Summary of Drinking Water Carcinogenicity Study of 2-Methyl-1-Propanol in F344 Rats

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Japan Bioassay Research Center

Japan Industrial Safety and Health Association

PREFACE

The tests were contracted and supported by the Ministry of Health, Labour and Welfare of Japan. The tests were conducted by Japan Bioassay Research Center (JBRC) and the report was prepared by JBRC and peer reviewed by outside expert pathologist. Complete report was submitted to Ministry of Health, Labour and Welfare of Japan on September 30, 2009.

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

Summary of Drinking Water Carcinogenicity Study of 2-Methyl-1-Propanol in F344 Rats

Purpose, materials and methods

2-Methyl-1-propanol (CAS No. 78-83-1) is a colorless clear liquid with a melting point of -108°C and a boiling point of 107.9°C. It is soluble in water (8.7 wt%), alcohol, and ether.

The carcinogenicity and chronic toxicity of 2-methyl-1-propanol were examined in F344/DuCrlCrlj rats. Groups of test animals were administered 2-methyl-1-propanol 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-methyl-1-propanol were 0, 3300, 10000 or 30000 ppm (w/w). Both sexes were administered each concentration of 2-Methyl-1-propanol. 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. 2-Methyl-1-propanol was analyzed for purity and stability by both infrared spectrometry and gas chromatography before and after its use. The concentrations of 2-methyl-1-propanol in the drinking water were determined by gas chromatography at the time of preparation and on the 4th day after preparation, while stored at room temperature. The animals were observed daily for clinical signs and mortality. Body weight, water consumption and food consumption were measured once a week for the first 14 weeks and every 4 weeks thereafter. Animals found dead, in a moribund state, or surviving to the end of the 2-year administration period underwent complete necropsy. Urinalysis was performed near the end of the administration period. For hematology and blood biochemistry at the terminal necropsy, surviving animals were fasted overnight and bled under deep ether anesthesia. Organs and tissues were removed, weighed and examined for macroscopic lesions at necropsy. The organs and tissues were then fixed and embedded in paraffin. Five μm thick tissue sections were prepared and stained with hematoxylin and eosin and examined microscopically. Incidences of neoplastic lesions were statistically analyzed by Fisher's exact test. Any positive dose-response trends of 2-methyl-1-propanol induction of neoplastic lesions were analyzed by Peto's test. Incidences of non-neoplastic lesions and urinalysis were analyzed by the Chi-square test. Changes in body weight, food consumption, hematological and blood biochemical parameters, and organ weights were analyzed by Dunnett's test. The present studies were conducted in accordance with the Organisation for Economic Co-operation and Development (OECD) Good Laboratory Practice and with

reference to the OECD Guideline for Testing of Chemicals 451 “Carcinogenicity Studies”.

Results

No significant differences in survival rates were found between any of the groups administered 2-methyl-1-propanol and their respective controls. Soiled fur around the genitalia was observed in the 30000 ppm-administered females. Growth rates of the 30000 ppm-administered males and females were suppressed, and food and water consumption was decreased in the 10000 and 30000 ppm-administered males and females through most of the 2-year administration period.

No significant increases in the incidence of neoplastic or tumor-related lesions was found in any of the 2-methyl-1-propanol-administered groups of either sex compared with their respective controls. Kidney weights (absolute and relative) were increased in the 10000 and 30000 ppm-administered females. Additionally, urinary occult blood, papillary necrosis and papillary mineralization in the kidney were increased in the 30000 ppm-administered females. Finally, urothelial hyperplasia of the pelvis was observed in the 30000 ppm-administered females. In males, kidney weights (absolute) were increased in 30000 ppm-administered group, but neither histopathological changes nor urinary occult blood were found.

Using kidney weight, renal lesions and body weight suppression (male only), as endpoint markers, the no-observed-adverse-effect-level (NOAEL) for males of 2-methyl-1-propanol in the drinking water was 10000 ppm (513 mg/kg body weight per day) and 3300 ppm (297 mg/kg body weight per day) for females.

Conclusions

There was no evidence of carcinogenic activity of 2-methyl-1-propanol in male or female rats.

Incidences of selected neoplastic lesions of male rats in the 2-year drinking water carcinogenicity study of 2-Methyl-1-propanol

Dose (ppm)		0	3300	10000	30000	Peto test	Cochran-Armitage test
Number of examined animals		50	50	50	50		
benign tumor							
subcutis	fibroma	2	1	5	2		
lung	bronchiolar-alveolar adenoma	3	3	2	2		
pituitary	adenoma	24	13 *	20	14 *		
thyroid	C-cell adenoma	8	3	6	10		
adrenal	pheochromocytoma	4	5	5	6		
testis	interstitial cell tumor	28	30	34	36		
malignant tumor							
lung	bronchiolar-alveolar carcinoma	1	1	3	1		
spleen	mononuclear cell leukemia	3	6	8	2		
pancreas	islet cell adenocarcinoma	0	3	2	1		
peritoneum	mesothelioma	1	0	2	4	↑	↑

Incidences of selected neoplastic lesions of female rats in the 2-year drinking water carcinogenicity study of 2-Methyl-1-propanol

Dose (ppm)		0	3300	10000	30000	Peto test	Cochran-Armitage test
Number of examined animals		50	50	50	50		
benign tumor							
pituitary	adenoma	11	7	8	11		
thyroid	C-cell adenoma	4	7	6	1		
adrenal	pheochromocytoma	2	3	2	0		
uterus	endometrial stromal polyp	8	7	7	9		
mammary gland	fibroadenoma	4	3	4	3		
malignant tumor							
spleen	mononuclear cell leukemia	4	5	5	3		
uterus	adenocarcinoma	1	1	2	3		

Significant difference

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

SELECTED TABLES

TABLE C 1

BODY WEIGHT CHANGES AND

SURVIVAL ANIMAL NUMBERS: MALE

STUDY NO. : 0612
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>	3300 ppm Av. Wt.	3300 ppm % of cont. <50>	3300 ppm No. of Surviv.	10000 ppm Av. Wt.	10000 ppm % of cont. <50>	10000 ppm No. of Surviv.	30000 ppm Av. Wt.	30000 ppm % of cont. <50>	30000 ppm No. of Surviv.
0-0	126 (50)	50/50	126 (50)	100	50/50	126 (50)	100	50/50	126 (50)	100	50/50
1-7	157 (50)	50/50	156 (50)	99	50/50	154 (50)	98	50/50	151 (50)	96	50/50
2-7	187 (50)	50/50	187 (50)	100	50/50	184 (50)	98	50/50	179 (50)	96	50/50
3-7	211 (50)	50/50	211 (50)	100	50/50	207 (50)	98	50/50	202 (50)	96	50/50
4-7	229 (50)	50/50	230 (50)	100	50/50	225 (50)	98	50/50	220 (50)	96	50/50
5-7	242 (50)	50/50	244 (50)	101	50/50	239 (50)	99	50/50	233 (50)	96	50/50
6-7	253 (50)	50/50	256 (50)	101	50/50	251 (50)	99	50/50	245 (50)	97	50/50
7-7	264 (50)	50/50	265 (50)	100	50/50	262 (50)	99	50/50	254 (50)	96	50/50
8-7	274 (50)	50/50	277 (50)	101	50/50	273 (50)	100	50/50	265 (50)	97	50/50
9-7	282 (50)	50/50	283 (50)	100	50/50	280 (50)	99	50/50	272 (50)	96	50/50
10-7	288 (50)	50/50	289 (50)	100	50/50	285 (50)	99	50/50	277 (50)	96	50/50
11-7	293 (50)	50/50	294 (50)	100	50/50	289 (50)	99	50/50	281 (50)	96	50/50
12-7	301 (50)	50/50	303 (50)	101	50/50	297 (50)	99	50/50	288 (50)	96	50/50
13-7	307 (50)	50/50	310 (50)	101	50/50	303 (50)	99	50/50	294 (50)	96	50/50
14-7	312 (50)	50/50	316 (50)	101	50/50	309 (50)	99	50/50	299 (50)	96	50/50
18-7	330 (50)	50/50	333 (50)	101	50/50	327 (50)	99	50/50	316 (50)	96	50/50
22-7	343 (50)	50/50	349 (49)	102	49/50	340 (50)	99	50/50	328 (50)	96	50/50
26-7	355 (50)	50/50	359 (49)	101	49/50	350 (50)	99	50/50	338 (50)	95	50/50
30-7	365 (50)	50/50	369 (49)	101	49/50	359 (50)	98	50/50	346 (50)	95	50/50
34-7	373 (50)	50/50	377 (49)	101	49/50	366 (50)	98	50/50	353 (50)	95	50/50
38-7	379 (50)	50/50	386 (49)	102	49/50	373 (50)	98	50/50	361 (50)	95	50/50
42-7	388 (49)	49/50	392 (49)	101	49/50	378 (49)	97	49/50	366 (50)	94	50/50
46-7	394 (49)	49/50	398 (48)	101	48/50	383 (49)	97	49/50	371 (50)	94	50/50
50-7	401 (49)	49/50	404 (48)	101	48/50	389 (49)	97	49/50	376 (50)	94	50/50
54-7	408 (49)	49/50	414 (47)	101	47/50	396 (49)	97	49/50	383 (50)	94	50/50
58-7	414 (49)	49/50	419 (47)	101	47/50	403 (49)	97	49/50	386 (50)	93	50/50
62-7	420 (49)	49/50	423 (46)	101	46/50	407 (49)	97	49/50	391 (50)	93	50/50
66-7	418 (49)	49/50	422 (46)	101	46/50	408 (49)	98	49/50	391 (50)	94	50/50
70-7	421 (49)	49/50	421 (45)	100	45/50	408 (49)	97	49/50	390 (50)	93	50/50
74-7	424 (49)	49/50	429 (43)	101	43/50	407 (49)	96	49/50	393 (50)	93	50/50
78-7	425 (49)	49/50	427 (42)	100	42/50	414 (48)	97	48/50	394 (50)	93	50/50
82-7	420 (49)	49/50	427 (40)	102	40/50	414 (48)	99	48/50	391 (50)	93	50/50
86-7	423 (48)	48/50	428 (40)	101	40/50	416 (48)	98	48/50	391 (49)	92	49/50
90-7	423 (47)	47/50	423 (40)	100	40/50	421 (47)	100	47/50	386 (48)	91	48/50
94-7	420 (46)	46/50	421 (38)	100	38/50	408 (45)	97	45/50	383 (46)	91	46/50
98-7	411 (43)	43/50	419 (36)	102	36/50	399 (44)	97	44/50	384 (43)	93	43/50
102-7	403 (40)	40/50	406 (35)	101	35/50	397 (40)	99	40/50	372 (43)	92	43/50
104-7	398 (40)	40/50	398 (35)	100	35/50	393 (39)	99	39/50	370 (40)	93	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. : 0612
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>	3300 ppm Av. Wt.	3300 ppm % of cont. <50>	3300 ppm No. of Surviv.	10000 ppm Av. Wt.	10000 ppm % of cont. <50>	10000 ppm No. of Surviv.	30000 ppm Av. Wt.	30000 ppm % of cont. <50>	30000 ppm No. of Surviv.
0-0	99 (50)	50/50	99 (50)	100	50/50	99 (50)	100	50/50	99 (50)	100	50/50
1-7	114 (50)	50/50	115 (50)	101	50/50	113 (50)	99	50/50	112 (50)	98	50/50
2-7	125 (50)	50/50	126 (50)	101	50/50	125 (50)	100	50/50	125 (50)	100	50/50
3-7	134 (50)	50/50	135 (50)	101	50/50	133 (50)	99	50/50	132 (50)	99	50/50
4-7	140 (50)	50/50	142 (50)	101	50/50	141 (50)	101	50/50	139 (50)	99	50/50
5-7	145 (50)	50/50	147 (50)	101	50/50	146 (50)	101	50/50	143 (50)	99	50/50
6-7	151 (50)	50/50	152 (50)	101	50/50	151 (50)	100	50/50	148 (50)	98	50/50
7-7	153 (50)	50/50	155 (50)	101	50/50	153 (50)	100	50/50	149 (50)	97	50/50
8-7	156 (50)	50/50	158 (50)	101	50/50	156 (50)	100	50/50	152 (50)	97	50/50
9-7	158 (50)	50/50	161 (50)	102	50/50	158 (50)	100	50/50	154 (50)	97	50/50
10-7	161 (50)	50/50	163 (50)	101	50/50	161 (50)	100	50/50	157 (50)	98	50/50
11-7	163 (50)	50/50	165 (50)	101	50/50	163 (50)	100	50/50	158 (50)	97	50/50
12-7	166 (50)	50/50	168 (50)	101	50/50	166 (50)	100	50/50	161 (50)	97	50/50
13-7	168 (50)	50/50	171 (50)	102	50/50	167 (50)	99	50/50	163 (50)	97	50/50
14-7	169 (50)	50/50	171 (50)	101	50/50	169 (50)	100	50/50	163 (50)	96	50/50
18-7	176 (50)	50/50	178 (50)	101	50/50	176 (50)	100	50/50	169 (50)	96	50/50
22-7	182 (50)	50/50	183 (50)	101	50/50	182 (50)	100	50/50	174 (50)	96	50/50
26-7	186 (50)	50/50	189 (50)	102	50/50	186 (50)	100	50/50	178 (50)	96	50/50
30-7	190 (50)	50/50	193 (50)	102	50/50	190 (50)	100	50/50	181 (50)	95	50/50
34-7	195 (49)	49/50	197 (50)	101	50/50	195 (50)	100	50/50	186 (50)	95	50/50
38-7	199 (49)	49/50	201 (50)	101	50/50	198 (50)	99	50/50	189 (50)	95	50/50
42-7	204 (49)	49/50	205 (50)	100	50/50	203 (50)	100	50/50	192 (50)	94	50/50
46-7	206 (49)	49/50	208 (50)	101	50/50	206 (50)	100	50/50	194 (50)	94	50/50
50-7	212 (48)	48/50	213 (50)	100	50/50	210 (50)	99	50/50	197 (50)	93	50/50
54-7	218 (47)	47/50	219 (50)	100	50/50	216 (50)	99	50/50	201 (50)	92	50/50
58-7	224 (47)	47/50	224 (50)	100	50/50	221 (50)	99	50/50	204 (50)	91	50/50
62-7	228 (47)	47/50	229 (49)	100	49/50	225 (50)	99	50/50	209 (50)	92	50/50
66-7	232 (47)	47/50	233 (49)	100	49/50	230 (50)	99	50/50	214 (50)	92	50/50
70-7	235 (46)	46/50	239 (49)	102	49/50	233 (50)	99	50/50	216 (48)	92	48/50
74-7	239 (46)	46/50	245 (48)	103	48/50	238 (50)	100	50/50	219 (47)	92	47/50
78-7	245 (45)	45/50	249 (47)	102	47/50	240 (50)	98	50/50	224 (46)	91	46/50
82-7	250 (43)	43/50	250 (45)	100	45/50	244 (49)	98	49/50	227 (46)	91	46/50
86-7	256 (40)	40/50	258 (45)	101	45/50	248 (49)	97	49/50	231 (45)	90	45/50
90-7	258 (38)	38/50	260 (44)	101	44/50	250 (48)	97	48/50	233 (44)	90	44/50
94-7	260 (38)	38/50	262 (43)	101	43/50	251 (47)	97	47/50	234 (44)	90	44/50
98-7	262 (38)	38/50	265 (43)	101	43/50	251 (45)	96	45/50	234 (43)	89	43/50
102-7	263 (35)	35/50	269 (40)	102	40/50	252 (44)	96	44/50	234 (40)	89	40/50
104-7	262 (35)	35/50	262 (39)	100	39/50	252 (44)	96	44/50	234 (39)	89	39/50

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

TABLE C 3

BODY WEIGHT CHANGES: MALE

STUDY NO. : 0612
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	126± 5	157± 6	187± 9	211± 10	229± 11	242± 12	253± 13
3300 ppm	126± 5	156± 7	187± 10	211± 12	230± 13	244± 15	256± 16
10000 ppm	126± 5	154± 7*	184± 10	207± 10	225± 12	239± 13	251± 13
30000 ppm	126± 5	151± 6**	179± 8**	202± 9**	220± 10**	233± 11**	245± 12**

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

STUDY NO. : 0612
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± 14	274± 14	282± 15	288± 15	293± 15	301± 15	307± 15
3300 ppm	265± 16	277± 17	283± 17	289± 18	294± 19	303± 19	310± 20
10000 ppm	262± 13	273± 14	280± 15	285± 14	289± 15	297± 15	303± 15
30000 ppm	254± 13**	265± 13**	272± 14**	277± 13**	281± 12**	288± 13**	294± 14**

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

STUDY NO. : 0612
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	312± 16	330± 17	343± 18	355± 18	365± 19	373± 21	379± 22
3300 ppm	316± 21	333± 21	349± 21	359± 21	369± 23	377± 24	386± 25
10000 ppm	309± 16	327± 17	340± 18	350± 20	359± 22	366± 24	373± 25
30000 ppm	299± 14**	316± 14**	328± 15**	338± 17**	346± 18**	353± 18**	361± 20**

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

(HAN260)

BAIS 4

STUDY NO. : 0612
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	388± 22	394± 22	401± 23	408± 23	414± 24	420± 23	418± 23
3300 ppm	392± 27	398± 29	404± 30	414± 26	419± 26	423± 26	422± 28
10000 ppm	378± 26	383± 26	389± 26	396± 26*	403± 27	407± 27*	408± 24
30000 ppm	366± 20**	371± 21**	376± 22**	383± 22**	386± 24**	391± 24**	391± 24**

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

STUDY NO. : 0612
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	421± 24	424± 24	425± 25	420± 33	423± 34	423± 25	420± 28
3300 ppm	421± 34	429± 27	427± 29	427± 24	428± 24	423± 29	421± 31
10000 ppm	408± 26*	407± 35*	414± 25	414± 25	416± 28	421± 46	408± 32
30000 ppm	390± 25**	393± 23**	394± 22**	391± 23**	391± 30**	386± 35**	383± 40**

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

(HAN260)

BAIS 4

STUDY NO. : 0612
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	411± 28	403± 34	398± 40
3300 ppm	419± 26	406± 33	398± 40
10000 ppm	399± 35	397± 35	393± 40
30000 ppm	384± 28**	372± 37**	370± 31**

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

TABLE C 4

BODY WEIGHT CHANGES: FEMALE

STUDY NO. : 0612
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	99± 3	114± 4	125± 5	134± 6	140± 7	145± 8	151± 8
3300 ppm	99± 3	115± 5	126± 5	135± 6	142± 6	147± 7	152± 7
10000 ppm	99± 3	113± 4	125± 5	133± 6	141± 7	146± 7	151± 7
30000 ppm	99± 3	112± 4*	125± 4	132± 5	139± 6	143± 6	148± 7

