50>				<50>				<50>				<50>			
	erosion:forestomach		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				800 ppm				2400 ppm				7200 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Digestive system)																		
stomach			<50>				<50>				<50>				<50>			
	ulcer:forestomach		1	1	1	0	0	1	0	0	1	2	0	0	0	2	0	0
			(2)	(2)	(2)	(0)	(0)	(2)	(0)	(0)	(2)	(4)	(0)	(0)	(0)	(4)	(0)	(0)
	hyperplasia:forestomach		0	0	0	0	1	1	0	0	3	0	0	0	2	2	0	0
			(0)	(0)	(0)	(0)	(2)	(2)	(0)	(0)	(6)	(0)	(0)	(0)	(4)	(4)	(0)	(0)
	erosion:glandular stomach		4	1	0	0	2	0	0	0	2	0	0	0	2	0	0	0
			(8)	(2)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	ulcer:glandular stomach		1	2	0	0	0	1	0	0	0	0	0	0	0	2	0	0
			(2)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)
	hyperplasia:glandular stomach		0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(2)	(0)	(0)	(0)
small intes			<50>				<50>				<50>				<50>			
	hyperplasia		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)
large intes			<50>				<50>				<50>				<50>			
	invagination		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				800 ppm				2400 ppm				7200 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>			
	herniation		9	0	0	0	7	0	0	0	7	0	0	0	8	0	0	0
			(18)	(0)	(0)	(0)	(14)	(0)	(0)	(0)	(14)	(0)	(0)	(0)	(16)	(0)	(0)	(0)
	peliosis-like lesion		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)
	necrosis:central		0	0	1	0	0	0	1	0	0	0	1	0	0	0	0	0
			(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)
	necrosis:focal		0	0	0	0	3	0	0	0	3	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	fatty change:central		0	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)
	fatty change:peripheral		1	1	0	0	0	0	0	0	1	1	0	0	0	0	0	0
			(2)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		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)
	inflammatory cell nest		28	4	0	0	31	1	0	0	27	4	0	0	27	2	0	0
			(56)	(8)	(0)	(0)	(62)	(2)	(0)	(0)	(54)	(8)	(0)	(0)	(54)	(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	Control				800 ppm				2400 ppm				7200 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>			
	acidophilic cell focus		5	0	0	0	6	1	0	0	5	1	0	0	0	2	0	0 *
			(10)	(0)	(0)	(0)	(12)	(2)	(0)	(0)	(10)	(2)	(0)	(0)	(0)	(4)	(0)	(0)
	basophilic cell focus		25	0	0	0	26	0	0	0	25	1	0	0	18	0	0	0
			(50)	(0)	(0)	(0)	(52)	(0)	(0)	(0)	(50)	(2)	(0)	(0)	(36)	(0)	(0)	(0)
	bile duct hyperplasia		28	0	0	0	24	0	0	0	19	0	0	0	22	0	0	0
			(56)	(0)	(0)	(0)	(48)	(0)	(0)	(0)	(38)	(0)	(0)	(0)	(44)	(0)	(0)	(0)
	bile ductular proliferation		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)
pancreas			<50>				<50>				<50>				<50>			
	atrophy:focal		1	0	0	0	1	0	0	0	2	0	0	0	2	0	0	0
			(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	islet cell hyperplasia		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)
{Urinary system}																		
kidney			<50>				<50>				<50>				<50>			
	cyst		0	0	0	0	0	1	0	0	0	1	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(4)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				800 ppm				2400 ppm				7200 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}																		
kidney			<50>				<50>				<50>				<50>			
	hyaline droplet		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)
	scar		0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(2)	(0)	(0)
	chronic nephropathy		17	4	1	0	19	4	1	0	19	0	0	0	7	3	1	0
			(34)	(8)	(2)	(0)	(38)	(8)	(2)	(0)	(38)	(0)	(0)	(0)	(14)	(6)	(2)	(0)
	hydronephrosis		0	0	0	0	0	0	0	0	0	0	0	0	2	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(2)	(0)	(0)
	papillary necrosis		0	0	0	0	0	0	0	0	17	0	0	0 **	13	18	14	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(34)	(0)	(0)	(0)	(26)	(36)	(28)	(0)
	mineralization:papilla		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:pelvis		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)
	mineralization:cortex		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)

