p-ニトロアニソールのラットを用いた
経口投与によるがん原性試験(混餌試験)報告書

試験番号：０４０１

TABLES

TABLES

TABLES (Continued)

TABLE 1 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF MALE RATS IN THE 2-YEAR FEED STUDY OF *p*-NITROANISOLE

Week on Study	Control		2000ppm			4000ppm			8000ppm		
	Av. Wt.	No. of Surviv.	Av. Wt.	% of cont.	No. of Surviv.	Av. Wt.	% of cont.	No. of Surviv.	Av. Wt.	% of cont.	No. of Surviv.
	< 50 >		< 50 >			< 50 >			< 50 >		
0	121 (50)	50 / 50	121 (50)	100	50 / 50	121 (50)	100	50 / 50	121 (50)	100	50 / 50
1	147 (50)	50 / 50	147 (50)	100	50 / 50	141 (50)	96	50 / 50	129 (50)	88	50 / 50
2	178 (50)	50 / 50	180 (50)	101	50 / 50	175 (50)	98	50 / 50	157 (50)	88	50 / 50
3	203 (50)	50 / 50	203 (50)	100	50 / 50	200 (50)	99	50 / 50	181 (50)	89	50 / 50
4	221 (50)	50 / 50	221 (50)	100	50 / 50	219 (50)	99	50 / 50	199 (50)	90	50 / 50
5	237 (50)	50 / 50	236 (50)	100	50 / 50	235 (50)	99	50 / 50	213 (50)	90	50 / 50
6	251 (50)	50 / 50	250 (50)	100	50 / 50	249 (50)	99	50 / 50	224 (50)	89	50 / 50
7	265 (50)	50 / 50	264 (50)	100	50 / 50	263 (50)	99	50 / 50	237 (50)	89	50 / 50
8	276 (50)	50 / 50	276 (50)	100	50 / 50	274 (50)	99	50 / 50	248 (50)	90	50 / 50
9	286 (50)	50 / 50	288 (50)	101	50 / 50	287 (50)	100	50 / 50	256 (50)	90	50 / 50
10	296 (50)	50 / 50	298 (50)	101	50 / 50	297 (50)	100	50 / 50	266 (50)	90	50 / 50
11	304 (50)	50 / 50	306 (50)	101	50 / 50	306 (50)	101	50 / 50	274 (50)	90	50 / 50
12	310 (50)	50 / 50	312 (50)	101	50 / 50	311 (50)	100	50 / 50	278 (50)	90	50 / 50
13	318 (50)	50 / 50	320 (50)	101	50 / 50	321 (50)	101	50 / 50	288 (50)	91	50 / 50
14	324 (50)	50 / 50	328 (50)	101	50 / 50	327 (50)	101	50 / 50	294 (50)	91	50 / 50
18	341 (50)	50 / 50	347 (50)	102	50 / 50	347 (50)	102	50 / 50	313 (50)	92	50 / 50
22	357 (50)	50 / 50	366 (50)	103	50 / 50	365 (50)	102	50 / 50	329 (50)	92	50 / 50
26	366 (50)	50 / 50	377 (50)	103	50 / 50	376 (50)	103	50 / 50	339 (50)	93	50 / 50
30	373 (50)	50 / 50	386 (50)	103	50 / 50	386 (49)	103	49 / 50	346 (50)	93	50 / 50
34	382 (50)	50 / 50	395 (50)	103	50 / 50	396 (49)	104	49 / 50	354 (50)	93	50 / 50
38	391 (50)	50 / 50	405 (50)	104	50 / 50	407 (49)	104	49 / 50	361 (50)	92	50 / 50
42	400 (50)	50 / 50	414 (50)	104	50 / 50	414 (49)	104	49 / 50	367 (50)	92	50 / 50
46	405 (50)	50 / 50	419 (49)	103	49 / 50	420 (49)	104	49 / 50	372 (49)	92	49 / 50
50	407 (50)	50 / 50	423 (49)	104	49 / 50	422 (49)	104	49 / 50	373 (49)	92	49 / 50
54	411 (50)	50 / 50	427 (49)	104	49 / 50	426 (49)	104	49 / 50	372 (48)	91	48 / 50
58	414 (50)	50 / 50	431 (49)	104	49 / 50	425 (48)	103	48 / 50	365 (48)	88	48 / 50
62	417 (49)	49 / 50	433 (49)	104	49 / 50	424 (48)	102	48 / 50	357 (48)	86	48 / 50
66	420 (49)	49 / 50	435 (49)	104	49 / 50	421 (48)	100	48 / 50	349 (48)	83	48 / 50
70	422 (49)	49 / 50	435 (49)	103	49 / 50	416 (48)	99	48 / 50	341 (47)	81	47 / 50
74	419 (49)	49 / 50	434 (49)	104	49 / 50	411 (47)	98	47 / 50	332 (45)	79	45 / 50
78	419 (49)	49 / 50	434 (49)	104	49 / 50	407 (47)	97	47 / 50	319 (41)	76	41 / 50
82	418 (49)	49 / 50	430 (49)	103	49 / 50	401 (47)	96	47 / 50	298 (34)	71	34 / 50
86	416 (49)	49 / 50	427 (47)	103	47 / 50	392 (45)	94	45 / 50	296 (23)	71	23 / 50
90	416 (46)	46 / 50	423 (45)	102	45 / 50	385 (45)	93	45 / 50	305 (16)	73	16 / 50
94	410 (44)	44 / 50	417 (43)	102	43 / 50	375 (44)	91	44 / 50	276 (14)	67	14 / 50
98	403 (42)	42 / 50	408 (39)	101	39 / 50	361 (38)	90	38 / 50	292 (4)	72	4 / 50
102	395 (38)	38 / 50	395 (39)	100	39 / 50	345 (35)	87	35 / 50	250 (4)	63	4 / 50
104	389 (37)	37 / 50	386 (39)	99	39 / 50	333 (32)	86	32 / 50	232 (2)	60	2 / 50

< > : No.of effective animals, ( ) : No.of measured animals, Av.Wt.: Averaged body weight (Unit : g)

