1,3,5,7-テトラアザトリシクロ〔3.3.1.1 ^{3,7}〕デカンのラット及びマウスを用いた経口投与によるがん原性試験（混水試験）報告書

試験番号

ラット/0224；マウス/0225

TABLES

TABLES

TABLES (CONTINUE)

TABLE 1 EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE DRINKING WATER STUDIES OF UROTROPIN

Two-year studies
<Method of Administration>
Drinking water
<Number of Groups>
Male 4, Female 4
<Size of Groups>
50 males and 50 females of each group
<Animals>
Strain and Species
F344/DuCrj (Fischer) rat
Crj:BDF_1 mouse
Animal Source
Charles River Japan, Inc.
Duration Held Before Study
2 wk
Age When Placed on Study
6 wk
Age When Killed
110～111 wk
<Doses>
Rat-------- <Male> 0, 7500, 15000, or 30000 ppm
<Female> 0, 7500, 15000, or 30000 ppm
Mouse---- <Male> 0, 10000, 20000, or 40000 ppm
<Female> 0, 10000, 20000, or 40000 ppm
<Duration of Dosing>
7d/wk for 104wk
<Animal Maintenance>
Feed
CRF-1 (Oriental Yeast Co., Ltd.)
Sterilized by γ-ray
Available *ad libitum*
Water
Filtrated and sterilized by ultraviolet ray
Automatic watering system in duration of quarantine
Glass bottle in duration of acclimation and administration
Available *ad libitum*
Animal per Cage
Single (stainless steel wire)
Animal Room Environment
Barrier system
Temperature : 24±2℃
Humidity : 55±10%
Fluorescent light 12h/d
15-17 room air changes /h
<Type and Frequency of Observation>
Clinical sign
Observed 1 per d
Body weight
Weighed 1 per wk for 14wk
Weighed 1 per 2wks thereafter
Water Consumption
Weighed 1 per wk for 14wk
Weighed 1 per 2wks thereafter
Food Consumption
Weighed 1 per wk for 14wk
Weighed 1 per 4wks thereafter

TABLE 1 (Continued) EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE DRINKING WATER STUDIES OF UROTROPIN

Two-year studies
<Hematology> Red blood cell (RBC), Hemoglobin, Hematocrit, Mean Corpuscular Volume (MCV), Mean Corpuscular hemoglobin (MCH), Mean Corpuscular hemoglobin concentrate (MCHC), Platelet, White blood cell (WBC), Differential WBC. <Biochemistry> Total protein, Albumin, A/G/ ratio, Total bilirubin, Glucose, Total cholesterol Triglyceride, Phospholipid <rat only>, Glutamic oxaloacetic transaminase (GOT), Glutamic pyruvic transaminase (GPT), Lactate dehydrogenase (LDH), Alkaline phosphatase (ALP), γ -Glutamyl transpeptidase (G-GTP) <rat only>, Creatine phosphokinase (CPK), Urea nitrogen, Creatinine <rat only>, Sodium, Potassium, Chloride, Calcium, Inorganic phosphorus. <Urinalysis> pH, Protein, Glucose, Ketone body, Bilirubin <rat only>, Occult blood, Urobilinogen. <Necropsy> Necropsy performed on all animals. <Organ Weight> Organ weight measurement performed on scheduled sacrificed animals. The following organs were weighed; brain, lung, liver, spleen, heart, kidney, adrenal, testis, ovary. <Histopathologic Examination> Histopathologic examination performed on all animals. The following organs were examined; skin, nasal cavity, trachea, lung, bone marrow, lymph node, thymus, spleen, heart, tongue, salivary gland, esophagus, stomach, small intestine, large intestine, liver, pancreas, kidney, urinary bladder, pituitary, thyroid, adrenal, testis, epididymis, seminal vesicle, prostate, ovary, uterus, vagina, mammary gland, brain, spinal cord, peripheral nerve, eye, Harderian gland, muscle, bone, other organs/tissues with gross lesions.

TABLE 2 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES IN MALE RAT (TWO-YEAR STUDY)

Week on Study	Control Av.Wt.	Control No.of Surviv. <50>	7500 ppm Av.Wt.	7500 ppm % of cont. <50>	7500 ppm No.of Surviv.	15000 ppm Av.Wt.	15000 ppm % of cont. <50>	15000 ppm No.of Surviv.	30000 ppm Av.Wt.	30000 ppm % of cont. <50>	30000 ppm No.of Surviv.
0	128 (50)	50/50	128 (50)	100	50/50	128 (50)	100	50/50	128 (50)	100	50/50
1	167 (50)	50/50	166 (50)	99	50/50	162 (50)	97	50/50	159 (50)	95	50/50
2	196 (50)	50/50	193 (50)	98	50/50	190 (50)	97	50/50	185 (50)	94	50/50
3	215 (50)	50/50	212 (50)	99	50/50	208 (50)	97	50/50	202 (50)	94	50/50
4	231 (50)	50/50	227 (50)	98	50/50	225 (50)	97	50/50	216 (50)	94	50/50
5	245 (50)	50/50	240 (50)	98	50/50	239 (50)	98	50/50	227 (50)	93	50/50
6	259 (50)	50/50	253 (50)	98	50/50	251 (50)	97	50/50	240 (50)	93	50/50
7	273 (50)	50/50	268 (50)	98	50/50	267 (50)	98	50/50	254 (50)	93	50/50
8	285 (50)	50/50	281 (50)	99	50/50	279 (50)	98	50/50	267 (50)	94	50/50
9	297 (50)	50/50	294 (50)	99	50/50	291 (50)	98	50/50	277 (50)	93	50/50
10	306 (50)	50/50	304 (50)	99	50/50	302 (50)	99	50/50	286 (50)	93	50/50
11	317 (50)	50/50	315 (50)	99	50/50	313 (50)	99	50/50	296 (50)	93	50/50
12	325 (50)	50/50	323 (50)	99	50/50	322 (50)	99	50/50	305 (50)	94	50/50
13	333 (50)	50/50	333 (50)	100	50/50	330 (50)	99	50/50	314 (50)	94	50/50
14	342 (50)	50/50	341 (50)	100	50/50	337 (50)	99	50/50	322 (50)	94	50/50
16	355 (50)	50/50	356 (50)	100	50/50	351 (50)	99	50/50	335 (50)	94	50/50
18	361 (50)	50/50	362 (50)	100	50/50	356 (50)	99	50/50	344 (50)	95	50/50
20	365 (50)	50/50	366 (50)	100	50/50	363 (50)	99	50/50	350 (50)	96	50/50
22	374 (50)	50/50	375 (50)	100	50/50	368 (50)	98	50/50	357 (50)	95	50/50
24	379 (50)	50/50	381 (50)	101	50/50	375 (50)	99	50/50	365 (50)	96	50/50
26	388 (50)	50/50	389 (50)	100	50/50	384 (50)	99	50/50	375 (50)	97	50/50
28	394 (50)	50/50	396 (50)	101	50/50	391 (50)	99	50/50	382 (50)	97	50/50
30	403 (50)	50/50	406 (50)	101	50/50	399 (50)	99	50/50	391 (50)	97	50/50
32	410 (50)	50/50	413 (50)	101	50/50	406 (50)	99	50/50	397 (50)	97	50/50
34	416 (50)	50/50	420 (50)	101	50/50	412 (50)	99	50/50	403 (50)	97	50/50
36	423 (50)	50/50	427 (50)	101	50/50	419 (50)	99	50/50	410 (50)	97	50/50
38	428 (50)	50/50	433 (50)	101	50/50	424 (50)	99	50/50	415 (50)	97	50/50
40	432 (50)	50/50	438 (50)	101	50/50	431 (50)	100	50/50	421 (50)	97	50/50
42	438 (50)	50/50	443 (50)	101	50/50	435 (50)	99	50/50	425 (50)	97	50/50
44	443 (50)	50/50	448 (50)	101	50/50	439 (50)	99	50/50	429 (50)	97	50/50
46	447 (50)	50/50	453 (50)	101	50/50	443 (50)	99	50/50	432 (50)	97	50/50
48	451 (50)	50/50	457 (50)	101	50/50	447 (50)	99	50/50	436 (50)	97	50/50
50	455 (50)	50/50	460 (50)	101	50/50	451 (50)	99	50/50	438 (50)	96	50/50
52	459 (50)	50/50	465 (50)	101	50/50	455 (50)	99	50/50	443 (50)	97	50/50
54	462 (50)	50/50	468 (50)	101	50/50	459 (50)	99	50/50	447 (50)	97	50/50
56	467 (50)	50/50	472 (50)	101	50/50	461 (50)	99	49/50	451 (50)	97	50/50
58	469 (50)	50/50	473 (50)	101	50/50	464 (49)	99	49/50	451 (50)	96	50/50
60	474 (50)	50/50	477 (50)	101	50/50	467 (49)	99	49/50	455 (50)	96	50/50
62	478 (50)	50/50	481 (49)	101	49/50	470 (48)	98	48/50	457 (50)	96	50/50
64	481 (50)	50/50	484 (49)	101	49/50	474 (48)	99	48/50	459 (50)	95	50/50
66	482 (50)	50/50	487 (49)	101	49/50	475 (48)	99	47/50	461 (50)	96	50/50
68	484 (49)	49/50	491 (49)	101	49/50	483 (47)	100	47/50	463 (50)	96	50/50
70	487 (48)	48/50	489 (49)	100	49/50	482 (47)	99	47/50	463 (50)	95	50/50
72	484 (48)	48/50	488 (49)	101	49/50	479 (47)	99	47/50	462 (50)	95	50/50
74	485 (48)	48/50	489 (49)	101	49/50	479 (47)	99	47/50	463 (50)	95	50/50
76	487 (48)	48/50	490 (49)	101	49/50	478 (47)	98	47/50	463 (50)	95	50/50
78	489 (48)	48/50	492 (47)	101	47/50	481 (46)	98	46/50	462 (50)	94	50/50
80	490 (48)	48/50	493 (47)	101	47/50	480 (46)	98	46/50	464 (48)	95	48/50
82	491 (48)	48/50	492 (46)	100	46/50	480 (46)	98	46/50	463 (48)	94	48/50
84	484 (48)	48/50	491 (46)	101	46/50	475 (45)	98	45/50	457 (48)	94	48/50
86	489 (46)	46/50	489 (46)	100	46/50	474 (45)	97	45/50	457 (46)	93	46/50
88	488 (46)	46/50	490 (46)	100	46/50	470 (45)	96	45/50	452 (46)	93	46/50
90	484 (45)	45/50	486 (46)	100	46/50	463 (45)	96	45/50	448 (46)	93	46/50
92	477 (45)	45/50	480 (46)	101	46/50	459 (42)	96	42/50	442 (46)	93	46/50
94	472 (44)	44/50	479 (46)	101	46/50	453 (42)	96	42/50	435 (44)	92	43/50
96	466 (43)	42/50	477 (46)	102	45/50	451 (40)	97	40/50	432 (41)	93	41/50
98	470 (41)	41/50	460 (43)	98	42/50	444 (40)	94	40/50	421 (39)	90	37/50
100	463 (39)	39/50	455 (42)	98	42/50	436 (38)	94	37/50	413 (33)	89	33/50
102	455 (39)	39/50	450 (40)	99	40/50	436 (35)	96	35/50	414 (30)	91	30/50
104	451 (38)	38/50	445 (39)	99	39/50	428 (34)	95	34/50	398 (30)	88	30/50

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

TABLE 3 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES IN FEMALE RAT (TWO-YEAR STUDY)

