Summary of Inhalation Carcinogenicity Study of 1-Bromobutane in F344 Rats

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Japan Bioassay Research Center

Japan Industrial Safety and Health Association

PREFACE

The tests were contracted and supported by the Ministry of Health, Labour and Welfare of Japan. The tests were conducted by Japan Bioassay Research Center (JBRC) and the report was prepared by JBRC and peer reviewed by outside expert pathologist. Complete report was submitted to Ministry of Health, Labour and Welfare of Japan on March 31, 2008.

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

Summary of Inhalation Carcinogenicity Study of 1-Bromobutane in F344 Rats

Purpose, materials and methods

1-Bromobutane (CAS No. 109-65-9) is a colorless liquid with a boiling point of 101.3°C. It is soluble in alcohol and ether and insoluble in water.

The carcinogenicity and chronic toxicity of 1-bromobutane (greater than 99.7% pure) were examined by inhalation exposure using groups of F344/DuCrlCrlj (Fischer) rats. Each group of test animals consisted of either 50 male or 50 female rats. Test animals were exposed to 1-bromobutane vapor at target concentrations of 0 (clean air), 125, 250 or 500 ppm (v/v) for 6 hours/day, 5 days/week for 2 years (104 weeks). Both sexes were exposed to each concentration of 1-bromobutane vapor. The highest dose level was chosen so as not to exceed the maximum tolerated dose (MTD), based on both growth rate and toxicity in a previous 13-week toxicity study. The identity of the 1-Bromobutane used in these experiments was confirmed by both infrared spectrometry and mass spectrometry, and it was analyzed by gas chromatography before and after its use to affirm its stability. Stainless-steel inhalation exposure chambers (volume: 8500 L) were used throughout the 2-year exposure period. 1-Bromobutane vapor-air mixtures were generated by bubbling clean air through 1-bromobutane liquid and the mixtures supplied to the inhalation exposure chambers. Air concentrations of 1-bromobutane vapor in the inhalation exposure chambers were monitored at 15 min intervals by gas chromatography. The animals were observed daily for clinical signs and mortality. Body weight and food consumption were measured once a week for the first 14 weeks and every 4 weeks thereafter. All animals, including those found dead or in a moribund state as well as those surviving to the end of the 2-year exposure period, underwent complete necropsy. Urinalysis was performed near the end of the exposure period. 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 1-Bromobutane 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

The body weights of the highest exposure groups, 500 ppm-exposed males and females, were slightly decreased: terminal body weights of the 500 ppm-exposed males and females were suppressed to 83% and 90% of their respective controls. No other significant differences in survival rate or clinical symptoms were found between the 1-bromobutane-exposed groups of either sex and their controls.

No significant increase in the incidence of neoplastic lesions was found in any of the 1-bromobutane-exposed groups of either sex compared with their controls. There was, however, an increase in the incidence of eosinophilic change in the respiratory epithelium in males exposed to 500 ppm 1-bromobutaneand an increase in the severity of eosinophilic change in the olfactory epithelium of males exposed to 250 ppm and 500 ppm 1-bromobutane.

Conclusions

There was no evidence of carcinogenic activity of 1-bromobutane in male or female rats.

SELECTED TABLES

TABLE A

CONCENTRATIONS OF 1 - BROMOBUTANE IN THE INHALATION CHAMBER OF THE 2-YEAR INHALATION STUDY

CONCENTRATIONS OF 1-BROMOBUTANE IN THE INHALATION CHAMBER OF THE 2-YEAR INHALATION STUDY

Group Name	Concentration(ppm) Mean ± S.D.
Control	0.0 ± 0.0
125 ppm	125.2 ± 0.4
250 ppm	250.5 ± 1.0
500 ppm	500.8 ± 1.9

TABLE D1

BODY WEIGHT CHANGES AND SURVIVAL ANIMAL NUMBERS : MALE

STUDY NO. : 0560
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>	125 ppm Av. Wt.	125 ppm % of cont. <50>	125 ppm No. of Surviv.	250 ppm Av. Wt.	250 ppm % of cont. <50>	250 ppm No. of Surviv.	500 ppm Av. Wt.	500 ppm % of cont. <50>	500 ppm No. of Surviv.
0-0	116 (50)	50/50	116 (50)	100	50/50	116 (50)	100	50/50	116 (50)	100	50/50
1-7	144 (50)	50/50	142 (50)	99	50/50	137 (50)	95	50/50	132 (50)	92	50/50
2-7	177 (50)	50/50	175 (50)	99	50/50	167 (50)	94	50/50	159 (50)	90	50/50
3-7	203 (50)	50/50	202 (50)	100	50/50	192 (50)	95	50/50	179 (50)	88	50/50
4-7	225 (50)	50/50	224 (50)	100	50/50	212 (50)	94	50/50	198 (50)	88	50/50
5-7	241 (50)	50/50	242 (50)	100	50/50	229 (50)	95	50/50	213 (50)	88	50/50
6-7	256 (50)	50/50	257 (50)	100	50/50	244 (50)	95	50/50	225 (50)	88	50/50
7-7	272 (50)	50/50	272 (50)	100	50/50	259 (50)	95	50/50	238 (50)	88	50/50
8-7	284 (50)	50/50	285 (50)	100	50/50	272 (50)	96	50/50	250 (50)	88	50/50
9-7	294 (50)	50/50	295 (50)	100	50/50	284 (50)	97	50/50	260 (50)	88	50/50
10-7	304 (50)	50/50	305 (50)	100	50/50	292 (50)	96	50/50	267 (50)	88	50/50
11-7	312 (50)	50/50	313 (50)	100	50/50	301 (50)	96	50/50	272 (50)	87	50/50
12-7	318 (50)	50/50	319 (50)	100	50/50	306 (50)	96	50/50	277 (50)	87	50/50
13-7	325 (50)	50/50	328 (50)	101	50/50	313 (50)	96	50/50	283 (50)	87	50/50
14-7	331 (50)	50/50	334 (50)	101	50/50	318 (50)	96	50/50	288 (50)	87	50/50
18-7	343 (50)	50/50	350 (50)	102	50/50	333 (50)	97	50/50	303 (50)	88	50/50
22-7	362 (50)	50/50	369 (50)	102	50/50	352 (50)	97	50/50	317 (50)	88	50/50
26-7	377 (50)	50/50	383 (50)	102	50/50	366 (49)	97	49/50	332 (50)	88	50/50
30-7	385 (50)	50/50	390 (50)	101	50/50	374 (49)	97	49/50	338 (50)	88	50/50
34-7	393 (50)	50/50	400 (50)	102	50/50	385 (49)	98	49/50	347 (50)	88	50/50
38-7	400 (50)	50/50	409 (50)	102	50/50	393 (49)	98	49/50	355 (50)	89	50/50
42-7	410 (50)	50/50	419 (50)	102	50/50	401 (49)	98	49/50	361 (50)	88	50/50
46-7	416 (50)	50/50	423 (50)	102	50/50	407 (49)	98	49/50	366 (50)	88	50/50
50-7	421 (50)	50/50	427 (50)	101	50/50	410 (49)	97	49/50	370 (50)	88	50/50
54-7	426 (50)	50/50	431 (50)	101	50/50	414 (49)	97	49/50	371 (50)	87	50/50
58-7	427 (50)	50/50	434 (50)	102	50/50	418 (49)	98	49/50	375 (50)	88	50/50
62-7	431 (50)	50/50	437 (50)	101	50/50	422 (49)	98	49/50	381 (50)	88	50/50
66-7	434 (50)	50/50	440 (50)	101	50/50	421 (49)	97	49/50	378 (50)	87	50/50
70-7	433 (50)	50/50	443 (49)	102	49/50	422 (49)	97	49/50	378 (49)	87	49/50
74-7	436 (50)	50/50	444 (47)	102	47/50	425 (49)	97	49/50	378 (49)	87	49/50
78-7	443 (49)	49/50	443 (46)	100	46/50	425 (49)	96	49/50	378 (48)	85	48/50
82-7	442 (48)	48/50	442 (44)	100	44/50	422 (49)	95	49/50	374 (48)	85	48/50
86-7	440 (48)	48/50	441 (43)	100	43/50	419 (49)	95	49/50	373 (45)	85	45/50
90-7	437 (47)	47/50	439 (42)	100	42/50	418 (48)	96	48/50	372 (44)	85	44/50
94-7	432 (46)	46/50	430 (40)	100	40/50	414 (46)	96	46/50	364 (43)	84	43/50
98-7	428 (45)	45/50	429 (38)	100	38/50	415 (44)	97	44/50	363 (41)	85	41/50
102-7	414 (44)	44/50	423 (37)	102	37/50	410 (43)	99	43/50	355 (40)	86	40/50
104-7	420 (39)	39/50	417 (35)	99	35/50	405 (41)	96	41/50	350 (37)	83	37/50

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

TABLE D2

BODY WEIGHT CHANGES AND SURVIVAL ANIMAL NUMBERS : FEMALE

STUDY NO. : 0560
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>	125 ppm Av. Wt.	125 ppm % of cont. <50>	125 ppm No. of Surviv.	250 ppm Av. Wt.	250 ppm % of cont. <50>	250 ppm No. of Surviv.	500 ppm Av. Wt.	500 ppm % of cont. <50>	500 ppm No. of Surviv.
0-0	96 (50)	50/50	96 (50)	100	50/50	96 (50)	100	50/50	96 (50)	100	50/50
1-7	110 (50)	50/50	108 (50)	98	50/50	107 (50)	97	50/50	104 (50)	95	50/50
2-7	123 (50)	50/50	122 (50)	99	50/50	120 (50)	98	50/50	116 (50)	94	50/50
3-7	134 (50)	50/50	133 (50)	99	50/50	130 (50)	97	50/50	125 (50)	93	50/50
4-7	143 (50)	50/50	142 (50)	99	50/50	139 (50)	97	50/50	132 (50)	92	50/50
5-7	152 (50)	50/50	149 (50)	98	50/50	148 (50)	97	50/50	140 (50)	92	50/50
6-7	156 (50)	50/50	154 (50)	99	50/50	153 (50)	98	50/50	145 (50)	93	50/50
7-7	162 (50)	50/50	160 (50)	99	50/50	160 (50)	99	50/50	150 (50)	93	50/50
8-7	165 (50)	50/50	166 (50)	101	50/50	164 (50)	99	50/50	155 (50)	94	50/50
9-7	169 (50)	50/50	169 (50)	100	50/50	168 (50)	99	50/50	160 (50)	95	50/50
10-7	173 (50)	50/50	174 (50)	101	50/50	173 (50)	100	50/50	163 (50)	94	50/50
11-7	177 (50)	50/50	179 (50)	101	50/50	177 (50)	100	50/50	167 (50)	94	50/50
12-7	178 (50)	50/50	180 (50)	101	50/50	180 (50)	101	50/50	168 (50)	94	50/50
13-7	180 (50)	50/50	183 (50)	102	50/50	182 (50)	101	50/50	172 (50)	96	50/50
14-7	183 (50)	50/50	185 (50)	101	50/50	183 (50)	100	50/50	172 (50)	94	50/50
18-7	188 (50)	50/50	191 (50)	102	50/50	191 (50)	102	50/50	179 (50)	95	50/50
22-7	195 (50)	50/50	197 (50)	101	50/50	198 (50)	102	50/50	186 (50)	95	50/50
26-7	201 (50)	50/50	202 (50)	100	50/50	202 (50)	100	50/50	190 (50)	95	50/50
30-7	204 (50)	50/50	206 (50)	101	50/50	208 (50)	102	50/50	195 (50)	96	50/50
34-7	209 (50)	50/50	210 (50)	100	50/50	214 (50)	102	50/50	200 (50)	96	50/50
38-7	215 (50)	50/50	216 (50)	100	50/50	218 (50)	101	50/50	206 (50)	96	50/50
42-7	221 (50)	50/50	223 (50)	101	50/50	226 (50)	102	50/50	214 (50)	97	50/50
46-7	225 (50)	50/50	224 (50)	100	50/50	228 (50)	101	50/50	215 (50)	96	50/50
50-7	228 (50)	50/50	230 (50)	101	50/50	233 (50)	102	50/50	219 (50)	96	50/50
54-7	235 (50)	50/50	233 (50)	99	50/50	236 (50)	100	50/50	220 (50)	94	50/50
58-7	238 (50)	50/50	237 (49)	100	49/50	240 (50)	101	50/50	225 (50)	95	50/50
62-7	242 (50)	50/50	242 (49)	100	49/50	242 (50)	100	50/50	228 (50)	94	50/50
66-7	249 (50)	50/50	250 (49)	100	49/50	250 (50)	100	50/50	236 (49)	95	49/50
70-7	255 (50)	50/50	255 (49)	100	49/50	253 (50)	99	50/50	240 (47)	94	47/50
74-7	261 (49)	49/50	260 (48)	100	48/50	259 (50)	99	50/50	245 (46)	94	46/50
78-7	266 (49)	49/50	265 (48)	100	48/50	261 (50)	98	50/50	247 (46)	93	46/50
82-7	269 (49)	49/50	270 (48)	100	48/50	265 (50)	99	50/50	253 (44)	94	44/50
86-7	273 (46)	46/50	273 (48)	100	48/50	267 (47)	98	47/50	255 (44)	93	44/50
90-7	279 (45)	45/50	275 (48)	99	48/50	270 (46)	97	46/50	257 (44)	92	44/50
94-7	277 (43)	43/50	275 (47)	99	47/50	271 (45)	98	45/50	258 (44)	93	44/50
98-7	283 (39)	39/50	277 (46)	98	46/50	274 (43)	97	43/50	256 (42)	90	42/50
102-7	284 (38)	38/50	279 (44)	98	44/50	276 (42)	97	42/50	256 (38)	90	38/50
104-7	283 (38)	38/50	279 (43)	99	43/50	273 (41)	96	41/50	254 (37)	90	37/50

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

TABLE D3

BODY WEIGHT CHANGES : MALE

STUDY NO. : 0560
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	116± 6	144± 8	177± 9	203± 9	225± 10	241± 11	256± 11
125 ppm	116± 6	142± 8	175± 10	202± 10	224± 10	242± 12	257± 13
250 ppm	116± 6	137± 8**	167± 10**	192± 11**	212± 12**	229± 13**	244± 13**
500 ppm	116± 6	132± 8**	159± 8**	179± 9**	198± 10**	213± 10**	225± 11**

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

(HAN260)

STUDY NO. : 0560
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	272± 12	284± 12	294± 13	304± 14	312± 15	318± 16	325± 17
125 ppm	272± 14	285± 14	295± 14	305± 15	313± 15	319± 15	328± 16
250 ppm	259± 14**	272± 15**	284± 16**	292± 16**	301± 17**	306± 17**	313± 17**
500 ppm	238± 12**	250± 13**	260± 14**	267± 14**	272± 14**	277± 15**	283± 15**

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

(HAN260)

BAIS 4

STUDY NO. : 0560
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	331± 17	343± 18	362± 18	377± 18	385± 20	393± 20	400± 22
125 ppm	334± 16	350± 17	369± 19	383± 21	390± 21	400± 22	409± 24
250 ppm	318± 18**	333± 18**	352± 19*	366± 18*	374± 18*	385± 20	393± 19
500 ppm	288± 15**	303± 16**	317± 18**	332± 19**	338± 20**	347± 21**	355± 22**

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

(HAN260)