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 (%)	800 ppm 50 1 (%)	800 ppm 50 2 (%)	800 ppm 50 3 (%)	800 ppm 50 4 (%)	2400 ppm 50 1 (%)	2400 ppm 50 2 (%)	2400 ppm 50 3 (%)	2400 ppm 50 4 (%)	7200 ppm 50 1 (%)	7200 ppm 50 2 (%)	7200 ppm 50 3 (%)	7200 ppm 50 4 (%)
{Urinary system}																		
kidney		<50>	0	0	0	0	0	0	0	0	1	0	0	0	20	3	0	0 **
	urothelial hyperplasia:pelvis		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(40)	(6)	(0)	(0)
	inflammation:papilla		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)
urin bladd		<50>	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
	dilatation		(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
{Endocrine system}																		
pituitary		<50>	6	3	0	0	4	4	0	0	7	4	0	0	3	8	0	0
	angiectasis		(12)	(6)	(0)	(0)	(8)	(8)	(0)	(0)	(14)	(8)	(0)	(0)	(6)	(16)	(0)	(0)
	cyst		17	1	0	0	11	0	0	0	9	1	0	0	13	2	0	0
			(34)	(2)	(0)	(0)	(22)	(0)	(0)	(0)	(18)	(2)	(0)	(0)	(26)	(4)	(0)	(0)
	deposit of hemosiderin		1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				800 ppm				2400 ppm				7200 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Endocrine system}																		
pituitary			<50>				<50>				<50>				<50>			
	hyperplasia		5	5	0	0	4	3	0	0	4	1	0	0	1	2	0	0
			(10)	(10)	(0)	(0)	(8)	(6)	(0)	(0)	(8)	(2)	(0)	(0)	(2)	(4)	(0)	(0)
	Rathke pouch		0	0	0	0	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)
thyroid			<50>				<50>				<50>				<50>			
	C-cell hyperplasia		6	1	0	0	7	2	0	0	5	0	0	0	3	0	0	0
			(12)	(2)	(0)	(0)	(14)	(4)	(0)	(0)	(10)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
adrenal			<50>				<50>				<50>				<50>			
	angiectasis		2	0	0	0	2	1	0	0	2	0	0	0	4	0	0	0
			(4)	(0)	(0)	(0)	(4)	(2)	(0)	(0)	(4)	(0)	(0)	(0)	(8)	(0)	(0)	(0)
	cyst		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)
	hyperplasia:cortical cell		5	0	0	0	4	0	0	0	1	0	0	0	2	1	0	0
			(10)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(4)	(2)	(0)	(0)
	hyperplasia:medulla		0	0	0	0	0	1	0	0	0	1	0	0	2	1	0	0
			(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(4)	(2)	(0)	(0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1 (%)	Control 50 2 (%)	Control 50 3 (%)	Control 50 4 (%)	800 ppm 50 1 (%)	800 ppm 50 2 (%)	800 ppm 50 3 (%)	800 ppm 50 4 (%)	2400 ppm 50 1 (%)	2400 ppm 50 2 (%)	2400 ppm 50 3 (%)	2400 ppm 50 4 (%)	7200 ppm 50 1 (%)	7200 ppm 50 2 (%)	7200 ppm 50 3 (%)	7200 ppm 50 4 (%)
{Endocrine system}																		
adrenal		<50>																
	focal fatty change:cortex		6 (12)	2 (4)	0 (0)	0 (0)	3 (6)	1 (2)	0 (0)	0 (0)	3 (6)	1 (2)	0 (0)	0 (0)	3 (6)	1 (2)	0 (0)	0 (0)
{Reproductive system}																		
ovary		<50>																
	cyst		1 (2)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
uterus		<50>																
	cystic endometrial hyperplasia		2 (4)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)
mammary gl		<50>																
	cyst		0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
{Special sense organs/appendage}																		
eye		<50>																
	cataract		4 (8)	1 (2)	0 (0)	0 (0)	3 (6)	2 (4)	0 (0)	0 (0)	2 (4)	1 (2)	0 (0)	0 (0)	0 (0)	3 (6)	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 / Grade	Control 1 (%)	Control 2 (%)	Control 3 (%)	Control 4 (%)	800 ppm 1 (%)	800 ppm 2 (%)	800 ppm 3 (%)	800 ppm 4 (%)	2400 ppm 1 (%)	2400 ppm 2 (%)	2400 ppm 3 (%)	2400 ppm 4 (%)	7200 ppm 1 (%)	7200 ppm 2 (%)	7200 ppm 3 (%)	7200 ppm 4 (%)
		No. of Animals on Study	50				50				50				50			
{Special sense organs/appendage}																		
eye			<50>				<50>				<50>				<50>			
	retinal atrophy		15 (30)	6 (12)	4 (8)	0 (0)	15 (30)	3 (6)	5 (10)	0 (0)	6 (12)	4 (8)	2 (4)	0 (0)	16 (32)	10 (20)	3 (6)	0 (0)
	keratitis		5 (10)	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)	1 (2)	0 * (0)
	iritis		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)
Harder gl			<50>				<50>				<50>				<50>			
	hyperplasia		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)
{Musculoskeletal system}																		
muscle			<50>				<50>				<50>				<50>			
	mineralization		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)
bone			<50>				<50>				<50>				<50>			
	osteosclerosis		5 (10)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	2 (4)	2 (4)	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

TABLE P 1

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS: MALE

STUDY No. : 0641
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

Group Name	Control	800 ppm	2400 ppm	7200 ppm
	SITE : skin/appendage			
	TUMOR : squamous cell papilloma			
Tumor rate				
Overall rates(a)	4/50(8.0)	0/50(0.0)	1/50(2.0)	0/50(0.0)
Adjusted rates(b)	10.00	0.0	2.63	0.0
Terminal rates(c)	4/40(10.0)	0/45(0.0)	1/38(2.6)	0/40(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P = 0.9725			
Combined analysis(d)	P = ----------			
Cochran-Armitage test(e)	P = 0.0856			
Fisher Exact test(e)		P = 0.0587	P = 0.1811	P = 0.0587
	SITE : skin/appendage			
	TUMOR : keratoacanthoma			
Tumor rate				
Overall rates(a)	6/50(12.0)	2/50(4.0)	2/50(4.0)	1/50(2.0)
Adjusted rates(b)	15.00	4.44	2.63	2.50
Terminal rates(c)	6/40(15.0)	2/45(4.4)	1/38(2.6)	1/40(2.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3775			
Prevalence method(d)	P = 0.9621			
Combined analysis(d)	P = 0.9554			
Cochran-Armitage test(e)	P = 0.0957			
Fisher Exact test(e)		P = 0.1343	P = 0.1343	P = 0.0559
	SITE : subcutis			
	TUMOR : fibroma			
Tumor rate				
Overall rates(a)	6/50(12.0)	1/50(2.0)	6/50(12.0)	4/50(8.0)
Adjusted rates(b)	12.20	2.22	10.53	10.00
Terminal rates(c)	4/40(10.0)	1/45(2.2)	4/38(10.5)	4/40(10.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.6908			
Prevalence method(d)	P = 0.3527			
Combined analysis(d)	P = 0.4684			
Cochran-Armitage test(e)	P = 0.9855			
Fisher Exact test(e)		P = 0.0559	P = 0.6202	P = 0.3703

Group Name	Control	800 ppm	2400 ppm	7200 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)	7.50	6.67	2.63	0.0
Terminal rates(c)	3/40(7.5)	3/45(6.7)	1/38(2.6)	0/40(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1415			
Prevalence method(d)	P = 0.9781			
Combined analysis(d)	P = 0.8614			
Cochran-Armitage test(e)	P = 0.2555			
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)	2/50(4.0)	7/50(14.0)	0/50(0.0)
Adjusted rates(b)	7.50	2.22	5.26	0.0
Terminal rates(c)	3/40(7.5)	1/45(2.2)	2/38(5.3)	0/40(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.7552			
Prevalence method(d)	P = 0.9371			
Combined analysis(d)	P = 0.9428			
Cochran-Armitage test(e)	P = 0.1137			
Fisher Exact test(e)		P = 0.3389	P = 0.2623	P = 0.0587
	SITE : pancreas			
	TUMOR : islet cell adenoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	5/50(10.0)	2/50(4.0)	4/50(8.0)
Adjusted rates(b)	7.50	11.11	4.76	10.00
Terminal rates(c)	3/40(7.5)	5/45(11.1)	0/38(0.0)	4/40(10.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P = 0.4460			
Combined analysis(d)	P = -------			
Cochran-Armitage test(e)	P = 0.9052			
Fisher Exact test(e)		P = 0.3575	P = 0.5000	P = 0.5000