TABLE 2 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF FEMALE RATS IN THE 2-YEAR FEED STUDY OF *p*-NITROANISOLE

Week on Study	Control		2000ppm			4000ppm			8000ppm		
	Av. Wt.	No. of Surviv.	Av. Wt.	% of cont.	No. of Surviv.	Av. Wt.	% of cont.	No. of Surviv.	Av. Wt.	% of cont.	No. of Surviv.
	< 50 >		< 50 >			< 50 >			< 49 >		
0	97 (50)	50 / 50	97 (50)	100	50 / 50	97 (50)	100	50 / 50	97 (49)	100	49 / 49
1	111 (50)	50 / 50	108 (50)	97	50 / 50	103 (50)	93	50 / 50	97 (49)	87	49 / 49
2	122 (50)	50 / 50	117 (50)	96	50 / 50	112 (50)	92	50 / 50	108 (49)	89	49 / 49
3	132 (50)	50 / 50	124 (50)	94	50 / 50	119 (50)	90	50 / 50	117 (49)	89	49 / 49
4	139 (50)	50 / 50	129 (50)	93	50 / 50	125 (50)	90	50 / 50	124 (49)	89	49 / 49
5	145 (50)	50 / 50	135 (50)	93	50 / 50	130 (50)	90	50 / 50	128 (49)	88	49 / 49
6	150 (50)	50 / 50	138 (50)	92	50 / 50	134 (50)	89	50 / 50	132 (49)	88	49 / 49
7	155 (50)	50 / 50	142 (50)	92	50 / 50	137 (50)	88	50 / 50	135 (49)	87	49 / 49
8	158 (50)	50 / 50	145 (50)	92	50 / 50	140 (50)	89	50 / 50	138 (49)	87	49 / 49
9	161 (50)	50 / 50	148 (50)	92	50 / 50	144 (50)	89	50 / 50	141 (49)	88	49 / 49
10	163 (50)	50 / 50	152 (50)	93	50 / 50	147 (50)	90	50 / 50	144 (49)	88	49 / 49
11	167 (50)	50 / 50	155 (50)	93	50 / 50	150 (50)	90	50 / 50	148 (49)	89	49 / 49
12	169 (50)	50 / 50	157 (50)	93	50 / 50	152 (50)	90	50 / 50	150 (49)	89	49 / 49
13	169 (50)	50 / 50	158 (50)	93	50 / 50	154 (50)	91	50 / 50	154 (49)	91	49 / 49
14	170 (50)	50 / 50	157 (50)	92	50 / 50	156 (50)	92	50 / 50	155 (49)	91	49 / 49
18	176 (50)	50 / 50	161 (50)	91	50 / 50	157 (50)	89	50 / 50	156 (49)	89	49 / 49
22	182 (50)	50 / 50	166 (50)	91	50 / 50	162 (50)	89	50 / 50	160 (49)	88	49 / 49
26	188 (50)	50 / 50	171 (50)	91	50 / 50	166 (50)	88	50 / 50	163 (49)	87	49 / 49
30	192 (50)	50 / 50	175 (50)	91	50 / 50	168 (50)	88	50 / 50	167 (49)	87	49 / 49
34	197 (50)	50 / 50	178 (50)	90	50 / 50	171 (49)	87	49 / 50	169 (49)	86	49 / 49
38	198 (50)	50 / 50	178 (50)	90	50 / 50	172 (49)	87	49 / 50	171 (49)	86	49 / 49
42	203 (50)	50 / 50	182 (50)	90	50 / 50	174 (49)	86	49 / 50	172 (49)	85	49 / 49
46	207 (50)	50 / 50	185 (50)	89	50 / 50	176 (49)	85	49 / 50	175 (49)	85	49 / 49
50	211 (50)	50 / 50	188 (50)	89	50 / 50	179 (49)	85	49 / 50	177 (49)	84	49 / 49
54	217 (50)	50 / 50	191 (50)	88	50 / 50	181 (49)	83	49 / 50	180 (49)	83	49 / 49
58	223 (50)	50 / 50	195 (49)	87	49 / 50	185 (48)	83	48 / 50	180 (49)	81	49 / 49
62	226 (50)	50 / 50	198 (49)	88	49 / 50	188 (48)	83	48 / 50	182 (49)	81	49 / 49
66	231 (50)	50 / 50	201 (49)	87	49 / 50	190 (48)	82	48 / 50	183 (49)	79	49 / 49
70	237 (50)	50 / 50	204 (48)	86	48 / 50	193 (47)	81	47 / 50	184 (49)	78	49 / 49
74	244 (50)	50 / 50	210 (48)	86	48 / 50	198 (47)	81	47 / 50	186 (48)	76	48 / 49
78	246 (50)	50 / 50	214 (48)	87	48 / 50	201 (47)	82	47 / 50	185 (48)	75	48 / 49
82	252 (49)	49 / 50	218 (47)	87	47 / 50	203 (46)	81	46 / 50	186 (48)	74	48 / 49
86	256 (49)	49 / 50	220 (45)	86	45 / 50	206 (45)	80	45 / 50	185 (48)	72	48 / 49
90	260 (48)	48 / 50	224 (45)	86	45 / 50	207 (43)	80	43 / 50	187 (44)	72	44 / 49
94	264 (47)	47 / 50	226 (42)	86	42 / 50	210 (42)	80	42 / 50	184 (43)	70	43 / 49
98	265 (46)	46 / 50	228 (42)	86	42 / 50	215 (39)	81	39 / 50	183 (38)	69	38 / 49
102	261 (46)	46 / 50	228 (40)	87	40 / 50	212 (37)	81	37 / 50	183 (32)	70	32 / 49
104	259 (45)	45 / 50	226 (38)	87	38 / 50	209 (35)	81	35 / 50	180 (31)	69	31 / 49

< > : No.of effective animals, ( ) : No.of measured animals, Av.Wt.: Averaged body weight (Unit : g)

