

p-ジクロロベンゼンのラット及びマウスを用いた
吸入によるがん原性試験報告書

試験番号 ラット/0158 ; マウス/0159

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TABLE1 EXPERIMENTAL DESIGN AND MATERIALS AND METHODS
IN THE INHALATION STUDIES OF p-DICHLOROBENZENE

Two-Year Studies

<Method of Administration>
Inhalation

<Number of Group>
Male 4, Female 4

<Size of Groups>
50 males and 50 females of each group

<Animals>
Strain and Species
F344/DuCrj(Fischer)rat
Crj:BDF1 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

<Exposure Concentration>
Rat---0, 20, 75 or 300ppm
Mouse--0, 20, 75 or 300ppm

<Duration of Exposure>
6 h/d, 5 d/wk, for 104 wk

<Animal Maintenance>
Feed
CRF-1(Oriental Yeast Co.,Ltd.)
Sterilized by γ -ray
Available *ad libitum*
Water
Sterilized by ultraviolet rays
Automatic Watering system.
Available *ad libitum*
Animal per Cage
Single(stainless steel wire)
Animal Chambers Room Environment
Barrier system
Temperature : $23 \pm 2^{\circ}\text{C}$
Humidity : $55 \pm 10\%$
Fluorescent light 12 h/d
15-17 room air changes/h
Inhalation Chamber Environment
Temperature : $23 \pm 2^{\circ}\text{C}$
Humidity : $55 \pm 10\%$
Fluorescent light 12 h/d
12 room air changes/h

<Type and Frequency of Observation>
Clinical Sign
Observed 1 per d
Body Weight
Weighed 1 per wk for 14 wk
Weighed 1 per 4 wks thereafter
Food Consumption
Weighed 1 per wk for 14 wk
Weighed 1 per 4 wks thereafter

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

Week on Study	Control		20 ppm		75 ppm		300 ppm				
	Au.Wt.	No.of Surviv. <50>	Au.Wt.	% of cont. <50>	No.of Surviv.	Au.Wt.	% of cont. <50>	No.of Surviv.	Au.Wt.	% of cont. <50>	No.of Surviv.
0	126 (50)	50/50	126 (50)	100	50/50	126 (50)	100	50/50	126 (50)	100	50/50
1	160 (50)	50/50	162 (50)	101	50/50	163 (50)	102	50/50	158 (50)	99	50/50
2	187 (50)	50/50	189 (50)	101	50/50	190 (50)	102	50/50	185 (50)	99	50/50
3	210 (50)	50/50	212 (50)	101	50/50	212 (50)	101	50/50	210 (50)	100	50/50
4	230 (50)	50/50	234 (50)	102	50/50	233 (50)	101	50/50	232 (50)	101	50/50
5	249 (50)	50/50	253 (50)	102	50/50	252 (50)	101	50/50	252 (50)	101	50/50
6	266 (50)	50/50	269 (50)	101	50/50	268 (50)	101	50/50	268 (50)	101	50/50
7	280 (50)	50/50	285 (50)	102	50/50	283 (50)	101	50/50	283 (50)	101	50/50
8	294 (50)	50/50	298 (50)	101	50/50	297 (50)	101	50/50	296 (50)	101	50/50
9	305 (50)	50/50	312 (50)	102	50/50	310 (50)	102	50/50	311 (50)	102	50/50
10	318 (50)	50/50	324 (50)	102	50/50	321 (50)	101	50/50	321 (50)	101	50/50
11	328 (50)	50/50	335 (50)	102	50/50	333 (50)	102	50/50	333 (50)	102	50/50
12	337 (50)	50/50	344 (50)	102	50/50	343 (50)	102	50/50	343 (50)	102	50/50
13	343 (50)	50/50	352 (50)	103	50/50	349 (50)	102	50/50	350 (50)	102	50/50
14	351 (50)	50/50	359 (50)	102	50/50	356 (50)	101	50/50	357 (50)	102	50/50
18	377 (50)	50/50	384 (50)	102	50/50	381 (50)	101	50/50	379 (50)	101	50/50
22	395 (50)	50/50	401 (50)	102	50/50	399 (50)	101	50/50	398 (50)	101	50/50
26	411 (50)	50/50	418 (50)	102	50/50	418 (50)	102	50/50	415 (50)	101	50/50
30	426 (50)	50/50	433 (50)	102	50/50	432 (50)	101	50/50	429 (50)	101	50/50
34	438 (50)	50/50	446 (50)	102	50/50	445 (50)	102	50/50	444 (50)	101	50/50
38	451 (50)	50/50	458 (49)	102	49/50	460 (50)	102	50/50	458 (50)	102	50/50
42	457 (50)	50/50	466 (49)	102	49/50	467 (50)	102	50/50	465 (50)	102	50/50
46	463 (50)	50/50	470 (49)	102	49/50	474 (50)	102	50/50	472 (50)	102	50/50
50	470 (50)	50/50	477 (49)	101	49/50	482 (50)	103	50/50	478 (50)	102	50/50
54	478 (50)	50/50	483 (49)	101	49/50	491 (50)	103	50/50	485 (50)	101	50/50
58	479 (50)	50/50	485 (49)	101	49/50	494 (50)	103	50/50	489 (50)	102	50/50
62	488 (50)	50/50	488 (49)	100	49/50	496 (49)	102	49/50	488 (50)	100	50/50
66	486 (49)	49/50	489 (49)	101	49/50	495 (49)	102	49/50	487 (50)	100	50/50
70	489 (49)	49/50	484 (49)	99	48/50	495 (48)	101	48/50	489 (49)	100	49/50
74	490 (49)	49/50	488 (48)	100	48/50	494 (47)	101	47/50	483 (48)	99	48/50
78	488 (49)	49/50	487 (47)	100	47/50	495 (46)	101	46/50	483 (47)	99	47/50
82	485 (49)	49/50	486 (45)	100	44/50	487 (46)	100	46/50	470 (46)	97	45/50
86	478 (49)	49/50	486 (43)	102	43/50	479 (46)	100	46/50	468 (39)	98	39/50
90	466 (47)	47/50	479 (42)	103	42/50	465 (45)	100	45/50	455 (38)	98	38/50
94	457 (45)	45/50	476 (38)	104	38/50	452 (42)	99	41/50	439 (33)	96	33/50
98	448 (41)	41/50	462 (35)	103	35/50	443 (36)	99	36/50	439 (27)	98	27/50
102	427 (37)	36/50	452 (34)	106	34/50	428 (32)	100	32/50	401 (23)	94	22/50
104	423 (34)	33/50	439 (34)	104	34/50	409 (31)	97	29/50	413 (18)	98	18/50