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

(HAN260)

BAIS 4

STUDY NO. : 0612
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	153± 8	156± 8	158± 9	161± 9	163± 10	166± 10	168± 10
3300 ppm	155± 8	158± 8	161± 9	163± 9	165± 9	168± 9	171± 9
10000 ppm	153± 8	156± 8	158± 8	161± 9	163± 9	166± 9	167± 10
30000 ppm	149± 7	152± 8	154± 8*	157± 9	158± 9	161± 9*	163± 9*

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

(HAN260)

BAIS 4

STUDY NO. : 0612
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	169± 10	176± 10	182± 11	186± 11	190± 12	195± 12	199± 13
3300 ppm	171± 10	178± 10	183± 10	189± 11	193± 11	197± 11	201± 12
10000 ppm	169± 10	176± 10	182± 10	186± 11	190± 12	195± 13	198± 12
30000 ppm	163± 9**	169± 9**	174± 9**	178± 10**	181± 10**	186± 10**	189± 10**

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

(HAN260)

BAIS 4

STUDY NO. : 0612
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	204± 14	206± 15	212± 16	218± 19	224± 21	228± 22	232± 22
3300 ppm	205± 12	208± 13	213± 13	219± 15	224± 16	229± 17	233± 18
10000 ppm	203± 14	206± 14	210± 16	216± 18	221± 19	225± 20	230± 21
30000 ppm	192± 10**	194± 11**	197± 11**	201± 12**	204± 13**	209± 13**	214± 17**

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

(HAN260)

BAIS 4

STUDY NO. : 0612
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	235± 23	239± 23	245± 24	250± 22	256± 21	258± 22	260± 23
3300 ppm	239± 20	245± 19	249± 20	250± 24	258± 22	260± 23	262± 25
10000 ppm	233± 21	238± 22	240± 25	244± 21	248± 21	250± 21	251± 23
30000 ppm	216± 15**	219± 16**	224± 15**	227± 15**	231± 15**	233± 14**	234± 14**

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

(HAN260)

BAIS 4

STUDY NO. : 0612
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	262± 24	263± 25	262± 28
3300 ppm	265± 32	269± 50	262± 34
10000 ppm	251± 27	252± 27	252± 27
30000 ppm	234± 17**	234± 17**	234± 18**

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

TABLE D 1

FOOD CONSUMPTION CHANGES AND

SURVIVAL ANIMAL NUMBERS: MALE

STUDY NO. : 0612
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>	3300 ppm Av. FC.	3300 ppm % of cont. <50>	3300 ppm No. of Surviv.	10000 ppm Av. FC.	10000 ppm % of cont. <50>	10000 ppm No. of Surviv.	30000 ppm Av. FC.	30000 ppm % of cont. <50>	30000 ppm No. of Surviv.
1-7	14.1 (50)	50/50	14.0 (50)	99	50/50	13.4 (50)	95	50/50	11.8 (50)	84	50/50
2-7	15.4 (50)	50/50	15.3 (50)	99	50/50	14.6 (50)	95	50/50	13.2 (50)	86	50/50
3-7	15.6 (50)	50/50	15.6 (50)	100	50/50	14.8 (50)	95	50/50	13.5 (50)	87	50/50
4-7	15.1 (50)	50/50	15.3 (50)	101	50/50	14.8 (50)	98	50/50	13.4 (50)	89	50/50
5-7	15.1 (50)	50/50	15.0 (50)	99	50/50	14.5 (50)	96	50/50	13.2 (50)	87	50/50
6-7	14.6 (50)	50/50	14.7 (50)	101	50/50	14.2 (50)	97	50/50	12.9 (50)	88	50/50
7-7	14.5 (50)	50/50	14.4 (50)	99	50/50	13.9 (50)	96	50/50	12.7 (50)	88	50/50
8-7	14.8 (50)	50/50	14.7 (50)	99	50/50	14.2 (50)	96	50/50	12.9 (50)	87	50/50
9-7	14.7 (50)	50/50	14.5 (50)	99	50/50	14.1 (50)	96	50/50	12.8 (50)	87	50/50
10-7	14.7 (25)	50/50	14.6 (50)	99	50/50	14.1 (50)	96	50/50	12.8 (50)	87	50/50
11-7	14.7 (50)	50/50	14.7 (50)	100	50/50	14.1 (50)	96	50/50	12.9 (50)	88	50/50
12-7	14.9 (50)	50/50	14.8 (50)	99	50/50	14.2 (50)	95	50/50	12.9 (50)	87	50/50
13-7	14.7 (50)	50/50	14.5 (50)	99	50/50	13.9 (50)	95	50/50	12.6 (50)	86	50/50
14-7	14.7 (50)	50/50	14.7 (50)	100	50/50	13.9 (50)	95	50/50	12.8 (50)	87	50/50
18-7	14.8 (50)	50/50	14.9 (50)	101	50/50	14.2 (50)	96	50/50	13.0 (50)	88	50/50
22-7	14.9 (50)	50/50	14.9 (49)	100	49/50	14.3 (50)	96	50/50	13.1 (50)	88	50/50
26-7	15.2 (50)	50/50	15.2 (49)	100	49/50	14.5 (50)	95	50/50	13.3 (50)	88	50/50
30-7	15.3 (50)	50/50	15.3 (49)	100	49/50	14.7 (50)	96	50/50	13.6 (50)	89	50/50
34-7	15.1 (50)	50/50	15.5 (49)	101	49/50	14.7 (50)	95	50/50	13.6 (50)	88	50/50
38-7	15.5 (50)	50/50	15.7 (49)	101	49/50	14.9 (50)	96	50/50	13.9 (50)	90	50/50
42-7	15.8 (49)	49/50	15.6 (49)	99	49/50	14.9 (49)	94	49/50	13.9 (50)	88	50/50
46-7	16.1 (49)	49/50	16.0 (48)	99	48/50	15.2 (49)	94	49/50	14.1 (50)	88	50/50
50-7	15.8 (49)	49/50	15.7 (48)	99	48/50	15.0 (49)	95	49/50	13.9 (50)	88	50/50
54-7	16.0 (49)	49/50	15.9 (47)	99	47/50	15.3 (49)	96	49/50	14.2 (50)	89	50/50
58-7	15.9 (49)	49/50	15.8 (47)	99	47/50	15.3 (49)	96	49/50	14.1 (50)	89	50/50
62-7	16.1 (49)	49/50	16.0 (46)	99	46/50	15.4 (49)	96	49/50	14.2 (50)	88	50/50
66-7	16.2 (49)	49/50	16.0 (46)	99	46/50	15.4 (49)	95	49/50	14.6 (50)	90	50/50
70-7	16.7 (49)	49/50	16.4 (45)	98	45/50	16.1 (49)	96	49/50	15.0 (50)	90	50/50
74-7	16.9 (49)	49/50	17.0 (43)	101	43/50	15.9 (49)	94	49/50	15.5 (50)	92	50/50
78-7	16.2 (49)	49/50	15.9 (42)	98	42/50	15.9 (48)	98	48/50	14.9 (49)	92	50/50
82-7	16.3 (49)	49/50	16.7 (40)	102	40/50	16.2 (48)	99	48/50	14.9 (50)	91	50/50
86-7	16.9 (47)	48/50	16.6 (40)	98	40/50	15.9 (48)	94	48/50	14.7 (49)	87	49/50
90-7	16.9 (46)	47/50	16.7 (40)	99	40/50	16.5 (46)	98	47/50	14.9 (48)	88	48/50
94-7	16.4 (45)	46/50	16.5 (38)	101	38/50	15.5 (45)	95	45/50	14.6 (46)	89	46/50
98-7	16.4 (43)	43/50	16.4 (36)	100	36/50	15.2 (44)	93	44/50	14.7 (43)	90	43/50
102-7	16.0 (40)	40/50	15.1 (35)	94	35/50	15.9 (40)	99	40/50	14.0 (43)	88	43/50
104-7	16.2 (40)	40/50	15.4 (34)	95	35/50	15.9 (39)	98	39/50	14.3 (40)	88	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. : 0612
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>	3300 ppm Av. FC.	3300 ppm % of cont. <50>	3300 ppm No. of Surviv.	10000 ppm Av. FC.	10000 ppm % of cont. <50>	10000 ppm No. of Surviv.	30000 ppm Av. FC.	30000 ppm % of cont. <50>	30000 ppm No. of Surviv.
1-7	10.8 (50)	50/50	10.5 (50)	97	50/50	10.0 (50)	93	50/50	9.0 (50)	83	50/50
2-7	10.8 (50)	50/50	10.5 (50)	97	50/50	10.3 (50)	95	50/50	9.6 (50)	89	50/50
3-7	10.4 (50)	50/50	10.2 (50)	98	50/50	9.9 (50)	95	50/50	9.2 (50)	88	50/50
4-7	10.1 (50)	50/50	9.9 (50)	98	50/50	9.8 (50)	97	50/50	9.1 (50)	90	50/50
5-7	9.8 (50)	50/50	9.6 (50)	98	50/50	9.3 (50)	95	50/50	8.7 (50)	89	50/50
6-7	9.8 (50)	50/50	9.4 (50)	96	50/50	9.0 (50)	92	50/50	8.4 (50)	86	50/50
7-7	9.4 (50)	50/50	9.2 (50)	98	50/50	8.8 (50)	94	50/50	8.2 (50)	87	50/50
8-7	9.4 (50)	50/50	9.1 (50)	97	50/50	8.8 (50)	94	50/50	8.2 (50)	87	50/50
9-7	9.4 (50)	50/50	9.1 (50)	97	50/50	8.7 (50)	93	50/50	8.0 (50)	85	50/50
10-7	9.6 (50)	50/50	9.4 (50)	98	50/50	9.0 (50)	94	50/50	8.2 (50)	85	50/50
11-7	9.7 (50)	50/50	9.3 (50)	96	50/50	9.0 (50)	93	50/50	8.2 (50)	85	50/50
12-7	9.8 (50)	50/50	9.6 (50)	98	50/50	9.2 (50)	94	50/50	8.4 (50)	86	50/50
13-7	9.6 (50)	50/50	9.2 (50)	96	50/50	8.9 (50)	93	50/50	8.1 (50)	84	50/50
14-7	9.6 (50)	50/50	9.3 (50)	97	50/50	9.0 (50)	94	50/50	8.2 (50)	85	50/50
18-7	9.9 (50)	50/50	9.7 (50)	98	50/50	9.3 (50)	94	50/50	8.4 (50)	85	50/50
22-7	9.9 (50)	50/50	9.5 (50)	96	50/50	9.4 (50)	95	50/50	8.6 (50)	87	50/50
26-7	10.1 (50)	50/50	9.9 (50)	98	50/50	9.6 (50)	95	50/50	8.8 (50)	87	50/50
30-7	10.2 (50)	50/50	9.9 (50)	97	50/50	9.7 (50)	95	50/50	8.9 (50)	87	50/50
34-7	10.2 (49)	49/50	9.8 (50)	96	50/50	9.9 (50)	97	50/50	9.0 (50)	88	50/50
38-7	10.4 (49)	49/50	10.1 (50)	97	50/50	10.0 (50)	96	50/50	9.1 (50)	88	50/50
42-7	10.5 (49)	49/50	10.4 (50)	99	50/50	10.2 (50)	97	50/50	9.2 (50)	88	50/50
46-7	10.8 (49)	49/50	10.5 (50)	97	50/50	10.3 (50)	95	50/50	9.4 (50)	87	50/50
50-7	10.7 (48)	48/50	10.3 (50)	96	50/50	10.1 (50)	94	50/50	9.2 (50)	86	50/50
54-7	11.0 (47)	47/50	10.4 (50)	95	50/50	10.2 (50)	93	50/50	9.2 (50)	84	50/50
58-7	10.9 (47)	47/50	10.4 (50)	95	50/50	10.3 (50)	94	50/50	9.3 (50)	85	50/50
62-7	11.0 (47)	47/50	10.7 (49)	97	49/50	10.4 (50)	95	50/50	9.7 (50)	88	50/50
66-7	11.0 (47)	47/50	10.9 (49)	99	49/50	10.5 (50)	95	50/50	9.5 (50)	86	50/50
70-7	11.3 (46)	46/50	11.3 (49)	100	49/50	10.7 (50)	95	50/50	9.7 (48)	86	48/50
74-7	11.5 (46)	46/50	11.7 (48)	102	48/50	11.2 (50)	97	50/50	10.1 (47)	88	47/50
78-7	11.6 (45)	45/50	11.3 (47)	97	47/50	10.9 (50)	94	50/50	10.1 (46)	87	46/50
82-7	11.5 (43)	43/50	11.4 (45)	99	45/50	10.9 (49)	95	49/50	10.0 (46)	87	46/50
86-7	11.9 (40)	40/50	11.9 (45)	100	45/50	11.0 (49)	92	49/50	10.1 (45)	85	45/50
90-7	12.0 (38)	38/50	12.0 (44)	100	44/50	11.2 (48)	93	48/50	10.5 (44)	88	44/50
94-7	11.9 (38)	38/50	11.7 (43)	98	43/50	11.1 (47)	93	47/50	10.4 (44)	87	44/50
98-7	12.1 (38)	38/50	12.0 (43)	99	43/50	11.5 (45)	95	45/50	10.3 (43)	85	43/50
102-7	12.2 (34)	35/50	11.9 (39)	98	40/50	11.2 (44)	92	44/50	10.3 (40)	84	40/50
104-7	12.3 (33)	35/50	11.7 (39)	95	39/50	11.3 (44)	92	44/50	10.2 (39)	83	39/50

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

TABLE D 3

FOOD CONSUMPTION CHANGES: MALE

STUDY NO. : 0612
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	14.1± 0.7	15.4± 0.8	15.6± 0.8	15.1± 0.9	15.1± 0.8	14.6± 0.9	14.5± 0.9
3300 ppm	14.0± 0.9	15.3± 1.1	15.6± 1.1	15.3± 1.1	15.0± 1.0	14.7± 1.1	14.4± 1.0
10000 ppm	13.4± 0.8**	14.6± 0.9**	14.8± 0.9**	14.8± 0.8	14.5± 0.8**	14.2± 1.0	13.9± 0.6**
30000 ppm	11.8± 0.8**	13.2± 0.8**	13.5± 0.8**	13.4± 0.8**	13.2± 0.8**	12.9± 0.8**	12.7± 0.7**

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

STUDY NO. : 0612
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	14.8± 0.9	14.7± 0.9	14.7± 0.9	14.7± 0.9	14.9± 1.0	14.7± 0.8	14.7± 1.0
3300 ppm	14.7± 1.0	14.5± 1.0	14.6± 1.0	14.7± 1.1	14.8± 1.0	14.5± 0.9	14.7± 1.0
10000 ppm	14.2± 0.7**	14.1± 0.7**	14.1± 0.7*	14.1± 0.8**	14.2± 0.8**	13.9± 0.7**	13.9± 0.8**
30000 ppm	12.9± 0.8**	12.8± 0.9**	12.8± 0.8**	12.9± 0.8**	12.9± 0.9**	12.6± 0.9**	12.8± 0.8**

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

STUDY NO. : 0612
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	14.8± 0.9	14.9± 1.1	15.2± 1.1	15.3± 1.0	15.4± 1.1	15.5± 1.1	15.8± 1.0
3300 ppm	14.9± 1.0	14.9± 0.8	15.2± 1.0	15.3± 1.0	15.5± 0.9	15.7± 1.0	15.6± 1.5
10000 ppm	14.2± 0.8**	14.3± 0.8**	14.5± 0.8**	14.7± 0.7**	14.7± 0.8**	14.9± 0.8**	14.9± 0.8**
30000 ppm	13.0± 0.8**	13.1± 0.8**	13.3± 0.8**	13.6± 0.9**	13.6± 0.9**	13.9± 0.9**	13.9± 0.8**

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

STUDY NO. : 0612
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 46-7(7)	50-7(7)	54-7(7)	58-7(7)	62-7(7)	66-7(7)	70-7(7)
Control	16.1± 1.0	15.8± 1.0	16.0± 1.0	15.9± 1.0	16.1± 0.8	16.2± 1.0	16.7± 1.1
3300 ppm	16.0± 1.1	15.7± 1.2	15.9± 0.9	15.8± 1.1	16.0± 0.9	16.0± 1.0	16.4± 2.2
10000 ppm	15.2± 0.8**	15.0± 0.8**	15.3± 0.7**	15.3± 0.8**	15.4± 0.8**	15.4± 0.6**	16.1± 0.8*
30000 ppm	14.1± 0.9**	13.9± 0.9**	14.2± 0.8**	14.1± 0.9**	14.2± 0.9**	14.6± 0.9**	15.0± 0.9**

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

STUDY NO. : 0612
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	16.9± 1.0	16.2± 1.0	16.3± 1.9	16.9± 1.3	16.9± 1.3	16.4± 1.3	16.4± 1.3
3300 ppm	17.0± 1.4	15.9± 2.3	16.7± 1.3	16.6± 1.0	16.7± 1.8	16.5± 1.3	16.4± 1.2
10000 ppm	15.9± 2.3**	15.9± 1.1	16.2± 0.9	15.9± 1.4**	16.5± 1.0	15.5± 1.6*	15.2± 2.1**
30000 ppm	15.5± 0.9**	14.9± 0.8**	14.9± 0.8**	14.7± 1.2**	14.9± 1.3**	14.6± 1.3**	14.7± 1.7**

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

(HAN260)

BAIS 4

STUDY NO. : 0612
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	16.0± 1.6	16.2± 1.7
3300 ppm	15.1± 2.9	15.4± 3.6
10000 ppm	15.9± 1.7	15.9± 2.0
30000 ppm	14.0± 2.2**	14.3± 1.3**

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

TABLE D 4

FOOD CONSUMPTION CHANGES: FEMALE

STUDY NO. : 0612
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	10.8± 0.6	10.8± 0.7	10.4± 0.7	10.1± 0.7	9.8± 0.7	9.8± 0.7	9.4± 0.7
3300 ppm	10.5± 0.6*	10.5± 0.6	10.2± 0.6	9.9± 0.7	9.6± 0.6	9.4± 0.7*	9.2± 0.7
10000 ppm	10.0± 0.5**	10.3± 0.6**	9.9± 0.6**	9.8± 0.6	9.3± 0.5**	9.0± 0.5**	8.8± 0.5**
30000 ppm	9.0± 0.5**	9.6± 0.6**	9.2± 0.6**	9.1± 0.6**	8.7± 0.7**	8.4± 0.6**	8.2± 0.6**