Week on Study	Control Av.Wt.	Control No.of Surviv. <50>	7500 ppm Av.Wt.	7500 ppm % of cont. <50>	7500 ppm No.of Surviv.	15000 ppm Av.Wt.	15000 ppm % of cont. <50>	15000 ppm No.of Surviv.	30000 ppm Av.Wt.	30000 ppm % of cont. <50>	30000 ppm No.of Surviv.
0	100 (50)	50/50	100 (50)	100	50/50	100 (50)	100	50/50	101 (50)	101	50/50
1	120 (50)	50/50	119 (50)	99	50/50	119 (50)	99	50/50	117 (50)	98	50/50
2	131 (50)	50/50	130 (50)	99	50/50	130 (50)	99	50/50	128 (50)	98	50/50
3	140 (50)	50/50	140 (50)	100	50/50	139 (50)	99	50/50	136 (50)	97	50/50
4	148 (50)	50/50	147 (50)	99	50/50	147 (50)	99	50/50	143 (50)	97	50/50
5	155 (50)	50/50	154 (50)	99	50/50	154 (50)	99	50/50	148 (50)	95	50/50
6	159 (50)	50/50	157 (50)	99	50/50	158 (50)	99	50/50	153 (50)	96	50/50
7	165 (50)	50/50	163 (50)	99	50/50	163 (50)	99	50/50	157 (50)	95	50/50
8	167 (50)	50/50	166 (50)	99	50/50	166 (50)	99	50/50	160 (50)	96	50/50
9	173 (50)	50/50	171 (50)	99	50/50	171 (50)	99	50/50	165 (50)	95	50/50
10	176 (50)	50/50	174 (50)	99	50/50	174 (50)	99	50/50	167 (50)	95	50/50
11	181 (50)	50/50	178 (50)	98	50/50	178 (50)	98	50/50	171 (50)	94	50/50
12	183 (50)	50/50	180 (50)	98	50/50	180 (50)	98	50/50	172 (50)	94	50/50
13	186 (50)	50/50	184 (50)	99	50/50	183 (50)	98	50/50	175 (50)	94	50/50
14	190 (50)	50/50	187 (50)	98	50/50	185 (50)	97	50/50	178 (50)	94	50/50
16	195 (50)	50/50	193 (50)	99	50/50	189 (50)	97	50/50	182 (50)	93	50/50
18	199 (50)	50/50	196 (50)	98	50/50	193 (50)	97	50/50	186 (50)	93	50/50
20	202 (50)	50/50	199 (50)	99	50/50	196 (50)	97	50/50	189 (50)	94	50/50
22	205 (50)	50/50	202 (50)	99	50/50	198 (50)	97	50/50	191 (50)	93	50/50
24	209 (50)	50/50	205 (50)	98	50/50	201 (50)	96	50/50	193 (50)	92	50/50
26	212 (50)	50/50	209 (50)	99	50/50	205 (50)	97	50/50	197 (50)	93	50/50
28	214 (50)	50/50	212 (50)	99	50/50	207 (50)	97	50/50	198 (50)	93	50/50
30	217 (50)	50/50	214 (50)	99	50/50	210 (50)	97	50/50	201 (50)	93	50/50
32	220 (50)	50/50	218 (50)	99	50/50	213 (50)	97	50/50	204 (50)	93	50/50
34	221 (50)	50/50	220 (50)	100	50/50	214 (50)	97	50/50	205 (50)	93	50/50
36	224 (50)	50/50	224 (50)	100	50/50	219 (50)	98	50/50	211 (49)	94	49/50
38	228 (50)	50/50	227 (50)	100	50/50	220 (50)	96	50/50	212 (49)	93	49/50
40	231 (50)	50/50	230 (50)	100	50/50	222 (50)	96	50/50	214 (49)	93	49/50
42	234 (50)	50/50	231 (50)	99	50/50	224 (50)	96	50/50	216 (49)	92	49/50
44	236 (50)	50/50	234 (50)	99	50/50	227 (50)	96	50/50	219 (49)	93	49/50
46	238 (50)	50/50	238 (49)	100	49/50	230 (50)	97	50/50	221 (49)	93	49/50
48	241 (50)	50/50	240 (49)	100	49/50	231 (50)	96	50/50	222 (49)	92	49/50
50	245 (50)	50/50	244 (49)	100	49/50	234 (50)	96	50/50	225 (49)	92	49/50
52	250 (50)	50/50	249 (49)	100	49/50	237 (50)	95	50/50	228 (49)	91	49/50
54	252 (50)	50/50	250 (49)	99	49/50	239 (50)	95	50/50	230 (49)	91	49/50
56	255 (50)	50/50	252 (49)	99	49/50	241 (50)	95	50/50	233 (49)	91	49/50
58	259 (50)	50/50	257 (49)	99	49/50	245 (50)	95	50/50	234 (49)	90	49/50
60	262 (50)	50/50	260 (49)	99	49/50	249 (50)	95	50/50	239 (49)	91	49/50
62	267 (50)	50/50	263 (49)	99	49/50	252 (50)	94	50/50	240 (48)	90	48/50
64	271 (50)	50/50	270 (49)	100	49/50	256 (50)	94	50/50	243 (47)	90	47/50
66	274 (50)	50/50	275 (49)	100	49/50	259 (50)	95	50/50	245 (47)	89	47/50
68	277 (50)	50/50	278 (49)	100	49/50	262 (50)	95	50/50	248 (46)	90	46/50
70	280 (50)	50/50	282 (49)	101	49/50	266 (50)	95	50/50	250 (45)	89	44/50
72	283 (50)	50/50	286 (48)	101	48/50	268 (50)	95	50/50	253 (44)	89	44/50
74	287 (50)	50/50	290 (48)	101	48/50	271 (50)	94	50/50	254 (43)	89	43/50
76	292 (50)	50/50	295 (48)	101	48/50	273 (50)	93	50/50	257 (38)	88	38/50
78	295 (50)	50/50	297 (47)	101	47/50	277 (50)	94	50/50	259 (36)	88	36/50
80	298 (50)	50/50	301 (47)	101	47/50	280 (49)	94	49/50	262 (34)	88	32/50
82	302 (50)	50/50	304 (47)	101	47/50	284 (48)	94	48/50	267 (31)	88	31/50
84	304 (50)	50/50	308 (46)	101	46/50	285 (48)	94	48/50	267 (31)	88	31/50
86	307 (50)	50/50	310 (46)	101	46/50	289 (47)	94	47/50	260 (29)	85	28/50
88	309 (50)	50/50	311 (46)	101	46/50	291 (46)	94	46/50	266 (26)	86	26/50
90	308 (50)	50/50	309 (46)	100	46/50	292 (45)	95	45/50	267 (26)	87	26/50
92	306 (50)	49/50	310 (45)	101	45/50	292 (45)	95	43/50	266 (26)	87	26/50
94	309 (49)	49/50	307 (45)	99	44/50	294 (43)	95	43/50	270 (24)	87	24/50
96	316 (48)	48/50	311 (42)	98	41/50	297 (42)	94	41/50	275 (23)	87	23/50
98	317 (47)	47/50	310 (41)	98	41/50	297 (41)	94	41/50	269 (23)	85	23/50
100	316 (47)	47/50	310 (40)	98	40/50	295 (40)	93	40/50	276 (20)	87	20/50
102	314 (47)	47/50	311 (39)	99	39/50	300 (35)	96	35/50	270 (16)	86	16/50
104	313 (47)	47/50	311 (39)	99	39/50	295 (35)	94	35/50	274 (14)	88	14/50

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

TABLE 4 INCIDENCE OF EXTERNAL AND INTERNAL MASS IN CLINICAL OBSERVATION IN MALE RAT

Time of mass occurrence (week)		0～13	14～26	27～39	40～52	53～65	66～78	79～91	92～104	0～104
External mass										
	Control	0/50	0/50	0/50	1/50	0/50	4/48	8/45	9/38	11/50(3/12)
	7500ppm	0/50	0/50	0/50	2/50	3/49	4/47	7/46	15/39	16/50(4/11)
	15000ppm	0/50	0/50	0/50	0/50	2/48	2/46	2/43	8/34	10/50(3/16)
	30000ppm	0/50	0/50	0/50	0/50	2/50	5/50	6/46	17/30	18/50(8/20)
Internal mass										
	Control	0/50	0/50	0/50	0/50	0/50	1/48	0/45	0/38	1/50(1/12)
	7500ppm	0/50	0/50	0/50	0/50	0/49	0/47	0/46	1/39	1/50(1/11)
	15000ppm	0/50	0/50	0/50	0/50	0/48	1/46	0/43	1/34	2/50(2/16)
	30000ppm	0/50	0/50	0/50	0/50	0/50	0/50	0/46	0/30	0/50(0/20)

No. of animals with mass / No. of survival animals at first week on each period.
(No. of dead and moribund animals with mass / No. of dead and moribund animals)

TABLE 5 INCIDENCE OF EXTERNAL AND INTERNAL MASS IN CLINICAL OBSERVATION IN FEMALE RAT

Time of mass occurrence (week)		0～13	14～26	27～39	40～52	53～65	66～78	79～91	92～104	0～104
External mass										
	Control	0/50	0/50	0/50	0/50	1/50	0/50	4/50	7/47	9/50(2/ 3)
	7500ppm	0/50	0/50	0/50	1/49	1/49	3/47	7/46	8/39	12/50(4/11)
	15000ppm	0/50	0/50	0/50	0/50	0/50	2/50	2/45	8/35	10/50(6/15)
	30000ppm	0/50	0/50	1/49	2/49	2/47	5/36	5/26	7/14	13/50(9/36)
Internal mass										
	Control	0/50	0/50	0/50	0/50	0/50	0/50	0/50	0/47	0/50(0/ 3)
	7500ppm	0/50	0/50	0/50	0/49	0/49	0/47	0/46	1/39	1/50(1/11)
	15000ppm	0/50	0/50	0/50	0/50	0/50	0/50	0/45	1/35	1/50(1/15)
	30000ppm	0/50	0/50	0/49	0/49	0/47	0/36	1/26	1/14	2/50(2/36)

No. of animals with mass / No. of survival animals at first week on each period.
(No. of dead and moribund animals with mass / No. of dead and moribund animals)

TABLE 6 WATER CONSUMPTION IN MALE RAT (TWO-YEAR STUDY)

Week on Study	Control Av.WC.	Control No.of Surviv. <50>	7500 ppm Av.WC.	7500 ppm % of cont. <50>	7500 ppm No.of Surviv.	15000 ppm Av.WC.	15000 ppm % of cont. <50>	15000 ppm No.of Surviv.	30000 ppm Av.WC.	30000 ppm % of cont. <50>	30000 ppm No.of Surviv.
1	19.6 (50)	50/50	20.6 (50)	105	50/50	21.7 (50)	111	50/50	20.4 (50)	104	50/50
2	20.8 (50)	50/50	21.9 (50)	105	50/50	22.8 (50)	110	50/50	20.1 (50)	97	50/50
3	21.8 (50)	50/50	21.6 (50)	99	50/50	22.6 (50)	104	50/50	20.2 (50)	93	50/50
4	22.3 (50)	50/50	22.3 (50)	100	50/50	23.0 (50)	103	50/50	20.8 (50)	93	50/50
5	21.6 (50)	50/50	22.9 (50)	106	50/50	22.9 (50)	106	50/50	20.4 (50)	94	50/50
6	20.8 (50)	50/50	21.9 (50)	105	50/50	22.8 (50)	110	50/50	20.3 (50)	98	50/50
7	20.8 (50)	50/50	21.5 (50)	103	50/50	22.7 (50)	109	50/50	19.9 (50)	96	50/50
8	21.7 (48)	50/50	22.2 (50)	102	50/50	23.0 (50)	106	50/50	20.4 (50)	94	50/50
9	21.9 (50)	50/50	22.4 (50)	102	50/50	23.1 (50)	105	50/50	20.7 (50)	95	50/50
10	21.4 (50)	50/50	21.9 (50)	102	50/50	22.5 (50)	105	50/50	21.0 (50)	98	50/50
11	21.7 (50)	50/50	21.7 (50)	100	50/50	22.1 (50)	102	50/50	21.0 (50)	97	50/50
12	20.7 (50)	50/50	20.9 (50)	101	50/50	21.4 (50)	103	50/50	21.0 (50)	101	50/50
13	21.6 (49)	50/50	21.8 (50)	101	50/50	22.1 (50)	102	50/50	21.4 (50)	99	50/50
14	22.2 (49)	50/50	21.8 (50)	98	50/50	22.8 (50)	103	50/50	21.4 (50)	96	50/50
16	19.7 (50)	50/50	19.6 (50)	99	50/50	20.1 (50)	102	50/50	19.7 (50)	100	50/50
18	19.3 (49)	50/50	19.3 (50)	100	50/50	19.8 (50)	103	50/50	19.8 (50)	103	50/50
20	20.1 (50)	50/50	19.9 (50)	99	50/50	20.7 (50)	103	50/50	19.7 (50)	98	50/50
22	19.1 (50)	50/50	19.4 (50)	102	50/50	19.4 (50)	102	50/50	19.3 (50)	101	50/50
24	18.6 (50)	50/50	19.0 (50)	102	50/50	19.9 (50)	107	50/50	19.7 (50)	106	50/50
26	19.1 (50)	50/50	19.1 (50)	100	50/50	20.3 (49)	106	50/50	20.3 (50)	106	50/50
28	18.6 (50)	50/50	19.5 (50)	105	50/50	19.7 (50)	106	50/50	20.3 (50)	109	50/50
30	18.8 (50)	50/50	19.2 (50)	102	50/50	19.6 (50)	104	50/50	20.0 (50)	106	50/50
32	18.4 (50)	50/50	19.0 (49)	103	50/50	18.9 (50)	103	50/50	19.8 (50)	108	50/50
34	17.5 (50)	50/50	18.0 (50)	103	50/50	18.4 (50)	105	50/50	18.6 (50)	106	50/50
36	18.6 (50)	50/50	18.9 (50)	102	50/50	19.6 (50)	105	50/50	19.9 (50)	107	50/50
38	18.5 (50)	50/50	18.9 (50)	102	50/50	19.2 (50)	104	50/50	19.6 (50)	106	50/50
40	18.8 (50)	50/50	19.2 (50)	102	50/50	19.6 (50)	104	50/50	20.1 (50)	107	50/50
42	18.9 (50)	50/50	19.4 (50)	103	50/50	19.8 (50)	105	50/50	20.3 (50)	107	50/50
44	19.4 (50)	50/50	19.8 (50)	102	50/50	20.7 (50)	107	50/50	21.3 (50)	110	50/50
46	19.5 (50)	50/50	20.0 (50)	103	50/50	20.6 (50)	106	50/50	21.0 (50)	108	50/50
48	20.0 (50)	50/50	20.3 (50)	102	50/50	21.6 (50)	108	50/50	22.0 (50)	110	50/50
50	20.2 (50)	50/50	20.5 (50)	101	50/50	21.1 (50)	104	50/50	21.7 (50)	107	50/50
52	20.0 (50)	50/50	20.5 (50)	103	50/50	20.8 (50)	104	50/50	21.7 (50)	109	50/50
54	20.1 (49)	50/50	20.4 (50)	101	50/50	21.4 (50)	106	50/50	22.6 (50)	112	50/50
56	20.3 (50)	50/50	20.4 (50)	100	50/50	21.1 (49)	104	49/50	22.1 (50)	109	50/50
58	20.5 (50)	50/50	20.5 (50)	100	50/50	21.4 (49)	104	49/50	22.0 (50)	107	50/50
60	20.1 (50)	50/50	20.1 (50)	100	50/50	20.6 (49)	102	49/50	21.7 (50)	108	50/50
62	20.3 (50)	50/50	19.7 (50)	97	49/50	20.9 (48)	103	48/50	22.1 (50)	109	50/50
64	20.0 (50)	50/50	20.3 (49)	102	49/50	21.3 (48)	106	48/50	22.0 (50)	110	50/50
66	20.0 (50)	50/50	20.6 (49)	103	49/50	21.4 (48)	107	47/50	22.0 (50)	110	50/50
68	19.1 (49)	49/50	19.9 (49)	104	49/50	20.5 (47)	107	47/50	21.3 (50)	112	50/50
70	20.6 (48)	48/50	20.4 (49)	99	49/50	21.4 (47)	104	47/50	22.2 (50)	108	50/50
72	19.4 (48)	48/50	19.5 (49)	101	49/50	20.8 (47)	107	47/50	21.6 (50)	111	50/50
74	20.3 (48)	48/50	21.1 (49)	104	49/50	21.9 (47)	108	47/50	22.7 (50)	112	50/50
76	20.8 (48)	48/50	20.9 (49)	100	49/50	22.1 (47)	106	47/50	22.4 (50)	108	50/50
78	22.1 (48)	48/50	22.6 (48)	102	47/50	23.2 (46)	105	46/50	24.4 (50)	110	50/50
80	20.6 (48)	48/50	21.3 (47)	103	47/50	22.0 (46)	107	46/50	23.0 (48)	112	48/50
82	22.1 (48)	48/50	22.3 (46)	101	46/50	23.3 (46)	105	46/50	24.0 (48)	109	48/50
84	21.5 (48)	48/50	22.2 (46)	103	46/50	23.3 (44)	108	45/50	24.3 (48)	113	48/50
86	23.5 (46)	46/50	23.2 (46)	99	46/50	24.3 (45)	103	45/50	24.3 (46)	103	46/50
88	23.5 (43)	46/50	23.8 (45)	101	46/50	23.6 (42)	100	45/50	24.2 (45)	103	46/50
90	23.9 (45)	45/50	23.2 (46)	97	46/50	23.8 (44)	100	45/50	23.9 (46)	100	46/50
92	24.2 (43)	45/50	24.8 (46)	102	46/50	23.9 (40)	99	42/50	25.1 (46)	104	46/50
94	23.8 (43)	44/50	23.4 (43)	98	46/50	24.2 (41)	102	42/50	24.7 (44)	104	43/50
96	23.9 (39)	42/50	24.7 (42)	103	45/50	26.3 (39)	110	40/50	26.5 (41)	111	41/50
98	26.4 (37)	41/50	25.8 (41)	98	42/50	27.6 (40)	105	40/50	25.1 (39)	95	37/50
100	26.1 (33)	39/50	26.2 (37)	100	42/50	26.2 (36)	100	37/50	25.4 (32)	97	33/50
102	29.4 (36)	39/50	26.4 (37)	90	40/50	28.7 (35)	98	35/50	26.7 (29)	91	30/50
104	26.8 (26)	38/50	26.1 (30)	97	39/50	26.2 (27)	98	34/50	26.1 (29)	97	30/50