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

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

Week on Study	Control		20 ppm		75 ppm		300 ppm				
	AU.Wt.	No.of Surviv. <50>	AU.Wt.	% of cont. <50>	No.of Surviv.	AU.Wt.	% of cont. <50>	No.of Surviv.	AU.Wt.	% of cont. <50>	No.of Surviv.
0	100 (50)	50/50	100 (50)	100	50/50	100 (50)	100	50/50	100 (50)	100	50/50
1	116 (50)	50/50	116 (50)	100	50/50	116 (50)	100	50/50	114 (50)	98	50/50
2	128 (50)	50/50	127 (50)	99	50/50	128 (50)	100	50/50	125 (50)	98	50/50
3	139 (50)	50/50	138 (50)	99	50/50	138 (50)	99	50/50	135 (50)	97	50/50
4	148 (50)	50/50	146 (50)	99	50/50	148 (50)	100	50/50	146 (50)	99	50/50
5	156 (50)	50/50	157 (50)	101	50/50	156 (50)	100	50/50	156 (50)	100	50/50
6	164 (50)	50/50	165 (50)	101	50/50	164 (50)	100	50/50	163 (50)	99	50/50
7	170 (50)	50/50	172 (50)	101	50/50	171 (50)	101	50/50	170 (50)	100	50/50
8	177 (50)	50/50	178 (50)	101	50/50	178 (50)	101	50/50	177 (50)	100	50/50
9	183 (50)	50/50	186 (50)	102	50/50	185 (50)	101	50/50	184 (50)	101	50/50
10	189 (50)	50/50	192 (50)	102	50/50	190 (50)	101	50/50	190 (50)	101	50/50
11	195 (50)	50/50	198 (50)	102	50/50	196 (50)	101	50/50	196 (50)	101	50/50
12	200 (50)	50/50	203 (50)	102	50/50	201 (50)	101	50/50	201 (50)	101	50/50
13	200 (50)	50/50	203 (50)	102	50/50	200 (50)	100	50/50	203 (50)	102	50/50
14	204 (50)	50/50	206 (50)	101	50/50	202 (50)	99	50/50	205 (50)	100	50/50
18	214 (50)	50/50	217 (50)	101	50/50	214 (50)	100	50/50	218 (50)	102	50/50
22	224 (50)	50/50	229 (50)	102	50/50	226 (50)	101	50/50	226 (50)	101	50/50
26	234 (50)	50/50	236 (50)	101	50/50	235 (50)	100	50/50	235 (50)	100	50/50
30	241 (50)	50/50	242 (50)	100	50/50	241 (50)	100	50/50	244 (50)	101	50/50
34	245 (50)	50/50	248 (50)	101	50/50	248 (50)	101	50/50	250 (50)	102	50/50
38	253 (50)	50/50	255 (50)	101	50/50	257 (50)	102	50/50	259 (50)	102	50/50
42	259 (50)	50/50	262 (49)	101	49/50	263 (50)	102	50/50	266 (50)	103	50/50
46	264 (50)	50/50	267 (49)	101	49/50	266 (50)	101	50/50	271 (50)	103	50/50
50	268 (50)	50/50	271 (49)	101	49/50	270 (50)	101	50/50	276 (50)	103	50/50
54	278 (50)	50/50	281 (49)	101	49/50	281 (50)	101	50/50	284 (50)	102	50/50
58	281 (50)	50/50	285 (49)	101	49/50	288 (50)	102	50/50	290 (50)	103	50/50
62	290 (50)	50/50	292 (48)	101	48/50	295 (49)	102	49/50	298 (49)	103	49/50
66	295 (50)	50/50	301 (48)	102	48/50	302 (49)	102	49/50	303 (49)	103	49/50
70	303 (50)	50/50	307 (48)	101	48/50	308 (49)	102	49/50	308 (49)	102	49/50
74	308 (49)	49/50	314 (48)	102	48/50	314 (49)	102	49/50	313 (49)	102	49/50
78	312 (49)	49/50	322 (48)	103	48/50	320 (49)	103	49/50	316 (49)	101	49/50
82	314 (48)	48/50	323 (48)	103	48/50	321 (49)	102	49/50	319 (47)	102	47/50
86	320 (48)	48/50	326 (46)	102	46/50	321 (49)	100	49/50	321 (47)	100	47/50
90	322 (47)	47/50	330 (42)	102	42/50	323 (47)	100	47/50	321 (46)	100	46/50
94	322 (44)	44/50	332 (40)	103	40/50	320 (42)	99	41/50	323 (45)	100	45/50
98	323 (41)	41/50	329 (40)	102	40/50	325 (40)	101	40/50	320 (42)	99	42/50
102	325 (38)	38/50	328 (36)	101	36/50	321 (39)	99	39/50	311 (39)	96	39/50
104	322 (38)	38/50	322 (35)	100	34/50	315 (39)	98	38/50	306 (38)	95	36/50

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

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

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	2/50	2/50	7/50	6/49	6/49	12/45	17/50 (6/17)
	20 ppm	0/50	0/50	0/50	1/49	4/49	8/49	7/47	13/41	17/50 (5/16)
	75 ppm	0/50	0/50	0/50	0/50	1/50	2/49	4/46	10/45	13/50 (2/21)
	300 ppm	0/50	0/50	0/50	2/50	5/50	10/50	11/47	10/36	21/50 (15/32)
Internal mass	Control	0/50	0/50	0/50	0/50	0/50	0/49	1/49	4/45	5/50 (3/17)
	20 ppm	0/50	0/50	0/50	0/49	0/49	0/49	1/47	5/41	5/50 (3/16)
	75 ppm	0/50	0/50	0/50	0/50	0/50	0/49	2/46	2/45	3/50 (3/21)
	300 ppm	0/50	0/50	0/50	0/50	1/50	1/50	1/47	4/36	5/50 (5/32)

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

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

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	1/50	0/50	1/50	2/50	4/49	9/47	10/50 (2/12)
	20 ppm	0/50	0/50	0/50	0/49	1/49	2/48	5/48	8/42	8/50 (2/16)
	75 ppm	0/50	0/50	0/50	0/50	0/50	3/49	5/49	10/46	11/50 (2/12)
	300 ppm	0/50	0/50	0/50	0/50	1/50	3/49	4/48	11/46	13/50 (3/14)
Internal mass	Control	0/50	0/50	0/50	0/50	0/50	1/50	2/49	1/47	2/50 (2/12)
	20 ppm	0/50	0/50	0/50	0/49	0/49	1/48	2/48	5/42	6/50 (5/16)
	75 ppm	0/50	0/50	0/50	0/50	0/50	0/49	1/49	5/46	5/50 (5/12)
	300 ppm	0/50	0/50	0/50	0/50	1/50	0/49	0/48	5/46	6/50 (4/14)