TABLE 3 FOOD CONSUMPTION CHANGES OF MALE RATS IN THE 2-YEAR FEED STUDY OF *p*-NITROANISOLE

Week on Study	Control		2000ppm			4000ppm			8000ppm		
	Av. Fc.	No. of Surviv. < 50 >	Av. Fc.	% of cont.	No. of Surviv. < 50 >	Av. Fc.	% of cont.	No. of Surviv. < 50 >	Av. Fc.	% of cont.	No. of Surviv. < 50 >
1	11.9 (50)	50 / 50	11.8 (50)	99	50 / 50	10.9 (50)	92	50 / 50	8.8 (50)	74	50 / 50
2	13.4 (50)	50 / 50	13.6 (50)	101	50 / 50	13.1 (50)	98	50 / 50	11.5 (50)	86	50 / 50
3	13.6 (50)	50 / 50	14.0 (50)	103	50 / 50	14.0 (50)	103	50 / 50	12.8 (50)	94	50 / 50
4	14.0 (50)	50 / 50	14.2 (50)	101	50 / 50	14.4 (50)	103	50 / 50	13.7 (49)	98	50 / 50
5	14.2 (50)	50 / 50	14.3 (50)	101	50 / 50	14.5 (50)	102	50 / 50	13.6 (49)	96	50 / 50
6	14.3 (50)	50 / 50	14.4 (50)	101	50 / 50	14.6 (50)	102	50 / 50	13.8 (50)	97	50 / 50
7	14.5 (50)	50 / 50	14.7 (50)	101	50 / 50	14.7 (50)	101	50 / 50	13.8 (50)	95	50 / 50
8	14.4 (50)	50 / 50	14.7 (50)	102	50 / 50	14.7 (50)	102	50 / 50	14.1 (50)	98	50 / 50
9	14.4 (50)	50 / 50	15.0 (50)	104	50 / 50	14.9 (50)	103	50 / 50	14.1 (50)	98	50 / 50
10	14.8 (50)	50 / 50	15.2 (50)	103	50 / 50	15.1 (50)	102	50 / 50	14.4 (50)	97	50 / 50
11	14.3 (50)	50 / 50	15.0 (50)	105	50 / 50	15.1 (50)	106	50 / 50	14.4 (50)	101	50 / 50
12	14.1 (50)	50 / 50	14.5 (50)	103	50 / 50	14.4 (50)	102	50 / 50	13.8 (50)	98	50 / 50
13	14.5 (50)	50 / 50	14.7 (50)	101	50 / 50	14.7 (50)	101	50 / 50	14.2 (50)	98	50 / 50
14	14.3 (50)	50 / 50	14.6 (50)	102	50 / 50	14.6 (50)	102	50 / 50	14.2 (50)	99	50 / 50
18	14.7 (50)	50 / 50	14.9 (50)	101	50 / 50	14.9 (50)	101	50 / 50	14.3 (50)	97	50 / 50
22	15.8 (50)	50 / 50	16.1 (50)	102	50 / 50	16.2 (50)	103	50 / 50	15.5 (50)	98	50 / 50
26	15.9 (50)	50 / 50	16.2 (50)	102	50 / 50	16.5 (50)	104	50 / 50	15.4 (50)	97	50 / 50
30	15.4 (50)	50 / 50	16.2 (50)	105	50 / 50	16.3 (49)	106	49 / 50	15.4 (50)	100	50 / 50
34	15.7 (50)	50 / 50	16.2 (50)	103	50 / 50	16.7 (48)	106	49 / 50	16.0 (50)	102	50 / 50
38	15.9 (50)	50 / 50	16.1 (49)	101	50 / 50	17.0 (48)	107	49 / 50	16.0 (50)	101	50 / 50
42	16.0 (50)	50 / 50	16.1 (50)	101	50 / 50	16.8 (49)	105	49 / 50	15.9 (50)	99	50 / 50
46	16.1 (50)	50 / 50	16.0 (48)	99	49 / 50	16.7 (48)	104	49 / 50	15.9 (49)	99	49 / 50
50	16.0 (50)	50 / 50	16.1 (48)	101	49 / 50	16.6 (47)	104	49 / 50	15.6 (49)	98	49 / 50
54	15.9 (50)	50 / 50	16.1 (48)	101	49 / 50	16.9 (48)	106	49 / 50	15.7 (48)	99	48 / 50
58	15.8 (50)	50 / 50	15.9 (48)	101	49 / 50	16.4 (47)	104	48 / 50	15.1 (48)	96	48 / 50
62	16.0 (49)	49 / 50	16.2 (48)	101	49 / 50	16.6 (47)	104	48 / 50	15.1 (48)	94	48 / 50
66	16.0 (49)	49 / 50	16.2 (49)	101	49 / 50	16.4 (48)	103	48 / 50	14.9 (48)	93	48 / 50
70	15.9 (49)	49 / 50	15.9 (47)	100	49 / 50	16.3 (46)	103	48 / 50	15.2 (46)	96	47 / 50
74	16.1 (48)	49 / 50	16.3 (47)	101	49 / 50	16.5 (46)	102	47 / 50	15.1 (44)	94	45 / 50
78	16.3 (49)	49 / 50	16.3 (48)	100	49 / 50	16.3 (46)	100	47 / 50	14.7 (40)	90	41 / 50
82	15.9 (49)	49 / 50	16.2 (49)	102	49 / 50	16.4 (44)	103	47 / 50	14.9 (34)	94	34 / 50
86	16.1 (49)	49 / 50	16.1 (47)	100	47 / 50	16.4 (42)	102	45 / 50	15.0 (23)	93	23 / 50
90	15.9 (45)	46 / 50	16.0 (44)	101	45 / 50	16.4 (42)	103	45 / 50	16.7 (15)	105	16 / 50
94	15.5 (44)	44 / 50	15.5 (43)	100	43 / 50	15.8 (39)	102	44 / 50	15.1 (13)	97	14 / 50
98	15.3 (41)	42 / 50	15.6 (39)	102	39 / 50	15.6 (35)	102	38 / 50	17.7 (4)	116	4 / 50
102	15.3 (38)	38 / 50	15.6 (39)	102	39 / 50	16.2 (35)	106	35 / 50	13.8 (4)	90	4 / 50
104	15.1 (37)	37 / 50	15.3 (39)	101	39 / 50	16.1 (32)	107	32 / 50	12.2 (2)	81	2 / 50

< > : No.of effective animals, ( ) : No.of measured animals, Av.Fc.: Averaged food consumption (Unit : g)