BAIS 4

STUDY NO. : 0560
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	410± 22	416± 23	421± 23	426± 24	427± 24	431± 24	434± 26
125 ppm	419± 26	423± 27	427± 28	431± 28	434± 30	437± 30	440± 30
250 ppm	401± 20	407± 19	410± 20	414± 22	418± 21	422± 23	421± 22*
500 ppm	361± 23**	366± 24**	370± 24**	371± 23**	375± 23**	381± 24**	378± 23**

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

(HAN260)

BAIS 4

STUDY NO. : 0560
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	433± 37	436± 39	443± 25	442± 26	440± 27	437± 27	432± 31
125 ppm	443± 29	444± 30	443± 30	442± 32	441± 31	439± 33	430± 35
250 ppm	422± 23**	425± 24*	425± 24**	422± 28**	419± 31**	418± 29**	414± 28*
500 ppm	378± 23**	378± 24**	378± 22**	374± 26**	373± 29**	372± 24**	364± 29**

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

(HAN260)

STUDY NO. : 0560
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	428± 32	414± 44	420± 32
125 ppm	429± 32	423± 30	417± 30
250 ppm	415± 26	410± 27	405± 26
500 ppm	363± 25**	355± 29**	350± 29**

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

(HAN260)

TABLE D4

BODY WEIGHT CHANGES : FEMALE

STUDY NO. : 0560
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	96± 5	110± 6	123± 6	134± 6	143± 7	152± 8	156± 7
125 ppm	96± 5	108± 6	122± 6	133± 6	142± 7	149± 7	154± 7
250 ppm	96± 5	107± 6**	120± 7*	130± 7**	139± 7*	148± 8	153± 8
500 ppm	96± 5	104± 5**	116± 5**	125± 5**	132± 6**	140± 5**	145± 7**

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

(HAN260)

BAIS 4

STUDY NO. : 0560
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	162± 8	165± 9	169± 9	173± 10	177± 9	178± 9	180± 9
125 ppm	160± 8	166± 9	169± 9	174± 9	179± 9	180± 10	183± 10
250 ppm	160± 9	164± 9	168± 9	173± 9	177± 10	180± 10	182± 10
500 ppm	150± 6**	155± 7**	160± 7**	163± 7**	167± 8**	168± 8**	172± 8**

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

STUDY NO. : 0560
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	183± 10	188± 10	195± 11	201± 12	204± 12	209± 13	215± 14
125 ppm	185± 10	191± 10	197± 12	202± 11	206± 12	210± 13	216± 13
250 ppm	183± 11	191± 11	198± 12	202± 13	208± 12	214± 13	218± 14
500 ppm	172± 8**	179± 8**	186± 9**	190± 10**	195± 10**	200± 10**	206± 10**

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

(HAN260)

BAIS 4

STUDY NO. : 0560
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	221± 14	225± 15	228± 16	235± 17	238± 19	242± 21	249± 22
125 ppm	223± 14	224± 14	230± 16	233± 16	237± 17	242± 17	250± 19
250 ppm	226± 16	228± 17	233± 17	236± 19	240± 21	242± 21	250± 24
500 ppm	214± 11*	215± 11**	219± 11**	220± 11**	225± 13**	228± 13**	236± 14**

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

STUDY NO. : 0560
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	255± 23	261± 22	266± 26	269± 32	273± 32	279± 36	277± 23
125 ppm	255± 21	260± 21	265± 21	270± 22	273± 23	275± 23	275± 25
250 ppm	253± 25	259± 26	261± 27	265± 24	267± 27	270± 26	271± 29
500 ppm	240± 14**	245± 14**	247± 17**	253± 16**	255± 18**	257± 19**	258± 23**

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

(HAN260)

BAIS 4

STUDY NO. : 0560
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	283± 23	284± 22	283± 23
125 ppm	277± 27	279± 25	279± 24
250 ppm	274± 27	276± 28	273± 28
500 ppm	256± 24**	256± 22**	254± 22**

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

TABLE E1

FOOD CONSUMPTION CHANGES AND SURVIVAL ANIMAL NUMBERS : MALE

STUDY NO. : 0560
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>	125 ppm Av. FC.	125 ppm % of cont. <50>	125 ppm No. of Surviv.	250 ppm Av. FC.	250 ppm % of cont. <50>	250 ppm No. of Surviv.	500 ppm Av. FC.	500 ppm % of cont. <50>	500 ppm No. of Surviv.
1-7	13.7 (50)	50/50	13.0 (50)	95	50/50	12.3 (50)	90	50/50	11.2 (50)	82	50/50
2-7	15.5 (50)	50/50	15.7 (50)	101	50/50	14.7 (50)	95	50/50	13.9 (50)	90	50/50
3-7	16.5 (50)	50/50	16.7 (50)	101	50/50	16.0 (50)	97	50/50	15.6 (50)	95	50/50
4-7	16.3 (50)	50/50	17.2 (50)	106	50/50	16.7 (50)	102	50/50	16.7 (50)	102	50/50
5-7	16.3 (50)	50/50	17.2 (50)	106	50/50	17.2 (50)	106	50/50	17.3 (50)	106	50/50
6-7	16.0 (50)	50/50	17.0 (50)	106	50/50	17.2 (50)	108	50/50	17.4 (50)	109	50/50
7-7	16.5 (50)	50/50	17.6 (50)	107	50/50	17.7 (50)	107	50/50	17.9 (50)	108	50/50
8-7	16.4 (50)	50/50	17.0 (50)	104	50/50	17.1 (50)	104	50/50	17.4 (50)	106	50/50
9-7	16.6 (50)	50/50	17.3 (50)	104	50/50	17.5 (50)	105	50/50	18.2 (50)	110	50/50
10-7	16.2 (50)	50/50	16.9 (50)	104	50/50	17.0 (50)	105	50/50	18.3 (50)	113	50/50
11-7	16.4 (45)	50/50	17.4 (50)	106	50/50	17.4 (50)	106	50/50	18.4 (50)	112	50/50
12-7	16.3 (50)	50/50	17.2 (50)	106	50/50	17.1 (50)	105	50/50	18.4 (50)	113	50/50
13-7	16.2 (50)	50/50	17.3 (50)	107	50/50	17.1 (50)	106	50/50	18.5 (50)	114	50/50
14-7	16.2 (50)	50/50	17.0 (50)	105	50/50	17.0 (50)	105	50/50	18.5 (50)	114	50/50
18-7	16.2 (50)	50/50	17.4 (50)	107	50/50	17.2 (50)	106	50/50	19.3 (50)	119	50/50
22-7	16.2 (50)	50/50	17.2 (50)	106	50/50	17.0 (50)	105	50/50	18.9 (50)	117	50/50
26-7	16.2 (50)	50/50	16.6 (50)	102	50/50	16.6 (49)	102	49/50	17.9 (50)	110	50/50
30-7	16.2 (50)	50/50	17.2 (50)	106	50/50	17.2 (49)	106	49/50	19.0 (50)	117	50/50
34-7	16.1 (50)	50/50	16.8 (50)	104	50/50	16.9 (49)	105	49/50	18.6 (50)	116	50/50
38-7	16.1 (50)	50/50	17.1 (50)	106	50/50	17.2 (49)	107	49/50	18.9 (50)	117	50/50
42-7	16.5 (50)	50/50	17.0 (50)	103	50/50	16.9 (49)	102	49/50	18.5 (50)	112	50/50
46-7	16.1 (50)	50/50	16.8 (50)	104	50/50	16.7 (49)	104	49/50	18.2 (50)	113	50/50
50-7	16.5 (50)	50/50	17.1 (50)	104	50/50	17.2 (49)	104	49/50	18.6 (50)	113	50/50
54-7	16.5 (50)	50/50	16.9 (50)	102	50/50	17.1 (49)	104	49/50	18.4 (50)	112	50/50
58-7	17.0 (50)	50/50	17.6 (50)	104	50/50	17.7 (49)	104	49/50	19.1 (50)	112	50/50
62-7	16.6 (50)	50/50	16.9 (50)	102	50/50	16.9 (49)	102	49/50	17.7 (50)	107	50/50
66-7	16.7 (50)	50/50	17.6 (50)	105	50/50	17.2 (49)	103	49/50	18.2 (50)	109	50/50
70-7	16.8 (50)	50/50	17.6 (49)	105	49/50	17.1 (49)	102	49/50	18.1 (49)	108	49/50
74-7	16.5 (50)	50/50	17.2 (47)	104	47/50	17.1 (49)	104	49/50	17.9 (49)	108	49/50
78-7	16.4 (49)	49/50	16.7 (46)	102	46/50	16.9 (49)	103	49/50	17.3 (48)	105	48/50
82-7	16.4 (48)	48/50	16.8 (44)	102	44/50	16.7 (49)	102	49/50	17.3 (48)	105	48/50
86-7	16.3 (48)	48/50	16.8 (43)	103	43/50	16.6 (49)	102	49/50	16.8 (45)	103	45/50
90-7	17.0 (47)	47/50	17.1 (42)	101	42/50	17.0 (48)	100	48/50	17.1 (44)	101	44/50
94-7	16.8 (46)	46/50	16.8 (40)	100	40/50	16.6 (46)	99	46/50	16.9 (43)	101	43/50
98-7	17.0 (45)	45/50	17.0 (38)	100	38/50	16.7 (44)	98	44/50	17.2 (41)	101	41/50
102-7	15.6 (44)	44/50	16.7 (37)	107	37/50	16.9 (43)	108	43/50	17.4 (40)	112	40/50
104-7	16.6 (39)	39/50	16.3 (35)	98	35/50	16.5 (41)	99	41/50	17.1 (37)	103	37/50

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

TABLE E2

FOOD CONSUMPTION CHANGES AND SURVIVAL ANIMAL NUMBERS : FEMALE

STUDY NO. : 0560
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>	125 ppm Av. FC.	125 ppm % of cont. <50>	125 ppm No. of Surviv.	250 ppm Av. FC.	250 ppm % of cont. <50>	250 ppm No. of Surviv.	500 ppm Av. FC.	500 ppm % of cont. <50>	500 ppm No. of Surviv.
1-7	10.3 (50)	50/50	10.1 (50)	98	50/50	9.6 (50)	93	50/50	9.0 (50)	87	50/50
2-7	10.9 (50)	50/50	11.1 (50)	102	50/50	10.7 (50)	98	50/50	10.6 (50)	97	50/50
3-7	11.1 (50)	50/50	11.4 (50)	103	50/50	11.3 (50)	102	50/50	11.0 (50)	99	50/50
4-7	10.9 (50)	50/50	11.3 (50)	104	50/50	11.5 (50)	106	50/50	11.2 (50)	103	50/50
5-7	11.1 (50)	50/50	11.4 (50)	103	50/50	12.1 (50)	109	50/50	11.8 (50)	106	50/50
6-7	10.5 (50)	50/50	11.0 (50)	105	50/50	11.4 (50)	109	50/50	11.7 (50)	111	50/50
7-7	10.7 (50)	50/50	11.2 (50)	105	50/50	11.8 (50)	110	50/50	11.9 (50)	111	50/50
8-7	10.4 (50)	50/50	10.7 (50)	103	50/50	10.9 (50)	105	50/50	11.3 (50)	109	50/50
9-7	10.5 (50)	50/50	11.2 (50)	107	50/50	11.8 (50)	112	50/50	12.1 (50)	115	50/50
10-7	10.3 (50)	50/50	11.0 (50)	107	50/50	11.5 (50)	112	50/50	12.2 (50)	118	50/50
11-7	10.6 (50)	50/50	11.5 (50)	108	50/50	12.1 (50)	114	50/50	12.6 (50)	119	50/50
12-7	10.1 (50)	50/50	11.2 (50)	111	50/50	11.8 (50)	117	50/50	12.4 (50)	123	50/50
13-7	10.5 (50)	50/50	11.3 (50)	108	50/50	11.7 (50)	111	50/50	12.9 (50)	123	50/50
14-7	10.6 (50)	50/50	11.2 (50)	106	50/50	11.3 (50)	107	50/50	12.4 (50)	117	50/50
18-7	10.6 (50)	50/50	11.3 (50)	107	50/50	11.8 (50)	111	50/50	13.6 (50)	128	50/50
22-7	10.4 (50)	50/50	10.9 (50)	105	50/50	11.7 (50)	113	50/50	13.2 (50)	127	50/50
26-7	10.6 (50)	50/50	10.5 (50)	99	50/50	10.5 (50)	99	50/50	11.6 (50)	109	50/50
30-7	10.3 (50)	50/50	11.1 (50)	108	50/50	11.6 (50)	113	50/50	13.4 (50)	130	50/50
34-7	10.6 (50)	50/50	11.0 (50)	104	50/50	12.0 (50)	113	50/50	12.8 (50)	121	50/50
38-7	11.0 (50)	50/50	11.3 (50)	103	50/50	12.1 (50)	110	50/50	13.6 (50)	124	50/50
42-7	10.8 (50)	50/50	11.2 (50)	104	50/50	12.2 (50)	113	50/50	13.6 (50)	126	50/50
46-7	11.3 (50)	50/50	11.1 (50)	98	50/50	11.9 (50)	105	50/50	12.8 (50)	113	50/50
50-7	11.0 (50)	50/50	11.6 (50)	105	50/50	12.4 (50)	113	50/50	13.8 (50)	125	50/50
54-7	11.4 (50)	50/50	11.5 (50)	101	50/50	12.1 (50)	106	50/50	13.4 (50)	118	50/50
58-7	11.6 (50)	50/50	11.9 (49)	103	49/50	12.5 (50)	108	50/50	14.0 (50)	121	50/50
62-7	11.1 (50)	50/50	11.6 (49)	105	49/50	11.9 (50)	107	50/50	12.8 (50)	115	50/50
66-7	11.4 (50)	50/50	12.1 (49)	106	49/50	12.5 (50)	110	50/50	13.6 (49)	119	49/50
70-7	11.8 (50)	50/50	11.9 (49)	101	49/50	12.3 (50)	104	50/50	13.4 (47)	114	47/50
74-7	11.7 (49)	49/50	12.0 (48)	103	48/50	12.4 (50)	106	50/50	13.1 (46)	112	46/50
78-7	11.5 (49)	49/50	11.8 (48)	103	48/50	11.7 (50)	102	50/50	12.5 (46)	109	46/50
82-7	11.5 (49)	49/50	11.9 (48)	103	48/50	12.4 (50)	108	50/50	13.3 (44)	116	44/50
86-7	11.3 (46)	46/50	11.9 (48)	105	48/50	11.9 (47)	105	47/50	12.8 (44)	113	44/50
90-7	12.6 (44)	45/50	12.2 (48)	97	48/50	12.8 (46)	102	46/50	13.5 (44)	107	44/50
94-7	12.1 (43)	43/50	12.2 (47)	101	47/50	12.7 (45)	105	45/50	13.1 (44)	108	44/50
98-7	12.7 (39)	39/50	12.2 (46)	96	46/50	12.3 (43)	97	43/50	12.7 (42)	100	42/50
102-7	12.4 (38)	38/50	12.5 (44)	101	44/50	12.6 (42)	102	42/50	13.0 (38)	105	38/50
104-7	12.4 (38)	38/50	12.1 (43)	98	43/50	12.2 (41)	98	41/50	13.0 (37)	105	37/50