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

(HAN260)

BAIS 4

STUDY NO. : 0612
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	9.4± 0.7	9.4± 0.6	9.6± 0.7	9.7± 0.7	9.8± 0.7	9.6± 0.7	9.6± 0.7
3300 ppm	9.1± 0.6	9.1± 0.7*	9.4± 0.6	9.3± 0.7*	9.6± 0.6	9.2± 0.6	9.3± 0.7**
10000 ppm	8.8± 0.5**	8.7± 0.6**	9.0± 0.6**	9.0± 0.7**	9.2± 0.7**	8.9± 0.7**	9.0± 0.6**
30000 ppm	8.2± 0.6**	8.0± 0.6**	8.2± 0.6**	8.2± 0.7**	8.4± 0.6**	8.1± 0.6**	8.2± 0.6**

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

(HAN260)

BAIS 4

STUDY NO. : 0612
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	9.9± 0.7	10.1± 0.7	10.2± 0.9	10.2± 0.7	10.4± 0.8	10.5± 0.9
3300 ppm	9.7± 0.6	9.5± 0.6*	9.9± 0.6	9.9± 0.6	9.8± 0.6*	10.1± 0.7*	10.4± 0.6
10000 ppm	9.3± 0.7**	9.4± 0.6**	9.6± 0.6**	9.7± 0.7**	9.9± 0.7	10.0± 0.7**	10.2± 0.7
30000 ppm	8.4± 0.6**	8.6± 0.6**	8.8± 0.6**	8.9± 0.5**	9.0± 0.5**	9.1± 0.5**	9.2± 0.5**

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

(HAN260)

BAIS 4

STUDY NO. : 0612
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	10.8± 0.9	10.7± 0.9	11.0± 1.0	10.9± 1.0	11.0± 0.9	11.0± 1.1	11.3± 1.0
3300 ppm	10.5± 0.9	10.3± 0.6	10.4± 0.8*	10.4± 0.7*	10.7± 0.8	10.9± 0.7	11.3± 0.8
10000 ppm	10.3± 0.6**	10.1± 0.8**	10.2± 0.8**	10.3± 0.8**	10.4± 0.7**	10.5± 0.9**	10.7± 0.7**
30000 ppm	9.4± 0.6**	9.2± 0.6**	9.2± 0.6**	9.3± 0.7**	9.7± 0.9**	9.5± 0.9**	9.7± 0.8**

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

(HAN260)

BAIS 4

STUDY NO. : 0612
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : AI 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	11.5± 1.2	11.6± 1.1	11.5± 1.3	11.9± 1.2	12.0± 0.8	11.9± 1.6	12.1± 1.3
3300 ppm	11.7± 0.9	11.3± 1.1	11.4± 0.8	11.9± 0.8	12.0± 0.7	11.7± 0.9	12.0± 1.3
10000 ppm	11.2± 0.8	10.9± 1.3*	10.9± 0.8**	11.0± 1.7**	11.2± 1.2**	11.1± 1.7**	11.5± 1.3
30000 ppm	10.1± 0.8**	10.1± 0.6**	10.0± 0.9**	10.1± 0.9**	10.5± 0.8**	10.4± 0.7**	10.3± 0.9**

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

(HAN260)

BAIS 4

STUDY NO. : 0612
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	12.2± 1.2	12.3± 1.1
3300 ppm	11.9± 1.1	11.7± 1.7
10000 ppm	11.2± 1.7**	11.3± 1.3**
30000 ppm	10.3± 0.8**	10.2± 1.0**

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

(HAN260)

TABLE E 1

WATER CONSUMPTION CHANGES AND SURVIVAL ANIMAL NUMBERS: MALE

STUDY NO. : 0612
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>	3300 ppm Av. WC.	3300 ppm % of cont. <50>	3300 ppm No. of Surviv.	10000 ppm Av. WC.	10000 ppm % of cont. <50>	10000 ppm No. of Surviv.	30000 ppm Av. WC.	30000 ppm % of cont. <50>	30000 ppm No. of Surviv.
1-7	16.9 (50)	50/50	17.6 (50)	104	50/50	15.6 (50)	92	50/50	13.9 (50)	82	50/50
2-7	18.4 (50)	50/50	19.2 (50)	104	50/50	16.4 (50)	89	50/50	14.5 (50)	79	50/50
3-7	19.1 (50)	50/50	19.3 (50)	101	50/50	16.6 (50)	87	50/50	14.6 (50)	76	50/50
4-7	19.5 (50)	50/50	19.9 (49)	102	50/50	17.3 (50)	89	50/50	14.9 (50)	76	50/50
5-7	19.0 (48)	50/50	19.6 (50)	103	50/50	17.5 (50)	92	50/50	15.4 (49)	81	50/50
6-7	17.7 (50)	50/50	18.2 (50)	103	50/50	16.6 (50)	94	50/50	14.4 (50)	81	50/50
7-7	17.9 (50)	50/50	18.2 (48)	102	50/50	16.2 (50)	91	50/50	14.3 (50)	80	50/50
8-7	18.1 (49)	50/50	18.6 (50)	103	50/50	16.3 (50)	90	50/50	14.3 (50)	79	50/50
9-7	17.5 (50)	50/50	18.8 (50)	107	50/50	15.9 (50)	91	50/50	13.9 (50)	79	50/50
10-7	17.6 (50)	50/50	18.0 (49)	102	50/50	15.5 (50)	88	50/50	13.7 (50)	78	50/50
11-7	17.8 (50)	50/50	18.0 (50)	101	50/50	15.6 (50)	88	50/50	13.6 (50)	76	50/50
12-7	17.1 (50)	50/50	17.4 (50)	102	50/50	15.3 (50)	89	50/50	13.7 (50)	80	50/50
13-7	17.4 (50)	50/50	17.2 (49)	99	50/50	15.5 (50)	89	50/50	13.7 (50)	79	50/50
14-7	17.1 (49)	50/50	17.3 (50)	101	50/50	15.1 (50)	88	50/50	13.2 (50)	77	50/50
18-7	16.5 (50)	50/50	16.1 (50)	98	50/50	14.8 (50)	90	50/50	12.8 (50)	78	50/50
22-7	16.3 (49)	50/50	16.1 (49)	99	49/50	14.7 (50)	90	50/50	13.1 (50)	80	50/50
26-7	16.4 (50)	50/50	16.3 (49)	99	49/50	15.2 (50)	93	50/50	13.4 (50)	82	50/50
30-7	16.4 (50)	50/50	16.4 (49)	100	49/50	14.9 (50)	91	50/50	13.9 (50)	85	50/50
34-7	16.0 (50)	50/50	16.2 (49)	101	49/50	14.8 (50)	93	50/50	13.5 (50)	84	50/50
38-7	15.9 (50)	50/50	15.9 (49)	100	49/50	14.7 (50)	92	50/50	13.7 (50)	86	50/50
42-7	16.1 (49)	49/50	15.6 (49)	97	49/50	14.8 (49)	92	49/50	13.6 (50)	84	50/50
46-7	16.4 (49)	49/50	16.3 (48)	99	48/50	15.0 (49)	91	49/50	13.9 (50)	85	50/50
50-7	16.6 (49)	49/50	16.3 (48)	98	48/50	15.6 (49)	94	49/50	14.5 (50)	87	50/50
54-7	16.5 (49)	49/50	16.5 (47)	100	47/50	15.9 (49)	96	49/50	14.6 (50)	88	50/50
58-7	17.2 (49)	49/50	17.1 (47)	99	47/50	16.4 (49)	95	49/50	15.3 (50)	89	50/50
62-7	17.1 (49)	49/50	17.1 (46)	100	46/50	16.0 (49)	94	49/50	14.6 (50)	85	50/50
66-7	17.0 (49)	49/50	16.6 (46)	98	46/50	15.7 (49)	92	49/50	14.4 (50)	85	50/50
70-7	17.9 (49)	49/50	17.4 (44)	97	45/50	16.7 (49)	93	49/50	15.4 (50)	86	50/50
74-7	18.0 (49)	49/50	18.5 (42)	103	43/50	16.9 (48)	94	49/50	15.7 (50)	87	50/50
78-7	18.1 (48)	49/50	17.5 (42)	97	42/50	17.4 (48)	96	48/50	15.9 (50)	88	50/50
82-7	18.4 (48)	49/50	18.2 (39)	99	40/50	17.5 (48)	95	48/50	15.6 (50)	85	50/50
86-7	19.2 (46)	48/50	18.9 (39)	98	40/50	17.5 (47)	91	48/50	15.3 (49)	80	49/50
90-7	19.7 (44)	47/50	19.1 (40)	97	40/50	18.5 (46)	94	47/50	16.1 (48)	82	48/50
94-7	19.9 (42)	46/50	19.6 (37)	98	38/50	18.1 (44)	91	45/50	15.8 (44)	79	46/50
98-7	19.7 (38)	43/50	19.4 (35)	98	36/50	18.1 (42)	92	44/50	16.5 (42)	84	43/50
102-7	20.9 (36)	40/50	19.0 (33)	91	35/50	19.4 (39)	93	40/50	16.3 (40)	78	43/50
104-7	21.0 (34)	40/50	18.7 (31)	89	35/50	18.7 (36)	89	39/50	16.2 (39)	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. : 0612
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>	3300 ppm Av. WC.	3300 ppm % of cont. <50>	3300 ppm No. of Surviv.	10000 ppm Av. WC.	10000 ppm % of cont. <50>	10000 ppm No. of Surviv.	30000 ppm Av. WC.	30000 ppm % of cont. <50>	30000 ppm No. of Surviv.
1-7	16.4 (50)	50/50	15.7 (50)	96	50/50	13.2 (50)	80	50/50	11.2 (50)	68	50/50
2-7	17.4 (47)	50/50	16.8 (48)	97	50/50	13.0 (50)	75	50/50	11.4 (50)	66	50/50
3-7	20.2 (48)	50/50	17.8 (49)	88	50/50	12.9 (50)	64	50/50	10.6 (50)	52	50/50
4-7	18.4 (41)	50/50	17.8 (45)	97	50/50	13.3 (50)	72	50/50	10.7 (50)	58	50/50
5-7	16.6 (33)	50/50	18.0 (47)	108	50/50	13.0 (50)	78	50/50	10.4 (50)	63	50/50
6-7	17.7 (36)	50/50	17.7 (44)	100	50/50	12.4 (50)	70	50/50	9.9 (50)	56	50/50
7-7	17.7 (41)	50/50	16.7 (43)	94	50/50	12.1 (50)	68	50/50	9.5 (50)	54	50/50
8-7	17.4 (35)	50/50	18.0 (44)	103	50/50	11.9 (50)	68	50/50	9.3 (50)	53	50/50
9-7	18.2 (41)	50/50	18.7 (45)	103	50/50	11.7 (50)	64	50/50	9.3 (50)	51	50/50
10-7	18.5 (41)	50/50	17.1 (44)	92	50/50	11.4 (50)	62	50/50	9.2 (50)	50	50/50
11-7	18.4 (41)	50/50	17.4 (43)	95	50/50	11.7 (50)	64	50/50	9.4 (50)	51	50/50
12-7	17.0 (40)	50/50	16.7 (44)	98	50/50	11.4 (50)	67	50/50	9.1 (50)	54	50/50
13-7	18.5 (40)	50/50	17.5 (44)	95	50/50	11.7 (50)	63	50/50	9.6 (50)	52	50/50
14-7	17.9 (38)	50/50	17.3 (44)	97	50/50	11.6 (50)	65	50/50	8.9 (50)	50	50/50
18-7	19.0 (37)	50/50	17.2 (44)	91	50/50	12.1 (50)	64	50/50	9.1 (50)	48	50/50
22-7	18.0 (37)	50/50	17.9 (46)	99	50/50	12.3 (50)	68	50/50	9.3 (50)	52	50/50
26-7	17.6 (38)	50/50	18.4 (45)	105	50/50	12.0 (49)	68	50/50	9.8 (49)	56	50/50
30-7	18.1 (40)	50/50	17.8 (44)	98	50/50	12.3 (50)	68	50/50	9.3 (50)	51	50/50
34-7	16.7 (36)	49/50	16.9 (47)	101	50/50	12.5 (50)	75	50/50	9.7 (49)	58	50/50
38-7	17.0 (41)	49/50	16.9 (46)	99	50/50	11.8 (50)	69	50/50	9.4 (50)	55	50/50
42-7	17.2 (38)	49/50	16.3 (45)	95	50/50	12.3 (50)	72	50/50	10.5 (50)	61	50/50
46-7	16.7 (45)	49/50	16.6 (48)	99	50/50	12.2 (50)	73	50/50	10.1 (50)	60	50/50
50-7	17.1 (43)	48/50	17.3 (46)	101	50/50	12.4 (50)	73	50/50	10.6 (50)	62	50/50
54-7	16.2 (41)	47/50	16.4 (47)	101	50/50	12.3 (50)	76	50/50	10.7 (50)	66	50/50
58-7	16.7 (44)	47/50	15.9 (49)	95	50/50	12.8 (50)	77	50/50	11.3 (50)	68	50/50
62-7	16.8 (45)	47/50	15.6 (48)	93	49/50	12.5 (50)	74	50/50	11.4 (50)	68	50/50
66-7	15.0 (46)	47/50	16.2 (48)	108	49/50	11.8 (50)	79	50/50	10.9 (50)	73	50/50
70-7	15.6 (46)	46/50	16.8 (47)	108	49/50	12.9 (50)	83	50/50	11.7 (48)	75	48/50
74-7	14.9 (44)	46/50	16.3 (48)	109	48/50	12.6 (50)	85	50/50	11.8 (47)	79	47/50
78-7	15.0 (43)	45/50	16.0 (47)	107	47/50	13.1 (50)	87	50/50	12.0 (46)	80	46/50
82-7	15.1 (43)	43/50	15.1 (43)	100	45/50	12.5 (49)	83	49/50	12.2 (46)	81	46/50
86-7	15.2 (39)	40/50	16.4 (45)	108	45/50	12.9 (49)	85	49/50	12.2 (45)	80	45/50
90-7	15.4 (38)	38/50	15.6 (43)	101	44/50	13.2 (48)	86	48/50	12.5 (44)	81	44/50
94-7	16.1 (38)	38/50	15.7 (43)	98	43/50	13.8 (47)	86	47/50	12.8 (43)	80	44/50
98-7	16.2 (37)	38/50	16.2 (43)	100	43/50	14.3 (45)	88	45/50	12.9 (43)	80	43/50
102-7	17.4 (34)	35/50	16.6 (38)	95	40/50	14.9 (44)	86	44/50	13.7 (39)	79	40/50
104-7	16.6 (35)	35/50	16.5 (39)	99	39/50	14.6 (44)	88	44/50	12.9 (39)	78	39/50

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

TABLE E 3

WATER CONSUMPTION CHANGES: MALE

STUDY NO. : 0612
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	16.9± 0.9	18.4± 1.4	19.1± 2.2	19.5± 1.6	19.0± 1.6	17.7± 1.6	17.9± 1.8
3300 ppm	17.6± 1.4*	19.2± 2.0	19.3± 2.5	19.9± 2.4	19.6± 2.6	18.2± 2.0	18.2± 2.2
10000 ppm	15.6± 1.4**	16.4± 1.4**	16.6± 1.9**	17.3± 1.7**	17.5± 1.8**	16.6± 1.9**	16.2± 1.7**
30000 ppm	13.9± 0.9**	14.5± 0.8**	14.6± 1.3**	14.9± 0.9**	15.4± 1.0**	14.4± 1.2**	14.3± 1.1**

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

STUDY NO. : 0612
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(3)	9-7(3)	10-7(3)	11-7(3)	12-7(3)	13-7(3)	14-7(3)
Control	18.1± 1.6	17.5± 1.6	17.6± 1.8	17.8± 1.8	17.1± 1.8	17.4± 1.6	17.1± 2.2
3300 ppm	18.6± 2.3	18.8± 3.1	18.0± 2.0	18.0± 2.1	17.4± 2.2	17.2± 1.3	17.3± 2.4
10000 ppm	16.3± 1.6**	15.9± 1.6**	15.5± 1.3**	15.6± 1.4**	15.3± 1.3**	15.5± 2.0**	15.1± 1.2**
30000 ppm	14.3± 1.1**	13.9± 1.2**	13.7± 1.7**	13.6± 1.2**	13.7± 1.0**	13.7± 1.1**	13.2± 1.0**

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

STUDY NO. : 0612
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	16.5± 1.5	16.3± 1.3	16.4± 1.7	16.4± 1.1	16.0± 1.5	15.9± 1.4	16.1± 1.1
3300 ppm	16.1± 1.7	16.1± 1.5	16.3± 1.7	16.4± 1.7	16.2± 2.0	15.9± 1.1	15.6± 2.7
10000 ppm	14.8± 1.7**	14.7± 1.2**	15.2± 1.5**	14.9± 1.6**	14.8± 1.2**	14.7± 1.4**	14.8± 1.2**
30000 ppm	12.8± 1.0**	13.1± 0.9**	13.4± 1.2**	13.9± 2.4**	13.5± 1.2**	13.7± 1.2**	13.6± 1.5**

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

STUDY NO. : 0612
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	16.4± 1.1	16.6± 1.3	16.5± 1.4	17.2± 1.4	17.1± 1.4	17.0± 1.7	17.9± 2.2
3300 ppm	16.3± 1.6	16.3± 1.7	16.5± 1.4	17.1± 1.6	17.1± 1.5	16.6± 1.5	17.4± 3.0
10000 ppm	15.0± 1.3**	15.6± 1.3**	15.9± 1.5	16.4± 1.3*	16.0± 1.3**	15.7± 1.4**	16.7± 1.6**
30000 ppm	13.9± 1.3**	14.5± 1.7**	14.6± 1.2**	15.3± 1.5**	14.6± 1.3**	14.4± 1.2**	15.4± 1.3**

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

STUDY NO. : 0612
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 74-7(3)	78-7(3)	82-7(3)	86-7(3)	90-7(3)	94-7(3)	98-7(3)
Control	18.0± 2.3	18.1± 2.5	18.4± 3.4	19.2± 3.2	19.7± 3.6	19.9± 3.5	19.7± 3.1
3300 ppm	18.5± 2.6	17.5± 3.5	18.2± 2.9	18.9± 2.6	19.1± 3.8	19.6± 3.0	19.4± 3.4
10000 ppm	16.9± 1.8*	17.4± 1.6	17.5± 2.4	17.5± 3.4**	18.5± 3.7	18.1± 3.1*	18.1± 3.5
30000 ppm	15.7± 2.1**	15.9± 1.6**	15.6± 1.7**	15.3± 1.9**	16.1± 3.2**	15.8± 2.6**	16.5± 3.1**