TABLE 4 FOOD CONSUMPTION CHANGES OF FEMALE RATS IN THE 2-YEAR FEED STUDY OF *p*-NITROANISOLE

Week on Study	Control		2000ppm			4000ppm			8000ppm		
	Av. Fc.	No. of Surviv.	Av. Fc.	% of cont.	No. of Surviv.	Av. Fc.	% of cont.	No. of Surviv.	Av. Fc.	% of cont.	No. of Surviv.
	< 50 >		< 50 >			< 50 >			< 49 >		
1	9.7 (50)	50 / 50	9.1 (50)	94	50 / 50	8.4 (50)	87	50 / 50	8.5 (49)	88	49 / 49
2	10.0 (50)	50 / 50	9.1 (50)	91	50 / 50	8.4 (50)	84	50 / 50	8.1 (49)	81	49 / 49
3	10.2 (50)	50 / 50	9.1 (50)	89	50 / 50	8.2 (50)	80	50 / 50	8.2 (49)	80	49 / 49
4	10.2 (50)	50 / 50	9.1 (50)	89	50 / 50	8.5 (50)	83	50 / 50	8.5 (49)	83	49 / 49
5	10.3 (50)	50 / 50	9.1 (50)	88	50 / 50	8.5 (50)	83	50 / 50	8.5 (49)	83	49 / 49
6	10.3 (50)	50 / 50	9.3 (50)	90	50 / 50	8.6 (50)	83	50 / 50	8.4 (48)	82	49 / 49
7	10.0 (50)	50 / 50	9.3 (50)	93	50 / 50	8.5 (50)	85	50 / 50	8.3 (48)	83	49 / 49
8	9.8 (50)	50 / 50	9.2 (50)	94	50 / 50	8.5 (50)	87	50 / 50	8.5 (49)	87	49 / 49
9	9.9 (50)	50 / 50	9.3 (50)	94	50 / 50	8.6 (50)	87	50 / 50	8.4 (49)	85	49 / 49
10	9.7 (50)	50 / 50	9.3 (50)	96	50 / 50	8.6 (50)	89	50 / 50	8.3 (45)	86	49 / 49
11	9.8 (50)	50 / 50	9.5 (50)	97	50 / 50	8.8 (50)	90	50 / 50	8.6 (49)	88	49 / 49
12	9.6 (50)	50 / 50	9.2 (50)	96	50 / 50	8.6 (50)	90	50 / 50	8.5 (49)	89	49 / 49
13	9.7 (50)	50 / 50	9.4 (50)	97	50 / 50	8.8 (49)	91	50 / 50	8.8 (49)	91	49 / 49
14	9.6 (50)	50 / 50	9.0 (50)	94	50 / 50	8.7 (50)	91	50 / 50	8.4 (49)	88	49 / 49
18	10.2 (50)	50 / 50	9.3 (50)	91	50 / 50	8.8 (50)	86	50 / 50	8.6 (49)	84	49 / 49
22	10.8 (50)	50 / 50	9.8 (50)	91	50 / 50	8.9 (50)	82	50 / 50	8.9 (49)	82	49 / 49
26	10.7 (50)	50 / 50	9.7 (50)	91	50 / 50	8.8 (50)	82	50 / 50	8.6 (49)	80	49 / 49
30	10.9 (50)	50 / 50	10.0 (50)	92	50 / 50	8.9 (50)	82	50 / 50	9.1 (49)	83	49 / 49
34	11.0 (50)	50 / 50	10.0 (50)	91	50 / 50	8.9 (49)	81	49 / 50	9.0 (49)	82	49 / 49
38	11.1 (50)	50 / 50	10.1 (50)	91	50 / 50	9.0 (49)	81	49 / 50	9.4 (49)	85	49 / 49
42	11.5 (50)	50 / 50	10.3 (50)	90	50 / 50	9.2 (49)	80	49 / 50	9.4 (49)	82	49 / 49
46	11.9 (50)	50 / 50	10.5 (50)	88	50 / 50	9.2 (49)	77	49 / 50	9.4 (49)	79	49 / 49
50	11.5 (50)	50 / 50	10.6 (50)	92	50 / 50	9.3 (49)	81	49 / 50	9.5 (49)	83	49 / 49
54	11.7 (50)	50 / 50	10.6 (50)	91	50 / 50	9.4 (49)	80	49 / 50	9.6 (49)	82	49 / 49
58	12.1 (50)	50 / 50	10.9 (49)	90	49 / 50	9.9 (48)	82	48 / 50	9.7 (49)	80	49 / 49
62	12.0 (50)	50 / 50	11.1 (49)	93	49 / 50	10.0 (48)	83	48 / 50	9.9 (49)	83	49 / 49
66	12.3 (50)	50 / 50	11.3 (49)	92	49 / 50	10.2 (48)	83	48 / 50	10.2 (49)	83	49 / 49
70	12.2 (50)	50 / 50	11.0 (48)	90	48 / 50	10.4 (47)	85	47 / 50	10.5 (49)	86	49 / 49
74	12.9 (50)	50 / 50	11.6 (48)	90	48 / 50	10.6 (47)	82	47 / 50	10.5 (48)	81	48 / 49
78	12.8 (50)	50 / 50	11.4 (48)	89	48 / 50	10.5 (47)	82	47 / 50	10.5 (48)	82	48 / 49
82	12.9 (49)	49 / 50	11.7 (47)	91	47 / 50	10.9 (46)	84	46 / 50	11.1 (48)	86	48 / 49
86	13.3 (49)	49 / 50	12.2 (45)	92	45 / 50	10.9 (45)	82	45 / 50	11.1 (48)	83	48 / 49
90	13.4 (48)	48 / 50	12.6 (45)	94	45 / 50	11.0 (43)	82	43 / 50	11.2 (43)	84	44 / 49
94	13.0 (47)	47 / 50	12.2 (42)	94	42 / 50	11.0 (42)	85	42 / 50	11.1 (43)	85	43 / 49
98	13.2 (46)	46 / 50	12.1 (42)	92	42 / 50	11.5 (39)	87	39 / 50	11.0 (38)	83	38 / 49
102	12.8 (46)	46 / 50	12.5 (40)	98	40 / 50	11.7 (37)	91	37 / 50	11.3 (32)	88	32 / 49
104	12.4 (45)	45 / 50	12.1 (38)	98	38 / 50	11.7 (35)	94	35 / 50	11.3 (31)	91	31 / 49

< > : No.of effective animals, ( ) : No.of measured animals, Av.Fc.: Averaged food consumption (Unit : g)

TABLE 5 INCIDENCES OF EXTERNAL AND INTERNAL MASSES IN CLINICAL OBSERVATION O
MALE RATS IN THE 2-YEAR FEED STUDY OF *p*-NITROANISOLE

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	1/50	2/50	1/50	5/49	7/49	8/45	13/50(2/13)
2000 ppm	0/50	1/50	0/50	0/50	0/49	2/49	3/49	6/45	9/50(1/11)
4000 ppm	0/50	1/50	2/50	1/49	5/49	6/48	11/47	16/44	22/50(5/18)
8000 ppm	0/50	1/50	2/50	5/50	9/48	7/48	2/41	0/16	15/50(15/48)
Internal mass									
Control	0/50	0/50	0/50	0/50	0/50	0/49	0/49	2/45	2/50(2/13)
2000 ppm	0/50	0/50	0/50	0/50	0/49	0/49	0/49	1/45	1/50(1/11)
4000 ppm	0/50	0/50	0/50	0/49	0/49	0/48	0/47	0/44	0/50(0/18)
8000 ppm	0/50	0/50	0/50	0/50	0/48	0/48	0/41	0/16	0/50(0/48)