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

TABLE 7 WATER CONSUMPTION IN FEMALE RAT (TWO-YEAR STUDY)

Week on Study	Control Av.WC.	Control No.of Surviv. <50>	7500 ppm Av.WC.	7500 ppm % of cont. <50>	7500 ppm No.of Surviv.	15000 ppm Av.WC.	15000 ppm % of cont. <50>	15000 ppm No.of Surviv.	30000 ppm Av.WC.	30000 ppm % of cont. <50>	30000 ppm No.of Surviv.
1	17.3 (50)	50/50	18.8 (50)	109	50/50	17.3 (50)	100	50/50	17.7 (50)	102	50/50
2	18.0 (50)	50/50	20.9 (50)	116	50/50	18.3 (50)	102	50/50	17.1 (50)	95	50/50
3	17.5 (49)	50/50	19.9 (49)	114	50/50	19.0 (50)	109	50/50	16.6 (48)	95	50/50
4	17.7 (50)	50/50	19.1 (46)	108	50/50	18.9 (49)	107	50/50	17.3 (50)	98	50/50
5	17.7 (47)	50/50	18.5 (46)	105	50/50	19.0 (49)	107	50/50	16.2 (48)	92	50/50
6	18.4 (48)	50/50	19.6 (47)	107	50/50	20.3 (49)	110	50/50	17.2 (50)	93	50/50
7	17.6 (47)	50/50	21.1 (48)	120	50/50	18.6 (49)	106	50/50	16.6 (50)	94	50/50
8	18.2 (48)	50/50	20.1 (45)	110	50/50	19.4 (47)	107	50/50	17.5 (48)	96	50/50
9	19.3 (47)	50/50	20.6 (45)	107	50/50	19.5 (47)	101	50/50	16.7 (50)	87	50/50
10	19.3 (48)	50/50	21.2 (44)	110	50/50	18.4 (44)	95	50/50	16.7 (48)	87	50/50
11	19.7 (48)	50/50	20.0 (41)	102	50/50	19.6 (45)	99	50/50	15.7 (46)	80	50/50
12	19.3 (49)	50/50	19.0 (44)	98	50/50	18.6 (47)	96	50/50	17.9 (50)	93	50/50
13	18.7 (44)	50/50	20.2 (46)	108	50/50	17.5 (45)	94	50/50	17.2 (49)	92	50/50
14	20.1 (42)	50/50	20.6 (44)	102	50/50	20.8 (45)	103	50/50	18.0 (49)	90	50/50
16	18.7 (46)	50/50	19.5 (43)	104	50/50	19.5 (49)	104	50/50	15.7 (48)	84	50/50
18	19.5 (44)	50/50	18.8 (41)	96	50/50	19.8 (44)	102	50/50	16.3 (47)	84	50/50
20	19.6 (46)	50/50	18.7 (40)	95	50/50	19.3 (44)	98	50/50	16.8 (47)	86	50/50
22	18.2 (46)	50/50	19.5 (45)	107	50/50	18.2 (45)	100	50/50	16.5 (48)	91	50/50
24	18.5 (45)	50/50	19.0 (41)	103	50/50	19.5 (42)	105	50/50	17.3 (47)	94	50/50
26	18.1 (48)	50/50	20.0 (46)	110	50/50	19.4 (45)	107	50/50	17.8 (48)	98	50/50
28	17.7 (49)	50/50	18.1 (46)	102	50/50	18.1 (45)	102	50/50	16.7 (48)	94	50/50
30	16.5 (46)	50/50	18.7 (43)	113	50/50	17.5 (46)	106	50/50	15.9 (46)	96	50/50
32	15.7 (46)	50/50	17.9 (46)	114	50/50	19.3 (45)	123	50/50	17.7 (49)	113	50/50
34	14.8 (50)	50/50	15.9 (49)	107	50/50	16.0 (49)	108	50/50	14.7 (50)	99	50/50
36	16.7 (49)	50/50	19.9 (48)	119	50/50	18.1 (45)	108	50/50	16.8 (47)	101	49/50
38	15.6 (47)	50/50	17.7 (47)	113	50/50	18.4 (49)	118	50/50	16.4 (47)	105	49/50
40	16.3 (47)	50/50	18.0 (48)	110	50/50	17.6 (46)	108	50/50	16.4 (46)	101	49/50
42	17.3 (50)	50/50	18.9 (50)	109	50/50	17.7 (47)	102	50/50	16.9 (47)	98	49/50
44	16.7 (48)	50/50	17.9 (47)	107	50/50	17.3 (44)	104	50/50	18.3 (49)	110	49/50
46	16.0 (48)	50/50	17.4 (46)	109	49/50	17.8 (47)	111	50/50	18.1 (48)	113	49/50
48	16.7 (48)	50/50	18.0 (46)	108	49/50	18.6 (48)	111	50/50	17.9 (48)	107	49/50
50	17.4 (49)	50/50	19.1 (48)	110	49/50	19.0 (47)	109	50/50	18.4 (48)	106	49/50
52	17.5 (50)	50/50	19.3 (49)	110	49/50	18.3 (50)	105	50/50	19.0 (49)	109	49/50
54	16.2 (49)	50/50	17.9 (48)	110	49/50	16.8 (46)	104	50/50	18.3 (46)	113	49/50
56	15.6 (48)	50/50	17.7 (46)	113	49/50	17.9 (46)	115	50/50	18.9 (48)	121	49/50
58	16.5 (49)	50/50	18.9 (46)	115	49/50	18.7 (50)	113	50/50	18.0 (47)	109	49/50
60	15.7 (48)	50/50	17.6 (47)	112	49/50	18.5 (50)	118	50/50	18.7 (48)	119	49/50
62	16.5 (49)	50/50	18.6 (49)	113	49/50	17.4 (50)	105	50/50	18.0 (47)	109	48/50
64	16.1 (49)	50/50	18.2 (49)	113	49/50	17.2 (50)	107	50/50	17.8 (45)	111	47/50
66	16.0 (49)	50/50	18.3 (49)	114	49/50	16.8 (50)	105	50/50	18.8 (46)	118	47/50
68	14.9 (49)	50/50	16.8 (48)	113	49/50	16.3 (50)	109	50/50	17.5 (43)	117	46/50
70	15.7 (49)	50/50	16.3 (49)	104	49/50	16.4 (50)	104	50/50	17.9 (43)	114	44/50
72	15.3 (48)	50/50	16.9 (47)	110	48/50	17.0 (50)	111	50/50	18.5 (42)	121	44/50
74	15.9 (50)	50/50	17.8 (48)	112	48/50	17.2 (50)	108	50/50	18.2 (43)	114	43/50
76	15.8 (48)	50/50	17.5 (48)	111	48/50	17.7 (50)	112	50/50	17.9 (38)	113	38/50
78	16.9 (49)	50/50	18.0 (47)	107	47/50	18.7 (50)	111	50/50	18.9 (35)	112	36/50
80	15.5 (49)	50/50	17.9 (47)	115	47/50	17.6 (49)	114	49/50	19.0 (33)	123	32/50
82	17.1 (48)	50/50	19.4 (47)	113	47/50	19.2 (48)	112	48/50	19.9 (29)	116	31/50
84	16.5 (48)	50/50	19.1 (46)	116	46/50	17.9 (48)	108	48/50	20.9 (30)	127	31/50
86	17.5 (48)	50/50	19.6 (46)	112	46/50	18.9 (47)	108	47/50	19.8 (27)	113	28/50
88	17.1 (48)	50/50	19.4 (46)	113	46/50	18.8 (46)	110	46/50	19.9 (26)	116	26/50
90	16.9 (49)	50/50	18.6 (46)	110	46/50	18.2 (46)	108	45/50	19.7 (26)	117	26/50
92	17.7 (49)	49/50	19.8 (44)	112	45/50	19.8 (45)	112	43/50	20.9 (25)	118	26/50
94	17.9 (49)	49/50	18.4 (45)	103	44/50	19.0 (43)	106	43/50	20.5 (24)	115	24/50
96	18.9 (47)	48/50	20.8 (42)	110	41/50	20.2 (41)	107	41/50	22.4 (23)	119	23/50
98	19.0 (46)	47/50	20.0 (41)	105	41/50	20.2 (41)	106	41/50	21.7 (23)	114	23/50
100	19.5 (47)	47/50	21.1 (38)	108	40/50	20.9 (40)	107	40/50	21.0 (20)	108	20/50
102	20.5 (45)	47/50	23.0 (38)	112	39/50	22.4 (35)	109	35/50	19.1 (14)	93	16/50
104	20.5 (47)	47/50	22.9 (39)	112	39/50	21.6 (35)	105	35/50	21.6 (14)	105	14/50

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

TABLE 8 FOOD COSUMPTION IN MALE RAT (TWO-YEAR STUDY)

Week on Study	Control Av.FC.	Control No.of Surviv. <50>	7500 ppm Av.FC.	7500 ppm % of cont. <50>	7500 ppm No.of Surviv.	15000 ppm Av.FC.	15000 ppm % of cont. <50>	15000 ppm No.of Surviv.	30000 ppm Av.FC.	30000 ppm % of cont. <50>	30000 ppm No.of Surviv.
1	15.8 (50)	50/50	15.7 (50)	99	50/50	15.4 (50)	97	50/50	14.5 (50)	92	50/50
2	16.3 (50)	50/50	16.2 (50)	99	50/50	16.0 (50)	98	50/50	15.2 (50)	93	50/50
3	16.0 (50)	50/50	15.9 (50)	99	50/50	16.0 (50)	100	50/50	15.1 (50)	94	50/50
4	16.3 (50)	50/50	16.1 (50)	99	50/50	16.3 (50)	100	50/50	15.4 (50)	94	50/50
5	16.4 (50)	50/50	16.0 (50)	98	50/50	16.1 (50)	98	50/50	15.2 (50)	93	50/50
6	15.8 (50)	50/50	15.6 (50)	99	50/50	15.9 (50)	101	50/50	14.4 (50)	91	50/50
7	16.4 (50)	50/50	16.2 (50)	99	50/50	16.5 (50)	101	50/50	14.9 (50)	91	50/50
8	16.4 (50)	50/50	16.3 (50)	99	50/50	16.2 (49)	99	50/50	15.1 (50)	92	50/50
9	16.2 (50)	50/50	16.5 (50)	102	50/50	16.6 (50)	102	50/50	15.2 (50)	94	50/50
10	16.1 (50)	50/50	16.2 (50)	101	50/50	16.5 (50)	102	50/50	15.1 (50)	94	50/50
11	16.5 (50)	50/50	16.7 (50)	101	50/50	16.8 (50)	102	50/50	15.5 (50)	94	50/50
12	16.1 (50)	50/50	16.4 (50)	102	50/50	16.5 (50)	102	50/50	15.3 (50)	95	50/50
13	16.6 (50)	50/50	16.5 (50)	99	50/50	16.7 (50)	101	50/50	15.4 (50)	93	50/50
14	16.5 (50)	50/50	16.3 (50)	99	50/50	16.7 (50)	101	50/50	15.6 (50)	95	50/50
18	15.8 (50)	50/50	16.0 (50)	101	50/50	16.1 (50)	102	50/50	15.4 (50)	97	50/50
22	16.1 (50)	50/50	16.3 (50)	101	50/50	16.0 (49)	99	50/50	15.7 (50)	98	50/50
26	16.2 (50)	50/50	16.5 (50)	102	50/50	16.4 (49)	101	50/50	16.2 (50)	100	50/50
30	16.6 (50)	50/50	17.0 (50)	102	50/50	17.1 (50)	103	50/50	16.3 (50)	98	50/50
34	16.1 (50)	50/50	16.4 (50)	102	50/50	16.7 (50)	104	50/50	15.8 (50)	98	50/50
38	16.1 (50)	50/50	16.5 (50)	102	50/50	16.3 (49)	101	50/50	16.0 (50)	99	50/50
42	16.8 (50)	50/50	17.1 (50)	102	50/50	17.3 (50)	103	50/50	16.4 (50)	98	50/50
46	16.9 (50)	50/50	17.1 (50)	101	50/50	17.1 (50)	101	50/50	16.2 (50)	96	50/50
50	17.0 (50)	50/50	17.1 (50)	101	50/50	17.2 (50)	101	50/50	16.3 (50)	96	50/50
54	17.4 (50)	50/50	17.7 (50)	102	50/50	18.0 (48)	103	50/50	17.1 (50)	98	50/50
58	17.5 (50)	50/50	17.3 (50)	99	50/50	17.4 (49)	99	49/50	17.3 (50)	99	50/50
62	18.0 (50)	50/50	17.7 (50)	98	49/50	18.0 (48)	100	48/50	16.9 (50)	94	50/50
66	17.7 (50)	50/50	18.1 (49)	102	49/50	17.8 (48)	101	47/50	16.7 (50)	94	50/50
70	17.5 (48)	48/50	17.2 (49)	98	49/50	16.7 (47)	95	47/50	16.3 (50)	93	50/50
74	17.6 (48)	48/50	17.5 (49)	99	49/50	17.3 (47)	98	47/50	16.6 (50)	94	50/50
78	17.6 (48)	48/50	17.5 (48)	99	47/50	17.4 (46)	99	46/50	16.4 (50)	93	50/50
82	17.5 (48)	48/50	17.2 (46)	98	46/50	16.7 (46)	95	46/50	16.3 (48)	93	48/50
86	17.3 (46)	46/50	16.9 (46)	98	46/50	16.9 (45)	98	45/50	16.1 (46)	93	46/50
90	17.2 (45)	45/50	17.1 (46)	99	46/50	16.3 (45)	95	45/50	15.9 (46)	92	46/50
94	16.6 (44)	44/50	16.9 (46)	102	46/50	16.1 (42)	97	42/50	15.2 (44)	92	43/50
98	16.9 (41)	41/50	16.4 (43)	97	42/50	16.0 (40)	95	40/50	14.0 (39)	83	37/50
102	16.9 (39)	39/50	16.2 (38)	96	40/50	15.9 (35)	94	35/50	14.6 (30)	86	30/50
104	17.2 (38)	38/50	16.7 (39)	97	39/50	15.7 (35)	91	34/50	13.9 (30)	81	30/50

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

TABLE 9 FOOD COSUMPTION IN FEMALE RAT (TWO-YEAR STUDY)