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

STUDY NO. : 0612
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	20.9± 4.2	21.0± 4.0
3300 ppm	19.0± 4.1	18.7± 4.9
10000 ppm	19.4± 4.2	18.7± 4.2
30000 ppm	16.3± 3.7**	16.2± 3.5**

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

TABLE E 4

WATER CONSUMPTION CHANGES: FEMALE

STUDY NO. : 0612
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	16.4± 3.4	17.4± 4.8	20.2± 8.1	18.4± 4.3	16.6± 3.1	17.7± 4.4	17.7± 5.4
3300 ppm	15.7± 1.5	16.8± 3.1	17.8± 4.3	17.8± 3.7	18.0± 4.1	17.7± 3.9	16.7± 3.5
10000 ppm	13.2± 3.0**	13.0± 2.1**	12.9± 1.8**	13.3± 2.0**	13.0± 2.0**	12.4± 1.5**	12.1± 1.8**
30000 ppm	11.2± 0.8**	11.4± 0.8**	10.6± 0.9**	10.7± 0.9**	10.4± 0.9**	9.9± 1.2**	9.5± 1.1**

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

STUDY NO. : 0612
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(3)	9-7(3)	10-7(3)	11-7(3)	12-7(3)	13-7(3)	14-7(3)
Control	17.4± 4.8	18.2± 5.2	18.5± 5.7	18.4± 5.0	17.0± 4.5	18.5± 4.9	17.9± 5.0
3300 ppm	18.0± 4.5	18.7± 5.3	17.1± 4.1	17.4± 4.0	16.7± 4.0	17.5± 4.6	17.3± 4.2
10000 ppm	11.9± 1.4**	11.7± 1.7**	11.4± 1.6**	11.7± 1.8**	11.4± 1.8**	11.7± 1.5**	11.6± 2.2**
30000 ppm	9.3± 1.0**	9.3± 1.0**	9.2± 1.8**	9.4± 1.3**	9.1± 0.8**	9.6± 1.6**	8.9± 0.7**

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

STUDY NO. : 0612
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 18-7(3)	22-7(3)	26-7(3)	30-7(3)	34-7(3)	38-7(3)	42-7(3)
Control	19.0± 5.1	18.0± 4.7	17.6± 4.2	18.1± 4.3	16.7± 3.9	17.0± 4.1	17.2± 5.3
3300 ppm	17.2± 4.6	17.9± 5.0	18.4± 5.0	17.8± 4.7	16.9± 4.4	16.9± 5.1	16.3± 4.1
10000 ppm	12.1± 1.8**	12.3± 3.2**	12.0± 1.9**	12.3± 2.4**	12.5± 2.8**	11.8± 1.7**	12.3± 3.1**
30000 ppm	9.1± 1.6**	9.3± 0.9**	9.8± 2.5**	9.3± 1.2**	9.7± 2.7**	9.4± 1.0**	10.5± 3.2**

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

STUDY NO. : 0612
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	16.7± 4.8	17.1± 4.8	16.2± 4.0	16.7± 4.2	16.8± 4.9	15.0± 3.5	15.6± 3.7
3300 ppm	16.6± 4.6	17.3± 5.0	16.4± 4.6	15.9± 4.0	15.6± 3.6	16.2± 4.3	16.8± 4.3
10000 ppm	12.2± 1.8**	12.4± 1.8**	12.3± 2.1**	12.8± 1.7**	12.5± 2.2**	11.8± 1.4**	12.9± 2.2**
30000 ppm	10.1± 1.0**	10.6± 1.8**	10.7± 1.3**	11.3± 1.7**	11.4± 2.0**	10.9± 1.3**	11.7± 1.5**

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

STUDY NO. : 0612
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	14.9± 3.3	15.0± 3.0	15.1± 3.5	15.2± 3.3	15.4± 2.7	16.1± 3.0	16.2± 3.4
3300 ppm	16.3± 3.5*	16.0± 3.6	15.1± 2.7	16.4± 3.8	15.6± 2.9	15.7± 3.0	16.2± 3.4
10000 ppm	12.6± 2.3**	13.1± 2.3**	12.5± 2.7**	12.9± 2.2**	13.2± 2.7**	13.8± 3.1**	14.3± 3.6**
30000 ppm	11.8± 2.2**	12.0± 1.8**	12.2± 3.2**	12.2± 1.7**	12.5± 1.6**	12.8± 1.6**	12.9± 2.0**

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

STUDY NO. : 0612
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 102-7(3)	104-7(3)
Control	17.4± 4.7	16.6± 4.5
3300 ppm	16.6± 3.4	16.5± 3.1
10000 ppm	14.9± 4.0*	14.6± 3.4*
30000 ppm	13.7± 2.8**	12.9± 2.6**

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

TABLE F 1

CHEMICAL INTAKE CHANGES: MALE

STUDY NO. : 0612
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
3300 ppm	372±	26	338±	27	302±	30	285±	29	265±	35	235±	24	227±	23
10000 ppm	1013±	63	894±	58	805±	77	772±	70	731±	70	661±	69	617±	53
30000 ppm	2779±	166	2435±	119	2158±	166	2031±	96	1984±	116	1764±	136	1683±	109

STUDY NO. : 0612
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : mg/kg/day
REPORT TYPE : A1 104
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8		9		10		11		12		13		14	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
3300 ppm	222±	24	219±	33	206±	22	202±	20	190±	24	184±	15	181±	24
10000 ppm	597±	46	569±	49	543±	39	541±	38	516±	37	512±	67	491±	33
30000 ppm	1618±	115	1530±	121	1489±	178	1451±	110	1422±	83	1394±	82	1329±	92

STUDY NO. : 0612
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : mg/kg/day
REPORT TYPE : A1 104
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 18		22		26		30		34		38		42	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
3300 ppm	160±	16	152±	14	150±	15	147±	14	142±	21	136±	8	131±	21
10000 ppm	452±	60	433±	40	436±	52	417±	55	404±	31	397±	46	392±	40
30000 ppm	1220±	79	1202±	69	1191±	89	1207±	203	1147±	72	1140±	86	1114±	107

(HAN300)

BAIS 4

STUDY NO. : 0612
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) 46		50		54		58		62		66		70	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
3300 ppm	135±	9	134±	10	132±	8	135±	10	133±	10	130±	9	136±	21
10000 ppm	394±	43	400±	34	402±	46	408±	33	393±	29	385±	39	410±	42
30000 ppm	1123±	79	1156±	128	1147±	93	1190±	101	1119±	82	1108±	91	1182±	89

STUDY NO. : 0612
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) 74		78		82		86		90		94		98	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
3300 ppm	142±	17	134±	24	140±	19	146±	18	148±	27	154±	24	153±	24
10000 ppm	413±	48	420±	45	424±	65	420±	83	446±	96	445±	74	450±	87
30000 ppm	1199±	169	1208±	121	1199±	150	1182±	192	1262±	279	1267±	308	1303±	283

STUDY NO. : 0612
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) 102		104	
Control	0±	0	0±	0
3300 ppm	154±	31	154±	38
10000 ppm	492±	125	486±	168
30000 ppm	1314±	366	1333±	405

TABLE F 2

CHEMICAL INTAKE CHANGES: FEMALE

STUDY NO. : 0612
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
3300 ppm	451±	37	439±	70	434±	99	415±	80	404±	83	383±	80	355±	68
10000 ppm	1169±	256	1043±	151	962±	117	941±	117	890±	126	824±	89	791±	101
30000 ppm	2989±	173	2753±	147	2400±	173	2315±	154	2170±	151	2001±	203	1903±	166

STUDY NO. : 0612
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) 8		9		10		11		12		13		14	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
3300 ppm	376±	89	384±	109	346±	79	347±	76	328±	74	338±	86	333±	76
10000 ppm	762±	78	736±	89	709±	86	719±	92	687±	88	701±	75	687±	108
30000 ppm	1832±	156	1798±	151	1756±	291	1778±	217	1702±	127	1764±	280	1638±	115

STUDY NO. : 0612
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) 18		22		26		30		34		38		42	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
3300 ppm	320±	84	323±	86	322±	87	305±	76	282±	69	279±	86	261±	61
10000 ppm	688±	91	676±	154	644±	84	645±	108	636±	123	596±	75	605±	134
30000 ppm	1625±	299	1601±	128	1646±	423	1532±	174	1561±	376	1500±	141	1631±	492

STUDY NO. : 0612
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
3300 ppm	262±	70	268±	78	246±	67	234±	58	225±	55	230±	62	233±	61
10000 ppm	591±	68	592±	64	569±	84	578±	78	552±	80	514±	42	558±	95
30000 ppm	1557±	127	1618±	254	1602±	179	1672±	253	1644±	293	1542±	201	1627±	203

STUDY NO. : 0612
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) 74		78		82		86		90		94		98	
Control	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0	0±	0
3300 ppm	222±	53	213±	53	199±	36	211±	55	200±	48	198±	42	204±	46
10000 ppm	529±	86	544±	82	510±	94	522±	80	529±	108	551±	121	573±	147
30000 ppm	1620±	293	1608±	273	1622±	466	1593±	249	1612±	211	1646±	245	1661±	277

STUDY NO. : 0612
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
3300 ppm	208±	52	210±	53
10000 ppm	592±	173	585±	152
30000 ppm	1768±	431	1666±	382

TABLE G 1

HEMATOLOGY: MALE

STUDY NO. : 0612
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV fℓ	MCH pg	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	40	8.22± 1.71	14.0± 2.8	42.0± 7.3	52.1± 5.7	17.1± 1.2	33.0± 2.2	978± 285
3300 ppm	34	8.37± 1.11	14.2± 2.0	43.1± 5.2	51.5± 1.7	17.0± 0.8	32.9± 1.2	1018± 279
10000 ppm	39	8.32± 1.33	14.1± 2.4	42.4± 6.2	51.1± 2.4	17.0± 1.2	33.2± 1.6	1015± 329
30000 ppm	40	8.52± 1.40	14.5± 2.4	43.4± 6.6	51.2± 2.3	17.0± 0.9	33.3± 1.0	916± 284

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

STUDY NO. : 0612
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	5.2±	8.0
3300 ppm	34	4.1±	2.5
10000 ppm	39	4.2±	3.0
30000 ppm	40	4.1±	3.7

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

STUDY NO. : 0612
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$		Differential WBC (%) N-BAND		N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHER	
Control	40	10.65±	28.46	1±	1	46±	12	2±	1	0±	0	5±	2	42±	11	4±	16
3300 ppm	34	5.40±	1.17	0±	1	49±	9	2±	1	0±	0	5±	1	43±	9	0±	1
10000 ppm	39	5.87±	2.94	1±	1	51±	13	1±	1	0±	0	5±	1	41±	13	1±	5
30000 ppm	40	5.41±	1.80	1±	1	51±	9	2±	1	0±	0	5±	2	40±	9	1±	2

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

(HCL070)

TABLE G 2

HEMATOLOGY: FEMALE

STUDY NO. : 0612
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV fℓ	MCH pg	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	34	8.40± 0.46	15.2± 0.8	44.4± 2.0	52.9± 1.7	18.1± 0.7	34.3± 0.7	730± 113
3300 ppm	38	8.47± 0.38	15.4± 0.6	44.7± 1.7	52.9± 1.2	18.2± 0.5	34.5± 0.5	698± 88
10000 ppm	44	8.10± 1.11	14.8± 1.7	43.2± 4.0	53.9± 4.4	18.4± 1.0	34.3± 1.1	728± 155
30000 ppm	39	8.22± 0.82	14.8± 1.7	43.2± 4.5	52.5± 1.7	17.9± 0.9	34.2± 1.2	704± 141

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

STUDY NO. : 0612
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	34	2.8± 1.2
3300 ppm	38	2.6± 0.8
10000 ppm	44	4.5± 6.3
30000 ppm	39	2.9± 1.5

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

STUDY NO. : 0612
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 $10^3/\mu l$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHER
Control	34	3.51± 4.78	1± 1	43± 10	2± 1	0± 0	5± 2	49± 10	1± 2
3300 ppm	38	2.70± 0.89	1± 1	40± 7	2± 1	0± 0	5± 2	52± 6	1± 1
10000 ppm	44	3.25± 1.75	1± 1	41± 11	2± 1	0± 0	5± 2	51± 11	1± 2
30000 ppm	39	2.99± 1.65	1± 1	41± 11	2± 1	0± 0	5± 2	50± 12	1± 2

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

(HCL070)

BAIS 4

TABLE H 1

BIOCHEMISTRY: MALE

STUDY NO. : 0612
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	TOTAL PROTEIN g／dℓ	ALBUMIN g／dℓ	A/G RATIO	T-BILIRUBIN mg／dℓ	GLUCOSE mg／dℓ	T-CHOLESTEROL mg／dℓ	TRIGLYCERIDE mg／dℓ
Control	40	6.8± 0.5	2.8± 0.3	0.7± 0.1	0.28± 0.76	149± 27	223± 80	149± 100
3300 ppm	34	6.8± 0.3	2.9± 0.3	0.7± 0.1	0.15± 0.03	155± 25	200± 53	125± 80
10000 ppm	39	6.7± 0.3	2.8± 0.3	0.7± 0.1	0.16± 0.07	146± 26	209± 76	142± 133
30000 ppm	40	6.6± 0.4**	2.8± 0.2	0.8± 0.1	0.17± 0.07	153± 21	193± 66	109± 94

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

(HCL074)

STUDY NO. : 0612
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	318± 129	158± 302	57± 84	331± 843	244± 393	8± 6	130± 85
3300 ppm	34	279± 67	81± 26	36± 10	171± 45	197± 61	7± 3	116± 43
10000 ppm	39	295± 105	86± 44	41± 26	178± 71	192± 75	7± 4	138± 107
30000 ppm	40	279± 90	80± 26	38± 21	158± 34	167± 46	6± 3	110± 36

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

STUDY NO. : 0612
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	24.0±	10.7	0.7±	0.2	143±	1	3.6±	0.3	106±	2	10.8±	0.5	4.4±	0.9
3300 ppm	34	24.2±	24.0	0.8±	1.1	142±	2	3.6±	0.3	105±	2	10.7±	0.7	4.6±	2.4
10000 ppm	39	27.2±	36.7	0.7±	0.7	142±	2	3.7±	0.4	105±	2	10.7±	0.7	4.8±	3.7
30000 ppm	40	22.8±	15.8	0.6±	0.2	142±	2	3.8±	0.3	105±	1	10.5±	0.6	4.2±	1.3

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

TABLE H 2

BIOCHEMISTRY: FEMALE

STUDY NO. : 0612
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	34	7.0±	0.3	3.5±	0.3	1.0±	0.1	0.14±	0.03	142±	14	141±	29	64±	64
3300 ppm	38	7.0±	0.4	3.6±	0.3	1.1±	0.1	0.14±	0.03	147±	11	141±	28	64±	55
10000 ppm	44	6.9±	0.4	3.5±	0.4	1.0±	0.2	0.17±	0.12	141±	14	136±	29	63±	34
30000 ppm	39	6.7±	0.4*	3.5±	0.2	1.1±	0.1	0.14±	0.03	149±	21	131±	20	50±	19

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

(HCL074)

STUDY NO. : 0612
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	34	244± 49	116± 46	46± 17	206± 72	121± 69	3± 2	99± 22
3300 ppm	38	247± 44	128± 93	53± 44	212± 104	116± 36	2± 1	103± 37
10000 ppm	44	240± 48	129± 81	46± 19	240± 262	115± 46	3± 1	103± 29
30000 ppm	39	233± 31	117± 93	44± 26	205± 145	120± 36	3± 1	100± 51

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

(HCL074)

STUDY NO. : 0612
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	34	18.0± 2.4	0.5± 0.1	142± 1	3.4± 0.3	105± 2	10.6± 0.3	3.7± 0.7
3300 ppm	38	17.9± 2.7	0.5± 0.1	142± 1	3.4± 0.3	104± 1	10.6± 0.3	3.7± 0.7
10000 ppm	44	16.6± 2.9	0.5± 0.1	142± 1	3.5± 0.4	104± 2	10.7± 0.4	3.9± 0.9
30000 ppm	39	23.0± 25.9	0.5± 0.1	141± 2	3.7± 0.5**	104± 1	10.6± 0.4	4.3± 1.2*

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

TABLE I 1

URINALYSIS: MALE

STUDY NO. : 0612
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Bilirubin −	+	2+	3+	CHI
Control	40	0	1	8	9	19	3	0		0	0	0	0	29	11		40	0	0	0	0	0		38	2	0	0	0	0		40	0	0	0	
3300 ppm	35	0	0	4	10	19	2	0		0	0	0	0	25	10		35	0	0	0	0	0		32	3	0	0	0	0		35	0	0	0	
10000 ppm	40	0	3	4	11	17	5	0		0	0	0	0	29	11		40	0	0	0	0	0		39	1	0	0	0	0		40	0	0	0	
30000 ppm	42	1	2	5	10	22	2	0		0	0	0	0	30	12		42	0	0	0	0	0		37	5	0	0	0	0		42	0	0	0	

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

(HCL101)

STUDY NO. : 0612
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : I
SEX : MALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	Occult blood −	±	+	2+	3+	CHI	Urobilinogen ±	+	2+	3+	4+	CHI
Control	40	38	1	0	0	1		40	0	0	0	0	
3300 ppm	35	34	0	1	0	0		35	0	0	0	0	
10000 ppm	40	40	0	0	0	0		40	0	0	0	0	
30000 ppm	42	40	0	1	1	0		42	0	0	0	0	

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

(HCL101)

TABLE I 2

URINALYSIS: FEMALE

STUDY NO. : 0612
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	35	0	1	5	4	10	9	6		0	3	11	14	7	0		35	0	0	0	0	0		31	3	1	0	0	0		35	0	0	0	
3300 ppm	39	0	0	0	11	13	11	4		0	2	12	18	6	1		39	0	0	0	0	0		38	0	1	0	0	0		39	0	0	0	
10000 ppm	43	0	3	2	12	16	3	7		0	3	14	8	18	0		43	0	0	0	0	0		37	3	3	0	0	0		43	0	0	0	
30000 ppm	40	0	4	4	9	6	6	11		0	1	7	18	13	1		40	0	0	0	0	0		33	3	4	0	0	0		39	1	0	0	

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

(HCL101)