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

TABLE E3

FOOD CONSUMPTION CHANGES : MALE

STUDY NO. : 0560
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(6)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	13.7± 0.8	15.5± 0.9	16.5± 1.1	16.3± 1.1	16.3± 0.9	16.0± 0.9	16.5± 0.8
125 ppm	13.0± 0.9**	15.7± 1.2	16.7± 1.0	17.2± 1.2**	17.2± 1.3**	17.0± 1.3**	17.6± 1.3**
250 ppm	12.3± 1.0**	14.7± 1.3**	16.0± 1.5	16.7± 1.5	17.2± 1.6**	17.2± 1.5**	17.7± 1.4**
500 ppm	11.2± 0.8**	13.9± 1.2**	15.6± 1.3**	16.7± 1.3	17.3± 1.4**	17.4± 1.3**	17.9± 1.3**

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

(HAN260)

BAIS 4

STUDY NO. : 0560
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	16.4± 0.9	16.6± 0.9	16.2± 1.1	16.4± 1.1	16.3± 1.1	16.2± 1.0	16.2± 1.0
125 ppm	17.0± 1.2**	17.3± 1.1**	16.9± 1.1*	17.4± 1.2**	17.2± 1.2**	17.3± 1.1**	17.0± 1.1**
250 ppm	17.1± 1.4**	17.5± 1.5**	17.0± 1.3**	17.4± 1.5**	17.1± 1.5**	17.1± 1.4**	17.0± 1.4**
500 ppm	17.4± 1.4**	18.2± 1.4**	18.3± 1.5**	18.4± 1.5**	18.4± 1.5**	18.5± 1.4**	18.5± 1.5**

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

STUDY NO. : 0560
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	16.2± 1.1	16.2± 0.9	16.2± 0.9	16.2± 1.0	16.1± 0.9	16.1± 0.9	16.5± 0.8
125 ppm	17.4± 1.4**	17.2± 1.4**	16.6± 1.3	17.2± 1.2**	16.8± 1.1**	17.1± 1.0**	17.0± 1.1**
250 ppm	17.2± 1.5**	17.0± 1.3**	16.6± 0.9	17.2± 0.9**	16.9± 0.9**	17.2± 1.1**	16.9± 0.9*
500 ppm	19.3± 1.9**	18.9± 1.9**	17.9± 1.7**	19.0± 1.8**	18.6± 1.9**	18.9± 2.0**	18.5± 2.0**

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

(HAN260)

BAIS 4

STUDY NO. : 0560
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 46-7(7)	50-7(7)	54-7(7)	58-7(7)	62-7(7)	66-7(7)	70-7(7)
Control	16.1± 0.7	16.5± 0.8	16.5± 0.9	17.0± 0.9	16.6± 1.0	16.7± 0.9	16.8± 1.2
125 ppm	16.8± 1.2**	17.1± 1.2**	16.9± 1.2	17.6± 1.3**	16.9± 1.1	17.6± 1.1**	17.6± 1.1**
250 ppm	16.7± 1.0*	17.2± 0.9**	17.1± 1.1**	17.7± 1.0**	16.9± 1.2	17.2± 1.2	17.1± 1.0
500 ppm	18.2± 1.8**	18.6± 1.8**	18.4± 1.7**	19.1± 2.1**	17.7± 1.6**	18.2± 2.1**	18.1± 2.0**

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

(HAN260)

STUDY NO. : 0560
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	16.5± 1.1	16.4± 1.0	16.4± 1.2	16.3± 2.1	17.0± 1.4	16.8± 2.0	17.0± 1.6
125 ppm	17.2± 1.1**	16.7± 1.2	16.8± 1.3	16.8± 1.1	17.1± 1.6	16.8± 2.0	17.0± 1.4
250 ppm	17.1± 1.2	16.9± 1.6	16.7± 1.3	16.6± 1.8	17.0± 1.7	16.6± 1.9	16.7± 1.3
500 ppm	17.9± 2.0**	17.3± 1.8	17.3± 2.7*	16.8± 3.0	17.1± 2.1	16.9± 2.6	17.2± 2.2

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

STUDY NO. : 0560
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 102-7(7)	104-7(7)
Control	15.6± 3.2	16.6± 1.6
125 ppm	16.7± 2.8	16.3± 1.5
250 ppm	16.9± 1.5	16.5± 1.3
500 ppm	17.4± 2.3*	17.1± 2.4

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

TABLE E4

FOOD CONSUMPTION CHANGES : FEMALE

STUDY NO. : 0560
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(6)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	10.3± 0.8	10.9± 0.8	11.1± 0.8	10.9± 0.7	11.1± 0.9	10.5± 0.7	10.7± 0.8
125 ppm	10.1± 0.7	11.1± 0.9	11.4± 0.8	11.3± 0.9	11.4± 0.8	11.0± 0.9*	11.2± 0.8*
250 ppm	9.6± 0.8**	10.7± 0.8	11.3± 0.9	11.5± 1.0**	12.1± 1.0**	11.4± 0.9**	11.8± 1.0**
500 ppm	9.0± 0.5**	10.6± 0.6	11.0± 0.7	11.2± 0.7	11.8± 0.7**	11.7± 0.9**	11.9± 1.0**

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

(HAN260)

STUDY NO. : 0560
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)	14-7(7)
Control	10.4± 0.9	10.5± 1.0	10.3± 0.8	10.6± 0.7	10.1± 0.7	10.5± 0.7	10.6± 0.8
125 ppm	10.7± 1.0	11.2± 1.1**	11.0± 0.8**	11.5± 0.9**	11.2± 1.0**	11.3± 1.2**	11.2± 1.0**
250 ppm	10.9± 0.8*	11.8± 1.1**	11.5± 0.9**	12.1± 1.0**	11.8± 1.0**	11.7± 1.0**	11.3± 0.9**
500 ppm	11.3± 0.9**	12.1± 0.8**	12.2± 0.9**	12.6± 0.9**	12.4± 1.0**	12.9± 1.0**	12.4± 1.0**

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

(HAN260)

BAIS 4

STUDY NO. : 0560
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration 18-7(7)	week-day(effective) 22-7(7)	26-7(7)	30-7(7)	34-7(7)	38-7(7)	42-7(7)
Control	10.6± 0.9	10.4± 0.9	10.6± 0.8	10.3± 1.0	10.6± 0.8	11.0± 1.0	10.8± 0.9
125 ppm	11.3± 1.1**	10.9± 1.0	10.5± 0.8	11.1± 1.1**	11.0± 1.1	11.3± 1.0	11.2± 1.0
250 ppm	11.8± 1.1**	11.7± 1.0**	10.5± 0.7	11.6± 0.7**	12.0± 1.0**	12.1± 1.2**	12.2± 1.2**
500 ppm	13.6± 1.2**	13.2± 1.2**	11.6± 1.0**	13.4± 1.4**	12.8± 1.1**	13.6± 1.3**	13.6± 1.5**

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

(HAN260)

BAIS 4

STUDY NO. : 0560
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration 46-7(7)	week-day(effective) 50-7(7)	54-7(7)	58-7(7)	62-7(7)	66-7(7)	70-7(7)
Control	11.3± 0.9	11.0± 1.1	11.4± 1.1	11.6± 1.0	11.1± 1.0	11.4± 1.0	11.8± 0.8
125 ppm	11.1± 0.9	11.6± 1.1*	11.5± 1.0	11.9± 1.0	11.6± 1.0	12.1± 1.1**	11.9± 1.0
250 ppm	11.9± 1.3	12.4± 0.9**	12.1± 1.2**	12.5± 1.1**	11.9± 1.0**	12.5± 1.1**	12.3± 1.1
500 ppm	12.8± 1.3**	13.8± 1.3**	13.4± 1.2**	14.0± 1.8**	12.8± 0.9**	13.6± 1.3**	13.4± 1.1**

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

(HAN260)

BAIS 4

STUDY NO. : 0560
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 104
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 74-7(7)	78-7(7)	82-7(7)	86-7(7)	90-7(7)	94-7(7)	98-7(7)
Control	11.7± 1.1	11.5± 1.2	11.5± 1.2	11.3± 1.3	12.6± 1.0	12.1± 1.4	12.7± 1.3
125 ppm	12.0± 1.0	11.8± 0.9	11.9± 1.1	11.9± 1.2*	12.2± 1.3	12.2± 1.2	12.2± 1.8
250 ppm	12.4± 1.0**	11.7± 1.0	12.4± 1.0**	11.9± 1.1*	12.8± 1.1	12.7± 1.2	12.3± 1.1
500 ppm	13.1± 1.1**	12.5± 1.7**	13.3± 1.0**	12.8± 1.1**	13.5± 1.0**	13.1± 1.3**	12.7± 1.9

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

(HAN260)

BAIS 4

STUDY NO. : 0560
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	12.4± 1.0	12.4± 1.3
125 ppm	12.5± 1.2	12.1± 1.3
250 ppm	12.6± 1.2	12.2± 1.2
500 ppm	13.0± 0.9	13.0± 1.0

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

(HAN260)

TABLE F1

HEMATOLOGY : MALE

STUDY NO. : 0560
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	38	8.13± 1.50	14.3± 2.8	39.5± 6.6	48.8± 2.8	17.5± 1.2	35.9± 1.7	811± 248
125 ppm	34	9.10± 1.22*	15.8± 2.0*	43.3± 5.1*	47.7± 1.7*	17.4± 0.6	36.5± 0.8	813± 119
250 ppm	41	8.96± 1.50*	15.5± 2.3	42.3± 5.7	47.7± 3.9**	17.4± 1.0	36.5± 1.2	834± 225
500 ppm	37	9.26± 1.60**	15.5± 2.8	42.8± 6.7	46.4± 2.2**	16.8± 0.8**	36.1± 1.6	906± 202**

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

(HCL070)

BAIS 4

STUDY NO. : 0560
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	38	4.3±	3.8
125 ppm	34	2.9±	2.5*
250 ppm	41	3.9±	6.2**
500 ppm	37	3.4±	3.6**

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

(HCL070)

BAIS 4

STUDY NO. : 0560
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	38	11.86± 22.20	0± 1	47± 13	2± 1	0± 0	5± 2	40± 11	6± 18
125 ppm	34	6.68± 1.80	0± 1	46± 10	2± 1	0± 0	6± 1	45± 10	1± 1
250 ppm	41	7.72± 3.85	0± 1	46± 9	2± 1	0± 0	6± 2	43± 10	3± 13
500 ppm	37	9.08± 5.44*	0± 1	47± 10	1± 1	0± 0	6± 2	44± 9	1± 3

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

(HCL070)

BAIS 4

TABLE F2

HEMATOLOGY : FEMALE

STUDY NO. : 0560
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	38	7.73± 1.28	14.5± 2.3	39.0± 5.7	50.7± 3.1	18.8± 0.7	37.1± 1.4	683± 226
125 ppm	43	8.02± 1.08	14.9± 2.0	40.3± 4.2	50.6± 3.3	18.6± 1.1	36.8± 1.8	680± 222
250 ppm	41	7.92± 1.21	14.9± 2.3	40.1± 5.0	51.3± 5.5	18.9± 1.7	36.8± 2.0	660± 181
500 ppm	37	8.37± 0.40**	15.8± 0.7**	42.4± 1.3**	50.7± 1.4	18.8± 0.3	37.2± 0.8	724± 84**

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

(HCL070)

BAIS 4

STUDY NO. : 0560
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	38	3.6±	4.9
125 ppm	43	3.8±	5.5
250 ppm	41	3.8±	5.4
500 ppm	37	2.6±	1.7

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

(HCL070)

BAIS 4

STUDY NO. : 0560
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHER
Control	38	5.17± 3.73	1± 1	44± 14	2± 1	0± 0	5± 2	47± 14	2± 7
125 ppm	43	4.55± 5.32	1± 1	38± 14	2± 1	0± 0	5± 2	51± 14	4± 14
250 ppm	41	7.90± 18.80	1± 1	34± 11**	2± 2	0± 0	5± 2	51± 14	7± 22
500 ppm	37	4.40± 1.66	0± 1	39± 8	2± 1	0± 0	6± 1**	52± 8	1± 1

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

(HCL070)

BAIS 4

TABLE G1

BIOCHEMISTRY : MALE

STUDY NO. : 0560
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	38	6.7± 0.3	3.0± 0.3	0.8± 0.1	0.17± 0.06	156± 24	207± 80	184± 131
125 ppm	34	6.9± 0.3	3.0± 0.2	0.8± 0.1	0.16± 0.04	158± 19	249± 70*	213± 99
250 ppm	41	6.8± 0.2	3.0± 0.2	0.8± 0.1	0.20± 0.24	155± 23	259± 65**	245± 130
500 ppm	37	6.7± 0.4	2.8± 0.3**	0.7± 0.1**	0.18± 0.08	155± 14	260± 79**	274± 126**

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

(HCL074)

BAIS 4

STUDY NO. : 0560
ANIMAL : RAT F344/DuCr1Cr1j[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	38	302± 114	98± 116	39± 19	228± 241	226± 148	7± 4	139± 176
125 ppm	34	351± 96	69± 18	31± 6	173± 56	166± 58*	9± 5	99± 26
250 ppm	41	358± 88*	86± 89	35± 18	187± 127	200± 69	13± 8**	95± 21
500 ppm	37	364± 111*	82± 42	41± 24	162± 50	237± 101	17± 10**	96± 25

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

(HCL074)

BAIS 4

STUDY NO. : 0560
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	38	21.3± 11.5	0.7± 0.4	143± 2	3.6± 0.4	105± 2	10.8± 0.6	4.4± 1.4
125 ppm	34	20.6± 4.6	0.6± 0.1	142± 1**	3.7± 0.3	107± 1**	10.8± 0.4	4.0± 0.7
250 ppm	41	20.8± 4.9	0.6± 0.1	142± 2**	3.7± 0.3	110± 2**	10.7± 0.4	4.1± 0.6
500 ppm	37	23.0± 6.2**	0.6± 0.1	142± 1**	3.8± 0.3*	112± 3**	10.9± 0.8	4.4± 0.6

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

(HCL074)

TABLE G2

BIOCHEMISTRY : FEMALE

STUDY NO. : 0560
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	TOTAL PROTEIN g／dℓ		ALBUMIN g／dℓ		A/G RATIO		T-BILIRUBIN mg／dℓ		GLUCOSE mg／dℓ		T-CHOLESTEROL mg／dℓ		TRIGLYCERIDE mg／dℓ	
Control	38	7.0±	0.4	3.6±	0.3	1.1±	0.2	0.14±	0.07	143±	18	140±	26	87±	59
125 ppm	43	7.1±	0.3	3.7±	0.3	1.1±	0.1	0.13±	0.04	145±	17	149±	35	98±	64
250 ppm	41	7.1±	0.3	3.7±	0.3	1.1±	0.1	0.15±	0.14	148±	19	160±	47	128±	91*
500 ppm	37	6.9±	0.3	3.4±	0.2**	1.0±	0.1**	0.12±	0.01	149±	13	192±	70**	134±	89*

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

(HCL074)

STUDY NO. : 0560
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dℓ	AST IU/ℓ	ALT IU/ℓ	LDH IU/ℓ	ALP IU/ℓ	G-GTP IU/ℓ	CK IU/ℓ
Control	38	256± 48	121± 78	48± 20	212± 81	132± 58	3± 2	91± 25
125 ppm	43	271± 64	116± 84	48± 21	206± 72	119± 59	3± 2	85± 25
250 ppm	41	286± 73	141± 146	56± 46	211± 112	131± 75	4± 5	91± 70
500 ppm	37	324± 110**	90± 38	43± 18	164± 47*	113± 42	3± 2*	75± 22**