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

TABLE 6 INCIDENCES OF EXTERNAL AND INTERNAL MASSES IN CLINICAL OBSERVATION O
FEMALE RATS IN THE 2-YEAR FEED STUDY OF *p*-NITROANISOLE

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	5/50	4/48	8/50(0/ 5)
2000 ppm	0/50	0/50	0/50	2/50	3/50	3/49	7/48	4/45	10/50(5/12)
4000 ppm	0/50	0/50	2/50	3/49	5/49	4/48	4/47	7/43	13/50(6/15)
8000 ppm	0/49	1/49	0/49	3/49	5/49	1/49	4/48	4/43	11/49(4/18)
Internal mass									
Control	0/50	0/50	0/50	0/50	0/50	0/50	1/50	0/48	1/50(1/ 5)
2000 ppm	0/50	0/50	0/50	0/50	1/50	1/49	2/48	3/45	6/50(6/12)
4000 ppm	0/50	0/50	0/50	0/49	1/49	0/48	1/47	2/43	4/50(2/15)
8000 ppm	0/49	0/49	0/49	0/49	0/49	0/49	0/48	0/43	0/49(0/18)

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

TABLE 7 HEMATOLOGY OF MALE RATS IN THE 2-YEAR FEED STUDYOF *p*-NITROANISOLE

Group name	Control	2000 ppm	4000 ppm	8000 ppm
No. of examined animals	37	38	31	2
Red blood cell ($10^6/\mu$ L)	8.66 ± 0.82	8.18 ± 1.59	6.51 ± 1.75 **	4.55 ± 1.43 ?
Hemoglobin (g/dL)	14.7 ± 1.5	13.4 ± 2.5 *	10.4 ± 2.9 **	8.2 ± 3.1 ?
Hematocrit (%)	44.0 ± 3.7	40.9 ± 6.7 *	32.9 ± 7.7 **	26.8 ± 7.8 ?
MCH (pg)	16.9 ± 1.0	16.5 ± 1.3	16.0 ± 1.1 **	17.9 ± 1.2 ?
MCHC (g/dL)	33.3 ± 1.1	32.6 ± 1.6 *	31.2 ± 2.4 **	30.3 ± 2.8 ?
Platelet ($10^3/\mu$ L)	886 ± 250	921 ± 312	1197 ± 243 **	1691 ± 74 ?
Differential WBC (%)				
N-seg	37 ± 10	39 ± 9	45 ± 10 **	66 ± 11 ?
Eosino	2 ± 2	2 ± 1	1 ± 1 **	0 ± 0 ?
Lympho	53 ± 9	51 ± 10	44 ± 10 **	28 ± 5 ?
Other	3 ± 5	3 ± 5	5 ± 3 **	5 ± 5 ?

Mean ± S.D.
*) Significant difference, $p<0.05$ (Test of Dunnett)
**) Significant difference, $p<0.01$ (Test of Dunnett)
?)The statistical test was not applied, because number of data in this group was less than three.

TABLE 8 HEMATOLOGY OF FEMALE RATS IN THE 2-YEAR FEED STUDY OF *p*-NITROANISOLE

Group name	Control	2000 ppm	4000 ppm	8000 ppm
No. of examined animals	43	37	33	29
Red blood cell ($10^6/\mu$ L)	8.08 ± 1.04	8.04 ± 0.74	7.30 ± 0.46 **	6.73 ± 0.89 **
Hemoglobin (g/dL)	14.9 ± 1.9	14.5 ± 1.3	13.2 ± 0.9 **	11.8 ± 1.3 **
Hematocrit (%)	43.1 ± 4.8	42.6 ± 3.6	39.7 ± 2.0 **	36.5 ± 3.5 **
MCV (fL)	53.7 ± 2.8	53.1 ± 1.8	54.4 ± 1.9 **	54.6 ± 3.4 *
MCH (pg)	18.4 ± 0.7	18.1 ± 0.7	18.1 ± 0.7	17.6 ± 0.8 **
MCHC (g/dL)	34.4 ± 1.5	34.0 ± 0.7 *	33.2 ± 0.7 **	32.2 ± 0.9 **
Platelet ($10^3/\mu$ L)	653 ± 122	643 ± 78	759 ± 120 **	1059 ± 210 **
WBC ($10^3/\mu$ L)	3.22 ± 2.56	6.03 ± 9.44	4.51 ± 2.13 **	6.12 ± 3.79 **
Differential WBC (%)				
N-band	1 ± 1	1 ± 1	2 ± 1 **	2 ± 1
N-seg	33 ± 8	38 ± 13	39 ± 10 *	49 ± 18 **
Eosino	2 ± 1	1 ± 1	1 ± 2	1 ± 1 **
Mono	4 ± 2	3 ± 2	3 ± 1 **	3 ± 2
Lympho	58 ± 9	54 ± 12	52 ± 10	42 ± 17 **

Mean ± S.D.
*) Significant difference, $p<0.05$ (Test of Dunnett)
**) Significant difference, $p<0.01$ (Test of Dunnett)

TABLE 9 BIOCHEMISTRY OF MALE RATS IN THE 2-YEAR FEED STUDY OF *p*-NITROANISOLE

Group name	Control	2000 ppm		4000 ppm		8000 ppm	
No. of examined animals	37	38		31		2	
Albumin (g/dL)	3.4 ± 0.2	3.3 ± 0.3	*	3.0 ± 0.3	**	2.3 ± 0.2	?
A/G ratio	1.1 ± 0.1	1.0 ± 0.1	*	0.9 ± 0.1	**	0.8 ± 0.1	?
Glucose (mg/dL)	173 ± 31	172 ± 28		156 ± 29	*	151 ± 6	?
T-cholesterol (mg/dL)	148 ± 40	172 ± 55		262 ± 66	**	281 ± 65	?
Triglyceride (mg/dL)	57 ± 40	79 ± 77		111 ± 60	**	29 ± 6	?
Phospholipid (mg/dL)	213 ± 54	249 ± 100		372 ± 88	**	387 ± 29	?
GPT (IU/L)	38 ± 8	39 ± 38	*	69 ± 84		123 ± 74	?
γ-GTP (IU/L)	7 ± 3	14 ± 6	**	49 ± 45	**	85 ± 2	?
Urea nitrogen (mg/dL)	18.6 ± 3.4	22.9 ± 9.8	*	56.7 ± 40.5	**	189.9 ± 58.5	?
Creatinine (mg/dL)	0.6 ± 0.1	0.6 ± 0.1		1.1 ± 0.7	**	2.0 ± 0.4	?
Potassium (mEq/L)	3.4 ± 0.3	3.5 ± 0.4		3.8 ± 0.5	**	4.9 ± 1.1	?
Chloride (mEq/L)	106 ± 2	107 ± 2		104 ± 3	**	102 ± 4	?
Calcium (mg/dL)	10.4 ± 0.5	10.4 ± 0.4		11.2 ± 1.1	**	12.0 ± 1.2	?
Inorganic phosphorus (mg/dL)	4.0 ± 0.5	4.1 ± 0.8		7.1 ± 4.1	**	19.0 ± 5.9	?