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

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

Week-Day on Study	Control		20 ppm			75 ppm			300 ppm		
	Au.FC.	No.of Surviv. <50>	Au.FC.	% of cont. <50>	No.of Surviv.	Au.FC.	% of cont. <50>	No.of Surviv.	Au.FC.	% of cont. <50>	No.of Surviv.
1-7	17.0 (50)	50/50	17.0 (50)	100	50/50	16.7 (50)	98	50/50	16.0 (50)	94	50/50
2-7	17.9 (50)	50/50	17.5 (50)	98	50/50	17.5 (50)	98	50/50	17.3 (50)	97	50/50
3-7	18.1 (50)	50/50	18.2 (50)	101	50/50	18.7 (50)	103	50/50	18.1 (50)	100	50/50
4-7	19.1 (50)	50/50	19.2 (50)	101	50/50	19.2 (50)	101	50/50	19.5 (50)	102	50/50
5-7	18.8 (50)	50/50	18.7 (50)	99	50/50	18.8 (50)	100	50/50	18.9 (50)	101	50/50
6-7	18.4 (50)	50/50	18.5 (50)	101	50/50	18.5 (50)	101	50/50	18.7 (50)	102	50/50
7-7	18.3 (50)	50/50	18.4 (50)	101	50/50	18.6 (50)	102	50/50	18.8 (50)	103	50/50
8-7	19.0 (50)	50/50	18.4 (50)	97	50/50	18.8 (50)	99	50/50	19.1 (50)	101	50/50
9-7	18.7 (50)	50/50	18.9 (50)	101	50/50	19.0 (50)	102	50/50	19.5 (50)	104	50/50
10-7	18.3 (50)	50/50	18.9 (50)	103	50/50	18.9 (50)	103	50/50	19.3 (48)	105	50/50
11-7	18.3 (50)	50/50	18.7 (50)	102	50/50	18.7 (50)	102	50/50	19.1 (50)	104	50/50
12-7	18.4 (50)	50/50	18.9 (50)	103	50/50	19.0 (50)	103	50/50	19.0 (50)	103	50/50
13-7	18.4 (50)	50/50	19.0 (50)	103	50/50	18.8 (50)	102	50/50	19.4 (49)	105	50/50
14-7	18.3 (50)	50/50	18.5 (50)	101	50/50	18.5 (50)	101	50/50	18.8 (50)	103	50/50
18-7	18.1 (50)	50/50	18.2 (50)	101	50/50	18.4 (50)	102	50/50	18.6 (50)	103	50/50
22-7	18.1 (50)	50/50	18.2 (50)	101	50/50	18.6 (50)	103	50/50	18.7 (50)	103	50/50
26-7	18.1 (50)	50/50	18.6 (50)	103	50/50	19.1 (50)	106	50/50	18.8 (50)	104	50/50
30-7	18.5 (50)	50/50	18.8 (50)	102	50/50	19.2 (50)	104	50/50	19.4 (50)	105	50/50
34-7	19.1 (50)	50/50	19.1 (50)	100	50/50	19.5 (50)	102	50/50	19.8 (50)	104	50/50
38-7	18.8 (50)	50/50	18.9 (49)	101	49/50	19.2 (50)	102	50/50	19.9 (50)	106	50/50
42-7	18.0 (50)	50/50	18.3 (49)	102	49/50	18.8 (50)	104	50/50	19.1 (50)	106	50/50
46-7	18.6 (50)	50/50	18.4 (49)	99	49/50	18.7 (50)	101	50/50	19.5 (50)	105	50/50
50-7	18.9 (50)	50/50	18.8 (49)	99	49/50	19.5 (50)	103	50/50	19.8 (50)	105	50/50
54-7	18.6 (50)	50/50	18.7 (49)	101	49/50	19.1 (50)	103	50/50	19.4 (50)	104	50/50
58-7	19.0 (50)	50/50	19.4 (49)	102	49/50	19.5 (50)	103	50/50	20.0 (50)	105	50/50
62-7	19.3 (50)	50/50	19.2 (49)	99	49/50	18.8 (49)	97	49/50	19.2 (50)	99	50/50
66-7	19.2 (49)	49/50	19.1 (49)	99	49/50	19.0 (49)	99	49/50	19.3 (50)	101	50/50
70-7	19.5 (49)	49/50	19.1 (49)	98	48/50	19.3 (48)	99	48/50	20.1 (49)	103	49/50
74-7	18.9 (49)	49/50	18.5 (48)	98	48/50	18.8 (47)	99	47/50	18.7 (49)	99	48/50
78-7	18.1 (49)	49/50	17.0 (48)	94	47/50	18.7 (46)	103	46/50	18.8 (47)	104	47/50
82-7	18.4 (49)	49/50	17.6 (45)	96	44/50	18.6 (46)	101	46/50	18.4 (46)	100	45/50
86-7	18.1 (49)	49/50	18.1 (43)	100	43/50	19.0 (46)	105	46/50	18.3 (40)	101	39/50
90-7	18.2 (47)	47/50	18.2 (42)	100	42/50	18.2 (45)	103	45/50	18.9 (38)	104	38/50
94-7	18.1 (45)	45/50	18.4 (38)	102	38/50	18.4 (42)	102	41/50	17.8 (33)	98	33/50
98-7	18.1 (42)	41/50	17.8 (35)	98	35/50	18.3 (36)	101	36/50	17.3 (29)	96	27/50
102-7	17.4 (38)	36/50	18.4 (35)	106	34/50	17.8 (33)	102	32/50	17.0 (23)	98	22/50
104-7	17.3 (35)	33/50	17.9 (34)	103	34/50	17.7 (32)	102	29/50	18.6 (18)	108	18/50

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

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

Week-Day on Study	Control		20 ppm		75 ppm		300 ppm				
	Au.F.C.	No.of Surviv. <50>	Au.F.C.	% of cont. <50>	No.of Surviv.	Au.F.C.	% of cont. <50>	No.of Surviv.	Au.F.C.	% of cont. <50>	No.of Surviv.
1-7	12.7 (50)	50/50	12.5 (50)	98	50/50	12.6 (50)	99	50/50	11.9 (50)	94	50/50
2-7	12.6 (50)	50/50	12.2 (50)	97	50/50	12.3 (50)	98	50/50	11.8 (50)	94	50/50
3-7	12.7 (50)	50/50	12.5 (50)	98	50/50	12.7 (50)	100	50/50	11.9 (50)	94	50/50
4-7	13.1 (50)	50/50	12.9 (50)	98	50/50	13.2 (50)	101	50/50	12.9 (50)	98	50/50
5-7	12.4 (49)	50/50	12.8 (50)	103	50/50	13.0 (50)	105	50/50	12.6 (50)	102	50/50
6-7	12.9 (50)	50/50	13.1 (50)	102	50/50	12.8 (50)	99	50/50	12.6 (50)	98	50/50
7-7	12.9 (50)	50/50	13.2 (50)	102	50/50	13.2 (50)	102	50/50	13.0 (50)	101	50/50
8-7	13.1 (50)	50/50	12.8 (50)	98	50/50	13.3 (50)	102	50/50	13.1 (50)	100	50/50
9-7	13.4 (50)	50/50	13.5 (50)	101	50/50	13.6 (50)	101	50/50	13.5 (50)	101	50/50
10-7	12.7 (50)	50/50	13.7 (50)	108	50/50	13.2 (50)	104	50/50	13.2 (50)	104	50/50
11-7	12.9 (50)	50/50	13.3 (50)	103	50/50	13.3 (50)	103	50/50	12.8 (50)	99	50/50
12-7	13.5 (50)	50/50	13.7 (49)	101	50/50	13.5 (50)	100	50/50	13.5 (50)	100	50/50
13-7	12.1 (50)	50/50	12.2 (50)	101	50/50	11.6 (50)	96	50/50	12.7 (50)	105	50/50
14-7	12.5 (50)	50/50	12.3 (50)	98	50/50	11.8 (50)	94	50/50	12.4 (50)	99	50/50
18-7	12.6 (50)	50/50	12.6 (50)	100	50/50	12.7 (50)	101	50/50	13.2 (50)	105	50/50
22-7	12.7 (50)	50/50	13.1 (49)	103	50/50	12.9 (50)	102	50/50	12.9 (50)	102	50/50
26-7	13.0 (49)	50/50	12.7 (50)	98	50/50	12.9 (50)	99	50/50	13.2 (50)	102	50/50
30-7	13.0 (50)	50/50	12.6 (50)	97	50/50	12.9 (50)	99	50/50	13.8 (50)	106	50/50
34-7	12.9 (50)	50/50	13.2 (50)	102	50/50	13.0 (50)	101	50/50	13.5 (50)	105	50/50
38-7	13.0 (50)	50/50	13.3 (50)	102	50/50	13.1 (50)	101	50/50	13.6 (50)	105	50/50
42-7	13.1 (50)	50/50	12.9 (49)	98	49/50	13.0 (50)	99	50/50	13.4 (50)	102	50/50
46-7	12.5 (50)	50/50	12.6 (49)	101	49/50	12.4 (50)	99	50/50	13.5 (50)	108	50/50
50-7	12.7 (50)	50/50	12.8 (49)	101	49/50	13.0 (50)	102	50/50	13.8 (50)	109	50/50
54-7	13.6 (50)	50/50	13.8 (49)	101	49/50	13.8 (50)	101	50/50	14.0 (50)	103	50/50
58-7	13.6 (50)	50/50	14.3 (49)	105	49/50	13.9 (50)	102	50/50	14.3 (50)	105	50/50
62-7	14.2 (50)	50/50	13.8 (49)	97	48/50	13.6 (50)	96	49/50	14.5 (49)	102	49/50
66-7	13.9 (50)	50/50	14.4 (48)	104	48/50	14.2 (49)	102	49/50	14.5 (49)	104	49/50
70-7	14.1 (50)	50/50	14.4 (48)	102	48/50	14.4 (49)	102	49/50	14.7 (49)	104	49/50
74-7	14.0 (49)	49/50	14.4 (48)	103	48/50	14.4 (49)	103	49/50	15.0 (49)	107	49/50
78-7	13.3 (49)	49/50	13.8 (48)	104	48/50	14.0 (49)	105	49/50	14.0 (49)	105	49/50
82-7	13.8 (48)	48/50	13.8 (48)	100	48/50	14.5 (49)	105	49/50	15.1 (47)	109	47/50
86-7	14.3 (48)	48/50	13.8 (46)	97	46/50	14.6 (49)	102	49/50	14.9 (47)	104	47/50
90-7	14.6 (47)	47/50	14.9 (43)	102	42/50	14.7 (47)	101	47/50	15.6 (46)	107	46/50
94-7	14.1 (45)	44/50	14.9 (40)	106	40/50	13.6 (44)	96	41/50	15.6 (45)	111	45/50
98-7	13.7 (42)	41/50	14.5 (40)	106	40/50	14.5 (40)	106	40/50	14.3 (44)	104	42/50
102-7	14.5 (38)	38/50	14.9 (36)	103	36/50	15.2 (39)	105	39/50	14.8 (40)	102	39/50
104-7	15.0 (38)	38/50	14.4 (36)	96	34/50	14.7 (39)	98	38/50	14.7 (39)	98	36/50