Week on Study	Control Av.FC.	Control No.of Suruiu. <50>	7500 ppm Av.FC.	7500 ppm % of cont. <50>	7500 ppm No.of Suruiu.	15000 ppm Av.FC.	15000 ppm % of cont. <50>	15000 ppm No.of Suruiu.	30000 ppm Av.FC.	30000 ppm % of cont. <50>	30000 ppm No.of Suruiu.
1	11.8 (50)	50/50	11.6 (50)	98	50/50	11.9 (50)	101	50/50	11.5 (50)	97	50/50
2	11.2 (50)	50/50	11.2 (50)	100	50/50	11.8 (50)	105	50/50	11.4 (50)	102	50/50
3	11.4 (50)	50/50	11.2 (50)	98	50/50	11.5 (50)	101	50/50	11.2 (50)	98	50/50
4	11.4 (50)	50/50	11.2 (50)	98	50/50	11.8 (50)	104	50/50	11.3 (50)	99	50/50
5	11.4 (50)	50/50	11.2 (50)	98	50/50	11.5 (50)	101	50/50	11.2 (50)	98	50/50
6	10.5 (50)	50/50	10.3 (50)	98	50/50	11.3 (50)	108	50/50	10.5 (50)	100	50/50
7	10.8 (50)	50/50	10.3 (50)	95	50/50	10.9 (50)	101	50/50	10.6 (50)	98	50/50
8	10.4 (50)	50/50	10.1 (50)	97	50/50	10.7 (50)	103	50/50	10.2 (50)	98	50/50
9	10.8 (50)	50/50	10.4 (50)	96	50/50	10.9 (50)	101	50/50	10.6 (50)	98	50/50
10	10.6 (50)	50/50	10.2 (50)	96	50/50	10.6 (50)	100	50/50	10.0 (50)	94	50/50
11	10.7 (50)	50/50	10.1 (50)	94	50/50	10.6 (50)	99	50/50	10.0 (50)	93	50/50
12	10.3 (50)	50/50	10.0 (50)	97	50/50	10.2 (50)	99	50/50	9.7 (50)	94	50/50
13	10.3 (50)	50/50	9.8 (50)	95	50/50	10.0 (50)	97	50/50	9.8 (50)	95	50/50
14	10.7 (50)	50/50	10.4 (50)	97	50/50	10.4 (50)	97	50/50	10.2 (50)	95	50/50
18	11.2 (50)	50/50	10.7 (50)	96	50/50	10.8 (50)	96	50/50	10.3 (50)	92	50/50
22	11.2 (50)	50/50	10.7 (50)	96	50/50	10.9 (50)	97	50/50	10.5 (50)	94	50/50
26	11.3 (50)	50/50	11.1 (50)	98	50/50	11.3 (50)	100	50/50	11.0 (50)	97	50/50
30	11.1 (50)	50/50	10.9 (50)	98	50/50	11.0 (50)	99	50/50	10.7 (50)	96	50/50
34	10.7 (50)	50/50	10.6 (50)	99	50/50	10.8 (50)	101	50/50	10.5 (50)	98	50/50
38	11.2 (50)	50/50	10.7 (50)	96	50/50	10.8 (50)	96	50/50	10.7 (49)	96	49/50
42	11.5 (50)	50/50	10.8 (50)	94	50/50	11.0 (50)	96	50/50	11.1 (49)	97	49/50
46	11.3 (50)	50/50	11.3 (49)	100	49/50	11.3 (50)	100	50/50	11.2 (49)	99	49/50
50	11.8 (50)	50/50	11.7 (49)	99	49/50	11.3 (50)	96	50/50	11.4 (49)	97	49/50
54	12.1 (50)	50/50	11.8 (49)	98	49/50	11.8 (50)	98	50/50	11.9 (49)	98	49/50
58	12.5 (50)	50/50	12.2 (49)	98	49/50	12.1 (50)	97	50/50	11.5 (49)	92	49/50
62	12.7 (50)	50/50	12.3 (49)	97	49/50	12.0 (50)	94	50/50	11.7 (48)	92	48/50
66	12.1 (50)	50/50	12.2 (49)	101	49/50	11.8 (50)	98	50/50	11.6 (47)	96	47/50
70	12.2 (50)	50/50	11.9 (49)	98	49/50	11.9 (50)	98	50/50	11.8 (45)	97	44/50
74	12.6 (50)	50/50	12.6 (48)	100	48/50	12.2 (50)	97	50/50	12.0 (44)	95	43/50
78	12.8 (50)	50/50	12.4 (47)	97	47/50	12.4 (50)	97	50/50	12.0 (36)	94	36/50
82	13.1 (50)	50/50	12.9 (47)	98	47/50	12.6 (48)	96	48/50	12.8 (31)	98	31/50
86	13.0 (50)	50/50	12.6 (46)	97	46/50	12.3 (47)	95	47/50	11.7 (29)	90	28/50
90	12.6 (50)	50/50	12.3 (46)	98	46/50	12.5 (45)	99	45/50	12.2 (26)	97	26/50
94	12.9 (49)	49/50	12.1 (45)	94	44/50	12.6 (43)	98	43/50	12.7 (24)	98	24/50
98	13.0 (47)	47/50	12.3 (41)	95	41/50	12.3 (41)	95	41/50	11.9 (23)	92	23/50
102	13.1 (47)	47/50	12.9 (39)	98	39/50	13.0 (35)	99	35/50	11.2 (16)	85	16/50
104	13.4 (46)	47/50	12.8 (39)	96	39/50	12.3 (35)	92	35/50	11.7 (14)	87	14/50

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

TABLE 10 NEOPLASTIC LESIONS INCIDENCE AND STATISTICAL ANALYSIS IN MALE RAT

Group Name	Control	7500ppm	15000ppm	30000ppm
SITE : skin/appendage				
TUMOR : sebaceous adenoma[f]				
Tumor rate				
Overall rates(a)	0/50(0.0)	0/50(0.0)	0/50(0.0)	3/50(6.0)
Adjusted rates(b)	0.0	0.0	0.0	8.82
Terminal rates(c)	0/38(0.0)	0/39(0.0)	0/34(0.0)	2/30(6.7)
Statistical analysis				
Peto test				
Standard method(d)	P=------			
Prevalence method(d)	P=0.0025**?			
Combined analysis (d)	P=------			
Cochran-Amitage test(e)	P=0.0079**?			
Fisher Exact test(e)		P=0.5000	P=0.5000	P=0.1325
SITE : thyroid				
TUMOR : C-cell adenoma[g]				
Tumor rate				
Overall rates(a)	12/50(24.0)	5/50(10.0)	5/50(10.0)	4/50(8.0)
Adjusted rates(b)	29.27	12.82	14.71	11.76
Terminal rates(c)	11/38(28.9)	5/39(12.8)	5/34(14.7)	3/30(10.0)
Statistical analysis				
Peto test				
Standard method(d)	P=------			
Prevalence method(d)	P=0.9671			
Combined analysis (d)	P=------			
Cochran-Amitage test(e)	P=0.0393*			
Fisher Exact test(e)		P=0.0942	P=0.0942	P=0.0539
SITE : mammary gland				
TUMOR : adenoma[h], fibroadenoma[i]				
Tumor rate				
Overall rates(a)	3/50(6.0)	1/50(2.0)	0/50(0.0)	0/50(0.0)
Adjusted rates(b)	7.89	2.44	0.0	0.0
Terminal rates(c)	3/38(7.9)	0/39(0.0)	0/34(0.0)	0/30(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P=------			
Prevalence method(d)	P=0.9858			
Combined analysis (d)	P=------			
Cochran-Amitage test(e)	P=0.0405*			
Fisher Exact test(e)		P=0.3235	P=0.1325	P=0.1325

(a):Number of tumor-bearing animals/number of animals examined at the site.
(b):Kaplan-Meire estimate tumor incidence at the end of the study after adjusting for intercurrent mortality.
(c):Observed tumor incidence at terminal kill.
(d):Beneth 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-Amitage and Fisher exact test compare directly the overall incidence rates.
(f):Historical incidence for 2-year studies: 2/850(0.2%); range 0% to 4%
(g):Historical incidence for 2-year studies: 105/850(12.4%); range 4% to 26%
(h):Historical incidence for 2-year studies: 8/850(0.9%); range 0% to 4%
(i):Historical incidence for 2-year studies: 16/850(1.9%); range 0% to 6%
?: The conditional probabilities of the largest and smallest possible out comes can not be 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

TABLE 11 NEOPLASTIC LESIONS INCIDENCE AND STATISTICAL ANALYSIS IN FEMALE RAT

Group Name	Control	7500ppm	15000ppm	30000ppm
SITE : spleen				
TUMOR : mononuclear cell leukemia[f]				
Tumor rate				
Overall rates(a)	1/50(2.0)	7/50(14.0)	3/50(6.0)	4/50(8.0)
Adjusted rates(b)	2.13	7.69	5.71	7.14
Terminal rates(c)	1/47(2.1)	3/39(7.7)	2/35(5.7)	1/14(7.1)
Statistical analysis				
Peto test				
Standard method(d)	P=0.0417*			
Prevalence method(d)	P=0.2161			
Combined analysis (d)	P=0.0349*			
Cochran-Amitage test(e)	P=0.6177			
Fisher Exact test(e)		P=0.0430*	P=0.3235	P=0.1998
SITE : pituitary gland				
TUMOR : adenoma[g]				
Tumor rate				
Overall rates(a)	18/49(36.7)	14/50(28.0)	12/50(24.0)	6/50(12.0)
Adjusted rates(b)	35.42	25.64	25.71	21.43
Terminal rates(c)	16/46(34.8)	10/39(25.6)	9/35(25.7)	3/14(21.4)
Statistical analysis				
Peto test				
Standard method(d)	P=0.4673			
Prevalence method(d)	P=0.9411			
Combined analysis (d)	P=0.9192			
Cochran-Amitage test(e)	P=0.0041**			
Fisher Exact test(e)		P=0.3228	P=0.2121	P=0.0201*
SITE : pituitary gland				
TUMOR : adenoma[g], adenocarcinoma[h]				
Tumor rate				
Overall rates(a)	19/49(38.8)	14/50(28.0)	14/50(28.0)	7/50(14.0)
Adjusted rates(b)	37.50	25.64	28.57	21.43
Terminal rates(c)	17/46(37.0)	10/39(25.6)	10/35(28.6)	3/14(21.4)
Statistical analysis				
Peto test				
Standard method(d)	P=0.1912			
Prevalence method(d)	P=0.9439			
Combined analysis (d)	P=0.8365			
Cochran-Amitage test(e)	P=0.0070**			
Fisher Exact test(e)		P=0.2736	P=0.2736	P=0.0256*
SITE : uterus				
TUMOR : endometrial stromal polyp[i]				
Tumor rate				
Overall rates(a)	14/50(28.0)	5/50(10.0)	7/50(14.0)	7/50(14.0)
Adjusted rates(b)	28.00	12.82	13.04	29.41
Terminal rates(c)	13/47(27.7)	5/39(12.8)	3/35(8.6)	4/14(28.6)
Statistical analysis				
Peto test				
Standard method(d)	P=0.0621			
Prevalence method(d)	P=0.6556			
Combined analysis (d)	P=0.4651			
Cochran-Amitage test(e)	P=0.1662			
Fisher Exact test(e)		P=0.0481*	P=0.1246	P=0.1246

TABLE 11 NEOPLASTIC LESIONS INCIDENCE AND STATISTICAL ANALYSIS IN FEMALE RAT (Continued)

Group Name	Control	7500ppm	15000ppm	30000ppm
SITE : uterus				
TUMOR : endometrial stromal polyp(i), endometrial stromal sarcoma(j)				
Tumor rate				
Overall rates(a)	14/50(28.0)	5/50(10.0)	9/50(18.0)	8/50(16.0)
Adjusted rates(b)	28.00	12.82	13.33	29.41
Terminal rates(c)	13/47(27.7)	5/39(12.8)	3/35(8.6)	4/14(28.6)
Statistical analysis				
Peto test				
Standard method(d)	P=0.0146*			
Prevalence method(d)	P=0.6429			
Combined analysis (d)	P=0.2632			
Cochran-Amitage test(e)	P=0.3195			
Fisher Exact test(e)		P=0.0481*	P=0.2397	P=0.1781

(a):Number of tumor-bearing animals/number of animals examined at the site.
(b):Kaplan-Meire estimate tumor incidence at the end of the study after adjusting for intercurrent mortality.
(c):Observed tumor incidence at terminal kill.
(d):Beneth 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-Amitage and Fisher exact test compare directly the overall incidence rates.
(f):Historical incidence for 2-year studies: 125/849(14.7%); range 8% to 26%
(g):Historical incidence for 2-year studies: 360/849(42.4%); range 16% to 70%
(h):Historical incidence for 2-year studies: 19/849(2.2%); range 0% to 14%
(i):Historical incidence for 2-year studies: 127/849(15.0%); range 2% to 28%
(j):Historical incidence for 2-year studies:4/849(0.5%); range 0% to 2%
?: The conditional probabilities of the largest and smallest possible out comes can not be estimated or this P-value is beyond the estimated P-value.
------:There is no data which should be statistical analysis.