STUDY NO. : 0612
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	Occult blood −	±	+	2+	3+	CHI	Urobilinogen ±	+	2+	3+	4+	CHI
Control	35	34	0	0	0	1		35	0	0	0	0	
3300 ppm	39	39	0	0	0	0		39	0	0	0	0	
10000 ppm	43	42	0	0	1	0		43	0	0	0	0	
30000 ppm	40	26	1	3	1	9	*	40	0	0	0	0	

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

(HCL101)

TABLE K 1

ORGAN WEIGHT, ABSOLUTE: MALE

STUDY NO. : 0612
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	370± 42	0.075± 0.013	2.556± 1.156	1.197± 0.110	1.405± 0.256	2.741± 0.390
3300 ppm	34	376± 33	0.074± 0.013	2.668± 0.993	1.215± 0.082	1.350± 0.096	2.717± 0.399
10000 ppm	39	367± 41	0.077± 0.016	2.636± 1.204	1.208± 0.101	1.368± 0.164	2.883± 0.485
30000 ppm	40	347± 30*	0.146± 0.472	3.129± 1.331	1.128± 0.086**	1.293± 0.065**	2.808± 0.414

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

STUDY NO. : 0612
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	1.186±	1.205	11.475±	2.481	2.088±	0.048
3300 ppm	34	0.934±	0.222	10.801±	1.055	2.106±	0.077
10000 ppm	39	1.135±	0.965	10.879±	1.681	2.090±	0.049
30000 ppm	40	1.016±	0.762	10.290±	1.223**	2.071±	0.039

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

(HCL040)

BAIS 4

TABLE K 2

ORGAN WEIGHT, ABSOLUTE: FEMALE

STUDY NO. : 0612
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	34	247± 24	0.074± 0.035	0.128± 0.022	0.846± 0.064	0.934± 0.069	1.691± 0.117
3300 ppm	38	249± 28	0.090± 0.116	0.124± 0.021	0.830± 0.050	0.939± 0.069	1.691± 0.113
10000 ppm	44	236± 27	0.077± 0.069	0.136± 0.042	0.850± 0.062	0.928± 0.068	1.845± 0.180**
30000 ppm	39	220± 19**	0.157± 0.491**	0.153± 0.118	0.815± 0.065	0.907± 0.066	1.842± 0.126**

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

(HCL040)

STUDY NO. : 0612
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	34	0.557±	0.224	6.259±	0.683	1.900±	0.042
3300 ppm	38	0.537±	0.172	6.184±	0.566	1.923±	0.050
10000 ppm	44	0.849±	1.465	6.332±	0.997	1.901±	0.042
30000 ppm	39	0.510±	0.137	5.833±	0.590**	1.879±	0.046

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

(HCL040)

TABLE L 1

ORGAN WEIGHT, RELATIVE: MALE

STUDY NO. : 0612
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	370± 42	0.021± 0.006	0.683± 0.287	0.327± 0.045	0.387± 0.112	0.752± 0.158
3300 ppm	34	376± 33	0.020± 0.005	0.710± 0.265	0.326± 0.044	0.362± 0.050	0.734± 0.186
10000 ppm	39	367± 41	0.022± 0.007	0.713± 0.315	0.333± 0.042	0.377± 0.057	0.810± 0.288
30000 ppm	40	347± 30*	0.042± 0.132	0.900± 0.368**	0.326± 0.024	0.374± 0.030	0.822± 0.214**

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

(HCL042)

BAIS 4

STUDY NO. : 0612
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	0.337± 0.433	3.133± 0.812	0.572± 0.073
3300 ppm	34	0.249± 0.059	2.889± 0.337	0.565± 0.059
10000 ppm	39	0.304± 0.241	2.977± 0.411	0.577± 0.075
30000 ppm	40	0.297± 0.241	2.988± 0.492	0.601± 0.058

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

(HCL042)

BAIS 4

TABLE L 2

ORGAN WEIGHT, RELATIVE: FEMALE

STUDY NO. : 0612
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	34	247± 24	0.030± 0.012	0.052± 0.010	0.345± 0.035	0.381± 0.044	0.691± 0.081
3300 ppm	38	249± 28	0.041± 0.081	0.051± 0.009	0.339± 0.061	0.383± 0.054	0.688± 0.081
10000 ppm	44	236± 27	0.033± 0.029	0.058± 0.018	0.364± 0.039*	0.398± 0.047	0.795± 0.155**
30000 ppm	39	220± 19**	0.073± 0.228	0.069± 0.052**	0.372± 0.033**	0.415± 0.046**	0.842± 0.088**

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

(HCL042)

BAIS 4

STUDY NO. : 0612
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	34	0.228± 0.105	2.548± 0.298	0.777± 0.078
3300 ppm	38	0.216± 0.065	2.501± 0.192	0.784± 0.101
10000 ppm	44	0.359± 0.614	2.699± 0.411*	0.816± 0.098
30000 ppm	39	0.233± 0.064	2.654± 0.200**	0.859± 0.071**

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

(HCL042)

BAIS 4

TABLE M 1

HISTOPATHOLOGICAL FINDINGS:

NON-NEOPLASTIC LESIONS:

MALE: ALL ANIMALS

STUDY NO. : 0612
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	Control				3300 ppm				10000 ppm				30000 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>			
	abscess		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)
	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)
	epidermal cyst		0	0	0	0	1	1	0	0	0	2	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(2)	(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)
{Respiratory system}																		
nasal cavit			<50>				<50>				<50>				<50>			
	thrombus		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)
	eosinophilic change:olfactory epithelium		30	7	0	0	29	3	0	0	30	5	0	0	28	9	2	0
			(60)	(14)	(0)	(0)	(58)	(6)	(0)	(0)	(60)	(10)	(0)	(0)	(56)	(18)	(4)	(0)
	eosinophilic change:respiratory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	inflammation:foreign body		9	3	0	0	14	2	0	0	7	2	0	0	7	1	0	0
			(18)	(6)	(0)	(0)	(28)	(4)	(0)	(0)	(14)	(4)	(0)	(0)	(14)	(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				3300 ppm				10000 ppm				30000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}																		
nasal cavit			<50>				<50>				<50>				<50>			
	inflammation:respiratory epithelium		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		1	0	0	0	2	0	0	0	1	0	0	0	1	0	0	0
			(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	respiratory metaplasia:gland		3	0	0	0	3	0	0	0	0	0	0	0	2	0	0	0
			(6)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	inflammation:transitional epithelium		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)
larynx			<50>				<50>				<50>				<50>			
	inflammation		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)
lung			<50>				<50>				<50>				<50>			
	edema		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)
	inflammation		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)	(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				3300 ppm				10000 ppm				30000 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>			
	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)
	accumulation of foamy cells		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)
	bronchiolar-alveolar cell hyperplasia		1	2	0	0	2	0	0	0	1	1	0	0	2	1	0	0
			(2)	(4)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(2)	(0)	(0)	(4)	(2)	(0)	(0)
{Hematopoietic system}																		
bone marrow			<50>				<50>				<50>				<50>			
	congestion		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)
	granulation		1	0	0	0	2	0	0	0	1	0	0	0	2	0	0	0
			(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	increased hematopoiesis		4	0	0	0	2	0	0	0	8	0	0	0	4	0	0	0
			(8)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(16)	(0)	(0)	(0)	(8)	(0)	(0)	(0)
lymph node			<50>				<50>				<50>				<50>			
	lymphadenitis		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1 (%)	Control 50 2 (%)	Control 50 3 (%)	Control 50 4 (%)	3300 ppm 50 1 (%)	3300 ppm 50 2 (%)	3300 ppm 50 3 (%)	3300 ppm 50 4 (%)	10000 ppm 50 1 (%)	10000 ppm 50 2 (%)	10000 ppm 50 3 (%)	10000 ppm 50 4 (%)	30000 ppm 50 1 (%)	30000 ppm 50 2 (%)	30000 ppm 50 3 (%)	30000 ppm 50 4 (%)
{Hematopoietic system}																		
thymus		<50>																
	ectopic tissue		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
spleen		<50>																
	atrophy		0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)
	congestion		6 (12)	3 (6)	0 (0)	0 (0)	6 (12)	0 (0)	0 (0)	0 (0)	6 (12)	1 (2)	0 (0)	0 (0)	10 (20)	0 (0)	0 (0)	0 (0)
	deposit of hemosiderin		10 (20)	2 (4)	0 (0)	0 (0)	10 (20)	4 (8)	0 (0)	0 (0)	8 (16)	1 (2)	0 (0)	0 (0)	10 (20)	3 (6)	0 (0)	0 (0)
	inflammation		0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	fibrosis		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)	1 (2)	0 (0)	0 (0)
	fibrosis:focal		0 (0)	2 (4)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	extramedullary hematopoiesis		4 (8)	1 (2)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	4 (8)	1 (2)	1 (2)	0 (0)	5 (10)	1 (2)	1 (2)	0 (0)

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

Organ	Findings	Group Name	Control				3300 ppm				10000 ppm				30000 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>			
	thrombus		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)
	mineralization		0	0	0	0	0	1	0	0	0	1	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)
	inflammatory cell nest		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)
	myocardial fibrosis		18	0	0	0	15	1	0	0	14	0	0	0	14	0	0	0
			(36)	(0)	(0)	(0)	(30)	(2)	(0)	(0)	(28)	(0)	(0)	(0)	(28)	(0)	(0)	(0)
{Digestive system}																		
stomach			<50>				<50>				<50>				<50>			
	hemorrhage		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)
	basal cell hyperplasia		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)	(0)	(0)	(0)	(0)
	erosion:forestomach		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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				3300 ppm				10000 ppm				30000 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	0	0	2	3	0	0	2	0	0	0	1	0	0	0
			(2)	(2)	(0)	(0)	(4)	(6)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	hyperplasia:forestomach		0	0	0	0	2	0	0	0	1	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(2)	(0)	(0)
	erosion:glandular stomach		2	0	0	0	4	0	0	0	1	0	0	0	1	0	0	0
			(4)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	hyperplasia:glandular stomach		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:glandular stomach		0	0	0	0	0	1	0	0	1	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(2)	(0)	(0)
small intes			<50>				<50>				<50>				<50>			
	inflammatory infiltration		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
large intes			<50>				<50>				<50>				<50>			
	inflammatory infiltration		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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				3300 ppm				10000 ppm				30000 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		7	0	0	0	8	0	0	0	4	0	0	0	7	0	0	0
			(14)	(0)	(0)	(0)	(16)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(14)	(0)	(0)	(0)
	necrosis:central		0	1	0	0	0	0	0	0	1	0	0	0	0	1	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(2)	(0)	(0)
	necrosis:focal		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)
	fatty change		0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0
			(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
	fatty change:central		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)
	fatty change:peripheral		0	0	0	0	1	0	0	0	0	0	0	0	1	1	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(2)	(0)	(0)
	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)
	granulation		5	0	0	0	3	0	0	0	4	1	0	0	3	1	0	0
			(10)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(8)	(2)	(0)	(0)	(6)	(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 (%)	3300 ppm 50 1 (%)	3300 ppm 50 2 (%)	3300 ppm 50 3 (%)	3300 ppm 50 4 (%)	10000 ppm 50 1 (%)	10000 ppm 50 2 (%)	10000 ppm 50 3 (%)	10000 ppm 50 4 (%)	30000 ppm 50 1 (%)	30000 ppm 50 2 (%)	30000 ppm 50 3 (%)	30000 ppm 50 4 (%)
(Digestive system)																		
liver			<50>				<50>				<50>				<50>			
	clear cell focus		12 (24)	0 (0)	0 (0)	0 (0)	6 (12)	4 (8)	0 (0)	0 * (0)	6 (12)	3 (6)	0 (0)	0 (0)	9 (18)	1 (2)	0 (0)	0 (0)
	acidophilic cell focus		4 (8)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	6 (12)	0 (0)	0 (0)	0 (0)
	basophilic cell focus		8 (16)	1 (2)	0 (0)	0 (0)	5 (10)	1 (2)	0 (0)	0 (0)	9 (18)	2 (4)	0 (0)	0 (0)	6 (12)	1 (2)	0 (0)	0 (0)
	mixed cell focus		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)
	spongiosis hepatis		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	bile duct hyperplasia		6 (12)	42 (84)	0 (0)	0 (0)	3 (6)	44 (88)	0 (0)	0 (0)	1 (2)	48 (96)	0 (0)	0 (0)	4 (8)	46 (92)	0 (0)	0 (0)
	biliary cyst		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
pancreas			<50>				<50>				<50>				<50>			
	atrophy		15 (30)	0 (0)	0 (0)	0 (0)	12 (24)	1 (2)	0 (0)	0 (0)	12 (24)	3 (6)	0 (0)	0 (0)	11 (22)	4 (8)	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				3300 ppm				10000 ppm				30000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
pancreas			<50>				<50>				<50>				<50>			
	arteritis		0	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(2)	(0)	(0)
{Urinary system}																		
kidney			<50>				<50>				<50>				<50>			
	cyst		1	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	inflammatory cell nest		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)
	scar		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)
	chronic nephropathy		12	16	15	4	15	19	10	1	15	21	9	2	17	21	9	2
			(24)	(32)	(30)	(8)	(30)	(38)	(20)	(2)	(30)	(42)	(18)	(4)	(34)	(42)	(18)	(4)
	tubular necrosis		0	0	0	0	0	0	0	0	0	2	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(4)	(0)	(0)	(0)
	mineralization:pelvis		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				3300 ppm				10000 ppm				30000 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>			
	mineralization:cortex		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)
	urothelial hyperplasia:pelvis		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)
	atypical tubule hyperplasia		2	1	0	0	1	0	0	0	1	1	0	0	0	0	0	0
			(4)	(2)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(2)	(0)	(0)	(0)	(0)	(0)	(0)
{Endocrine system}																		
pituitary			<50>				<50>				<50>				<50>			
	angiectasis		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)
	hyperplasia		6	8	0	0	10	12	0	0	6	4	0	0	3	7	0	0
			(12)	(16)	(0)	(0)	(20)	(24)	(0)	(0)	(12)	(8)	(0)	(0)	(6)	(14)	(0)	(0)
	Rathke pouch		1	0	0	0	2	0	0	0	1	0	0	0	1	0	0	0
			(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	aberrant craniopharyngeal tissue		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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				3300 ppm				10000 ppm				30000 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>			
	follicular 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)
	C-cell hyperplasia		12	2	0	0	14	4	0	0	9	6	0	0	5	2	0	0
			(24)	(4)	(0)	(0)	(28)	(8)	(0)	(0)	(18)	(12)	(0)	(0)	(10)	(4)	(0)	(0)
parathyroid			<50>				<50>				<50>				<50>			
	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)
adrenal			<50>				<50>				<50>				<50>			
	congestion		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)
	hyperplasia:cortical cell		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia:medulla		2	1	0	0	4	1	0	0	4	2	0	0	2	3	0	0
			(4)	(2)	(0)	(0)	(8)	(2)	(0)	(0)	(8)	(4)	(0)	(0)	(4)	(6)	(0)	(0)
	focal fatty change:cortex		0	0	0	0	3	1	0	0	4	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(6)	(2)	(0)	(0)	(8)	(0)	(0)	(0)	(4)	(0)	(0)	(0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50				3300 ppm 50				10000 ppm 50				30000 ppm 50			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Reproductive system}																		
testis			<50>				<50>				<50>				<50>			
	mineralization		0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	arteritis		8 (16)	3 (6)	0 (0)	0 (0)	2 (4)	1 (2)	0 (0)	0 (0)	3 (6)	2 (4)	0 (0)	0 (0)	2 (4)	1 (2)	0 (0)	0 (0)
	interstitial cell hyperplasia		17 (34)	3 (6)	0 (0)	0 (0)	17 (34)	0 (0)	0 (0)	0 (0)	15 (30)	2 (4)	0 (0)	0 (0)	10 (20)	8 (16)	0 (0)	0 (0)
prostate			<50>				<50>				<50>				<50>			
	inflammation		0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hyperplasia		8 (16)	2 (4)	0 (0)	0 (0)	9 (18)	1 (2)	0 (0)	0 (0)	3 (6)	2 (4)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)
mammary gl			<50>				<50>				<50>				<50>			
	galactocele		0 (0)	2 (4)	1 (2)	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)
{Nervous system}																		
brain			<50>				<50>				<50>				<50>			
	hemorrhage		0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	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				3300 ppm				10000 ppm				30000 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Nervous system}																		
brain			<50>				<50>				<50>				<50>			
	dilatation:cerebral ventricle		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)
spinal cord			<50>				<50>				<50>				<50>			
	hemorrhage		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)
	hematoma		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)
{Special sense organs/appendage}																		
eye			<50>				<50>				<50>				<50>			
	cataract		12	0	0	0	4	0	0	0	7	0	0	0	3	0	0	0 *
			(24)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(14)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
	retinal atrophy		25	12	4	0	19	14	3	0	26	14	3	0	23	17	3	0
			(50)	(24)	(8)	(0)	(38)	(28)	(6)	(0)	(52)	(28)	(6)	(0)	(46)	(34)	(6)	(0)
	squamous cell metaplasia:cornea		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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				3300 ppm 50				10000 ppm 50				30000 ppm 50			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Special sense organs/appendage}																		
Harder gl			<50>				<50>				<50>				<50>			
	inflammatory infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)
nasolacr d			<50>				<50>				<50>				<50>			
	inflammation		2 (4)	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)
{Musculoskeletal system}																		
muscle			<50>				<50>				<50>				<50>			
	atrophy		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
bone			<50>				<50>				<50>				<50>			
	osteosclerosis		0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
{Body cavities}																		
peritoneum			<50>				<50>				<50>				<50>			
	inflammation		0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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				3300 ppm				10000 ppm				30000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Body cavities}																		
mesenterium			<50>				<50>				<50>				<50>			
	inflammation		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)
	arteritis		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

TABLE M 4

HISTOPATHOLOGICAL FINDINGS:

NON-NEOPLASTIC LESIONS:

FEMALE: ALL ANIMALS

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50				3300 ppm 50				10000 ppm 50				30000 ppm 50			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Respiratory system}																		
nasal cavit			<50>				<50>				<50>				<50>			
	thrombus		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	eosinophilic change:olfactory epithelium		8 (16)	29 (58)	10 (20)	0 (0)	7 (14)	31 (62)	7 (14)	0 (0)	8 (16)	32 (64)	9 (18)	0 (0)	4 (8)	35 (70)	11 (22)	0 (0)
	eosinophilic change:respiratory epithelium		34 (68)	0 (0)	0 (0)	0 (0)	32 (64)	0 (0)	0 (0)	0 (0)	32 (64)	0 (0)	0 (0)	0 (0)	37 (74)	0 (0)	0 (0)	0 (0)
	inflammation:foreign body		1 (2)	0 (0)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
	inflammation:respiratory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	inflammation:olfactory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:olfactory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:gland		7 (14)	0 (0)	0 (0)	0 (0)	7 (14)	0 (0)	0 (0)	0 (0)	6 (12)	0 (0)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50				3300 ppm 50				10000 ppm 50				30000 ppm 50			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Respiratory system}																		
nasal cavit			<50>				<50>				<50>				<50>			
	inflammation:transitional epithelium		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	squamous cell metaplasia:respiratory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
larynx			<50>				<50>				<50>				<50>			
	inflammation		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)
lung			<50>				<50>				<50>				<50>			
	congestion		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)	1 (2)	0 (0)	0 (0)
	edema		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)
	bronchiolar-alveolar cell hyperplasia		0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	2 (4)	1 (2)	0 (0)	0 (0)
	emphysema		0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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 (%)	3300 ppm 50 1 (%)	3300 ppm 50 2 (%)	3300 ppm 50 3 (%)	3300 ppm 50 4 (%)	10000 ppm 50 1 (%)	10000 ppm 50 2 (%)	10000 ppm 50 3 (%)	10000 ppm 50 4 (%)	30000 ppm 50 1 (%)	30000 ppm 50 2 (%)	30000 ppm 50 3 (%)	30000 ppm 50 4 (%)
{Hematopoietic system}																		
bone marrow			<50>				<50>				<50>				<50>			
	granulation		5 (10)	2 (4)	0 (0)	0 (0)	7 (14)	0 (0)	0 (0)	0 (0)	4 (8)	2 (4)	0 (0)	0 (0)	7 (14)	2 (4)	0 (0)	0 (0)
	increased hematopoiesis		5 (10)	0 (0)	0 (0)	0 (0)	6 (12)	0 (0)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)
thymus			<50>				<50>				<50>				<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)
spleen			<50>				<50>				<50>				<50>			
	atrophy		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)
	congestion		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)
	deposit of hemosiderin		29 (58)	4 (8)	0 (0)	0 (0)	27 (54)	3 (6)	0 (0)	0 (0)	30 (60)	3 (6)	0 (0)	0 (0)	26 (52)	1 (2)	0 (0)	0 (0)
	fibrosis		0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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				3300 ppm				10000 ppm				30000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}																		
spleen			<50>				<50>				<50>				<50>			
	extramedullary hematopoiesis		4	1	1	0	5	4	0	0	7	2	0	0	6	2	0	0
			(8)	(2)	(2)	(0)	(10)	(8)	(0)	(0)	(14)	(4)	(0)	(0)	(12)	(4)	(0)	(0)
{Circulatory system}																		
heart			<50>				<50>				<50>				<50>			
	thrombus		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	myocardial fibrosis		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)
	subendocardial fibrosis		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)
{Digestive system}																		
oral cavity			<50>				<50>				<50>				<50>			
	squamous cell hyperplasia		0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)

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				3300 ppm				10000 ppm				30000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
tongue			<50>				<50>				<50>				<50>			
	squamous cell hyperplasia		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	arteritis		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)
salivary gl			<50>				<50>				<50>				<50>			
	atrophy		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)
stomach			<50>				<50>				<50>				<50>			
	ulcer:forestomach		0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	hyperplasia:forestomach		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	erosion:glandular stomach		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	ulcer: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)

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 (%)	3300 ppm 50 1 (%)	3300 ppm 50 2 (%)	3300 ppm 50 3 (%)	3300 ppm 50 4 (%)	10000 ppm 50 1 (%)	10000 ppm 50 2 (%)	10000 ppm 50 3 (%)	10000 ppm 50 4 (%)	30000 ppm 50 1 (%)	30000 ppm 50 2 (%)	30000 ppm 50 3 (%)	30000 ppm 50 4 (%)
{Digestive system}																		
stomach			<50>				<50>				<50>				<50>			
	mineralization:glandular stomach		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
large intes			<50>				<50>				<50>				<50>			
	cyst		0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
liver			<50>				<50>				<50>				<50>			
	herniation		7 (14)	0 (0)	0 (0)	0 (0)	7 (14)	0 (0)	0 (0)	0 (0)	10 (20)	0 (0)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)
	necrosis:central		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	necrosis:focal		2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)
	fatty change		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)
	lymphocytic infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	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				3300 ppm				10000 ppm				30000 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		14	1	0	0	11	0	0	0	10	0	0	0	15	1	0	0
			(28)	(2)	(0)	(0)	(22)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(30)	(2)	(0)	(0)
	inflammatory cell nest		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)
	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)
	clear cell focus		1	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(2)	(2)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	basophilic cell focus		27	2	0	0	30	2	0	0	32	2	0	0	26	2	0	0
			(54)	(4)	(0)	(0)	(60)	(4)	(0)	(0)	(64)	(4)	(0)	(0)	(52)	(4)	(0)	(0)
	mixed cell focus		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)
	bile duct hyperplasia		20	1	0	0	16	2	0	0	16	5	0	0	14	5	0	0
			(40)	(2)	(0)	(0)	(32)	(4)	(0)	(0)	(32)	(10)	(0)	(0)	(28)	(10)	(0)	(0)
	biliary 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)

Grade 1 : SIight 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				3300 ppm				10000 ppm				30000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
pancreas			<50>				<50>				<50>				<50>			
	atrophy		3	1	0	0	4	1	0	0	4	0	0	0	6	2	0	0
			(6)	(2)	(0)	(0)	(8)	(2)	(0)	(0)	(8)	(0)	(0)	(0)	(12)	(4)	(0)	(0)
	lymphocytic infiltration		0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	islet cell hyperplasia		0	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)
{Urinary system}																		
kidney			<50>				<50>				<50>				<50>			
	cyst		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)
	hyaline droplet		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)
	deposit of hemosiderin		0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(2)	(0)	(0)	(0)
	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)

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				3300 ppm				10000 ppm				30000 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>			
	chronic nephropathy		28	2	1	0	27	2	1	0	29	5	1	0	26	2	2	0
			(56)	(4)	(2)	(0)	(54)	(4)	(2)	(0)	(58)	(10)	(2)	(0)	(52)	(4)	(4)	(0)
	tubular necrosis		0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)
	papillary necrosis		0	0	0	0	0	0	0	0	0	0	0	0	6	0	0	0 *
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(12)	(0)	(0)	(0)
	mineralization:cortico-medullary junction		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)
	mineralization:papilla		0	0	0	0	0	0	0	0	0	0	0	0	6	0	0	0 *
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(12)	(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	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)
	regeneration:proximal tubule		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 / No. of Animals on Study / Grade	Control 50 1 (%)	Control 50 2 (%)	Control 50 3 (%)	Control 50 4 (%)	3300 ppm 50 1 (%)	3300 ppm 50 2 (%)	3300 ppm 50 3 (%)	3300 ppm 50 4 (%)	10000 ppm 50 1 (%)	10000 ppm 50 2 (%)	10000 ppm 50 3 (%)	10000 ppm 50 4 (%)	30000 ppm 50 1 (%)	30000 ppm 50 2 (%)	30000 ppm 50 3 (%)	30000 ppm 50 4 (%)
{Urinary system}																		
kidney			<50>				<50>				<50>				<50>			
	urothelial hyperplasia:pelvis		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)
	atypical tubule hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	dilated pelvis		0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
{Endocrine system}																		
pituitary			<50>				<50>				<50>				<50>			
	angiectasis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	2 (4)	2 (4)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)
	cyst		5 (10)	1 (2)	0 (0)	0 (0)	3 (6)	3 (6)	0 (0)	0 (0)	4 (8)	1 (2)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)
	hyperplasia		7 (14)	2 (4)	0 (0)	0 (0)	4 (8)	4 (8)	0 (0)	0 (0)	6 (12)	7 (14)	0 (0)	0 (0)	10 (20)	5 (10)	0 (0)	0 (0)
	Rathke pouch		2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)

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				3300 ppm				10000 ppm				30000 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	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)
	C-cell hyperplasia		9	2	0	0	14	5	0	0	10	4	0	0	5	1	0	0
			(18)	(4)	(0)	(0)	(28)	(10)	(0)	(0)	(20)	(8)	(0)	(0)	(10)	(2)	(0)	(0)
adrenal			<50>				<50>				<50>				<50>			
	peliosis-like lesion		3	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(6)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	extramedullary hematopoiesis		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)
	hyperplasia:cortical cell		0	1	0	0	0	0	0	0	1	1	0	0	0	1	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(2)	(0)	(0)	(0)	(2)	(0)	(0)
	hyperplasia:medulla		1	0	0	0	0	0	0	0	1	2	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(4)	(0)	(0)	(0)	(0)	(0)	(0)
	focal fatty change:cortex		6	0	0	0	2	0	0	0	4	0	0	0	3	3	0	0
			(12)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(8)	(0)	(0)	(0)	(6)	(6)	(0)	(0)
{Reproductive system}																		
ovary			<50>				<50>				<50>				<50>			
	cyst		1	0	0	0	0	0	0	0	2	0	0	0	2	1	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(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				3300 ppm				10000 ppm				30000 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Reproductive system}																		
uterus			<50>				<50>				<50>				<50>			
	decidual change		0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	cystic endometrial hyperplasia		1	0	0	0	0	0	0	0	1	1	0	0	4	2	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(2)	(0)	(0)	(8)	(4)	(0)	(0)
{Special sense organs/appendage}																		
eye			<50>				<50>				<50>				<50>			
	inflammatory 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)
	cataract		6	0	0	0	6	0	0	0	6	0	0	0	2	0	0	0
			(12)	(0)	(0)	(0)	(12)	(0)	(0)	(0)	(12)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	retinal atrophy		18	18	2	0	20	15	5	0	21	20	5	0	22	18	2	0
			(36)	(36)	(4)	(0)	(40)	(30)	(10)	(0)	(42)	(40)	(10)	(0)	(44)	(36)	(4)	(0)
	squamous cell metaplasia:cornea		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)
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)

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				3300 ppm				10000 ppm				30000 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}																		
Harder gl			<50>				<50>				<50>				<50>			
	lymphocytic infiltration		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
nasolacr d			<50>				<50>				<50>				<50>			
	inflammation		7	0	0	0	3	0	0	0	5	0	0	0	2	0	0	0
			(14)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
{Musculoskeletal system}																		
bone			<50>				<50>				<50>				<50>			
	osteosclerosis		3	1	0	0	2	2	1	0	5	1	0	0	2	1	2	0
			(6)	(2)	(0)	(0)	(4)	(4)	(2)	(0)	(10)	(2)	(0)	(0)	(4)	(2)	(4)	(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. : 0612
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

Group Name	Control	3300 ppm	10000 ppm	30000 ppm
	SITE : subcutis			
	TUMOR : fibroma			
Tumor rate				
Overall rates(a)	2/50(4.0)	1/50(2.0)	5/50(10.0)	2/50(4.0)
Adjusted rates(b)	5.00	2.86	9.52	2.17
Terminal rates(c)	2/40(5.0)	1/35(2.9)	3/39(7.7)	0/40(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1730			
Prevalence method(d)	P = 0.6644			
Combined analysis(d)	P = 0.4621			
Cochran-Armitage test(e)	P = 0.8881			
Fisher Exact test(e)		P = 0.5000	P = 0.2180	P = 0.6913
	SITE : subcutis			
	TUMOR : fibroma, fibrosarcoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	1/50(2.0)	6/50(12.0)	2/50(4.0)
Adjusted rates(b)	5.00	2.86	11.90	2.17
Terminal rates(c)	2/40(5.0)	1/35(2.9)	4/39(10.3)	0/40(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3557			
Prevalence method(d)	P = 0.6745			
Combined analysis(d)	P = 0.5902			
Cochran-Armitage test(e)	P = 0.8660			
Fisher Exact test(e)		P = 0.3087	P = 0.2435	P = 0.5000
	SITE : lung			
	TUMOR : bronchiolar-alveolar adenoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	3/50(6.0)	2/50(4.0)	2/50(4.0)
Adjusted rates(b)	7.50	8.57	4.88	5.00
Terminal rates(c)	3/40(7.5)	3/35(8.6)	1/39(2.6)	2/40(5.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.7246			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.6091			
Fisher Exact test(e)		P = 0.6611	P = 0.5000	P = 0.5000

Group Name	Control	3300 ppm	10000 ppm	30000 ppm
	SITE : lung			
	TUMOR : bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	1/50(2.0)	3/50(6.0)	1/50(2.0)
Adjusted rates(b)	2.50	2.86	7.69	2.50
Terminal rates(c)	1/40(2.5)	1/35(2.9)	3/39(7.7)	1/40(2.5)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.5193			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.9532			
Fisher Exact test(e)		P = 0.7525	P = 0.3087	P = 0.7525
	SITE : lung			
	TUMOR : bronchiolar-alveolar adenoma, bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	3/50(6.0)	5/50(10.0)	3/50(6.0)
Adjusted rates(b)	10.00	8.57	12.20	7.50
Terminal rates(c)	4/40(10.0)	3/35(8.6)	4/39(10.3)	3/40(7.5)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.6611			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.7736			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.5000
	SITE : spleen			
	TUMOR : mononuclear cell leukemia			
Tumor rate				
Overall rates(a)	3/50(6.0)	6/50(12.0)	8/50(16.0)	2/50(4.0)
Adjusted rates(b)	5.00	10.00	15.38	2.50
Terminal rates(c)	2/40(5.0)	3/35(8.6)	6/39(15.4)	1/40(2.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.6141			
Prevalence method(d)	P = 0.8435			
Combined analysis(d)	P = 0.8496			
Cochran-Armitage test(e)	P = 0.3420			
Fisher Exact test(e)		P = 0.2435	P = 0.0999	P = 0.5000

Group Name	Control	3300 ppm	10000 ppm	30000 ppm
	SITE : liver			
	TUMOR : hepatocellular adenoma, hepatocellular carcinoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	1/50(2.0)	0/50(0.0)	3/50(6.0)
Adjusted rates(b)	7.50	2.86	0.0	7.14
Terminal rates(c)	3/40(7.5)	1/35(2.9)	0/39(0.0)	2/40(5.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.3145			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.5625			
Fisher Exact test(e)		P = 0.3087	P = 0.1212	P = 0.6611
	SITE : pancreas			
	TUMOR : islet cell adenocarcinoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	3/50(6.0)	2/50(4.0)	1/50(2.0)
Adjusted rates(b)	0.0	5.71	5.13	2.50
Terminal rates(c)	0/40(0.0)	2/35(5.7)	2/39(5.1)	1/40(2.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5374			
Prevalence method(d)	P = 0.4560			
Combined analysis(d)	P = 0.5654			
Cochran-Armitage test(e)	P = 0.8573			
Fisher Exact test(e)		P = 0.1212	P = 0.2475	P = 0.5000
	SITE : pancreas			
	TUMOR : islet cell adenoma, islet cell adenocarcinoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	4/50(8.0)	2/50(4.0)	1/50(2.0)
Adjusted rates(b)	2.50	8.57	5.13	2.50
Terminal rates(c)	1/40(2.5)	3/35(8.6)	2/39(5.1)	1/40(2.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5374			
Prevalence method(d)	P = 0.6995			
Combined analysis(d)	P = 0.7700			
Cochran-Armitage test(e)	P = 0.4683			
Fisher Exact test(e)		P = 0.1811	P = 0.5000	P = 0.7525

Group Name	Control	3300 ppm	10000 ppm	30000 ppm
	SITE : pituitary gland			
	TUMOR : adenoma			
Tumor rate				
Overall rates(a)	24/50(48.0)	13/50(26.0)	20/50(40.0)	14/50(28.0)
Adjusted rates(b)	50.00	20.00	41.03	25.00
Terminal rates(c)	20/40(50.0)	7/35(20.0)	16/39(41.0)	10/40(25.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5012			
Prevalence method(d)	P = 0.9579			
Combined analysis(d)	P = 0.9300			
Cochran-Armitage test(e)	P = 0.1798			
Fisher Exact test(e)		P = 0.0188*	P = 0.2729	P = 0.0315*
	SITE : pituitary gland			
	TUMOR : adenoma, adenocarcinoma			
Tumor rate				
Overall rates(a)	25/50(50.0)	13/50(26.0)	20/50(40.0)	15/50(30.0)
Adjusted rates(b)	50.00	20.00	41.03	27.50
Terminal rates(c)	20/40(50.0)	7/35(20.0)	16/39(41.0)	11/40(27.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5948			
Prevalence method(d)	P = 0.9279			
Combined analysis(d)	P = 0.9154			
Cochran-Armitage test(e)	P = 0.2195			
Fisher Exact test(e)		P = 0.0114*	P = 0.2108	P = 0.0328*
	SITE : thyroid			
	TUMOR : C-cell adenoma			
Tumor rate				
Overall rates(a)	8/50(16.0)	3/50(6.0)	6/50(12.0)	10/50(20.0)
Adjusted rates(b)	17.78	8.57	13.95	22.50
Terminal rates(c)	6/40(15.0)	3/35(8.6)	4/39(10.3)	9/40(22.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1446			
Prevalence method(d)	P = 0.1660			
Combined analysis(d)	P = 0.1022			
Cochran-Armitage test(e)	P = 0.1677			
Fisher Exact test(e)		P = 0.0999	P = 0.3871	P = 0.3976

Group Name	Control	3300 ppm	10000 ppm	30000 ppm
	SITE : thyroid			
	TUMOR : C-cell adenoma, C-cell carcinoma			
Tumor rate				
Overall rates(a)	8/50(16.0)	3/50(6.0)	8/50(16.0)	10/50(20.0)
Adjusted rates(b)	17.78	8.57	18.60	22.50
Terminal rates(c)	6/40(15.0)	3/35(8.6)	6/39(15.4)	9/40(22.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1446			
Prevalence method(d)	P = 0.1817			
Combined analysis(d)	P = 0.1146			
Cochran-Armitage test(e)	P = 0.1900			
Fisher Exact test(e)		P = 0.0999	P = 0.6071	P = 0.3976
	SITE : adrenal gland			
	TUMOR : pheochromocytoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	5/50(10.0)	5/50(10.0)	6/50(12.0)
Adjusted rates(b)	9.30	13.16	12.82	13.95
Terminal rates(c)	3/40(7.5)	4/35(11.4)	5/39(12.8)	4/40(10.0)
Statistical analysis				
Peto test				
Standard method(d)	P = -------			
Prevalence method(d)	P = 0.3182			
Combined analysis(d)	P = -------			
Cochran-Armitage test(e)	P = 0.5436			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.3703
	SITE : adrenal gland			
	TUMOR : pheochromocytoma, pheochromocytoma:malignant			
Tumor rate				
Overall rates(a)	4/50(8.0)	5/50(10.0)	5/50(10.0)	8/50(16.0)
Adjusted rates(b)	9.30	13.16	12.82	16.28
Terminal rates(c)	3/40(7.5)	4/35(11.4)	5/39(12.8)	5/40(12.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1430			
Prevalence method(d)	P = 0.1949			
Combined analysis(d)	P = 0.1186			
Cochran-Armitage test(e)	P = 0.1846			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.1783