< >:No.of effective animals,():No.of measured animals Au.F.C.: g

TABLE 8 NUMBER OF RATS WITH SELECTED NASAL CAVITY LESIONS

Group Name	Male				Female			
	Control	20ppm	75ppm	300ppm	Control	20ppm	75ppm	300ppm
Number of examined	50	50	50	50	50	50	50	50
eosinophilic change:								
olfactory epithelium	33 ²³	22 ¹⁷	21 ¹⁵	26 ⁶	49	46	46	50
(+)	(32)	(20)	(19)	(19) ¹³	(22)	(17)	(17)	(13) ²
(2+)	(1)	(1)	(1)	(7) ⁴⁶	(21)	(27)	(16)	(27) ⁹
(3+)	(0)	(1)	(1)	(0)	(8)	(12)	(23) ⁴	(20) ³
eosinophilic change:								
respiratory epithelium	4	1	5	4	11	10	14 ³	38 ³
(+)	(4)	(1)	(5)	(4) ²	(11)	(10)	(14)	(38)
respiratory metaplasia:gland	3	0	0	0	5	4	4	33
(+)	(3)	(0)	(0)	(0)	(5)	(4)	(4)	(33) ³
Grade	(+):Slight	(2+):Moderate	(3+):Marked					

TABLE 9 NUMBER OF RATS WITH SELECTED KIDNEY LESIONS IN RENAL PELIVIS

Group Name	Male				Female			
	Control	20ppm	75ppm	300ppm	Control	20ppm	75ppm	300ppm
Number of examined	50	50	50	50	50	50	50	50
mineralization:papilla	0	1	0	41	1	0	0	0
(+)	(0)	(1)	(0)	(40) ⁶	(1)	(0)	(0)	(0)
(2+)	(0)	(0)	(0)	(1)	(0)	(0)	(0)	(0)
urothelial hyperplasia:pelivis	7	8	13	32	0	0	0	0
(+)	(7) ⁴	(8)	(13)	(32) ⁷	(0)	(0)	(0)	(0)
chronic nephropathy	50	49	49	50	43	46	45	48
(+)	(0)	(0)	(0)	(0)	(28) ²	(29) ³	(15) ³	(29) ³
(2+)	(8) ⁴	(8) ⁴	(8) ³	(6) ⁶	(17) ³	(21) ³	(24) ²	(21) ³
(3+)	(18)	(20) ⁶	(26) ⁸	(14) ⁷	(16) ²	(16) ²	(16) ³	(13) ¹
(4+)	(24) ²	(21) ⁴	(20) ⁹	(20) ¹¹	(2)	(0)	(0)	(5) ³
Grade	(+):Slight	(2+):Moderate	(3+):Marked	(4+):Severe				

TABLE 10 CAUSE OF DEATH:RAT

Group Name	Male				Female			
	Control	20ppm	75ppm	300ppm	Control	20ppm	75ppm	300ppm
Number of Dead/Moribund Animal	17	16	21	32	12	16	12	14
No microscopical confirmation	0	2	0	2	1	1	0	1
Respiratory system lesion	0	0	0	0	0	0	0	1
Renal lesion	0	0	0	0	0	0	1	0
Chronic nephropathy	6	3	4	11	1	0	0	3
Tumor death : leukemia	3(17.6)	7(43.8)	5(23.8)	10(31.3)	2	5	6	3
: subcutis	1	0	0	2	0	0	0	0
: bone marrow	1	0	0	0	0	0	0	0
: spleen	1	0	0	1	0	0	0	0
: oral cavity	0	0	0	1	0	0	0	0
: small intestine	0	1	0	0	0	1	0	0
: pituitary gland	4	2	7	1	7	6	2	4
: uterus	0	0	0	0	1	2	2	0
: mammary gland	1	0	0	0	0	1	0	1
: brain	0	0	1	0	0	0	1	0
: Zymbal gland	0	1	0	2	0	0	0	0
: muscle	0	0	0	1	0	0	0	0
: vertebra	0	0	1	0	0	0	0	0
: pleura	0	0	0	0	0	0	0	1
: peritoneum	0	0	3	1	0	0	0	0

TABLE 11 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES IN MALE MOUSE (TWO-YEAR STUDY)