TABLE 12 NUMBER OF RATS WITH MINERALIZATION OF HEART

Group name		Control	7500ppm	15000ppm	30000ppm
Male					
Dead and moribund animals		<12>	<11>	<16>	<20>
		2	0	1	11
	+	(1)		(1)	(3)
	2+	(1)			(6)
	3+				(2)
Sacrificed animals		<38>	<39>	<34>	<30>
		0	0	0	2
	+				(2)
	2+				
	3+				
All animals		<50>	<50>	<50>	<50>*
		2	0	1	13
	+	(1)		(1)	(5)
	2+	(1)			(6)
	3+				(2)
Female					
Dead and moribund animals		<3>	<11>	<15>	<36>
		1	0	2	18
	+	(1)			(2)
	2+				(12)
	3+			(2)	(4)
Sacrificed animals		<47>	<39>	<35>	<14>
		0	0	1	0
	+				
	2+				
	3+			(1)	
All animals		<50>	<50>	<50>	<50>**
		1	0	3	18
	+	(1)			(2)
	2+				(12)
	3+			(3)	(4)

Grade +:Slight 2+:Moderate 3+:Marked
<a> a:Number of animals examined at the site
b b:Number of animals with lesion
(c) c:Number of animals with lesion in each grade
Significant difference *:P≦0.05 **:P≦0.01 Test of Chi square

TABLE 13 NUMBER OF RATS WITH MINERALIZATION OF KIDNEY (CORTEX)

Group name		Control	7500ppm	15000ppm	30000ppm
Male					
Dead and moribund animals		<12>	<11>	<16>	<20>
		2	0	2	11
	+	(1)		(2)	(8)
	2+	(1)			(3)
	3+				
Sacrificed animals		<38>	<39>	<34>	<30>
		0	0	0	2
	+				(2)
	2+				
	3+				
All animals		<50>	<50>	<50>	<50>**
		2	0	2	13
	+	(1)		(2)	(10)
	2+	(1)			(3)
	3+				
Female					
Dead and moribund animals		<3>	<11>	<15>	<36>
		1	1	1	26
	+	(1)	(1)		(10)
	2+				(9)
	3+			(1)	(6)
	4+				(1)
Sacrificed animals		<47>	<39>	<35>	<14>
		0	0	1	0
	+				
	2+			(1)	
	3+				
	4+				
All animals		<50>	<50>	<50>	<50>**
		1	1	2	26
	+	(1)	(1)		(10)
	2+			(1)	(9)
	3+			(1)	(6)
	4+				(1)

Grade +: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:Number of animals with lesion in each grade
Significant difference *:P≦0.05 **:P≦0.01 Test of Chi square

TABLE 14 CAUSE OF DEATH IN RATS

	Male				Female			
Group	Control	7500ppm	15000ppm	30000ppm	Control	7500ppm	15000ppm	30000ppm
Number of dead or moribund animals	12	11	16	20	3	11	15	36
No microscopical confirmation	3	2	1	0	0	0	0	3
Integmentary system lesion	0	0	0	0	0	0	0	1
Cardiovascular lesion	0	0	0	9	0	0	1	14
Renal lesion	0	0	0	0	0	0	0	8
CNS Disorders	0	0	1	0	0	0	0	0
Thrombosis	0	0	1	0	0	0	0	0
Ileus	0	0	0	0	0	0	1	0
Chronic nephropathy	1	0	1	0	1	0	1	1
Tumor death : leukemia	5	0	2	2	0	4	1	3
subcutis	1	3	0	1	0	0	0	1
oral cavity	0	0	0	0	1	0	0	0
tooth	0	0	0	0	0	1	0	0
large intestine	0	0	0	0	0	0	1	0
liver	0	0	1	0	0	0	1	0
pituitary	2	3	3	2	1	3	2	2
adrenal	0	0	1	1	0	0	0	0
uterus	–	–	–	–	0	0	4	2
mammary gland	0	0	0	0	0	1	1	0
preptual/clitoral gland	0	0	1	0	0	1	1	1
brain	0	1	2	1	0	1	0	0
Zymbal gland	0	0	0	1	0	0	1	0
bone	0	0	0	1	0	0	0	0
peritoneum	0	2	2	2	0	0	0	0

TABLE 15 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES IN MALE MOUSE (TWO-YEAR STUDY)

Week on Study	Control Av.Wt.	Control No.of Surviv. <50>	10000 ppm Av.Wt.	10000 ppm % of cont. <50>	10000 ppm No.of Surviv.	20000 ppm Av.Wt.	20000 ppm % of cont. <50>	20000 ppm No.of Surviv.	40000 ppm Av.Wt.	40000 ppm % of cont. <50>	40000 ppm No.of Surviv.
0	22.5 (50)	50/50	22.5 (50)	100	50/50	22.5 (50)	100	50/50	22.5 (50)	100	50/50
1	24.1 (50)	50/50	23.9 (50)	99	50/50	23.6 (50)	98	50/50	23.4 (50)	97	50/50
2	24.9 (50)	50/50	24.7 (50)	99	50/50	24.7 (50)	99	50/50	24.4 (50)	98	50/50
3	25.9 (50)	50/50	25.9 (50)	100	50/50	25.8 (50)	100	50/50	25.5 (50)	98	50/50
4	27.0 (50)	50/50	26.9 (50)	100	50/50	26.9 (50)	100	50/50	26.4 (50)	98	50/50
5	27.9 (50)	50/50	27.1 (50)	97	50/50	27.3 (50)	98	50/50	26.8 (50)	96	50/50
6	28.6 (50)	50/50	28.3 (50)	99	50/50	28.4 (50)	99	50/50	27.7 (50)	97	50/50
7	29.0 (50)	50/50	28.9 (50)	100	50/50	28.9 (50)	100	50/50	28.2 (50)	97	50/50
8	29.7 (50)	50/50	29.9 (50)	101	50/50	29.7 (50)	100	50/50	29.0 (50)	98	50/50
9	30.4 (50)	50/50	30.8 (50)	101	50/50	30.6 (50)	101	50/50	29.7 (50)	98	50/50
10	31.4 (50)	50/50	31.8 (50)	101	50/50	31.6 (50)	101	50/50	30.7 (50)	98	50/50
11	31.9 (50)	50/50	32.2 (50)	101	50/50	32.1 (50)	101	50/50	31.2 (50)	98	50/50
12	33.1 (50)	50/50	33.3 (50)	101	50/50	33.2 (50)	100	50/50	32.3 (50)	98	50/50
13	33.6 (50)	50/50	33.9 (50)	101	50/50	34.0 (50)	101	50/50	32.9 (50)	98	50/50
14	34.4 (50)	50/50	34.8 (50)	101	50/50	35.1 (50)	102	50/50	33.9 (50)	99	50/50
16	35.7 (50)	50/50	36.0 (50)	101	50/50	36.2 (50)	101	50/50	35.1 (50)	98	50/50
18	37.5 (50)	50/50	38.1 (50)	102	50/50	38.0 (50)	101	50/50	36.6 (50)	98	50/50
20	38.9 (50)	50/50	39.5 (50)	102	50/50	39.5 (50)	102	50/50	38.0 (50)	98	50/50
22	39.4 (50)	50/50	40.3 (50)	102	50/50	40.4 (50)	103	50/50	38.7 (50)	98	50/50
24	40.4 (50)	50/50	40.9 (50)	101	50/50	41.5 (50)	103	50/50	39.5 (50)	98	50/50
26	41.4 (50)	50/50	42.0 (50)	101	50/50	42.6 (50)	103	50/50	40.6 (50)	98	50/50
28	42.3 (50)	50/50	43.0 (50)	102	50/50	43.9 (50)	104	50/50	41.6 (50)	98	50/50
30	43.3 (50)	50/50	44.1 (50)	102	50/50	44.8 (50)	103	50/50	42.6 (50)	98	50/50
32	44.7 (50)	50/50	45.4 (50)	102	50/50	46.4 (50)	104	50/50	43.9 (50)	98	50/50
34	45.2 (50)	50/50	45.8 (50)	101	50/50	46.8 (50)	104	50/50	44.3 (50)	98	50/50
36	45.9 (50)	50/50	46.1 (50)	100	50/50	46.8 (50)	102	50/50	44.4 (50)	97	50/50
38	46.2 (50)	50/50	46.5 (50)	101	50/50	47.1 (50)	102	50/50	44.6 (50)	97	50/50
40	46.6 (50)	50/50	47.0 (50)	101	50/50	47.8 (50)	103	50/50	45.1 (50)	97	50/50
42	47.0 (50)	50/50	47.4 (50)	101	50/50	48.3 (50)	103	50/50	45.2 (50)	96	50/50
44	47.6 (50)	50/50	48.6 (50)	102	50/50	49.1 (50)	103	50/50	46.2 (50)	97	50/50
46	47.8 (50)	50/50	48.3 (50)	101	50/50	49.2 (50)	103	50/50	46.4 (50)	97	50/50
48	48.0 (50)	49/50	48.4 (50)	101	50/50	49.3 (50)	103	50/50	46.7 (50)	97	50/50
50	49.2 (49)	49/50	49.0 (50)	100	50/50	50.0 (50)	102	50/50	47.1 (50)	96	50/50
52	50.2 (49)	49/50	50.0 (50)	100	50/50	50.9 (50)	101	50/50	47.6 (50)	95	50/50
54	49.2 (49)	49/50	49.7 (50)	101	50/50	49.9 (50)	101	50/50	46.8 (49)	95	49/50
56	49.5 (49)	49/50	49.6 (50)	100	50/50	49.8 (50)	101	50/50	46.6 (49)	94	49/50
58	49.2 (49)	49/50	49.4 (50)	100	50/50	50.0 (50)	102	50/50	46.5 (48)	95	48/50
60	50.4 (49)	49/50	50.2 (50)	100	50/50	51.4 (50)	102	50/50	47.9 (48)	95	48/50
62	51.4 (49)	49/50	51.0 (50)	99	50/50	51.9 (50)	101	50/50	49.0 (47)	95	47/50
64	51.5 (49)	49/50	51.5 (50)	100	50/50	52.3 (50)	102	50/50	49.4 (47)	96	47/50
66	51.5 (49)	49/50	51.1 (50)	99	50/50	51.9 (50)	101	50/50	48.9 (46)	95	46/50
68	51.8 (49)	49/50	52.2 (49)	101	49/50	51.9 (50)	100	50/50	48.8 (45)	94	45/50
70	52.2 (48)	48/50	52.1 (49)	100	49/50	52.5 (49)	101	49/50	49.2 (43)	94	43/50
72	52.7 (48)	48/50	52.7 (49)	100	49/50	52.4 (49)	99	49/50	49.5 (43)	94	43/50
74	52.9 (48)	48/50	52.9 (49)	100	49/50	52.6 (48)	99	48/50	49.9 (42)	94	42/50
76	52.9 (47)	47/50	52.7 (49)	100	49/50	53.2 (46)	101	46/50	50.0 (42)	95	42/50
78	53.2 (46)	46/50	53.0 (48)	100	48/50	53.1 (46)	100	46/50	50.0 (42)	94	42/50
80	53.3 (44)	44/50	53.5 (48)	100	48/50	53.3 (46)	100	46/50	51.0 (41)	96	41/50
82	53.7 (44)	44/50	53.1 (48)	99	48/50	52.9 (46)	99	46/50	50.4 (41)	94	41/50
84	53.7 (44)	44/50	53.3 (47)	99	46/50	52.4 (45)	98	45/50	50.9 (40)	95	40/50
86	53.0 (44)	44/50	53.1 (46)	100	46/50	52.9 (43)	100	43/50	50.1 (40)	95	40/50
88	52.4 (44)	44/50	53.6 (45)	102	45/50	52.7 (43)	101	43/50	49.9 (39)	95	39/50
90	51.6 (44)	44/50	53.0 (45)	103	45/50	51.3 (42)	99	42/50	49.3 (38)	96	38/50
92	51.8 (42)	42/50	54.1 (43)	104	43/50	51.9 (41)	100	41/50	50.3 (35)	97	35/50
94	51.5 (42)	42/50	53.4 (43)	104	43/50	50.9 (41)	99	41/50	49.4 (35)	96	34/50
96	51.4 (41)	41/50	53.2 (42)	104	42/50	50.0 (39)	97	39/50	48.1 (33)	94	33/50
98	50.8 (40)	40/50	53.8 (39)	106	39/50	49.3 (37)	97	37/50	47.3 (32)	93	32/50
100	49.9 (39)	39/50	53.1 (38)	106	38/50	49.3 (33)	99	33/50	46.0 (31)	92	31/50
102	49.9 (36)	36/50	52.6 (36)	105	36/50	48.5 (32)	97	32/50	46.4 (29)	93	29/50
104	49.5 (34)	34/50	52.3 (35)	106	35/50	48.0 (30)	97	30/50	46.6 (25)	94	25/50

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

TABLE 16 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES IN FEMALE MOUSE (TWO-YEAR STUDY)