Group Name	Control	3300 ppm	10000 ppm	30000 ppm
	SITE : testis			
	TUMOR : interstitial cell tumor			
Tumor rate				
Overall rates(a)	28/50(56.0)	30/50(60.0)	34/50(68.0)	36/50(72.0)
Adjusted rates(b)	67.50	78.38	75.00	80.00
Terminal rates(c)	27/40(67.5)	27/35(77.1)	29/39(74.4)	32/40(80.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.1199			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0914			
Fisher Exact test(e)		P = 0.4198	P = 0.1515	P = 0.0721
	SITE : peritoneum			
	TUMOR : mesothelioma			
Tumor rate				
Overall rates(a)	1/50(2.0)	0/50(0.0)	2/50(4.0)	4/50(8.0)
Adjusted rates(b)	2.50	0.0	4.65	7.50
Terminal rates(c)	1/40(2.5)	0/35(0.0)	1/39(2.6)	3/40(7.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1465			
Prevalence method(d)	P = 0.0751			
Combined analysis(d)	P = 0.0293*			
Cochran-Armitage test(e)	P = 0.0338*			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.1811

(a): Number of tumor-bearing animals/number of animals examined at the site.
(b): Kaplan-Meier estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.
(c): Observed tumor incidence at terminal kill.
(d): Beneath the control incidence are the P-values associated with the trend test.
Standard method : Death analysis
Prevalence method : Incidental tumor test
Combined analysis : Death analysis + Incidental tumor test
(e): The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.
? : The conditional probabilities of the largest and smallest possible out comes can not estimated or this P-value is beyond the estimated P-value.
------ : There is no data which should be statistical analysis.
Significant difference : * : P ≦ 0.05 ** : P ≦ 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	3300 ppm	10000 ppm	30000 ppm
	SITE : spleen			
	TUMOR : mononuclear cell leukemia			
Tumor rate				
Overall rates(a)	4/50(8.0)	5/50(10.0)	5/50(10.0)	3/50(6.0)
Adjusted rates(b)	2.86	5.13	4.55	0.0
Terminal rates(c)	1/35(2.9)	2/39(5.1)	2/44(4.5)	0/39(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5129			
Prevalence method(d)	P = 0.8723			
Combined analysis(d)	P = 0.7402			
Cochran-Armitage test(e)	P = 0.5489			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.5000
	SITE : oral cavity			
	TUMOR : squamous cell papilloma, squamous cell carcinoma			
Tumor rate				
Overall rates(a)	0/50(0.0)	0/50(0.0)	3/50(6.0)	0/50(0.0)
Adjusted rates(b)	0.0	0.0	4.55	0.0
Terminal rates(c)	0/35(0.0)	0/39(0.0)	2/44(4.5)	0/39(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3810			
Prevalence method(d)	P = 0.4871			
Combined analysis(d)	P = 0.5188			
Cochran-Armitage test(e)	P = 0.9016			
Fisher Exact test(e)		P = N.C.	P = 0.1212	P = N.C.
	SITE : pituitary gland			
	TUMOR : adenoma			
Tumor rate				
Overall rates(a)	11/50(22.0)	7/50(14.0)	8/50(16.0)	11/50(22.0)
Adjusted rates(b)	18.18	15.38	16.33	21.43
Terminal rates(c)	6/35(17.1)	6/39(15.4)	7/44(15.9)	8/39(20.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5218			
Prevalence method(d)	P = 0.3383			
Combined analysis(d)	P = 0.3722			
Cochran-Armitage test(e)	P = 0.6104			
Fisher Exact test(e)		P = 0.2178	P = 0.3055	P = 0.5952

Group Name	Control	3300 ppm	10000 ppm	30000 ppm
	SITE : pituitary gland			
	TUMOR : adenoma, adenocarcinoma			
Tumor rate				
Overall rates(a)	11/50(22.0)	7/50(14.0)	9/50(18.0)	11/50(22.0)
Adjusted rates(b)	18.18	15.38	18.37	21.43
Terminal rates(c)	6/35(17.1)	6/39(15.4)	8/44(18.2)	8/39(20.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.5218			
Prevalence method(d)	P = 0.3483			
Combined analysis(d)	P = 0.3810			
Cochran-Armitage test(e)	P = 0.6230			
Fisher Exact test(e)		P = 0.2178	P = 0.4016	P = 0.5952
	SITE : thyroid			
	TUMOR : C-cell adenoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	7/50(14.0)	6/50(12.0)	1/50(2.0)
Adjusted rates(b)	9.30	17.95	13.64	2.56
Terminal rates(c)	3/35(8.6)	7/39(17.9)	6/44(13.6)	1/39(2.6)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.9737			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0827			
Fisher Exact test(e)		P = 0.2623	P = 0.3703	P = 0.1811
	SITE : thyroid			
	TUMOR : C-cell adenoma, C-cell carcinoma			
Tumor rate				
Overall rates(a)	5/50(10.0)	7/50(14.0)	8/50(16.0)	1/50(2.0)
Adjusted rates(b)	11.63	17.95	18.18	2.56
Terminal rates(c)	4/35(11.4)	7/39(17.9)	8/44(18.2)	1/39(2.6)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.9820			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0619			
Fisher Exact test(e)		P = 0.3798	P = 0.2768	P = 0.1022

Group Name	Control	3300 ppm	10000 ppm	30000 ppm
	SITE : adrenal gland			
	TUMOR : pheochromocytoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	3/50(6.0)	2/50(4.0)	0/50(0.0)
Adjusted rates(b)	5.71	7.69	4.55	0.0
Terminal rates(c)	2/35(5.7)	3/39(7.7)	2/44(4.5)	0/39(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.9569			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.1295			
Fisher Exact test(e)		P = 0.5000	P = 0.6913	P = 0.2475
	SITE : adrenal gland			
	TUMOR : pheochromocytoma, pheochromocytoma:malignant			
Tumor rate				
Overall rates(a)	3/50(6.0)	4/50(8.0)	3/50(6.0)	2/50(4.0)
Adjusted rates(b)	8.57	10.26	6.82	5.13
Terminal rates(c)	3/35(8.6)	4/39(10.3)	3/44(6.8)	2/39(5.1)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.7727			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.4947			
Fisher Exact test(e)		P = 0.5000	P = 0.6611	P = 0.5000
	SITE : uterus			
	TUMOR : endometrial stromal polyp			
Tumor rate				
Overall rates(a)	8/50(16.0)	7/50(14.0)	7/50(14.0)	9/50(18.0)
Adjusted rates(b)	14.89	17.95	15.91	20.00
Terminal rates(c)	4/35(11.4)	7/39(17.9)	7/44(15.9)	7/39(17.9)
Statistical analysis				
Peto test				
Standard method(d)	P = 1.0000 ?			
Prevalence method(d)	P = 0.2896			
Combined analysis(d)	P = 0.3577			
Cochran-Armitage test(e)	P = 0.6441			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.5000

Group Name	Control	3300 ppm	10000 ppm	30000 ppm
	SITE : uterus TUMOR : adenocarcinoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	1/50(2.0)	2/50(4.0)	3/50(6.0)
Adjusted rates(b)	2.86	2.56	2.27	5.13
Terminal rates(c)	1/35(2.9)	1/39(2.6)	1/44(2.3)	2/39(5.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1670			
Prevalence method(d)	P = 0.2378			
Combined analysis(d)	P = 0.1273			
Cochran-Armitage test(e)	P = 0.2149			
Fisher Exact test(e)		P = 0.7525	P = 0.5000	P = 0.3087
	SITE : uterus TUMOR : adenoma, adenocarcinoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	2/50(4.0)	2/50(4.0)	3/50(6.0)
Adjusted rates(b)	5.71	5.13	2.27	5.13
Terminal rates(c)	2/35(5.7)	2/39(5.1)	1/44(2.3)	2/39(5.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1670			
Prevalence method(d)	P = 0.4899			
Combined analysis(d)	P = 0.3031			
Cochran-Armitage test(e)	P = 0.5743			
Fisher Exact test(e)		P = 0.6913	P = 0.6913	P = 0.5000
	SITE : mammary gland TUMOR : fibroadenoma			
Tumor rate				
Overall rates(a)	4/50(8.0)	3/50(6.0)	4/50(8.0)	3/50(6.0)
Adjusted rates(b)	11.43	7.69	8.89	7.14
Terminal rates(c)	4/35(11.4)	3/39(7.7)	3/44(6.8)	2/39(5.1)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.6509			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.7815			
Fisher Exact test(e)		P = 0.5000	P = 0.6425	P = 0.5000

Group Name	Control	3300 ppm	10000 ppm	30000 ppm
	SITE : mammary gland			
	TUMOR : adenoma, fibroadenoma, adenocarcinoma			
Tumor rate				
Overall rates(a)	5/50(10.0)	5/50(10.0)	4/50(8.0)	4/50(8.0)
Adjusted rates(b)	14.29	7.69	8.89	9.30
Terminal rates(c)	5/35(14.3)	3/39(7.7)	3/44(6.8)	2/39(5.1)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.7957			
Prevalence method(d)	P = 0.5777			
Combined analysis(d)	P = 0.6942			
Cochran-Armitage test(e)	P = 0.6969			
Fisher Exact test(e)		P = 0.6297	P = 0.5000	P = 0.5000

(HPT360A)

BAIS4

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

TABLE R

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

F344/DuCrlCrlj MALE RATS

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

Organs Tumors	No. of animals examined	No. of animals bearing tumor	Incidence (%)	Min. - Max. (%)
Peritoneum	2399			
Mesothelioma		63	2.6	0 - 8

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

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

TABLE S 1

CAUSE OF DEATH: MALE

STUDY NO. : 0612
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
SEX : MALE

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

Group Name	Control	3300 ppm	10000 ppm	30000 ppm
Number of Dead and Moribund Animal	10	15	11	10
no microscop confirm	1	5	0	1
chronic nephropathy	1	0	0	0
peritonitis	1	0	0	0
tumor d:leukemia	1	2	2	1
tumor d:subcutis	1	1	1	1
tumor d:pancreas	0	1	0	0
tumor d:urin bladd	0	0	1	0
tumor d:pituitary	4	5	3	3
tumor d:thyroid	0	0	0	1
tumor d:adrenal	0	0	0	1
tumor d:periph nerv	1	0	0	0
tumor d:Zymbal gl	0	0	2	0
tumor d:bone	0	1	0	0
tumor d:pleura	0	0	0	1
tumor d:peritoneum	0	0	1	1
tumor d:adipose	0	0	1	0

TABLE S 2

CAUSE OF DEATH: FEMALE

STUDY NO. : 0612
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
SEX : FEMALE

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

Group Name	Control	3300 ppm	10000 ppm	30000 ppm
Number of Dead and Moribund Animal	15	11	6	11
no microscop confirm	4	3	1	2
tumor d:leukemia	3	3	3	3
tumor d:subcutis	0	1	0	1
tumor d:oral cavity	0	0	1	0
tumor d:pituitary	3	0	0	2
tumor d:ovary	1	0	0	0
tumor d:uterus	3	2	1	3
tumor d:mammary gl	0	2	0	0
tumor d:retroperit	1	0	0	0

(BIO120)