Week on Study	Control		20ppm			75ppm			300ppm		
	Au.Wt.	No.of Surviv. <49>	Au.Wt.	% of cont. <49>	No.of Surviv.	Au.Wt.	% of cont. <50>	No.of Surviv.	Au.Wt.	% of cont. <49>	No.of Surviv.
0	22.4 (49)	50/50	22.4 (49)	100	50/50	22.4 (50)	100	50/50	22.4 (49)	100	50/50
1	24.4 (49)	50/50	24.1 (49)	99	50/50	23.6 (50)	97	50/50	24.8 (49)	102	50/50
2	25.1 (49)	49/49	24.5 (49)	98	50/50	24.4 (50)	97	50/50	25.4 (49)	101	50/50
3	26.0 (49)	49/49	25.4 (49)	98	50/50	25.4 (50)	98	50/50	26.6 (49)	102	50/50
4	26.8 (49)	49/49	25.7 (49)	96	50/50	26.0 (50)	97	50/50	26.8 (49)	100	50/50
5	27.6 (49)	49/49	26.5 (49)	96	50/50	26.9 (50)	97	50/50	27.7 (49)	100	49/49
6	28.2 (49)	49/49	27.1 (49)	96	50/50	27.5 (50)	98	50/50	28.1 (49)	100	49/49
7	29.2 (49)	49/49	27.8 (49)	95	50/50	28.2 (50)	97	50/50	28.7 (49)	98	49/49
8	29.6 (49)	49/49	28.3 (49)	96	50/50	29.1 (50)	98	50/50	29.3 (49)	99	49/49
9	30.0 (49)	49/49	28.6 (49)	95	50/50	29.5 (50)	98	50/50	29.6 (49)	99	49/49
10	31.3 (49)	49/49	29.8 (49)	95	50/50	30.5 (50)	97	50/50	30.3 (49)	97	49/49
11	32.2 (49)	49/49	31.1 (49)	97	50/50	31.6 (50)	98	50/50	31.6 (49)	98	49/49
12	32.8 (49)	49/49	31.6 (49)	96	50/50	32.4 (50)	99	50/50	32.2 (49)	98	49/49
13	33.3 (49)	49/49	32.4 (49)	97	50/50	33.1 (50)	99	50/50	33.0 (49)	99	49/49
14	34.1 (49)	49/49	32.8 (49)	96	50/50	33.8 (50)	99	50/50	33.4 (49)	98	49/49
18	36.3 (49)	49/49	35.0 (49)	96	50/50	36.2 (50)	100	50/50	35.4 (49)	98	49/49
22	38.6 (49)	49/49	37.6 (49)	97	49/49	38.7 (50)	100	50/50	37.0 (48)	96	48/49
26	40.8 (49)	49/49	40.0 (49)	98	49/49	40.6 (50)	100	50/50	39.2 (48)	96	48/49
30	42.4 (49)	49/49	41.7 (49)	98	49/49	42.9 (50)	101	50/50	40.8 (48)	96	48/49
34	43.8 (49)	49/49	43.2 (49)	99	49/49	44.6 (49)	102	49/50	42.3 (48)	97	48/49
38	44.4 (49)	49/49	43.7 (49)	98	49/49	45.0 (49)	101	49/50	42.9 (48)	97	48/49
42	45.5 (48)	48/49	44.1 (49)	97	49/49	45.9 (49)	101	49/50	43.7 (48)	96	48/49
46	46.4 (48)	48/49	44.7 (49)	96	49/49	46.4 (49)	100	49/50	44.6 (48)	96	48/49
50	46.9 (48)	48/49	45.4 (49)	97	49/49	46.9 (49)	100	49/50	45.2 (48)	96	48/49
54	47.2 (47)	47/49	45.9 (49)	97	49/49	47.2 (49)	100	49/50	45.5 (48)	96	48/49
58	47.8 (47)	47/49	46.3 (49)	97	49/49	48.5 (47)	101	47/50	46.6 (48)	97	48/49
62	48.5 (46)	46/49	47.3 (49)	98	49/49	49.3 (46)	102	46/50	47.3 (48)	98	48/49
66	49.8 (46)	46/49	48.0 (49)	96	49/49	49.9 (46)	100	46/50	47.9 (46)	96	46/49
70	50.2 (46)	46/49	49.2 (48)	98	48/49	50.6 (46)	101	46/50	48.2 (45)	96	45/49
74	50.5 (45)	45/49	49.4 (48)	98	48/49	50.4 (46)	100	46/50	48.9 (44)	97	44/49
78	51.3 (45)	45/49	49.6 (47)	97	47/49	51.2 (45)	100	45/50	48.5 (44)	95	44/49
82	52.0 (45)	45/49	49.7 (47)	96	47/49	52.1 (43)	100	43/50	47.9 (43)	92	43/49
86	52.2 (45)	45/49	50.5 (43)	97	43/49	52.6 (42)	101	42/50	47.4 (42)	91	42/49
90	51.7 (45)	45/49	49.6 (40)	96	40/49	51.9 (40)	100	40/50	46.7 (39)	90	39/49
94	51.0 (43)	43/49	48.3 (38)	95	38/49	51.9 (38)	102	38/50	45.6 (36)	89	36/49
98	49.3 (42)	42/49	47.1 (36)	96	36/49	49.5 (37)	100	37/50	43.2 (34)	88	34/49
102	47.5 (41)	41/49	45.6 (34)	96	34/49	47.7 (33)	100	33/50	41.5 (33)	87	33/49
104	46.8 (39)	39/49	44.6 (31)	95	31/49	46.4 (32)	99	32/50	41.5 (30)	89	30/49

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

TABLE 12 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES IN FEMALE MOUSE (TWO-YEAR STUDY)

Week on Study	Control		20ppm			75ppm			300ppm		
	Au.Wt.	No.of Surviv. <50>	Au.Wt.	% of cont. <50>	No.of Surviv.	Au.Wt.	% of cont. <49>	No.of Surviv.	Au.Wt.	% of cont. <50>	No.of Surviv.
0	18.9 (50)	50/50	18.9 (50)	100	50/50	18.9 (49)	100	50/50	18.9 (50)	100	50/50
1	19.9 (50)	50/50	20.0 (50)	101	50/50	20.0 (49)	101	50/50	20.4 (50)	103	50/50
2	20.7 (50)	50/50	20.5 (50)	99	50/50	20.9 (49)	101	49/49	20.6 (50)	100	50/50
3	21.6 (50)	50/50	21.6 (50)	100	50/50	21.8 (49)	101	49/49	22.1 (50)	102	50/50
4	22.2 (50)	50/50	21.9 (50)	99	50/50	22.3 (49)	100	49/49	22.6 (50)	102	50/50
5	23.0 (50)	50/50	22.9 (50)	100	50/50	22.7 (49)	99	49/49	23.5 (50)	102	50/50
6	23.3 (50)	50/50	23.2 (50)	100	50/50	23.6 (49)	101	49/49	23.8 (50)	102	50/50
7	23.9 (50)	50/50	24.0 (50)	100	50/50	24.1 (49)	101	49/49	24.5 (50)	103	50/50
8	24.3 (50)	50/50	24.0 (50)	99	50/50	24.7 (49)	102	49/49	24.6 (50)	101	50/50
9	24.0 (50)	50/50	24.0 (50)	100	50/50	24.5 (49)	102	49/49	24.9 (50)	104	50/50
10	25.3 (50)	50/50	24.6 (50)	97	50/50	25.4 (49)	100	49/49	25.4 (50)	100	50/50
11	25.6 (50)	50/50	25.3 (50)	99	50/50	26.1 (49)	102	49/49	26.1 (50)	102	50/50
12	25.4 (50)	50/50	25.2 (50)	99	50/50	26.2 (49)	103	49/49	26.1 (50)	103	50/50
13	25.8 (50)	50/50	25.5 (50)	99	50/50	26.5 (49)	103	49/49	26.7 (50)	103	50/50
14	26.3 (50)	50/50	26.1 (50)	99	50/50	26.7 (49)	102	49/49	26.7 (50)	102	50/50
18	27.0 (50)	50/50	27.0 (50)	100	50/50	28.1 (49)	104	49/49	28.1 (50)	104	50/50
22	29.0 (50)	50/50	28.4 (50)	98	50/50	29.4 (49)	101	49/49	29.3 (50)	101	50/50
26	29.8 (50)	50/50	30.4 (50)	102	50/50	30.1 (49)	101	49/49	30.4 (50)	102	50/50
30	30.7 (50)	50/50	31.0 (50)	101	50/50	31.8 (49)	104	49/49	31.5 (50)	103	50/50
34	30.9 (50)	50/50	31.5 (50)	102	50/50	32.7 (49)	106	49/49	32.3 (50)	105	50/50
38	31.6 (50)	50/50	32.1 (50)	102	50/50	32.4 (49)	103	49/49	32.6 (50)	103	50/50
42	31.9 (49)	49/50	32.6 (50)	102	50/50	32.9 (49)	103	49/49	32.8 (50)	103	50/50
46	32.6 (49)	49/50	32.9 (50)	101	50/50	33.3 (49)	102	49/49	33.8 (50)	104	50/50
50	33.6 (48)	48/50	33.7 (50)	100	50/50	34.3 (49)	102	49/49	34.3 (50)	102	50/50
54	33.6 (46)	46/50	34.6 (49)	103	49/50	34.5 (48)	103	48/49	34.8 (49)	104	49/50
58	34.6 (46)	46/50	35.0 (49)	101	49/50	35.5 (48)	103	48/49	35.7 (48)	103	48/50
62	35.2 (46)	46/50	36.0 (49)	102	49/50	36.2 (48)	103	48/49	37.0 (48)	105	48/50
66	36.2 (45)	45/50	36.8 (46)	102	46/50	36.7 (47)	101	47/49	37.0 (45)	102	45/50
70	36.7 (44)	44/50	37.5 (46)	102	46/50	37.2 (47)	101	47/49	37.4 (45)	102	45/50
74	36.4 (43)	43/50	36.8 (45)	101	45/50	37.6 (46)	103	46/49	37.8 (45)	104	45/50
78	37.7 (41)	41/50	37.8 (42)	100	42/50	38.6 (44)	102	44/49	38.2 (45)	101	45/50
82	38.2 (41)	41/50	38.7 (39)	101	39/50	38.4 (43)	101	43/49	38.0 (44)	99	44/50
86	38.6 (37)	37/50	39.1 (38)	101	38/50	39.3 (41)	102	41/49	36.8 (42)	95	42/50
90	38.8 (36)	36/50	38.9 (38)	100	38/50	39.0 (36)	101	36/49	36.3 (37)	94	37/50
94	39.2 (35)	35/50	38.6 (36)	98	36/50	39.5 (33)	101	33/49	36.2 (34)	92	34/50
98	37.7 (34)	34/50	38.6 (32)	102	32/50	37.8 (28)	100	28/49	34.8 (33)	92	33/50
102	37.0 (30)	30/50	37.7 (28)	102	27/50	36.6 (26)	99	26/49	33.8 (27)	91	27/50
104	36.5 (28)	28/50	38.8 (25)	106	25/50	35.6 (23)	98	23/49	33.5 (26)	92	26/50