Week on Study	Control Av.Wt.	Control No.of Surviv. <50>	10000 ppm Av.Wt.	10000 ppm % of cont. <50>	10000 ppm No.of Surviv.	20000 ppm Av.Wt.	20000 ppm % of cont. <50>	20000 ppm No.of Surviv.	40000 ppm Av.Wt.	40000 ppm % of cont. <50>	40000 ppm No.of Surviv.
0	18.1 (50)	50/50	18.1 (50)	100	50/50	18.1 (50)	100	50/50	18.1 (50)	100	50/50
1	19.2 (50)	50/50	19.2 (50)	100	50/50	19.0 (50)	99	50/50	19.3 (50)	101	50/50
2	19.8 (50)	50/50	19.9 (50)	101	50/50	19.6 (50)	99	50/50	19.7 (50)	99	50/50
3	20.6 (50)	50/50	20.7 (50)	100	50/50	20.5 (50)	100	50/50	20.7 (50)	100	50/50
4	21.5 (50)	50/50	21.6 (50)	100	50/50	21.3 (50)	99	50/50	21.5 (50)	100	50/50
5	22.0 (50)	50/50	21.7 (50)	99	50/50	21.4 (50)	97	50/50	21.2 (50)	96	50/50
6	22.5 (50)	50/50	22.4 (50)	100	50/50	22.4 (50)	100	50/50	22.2 (50)	99	50/50
7	22.8 (50)	50/50	22.5 (50)	99	50/50	22.6 (50)	99	50/50	22.6 (50)	99	50/50
8	23.2 (50)	50/50	23.1 (50)	100	50/50	23.2 (50)	100	50/50	23.0 (50)	99	50/50
9	23.6 (50)	50/50	23.7 (50)	100	50/50	23.7 (49)	100	49/50	23.5 (50)	100	50/50
10	24.0 (50)	50/50	24.1 (50)	100	50/50	24.0 (49)	100	49/50	24.0 (50)	100	50/50
11	23.9 (50)	50/50	23.9 (50)	100	50/50	23.7 (49)	99	49/50	23.9 (50)	100	50/50
12	24.9 (50)	50/50	24.4 (50)	98	50/50	24.4 (49)	98	49/50	24.3 (50)	98	50/50
13	24.4 (50)	50/50	24.1 (50)	99	50/50	24.1 (49)	99	49/50	24.1 (50)	99	50/50
14	24.7 (50)	50/50	24.7 (50)	100	50/50	24.5 (49)	99	49/50	24.6 (50)	100	50/50
16	25.4 (50)	50/50	25.4 (50)	100	50/50	25.0 (49)	98	49/50	25.0 (50)	98	50/50
18	26.4 (50)	50/50	26.2 (50)	99	50/50	26.1 (49)	99	49/50	25.9 (50)	98	50/50
20	26.8 (50)	50/50	26.8 (50)	100	50/50	26.4 (49)	99	49/50	26.4 (50)	99	50/50
22	27.0 (50)	50/50	27.4 (50)	101	50/50	27.2 (49)	101	49/50	26.9 (50)	100	50/50
24	27.4 (50)	50/50	26.9 (50)	98	50/50	27.5 (49)	100	49/50	27.1 (50)	99	50/50
26	28.1 (50)	50/50	27.9 (50)	99	50/50	27.5 (49)	98	49/50	27.3 (50)	97	50/50
28	29.0 (49)	49/50	28.6 (50)	99	50/50	28.3 (49)	98	49/50	27.4 (50)	94	50/50
30	29.4 (49)	49/50	29.1 (50)	99	50/50	28.4 (49)	97	49/50	28.1 (50)	96	50/50
32	30.4 (49)	49/50	30.4 (50)	100	50/50	30.0 (48)	99	48/50	29.0 (50)	95	50/50
34	30.4 (49)	49/50	30.3 (50)	100	50/50	29.6 (48)	97	48/50	29.6 (50)	97	50/50
36	30.9 (49)	49/50	31.0 (49)	100	49/50	30.5 (48)	99	48/50	29.8 (50)	96	50/50
38	30.6 (49)	49/50	30.8 (49)	101	49/50	30.1 (48)	98	48/50	29.7 (50)	97	50/50
40	31.7 (49)	49/50	31.6 (49)	100	49/50	31.0 (48)	98	48/50	30.3 (50)	96	50/50
42	31.9 (49)	49/50	31.6 (49)	99	49/50	31.3 (48)	98	48/50	29.7 (50)	93	50/50
44	31.9 (49)	49/50	32.0 (49)	100	49/50	31.6 (48)	99	48/50	30.4 (50)	95	50/50
46	31.6 (47)	47/50	31.8 (49)	101	49/50	31.2 (47)	99	47/50	30.4 (50)	96	50/50
48	32.8 (47)	47/50	33.0 (49)	101	49/50	32.1 (47)	98	47/50	30.9 (50)	94	50/50
50	32.6 (47)	47/50	32.8 (49)	101	49/50	32.2 (47)	99	47/50	31.3 (50)	96	50/50
52	33.0 (47)	47/50	32.8 (49)	99	49/50	33.0 (47)	100	47/50	32.0 (50)	97	50/50
54	32.3 (47)	47/50	32.3 (49)	100	49/50	32.4 (46)	100	46/50	31.6 (49)	98	49/50
56	32.8 (46)	46/50	31.6 (49)	96	49/50	31.9 (46)	97	46/50	31.7 (49)	97	49/50
58	33.2 (46)	46/50	32.6 (48)	98	48/50	32.6 (46)	98	46/50	32.4 (49)	98	49/50
60	34.1 (46)	46/50	34.1 (48)	100	48/50	33.9 (46)	99	46/50	33.0 (49)	97	49/50
62	35.3 (45)	45/50	34.8 (48)	99	48/50	34.3 (45)	97	45/50	33.5 (49)	95	49/50
64	35.8 (45)	45/50	35.3 (48)	99	48/50	35.6 (45)	99	45/50	34.6 (49)	97	49/50
66	36.3 (45)	45/50	35.9 (47)	99	47/50	35.2 (44)	97	44/50	34.3 (48)	94	48/50
68	36.5 (45)	45/50	36.2 (47)	99	47/50	35.1 (43)	96	43/50	34.4 (47)	94	47/50
70	36.4 (45)	45/50	36.2 (47)	99	47/50	35.3 (43)	97	43/50	34.4 (47)	95	47/50
72	36.7 (45)	45/50	36.3 (47)	99	47/50	36.3 (43)	99	43/50	34.9 (47)	95	47/50
74	37.4 (43)	43/50	36.7 (46)	98	46/50	36.3 (43)	97	43/50	35.0 (47)	94	47/50
76	37.2 (43)	43/50	37.5 (45)	101	45/50	37.0 (42)	99	42/50	35.9 (46)	97	46/50
78	38.1 (43)	43/50	37.4 (44)	98	44/50	37.1 (42)	97	42/50	36.0 (46)	94	46/50
80	37.8 (42)	42/50	37.8 (42)	100	42/50	37.6 (42)	99	42/50	36.4 (46)	96	46/50
82	38.3 (42)	42/50	38.0 (41)	99	41/50	37.8 (41)	99	41/50	36.2 (45)	95	45/50
84	37.7 (41)	41/50	38.1 (41)	101	41/50	37.6 (39)	100	39/50	36.6 (44)	97	44/50
86	38.0 (40)	40/50	37.1 (41)	98	41/50	37.6 (37)	99	37/50	36.1 (43)	95	43/50
88	37.8 (38)	38/50	36.9 (40)	98	39/50	37.5 (35)	99	35/50	36.3 (43)	96	43/50
90	37.6 (37)	37/50	36.4 (36)	97	36/50	37.1 (32)	99	32/50	35.9 (43)	95	43/50
92	36.8 (37)	37/50	36.7 (35)	100	35/50	36.0 (31)	98	31/50	35.9 (41)	98	41/50
94	37.1 (37)	37/50	36.0 (34)	97	34/50	36.7 (29)	99	29/50	35.9 (39)	97	39/50
96	36.3 (35)	35/50	35.3 (32)	97	32/50	35.9 (27)	99	27/50	35.3 (37)	97	37/50
98	37.6 (33)	33/50	35.3 (31)	94	31/50	35.8 (26)	95	26/50	35.0 (36)	93	36/50
100	36.4 (32)	32/50	36.3 (28)	100	28/50	35.4 (24)	97	24/50	35.4 (35)	97	35/50
102	36.6 (30)	30/50	36.5 (25)	100	25/50	34.7 (23)	95	22/50	34.5 (33)	94	32/50
104	36.2 (29)	29/50	35.4 (25)	98	24/50	36.1 (19)	100	19/50	34.9 (28)	96	28/50

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

TABLE 17 INCIDENCE OF EXTERNAL AND INTERNAL MASS IN CLINICAL OBSERVATION IN MALE MOUSE

Time of mass occurrence (week)		0～13	14～26	27～39	40～52	53～65	66～78	79～91	92～104	0～104
External mass										
	Control	0/50	0/50	0/50	0/49	0/49	1/46	1/44	2/34	4/50(2/16)
	10000ppm	0/50	0/50	0/50	0/50	0/50	3/48	2/43	4/35	5/50(2/15)
	20000ppm	0/50	0/50	0/50	0/50	0/50	0/46	0/42	1/30	1/50(0/20)
	40000ppm	0/50	0/50	0/50	0/50	0/46	0/42	2/36	1/25	3/50(2/25)
Internal mass										
	Control	0/50	0/50	0/50	0/49	0/49	2/46	3/44	4/34	6/50(3/16)
	10000ppm	0/50	0/50	0/50	0/50	1/50	1/48	2/43	1/35	4/50(4/15)
	20000ppm	0/50	0/50	0/49	0/50	1/50	2/46	2/42	3/30	4/50(4/20)
	40000ppm	0/50	0/50	0/50	0/50	1/46	0/42	0/36	1/25	2/50(2/25)

No. of animals with mass / No. of survival animals at first week on each period.
(No. of dead and moribund animals with mass / No. of dead and moribund animals)

TABLE 18 INCIDENCE OF EXTERNAL AND INTERNAL MASS IN CLINICAL OBSERVATION IN FEMALE MOUSE

Time of mass occurrence (week)		0～13	14～26	27～39	40～52	53～65	66～78	79～91	92～104	0～104
External mass										
	Control	0/50	0/50	0/49	0/47	1/45	1/43	0/37	6/29	7/50(4/21)
	10000ppm	0/50	0/50	0/49	0/49	0/48	1/44	3/36	2/24	3/50(3/26)
	20000ppm	1/49	0/49	0/48	2/47	0/45	1/42	1/32	1/19	3/50(3/31)
	40000ppm	0/50	0/50	0/50	0/50	1/48	3/46	4/43	7/28	7/49(4/22)
Internal mass										
	Control	0/50	0/50	0/49	0/47	4/45	4/43	5/37	2/29	12/50(11/21)
	10000ppm	0/50	0/50	0/49	0/49	0/48	3/44	5/36	2/24	7/50(7/26)
	20000ppm	0/49	0/49	0/48	2/47	1/45	0/42	8/32	5/19	12/50(11/31)
	40000ppm	0/50	0/50	0/50	0/50	3/48	4/46	4/43	4/28	9/49(9/22)

No. of animals with mass / No. of survival animals at first week on each period.
(No. of dead and moribund animals with mass / No. of dead and moribund animals)

TABLE 19 WATER CONSUMPTION IN MALE MOUSE (TWO-YEAR STUDY)

Week on Study	Control Av.WC.	Control No.of Surviv. <50>	10000 ppm Av.WC.	10000 ppm % of cont. <50>	10000 ppm No.of Surviv.	20000 ppm Av.WC.	20000 ppm % of cont. <50>	20000 ppm No.of Surviv.	40000 ppm Av.WC.	40000 ppm % of cont. <50>	40000 ppm No.of Surviv.
1	4.9 (50)	50/50	5.3 (50)	108	50/50	5.2 (50)	106	50/50	5.6 (49)	114	50/50
2	5.0 (49)	50/50	5.1 (50)	102	50/50	5.2 (50)	104	50/50	5.6 (49)	112	50/50
3	4.7 (49)	50/50	5.0 (50)	106	50/50	5.2 (49)	111	50/50	5.7 (47)	121	50/50
4	6.1 (50)	50/50	5.5 (50)	90	50/50	5.9 (50)	97	50/50	7.0 (50)	115	50/50
5	6.9 (50)	50/50	5.2 (50)	75	50/50	5.6 (50)	81	50/50	7.2 (50)	104	50/50
6	6.6 (50)	50/50	6.3 (50)	95	50/50	6.7 (50)	102	50/50	7.2 (50)	109	50/50
7	9.7 (50)	50/50	6.4 (50)	66	50/50	6.9 (50)	71	50/50	7.8 (50)	80	50/50
8	7.2 (50)	50/50	6.4 (50)	89	50/50	6.9 (50)	96	50/50	7.6 (50)	106	50/50
9	6.3 (50)	50/50	6.2 (50)	98	50/50	6.7 (50)	106	50/50	7.0 (50)	111	50/50
10	5.9 (49)	50/50	5.7 (50)	97	50/50	6.0 (50)	102	50/50	6.4 (50)	108	50/50
11	6.4 (50)	50/50	5.4 (50)	84	50/50	6.5 (50)	102	50/50	6.6 (50)	103	50/50
12	6.4 (49)	50/50	5.8 (50)	91	50/50	5.9 (49)	92	50/50	6.4 (50)	100	50/50
13	6.9 (50)	50/50	5.5 (50)	80	50/50	5.6 (50)	81	50/50	6.0 (50)	87	50/50
14	6.4 (48)	50/50	5.4 (50)	84	50/50	6.1 (50)	95	50/50	6.2 (50)	97	50/50
16	7.2 (49)	50/50	5.6 (50)	78	50/50	5.5 (50)	76	50/50	5.9 (50)	82	50/50
18	6.8 (50)	50/50	4.9 (50)	72	50/50	5.3 (50)	78	50/50	5.7 (50)	84	50/50
20	5.3 (50)	50/50	4.6 (50)	87	50/50	4.9 (50)	92	50/50	5.3 (50)	100	50/50
22	5.2 (50)	50/50	4.7 (50)	90	50/50	5.0 (50)	96	50/50	5.6 (50)	108	50/50
24	5.2 (50)	50/50	4.7 (50)	90	50/50	4.4 (50)	85	50/50	5.2 (50)	100	50/50
26	4.9 (50)	50/50	4.7 (50)	96	50/50	4.5 (50)	92	50/50	4.8 (50)	98	50/50
28	5.2 (50)	50/50	4.4 (50)	85	50/50	4.8 (50)	92	50/50	4.9 (50)	94	50/50
30	5.2 (50)	50/50	4.4 (50)	85	50/50	4.6 (49)	88	50/50	4.7 (50)	90	50/50
32	5.5 (50)	50/50	4.3 (50)	78	50/50	4.6 (50)	84	50/50	5.1 (49)	93	50/50
34	5.0 (50)	50/50	4.4 (50)	88	50/50	4.8 (50)	96	50/50	4.9 (50)	98	50/50
36	4.9 (50)	50/50	4.6 (50)	94	50/50	4.5 (50)	92	50/50	4.8 (50)	98	50/50
38	4.4 (50)	50/50	4.2 (50)	95	50/50	4.6 (50)	105	50/50	4.6 (50)	105	50/50
40	4.9 (50)	50/50	4.4 (50)	90	50/50	4.9 (50)	100	50/50	5.0 (50)	102	50/50
42	4.9 (50)	50/50	4.6 (50)	94	50/50	4.9 (50)	100	50/50	4.8 (50)	98	50/50
44	5.3 (50)	50/50	4.6 (50)	87	50/50	4.9 (50)	92	50/50	5.2 (48)	98	50/50
46	5.6 (50)	50/50	4.4 (50)	79	50/50	4.7 (50)	84	50/50	5.0 (50)	89	50/50
48	6.2 (50)	49/50	4.7 (50)	76	50/50	4.9 (50)	79	50/50	5.4 (50)	87	50/50
50	5.1 (49)	49/50	4.6 (50)	90	50/50	4.7 (50)	92	50/50	5.0 (50)	98	50/50
52	4.5 (49)	49/50	4.3 (50)	96	50/50	4.5 (50)	100	50/50	4.8 (50)	107	50/50
54	5.4 (49)	49/50	4.6 (50)	85	50/50	4.8 (50)	89	50/50	5.2 (49)	96	49/50
56	5.1 (49)	49/50	4.7 (50)	92	50/50	5.0 (50)	98	50/50	5.5 (49)	108	49/50
58	5.2 (49)	49/50	4.5 (50)	87	50/50	5.0 (50)	96	50/50	5.3 (46)	102	48/50
60	5.3 (49)	49/50	4.6 (50)	87	50/50	5.0 (50)	94	50/50	5.2 (47)	98	48/50
62	4.9 (49)	49/50	4.5 (50)	92	50/50	4.5 (50)	92	50/50	4.8 (47)	98	47/50
64	5.3 (49)	49/50	5.5 (50)	104	50/50	4.8 (50)	91	50/50	5.2 (47)	98	47/50
66	5.0 (49)	49/50	5.0 (50)	100	50/50	4.9 (50)	98	50/50	5.2 (46)	104	46/50
68	5.2 (49)	49/50	4.6 (49)	88	49/50	4.9 (50)	94	50/50	5.3 (45)	102	45/50
70	4.7 (48)	48/50	4.4 (48)	94	49/50	4.6 (49)	98	49/50	5.1 (42)	109	43/50
72	5.1 (48)	48/50	4.4 (49)	86	49/50	4.8 (49)	94	49/50	5.5 (43)	108	43/50
74	4.8 (48)	48/50	4.6 (49)	96	49/50	4.8 (48)	100	48/50	5.8 (42)	121	42/50
76	5.6 (47)	47/50	4.5 (49)	80	49/50	5.1 (46)	91	46/50	5.9 (42)	105	42/50
78	5.0 (46)	46/50	4.5 (48)	90	48/50	4.9 (46)	98	46/50	5.5 (42)	110	42/50
80	5.2 (44)	44/50	4.7 (48)	90	48/50	5.1 (46)	98	46/50	5.5 (41)	106	41/50
82	5.2 (44)	44/50	4.6 (48)	88	48/50	5.0 (46)	96	46/50	5.6 (41)	108	41/50
84	5.1 (44)	44/50	4.7 (47)	92	46/50	5.1 (45)	100	45/50	6.0 (40)	118	40/50
86	5.1 (44)	44/50	5.0 (46)	98	46/50	5.4 (43)	106	43/50	6.3 (40)	124	40/50
88	5.8 (44)	44/50	5.0 (45)	85	45/50	5.9 (43)	100	43/50	6.6 (39)	112	39/50
90	5.9 (44)	44/50	4.9 (45)	83	45/50	6.6 (43)	112	42/50	7.2 (38)	122	38/50
92	5.5 (42)	42/50	5.0 (43)	91	43/50	6.7 (41)	122	41/50	7.1 (35)	129	35/50
94	5.3 (42)	42/50	4.7 (43)	89	43/50	6.8 (41)	128	41/50	7.3 (35)	138	34/50
96	5.6 (41)	41/50	5.1 (42)	91	42/50	7.4 (39)	132	39/50	7.3 (33)	130	33/50
98	5.5 (40)	40/50	4.9 (39)	89	39/50	6.9 (37)	125	37/50	8.2 (32)	149	32/50
100	6.2 (39)	39/50	5.0 (38)	81	38/50	6.5 (33)	105	33/50	8.0 (29)	129	31/50
102	6.2 (37)	36/50	5.3 (36)	85	36/50	6.1 (32)	98	32/50	8.0 (30)	129	29/50
104	6.3 (35)	34/50	5.2 (35)	83	35/50	6.5 (30)	103	30/50	8.0 (25)	127	25/50