Mean ± S.D.
*) Significant difference, $p<0.05$ (Test of Dunnett)
**) Significant difference, $p<0.01$ (Test of Dunnett)
?)The statistical test was not applied, because number of data in this group was less than three.

TABLE 10 BIOCHEMISTRY OF FEMALE RATS IN THE 2-YEAR FEED STUDY OF *p*-NITROANISOLE

Group name	Control	2000 ppm		4000 ppm		8000 ppm	
No. of examined animals	43	37		34		30	
Total protein (g/dL)	6.9 ± 0.5	6.8 ± 0.5		7.4 ± 0.4	**	6.8 ± 0.9	
Albumin (g/dL)	3.9 ± 0.4	3.8 ± 0.3		3.9 ± 0.3		3.3 ± 0.6	**
A/G ratio	1.3 ± 0.2	1.3 ± 0.1		1.2 ± 0.1	**	1.0 ± 0.2	**
T-cholesterol (mg/dL)	127 ± 37	122 ± 27		214 ± 104	**	330 ± 101	**
Phospholipid (mg/dL)	224 ± 59	212 ± 43		332 ± 146	**	467 ± 142	**
GOT (IU/L)	115 ± 33	155 ± 192		74 ± 42	**	117 ± 113	**
GPT (IU/L)	50 ± 14	74 ± 97		37 ± 17	**	61 ± 58	
LDH (IU/L)	272 ± 83	279 ± 165		197 ± 60	**	240 ± 143	*
ALP (IU/L)	120 ± 73	186 ± 290		93 ± 32	*	127 ± 84	
γ-GTP (IU/L)	3 ± 2	4 ± 3		4 ± 3		20 ± 24	**
Urea nitrogen (mg/dL)	17.0 ± 3.0	20.4 ± 4.8	**	21.7 ± 3.5	**	53.8 ± 63.5	**
Creatinine (mg/dL)	0.5 ± 0.1	0.6 ± 0.1		0.6 ± 0.1		0.7 ± 0.3	**
Sodium (mEq/L)	141 ± 1	141 ± 2		140 ± 2		139 ± 2	**
Potassium (mEq/L)	3.4 ± 0.3	3.4 ± 0.3		3.4 ± 0.3		4.0 ± 0.7	**
Chloride (mEq/L)	105 ± 3	105 ± 3		104 ± 3	*	102 ± 5	**
Calcium (mg/dL)	10.3 ± 0.5	10.2 ± 0.5		10.7 ± 0.6	**	11.1 ± 0.9	**
Inorganic phosphorus (mg/dL)	3.5 ± 0.7	3.9 ± 0.6		4.0 ± 0.8	*	7.1 ± 6.6	**

Mean ± S.D.
*) Significant difference, $p<0.05$ (Test of Dunnett)
**) Significant difference, $p<0.01$ (Test of Dunnett)

TABLE 11 URINALYSIS OF MALE RATS IN THE 2-YEAR FEED STUDY OF *p*-NITROANISOLE

Group name	Grade	Control	2000 ppm	4000 ppm	8000 ppm
Number of examined animals		37	39	34	3
pH	6.0	1	1	1	0
	6.5	4	2	8	2
	7.0	7	3	6	1
	7.5	14	20	16	0
	8.0	11	10	3	0
	8.5	0	3	0	0
	Chi square test				**
Glucose	−	37	39	31	2
	±	0	0	1	1
	+	0	0	2	0
	2+	0	0	0	0
	3+	0	0	0	0
	Chi square test				**

Significant difference : * : $p<0.05$ ** : $p<0.01$

TABLE 12 URINALYSIS OF FEMALE RATS IN THE 2-YEAR FEED STUDY OF *p*-NITROANISOLE

Group name	Grade	Control	2000 ppm	4000 ppm	8000 ppm
Number of examined animals		45	39	35	31
Protein	−	0	0	0	0
	±	3	1	0	0
	+	16	18	0	0
	2+	15	12	15	3
	3+	10	8	19	26
	4+	1	0	1	2
	Chi square test			**	**
Occult blood	−	43	29	28	23
	±	0	1	1	5
	+	1	1	2	0
	2+	0	3	0	0
	3+	1	5	4	3
	Chi square test				*

Significant difference : * : $p<0.05$ ** : $p<0.01$

TABLE 13 ORGAN WEIGHTS OF MALE RATS IN THE 2-YEAR FEED STUDY OF *p*-NITROANISOLE

Group name	Control	2000 ppm	4000 ppm	8000 ppm
No. of examined animals	37	39	32	2
Body weight (g)	371 ± 34	366 ± 39	313 ± 34 **	216 ± 6 ?
Adrenals (g)	0.072 ± 0.014	0.139 ± 0.368	0.089 ± 0.066	0.077 ± 0.030 ?
Adrenals (%)	0.020 ± 0.006	0.038 ± 0.096	0.030 ± 0.025 **	0.036 ± 0.013 ?
Testes (g)	3.484 ± 1.254	4.411 ± 3.496	4.515 ± 2.197	1.735 ± 0.738 ?
Testes (%)	0.939 ± 0.338	1.182 ± 0.861	1.442 ± 0.668 **	0.799 ± 0.321 ?
Heart (g)	1.198 ± 0.091	1.270 ± 0.182	1.236 ± 0.169	1.270 ± 0.301 ?
Heart (%)	0.325 ± 0.034	0.351 ± 0.065	0.403 ± 0.090 **	0.587 ± 0.124 ?
Lungs (g)	1.362 ± 0.087	1.562 ± 0.394 **	1.560 ± 0.284 **	1.247 ± 0.021 ?
Lungs (%)	0.369 ± 0.031	0.437 ± 0.156 **	0.506 ± 0.126 **	0.578 ± 0.025 ?
Kidneys (g)	2.577 ± 0.287	2.839 ± 0.419 **	3.358 ± 0.541 **	3.559 ± 0.054 ?
Kidneys (%)	0.703 ± 0.128	0.791 ± 0.200 *	1.094 ± 0.264 **	1.649 ± 0.069 ?
Spleen (g)	0.962 ± 0.448	1.452 ± 2.882	1.098 ± 0.262 **	0.531 ± 0.081 ?
Spleen (%)	0.259 ± 0.112	0.417 ± 0.915	0.349 ± 0.072 **	0.246 ± 0.030 ?
Liver (g)	9.809 ± 1.142	11.564 ± 2.085 **	14.804 ± 1.525 **	16.305 ± 4.564 ?
Liver (%)	2.655 ± 0.299	3.194 ± 0.715 **	4.768 ± 0.551 **	7.523 ± 1.916 ?
Brain (g)	2.069 ± 0.092	2.084 ± 0.061	2.118 ± 0.054 **	2.042 ± 0.131 ?
Brain (%)	0.562 ± 0.050	0.576 ± 0.067	0.685 ± 0.079 **	0.945 ± 0.036 ?