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

TABLE 13 INCIDENCE OF EXTERNAL AND INTERNAL MASS IN CLINICAL OBSERVATION :MOUSE :MALE

week		0~13	14~26	27~39	40~52	53~65	66~78	79~91	92~104	0~104
External mass	Control	0/49	0/49	0/49	0/49	0/47	0/46	0/45	1/45	1/49 (0/10)
	20 ppm	0/49	0/49	0/49	0/49	0/49	0/49	1/47	2/47	2/49 (0/18)
	75 ppm	0/50	0/50	0/50	0/49	1/49	1/46	3/45	3/45	4/50 (1/18)
	300 ppm	0/49	0/49	1/48	1/48	1/48	1/46	3/44	3/44	5/49 (4/19)
Internal mass	Control	2/49	2/49	3/49	3/49	1/47	2/46	3/45	9/44	12/49 (5/10)
	20 ppm	0/49	0/49	0/49	0/49	0/49	3/49	7/47	14/38	19/49 (9/18)
	75 ppm	0/50	0/50	0/50	0/49	1/49	0/46	2/45	7/39	9/50 (4/18)
	300 ppm	0/49	1/49	0/48	0/48	2/48	4/46	5/44	10/37	18/49 (11/19)

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

TABLE 14 INCIDENCE OF EXTERNAL AND INTERNAL MASS IN CLINICAL OBSERVATION :MOUSE :FEMALE

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	0/47	0/45	1/41	2/36	2/50 (2/22)
	20 ppm	0/50	0/50	0/50	0/50	0/49	1/46	1/41	2/37	3/50 (3/25)
	75 ppm	0/49	0/49	0/49	0/49	0/48	0/47	1/44	3/34	3/49 (3/26)
	300 ppm	0/50	0/50	0/50	0/50	0/49	0/45	2/45	1/35	2/50 (2/24)
Internal mass	Control	1/50	1/50	0/50	2/50	3/47	0/45	4/41	5/36	13/50 (8/22)
	20 ppm	0/50	0/50	2/50	2/50	2/49	3/46	2/41	6/37	13/50 (11/25)
	75 ppm	0/49	0/49	0/49	0/49	0/48	2/47	7/44	8/34	12/49 (10/26)
	300 ppm	0/50	0/50	0/50	0/50	4/49	2/45	16/45	27/35	36/50 (18/24)

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

TABLE 15 FOOD CONSUMPTION IN MALE MOUSE (TWO-YEAR STUDY)

Week-Day on Study	Control		20ppm			75ppm			300ppm		
	AU.FC.	No. of Surviv. <49>	AU.FC.	% of cont. <49>	No. of Surviv.	AU.FC.	% of cont. <50>	No. of Surviv.	AU.FC.	% of cont. <49>	No. of Surviv.
1-7	4.2 (49)	50/50	4.2 (49)	100	50/50	4.1 (50)	98	50/50	4.3 (49)	102	50/50
2-7	4.1 (48)	49/49	4.0 (49)	98	50/50	4.2 (50)	102	50/50	4.3 (49)	105	50/50
3-7	4.1 (49)	49/49	4.0 (49)	98	50/50	4.2 (50)	102	50/50	4.4 (49)	107	50/50
4-7	4.3 (49)	49/49	4.0 (49)	93	50/50	4.2 (50)	98	50/50	4.3 (49)	100	50/50
5-7	4.4 (49)	49/49	4.2 (49)	95	50/50	4.3 (50)	98	50/50	4.4 (49)	100	49/49
6-7	4.5 (49)	49/49	4.4 (49)	98	50/50	4.5 (50)	100	50/50	4.6 (49)	102	49/49
7-7	4.3 (49)	49/49	4.1 (49)	95	50/50	4.2 (50)	98	50/50	4.4 (49)	102	49/49
8-7	4.3 (49)	49/49	4.2 (49)	98	50/50	4.3 (50)	100	50/50	4.4 (49)	102	49/49
9-7	4.3 (49)	49/49	4.1 (49)	95	50/50	4.1 (50)	95	50/50	4.2 (49)	98	49/49
10-7	4.5 (49)	49/49	4.5 (49)	100	50/50	4.4 (50)	98	50/50	4.4 (49)	98	49/49
11-7	4.4 (49)	49/49	4.4 (49)	100	50/50	4.4 (50)	100	50/50	4.5 (49)	102	49/49
12-7	4.4 (49)	49/49	4.4 (49)	100	50/50	4.4 (50)	100	50/50	4.5 (49)	102	49/49
13-7	4.3 (49)	49/49	4.3 (49)	100	50/50	4.3 (50)	100	50/50	4.5 (49)	105	49/49
14-7	4.4 (49)	49/49	4.4 (49)	100	50/50	4.4 (50)	100	50/50	4.5 (49)	102	49/49
18-7	4.5 (49)	49/49	4.5 (49)	100	50/50	4.3 (50)	96	50/50	4.4 (49)	98	49/49
22-7	4.6 (49)	49/49	4.6 (49)	100	49/49	4.6 (50)	100	50/50	4.6 (48)	100	48/49
26-7	4.6 (49)	49/49	4.6 (49)	100	49/49	4.6 (50)	100	50/50	4.7 (48)	102	48/49
30-7	4.8 (49)	49/49	4.7 (49)	98	49/49	4.7 (50)	98	50/50	4.8 (48)	100	48/49
34-7	4.8 (49)	49/49	4.7 (49)	98	49/49	4.7 (49)	98	49/50	4.8 (48)	100	48/49
38-7	4.7 (49)	49/49	4.6 (49)	98	49/49	4.6 (49)	98	49/50	4.7 (48)	100	48/49
42-7	4.6 (49)	48/49	4.6 (49)	100	49/49	4.6 (49)	100	49/50	4.8 (48)	104	48/49
46-7	4.9 (48)	48/49	4.7 (49)	96	49/49	4.7 (49)	96	49/50	4.8 (48)	98	48/49
50-7	4.8 (48)	48/49	4.8 (49)	100	49/49	4.7 (49)	98	49/50	4.9 (48)	102	48/49
54-7	5.1 (47)	47/49	4.9 (49)	96	49/49	5.0 (49)	98	49/50	5.0 (48)	98	48/49
58-7	5.2 (47)	47/49	5.1 (49)	98	49/49	5.2 (47)	100	47/50	5.0 (48)	96	48/49
62-7	5.2 (46)	46/49	5.0 (24)	96	49/49	5.2 (46)	100	46/50	5.1 (48)	98	48/49
66-7	5.2 (46)	46/49	5.1 (49)	98	49/49	5.2 (46)	100	46/50	5.2 (46)	100	46/49
70-7	5.2 (46)	46/49	5.1 (47)	98	48/49	5.2 (46)	100	46/50	4.9 (45)	94	45/49
74-7	5.1 (45)	45/49	5.0 (48)	98	48/49	4.9 (46)	96	46/50	4.8 (44)	94	44/49
78-7	5.2 (45)	45/49	4.9 (47)	94	47/49	5.1 (45)	98	45/50	5.1 (44)	98	44/49
82-7	5.3 (45)	45/49	5.1 (47)	96	47/49	5.2 (43)	98	43/50	5.3 (44)	100	43/49
86-7	5.6 (45)	45/49	5.2 (43)	93	43/49	5.4 (42)	96	42/50	5.5 (42)	98	42/49
90-7	5.5 (45)	45/49	5.0 (40)	91	40/49	5.4 (41)	98	40/50	5.2 (40)	95	39/49
94-7	5.4 (39)	43/49	5.0 (20)	93	38/49	5.2 (38)	96	38/50	5.0 (36)	93	36/49
98-7	5.3 (42)	42/49	5.1 (36)	96	36/49	4.9 (37)	92	37/50	5.0 (34)	94	34/49
102-7	4.9 (41)	41/49	4.6 (35)	94	34/49	4.8 (33)	98	33/50	4.9 (34)	100	33/49
104-7	5.0 (40)	39/49	4.4 (34)	88	31/49	4.8 (33)	96	32/50	5.2 (32)	104	30/49