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

TABLE 20 WATER CONSUMPTION IN FEMALE MOUSE (TWO-YEAR STUDY)

Week on Study	Control Av.WC.	Control No.of Surviv. <50>	10000 ppm Av.WC.	10000 ppm % of cont. <50>	10000 ppm No.of Surviv.	20000 ppm Av.WC.	20000 ppm % of cont. <50>	20000 ppm No.of Surviv.	40000 ppm Av.WC.	40000 ppm % of cont. <50>	40000 ppm No.of Surviv.
1	4.7 (50)	50/50	4.8 (50)	102	50/50	4.9 (50)	104	50/50	5.6 (50)	119	50/50
2	4.6 (48)	50/50	5.0 (50)	109	50/50	5.3 (50)	115	50/50	5.6 (50)	122	50/50
3	4.6 (50)	50/50	4.9 (49)	107	50/50	5.4 (50)	117	50/50	5.7 (50)	124	50/50
4	5.8 (50)	50/50	5.5 (50)	95	50/50	7.2 (50)	124	50/50	7.8 (50)	134	50/50
5	6.0 (49)	50/50	6.3 (50)	105	50/50	7.5 (50)	125	50/50	6.8 (50)	113	50/50
6	6.1 (50)	50/50	7.4 (45)	121	50/50	8.1 (50)	133	50/50	7.7 (49)	126	50/50
7	7.8 (49)	50/50	8.3 (50)	106	50/50	7.4 (50)	95	50/50	8.0 (50)	103	50/50
8	6.3 (50)	50/50	8.9 (50)	141	50/50	7.6 (50)	121	50/50	8.1 (50)	129	50/50
9	7.5 (50)	50/50	8.1 (50)	108	50/50	7.4 (49)	99	49/50	7.5 (50)	100	50/50
10	7.0 (50)	50/50	7.5 (50)	107	50/50	7.6 (49)	109	49/50	6.8 (50)	97	50/50
11	8.0 (50)	50/50	8.1 (50)	101	50/50	8.7 (49)	109	49/50	7.1 (50)	89	50/50
12	7.7 (50)	50/50	8.1 (50)	105	50/50	7.8 (47)	101	49/50	7.3 (50)	95	50/50
13	8.5 (50)	50/50	7.8 (50)	92	50/50	9.4 (49)	111	49/50	8.0 (50)	94	50/50
14	10.0 (49)	50/50	9.4 (50)	94	50/50	9.3 (48)	93	49/50	8.3 (49)	83	50/50
16	8.3 (49)	50/50	7.9 (50)	95	50/50	7.2 (48)	87	49/50	7.0 (50)	84	50/50
18	8.0 (49)	50/50	7.5 (49)	94	50/50	7.7 (49)	96	49/50	7.3 (50)	91	50/50
20	8.4 (49)	50/50	6.7 (50)	80	50/50	6.1 (48)	73	49/50	6.8 (50)	81	50/50
22	7.0 (50)	50/50	6.9 (50)	99	50/50	6.3 (48)	90	49/50	6.1 (50)	87	50/50
24	7.7 (49)	50/50	6.4 (49)	83	50/50	6.2 (49)	81	49/50	7.1 (50)	92	50/50
26	6.7 (48)	50/50	6.1 (50)	91	50/50	6.5 (48)	97	49/50	6.1 (50)	91	50/50
28	7.9 (49)	49/50	6.2 (50)	78	50/50	6.2 (48)	78	49/50	6.4 (50)	81	50/50
30	7.2 (48)	49/50	6.9 (49)	96	50/50	5.9 (47)	82	49/50	6.1 (50)	85	50/50
32	7.3 (48)	49/50	5.8 (50)	79	50/50	6.0 (47)	82	48/50	6.8 (50)	93	50/50
34	6.6 (49)	49/50	5.6 (50)	85	50/50	6.5 (48)	98	48/50	6.1 (50)	92	50/50
36	6.6 (49)	49/50	6.2 (49)	94	49/50	6.4 (48)	97	48/50	6.0 (50)	91	50/50
38	5.9 (49)	49/50	5.8 (49)	98	49/50	6.0 (47)	102	48/50	5.4 (49)	92	50/50
40	6.0 (49)	49/50	6.0 (49)	100	49/50	6.6 (48)	110	48/50	5.8 (50)	97	50/50
42	6.1 (49)	49/50	6.8 (49)	111	49/50	6.6 (48)	108	48/50	5.4 (50)	89	50/50
44	6.1 (49)	49/50	6.6 (49)	108	49/50	7.0 (48)	115	48/50	5.6 (49)	92	50/50
46	5.4 (48)	47/50	6.2 (49)	115	49/50	6.2 (46)	115	47/50	5.6 (50)	104	50/50
48	5.6 (47)	47/50	6.5 (49)	116	49/50	5.9 (47)	105	47/50	5.8 (50)	104	50/50
50	6.3 (47)	47/50	6.5 (48)	103	49/50	6.6 (47)	105	47/50	6.0 (50)	95	50/50
52	5.2 (47)	47/50	5.5 (49)	106	49/50	5.7 (46)	110	47/50	5.3 (50)	102	50/50
54	6.3 (47)	47/50	7.2 (49)	114	49/50	6.1 (46)	97	46/50	5.5 (49)	87	49/50
56	6.5 (47)	46/50	6.2 (49)	95	49/50	5.9 (46)	91	46/50	5.6 (49)	86	49/50
58	5.5 (46)	46/50	5.5 (48)	100	48/50	5.6 (46)	102	46/50	5.1 (49)	93	49/50
60	5.3 (46)	46/50	5.9 (48)	111	48/50	5.9 (46)	111	46/50	5.6 (46)	106	49/50
62	5.1 (45)	45/50	5.1 (48)	100	48/50	5.0 (46)	98	45/50	4.7 (49)	92	49/50
64	4.9 (45)	45/50	5.4 (47)	110	48/50	5.8 (45)	118	45/50	5.3 (49)	108	49/50
66	5.6 (45)	45/50	5.2 (46)	93	47/50	6.0 (44)	107	44/50	4.9 (48)	88	48/50
68	5.0 (45)	45/50	5.1 (47)	102	47/50	5.7 (42)	114	43/50	4.9 (47)	98	47/50
70	4.7 (45)	45/50	4.7 (47)	100	47/50	5.0 (43)	106	43/50	4.9 (46)	104	47/50
72	4.8 (45)	45/50	4.8 (47)	100	47/50	5.5 (43)	115	43/50	5.0 (47)	104	47/50
74	5.1 (43)	43/50	5.1 (46)	100	46/50	5.2 (43)	102	43/50	5.1 (47)	100	47/50
76	4.7 (43)	43/50	5.0 (44)	106	45/50	5.2 (42)	111	42/50	5.0 (46)	106	46/50
78	4.7 (43)	43/50	4.2 (45)	89	44/50	4.9 (42)	104	42/50	4.8 (46)	102	46/50
80	4.8 (43)	42/50	4.8 (42)	100	42/50	5.5 (42)	115	42/50	5.4 (46)	113	46/50
82	4.5 (42)	42/50	4.6 (41)	102	41/50	5.0 (41)	111	41/50	5.1 (45)	113	45/50
84	4.4 (41)	41/50	4.7 (41)	107	41/50	5.0 (40)	114	39/50	5.4 (45)	123	44/50
86	4.4 (40)	40/50	4.5 (41)	102	41/50	5.0 (38)	114	37/50	5.0 (43)	114	43/50
88	4.7 (38)	38/50	4.8 (40)	102	39/50	5.3 (35)	113	35/50	5.4 (43)	115	43/50
90	4.6 (37)	37/50	4.5 (35)	98	36/50	5.4 (32)	117	32/50	5.2 (43)	113	43/50
92	4.3 (37)	37/50	4.6 (36)	107	35/50	5.3 (32)	123	31/50	5.6 (41)	130	41/50
94	4.3 (37)	37/50	4.4 (34)	102	34/50	5.2 (29)	121	29/50	5.9 (39)	137	39/50
96	4.8 (36)	35/50	4.6 (32)	96	32/50	5.4 (27)	113	27/50	6.6 (37)	138	37/50
98	4.7 (33)	33/50	4.4 (31)	94	31/50	5.5 (26)	117	26/50	6.1 (35)	130	36/50
100	4.9 (32)	32/50	5.1 (28)	104	28/50	6.3 (24)	129	24/50	5.8 (35)	118	35/50
102	4.7 (31)	30/50	4.8 (25)	102	25/50	6.4 (23)	136	22/50	5.8 (34)	123	32/50
104	4.7 (29)	29/50	4.7 (25)	100	24/50	5.5 (19)	117	19/50	6.3 (29)	134	28/50

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

TABLE 21 FOOD COSUMPTION IN MALE MOUSE (TWO-YEAR STUDY)

Week on Study	Control Av.FC.	Control No.of Surviv. <50>	10000 ppm Av.FC.	10000 ppm % of cont. <50>	10000 ppm No.of Surviv.	20000 ppm Av.FC.	20000 ppm % of cont. <50>	20000 ppm No.of Surviv.	40000 ppm Av.FC.	40000 ppm % of cont. <50>	40000 ppm No.of Surviv.
1	3.7 (50)	50/50	3.7 (50)	100	50/50	3.7 (50)	100	50/50	3.6 (50)	97	50/50
2	3.7 (50)	50/50	3.7 (50)	100	50/50	3.7 (50)	100	50/50	3.6 (50)	97	50/50
3	3.8 (50)	50/50	3.7 (50)	97	50/50	3.7 (50)	97	50/50	3.7 (50)	97	50/50
4	3.7 (50)	50/50	3.6 (50)	97	50/50	3.6 (50)	97	50/50	3.7 (50)	100	50/50
5	3.8 (50)	50/50	3.7 (50)	97	50/50	3.7 (50)	97	50/50	3.6 (50)	95	50/50
6	4.1 (50)	50/50	4.0 (50)	98	50/50	4.0 (50)	98	50/50	3.9 (50)	95	50/50
7	3.7 (50)	50/50	3.7 (50)	100	50/50	3.3 (50)	89	50/50	3.3 (50)	89	50/50
8	3.9 (50)	50/50	3.8 (50)	97	50/50	3.8 (50)	97	50/50	3.7 (50)	95	50/50
9	3.8 (49)	50/50	3.8 (50)	100	50/50	3.8 (50)	100	50/50	3.8 (50)	100	50/50
10	4.0 (50)	50/50	3.9 (50)	98	50/50	3.9 (50)	98	50/50	3.8 (50)	95	50/50
11	3.9 (50)	50/50	3.8 (50)	97	50/50	3.8 (50)	97	50/50	3.8 (50)	97	50/50
12	4.0 (50)	50/50	3.9 (50)	98	50/50	3.9 (50)	98	50/50	3.8 (50)	95	50/50
13	3.9 (50)	50/50	3.8 (50)	97	50/50	3.9 (50)	100	50/50	3.8 (50)	97	50/50
14	3.8 (50)	50/50	3.8 (50)	100	50/50	3.8 (50)	100	50/50	3.7 (50)	97	50/50
18	4.1 (50)	50/50	4.1 (50)	100	50/50	4.1 (50)	100	50/50	3.9 (50)	95	50/50
22	4.2 (50)	50/50	4.1 (50)	98	50/50	4.2 (50)	100	50/50	4.1 (50)	98	50/50
26	4.1 (50)	50/50	4.1 (50)	100	50/50	4.1 (50)	100	50/50	4.0 (50)	98	50/50
30	4.4 (50)	50/50	4.4 (50)	100	50/50	4.4 (50)	100	50/50	4.3 (50)	98	50/50
34	4.4 (50)	50/50	4.4 (50)	100	50/50	4.4 (50)	100	50/50	4.3 (50)	98	50/50
38	4.6 (50)	50/50	4.5 (50)	98	50/50	4.5 (50)	98	50/50	4.4 (50)	96	50/50
42	4.6 (50)	50/50	4.5 (50)	98	50/50	4.5 (50)	98	50/50	4.3 (50)	93	50/50
46	4.6 (50)	50/50	4.5 (50)	98	50/50	4.5 (50)	98	50/50	4.5 (50)	98	50/50
50	4.7 (49)	49/50	4.7 (50)	100	50/50	4.7 (50)	100	50/50	4.6 (50)	98	50/50
54	4.5 (49)	49/50	4.5 (50)	100	50/50	4.5 (50)	100	50/50	4.3 (49)	96	49/50
58	4.5 (49)	49/50	4.5 (50)	100	50/50	4.5 (50)	100	50/50	4.3 (48)	96	48/50
62	4.7 (49)	49/50	4.4 (50)	94	50/50	4.5 (50)	96	50/50	4.4 (47)	94	47/50
66	4.7 (49)	49/50	4.5 (50)	96	50/50	4.6 (50)	98	50/50	4.5 (46)	96	46/50
70	4.8 (48)	48/50	4.6 (49)	96	49/50	4.6 (49)	96	49/50	4.6 (43)	96	43/50
74	4.8 (48)	48/50	4.7 (49)	98	49/50	4.7 (48)	98	48/50	4.7 (42)	98	42/50
78	4.8 (46)	46/50	4.7 (48)	98	48/50	4.8 (46)	100	46/50	4.8 (42)	100	42/50
82	5.1 (44)	44/50	4.8 (48)	94	48/50	4.9 (46)	96	46/50	4.8 (41)	94	41/50
86	4.9 (44)	44/50	4.9 (46)	100	46/50	4.8 (43)	98	43/50	4.7 (40)	96	40/50
90	4.9 (44)	44/50	4.9 (45)	100	45/50	4.7 (43)	96	42/50	4.8 (38)	98	38/50
94	4.7 (42)	42/50	4.7 (43)	100	43/50	4.8 (41)	102	41/50	4.6 (35)	98	34/50
98	4.6 (40)	40/50	4.8 (39)	104	39/50	4.7 (37)	102	37/50	4.7 (32)	102	32/50
102	4.6 (37)	36/50	4.7 (36)	102	36/50	4.5 (32)	98	32/50	4.4 (30)	96	29/50
104	4.6 (35)	34/50	4.5 (35)	98	35/50	4.4 (30)	96	30/50	4.5 (25)	98	25/50