Mean ± S.D.

*) Significant difference, $p<0.05$ (Test of Dunnett)

**) Significant difference, $p<0.01$ (Test of Dunnett)

?)The statistical test was not applied, because number of data in this group was less than three.

TABLE 14 ORGAN WEIGHTS OF FEMALE RATS IN THE 2-YEAR FEED STUDY OF *p*-NITROANISOLE

Group name	Control	2000 ppm		4000 ppm		8000 ppm	
No. of examined animals	45	38		35		31	
Body weight (g)	244 ± 29	211 ± 31	**	194 ± 25	**	165 ± 20	**
Adrenals (g)	0.072 ± 0.010	0.067 ± 0.011	*	0.065 ± 0.010	**	0.064 ± 0.010	**
Adrenals (%)	0.030 ± 0.005	0.032 ± 0.007		0.034 ± 0.007	*	0.039 ± 0.008	**
Ovaries (g)	0.169 ± 0.226	0.155 ± 0.168		0.265 ± 0.763		0.124 ± 0.089	
Overies (%)	0.069 ± 0.092	0.079 ± 0.109	**	0.140 ± 0.410	**	0.075 ± 0.052	**
Heart (g)	0.877 ± 0.069	0.827 ± 0.092	*	0.819 ± 0.070	**	0.842 ± 0.088	
Heart (%)	0.363 ± 0.041	0.396 ± 0.050	*	0.425 ± 0.042	**	0.518 ± 0.082	**
Lungs (g)	1.025 ± 0.095	1.026 ± 0.075		1.006 ± 0.073		1.013 ± 0.096	
Lungs (%)	0.427 ± 0.074	0.497 ± 0.087	**	0.524 ± 0.064	**	0.624 ± 0.108	**
Kidneys (g)	1.699 ± 0.152	1.649 ± 0.178		1.870 ± 0.283	*	2.318 ± 0.501	**
Kidneys (%)	0.703 ± 0.077	0.793 ± 0.111	*	0.975 ± 0.179	**	1.423 ± 0.344	**
Spleen (g)	0.691 ± 0.594	0.524 ± 0.201		0.618 ± 0.150	*	0.689 ± 0.230	*
Spleen (%)	0.286 ± 0.247	0.249 ± 0.084		0.318 ± 0.063	**	0.411 ± 0.110	**
Liver (g)	6.287 ± 0.966	5.997 ± 1.233		7.447 ± 1.405	**	10.078 ± 2.085	**
Liver (%)	2.590 ± 0.331	2.854 ± 0.456		3.841 ± 0.596	**	6.098 ± 0.944	**
Brain (g)	1.895 ± 0.047	1.922 ± 0.042	*	1.933 ± 0.046	**	1.932 ± 0.056	**
Brain (%)	0.789 ± 0.104	0.931 ± 0.148	**	1.010 ± 0.125	**	1.188 ± 0.131	**

Mean ± S.D.

*) Significant difference, $p<0.05$ (Test of Dunnett)

**) Significant difference, $p<0.01$ (Test of Dunnett)

TABLE 15
INCIDENCES OF SELECTED NEOPLASTIC LESIONS OF MALE RATS IN THE 2-YEAR FEED STUDY OF *p*-NITROANISOLE

Group name No. of examined animals	Control <50>	2000 ppm <50>	4000 ppm <50>	8000 ppm <50>		
Liver						
Hepatocellular adenoma	0 (0%) [a]	1 (2%)	13(26%) **	11 (22%) **	⬆⬆	⇧⇧
Testis						
Interstitial cell tumor	34 (64%)	45 (90%) **	48 (96%) **	48 (96%) **	⬆⬆	⇧⇧
Spleen						
Mononuclear cell leukemia	8 (16%)	5 (10%)	3 (6%)	0 (0%) **		⇩⇩

[a] : No. of animals bearing tumor (incidence ; %)
** : Significant difference, $p<0.01$ (Fisher's exact test for neoplastic lesion)
⬆⬆ : Significant difference, $p<0.01$ (Peto test for neoplastic lesion)
⇩⇩and ⇧⇧ : Significant difference, $p<0.01$ (Cochran-Armitage test for neoplastic lesion)

TABLE 16
INCIDENCES OF SELECTED NEOPLASTIC LESIONS OF FEMALE RATS IN THE 2-YEAR FEED STUDY OF *p*-NITROANISOLE

Group name No. of examined animals	Control <50>	2000 ppm <50>	4000 ppm <50>	8000 ppm <49>		
Uterus						
Adenocarcinoma	1 (2%) [a]	4 (8%)	8 (16%) *	8 (16%) *	⬆⬆	⇧
Liver						
Hepatocellular adenoma	0 (0%)	0 (0%)	0 (0%)	5 (10%) *	⬆⬆	⇧⇧
Spleen						
Mononuclear cell leukemia	8 (16%)	7 (14%)	1 (2%) *	1 (2%) *		⇩⇩

[a] : No. of animals bearing tumor (incidence ; %)
* : Significant difference, $p<0.05$ (Fisher's exact test for neoplastic lesion)
⬆⬆ : Significant difference, $p<0.01$ (Peto test for neoplastic lesion)
⇩⇩and ⇧⇧ : Significant difference, $p<0.01$ (Cochran-Armitage test for neoplastic lesion)
⇧ : Significant difference, $p<0.05$ (Cochran-Armitage test for neoplastic lesion)