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

(HCL074)

STUDY NO. : 0560
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (105W)

Group Name	NO. of Animals	UREA NITROGEN mg／dℓ	CREATININE mg／dℓ	SODIUM mEq／ℓ	POTASSIUM mEq／ℓ	CHLORIDE mEq／ℓ	CALCIUM mg／dℓ	INORGANIC PHOSPHORUS mg／dℓ
Control	38	17.1± 1.8	0.5± 0.0	142± 1	3.4± 0.4	104± 2	10.5± 0.3	3.7± 0.7
125 ppm	43	17.2± 2.1	0.5± 0.1	142± 1	3.3± 0.4	107± 2**	10.6± 0.4	3.5± 0.7
250 ppm	41	17.5± 2.0	0.5± 0.0	142± 1	3.4± 0.4	109± 2**	10.6± 0.3	3.8± 0.9
500 ppm	37	18.0± 2.4	0.5± 0.0	140± 1**	3.4± 0.3	111± 4**	10.5± 0.4	3.9± 0.6

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

(HCL074)

BAIS 4

TABLE H1

URINALYSIS : MALE

STUDY NO. : 0560
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	42	0	0	6	7	19	8	2		0	0	0	3	31	8		42	0	0	0	0	0		41	1	0	0	0	0		42	0	0	0	
125 ppm	35	0	0	4	10	14	7	0		0	0	0	2	27	6		35	0	0	0	0	0		35	0	0	0	0	0		35	0	0	0	
250 ppm	42	0	1	6	12	18	5	0		0	0	0	1	25	16		42	0	0	0	0	0		40	1	1	0	0	0		42	0	0	0	
500 ppm	40	0	1	8	13	14	3	1		0	0	0	0	11	29	**	40	0	0	0	0	0		39	1	0	0	0	0		40	0	0	0	

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01

Test of CHI SQUARE

(HCL101)

BAIS 4

STUDY NO. : 0560
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	Occult blood −	±	+	2+	3+	CHI	Urobilinogen ±	+	2+	3+	4+	CHI
Control	42	42	0	0	0	0		42	0	0	0	0	
125 ppm	35	35	0	0	0	0		35	0	0	0	0	
250 ppm	42	40	0	1	0	1		42	0	0	0	0	
500 ppm	40	39	0	0	0	1		40	0	0	0	0	

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

(HCL101)

TABLE H2

URINALYSIS : FEMALE

STUDY NO. : 0560
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Bilirubin −	+	2+	3+	CHI
Control	38	0	0	1	3	9	21	4		0	2	7	6	16	7		38	0	0	0	0	0		27	11	0	0	0	0		38	0	0	0	
125 ppm	44	0	2	5	7	13	15	2		0	4	6	10	18	6		44	0	0	0	0	0		29	15	0	0	0	0		44	0	0	0	
250 ppm	41	0	0	6	11	12	9	3	**	0	2	5	6	21	7		41	0	0	0	0	0		30	11	0	0	0	0		41	0	0	0	
500 ppm	37	0	0	5	7	11	13	1		0	0	0	0	18	19	**	37	0	0	0	0	0		21	16	0	0	0	0		37	0	0	0	

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01

Test of CHI SQUARE

(HCL101)

STUDY NO. : 0560
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	38	38	0	0	0	0		38	0	0	0	0	
125 ppm	44	41	2	0	1	0		44	0	0	0	0	
250 ppm	41	40	0	0	0	1		41	0	0	0	0	
500 ppm	37	36	0	0	1	0		37	0	0	0	0	

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

(HCL101)

BAIS 4

TABLE J1

ORGAN WEIGHT, ABSOLUTE : MALE

STUDY NO. : 0560
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	Body Weight	ADRENALS	TESTES	HEART	LUNGS	KIDNEYS
Control	39	394± 34	0.071± 0.013	3.177± 1.347	1.217± 0.125	1.390± 0.227	2.761± 0.447
125 ppm	35	390± 29	0.106± 0.174	3.681± 1.275	1.207± 0.092	1.405± 0.359	2.880± 0.337
250 ppm	41	380± 26	0.098± 0.151	3.297± 1.276	1.191± 0.088	1.381± 0.141	2.843± 0.236
500 ppm	37	326± 28**	0.067± 0.018	4.008± 1.605*	1.165± 0.141*	1.321± 0.095	2.752± 0.264

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

(HCL040)

BAIS 4

STUDY NO. : 0560
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	SPLEEN		LIVER		BRAIN	
Control	39	1.337±	1.360	11.551±	1.295	2.032±	0.044
125 ppm	35	0.993±	0.400*	12.328±	1.684	2.043±	0.044
250 ppm	41	1.240±	1.647*	12.787±	1.806**	2.027±	0.043
500 ppm	37	0.916±	0.178**	12.564±	2.184*	1.978±	0.047**

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

(HCL040)

TABLE J2

ORGAN WEIGHT, ABSOLUTE : FEMALE

STUDY NO. : 0560
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	Body Weight	ADRENALS	OVARIES	HEART	LUNGS	KIDNEYS
Control	38	264± 22	0.090± 0.135	0.240± 0.725	0.859± 0.061	0.928± 0.065	1.720± 0.131
125 ppm	43	260± 24	0.068± 0.008	0.115± 0.027	0.857± 0.073	0.938± 0.157	1.713± 0.127
250 ppm	41	255± 27	0.068± 0.013	0.139± 0.126	0.882± 0.086	0.990± 0.248	1.709± 0.128
500 ppm	37	237± 22**	0.065± 0.005	0.118± 0.020	0.875± 0.060	0.947± 0.049	1.758± 0.104

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

(HCL040)

BAIS 4

STUDY NO. : 0560
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	SPLEEN		LIVER		BRAIN	
Control	38	0.624±	0.289	6.690±	1.131	1.862±	0.040
125 ppm	43	0.617±	0.401	6.759±	1.061	1.836±	0.036**
250 ppm	41	0.974±	1.775	6.904±	1.462	1.829±	0.044**
500 ppm	37	0.526±	0.088	7.039±	0.689*	1.787±	0.029**

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

(HCL040)

TABLE K1

ORGAN WEIGHT, RELATIVE : MALE

STUDY NO. : 0560
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	Body Weight (g)	ADRENALS	TESTES	HEART	LUNGS	KIDNEYS
Control	39	394± 34	0.018± 0.004	0.805± 0.334	0.311± 0.042	0.357± 0.081	0.709± 0.159
125 ppm	35	390± 29	0.027± 0.047	0.941± 0.309	0.310± 0.027	0.361± 0.091	0.740± 0.088*
250 ppm	41	380± 26	0.026± 0.043	0.868± 0.327	0.314± 0.027	0.364± 0.042**	0.749± 0.061**
500 ppm	37	326± 28**	0.021± 0.005**	1.237± 0.496**	0.360± 0.051**	0.408± 0.038**	0.848± 0.093**

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

(HCL042)

STUDY NO. : 0560
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	SPLEEN	LIVER	BRAIN
Control	39	0.349± 0.410	2.954± 0.467	0.519± 0.044
125 ppm	35	0.254± 0.095*	3.161± 0.371	0.527± 0.041
250 ppm	41	0.330± 0.456	3.368± 0.459**	0.535± 0.035
500 ppm	37	0.283± 0.064	3.850± 0.517**	0.611± 0.048**

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

(HCL042)

TABLE K2

ORGAN WEIGHT, RELATIVE : FEMALE

STUDY NO. : 0560
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	Body Weight (g)	ADRENALS	OVARIES	HEART	LUNGS	KIDNEYS
Control	38	264± 22	0.034± 0.049	0.094± 0.293	0.326± 0.028	0.353± 0.035	0.653± 0.053
125 ppm	43	260± 24	0.026± 0.003	0.045± 0.012	0.330± 0.030	0.363± 0.069	0.661± 0.046
250 ppm	41	255± 27	0.027± 0.006	0.056± 0.054	0.349± 0.052*	0.392± 0.113**	0.675± 0.064
500 ppm	37	237± 22**	0.028± 0.004	0.050± 0.009	0.373± 0.044**	0.403± 0.039**	0.749± 0.091**

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

(HCL042)

STUDY NO. : 0560
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	SPLEEN	LIVER	BRAIN
Control	38	0.238± 0.116	2.532± 0.366	0.709± 0.056
125 ppm	43	0.240± 0.163	2.599± 0.375	0.711± 0.064
250 ppm	41	0.392± 0.724	2.719± 0.586*	0.724± 0.073
500 ppm	37	0.224± 0.041	2.995± 0.378**	0.762± 0.078**

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

(HCL042)

TABLE L1

HISTOPATHOLOGICAL FINDINGS :

NON-NEOPLASTIC LESIONS : MALE

ALL ANIMALS

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1 (%)	2 (%)	3 (%)	4 (%)	125 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)	250 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)	500 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)
{Integumentary system/appandage}																		
skin/app			<50>				<50>				<50>				<50>			
	scab		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)
subcutis			<50>				<50>				<50>				<50>			
	inflammation		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	epidermal cyst		0	0	0	0	2	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Respiratory system}																		
nasal cavit			<50>				<50>				<50>				<50>			
	hyperplasia:gland		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)
	eosinophilic change:olfactory epithelium		34	14	0	0	33	10	0	0	16	25	4	0 **	10	34	6	0 **
			(68)	(28)	(0)	(0)	(66)	(20)	(0)	(0)	(32)	(50)	(8)	(0)	(20)	(68)	(12)	(0)
	eosinophilic change:respiratory epithelium		26	0	0	0	28	0	0	0	31	0	0	0	44	0	0	0 **
			(52)	(0)	(0)	(0)	(56)	(0)	(0)	(0)	(62)	(0)	(0)	(0)	(88)	(0)	(0)	(0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1 (%)	2 (%)	3 (%)	4 (%)	125 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)	250 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)	500 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)
{Respiratory system}																		
nasal cavit			<50>				<50>				<50>				<50>			
	inflammation:foreign body		8	7	0	0	13	6	0	0	9	8	0	0	16	10	0	0
			(16)	(14)	(0)	(0)	(26)	(12)	(0)	(0)	(18)	(16)	(0)	(0)	(32)	(20)	(0)	(0)
	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)
	inflammation:olfactory epithelium		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)
	respiratory metaplasia:olfactory epithelium		4	0	0	0	1	0	0	0	2	0	0	0	8	0	0	0
			(8)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(16)	(0)	(0)	(0)
	respiratory metaplasia:gland		10	0	0	0	12	0	0	0	8	1	0	0	15	0	0	0
			(20)	(0)	(0)	(0)	(24)	(0)	(0)	(0)	(16)	(2)	(0)	(0)	(30)	(0)	(0)	(0)
	squamous cell metaplasia:respiratory epithelium		3	0	0	0	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)
	atrophy:olfactory epithelium		0	0	0	0	0	0	3	0	1	1	0	0	2	2	1	0
			(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(2)	(2)	(0)	(0)	(4)	(4)	(2)	(0)
lung			<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)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1 (%)	2 (%)	3 (%)	4 (%)	125 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)	250 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)	500 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)
{Respiratory system}																		
lung			<50>				<50>				<50>				<50>			
	edema		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)
	inflammation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	inflammatory infiltration		0 (0)	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)	0 (0)
	accumulation of foamy cells		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)
	bronchiolar-alveolar cell hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	4 (8)	2 (4)	0 (0)	0 * (0)	4 (8)	0 (0)	0 (0)	0 (0)	2 (4)	1 (2)	0 (0)	0 (0)
	inflammation:foreign body		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
{Hematopoietic system}																		
bone marrow			<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 / No. of Animals on Study / Grade	Control 50 1 (%)	2 (%)	3 (%)	4 (%)	125 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)	250 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)	500 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)
{Hematopoietic system}																		
bone marrow			<50>				<50>				<50>				<50>			
	increased hematopoiesis		5	0	0	0	3	2	0	0	7	0	0	0	5	0	0	0
			(10)	(0)	(0)	(0)	(6)	(4)	(0)	(0)	(14)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	granulopoiesis:increased		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)
	xanthogranuloma		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)
lymph node			<50>				<50>				<50>				<50>			
	lymphadenitis		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)
spleen			<50>				<50>				<50>				<50>			
	congestion		2	3	0	0	0	2	0	0	0	1	0	0	1	0	0	0
			(4)	(6)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(2)	(0)	(0)	(0)
	hemorrhage		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	deposit of hemosiderin		4	0	0	0	3	3	0	0	3	0	1	0	4	3	0	0
			(8)	(0)	(0)	(0)	(6)	(6)	(0)	(0)	(6)	(0)	(2)	(0)	(8)	(6)	(0)	(0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1 (%)	2 (%)	3 (%)	4 (%)	125 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)	250 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)	500 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)
{Hematopoietic system}																		
spleen																		
	fibrosis:focal		1 (2)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
		<50>					<50>				<50>				<50>			
	increased extramedullary hematopoiesis		7 (14)	3 (6)	0 (0)	0 (0)	4 (8)	2 (4)	2 (4)	0 (0)	1 (2)	4 (8)	0 (0)	0 (0)	2 (4)	3 (6)	1 (2)	0 (0)
{Circulatory system}																		
heart																		
	myocardial fibrosis		29 (58)	1 (2)	0 (0)	0 (0)	23 (46)	1 (2)	0 (0)	0 (0)	20 (40)	1 (2)	0 (0)	0 (0)	20 (40)	2 (4)	0 (0)	0 (0)
		<50>					<50>				<50>				<50>			
{Digestive system}																		
oral cavity																		
	squamous cell 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)
		<50>					<50>				<50>				<50>			
esophagus																		
	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)
		<50>					<50>				<50>				<50>			