BAIS4

FIGURES

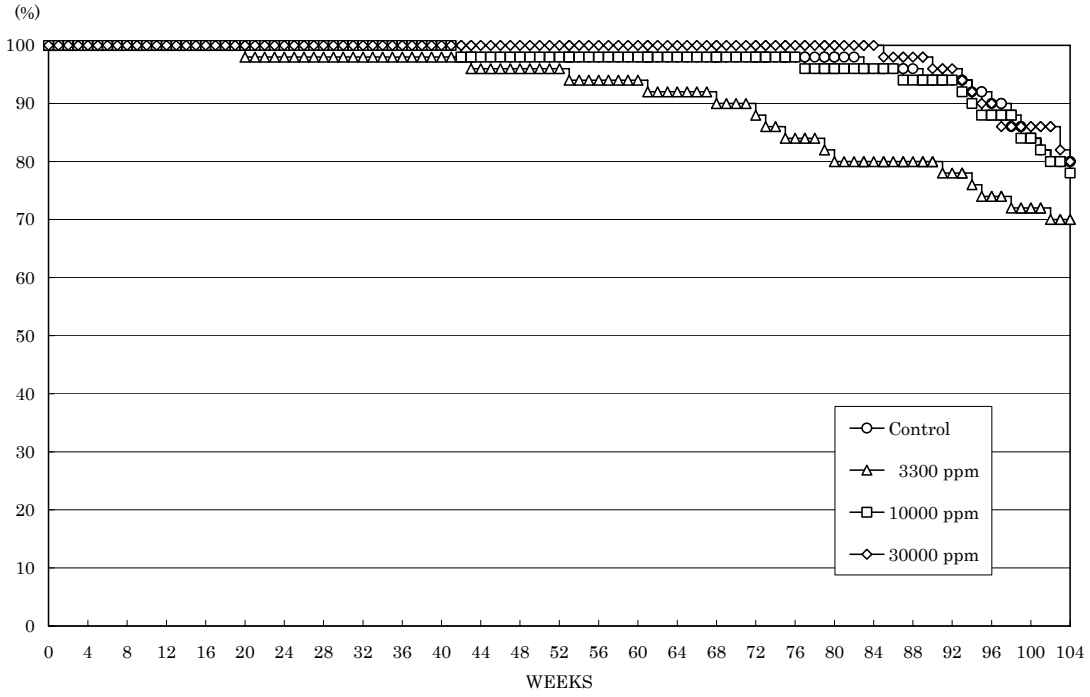


FIGURE 1　SURVIVAL ANIMAL RATE OF MALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF 2-METHYL-1-PROPANOL

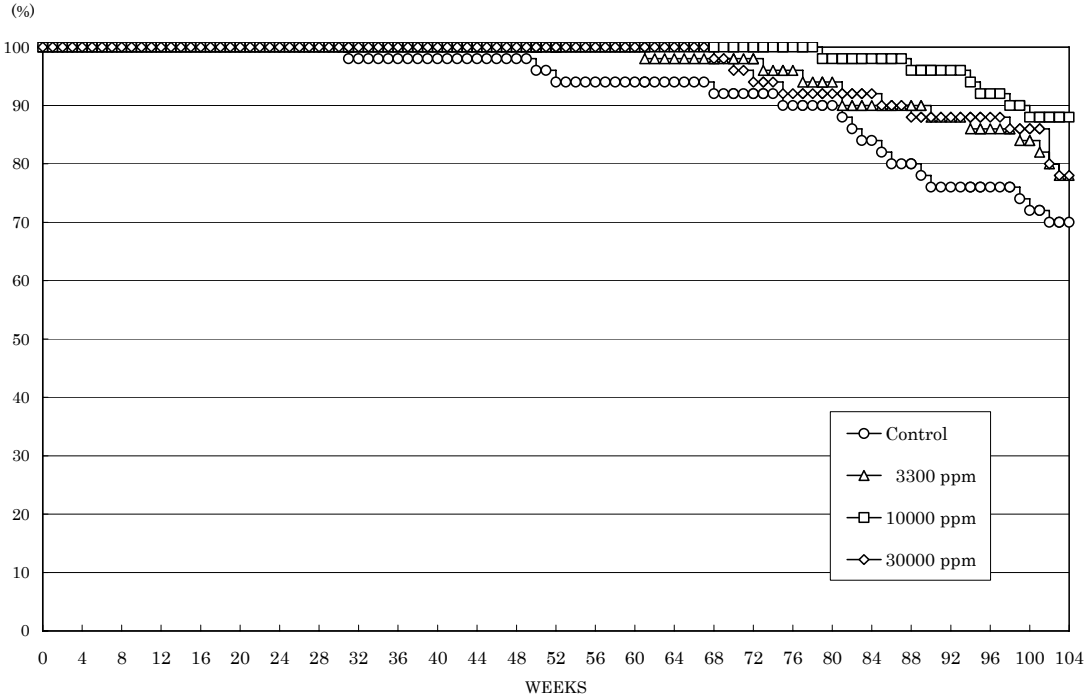


FIGURE 2　SURVIVAL ANIMAL RATE OF FEMALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF 2-METHYL-1-PROPANOL

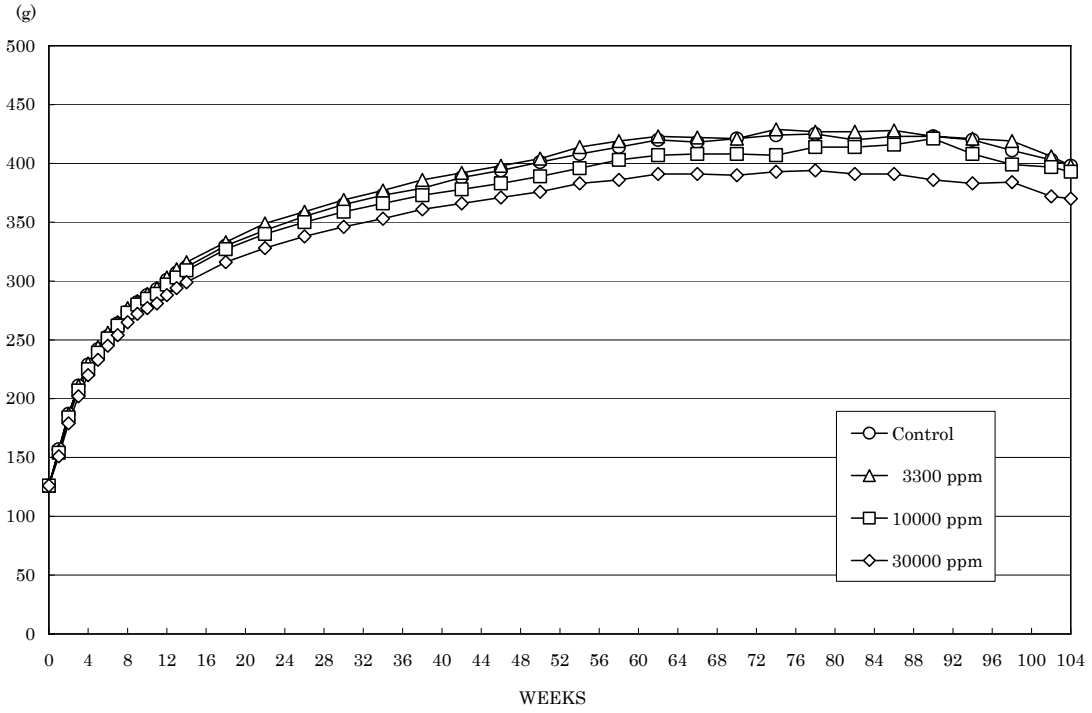


FIGURE 3 BODY WEIGHT CHANGES OF MALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF 2-METHYL-1-PROPANOL

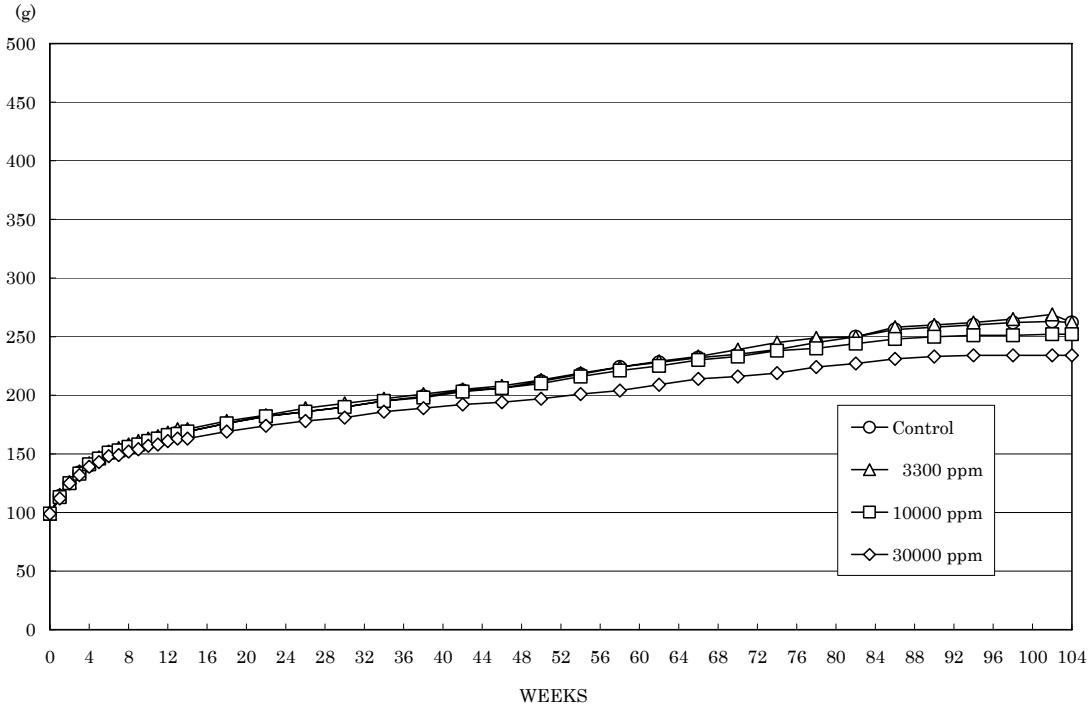


FIGURE 4 BODY WEIGHT CHANGES OF FEMALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF 2-METHYL-1-PROPANOL

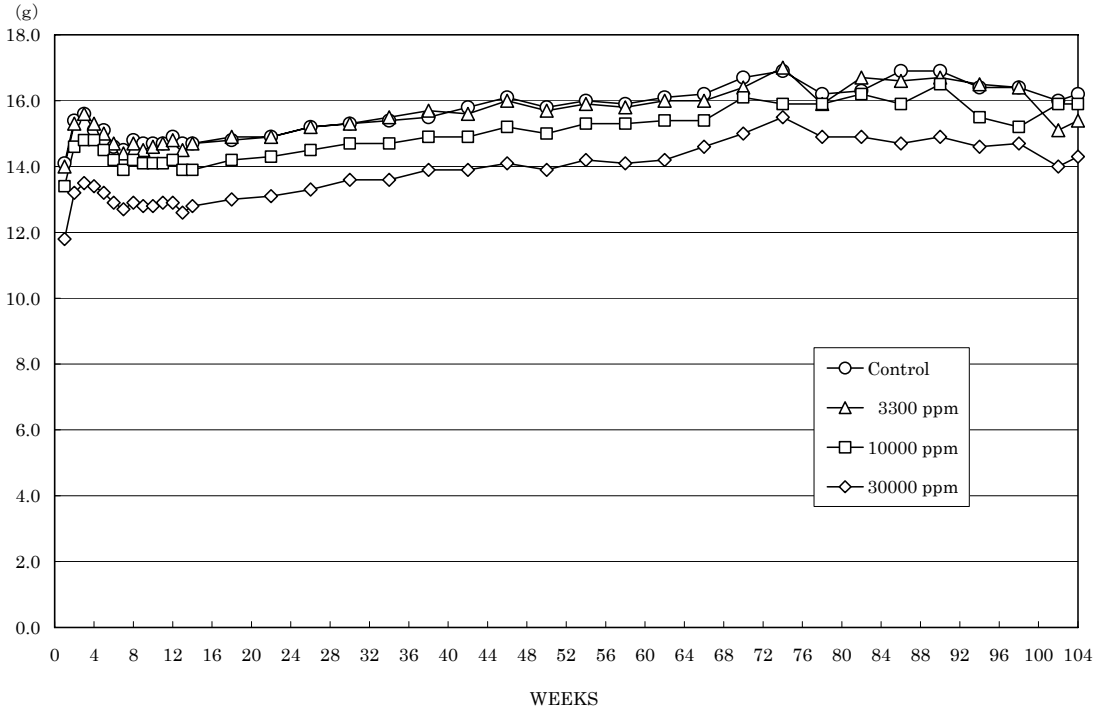


FIGURE 5 FOOD CONSUMPTION CHANGES OF MALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF 2-METHYL-1-PROPANOL

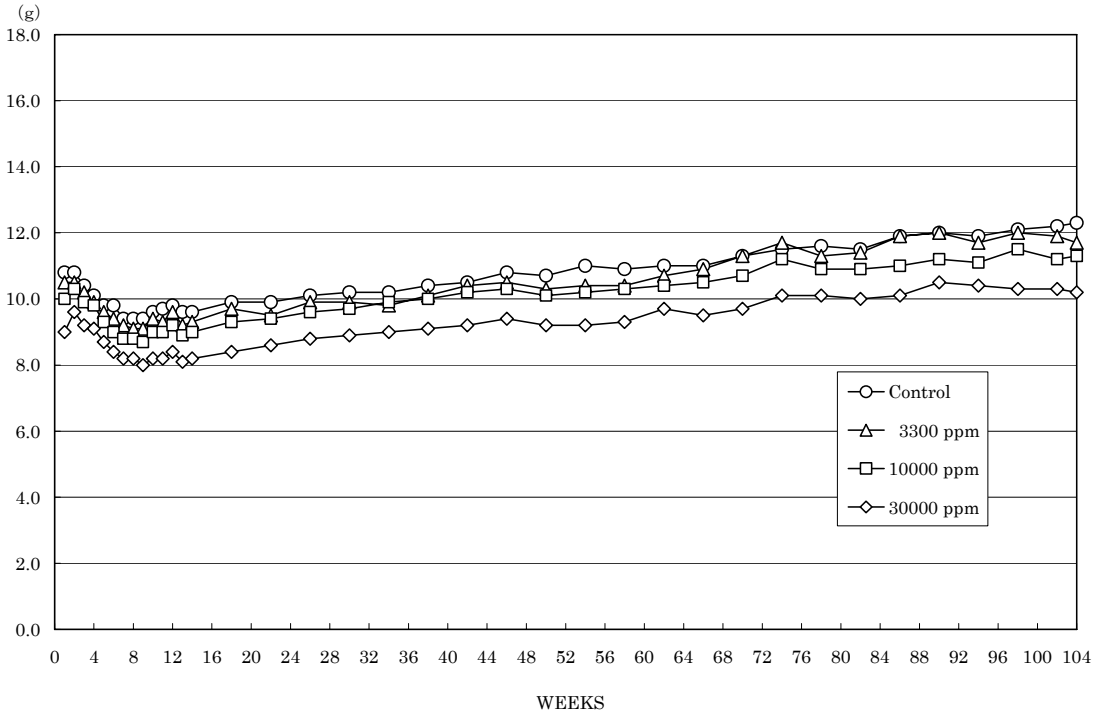


FIGURE 6 FOOD CONSUMPTION CHANGES OF FEMALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF 2-METHYL-1-PROPANOL

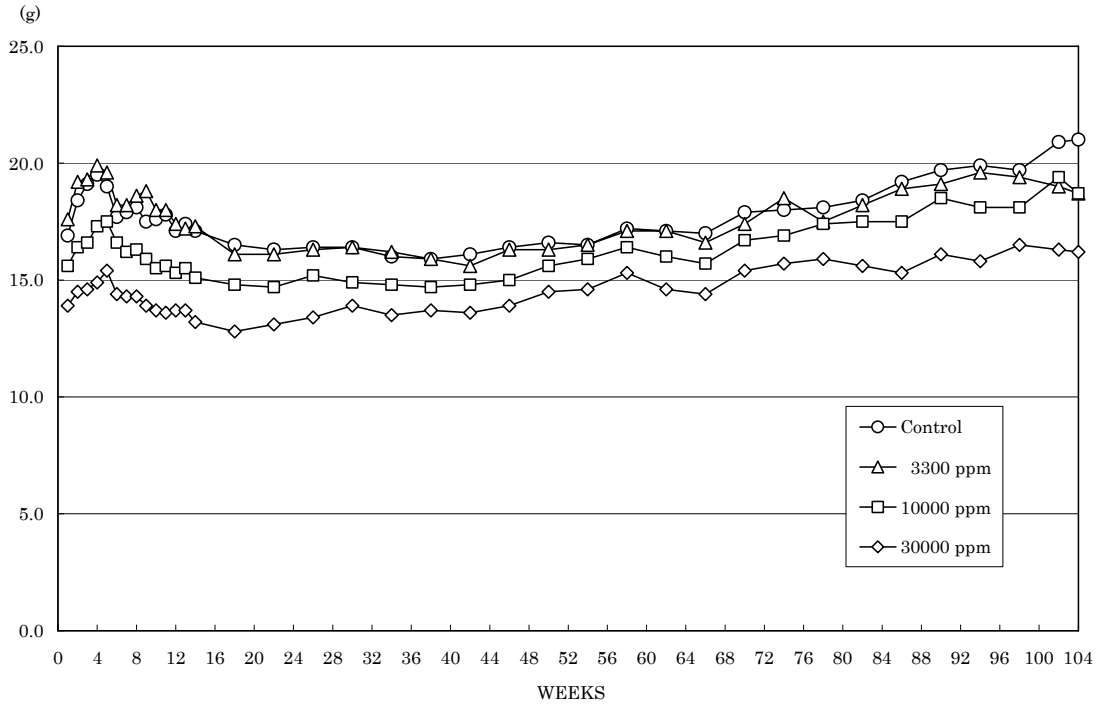


FIGURE 7 WATER CONSUMPTION CHANGES OF MALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF 2-METHYL-1-PROPANOL

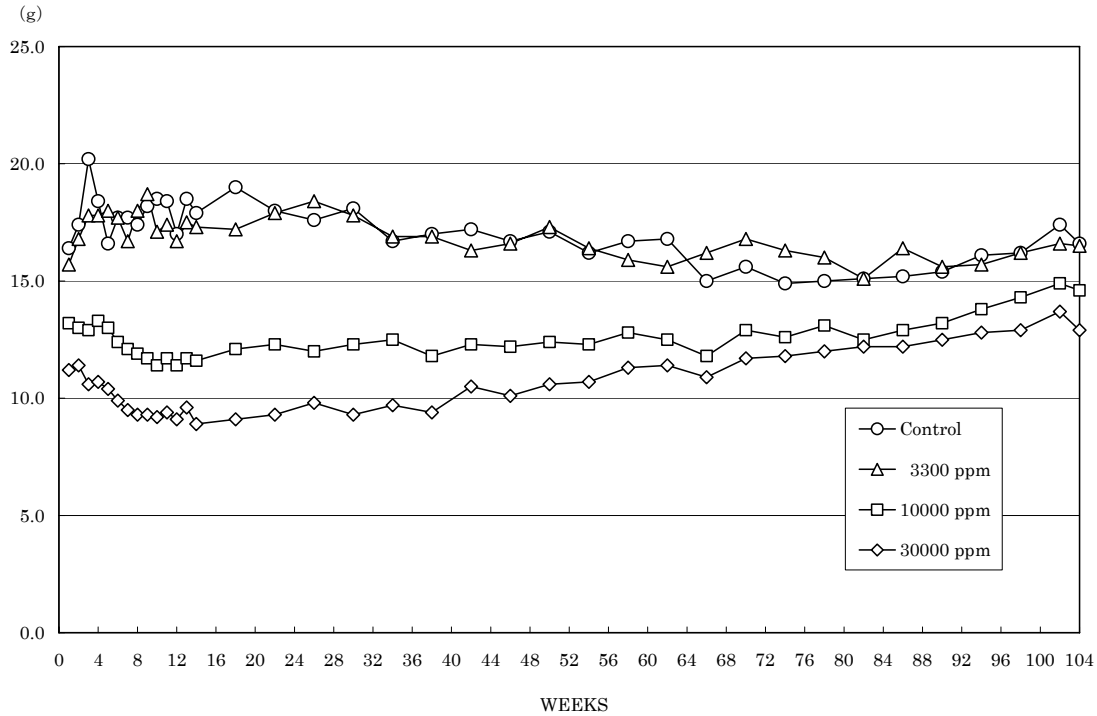
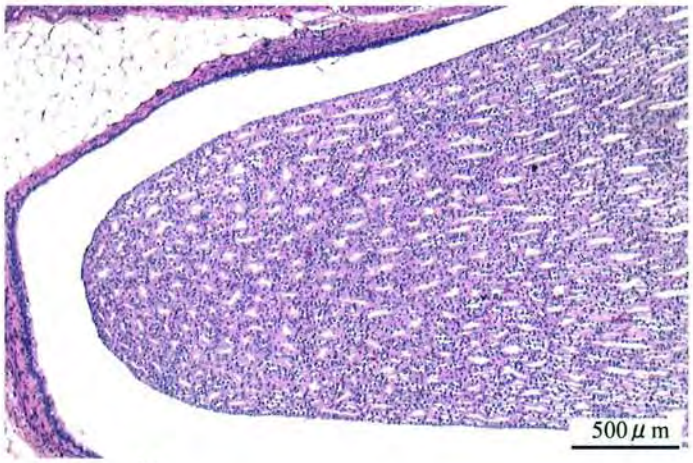
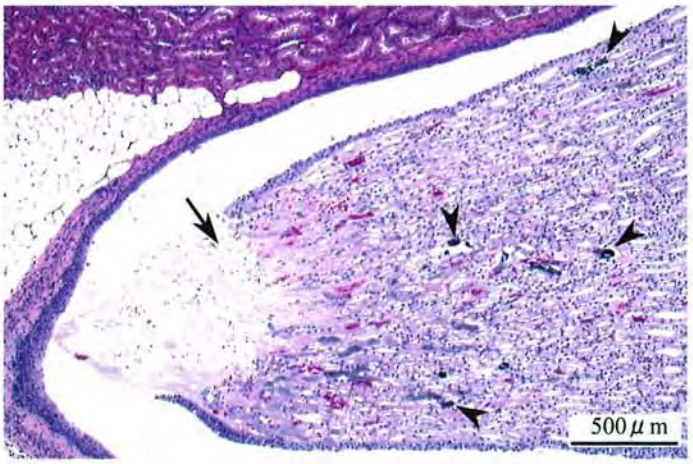


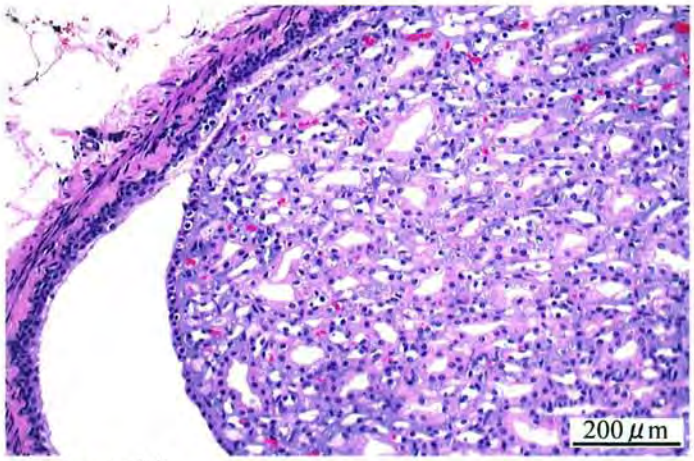
FIGURE 8 WATER CONSUMPTION CHANGES OF FEMALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF 2-METHYL-1-PROPANOL



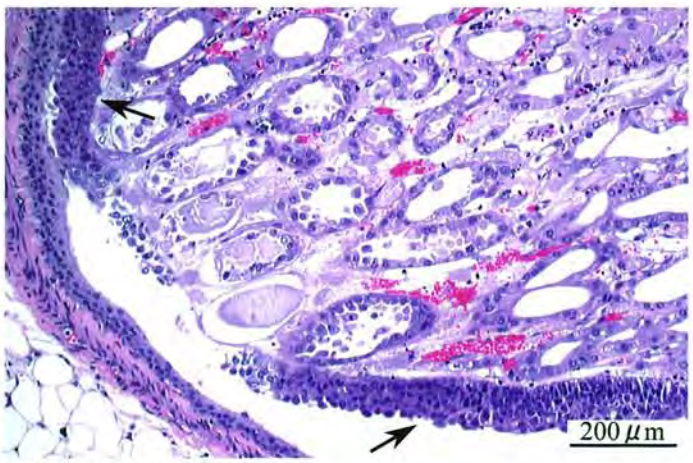
Photograph1
Kidney: Normal
Rat, Female, Control, Animal No. 0612-2012 (H&E)



Photograph 2
Kidney: Papillary necrosis (Arrow), Mineralization of papilla (Arrowheads)
Rat, Female, 30000ppm, Animal No. 0612-2346 (H&E)



Photograph 3
Kidney: Normal
Rat, Female, Control, Animal No. 0612-2036 (H&E)



Photograph 4
Kidney: Urothelial hyperplasia of pelvis (Arrows)
Rat, Female, 30000ppm, Animal No. 0612-2337 (H&E)