Group Name	Control	800 ppm	2400 ppm	7200 ppm
	SITE : pancreas			
	TUMOR : islet cell adenocarcinoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	3/50(6.0)	1/50(2.0)	3/50(6.0)
Adjusted rates(b)	2.50	6.67	2.63	7.50
Terminal rates(c)	1/40(2.5)	3/45(6.7)	1/38(2.6)	3/40(7.5)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P = 0.2165			
Combined analysis(d)	P = ----------			
Cochran-Armitage test(e)	P = 0.4694			
Fisher Exact test(e)		P = 0.3087	P = 0.7525	P = 0.3087
	SITE : pancreas			
	TUMOR : islet cell adenoma, islet cell adenocarcinoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	8/50(16.0)	3/50(6.0)	7/50(14.0)
Adjusted rates(b)	10.00	17.78	7.14	17.50
Terminal rates(c)	4/40(10.0)	8/45(17.8)	1/38(2.6)	7/40(17.5)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P = 0.2846			
Combined analysis(d)	P = -------			
Cochran-Armitage test(e)	P = 0.5822			
Fisher Exact test(e)		P = 0.1783	P = 0.5000	P = 0.2623
	SITE : pituitary gland			
	TUMOR : adenoma			
Tumor rate				
Overall rates(a)	13/49(26.5)	7/50(14.0)	6/50(12.0)	8/50(16.0)
Adjusted rates(b)	27.50	15.56	15.00	17.50
Terminal rates(c)	10/39(25.6)	7/45(15.6)	5/38(13.2)	7/40(17.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5007			
Prevalence method(d)	P = 0.7361			
Combined analysis(d)	P = 0.7375			
Cochran-Armitage test(e)	P = 0.4484			
Fisher Exact test(e)		P = 0.0961	P = 0.0564	P = 0.1502

Group Name	Control	800 ppm	2400 ppm	7200 ppm
	SITE : pituitary gland			
	TUMOR : adenocarcinoma			
Tumor rate				
Overall rates(a)	1/49(2.0)	1/50(2.0)	2/50(4.0)	3/50(6.0)
Adjusted rates(b)	2.56	2.22	5.26	5.00
Terminal rates(c)	1/39(2.6)	1/45(2.2)	2/38(5.3)	2/40(5.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1345			
Prevalence method(d)	P = 0.2426			
Combined analysis(d)	P = 0.1111			
Cochran-Armitage test(e)	P = 0.2198			
Fisher Exact test(e)		P = 0.7576	P = 0.5077	P = 0.3163
	SITE : pituitary gland			
	TUMOR : adenoma, adenocarcinoma			
Tumor rate				
Overall rates(a)	14/49(28.6)	8/50(16.0)	8/50(16.0)	11/50(22.0)
Adjusted rates(b)	30.00	17.78	20.00	22.50
Terminal rates(c)	11/39(28.2)	8/45(17.8)	7/38(18.4)	9/40(22.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.2342			
Prevalence method(d)	P = 0.6103			
Combined analysis(d)	P = 0.5031			
Cochran-Armitage test(e)	P = 0.8835			
Fisher Exact test(e)		P = 0.1032	P = 0.1032	P = 0.3013
	SITE : thyroid			
	TUMOR : C-cell adenoma			
Tumor rate				
Overall rates(a)	12/50(24.0)	12/50(24.0)	8/50(16.0)	7/50(14.0)
Adjusted rates(b)	25.00	26.67	21.05	16.67
Terminal rates(c)	10/40(25.0)	12/45(26.7)	8/38(21.1)	6/40(15.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 1.0000 ?			
Prevalence method(d)	P = 0.8906			
Combined analysis(d)	P = 0.9165			
Cochran-Armitage test(e)	P = 0.1560			
Fisher Exact test(e)		P = 0.5924	P = 0.2270	P = 0.1540

Group Name	Control	800 ppm	2400 ppm	7200 ppm
	SITE : thyroid			
	TUMOR : C-cell adenoma, C-cell carcinoma			
Tumor rate				
Overall rates(a)	12/50(24.0)	13/50(26.0)	9/50(18.0)	8/50(16.0)
Adjusted rates(b)	25.00	28.89	21.05	19.05
Terminal rates(c)	10/40(25.0)	13/45(28.9)	8/38(21.1)	7/40(17.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.6947			
Prevalence method(d)	P = 0.8459			
Combined analysis(d)	P = 0.8773			
Cochran-Armitage test(e)	P = 0.2231			
Fisher Exact test(e)		P = 0.5000	P = 0.3121	P = 0.2270
	SITE : adrenal gland			
	TUMOR : pheochromocytoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	4/50(8.0)	3/50(6.0)	5/50(10.0)
Adjusted rates(b)	7.50	8.89	7.14	12.20
Terminal rates(c)	3/40(7.5)	4/45(8.9)	2/38(5.3)	4/40(10.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 1.0000 ?			
Prevalence method(d)	P = 0.2410			
Combined analysis(d)	P = 0.3277			
Cochran-Armitage test(e)	P = 0.6542			
Fisher Exact test(e)		P = 0.6425	P = 0.5000	P = 0.5000
	SITE : adrenal gland			
	TUMOR : pheochromocytoma, pheochromocytoma:malignant			
Tumor rate				
Overall rates(a)	5/50(10.0)	5/50(10.0)	3/50(6.0)	6/50(12.0)
Adjusted rates(b)	10.00	11.11	7.14	12.20
Terminal rates(c)	4/40(10.0)	5/45(11.1)	2/38(5.3)	4/40(10.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3001			
Prevalence method(d)	P = 0.3898			
Combined analysis(d)	P = 0.3358			
Cochran-Armitage test(e)	P = 0.6659			
Fisher Exact test(e)		P = 0.6297	P = 0.3575	P = 0.5000

Group Name	Control	800 ppm	2400 ppm	7200 ppm
	SITE : testis			
	TUMOR : interstitial cell tumor			
Tumor rate				
Overall rates(a)	35/50(70.0)	31/50(62.0)	31/50(62.0)	20/50(40.0)
Adjusted rates(b)	85.00	67.39	71.79	50.00
Terminal rates(c)	34/40(85.0)	30/45(66.7)	27/38(71.1)	20/40(50.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.9994			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0017**			
Fisher Exact test(e)		P = 0.2634	P = 0.2634	P = 0.0023**