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1 (%)	2 (%)	3 (%)	4 (%)	125 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)	250 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)	500 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)
{Digestive system}																		
stomach			<50>				<50>				<50>				<50>			
	ulcer:forestomach		2 (4)	0 (0)	2 (4)	1 (2)	2 (4)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	4 (8)	1 (2)
	hyperplasia:forestomach		2 (4)	1 (2)	0 (0)	0 (0)	3 (6)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	3 (6)	2 (4)	0 (0)	0 (0)
	erosion:glandular stomach		3 (6)	0 (0)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	2 (4)	1 (2)	0 (0)	0 (0)	7 (14)	0 (0)	0 (0)	0 (0)
	ulcer:glandular stomach		0 (0)	3 (6)	0 (0)	0 (0)	1 (2)	0 (0)	1 (2)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	3 (6)	1 (2)	0 (0)	0 (0)
	hyperplasia:glandular stomach		3 (6)	0 (0)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)
	mineralization:glandular stomach		0 (0)	1 (2)	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)
	dilated glands		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)
small intes			<50>				<50>				<50>				<50>			
	erosion		0 (0)	0 (0)	0 (0)	0 (0)	4 (8)	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				125 ppm				250 ppm				500 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																		
	herniation		<50>				<50>				<50>				<50>			
			6	0	0	0	9	0	0	0	6	0	0	0	3	0	0	0
			(12)	(0)	(0)	(0)	(18)	(0)	(0)	(0)	(12)	(0)	(0)	(0)	(6)	(0)	(0)	(0)
	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)
	necrosis:central		0	0	0	0	1	2	0	0	0	0	0	0	0	2	0	0
			(0)	(0)	(0)	(0)	(2)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)
	necrosis:focal		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	fatty change		0	2	1	0	1	1	1	0	0	0	0	0	0	0	0	0
			(0)	(4)	(2)	(0)	(2)	(2)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	fatty change:central		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)
	fatty change:peripheral		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)
	degeneration:central		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 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1 (%)	2 (%)	3 (%)	4 (%)	125 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)	250 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)	500 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)
{Digestive system}																		
liver			<50>				<50>				<50>				<50>			
	granulation		3 (6)	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)
	clear cell focus		7 (14)	1 (2)	0 (0)	0 (0)	11 (22)	3 (6)	0 (0)	0 (0)	8 (16)	0 (0)	0 (0)	0 (0)	6 (12)	0 (0)	0 (0)	0 (0)
	acidophilic cell focus		1 (2)	1 (2)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	basophilic cell focus		5 (10)	0 (0)	0 (0)	0 (0)	3 (6)	1 (2)	0 (0)	0 (0)	5 (10)	3 (6)	0 (0)	0 (0)	5 (10)	2 (4)	0 (0)	0 (0)
	spongiosis hepatis		3 (6)	1 (2)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	bile duct hyperplasia		7 (14)	42 (84)	0 (0)	0 (0)	9 (18)	40 (80)	0 (0)	0 (0)	2 (4)	47 (94)	0 (0)	0 (0)	5 (10)	45 (90)	0 (0)	0 (0)
pancreas			<50>				<50>				<50>				<50>			
	atrophy		9 (18)	8 (16)	1 (2)	0 (0)	5 (10)	4 (8)	0 (0)	0 (0)	9 (18)	2 (4)	2 (4)	0 (0)	5 (10)	5 (10)	0 (0)	0 (0)
	islet cell hyperplasia		1 (2)	2 (4)	0 (0)	0 (0)	2 (4)	1 (2)	2 (4)	0 (0)	1 (2)	1 (2)	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				125 ppm				250 ppm				500 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>			
	ectopic 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)
	cyst		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	scar		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)
	chronic nephropathy		11	22	11	5	16	14	17	0 *	8	18	22	0 *	8	25	16	1
			(22)	(44)	(22)	(10)	(32)	(28)	(34)	(0)	(16)	(36)	(44)	(0)	(16)	(50)	(32)	(2)
	hydronephrosis		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)
	tubular necrosis		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)
	papillary necrosis		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)
	mineralization:papilla		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	Control				125 ppm				250 ppm				500 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:pelvis		1	0	0	0	3	0	0	0	1	0	0	0	2	0	0	0
			(2)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	urothelial hyperplasia:pelvis		1	2	0	0	2	0	0	0	2	1	1	0	2	2	0	0
			(2)	(4)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(2)	(2)	(0)	(4)	(4)	(0)	(0)
	atypical tubule 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)
urin bladd			<50>				<50>				<50>				<50>			
	dilatation		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		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)
{Endocrine system}																		
pituitary			<50>				<50>				<50>				<50>			
	cyst		0	0	0	0	1	0	0	0	1	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(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				125 ppm				250 ppm				500 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Endocrine system}																		
pituitary			<50>				<50>				<50>				<50>			
	hyperplasia		2 (4)	9 (18)	0 (0)	0 (0)	3 (6)	10 (20)	0 (0)	0 (0)	2 (4)	6 (12)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 ** (0)
	Rathke pouch		0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	1 (2)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)
thyroid			<50>				<50>				<50>				<50>			
	follicular hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
	C-cell hyperplasia		14 (28)	4 (8)	1 (2)	0 (0)	13 (26)	3 (6)	2 (4)	0 (0)	13 (26)	6 (12)	0 (0)	0 (0)	14 (28)	2 (4)	0 (0)	0 (0)
adrenal			<50>				<50>				<50>				<50>			
	osseous metaplasia		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)
	hyperplasia:medulla		1 (2)	5 (10)	0 (0)	0 (0)	1 (2)	3 (6)	0 (0)	0 (0)	1 (2)	2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)
	focal fatty change:cortex		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1 (%)	2 (%)	3 (%)	4 (%)	125 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)	250 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)	500 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)
{Reproductive system}																		
testis			<50>				<50>				<50>				<50>			
	mineralization		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	arteritis		0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	interstitial cell hyperplasia		15	1	0	0	9	1	0	0	7	0	0	0	8	0	0	0
			(30)	(2)	(0)	(0)	(18)	(2)	(0)	(0)	(14)	(0)	(0)	(0)	(16)	(0)	(0)	(0)
prostate			<50>				<50>				<50>				<50>			
	inflammation		2	0	0	0	0	1	0	0	0	1	0	0	0	1	0	0
			(4)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)
	hyperplasia		12	1	0	0	7	5	0	0	6	2	0	0	6	1	0	0
			(24)	(2)	(0)	(0)	(14)	(10)	(0)	(0)	(12)	(4)	(0)	(0)	(12)	(2)	(0)	(0)
{Nervous system}																		
brain			<50>				<50>				<50>				<50>			
	necrosis:focal		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 1 (%)	2 (%)	3 (%)	4 (%)	125 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)	250 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)	500 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)
{Nervous system}																		
brain																		
	mineralization	<50>	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)
	dilatation:cerebral ventricle		0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
{Special sense organs/appendage}																		
eye																		
	cataract	<50>	3 (6)	2 (4)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	3 (6)	1 (2)	0 (0)	0 (0)	4 (8)	1 (2)	0 (0)	0 (0)
	retinal atrophy		2 (4)	3 (6)	2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	1 (2)	2 (4)	2 (4)
	keratitis		1 (2)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	iritis		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)
	degeneration:cornea		3 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	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				125 ppm				250 ppm				500 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Special sense organs/appendage}																		
eye																		
	squamous cell metaplasia:cornea		<50>				<50>				<50>				<50>			
			0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
Harder gl																		
	lymphocytic infiltration		<50>				<50>				<50>				<50>			
			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)
nasolacr d																		
	inflammation		<50>				<50>				<50>				<50>			
			0	0	0	0	1	0	0	0	0	2	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)
{Body cavities}																		
peritoneum																		
	abscess		<50>				<50>				<50>				<50>			
			0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)

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

TABLE L4

HISTOPATHOLOGICAL FINDINGS :

NON-NEOPLASTIC LESIONS : FEMALE

ALL ANIMALS

Organ	Findings	Group Name	Control				125 ppm				250 ppm				500 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Integumentary system/appandage}																		
subcutis			<50>				<50>				<50>				<50>			
	abscess		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)
{Respiratory system}																		
nasal cavit			<50>				<50>				<50>				<50>			
	goblet cell hyperplasia		0	0	0	0	0	0	0	0	0	1	0	0	0	3	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(6)	(0)	(0)
	eosinophilic change:olfactory epithelium		1	28	20	0	1	31	17	0	0	28	22	0	1	21	28	0
			(2)	(56)	(40)	(0)	(2)	(62)	(34)	(0)	(0)	(56)	(44)	(0)	(2)	(42)	(56)	(0)
	eosinophilic change:respiratory epithelium		37	7	0	0	41	7	0	0	38	11	0	0	37	11	0	0
			(74)	(14)	(0)	(0)	(82)	(14)	(0)	(0)	(76)	(22)	(0)	(0)	(74)	(22)	(0)	(0)
	inflammation:foreign body		2	0	0	0	1	0	0	0	0	0	0	0	2	0	0	0
			(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	inflammation:respiratory epithelium		1	0	0	0	1	1	0	0	0	1	0	0	1	0	0	0
			(2)	(0)	(0)	(0)	(2)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(2)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		1	0	0	0	3	0	0	0	5	0	0	0	3	0	0	0
			(2)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(6)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				125 ppm				250 ppm				500 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}																		
nasal cavit			<50>				<50>				<50>				<50>			
	respiratory metaplasia:gland		14	0	0	0	15	2	0	0	16	0	0	0	16	1	0	0
			(28)	(0)	(0)	(0)	(30)	(4)	(0)	(0)	(32)	(0)	(0)	(0)	(32)	(2)	(0)	(0)
	atrophy:olfactory epithelium		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)
larynx			<50>				<50>				<50>				<50>			
	inflammation		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)
lung			<50>				<50>				<50>				<50>			
	edema		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)
	inflammatory infiltration		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	accumulation of foamy cells		1	0	0	0	2	0	0	0	0	0	0	0	1	1	0	0
			(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(2)	(0)	(0)
	bronchiolar-alveolar cell hyperplasia		1	0	0	0	2	0	0	0	3	0	0	0	0	0	0	0
			(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(6)	(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				125 ppm				250 ppm				500 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>			
	inflammation:foreign body		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)
{Hematopoietic system}																		
bone marrow			<50>				<50>				<50>				<50>			
	granulation		0	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	increased hematopoiesis		6	1	0	0	4	1	0	0	4	2	0	0	6	1	0	0
			(12)	(2)	(0)	(0)	(8)	(2)	(0)	(0)	(8)	(4)	(0)	(0)	(12)	(2)	(0)	(0)
spleen			<50>				<50>				<50>				<50>			
	atrophy		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)
	congestion		0	0	0	0	0	0	0	0	1	0	0	0	0	1	1	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(2)	(2)	(0)
	deposit of hemosiderin		28	6	0	0	30	7	0	0	25	12	0	0	33	9	1	0
			(56)	(12)	(0)	(0)	(60)	(14)	(0)	(0)	(50)	(24)	(0)	(0)	(66)	(18)	(2)	(0)

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

Organ	Findings	Group Name	Control				125 ppm				250 ppm				500 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>			
	fibrosis:focal		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)
	increased extramedullary hematopoiesis		8	3	1	0	2	4	0	0	3	4	1	0	4	4	2	0
			(16)	(6)	(2)	(0)	(4)	(8)	(0)	(0)	(6)	(8)	(2)	(0)	(8)	(8)	(4)	(0)
{Circulatory system}																		
heart			<50>				<50>				<50>				<50>			
	necrosis:focal		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	myocardial fibrosis		6	0	0	0	11	0	0	0	5	0	0	0	8	0	0	0
			(12)	(0)	(0)	(0)	(22)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(16)	(0)	(0)	(0)
{Digestive system}																		
esophagus			<50>				<50>				<50>				<50>			
	inflammation		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				125 ppm				250 ppm				500 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>			
	inflammation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	ulcer:forestomach		1 (2)	0 (0)	0 (0)	1 (2)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	3 (6)	1 (2)	0 (0)	0 (0)
	hyperplasia:forestomach		2 (4)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	1 (2)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)
	erosion:glandular stomach		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	ulcer:glandular stomach		2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	2 (4)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)
	hyperplasia: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)
small intes			<50>				<50>				<50>				<50>			
	erosion		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)
liver			<50>				<50>				<50>				<50>			
	herniation		15 (30)	0 (0)	0 (0)	0 (0)	8 (16)	0 (0)	0 (0)	0 (0)	9 (18)	0 (0)	0 (0)	0 (0)	8 (16)	0 (0)	0 (0)	0 (0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1 (%)	2 (%)	3 (%)	4 (%)	125 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)	250 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)	500 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)
{Digestive system}																		
liver			<50>				<50>				<50>				<50>			
	peliosis-like lesion		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	necrosis:central		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	4 (8)	0 (0)	0 (0)	0 (0)
	necrosis:focal		3 (6)	2 (4)	0 (0)	0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	2 (4)	1 (2)	0 (0)	0 (0)
	fatty change		0 (0)	2 (4)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	fatty change:central		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)
	lymphocytic infiltration		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)
	granulation		7 (14)	3 (6)	0 (0)	0 (0)	5 (10)	1 (2)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)	10 (20)	0 (0)	0 (0)	0 (0)
	inflammatory cell nest		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1 (%)	Control 50 2 (%)	Control 50 3 (%)	Control 50 4 (%)	125 ppm 50 1 (%)	125 ppm 50 2 (%)	125 ppm 50 3 (%)	125 ppm 50 4 (%)	250 ppm 50 1 (%)	250 ppm 50 2 (%)	250 ppm 50 3 (%)	250 ppm 50 4 (%)	500 ppm 50 1 (%)	500 ppm 50 2 (%)	500 ppm 50 3 (%)	500 ppm 50 4 (%)
{Digestive system}																		
liver			<50>				<50>				<50>				<50>			
	fibrosis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	clear cell focus		1 (2)	1 (2)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)
	basophilic cell focus		17 (34)	5 (10)	0 (0)	0 (0)	21 (42)	4 (8)	0 (0)	0 (0)	22 (44)	0 (0)	0 (0)	0 (0)	9 (18)	1 (2)	0 (0)	0 * (0)
	bile duct hyperplasia		7 (14)	2 (4)	0 (0)	0 (0)	6 (12)	1 (2)	0 (0)	0 (0)	3 (6)	1 (2)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)
pancreas			<50>				<50>				<50>				<50>			
	atrophy		1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	4 (8)	1 (2)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)
	islet cell hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
{Urinary system}																		
kidney			<50>				<50>				<50>				<50>			
	chronic nephropathy		39 (78)	7 (14)	0 (0)	0 (0)	39 (78)	7 (14)	0 (0)	0 (0)	38 (76)	6 (12)	1 (2)	0 (0)	36 (72)	10 (20)	3 (6)	0 (0)