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

AU.FC.: g

TABLE 16 FOOD CONSUMPTION IN FEMALE MOUSE (TWO-YEAR STUDY)

Week-Day on Study	Control		20ppm		75ppm		300ppm				
	Au.F.C.	No.of Surviv. <50>	Au.F.C.	% of cont. <50>	No.of Surviv.	Au.F.C.	% of cont. <49>	No.of Surviv.	Au.F.C.	% of cont. <50>	No.of Surviv.
1-7	3.6 (50)	50/50	3.6 (50)	100	50/50	3.6 (49)	100	50/50	3.7 (50)	103	50/50
2-7	3.5 (50)	50/50	3.6 (50)	103	50/50	3.7 (49)	106	49/49	3.8 (50)	109	50/50
3-7	3.6 (50)	50/50	3.9 (50)	108	50/50	3.9 (49)	108	49/49	4.0 (50)	111	50/50
4-7	3.8 (50)	50/50	3.9 (50)	103	50/50	4.0 (49)	105	49/49	4.1 (50)	108	50/50
5-7	4.1 (50)	50/50	4.3 (50)	105	50/50	4.2 (49)	102	49/49	4.3 (50)	105	50/50
6-7	4.2 (50)	50/50	4.4 (50)	105	50/50	4.5 (49)	107	49/49	4.5 (50)	107	50/50
7-7	4.1 (50)	50/50	4.3 (50)	105	50/50	4.2 (49)	102	49/49	4.5 (50)	110	50/50
8-7	4.2 (50)	50/50	4.3 (50)	102	50/50	4.3 (49)	102	49/49	4.5 (50)	107	50/50
9-7	4.1 (50)	50/50	4.4 (50)	107	50/50	4.1 (49)	100	49/49	4.2 (50)	102	50/50
10-7	4.4 (50)	50/50	4.7 (50)	107	50/50	4.4 (49)	100	49/49	4.4 (50)	100	50/50
11-7	4.1 (50)	50/50	4.3 (49)	105	50/50	4.3 (49)	105	49/49	4.2 (50)	102	50/50
12-7	4.1 (50)	50/50	4.3 (48)	105	50/50	4.2 (49)	102	49/49	4.4 (50)	107	50/50
13-7	4.1 (50)	50/50	4.2 (50)	102	50/50	4.2 (49)	102	49/49	4.3 (50)	105	50/50
14-7	4.2 (50)	50/50	4.4 (50)	105	50/50	4.2 (49)	100	49/49	4.4 (50)	105	50/50
18-7	4.4 (50)	50/50	4.7 (50)	107	50/50	4.3 (49)	98	49/49	4.5 (50)	102	50/50
22-7	4.6 (50)	50/50	4.7 (50)	102	50/50	4.6 (49)	100	49/49	4.7 (50)	102	50/50
26-7	4.5 (50)	50/50	4.7 (50)	104	50/50	4.6 (49)	102	49/49	4.9 (50)	109	50/50
30-7	4.8 (50)	50/50	4.8 (50)	100	50/50	4.9 (49)	102	49/49	4.9 (50)	102	50/50
34-7	4.6 (50)	50/50	4.6 (50)	100	50/50	4.7 (49)	102	49/49	4.8 (50)	104	50/50
38-7	4.7 (50)	50/50	4.5 (50)	96	50/50	4.5 (49)	96	49/49	4.7 (50)	100	50/50
42-7	4.5 (49)	49/50	4.6 (50)	102	50/50	4.4 (49)	98	49/49	4.5 (50)	100	50/50
46-7	4.4 (49)	49/50	4.5 (50)	102	50/50	4.5 (49)	102	49/49	4.6 (50)	105	50/50
50-7	4.5 (48)	48/50	4.5 (50)	100	50/50	4.5 (49)	100	49/49	4.7 (50)	104	50/50
54-7	4.8 (46)	46/50	4.8 (49)	100	49/50	4.9 (48)	102	48/49	4.9 (49)	102	49/50
58-7	5.0 (46)	46/50	5.0 (49)	100	49/50	4.9 (48)	98	48/49	4.9 (49)	98	48/50
62-7	4.9 (46)	46/50	4.7 (49)	96	49/50	4.9 (48)	100	48/49	4.9 (48)	100	48/50
66-7	4.8 (45)	45/50	4.9 (46)	102	46/50	4.8 (47)	100	47/49	4.9 (45)	102	45/50
70-7	4.8 (45)	44/50	4.7 (46)	98	46/50	4.7 (47)	98	47/49	4.7 (45)	98	45/50
74-7	4.4 (43)	43/50	4.5 (45)	102	45/50	4.6 (47)	105	46/49	4.6 (45)	105	45/50
78-7	4.8 (41)	41/50	4.6 (43)	96	42/50	4.6 (44)	96	44/49	4.9 (45)	102	45/50
82-7	5.1 (41)	41/50	4.9 (40)	96	39/50	5.0 (43)	98	43/49	5.4 (45)	106	44/50
86-7	5.2 (37)	37/50	4.7 (39)	90	38/50	4.9 (42)	94	41/49	5.7 (43)	110	42/50
90-7	5.0 (37)	36/50	4.8 (38)	96	38/50	5.1 (37)	102	36/49	5.6 (39)	112	37/50
94-7	5.1 (31)	35/50	4.7 (28)	92	36/50	5.0 (33)	98	33/49	5.7 (34)	112	34/50
98-7	4.7 (35)	34/50	4.8 (32)	102	32/50	4.8 (30)	102	28/49	5.7 (34)	121	33/50
102-7	4.5 (31)	30/50	4.5 (28)	100	27/50	4.5 (26)	100	26/49	5.3 (29)	118	27/50
104-7	4.6 (30)	28/50	4.8 (26)	104	25/50	4.3 (25)	93	23/49	5.4 (26)	117	26/50