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

TABLE 22 FOOD COSUMPTION IN FEMALE MOUSE (TWO-YEAR STUDY)

Week on Study	Control Av.FC.	Control No.of Surviv. <50>	10000 ppm Av.FC.	10000 ppm % of cont. <50>	10000 ppm No.of Surviv.	20000 ppm Av.FC.	20000 ppm % of cont. <50>	20000 ppm No.of Surviv.	40000 ppm Av.FC.	40000 ppm % of cont. <50>	40000 ppm No.of Surviv.
1	3.2 (50)	50/50	3.2 (50)	100	50/50	3.2 (50)	100	50/50	3.2 (50)	100	50/50
2	3.2 (50)	50/50	3.3 (50)	103	50/50	3.2 (50)	100	50/50	3.2 (50)	100	50/50
3	3.4 (50)	50/50	3.4 (50)	100	50/50	3.5 (50)	103	50/50	3.5 (50)	103	50/50
4	3.4 (50)	50/50	3.3 (50)	97	50/50	3.5 (50)	103	50/50	3.5 (50)	103	50/50
5	3.4 (50)	50/50	3.5 (50)	103	50/50	3.4 (50)	100	50/50	3.4 (50)	100	50/50
6	3.7 (50)	50/50	3.6 (50)	97	50/50	3.7 (50)	100	50/50	3.7 (50)	100	50/50
7	3.5 (50)	50/50	3.4 (50)	97	50/50	3.5 (50)	100	50/50	3.5 (50)	100	50/50
8	3.6 (50)	50/50	3.6 (50)	100	50/50	3.6 (50)	100	50/50	3.6 (50)	100	50/50
9	3.6 (50)	50/50	3.6 (50)	100	50/50	3.7 (49)	103	49/50	3.7 (50)	103	50/50
10	3.6 (50)	50/50	3.6 (50)	100	50/50	3.6 (49)	100	49/50	3.6 (50)	100	50/50
11	3.6 (50)	50/50	3.6 (50)	100	50/50	3.6 (49)	100	49/50	3.6 (50)	100	50/50
12	3.7 (50)	50/50	3.7 (50)	100	50/50	3.7 (49)	100	49/50	3.6 (50)	97	50/50
13	3.5 (50)	50/50	3.5 (50)	100	50/50	3.6 (49)	103	49/50	3.5 (50)	100	50/50
14	3.3 (50)	50/50	3.4 (50)	103	50/50	3.4 (49)	103	49/50	3.4 (50)	103	50/50
18	3.8 (50)	50/50	3.8 (50)	100	50/50	3.9 (49)	103	49/50	3.8 (50)	100	50/50
22	3.7 (50)	50/50	3.9 (50)	105	50/50	3.9 (49)	105	49/50	3.7 (50)	100	50/50
26	3.8 (50)	50/50	3.9 (50)	103	50/50	3.8 (49)	100	49/50	3.9 (50)	103	50/50
30	4.1 (49)	49/50	4.1 (50)	100	50/50	4.0 (49)	98	49/50	3.9 (50)	95	50/50
34	4.0 (49)	49/50	4.0 (50)	100	50/50	3.9 (48)	98	48/50	4.2 (50)	105	50/50
38	4.0 (49)	49/50	4.2 (49)	105	49/50	4.1 (48)	103	48/50	4.1 (50)	103	50/50
42	4.1 (49)	49/50	4.1 (49)	100	49/50	4.1 (48)	100	48/50	3.9 (50)	95	50/50
46	4.0 (48)	47/50	4.1 (49)	103	49/50	4.2 (47)	105	47/50	4.2 (50)	105	50/50
50	4.2 (47)	47/50	4.3 (49)	102	49/50	4.4 (47)	105	47/50	4.4 (50)	105	50/50
54	3.9 (47)	47/50	4.1 (49)	105	49/50	4.1 (46)	105	46/50	4.1 (49)	105	49/50
58	4.1 (46)	46/50	4.1 (48)	100	48/50	4.2 (46)	102	46/50	4.2 (49)	102	49/50
62	4.4 (45)	45/50	4.3 (48)	98	48/50	4.3 (46)	98	45/50	4.3 (49)	98	49/50
66	4.1 (45)	45/50	4.1 (47)	100	47/50	4.1 (44)	100	44/50	4.1 (48)	100	48/50
70	4.3 (45)	45/50	4.2 (47)	98	47/50	4.3 (43)	100	43/50	4.2 (47)	98	47/50
74	4.5 (43)	43/50	4.3 (46)	96	46/50	4.3 (43)	96	43/50	4.4 (47)	98	47/50
78	4.4 (43)	43/50	4.2 (45)	95	44/50	4.2 (42)	95	42/50	4.4 (46)	100	46/50
82	4.6 (42)	42/50	4.5 (41)	98	41/50	4.7 (41)	102	41/50	4.6 (45)	100	45/50
86	4.4 (40)	40/50	4.5 (41)	102	41/50	4.4 (38)	100	37/50	4.4 (43)	100	43/50
90	4.4 (37)	37/50	4.3 (36)	98	36/50	4.4 (32)	100	32/50	4.4 (43)	100	43/50
94	4.3 (37)	37/50	4.1 (34)	95	34/50	4.4 (29)	102	29/50	4.5 (39)	105	39/50
98	4.4 (33)	33/50	4.2 (31)	95	31/50	4.1 (26)	93	26/50	4.3 (36)	98	36/50
102	4.6 (31)	30/50	4.5 (25)	98	25/50	4.7 (23)	102	22/50	4.3 (34)	93	32/50
104	4.3 (29)	29/50	4.2 (25)	98	24/50	4.5 (19)	105	19/50	4.7 (29)	109	28/50

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

TABLE 23 NEOPLASTIC LESIONS INCIDENCE AND STATISTICAL ANALYSIS IN MALE MOUSE

Group Name	Control	10000ppm	20000ppm	40000ppm
SITE : spleen				
TUMOR : malignant lymphoma(f)				
Tumor rate				
Overall rates(a)	1/50(2.0)	0/50(0.0)	3/50(6.0)	3/50(6.0)
Adjusted rates(b)	2.94	0.0	6.67	0.0
Terminal rates(c)	1/34(2.9)	0/35(0.0)	2/30(6.7)	0/25(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P=0.0074**			
Prevalence method(d)	P=0.5831			
Combined analysis (d)	P=0.0462*			
Cochran-Amitage test(e)	P=0.1347			
Fisher Exact test(e)		P=0.4950	P=0.3235	P=0.3235
SITE : all organ				
TUMOR : malignant lymphoma				
Tumor rate				
Overall rates(a)	8/50(16.0)	3/50(6.0)	9/50(18.0)	9/50(18.0)
Adjusted rates(b)	14.71	5.71	16.67	10.00
Terminal rates(c)	5/34(14.7)	2/35(5.7)	5/30(16.7)	2/25(8.0)
Statistical analysis				
Peto test				
Standard method(d)	P=0.0350*			
Prevalence method(d)	P=0.4813			
Combined analysis (d)	P=0.0895			
Cochran-Amitage test(e)	P=0.3961			
Fisher Exact test(e)		P=0.1322	P=0.4846	P=0.4846

(a):Number of tumor-bearing animals/number of animals examined at the site.
(b):Kaplan-Meire estimate tumor incidence at the end of the study after adjusting for intercurrent mortality.
(c):Observed tumor incidence at terminal kill.
(d):Beneth 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-Amitage and Fisher exact test compare directly the overall incidence rates.
(f):Historical incidence for 2-year studies: 35/800(4.4%); range 2% to 10%
?: The conditional probabilities of the largest and smallest possible out comes can not be 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

TABLE 24 NEOPLASTIC LESIONS INCIDENCE AND STATISTICAL ANALYSIS IN FEMALE MOUSE

Group Name	Control	10000ppm	20000ppm	40000ppm
SITE : uterus				
TUMOR : endometrial stromal polyp[f]				
Tumor rate				
Overall rates(a)	5/50(10.0)	2/50(4.0)	0/50(0.0)	2/50(4.0)
Adjusted rates(b)	17.24	8.33	0.0	4.76
Terminal rates(c)	5/29(17.2)	2/24(8.3)	0/19(0.0)	1/28(3.6)
Statistical analysis				
Peto test				
Standard method(d)	P=------			
Prevalence method(d)	P=0.9062			
Combined analysis (d)	P=------			
Cochran-Amitage test(e)	P=0.1848			
Fisher Exact test(e)		P=0.2425	P=0.0360*	P=0.2425
SITE : mammary gland				
TUMOR : adenoma[g]				
Tumor rate				
Overall rates(a)	0/50(0.0)	0/50(0.0)	1/50(2.0)	3/50(6.0)
Adjusted rates(b)	0.0	0.0	5.26	7.69
Terminal rates(c)	0/29(0.0)	0/24(0.0)	1/19(5.3)	2/28(7.1)
Statistical analysis				
Peto test				
Standard method(d)	P=------			
Prevalence method(d)	P=0.0146*			
Combined analysis (d)	P=------			
Cochran-Amitage test(e)	P=0.0168*			
Fisher Exact test(e)		P=0.5000	P=0.4950	P=0.1325
SITE : mammary gland				
TUMOR : adenoma[g], adenocarcinoma[h]				
Tumor rate				
Overall rates(a)	1/50(2.0)	1/50(2.0)	3/50(6.0)	6/50(12.0)
Adjusted rates(b)	2.94	0.0	5.26	13.16
Terminal rates(c)	0/29(0.0)	0/24(0.0)	1/19(5.3)	3/28(10.7)
Statistical analysis				
Peto test				
Standard method(d)	P=0.2823			
Prevalence method(d)	P=0.0098**			
Combined analysis (d)	P=0.0142*			
Cochran-Amitage test(e)	P=0.0137*			
Fisher Exact test(e)		P=0.2475	P=0.3235	P=0.0724

TABLE 24 NEOPLASTIC LESIONS INCIDENCE AND STATISTICAL ANALYSIS IN FEMALE MOUSE
(Continued)

Group Name	Control	10000ppm	20000ppm	40000ppm
SITE : all organ				
TUMOR : malignant lymphoma				
Tumor rate				
Overall rates(a)	12/50(24.0)	16/50(32.0)	12/50(24.0)	16/50(32.0)
Adjusted rates(b)	17.24	16.67	15.79	35.71
Terminal rates(c)	5/29(17.2)	4/24(16.7)	3/19(15.8)	10/28(35.7)
Statistical analysis				
Peto test				
Standard method(d)	P=0.7741			
Prevalence method(d)	P=0.0378*			
Combined analysis (d)	P=0.3240			
Cochran-Amitage test(e)	P=0.5229			
Fisher Exact test(e)		P=0.3253	P=0.4103	P=0.3253

(a):Number of tumor-bearing animals/number of animals examined at the site.
(b):Kaplan-Meire estimate tumor incidence at the end of the study after adjusting for intercurrent mortality.
(c):Observed tumor incidence at terminal kill.
(d):Beneth 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-Amitage and Fisher exact test compare directly the overall incidence rates.
(f):Historical incidence for 2-year studies: 22/799(2.8%); range 0% to 10%
(g):Historical incidence for 2-year studies: 0/799(0%)
(h):Historical incidence for 2-year studies: 11/799(1.4%); range 0% to 4%
?: The conditional probabilities of the largest and smallest possible out comes can not be 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

TABLE 25 NUMBER OF MICE WITH SELECTED LESIONS OF NASAL CAVITY

Group name		Male				Female			
		Control	10000ppm	20000ppm	40000ppm	Control	10000ppm	20000ppm	40000ppm
Number of examined		50	50	50	50	50	50	50	50
Duct ectasia:									
olfactory gland		0	0	10	39	0	0	5	40
	+	(0)	(0)	(10)	(39)	(0)	(0)	(5)	(40)
	2+	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	3+	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
Respiratory metaplasia:									
gland		14	26	21	37	1	6	9	14
	+	(8)	(19)	(17)	(31)	(1)	(6)	(9)	(13)
	2+	(6)	(7)	(4)	(6)	(0)	(0)	(0)	(1)
	3+	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
Respiratory metaplasia:									
olfactory epithelium		13	11	25	32	3	2	10	8
	+	(13)	(11)	(25)	(30)	(2)	(2)	(10)	(8)
	2+	(0)	(0)	(0)	(2)	(1)	(0)	(0)	(0)
	3+	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
Eosinophilic change:									
olfactory epithelium		15	12	20	10	3	3	3	15
	+	(15)	(12)	(20)	(10)	(1)	(1)	(2)	(14)
	2+	(0)	(0)	(0)	(0)	(0)	(2)	(1)	(1)
	3+	(0)	(0)	(0)	(0)	(2)	(0)	(0)	(0)

Grade +:Slight 2+:Moderate 3+:Marked
a a:Number of animals with lesion
(b) b:Number of animals with lesion in each grade

TABLE 26 CAUSE OF DEATH IN MICE

Group		Male				Female			
		Control	10000ppm	20000ppm	40000ppm	Control	10000ppm	20000ppm	40000ppm
Number of dead or moribund animals		16	15	20	25	21	26	31	22
No microscopical confirmation		2	0	0	2	1	1	2	2
Integmentary system lesion		0	0	0	0	0	1	0	0
Hepatic lesion		0	0	1	3	0	2	0	0
Renal lesion		0	0	0	2	1	0	0	0
Urinary retention		3	4	5	3	0	0	0	0
Reproductive system lesion		0	0	0	0	0	0	1	1
Body cavity lesion		0	0	0	0	1	0	0	0
Arteritis		0	0	0	0	0	0	2	0
Hydronephrosis		0	0	0	1	2	0	1	1
Tumor death :	leukemia	3	1	4	6	7	12	10	6
	subcutis	1	3	0	1	0	1	0	2
	lung	0	0	1	0	1	0	0	0
	spleen	0	0	1	0	0	0	0	0
	liver	4	7	7	6	1	3	2	0
	pituitary	0	0	0	0	1	1	2	1
	adrenal	0	0	0	0	0	0	0	1
	ovary	–	–	–	–	0	1	0	0
	uterus	–	–	–	–	6	2	9	7
	mammary gland	0	0	0	0	0	1	2	1
	brain	0	0	1	0	0	0	0	0
	peripheral nerve	0	0	0	1	0	1	0	0
	Harder gland	1	0	0	0	0	0	0	0