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

Organ	Findings	Group Name	Control				125 ppm				250 ppm				500 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>			
	hydronephrosis		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)
	tubular necrosis		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)	(0)	(0)	(0)	(0)	(0)
	mineralization:papilla		2	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
			(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)
	mineralization:pelvis		0	0	0	0	0	0	0	0	3	0	0	0	4	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(8)	(0)	(0)	(0)
	desquamation:pelvis		1	0	0	0	2	0	0	0	2	1	0	0	1	0	0	0
			(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(4)	(2)	(0)	(0)	(2)	(0)	(0)	(0)
	urothelial hyperplasia:pelvis		0	1	0	0	1	0	0	0	1	0	0	0	1	0	0	0
			(0)	(2)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
	atypical tubule hyperplasia		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
urin bladd			<50>				<50>				<50>				<50>			
	dilatation		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				125 ppm				250 ppm				500 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}																		
urin bladd			<50>				<50>				<50>				<50>			
	transitional 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)
{Endocrine system}																		
pituitary			<50>				<50>				<50>				<50>			
	angiectasis		1	0	0	0	0	2	0	0	0	0	0	0	0	1	0	0
			(2)	(0)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)
	cyst		4	4	0	0	4	0	0	0	6	1	0	0	3	0	0	0
			(8)	(8)	(0)	(0)	(8)	(0)	(0)	(0)	(12)	(2)	(0)	(0)	(6)	(0)	(0)	(0)
	hyperplasia		7	7	0	0	11	6	0	0	5	6	0	0	7	6	0	0
			(14)	(14)	(0)	(0)	(22)	(12)	(0)	(0)	(10)	(12)	(0)	(0)	(14)	(12)	(0)	(0)
	Rathke pouch		2	0	0	0	1	0	0	0	2	0	0	0	1	0	0	0
			(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(4)	(0)	(0)	(0)	(2)	(0)	(0)	(0)
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)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 50 1 (%)	2 (%)	3 (%)	4 (%)	125 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)	250 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)	500 ppm 50 1 (%)	2 (%)	3 (%)	4 (%)
{Endocrine system}																		
thyroid			<50>				<50>				<50>				<50>			
	C-cell hyperplasia		13 (26)	3 (6)	0 (0)	0 (0)	13 (26)	3 (6)	1 (2)	0 (0)	8 (16)	5 (10)	0 (0)	0 (0)	11 (22)	4 (8)	0 (0)	0 (0)
adrenal			<50>				<50>				<50>				<50>			
	peliosis-like lesion		0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hyperplasia:cortical cell		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hyperplasia:medulla		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	1 (2)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
	focal fatty change:cortex		8 (16)	4 (8)	0 (0)	0 (0)	5 (10)	4 (8)	0 (0)	0 (0)	5 (10)	2 (4)	0 (0)	0 (0)	10 (20)	3 (6)	0 (0)	0 (0)
{Reproductive system}																		
ovary			<50>				<50>				<50>				<50>			
	cyst		1 (2)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	3 (6)	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				125 ppm				250 ppm				500 ppm			
		No. of Animals on Study	50				50				50				50			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Reproductive system}																		
uterus			<50>				<50>				<50>				<50>			
	cystic endometrial hyperplasia		5	2	0	0	4	0	0	0	1	2	0	0	6	1	0	0
			(10)	(4)	(0)	(0)	(8)	(0)	(0)	(0)	(2)	(4)	(0)	(0)	(12)	(2)	(0)	(0)
{Nervous system}																		
brain			<50>				<50>				<50>				<50>			
	hemorrhage		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)
{Special sense organs/appendage}																		
eye			<50>				<50>				<50>				<50>			
	cataract		2	1	0	0	0	3	0	0	0	4	0	0	1	3	0	0
			(4)	(2)	(0)	(0)	(0)	(6)	(0)	(0)	(0)	(8)	(0)	(0)	(2)	(6)	(0)	(0)
	retinal atrophy		1	0	2	0	0	0	1	2	0	0	3	1	0	0	3	1
			(2)	(0)	(4)	(0)	(0)	(0)	(2)	(4)	(0)	(0)	(6)	(2)	(0)	(0)	(6)	(2)
	keratitis		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)

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				125 ppm 50				250 ppm 50				500 ppm 50			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Special sense organs/appendage}																		
eye			<50>				<50>				<50>				<50>			
	degeneration:cornea		1 (2)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)
Harder gl			<50>				<50>				<50>				<50>			
	degeneration		4 (8)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (6)	0 (0)	0 (0)	0 (0)
	lymphocytic infiltration		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)
nasolacr d			<50>				<50>				<50>				<50>			
	inflammation		1 (2)	5 (10)	0 (0)	0 (0)	0 (0)	5 (10)	0 (0)	0 (0)	0 (0)	5 (10)	1 (2)	0 (0)	0 (0)	6 (12)	0 (0)	0 (0)
{Musculoskeletal system}																		
muscle			<50>				<50>				<50>				<50>			
	fibrosis		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)
bone			<50>				<50>				<50>				<50>			
	osteosclerosis		3 (6)	0 (0)	0 (0)	0 (0)	2 (4)	2 (4)	0 (0)	0 (0)	3 (6)	2 (4)	2 (4)	0 (0)	1 (2)	2 (4)	0 (0)	0 (0)

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

Organ	Findings	Group Name	Control				125 ppm				250 ppm				500 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}																		
peritoneum			<50>				<50>				<50>				<50>			
	inflammation		0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

TABLE O1

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS : MALE

STUDY No. : 0560
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
SEX : MALE

NEOPLASTIC LESIONS-INCIDENCE AND STATISTICAL ANALYSIS

Group Name	Control	125 ppm	250 ppm	500 ppm
	SITE : subcutis			
	TUMOR : fibroma			
Tumor rate				
Overall rates(a)	3/50(6.0)	1/50(2.0)	5/50(10.0)	5/50(10.0)
Adjusted rates(b)	7.69	2.86	9.76	13.51
Terminal rates(c)	3/39(7.7)	1/35(2.9)	4/41(9.8)	5/37(13.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3942			
Prevalence method(d)	P = 0.1098			
Combined analysis(d)	P = 0.1088			
Cochran-Armitage test(e)	P = 0.2232			
Fisher Exact test(e)		P = 0.3087	P = 0.3575	P = 0.3575
	SITE : lung			
	TUMOR : bronchiolar-alveolar adenoma			
Tumor rate				
Overall rates(a)	2/50(4.0)	1/50(2.0)	3/50(6.0)	6/50(12.0)
Adjusted rates(b)	5.13	2.86	6.98	15.00
Terminal rates(c)	2/39(5.1)	1/35(2.9)	2/41(4.9)	5/37(13.5)
Statistical analysis				
Peto test				
Standard method(d)	P = --------			
Prevalence method(d)	P = 0.0252*			
Combined analysis(d)	P = -------			
Cochran-Armitage test(e)	P = 0.0441*			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.1343
	SITE : lung			
	TUMOR : bronchiolar-alveolar adenoma,bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	3/50(6.0)	1/50(2.0)	5/50(10.0)	7/50(14.0)
Adjusted rates(b)	7.69	2.86	11.63	17.50
Terminal rates(c)	3/39(7.7)	1/35(2.9)	4/41(9.8)	6/37(16.2)
Statistical analysis				
Peto test				
Standard method(d)	P = -------			
Prevalence method(d)	P = 0.0292*			
Combined analysis(d)	P = -------			
Cochran-Armitage test(e)	P = 0.0526			
Fisher Exact test(e)		P = 0.3087	P = 0.3575	P = 0.1589

Group Name	Control	125 ppm	250 ppm	500 ppm
SITE : spleen				
TUMOR : mononuclear cell leukemia				
Tumor rate				
Overall rates(a)	7/50(14.0)	4/50(8.0)	2/50(4.0)	1/50(2.0)
Adjusted rates(b)	12.82	5.71	2.44	0.0
Terminal rates(c)	5/39(12.8)	2/35(5.7)	1/41(2.4)	0/37(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.7385			
Prevalence method(d)	P = 0.9963			
Combined analysis(d)	P = 0.9916			
Cochran-Armitage test(e)	P = 0.0192*			
Fisher Exact test(e)		P = 0.2623	P = 0.0798	P = 0.0297*
SITE : stomach				
TUMOR : squamous cell papilloma, squamous cell carcinoma				
Tumor rate				
Overall rates(a)	0/50(0.0)	3/50(6.0)	0/50(0.0)	2/50(4.0)
Adjusted rates(b)	0.0	6.00	0.0	4.88
Terminal rates(c)	0/39(0.0)	2/35(5.7)	0/41(0.0)	1/37(2.7)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.2412			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.4908			
Fisher Exact test(e)		P = 0.1212	P = N.C.	P = 0.2475
SITE : liver				
TUMOR : hepatocellular adenoma				
Tumor rate				
Overall rates(a)	0/50(0.0)	1/50(2.0)	3/50(6.0)	3/50(6.0)
Adjusted rates(b)	0.0	2.86	7.32	7.50
Terminal rates(c)	0/39(0.0)	1/35(2.9)	3/41(7.3)	2/37(5.4)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.0455*			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.0791			
Fisher Exact test(e)		P = 0.5000	P = 0.1212	P = 0.1212

Group Name	Control	125 ppm	250 ppm	500 ppm
SITE : liver				
TUMOR : hepatocellular adenoma, hepatocellular carcinoma				
Tumor rate				
Overall rates(a)	0/50(0.0)	1/50(2.0)	4/50(8.0)	3/50(6.0)
Adjusted rates(b)	0.0	2.86	9.76	7.50
Terminal rates(c)	0/39(0.0)	1/35(2.9)	4/41(9.8)	2/37(5.4)
Statistical analysis				
Peto test				
Standard method(d)	P = -------			
Prevalence method(d)	P = 0.0497*			
Combined analysis(d)	P = -------			
Cochran-Armitage test(e)	P = 0.0877			
Fisher Exact test(e)		P = 0.5000	P = 0.0587	P = 0.1212
SITE : pancreas				
TUMOR : islet cell adenoma				
Tumor rate				
Overall rates(a)	1/50(2.0)	7/50(14.0)	2/50(4.0)	1/50(2.0)
Adjusted rates(b)	2.27	17.50	4.88	2.50
Terminal rates(c)	0/39(0.0)	6/35(17.1)	2/41(4.9)	0/37(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = -------			
Prevalence method(d)	P = 0.7934			
Combined analysis(d)	P = -------			
Cochran-Armitage test(e)	P = 0.3728			
Fisher Exact test(e)		P = 0.0297*	P = 0.5000	P = 0.7525
SITE : pancreas				
TUMOR : islet cell adenoma, islet cell adenocarcinoma				
Tumor rate				
Overall rates(a)	2/50(4.0)	7/50(14.0)	3/50(6.0)	1/50(2.0)
Adjusted rates(b)	4.55	17.50	7.32	2.50
Terminal rates(c)	1/39(2.6)	6/35(17.1)	3/41(7.3)	0/37(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = -------			
Prevalence method(d)	P = 0.8528			
Combined analysis(d)	P = -------			
Cochran-Armitage test(e)	P = 0.2648			
Fisher Exact test(e)		P = 0.0798	P = 0.5000	P = 0.5000

Group Name	Control	125 ppm	250 ppm	500 ppm
	SITE : pituitary gland			
	TUMOR : adenoma			
Tumor rate				
Overall rates(a)	12/50(24.0)	9/50(18.0)	9/50(18.0)	5/50(10.0)
Adjusted rates(b)	17.95	15.38	19.57	7.32
Terminal rates(c)	7/39(17.9)	4/35(11.4)	7/41(17.1)	2/37(5.4)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.9168			
Prevalence method(d)	P = 0.8786			
Combined analysis(d)	P = 0.9607			
Cochran-Armitage test(e)	P = 0.0730			
Fisher Exact test(e)		P = 0.3121	P = 0.3121	P = 0.0542
	SITE : thyroid			
	TUMOR : C-cell adenoma			
Tumor rate				
Overall rates(a)	7/50(14.0)	11/50(22.0)	9/50(18.0)	6/50(12.0)
Adjusted rates(b)	17.95	27.78	20.45	13.64
Terminal rates(c)	7/39(17.9)	9/35(25.7)	8/41(19.5)	5/37(13.5)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.7099			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.5407			
Fisher Exact test(e)		P = 0.2178	P = 0.3929	P = 0.5000
	SITE : thyroid			
	TUMOR : C-cell carcinoma			
Tumor rate				
Overall rates(a)	6/50(12.0)	1/50(2.0)	3/50(6.0)	1/50(2.0)
Adjusted rates(b)	5.13	2.86	4.88	0.0
Terminal rates(c)	2/39(5.1)	1/35(2.9)	2/41(4.9)	0/37(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8887			
Prevalence method(d)	P = 0.8717			
Combined analysis(d)	P = 0.9570			
Cochran-Armitage test(e)	P = 0.0836			
Fisher Exact test(e)		P = 0.0559	P = 0.2435	P = 0.0559

Group Name	Control	125 ppm	250 ppm	500 ppm
SITE : thyroid				
TUMOR : C-cell adenoma, C-cell carcinoma				
Tumor rate				
Overall rates(a)	13/50(26.0)	12/50(24.0)	12/50(24.0)	7/50(14.0)
Adjusted rates(b)	23.08	30.56	25.00	13.95
Terminal rates(c)	9/39(23.1)	10/35(28.6)	10/41(24.4)	5/37(13.5)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.8887			
Prevalence method(d)	P = 0.8525			
Combined analysis(d)	P = 0.9287			
Cochran-Armitage test(e)	P = 0.1335			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.1054
SITE : thyroid				
TUMOR : follicular adenoma, follicular adenocarcinoma				
Tumor rate				
Overall rates(a)	0/50(0.0)	3/50(6.0)	2/50(4.0)	2/50(4.0)
Adjusted rates(b)	0.0	7.14	4.88	5.41
Terminal rates(c)	0/39(0.0)	2/35(5.7)	2/41(4.9)	2/37(5.4)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.2219			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.4744			
Fisher Exact test(e)		P = 0.1212	P = 0.2475	P = 0.2475
SITE : adrenal gland				
TUMOR : pheochromocytoma				
Tumor rate				
Overall rates(a)	4/50(8.0)	4/50(8.0)	1/50(2.0)	2/50(4.0)
Adjusted rates(b)	8.70	10.81	2.44	5.41
Terminal rates(c)	2/39(5.1)	3/35(8.6)	1/41(2.4)	2/37(5.4)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.8442			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.2709			
Fisher Exact test(e)		P = 0.6425	P = 0.1811	P = 0.3389

Group Name	Control	125 ppm	250 ppm	500 ppm
	SITE : adrenal gland TUMOR : pheochromocytoma:malignant			
Tumor rate				
Overall rates(a)	0/50(0.0)	1/50(2.0)	3/50(6.0)	0/50(0.0)
Adjusted rates(b)	0.0	2.86	4.88	0.0
Terminal rates(c)	0/39(0.0)	1/35(2.9)	2/41(4.9)	0/37(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4074			
Prevalence method(d)	P = 0.5147			
Combined analysis(d)	P = 0.4826			
Cochran-Armitage test(e)	P = 1.0000			
Fisher Exact test(e)		P = 0.5000	P = 0.1212	P = N.C.
	SITE : adrenal gland TUMOR : pheochromocytoma, pheochromocytoma:malignant			
Tumor rate				
Overall rates(a)	4/50(8.0)	5/50(10.0)	4/50(8.0)	2/50(4.0)
Adjusted rates(b)	8.70	13.51	7.32	5.41
Terminal rates(c)	2/39(5.1)	4/35(11.4)	3/41(7.3)	2/37(5.4)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.4074			
Prevalence method(d)	P = 0.8223			
Combined analysis(d)	P = 0.8008			
Cochran-Armitage test(e)	P = 0.3406			
Fisher Exact test(e)		P = 0.5000	P = 0.6425	P = 0.3389
	SITE : testis TUMOR : interstitial cell tumor			
Tumor rate				
Overall rates(a)	42/50(84.0)	44/50(88.0)	46/50(92.0)	43/50(86.0)
Adjusted rates(b)	94.87	97.37	97.73	97.50
Terminal rates(c)	37/39(94.9)	34/35(97.1)	40/41(97.6)	36/37(97.3)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.2809			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.8003			
Fisher Exact test(e)		P = 0.3871	P = 0.1783	P = 0.5000

Group Name	Control	125 ppm	250 ppm	500 ppm
	SITE : preputial/clitoral gland TUMOR : adenoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	2/50(4.0)	2/50(4.0)	3/50(6.0)
Adjusted rates(b)	2.38	2.86	4.88	5.41
Terminal rates(c)	0/39(0.0)	1/35(2.9)	2/41(4.9)	2/37(5.4)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.2456			
Prevalence method(d)	P = 0.2389			
Combined analysis(d)	P = 0.1663			
Cochran-Armitage test(e)	P = 0.3291			
Fisher Exact test(e)		P = 0.5000	P = 0.5000	P = 0.3087
	SITE : brain TUMOR : glioma			
Tumor rate				
Overall rates(a)	0/50(0.0)	3/50(6.0)	1/50(2.0)	1/50(2.0)
Adjusted rates(b)	0.0	8.57	0.0	0.0
Terminal rates(c)	0/39(0.0)	3/35(8.6)	0/41(0.0)	0/37(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1385			
Prevalence method(d)	P = 0.7956			
Combined analysis(d)	P = 0.4569			
Cochran-Armitage test(e)	P = 0.9390			
Fisher Exact test(e)		P = 0.1212	P = 0.5000	P = 0.5000