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

TABLE P 2

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS: FEMALE

Group Name	Control	800 ppm	2400 ppm	7200 ppm
SITE : spleen				
TUMOR : mononuclear cell leukemia				
Tumor rate				
Overall rates(a)	4/50(8.0)	7/50(14.0)	5/50(10.0)	5/50(10.0)
Adjusted rates(b)	5.26	10.53	7.14	3.03
Terminal rates(c)	2/38(5.3)	4/38(10.5)	3/42(7.1)	1/33(3.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1545			
Prevalence method(d)	P = 0.7892			
Combined analysis(d)	P = 0.4100			
Cochran-Armitage test(e)	P = 0.9342			
Fisher Exact test(e)		P = 0.2623	P = 0.5000	P = 0.5000
SITE : pituitary gland				
TUMOR : adenoma				
Tumor rate				
Overall rates(a)	12/50(24.0)	17/50(34.0)	16/50(32.0)	14/50(28.0)
Adjusted rates(b)	14.63	29.27	33.33	30.30
Terminal rates(c)	5/38(13.2)	11/38(28.9)	14/42(33.3)	10/33(30.3)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.9062			
Prevalence method(d)	P = 0.1222			
Combined analysis(d)	P = 0.3917			
Cochran-Armitage test(e)	P = 0.9734			
Fisher Exact test(e)		P = 0.1891	P = 0.2522	P = 0.4100
SITE : pituitary gland				
TUMOR : adenoma,adenocarcinoma				
Tumor rate				
Overall rates(a)	14/50(28.0)	19/50(38.0)	17/50(34.0)	14/50(28.0)
Adjusted rates(b)	17.50	31.71	35.71	30.30
Terminal rates(c)	6/38(15.8)	12/38(31.6)	15/42(35.7)	10/33(30.3)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.9510			
Prevalence method(d)	P = 0.2005			
Combined analysis(d)	P = 0.5784			
Cochran-Armitage test(e)	P = 0.6023			
Fisher Exact test(e)		P = 0.1976	P = 0.3329	P = 0.5880

Group Name	Control	800 ppm	2400 ppm	7200 ppm
	SITE : thyroid			
	TUMOR : C-cell adenoma			
Tumor rate				
Overall rates(a)	6/50(12.0)	8/50(16.0)	11/50(22.0)	4/50(8.0)
Adjusted rates(b)	13.16	17.39	22.45	12.12
Terminal rates(c)	5/38(13.2)	5/38(13.2)	9/42(21.4)	4/33(12.1)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P = 0.7582			
Combined analysis(d)	P = ----------			
Cochran-Armitage test(e)	P = 0.3210			
Fisher Exact test(e)		P = 0.3871	P = 0.1434	P = 0.3703
	SITE : thyroid			
	TUMOR : C-cell adenoma,C-cell carcinoma			
Tumor rate				
Overall rates(a)	6/50(12.0)	8/50(16.0)	12/50(24.0)	4/50(8.0)
Adjusted rates(b)	13.16	17.39	22.92	12.12
Terminal rates(c)	5/38(13.2)	5/38(13.2)	9/42(21.4)	4/33(12.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3509			
Prevalence method(d)	P = 0.7579			
Combined analysis(d)	P = 0.7545			
Cochran-Armitage test(e)	P = 0.3209			
Fisher Exact test(e)		P = 0.3871	P = 0.0961	P = 0.3703
	SITE : adrenal gland			
	TUMOR : pheochromocytoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	1/50(2.0)	1/50(2.0)	3/50(6.0)
Adjusted rates(b)	2.33	2.04	2.38	7.69
Terminal rates(c)	0/38(0.0)	0/38(0.0)	1/42(2.4)	2/33(6.1)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P = 0.0800			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.1721			
Fisher Exact test(e)		P = 0.7525	P = 0.7525	P = 0.3087

Group Name	Control	800 ppm	2400 ppm	7200 ppm
	SITE : adrenal gland			
	TUMOR : pheochromocytoma, pheochromocytoma:malignant			
Tumor rate				
Overall rates(a)	1/50(2.0)	1/50(2.0)	1/50(2.0)	4/50(8.0)
Adjusted rates(b)	2.33	2.04	2.38	10.26
Terminal rates(c)	0/38(0.0)	0/38(0.0)	1/42(2.4)	3/33(9.1)
Statistical analysis				
Peto test				
Standard method(d)	P = ----------			
Prevalence method(d)	P = 0.0284*			
Combined analysis(d)	P = ----------			
Cochran-Armitage test(e)	P = 0.0573			
Fisher Exact test(e)		P = 0.7525	P = 0.7525	P = 0.1811
	SITE : uterus			
	TUMOR : endometrial stromal polyp			
Tumor rate				
Overall rates(a)	7/50(14.0)	5/50(10.0)	9/50(18.0)	5/50(10.0)
Adjusted rates(b)	14.29	10.53	19.05	15.15
Terminal rates(c)	5/38(13.2)	4/38(10.5)	8/42(19.0)	5/33(15.2)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3536			
Prevalence method(d)	P = 0.5626			
Combined analysis(d)	P = 0.5630			
Cochran-Armitage test(e)	P = 0.6515			
Fisher Exact test(e)		P = 0.3798	P = 0.3929	P = 0.3798
	SITE : mammary gland			
	TUMOR : fibroadenoma			
Tumor rate				
Overall rates(a)	7/50(14.0)	7/50(14.0)	10/50(20.0)	4/50(8.0)
Adjusted rates(b)	14.00	13.04	20.93	12.12
Terminal rates(c)	3/38(7.9)	4/38(10.5)	8/42(19.0)	4/33(12.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5859			
Prevalence method(d)	P = 0.7653			
Combined analysis(d)	P = 0.7933			
Cochran-Armitage test(e)	P = 0.2934			
Fisher Exact test(e)		P = 0.6129	P = 0.2977	P = 0.2623

Group Name	Control	800 ppm	2400 ppm	7200 ppm
	SITE : mammary gland			
	TUMOR : adenoma, fibroadenoma, adenocarcinoma			
Tumor rate				
Overall rates(a)	11/50(22.0)	10/50(20.0)	11/50(22.0)	6/50(12.0)
Adjusted rates(b)	22.00	20.00	20.93	15.15
Terminal rates(c)	6/38(15.8)	6/38(15.8)	8/42(19.0)	5/33(15.2)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.2528			
Prevalence method(d)	P = 0.9141			
Combined analysis(d)	P = 0.8625			
Cochran-Armitage test(e)	P = 0.1712			
Fisher Exact test(e)		P = 0.5000	P = 0.5952	P = 0.1434
	SITE : preputial/clitoral gland			
	TUMOR : adenoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	3/50(6.0)	1/50(2.0)	2/50(4.0)
Adjusted rates(b)	5.26	4.88	2.38	6.06
Terminal rates(c)	2/38(5.3)	1/38(2.6)	1/42(2.4)	2/33(6.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8633			
Prevalence method(d)	P = 0.3970			
Combined analysis(d)	P = 0.6076			
Cochran-Armitage test(e)	P = 0.6080			
Fisher Exact test(e)		P = 0.6611	P = 0.3087	P = 0.5000