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

Au.F.C.: g

TABLE 17 NEOPLASTIC LESIONS(LIVER) INCIDENCE AND STATISTICAL ANALYSIS:MOUSE:MALE

Group Name	Control	20 ppm	75 ppm	300 ppm
SITE : liver				
TUMOUR : hepatocellular adenoma				
Tumor Rates				
Overall Rates(a)	13/49 (26.5)	9/49 (18.4)	7/50 (14.0)	13/49 (26.5)
Adjusted Rates(b)	28.89	22.58	18.75	36.67
Terminal Rates(c)	11/39 (28.2)	7/31 (22.6)	6/32 (18.8)	11/30 (36.7)
Statistical Analysis				
Peto Test				
Standard metod(d)	P=-----			
Prevalence method(d)	P=0.1723			
Combined analysis(d)	P=-----			
Cochran-Armitage Test(e)	P=0.4993			
Fisher Exact Test(e)		P=0.2971	P=0.1537	P=0.4129
SITE : liver				
TUMOUR : hepatocellular carcinoma				
Tumor Rates				
Overall Rates(a)	12/49 (24.5)	17/49 (34.7)	16/50 (32.0)	38/49 (77.6)
Adjusted Rates(b)	25.64	41.94	39.39	81.58
Terminal Rates(c)	10/39 (25.6)	13/31 (41.9)	12/32 (37.5)	23/30 (76.7)
Statistical Analysis				
Peto Test				
Standard metod(d)	P=0.0507			
Prevalence method(d)	P<0.0001**?			
Combined analysis(d)	P<0.0001**			
Cochran-Armitage Test(e)	P<0.0001**			
Fisher Exact Test(e)		P=0.2733	P=0.3429	P=0.0018**
SITE : liver				
TUMOUR : hepatocellular adenoma,hepatocellular carcinoma				
Tumor Rates				
Overall Rates(a)	20/49 (40.8)	21/49 (42.9)	18/50 (36.0)	41/49 (83.7)
Adjusted Rates(b)	43.59	51.61	42.42	89.47
Terminal Rates(c)	17/39 (43.6)	16/31 (51.6)	13/32 (40.6)	26/30 (86.7)
Statistical Analysis				
Peto Test				
Standard metod(d)	P=0.0507			
Prevalence method(d)	P<0.0001**			
Combined analysis(d)	P<0.0001**			
Cochran-Armitage Test(e)	P<0.0001**			
Fisher Exact Test(e)		P=0.4781	P=0.4453	P=0.0242*
SITE : liver				
TUMOUR : histiocytic sarcoma				
Tumor Rates				
Overall Rates(a)	0/49 (0.0)	3/49 (6.1)	1/50 (2.0)	6/49 (12.2)
Adjusted Rates(b)	0.0	3.23	0.0	0.0
Terminal Rates(c)	0/39 (0.0)	1/31 (3.2)	0/32 (0.0)	0/30 (0.0)
Statistical Analysis				
Peto Test				
Standard metod(d)	P=0.0029**			
Prevalence method(d)	P=0.4473			
Combined analysis(d)	P=0.0072**			
Cochran-Armitage Test(e)	P=0.0097**			
Fisher Exact Test(e)		P=0.1326	P=0.4900	P=0.0191*

(a):Number of tumor-bearing animals/number of animals examined at the site.

(b):Kaplan-Weire estimated tumor incidence at the end of study after adjusting for intercurrent mortality.

(c):Observed tumor incidence at terminal kill.

(d):Beneath the control incidence are the P-values associated with the trend test.

Standard method : Death analysis

Prevalence method : Incidental tumor test

Combined analysis : Death analysis + Incidental tumor test

(e):The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.

?:The conditional probabilities of the largest and smallest possible out comes can not estimated or this p-value is beyond the estimated p-value.

-----:There is no data which should be statistical analysis.

Significant difference; * : $P \leq 0.05$ ** : $P \leq 0.01$

TABLE 18 NEOPLASTIC LESIONS(LIVER) INCIDENCE AND STATISTICAL ANALYSIS:MOUSE:FEMALE

Group Name	Control	20 ppm	75 ppm	300 ppm
SITE : liver				
TUMOUR : hepatocellular adenoma				
Tumor Rates				
Overall Rates(a)	2/50 (4.0)	10/50 (20.0)	6/49 (12.2)	20/50 (40.0)
Adjusted Rates(b)	4.76	36.00	21.74	50.00
Terminal Rates(c)	1/28 (3.6)	9/25 (36.0)	5/23 (21.7)	13/26 (50.0)
Statistical Analysis				
Peto Test				
Standard metod(d)	P=-----			
Prevalence method(d)	P<0.0001**			
Combined analysis(d)	P=-----			
Cochran-Armitage Test(e)	P<0.0001**			
Fisher Exact Test(e)		P=0.0270*	P=0.1540	P=0.0003**
SITE : liver				
TUMOUR : hepatocellular carcinoma				
Tumor Rates				
Overall Rates(a)	2/50 (4.0)	4/50 (8.0)	2/49 (4.1)	41/50 (82.0)
Adjusted Rates(b)	7.14	12.00	8.33	100.00
Terminal Rates(c)	2/28 (7.1)	3/25 (12.0)	1/23 (4.3)	26/26 (100.0)
Statistical Analysis				
Peto Test				
Standard metod(d)	P<0.0001**			
Prevalence method(d)	P<0.0001**?			
Combined analysis(d)	P<0.0001**?			
Cochran-Armitage Test(e)	P<0.0001**			
Fisher Exact Test(e)		P=0.3574	P=0.3162	P<0.0001**
SITE : liver				
TUMOUR : hepatocellular adenoma,hepatocellular carcinoma				
Tumor Rates				
Overall Rates(a)	4/50 (8.0)	13/50 (26.0)	7/49 (14.3)	45/50 (90.0)
Adjusted Rates(b)	10.71	44.00	25.00	100.00
Terminal Rates(c)	3/28 (10.7)	11/25 (44.0)	5/23 (21.7)	26/26 (100.0)
Statistical Analysis				
Peto Test				
Standard metod(d)	P<0.0001**			
Prevalence method(d)	P<0.0001**?			
Combined analysis(d)	P<0.0001**?			
Cochran-Armitage Test(e)	P<0.0001**			
Fisher Exact Test(e)		P=0.0371*	P=0.2850	P<0.0001**

TABLE 19 NEOPLASTIC LESIONS(LUNG) INCIDENCE AND STATISTICAL ANALYSIS:MOUSE:FEMALE

Group Name	Control	20 ppm	75 ppm	300 ppm
SITE : lung				
TUMOUR : bronchiolar-alveolar carcinoma				
Tumor Rates				
Overall Rates(a)	2/50 (2.0)	1/50 (2.0)	1/49 (2.0)	4/50 (8.0)
Adjusted Rates(b)	3.57	4.00	4.35	10.53
Terminal Rates(c)	1/28 (3.6)	1/25 (4.0)	1/23 (4.3)	2/26 (7.7)
Statistical Analysis				
Peto Test				
Standard metod(d)	P=-----			
Prevalence method(d)	P=0.0377*			
Combined analysis(d)	P=-----			
Cochran-Armitage Test(e)	P=0.0526			
Fisher Exact Test(e)		P=0.2475	P=0.2525	P=0.1998

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

TABLE 20 NUMBER OF MOUSE WITH CENTRAL HEPATOCELLULAR HYPERTROPHY

Group Name	Male				Female			
	Control	20ppm	75ppm	300ppm	Control	20ppm	75ppm	300ppm
Number of examined	49	49	50	49	50	50	49	50
hepatocellular hypertrophy:								
central	0	0	0	34	0	0	0	2

TABLE 21 NUMBER OF MALE MOUSE WITH MINERALIZATION IN TESTIS

Group Name	Male			
	Control	20ppm	75ppm	300ppm
Number of examined	49	49	50	49
mineralization	27	35	42	41

TABLE 22 CAUSE OF DEATH:MOUSE

Group Name	Male				Female			
	Control	20ppm	75ppm	300ppm	Control	20ppm	75ppm	300ppm
Number of Dead/Moribund Animal	10	18	18	19	22	25	26	24
No microscopical confirmation	0	0	2	0	2	1	1	0
Cardiovascular lesion	0	0	0	0	0	1	0	0
Renal lesion	1	1	1	0	2	1	0	0
Reproductive system lesion	0	1	0	0	0	0	0	0
Body cavity lesion	0	1	0	0	0	0	0	0
Urinary retention	2	0	1	3	0	1	0	0
Arteritis	0	2	1	0	0	0	0	0
Hydronephrosis	1	1	0	1	1	1	0	0
Tumor death : leukemia	1	2	3	2	8	11	10	6
: skin/apendage	0	0	0	0	0	2	0	0
: subcutis	0	0	1	0	0	0	0	0
: spleen	0	2	1	0	0	0	1	0
: stomach	1	0	0	0	0	0	0	0
: liver	3	7	4	12	1	2	3	10
: urinary bladder	0	0	1	0	0	0	0	0
: pituitary	1	0	1	1	1	1	2	0
: uterus	0	0	0	0	7	4	9	8
: peripheral nerves	0	1	0	0	0	0	0	0
: bone	0	0	1	0	0	0	0	0
: peritoneum	0	0	1	0	0	0	0	0