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

TABLE O2

NEOPLASTIC LESIONS-INCIDENCE

AND STATISTICAL ANALYSIS : FEMALE

Group Name	Control	125 ppm	250 ppm	500 ppm
	SITE : lung			
	TUMOR : bronchiolar-alveolar adenoma, bronchiolar-alveolar carcinoma			
Tumor rate				
Overall rates(a)	1/50(2.0)	0/50(0.0)	1/50(2.0)	3/50(6.0)
Adjusted rates(b)	2.33	0.0	2.44	8.11
Terminal rates(c)	0/38(0.0)	0/43(0.0)	1/41(2.4)	3/37(8.1)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.0595			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.1079			
Fisher Exact test(e)		P = 0.5000	P = 0.7525	P = 0.3087
	SITE : spleen			
	TUMOR : mononuclear cell leukemia			
Tumor rate				
Overall rates(a)	5/50(10.0)	5/50(10.0)	6/50(12.0)	1/50(2.0)
Adjusted rates(b)	7.89	6.98	7.32	0.0
Terminal rates(c)	3/38(7.9)	3/43(7.0)	3/41(7.3)	0/37(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.6530			
Prevalence method(d)	P = 0.9415			
Combined analysis(d)	P = 0.9206			
Cochran-Armitage test(e)	P = 0.1336			
Fisher Exact test(e)		P = 0.6297	P = 0.5000	P = 0.1022
	SITE : pituitary gland			
	TUMOR : adenoma			
Tumor rate				
Overall rates(a)	13/50(26.0)	14/50(28.0)	13/50(26.0)	7/50(14.0)
Adjusted rates(b)	23.68	27.91	26.83	16.22
Terminal rates(c)	9/38(23.7)	12/43(27.9)	11/41(26.8)	6/37(16.2)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.9002			
Prevalence method(d)	P = 0.8232			
Combined analysis(d)	P = 0.9256			
Cochran-Armitage test(e)	P = 0.1081			
Fisher Exact test(e)		P = 0.5000	P = 0.5900	P = 0.1054

Group Name	Control	125 ppm	250 ppm	500 ppm
	SITE : pituitary gland TUMOR : adenoma, adenocarcinoma			
Tumor rate				
Overall rates(a)	14/50(28.0)	14/50(28.0)	13/50(26.0)	8/50(16.0)
Adjusted rates(b)	26.32	27.91	26.83	16.22
Terminal rates(c)	10/38(26.3)	12/43(27.9)	11/41(26.8)	6/37(16.2)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.7569			
Prevalence method(d)	P = 0.8733			
Combined analysis(d)	P = 0.9123			
Cochran-Armitage test(e)	P = 0.1264			
Fisher Exact test(e)		P = 0.5880	P = 0.5000	P = 0.1135
	SITE : thyroid TUMOR : C-cell adenoma			
Tumor rate				
Overall rates(a)	6/50(12.0)	6/50(12.0)	2/50(4.0)	3/50(6.0)
Adjusted rates(b)	13.16	13.33	4.88	8.11
Terminal rates(c)	5/38(13.2)	5/43(11.6)	2/41(4.9)	3/37(8.1)
Statistical analysis				
Peto test				
Standard method(d)	P = -------			
Prevalence method(d)	P = 0.8950			
Combined analysis(d)	P = -------			
Cochran-Armitage test(e)	P = 0.1840			
Fisher Exact test(e)		P = 0.6202	P = 0.1343	P = 0.2435
	SITE : thyroid TUMOR : C-cell adenoma, C-cell carcinoma			
Tumor rate				
Overall rates(a)	7/50(14.0)	6/50(12.0)	2/50(4.0)	4/50(8.0)
Adjusted rates(b)	15.79	13.33	4.88	10.81
Terminal rates(c)	6/38(15.8)	5/43(11.6)	2/41(4.9)	4/37(10.8)
Statistical analysis				
Peto test				
Standard method(d)	P = -------			
Prevalence method(d)	P = 0.8633			
Combined analysis(d)	P = -------			
Cochran-Armitage test(e)	P = 0.2372			
Fisher Exact test(e)		P = 0.5000	P = 0.0798	P = 0.2623

Group Name	Control	125 ppm	250 ppm	500 ppm
SITE : uterus TUMOR : endometrial stromal polyp				
Tumor rate				
Overall rates(a)	5/50(10.0)	3/50(6.0)	5/50(10.0)	3/50(6.0)
Adjusted rates(b)	13.16	6.98	11.90	8.11
Terminal rates(c)	5/38(13.2)	3/43(7.0)	4/41(9.8)	3/37(8.1)
Statistical analysis				
Peto test				
Standard method(d)	P = ------			
Prevalence method(d)	P = 0.6791			
Combined analysis(d)	P = ------			
Cochran-Armitage test(e)	P = 0.5970			
Fisher Exact test(e)		P = 0.3575	P = 0.6297	P = 0.3575
SITE : uterus TUMOR : endometrial stromal sarcoma				
Tumor rate				
Overall rates(a)	3/50(6.0)	1/50(2.0)	1/50(2.0)	3/50(6.0)
Adjusted rates(b)	0.0	0.0	2.27	2.13
Terminal rates(c)	0/38(0.0)	0/43(0.0)	0/41(0.0)	0/37(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.6383			
Prevalence method(d)	P = 0.1356			
Combined analysis(d)	P = 0.3917			
Cochran-Armitage test(e)	P = 0.8073			
Fisher Exact test(e)		P = 0.3087	P = 0.3087	P = 0.6611
SITE : mammary gland TUMOR : fibroadenoma				
Tumor rate				
Overall rates(a)	8/50(16.0)	5/50(10.0)	5/50(10.0)	1/50(2.0)
Adjusted rates(b)	18.42	11.63	10.00	0.0
Terminal rates(c)	7/38(18.4)	5/43(11.6)	3/41(7.3)	0/37(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3865			
Prevalence method(d)	P = 0.9958			
Combined analysis(d)	P = 0.9907			
Cochran-Armitage test(e)	P = 0.0202*			
Fisher Exact test(e)		P = 0.2768	P = 0.2768	P = 0.0154*

Group Name	Control	125 ppm	250 ppm	500 ppm
	SITE : mammary gland TUMOR : adenoma, fibroadenoma			
Tumor rate				
Overall rates(a)	8/50(16.0)	5/50(10.0)	6/50(12.0)	1/50(2.0)
Adjusted rates(b)	18.42	11.63	12.00	0.0
Terminal rates(c)	7/38(18.4)	5/43(11.6)	4/41(9.8)	0/37(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.3865			
Prevalence method(d)	P = 0.9938			
Combined analysis(d)	P = 0.9877			
Cochran-Armitage test(e)	P = 0.0257*			
Fisher Exact test(e)		P = 0.2768	P = 0.3871	P = 0.0154*
	SITE : mammary gland TUMOR : adenoma, fibroadenoma, adenocarcinoma			
Tumor rate				
Overall rates(a)	8/50(16.0)	5/50(10.0)	6/50(12.0)	2/50(4.0)
Adjusted rates(b)	18.42	11.63	12.00	0.0
Terminal rates(c)	7/38(18.4)	5/43(11.6)	4/41(9.8)	0/37(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1467			
Prevalence method(d)	P = 0.9933			
Combined analysis(d)	P = 0.9607			
Cochran-Armitage test(e)	P = 0.0669			
Fisher Exact test(e)		P = 0.2768	P = 0.3871	P = 0.0458*

Group Name	Control	125 ppm	250 ppm	500 ppm
SITE : preputial/clitoral gland				
TUMOR : adenoma				
Tumor rate				
Overall rates(a)	2/50(4.0)	4/50(8.0)	6/50(12.0)	3/50(6.0)
Adjusted rates(b)	5.26	9.09	9.76	5.41
Terminal rates(c)	2/38(5.3)	3/43(7.0)	4/41(9.8)	2/37(5.4)
Statistical analysis				
Peto test				
Standard method(d)	P = 0.1474			
Prevalence method(d)	P = 0.5361			
Combined analysis(d)	P = 0.3365			
Cochran-Armitage test(e)	P = 0.7508			
Fisher Exact test(e)		P = 0.3389	P = 0.1343	P = 0.5000

(HPT360A)

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

TABLE Q

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

TABLE Q 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. (%)
Lung	2199			
Bronchio-alveolar adenoma 1)		84	3.8	0 - 12
Bronchio-alveolar carcinoma 2)		19	0.9	0 - 8
1)+2)		103	4.7	0 - 14
Liver	2199			
Hepatocellular adenoma 1)		41	1.9	0 - 8
Hepatocellular carcinoma 2)		7	0.3	0 - 2
1)+2)		47	2.1	0 - 8
Pncreas	2199			
Islet cell adenoma		46	2.1	0 - 14

Forty four 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

TABLE R

CAUSE OF DEATH OF RATS IN THE 2-YEAR INHALATION STUDY OF 1 - BROMOBUTANE

TABLE R CAUSE OF DEATH OF RATS IN THE 2-YEAR INHALATION STUDY OF 1-BROMOBUTANE

	Male				Female			
Group name	Control	125 ppm	250 ppm	500 ppm	Control	125 ppm	250 ppm	500 ppm
Number of dead or moribund animals	11	15	9	13	12	7	9	13
Urinary system lesion	0	2	0	0	0	0	0	0
Chronic nephropathy	0	0	0	1	0	0	0	0
Peritonitis	0	0	0	0	0	1	0	0
Tumor death : leukemia	2	2	1	1	2	2	3	1
skin / appendage	0	1	1	0	0	0	0	0
subcutis	0	1	1	1	0	0	0	0
lymph node	0	0	0	0	1	0	0	0
spleen	0	0	0	1	0	0	0	0
kidney	0	1	0	0	0	0	0	0
urinary bladder	0	0	0	0	0	0	0	1
pituitary gland	5	3	0	2	4	2	2	2
thyroid	4	0	1	1	0	0	0	0
adrenal gland	0	0	1	0	0	0	0	0
uterus	—	—	—	—	3	1	0	2
mammary gland	0	0	0	0	1	0	0	2
preputial/clitoral gland	0	1	0	1	0	0	2	1
brain	0	0	2	1	0	0	0	0
Zymbal gland	0	1	1	2	0	0	1	2
vertebra	—	—	—	—	0	0	0	1
bone	0	2	0	0	0	0	0	0
No microscopical confirmation	0	1	1	2	1	1	1	1

FIGURES

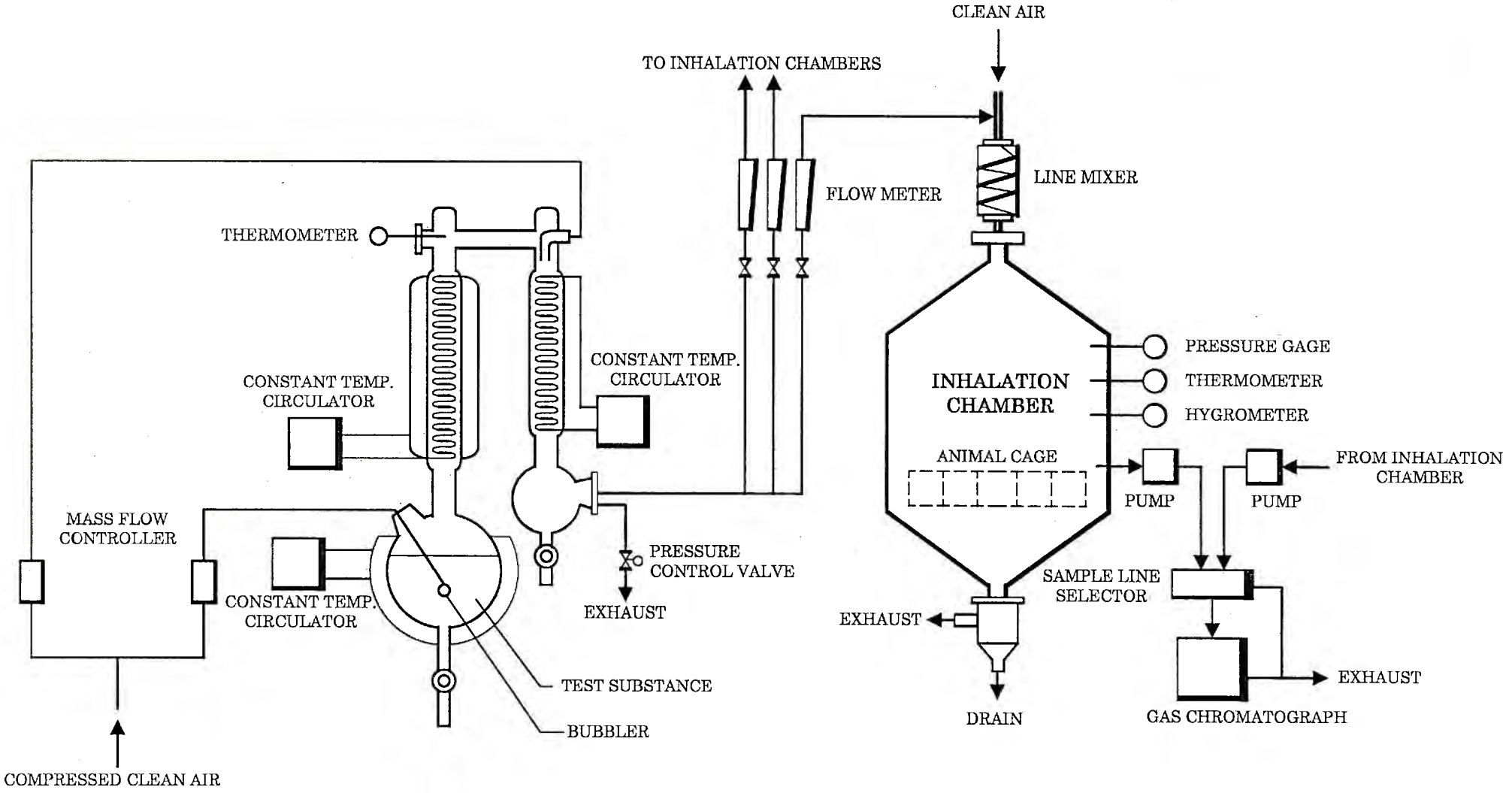

FIGURE 1 1-BROMOBUTANE VAPOR GENERATION SYSTEM AND INHALATION SYSTEM

(Study No. 0560)