(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 R

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

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

Organs Tumors	No. of animals examined	No. of animals bearing tumor	Incidence (%)	Min. - Max. (%)
Adrenal	2446			
Pheochromocytoma 1)		81	3.3	0 - 16
Pheochromocytoma:malignant 2)		22	0.9	0 - 6
1)+2)		103	4.2	0 - 18

49 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, 0296, 0318, 0328, 0342, 0347, 0365, 0371, 0399, 0401, 0417, 0421, 0437, 0448, 0457, 0461, 0497, 0535, 0560, 0579, 0610, 0612, 0667, 0675, 0686, 0691

TABLE S 1

CAUSE OF DEATH: MALE

STUDY NO. : 0641
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
SEX : MALE

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

Group Name	Control	800 ppm	2400 ppm	7200 ppm
Number of Dead and Moribund Animal	10	5	12	10
no microscop confirm	1	1	0	1
integumentary sy les	0	0	1	0
renal lesion	0	0	0	1
chronic nephropathy	1	0	0	0
tumor d:leukemia	1	1	5	0
tumor d:skin/app	1	0	1	0
tumor d:subcutis	1	0	2	0
tumor d:lung	0	0	0	1
tumor d:urin bladd	0	0	0	1
tumor d:pituitary	2	0	0	2
tumor d:thyroid	1	1	1	1
tumor d:adrenal	1	0	0	1
tumor d:brain	1	0	0	0
tumor d:Zymbal gl	0	0	1	1
tumor d:bone	0	1	1	0
tumor d:peritoneum	0	1	0	1

TABLE S 2

CAUSE OF DEATH: FEMALE

STUDY NO. : 0641
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
SEX : FEMALE

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

Group Name	Control	800 ppm	2400 ppm	7200 ppm
Number of Dead and Moribund Animal	12	12	8	17
no microscop confirm	0	1	1	2
renal lesion	0	0	0	2
tumor d:leukemia	2	3	2	6
tumor d:thymus	1	0	0	0
tumor d:pituitary	7	6	2	2
tumor d:thyroid	0	0	1	0
tumor d:uterus	1	0	1	3
tumor d:mammary gl	0	1	1	1
tumor d:prep/cli gl	1	1	0	0
tumor d:Zymbal gl	0	0	0	1

(BIO120)

BAIS4

FIGURES

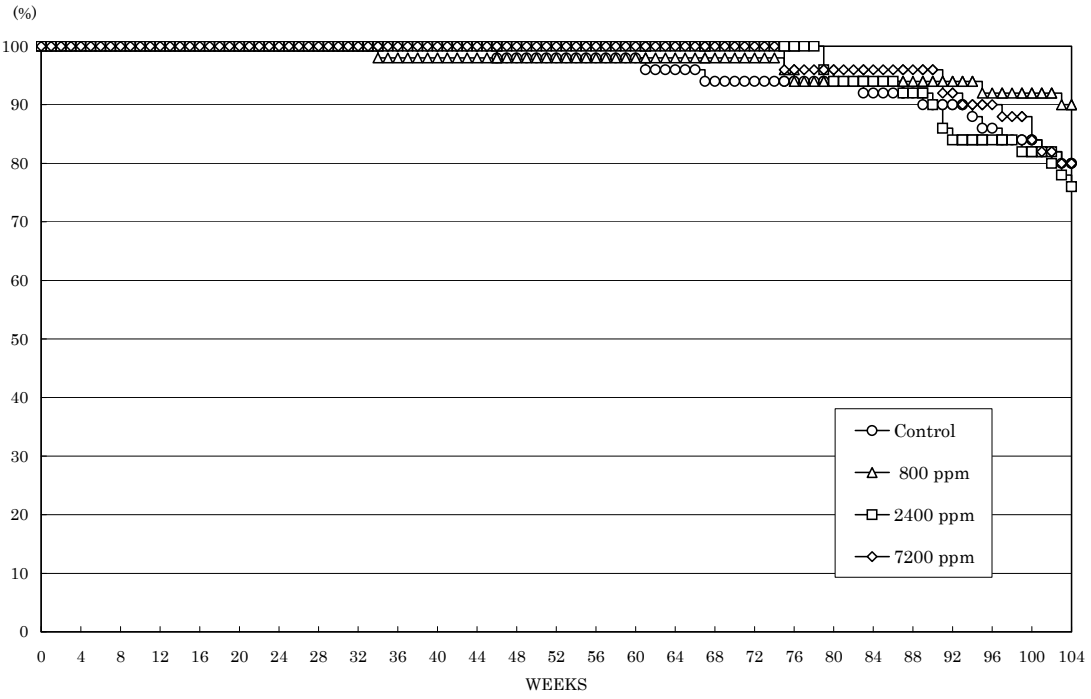


FIGURE 1 SURVIVAL ANIMAL RATE OF MALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF 2-AMINOETHANOL

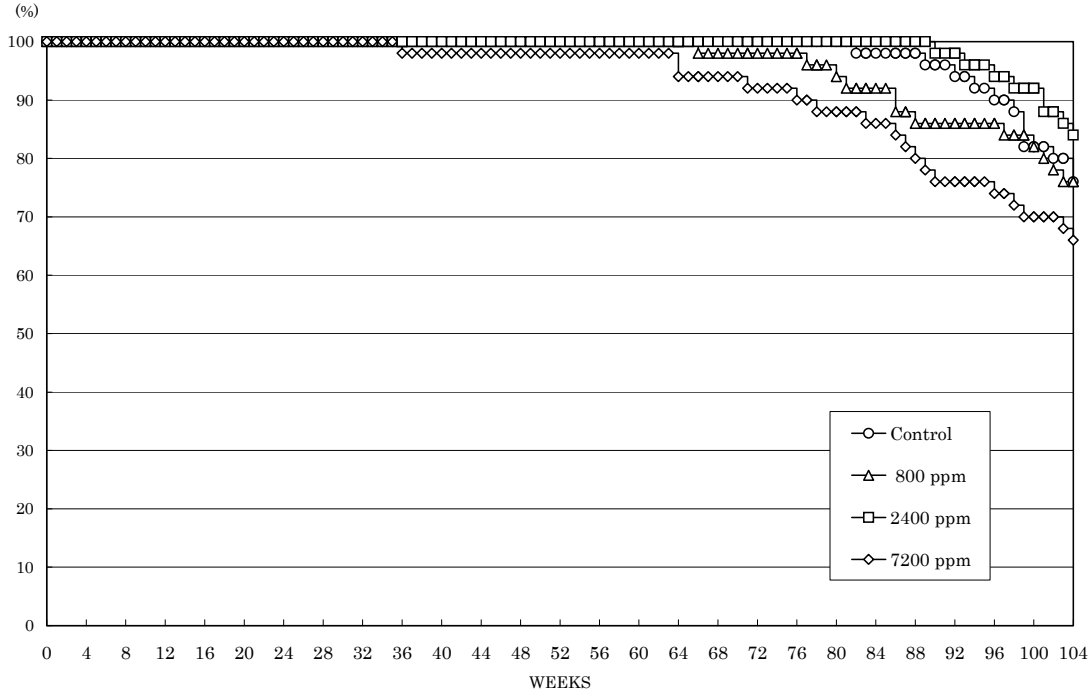


FIGURE 2 SURVIVAL ANIMAL RATE OF FEMALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF 2-AMINOETHANOL

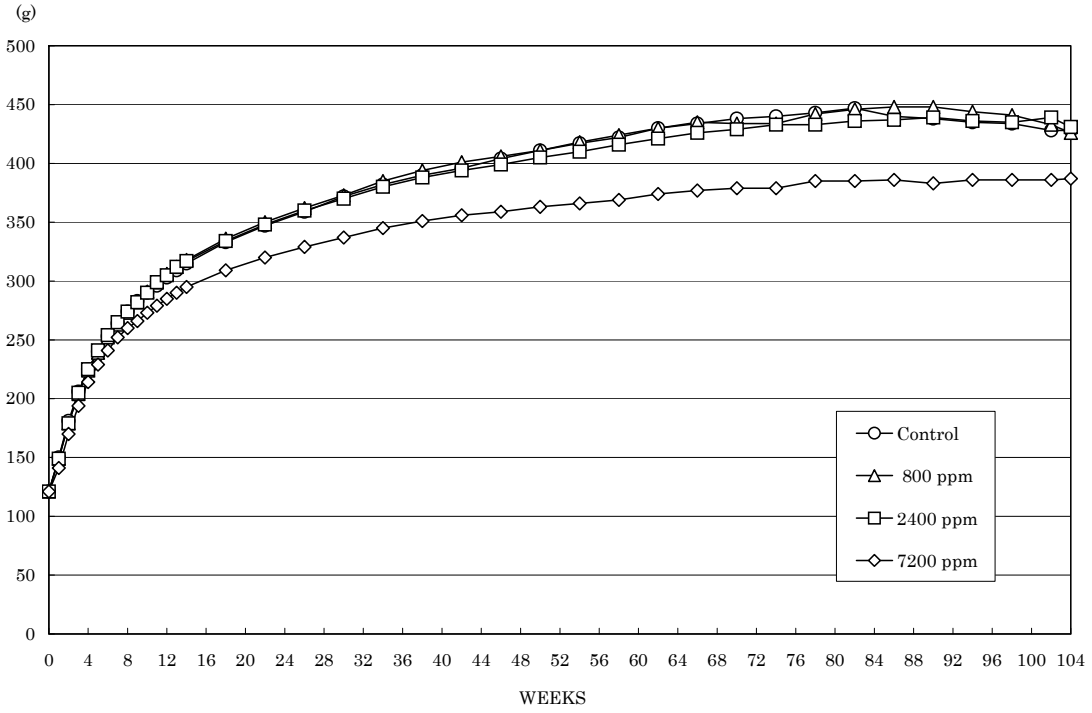


FIGURE 3 BODY WEIGHT CHANGES OF MALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF 2-AMINOETHANOL

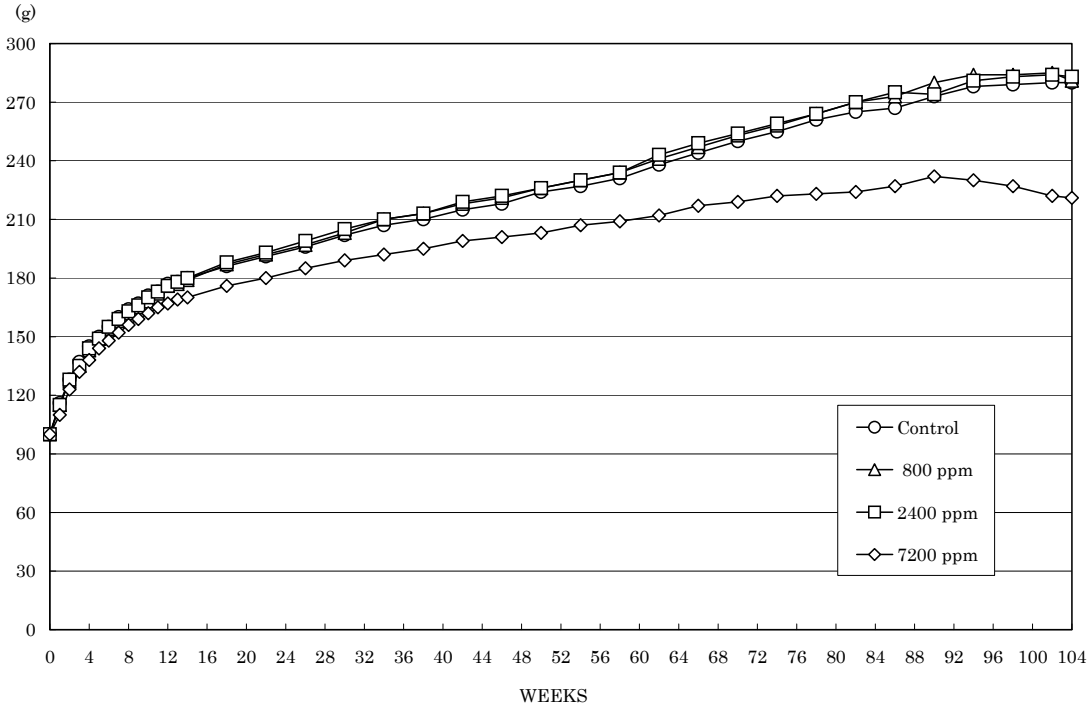