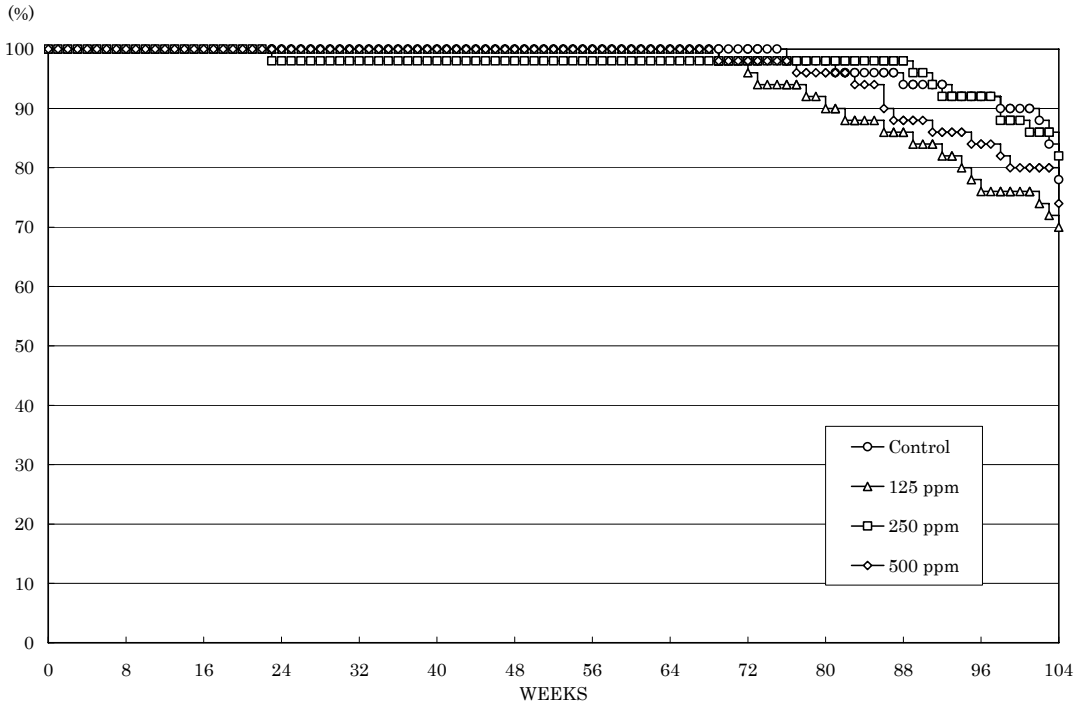

FIGURE 2 SURVIVAL ANIMAL RATE OF MALE RATS IN THE 2-YEAR INHALATION STUDY OF 1-BROMOBUTANE

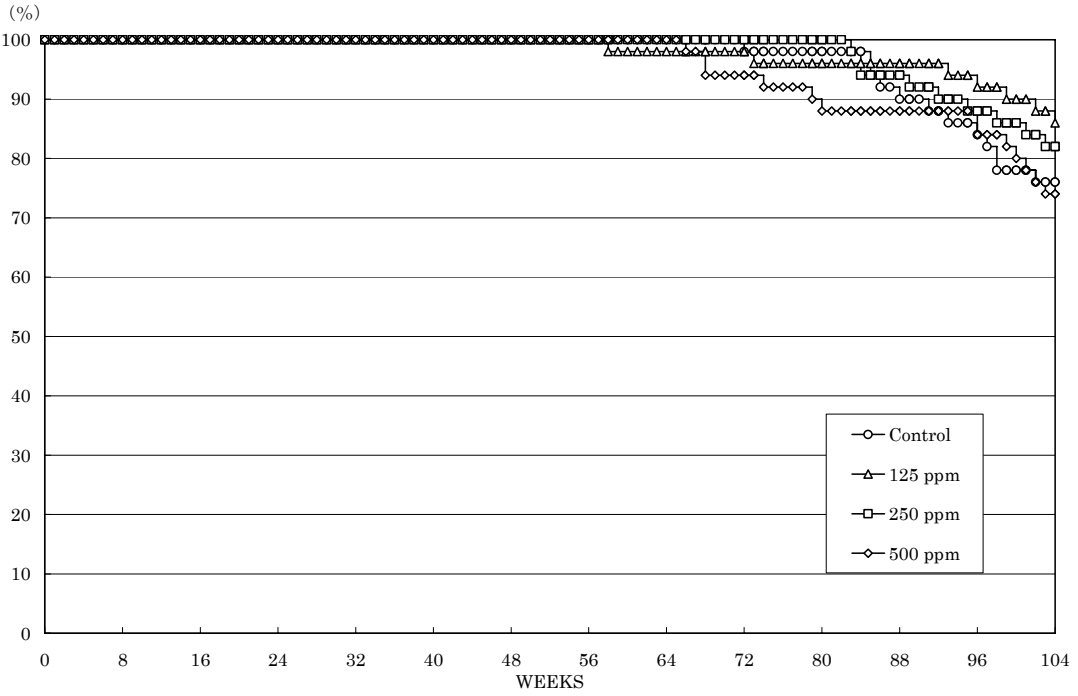

FIGURE 3 SURVIVAL ANIMAL RATE OF FEMALE RATS IN THE 2-YEAR INHALATION STUDY OF 1-BROMOBUTANE

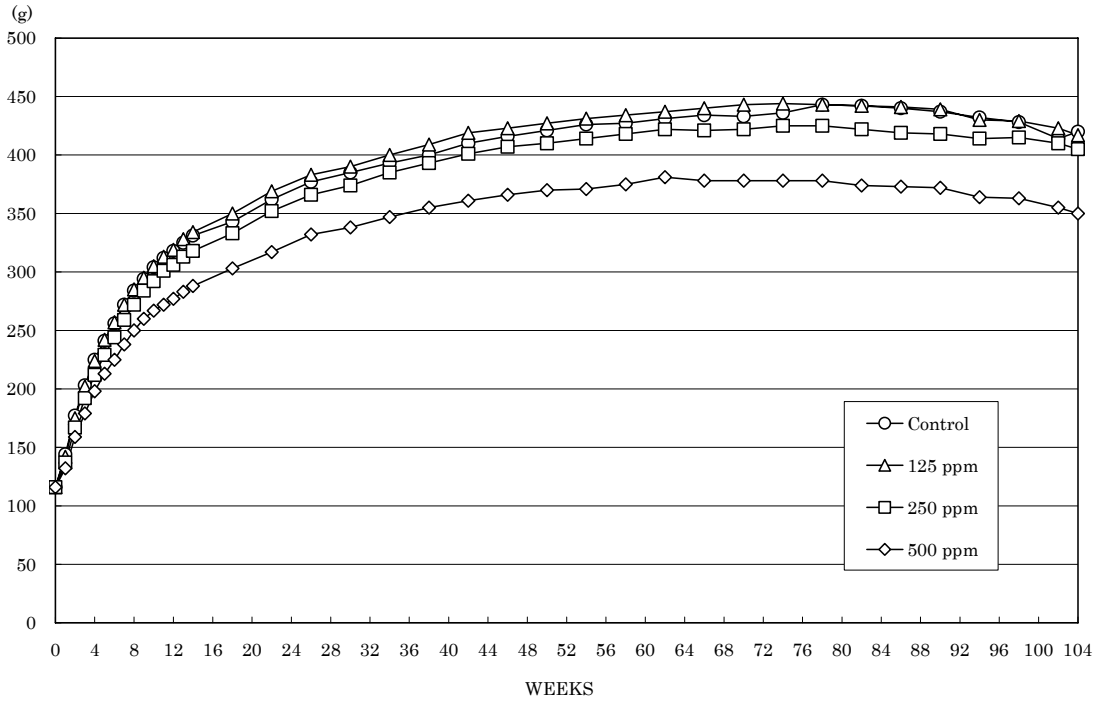

FIGURE 4 BODY WEIGHT CHANGES OF MALE RATS IN THE 2-YEAR INHALATION STUDY OF 1-BROMOBUTANE

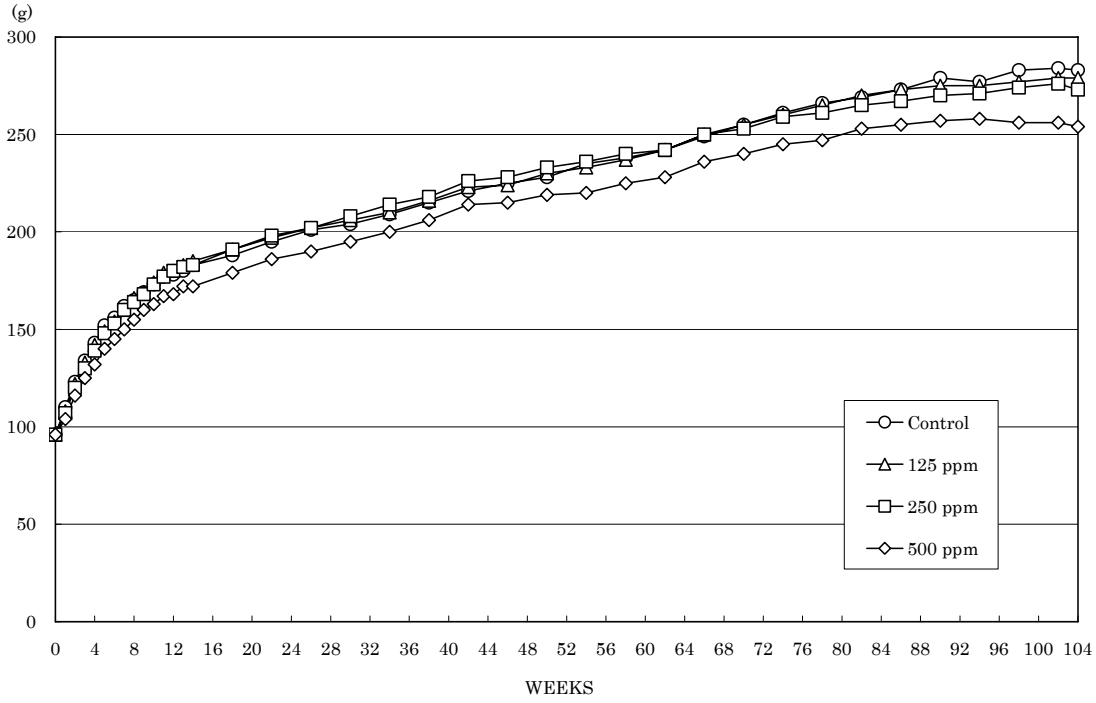

FIGURE 5 BODY WEIGHT CHANGES OF FEMALE RATS IN THE 2-YEAR INHALATION STUDY OF 1-BROMOBUTANE

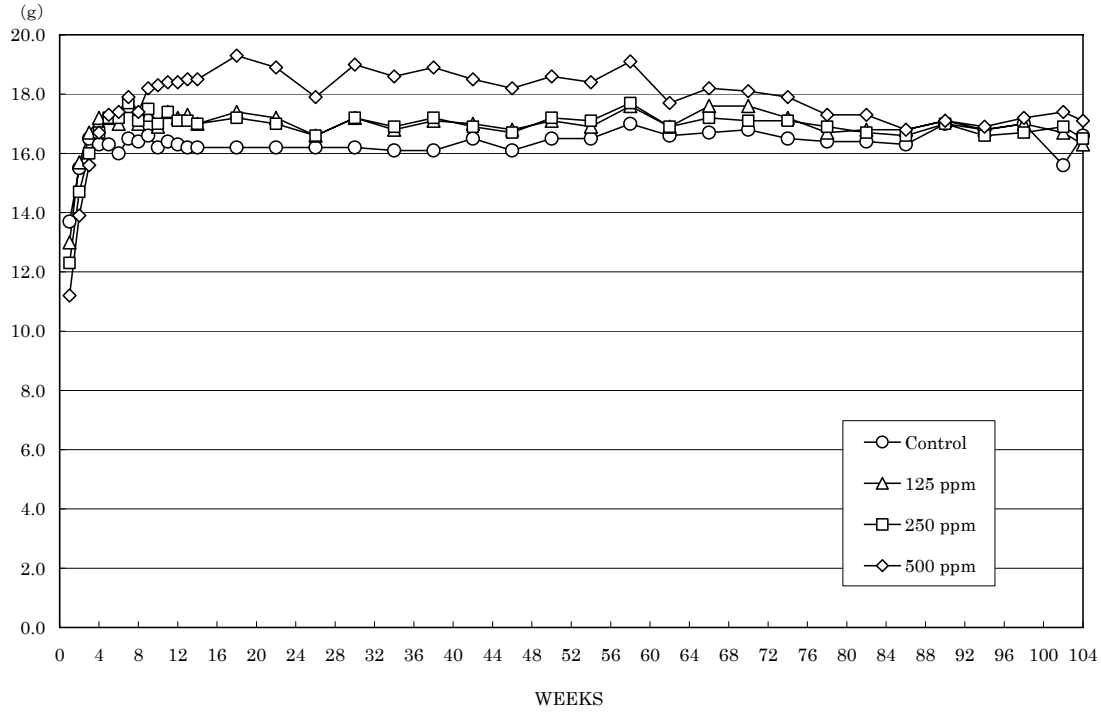

FIGURE 6 FOOD CONSUMPTION CHANGES OF MALE RATS IN THE 2-YEAR INHALATION STUDY OF 1-BROMOBUTANE

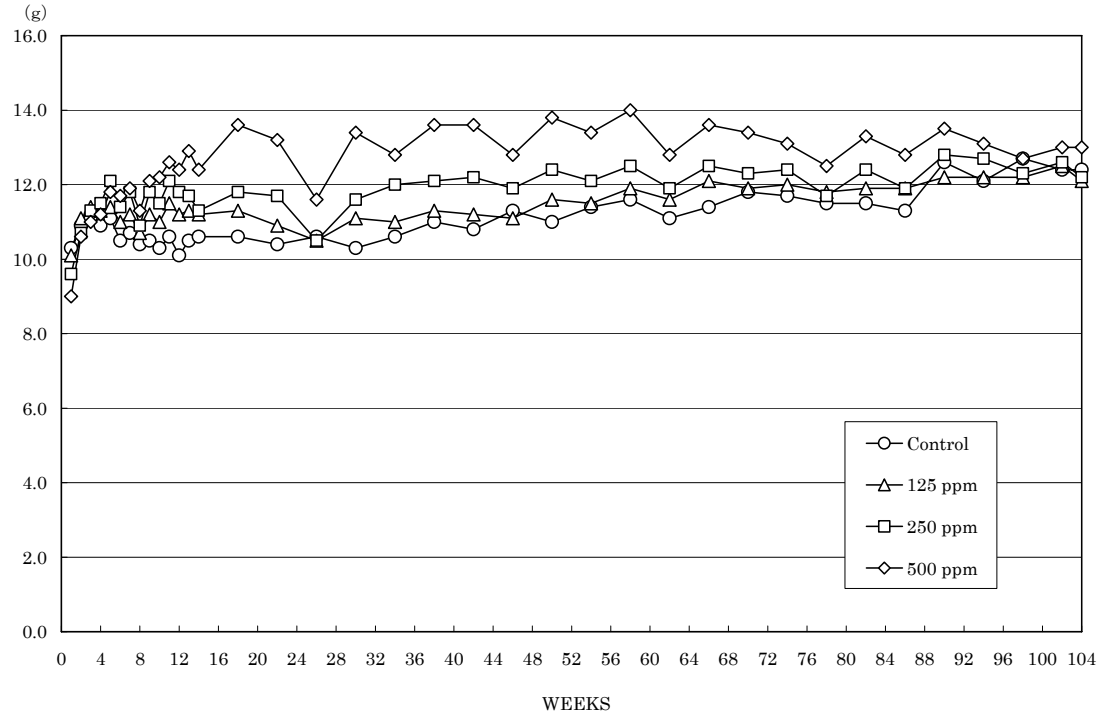

FIGURE 7 FOOD CONSUMPTION CHANGES OF FEMALE RATS IN THE 2-YEAR INHALATION STUDY OF 1-BROMOBUTANE