FIGURE 4 BODY WEIGHT CHANGES OF FEMALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF 2-AMINOETHANOL

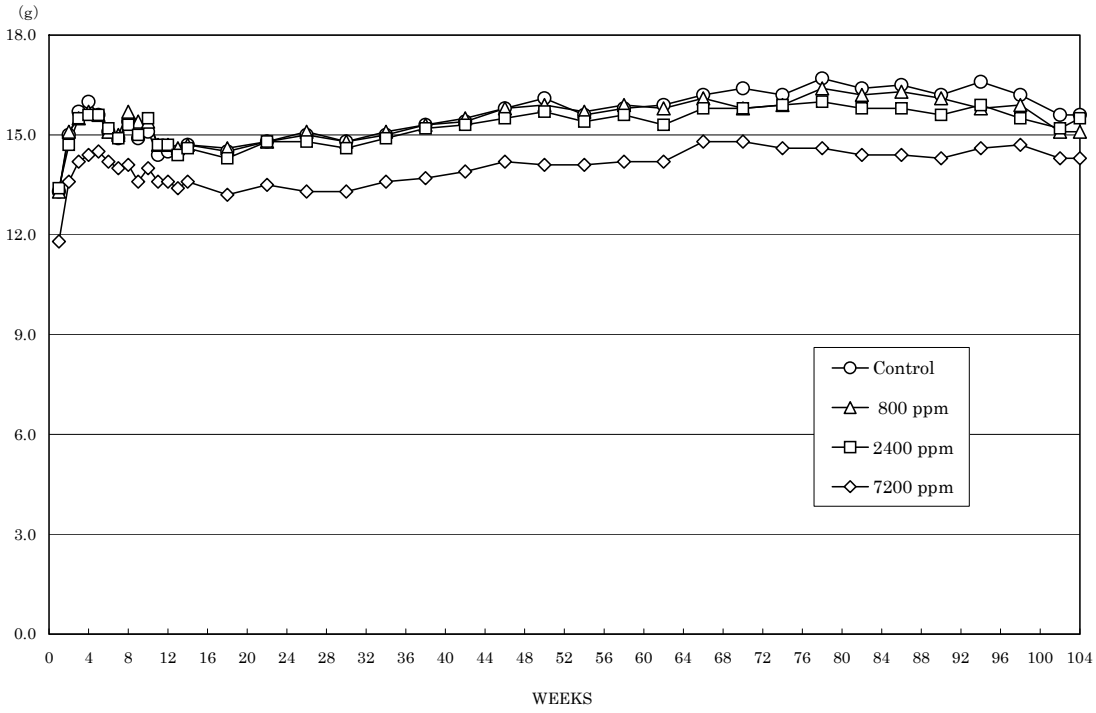


FIGURE 5 FOOD CONSUMPTION CHANGES OF MALE RATS IN THE 2-YEAR DRINKING WATER STUDY 2-AMINOETHANOL

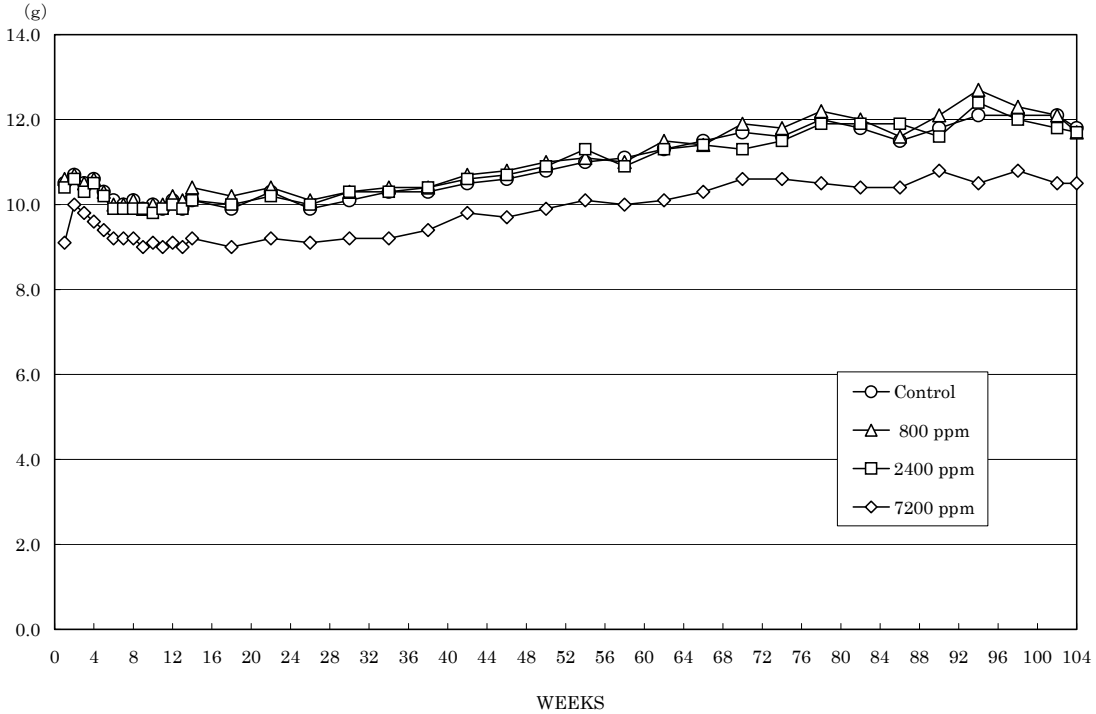


FIGURE 6 FOOD CONSUMPTION CHANGES OF FEMALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF 2-AMINOETHANOL

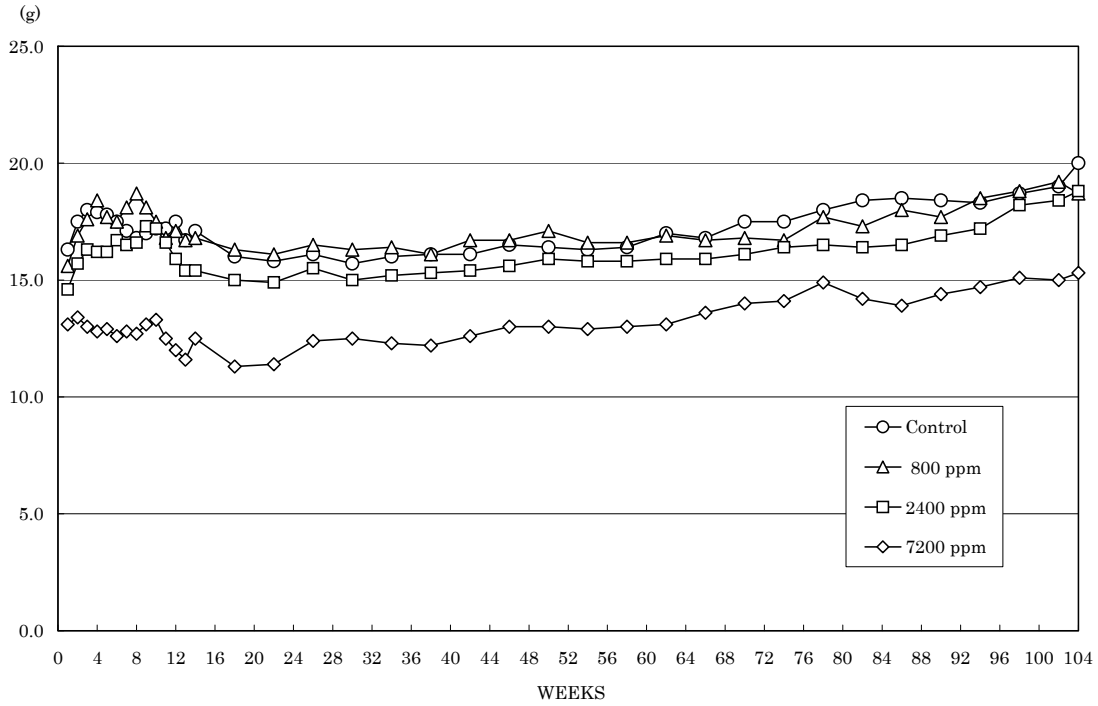


FIGURE 7 WATER CONSUMPTION CHANGES OF MALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF 2-AMINOETHANOL

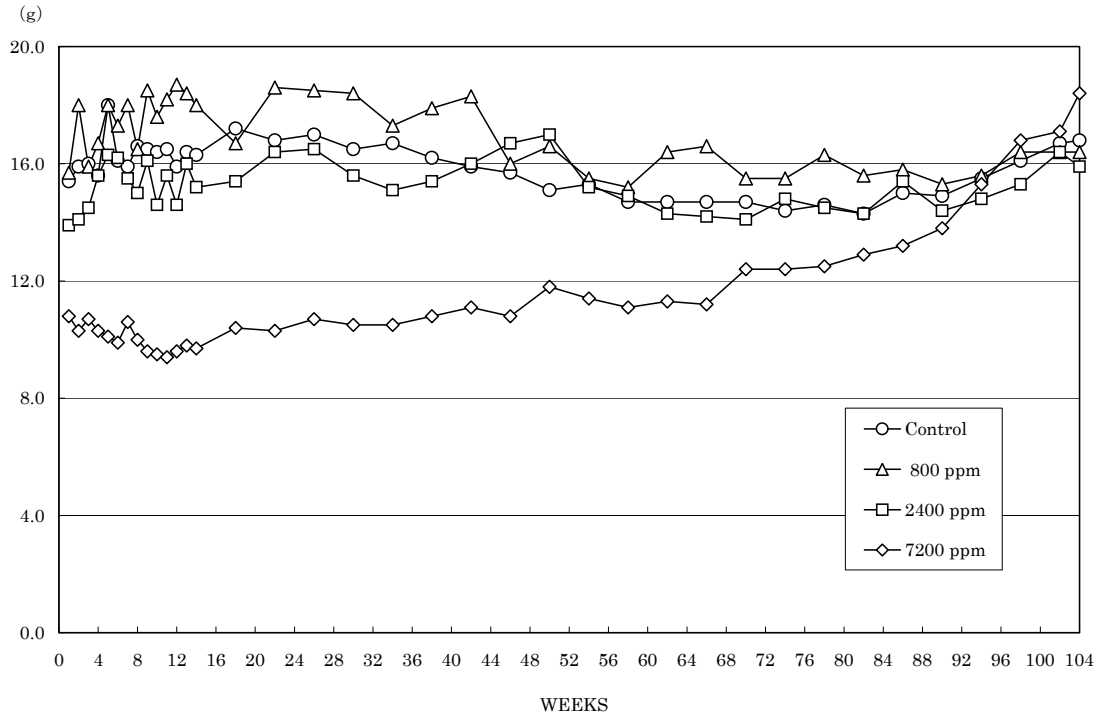
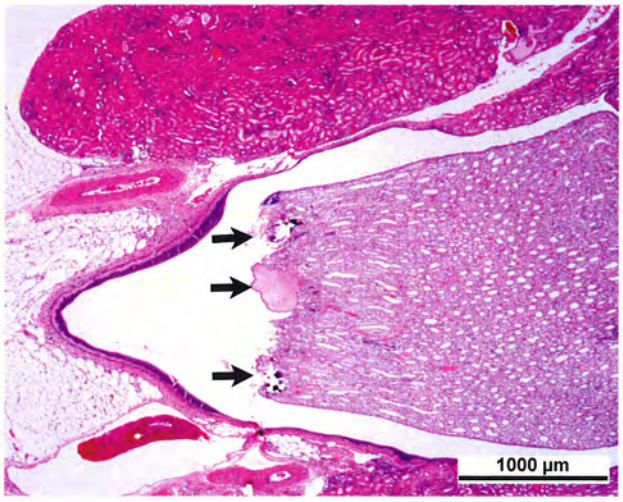
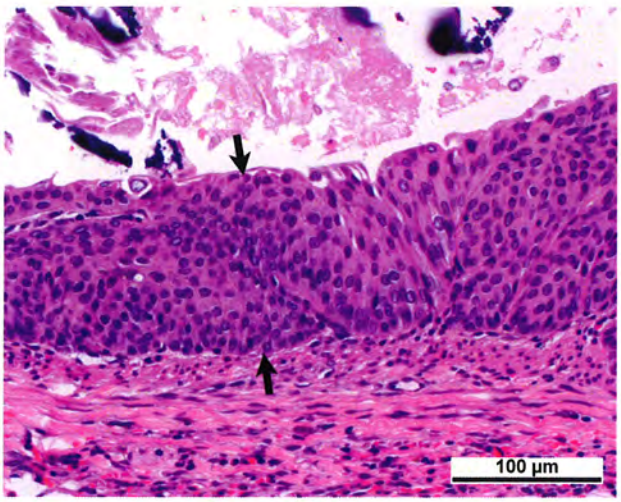


FIGURE 8 WATER CONSUMPTION CHANGES OF FEMALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF 2-AMINOETHANOL

Photograph 1
Kidney: Normal
Rat, Female, Control, Animal No. 0641-2007 (H&E)



Photograph 2
Kidney: Papillary necrosis (arrows)
Rat, Female, 7200 ppm, Animal No. 0641-2304 (H&E)



Photograph 3
Kidney: Urothelial hyperplasia of pelvis (arrows)
Rat, Female, 7200 ppm, Animal No. 0641-2313 (H&E)