TABLE 17
INCIDENCES OF SELECTED NON-NEOPLASTIC LESIONS OF MALE RATS IN THE 2-YEAR FEED STUDY OF *p*-NITROANISOLE

Group name	Control				2000 ppm				4000 ppm				8000 ppm			
No. of examined animals	50				50				50				50			
Grade	<1>	<2>	<3>	<4>	<1>	<2>	<3>	<4>	<1>	<2>	<3>	<4>	<1>	<2>	<3>	<4>
Nasal cavity																
Eosinophilic change : olfactory epithelium	12	14	7	0	13	9	7	0	13	14	12	0	8	2	0	0 **
Lung																
Bronchiolar-alveolar cell hyperplasia	8	1	0	0	0	1	0	0 *	0	0	0	0 **	0	0	0	0 **
Uremic pneumonitis	0	0	0	0	0	0	0	0	5	0	1	0 *	18	3	0	0 **
Spleen																
Deposit of hemosiderin	35	5	0	0	24	15	1	0 *	18	22	6	0 **	34	12	0	0
Heart																
Mineralization	0	0	0	0	0	0	0	0	4	1	0	0	18	0	0	0 **
Artery/aort																
Mineralization	0	0	0	0	0	0	0	0	3	0	0	0	16	0	0	0 **
Tongue																
Edema	0	0	0	0	0	0	0	0	0	0	0	0	11	0	0	0 **
Mineralization	0	0	0	0	0	0	0	0	5	0	0	0	19	0	0	0 **
Stmach																
Mineralization	0	0	0	0	1	0	0	0	4	5	0	0 **	16	15	4	0 **
Liver																
Granulation	11	1	0	0	8	2	2	0	11	8	1	0	2	0	0	0 *
Basophilic cell focus	4	0	0	0	7	1	0	0	23	4	0	0 **	19	2	0	0 **
Spongiosis hepatis	0	0	0	0	5	0	0	0	8	1	1	0 *	11	1	0	0 **
Pancreas																
Atrophy	6	0	0	0	7	0	0	0	3	0	0	0	0	0	0	0 *
Kidney																
Cyst	0	0	0	0	1	0	0	0	2	0	0	0	8	0	0	0 **
Chronic nephropathy	22	15	8	1	10	14	24	1 **	0	1	25	23 **	1	0	1	48 **
Mineralization : papilla	8	0	0	0	7	0	0	0	8	26	14	0 **	37	9	0	0 **
Urothelial hyperplasia : pelvis	12	0	0	0	6	0	0	0	34	1	0	0 **	35	0	0	0 **
Parathyroid																
Hyperplasia	0	0	0	0	0	0	0	0	6	0	0	0 *	23	0	0	0 **
Adrenal																
Hemorrhage	0	0	0	0	0	0	0	0	2	0	0	0	13	0	0	0 **
Necrosis : cortex	0	0	0	0	0	0	0	0	2	0	0	0	10	0	0	0 **
Prostate																
Hyperplasia	8	0	0	0	9	0	0	0	6	1	0	0	0	0	0	0 **
Muscle																
Mineralization	0	0	0	0	0	0	0	0	4	0	0	0	7	0	0	0 *

Grade <1>:Slight, <2>:Moderate, <3>:Marked, <4>:Severe
*) Significant difference, $p<0.05$ (Test of Chi Square)
**) Significant difference, $p<0.01$ (Test of Chi Square)

TABLE 18
INCIDENCES OF SELECTED NON-NEOPLASTIC LESIONS OF FEMALE RATS IN THE 2-YEAR FEED STUDY OF *p*-NITROANISOLE

Group name	Control				2000 ppm				4000 ppm				8000 ppm			
No. of examined animals	50				50				50				49			
Grade	<1>	<2>	<3>	<4>	<1>	<2>	<3>	<4>	<1>	<2>	<3>	<4>	<1>	<2>	<3>	<4>
Nasal cavity																
Mineralization	25	0	0	0	13	0	0	0 *	16	0	0	0	8	0	0	0 **
Eosinophilic change : olfactory epithelium	3	15	31	0	4	15	25	0	11	15	22	0	7	23	12	0 **
Lung																
Uremic pneumonitis	0	0	0	0	0	0	0	0	0	0	0	0	5	3	0	0 *
Spleen																
Deposit of hemosiderin	7	30	7	0	6	25	12	0	5	17	25	0 **	12	18	14	0
Heart																
Mineralization	0	0	0	0	0	0	0	0	1	0	0	0	5	0	0	0
Myocardial fibrosis	16	0	0	0	21	0	0	0	24	0	0	0	27	0	0	0 *
Tongue																
Edema	0	0	0	0	0	0	0	0	1	0	0	0	6	0	0	0 *
Mineralization	0	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0
Stmach																
Mineralization	0	0	0	0	0	0	0	0	0	0	0	0	10	1	0	0 **
Liver																
Granulation	26	2	5	0	21	5	4	0	26	1	5	0	11	5	3	0 **
Kidney																
Chronic nephropathy	12	2	3	0	8	2	1	0	9	16	9	1 **	4	5	22	17 **
Mineralization : cortico-medullary junction	6	0	0	0	5	0	0	0	2	0	0	0	0	0	0	0 *
Mineralization : papilla	5	0	0	0	14	0	0	0 *	19	15	7	0 **	17	15	11	0 **
Urothelial hyperplasia : pelvis	1	0	0	0	2	0	0	0	4	1	0	0	11	0	0	0 **
Adrenal																
Hemorrhage	0	0	0	0	1	0	0	0	1	0	0	0	2	4	0	0 *
Peliosis-like lesion	31	0	0	0	23	0	0	0	18	0	0	0 *	6	0	0	0 **

Grade <1>:Slight, <2>:Moderate, <3>:Marked, <4>:Severe
*) Significant difference, $p<0.05$ (Test of Chi Square)
**) Significant difference, $p<0.01$ (Test of Chi Square)

TABLE 19
CAUSE OF DEATH OF RATS IN THE 2-YEAR FEED STUDY OF *p*-NITROANISOLE

		Male				Female			
Group name		Control	2000ppm	4000ppm	8000ppm	Control	2000ppm	4000ppm	8000ppm
Number of dead or moribund animals		13	11	18	48	5	12	15	18
No microscopical confirmation		0	0	1	0	0	0	1	0
Cadiovascular lesion		0	1	0	0	0	0	1	0
Digestive system lesion		1	0	0	0	0	0	0	0
Urinary retention		0	0	1	0	0	0	0	0
Chronic nephropathy		0	0	4	45	0	0	0	12
Arteritis		0	0	0	1	0	0	0	0
Tumor death	leukemia	6	4	3	0	2	6	0	1
	skin/app	0	0	0	1	0	0	0	0
	subcutis	0	0	1	0	0	1	0	0
	tongue	0	0	0	0	0	0	0	1
	spleen	1	0	1	0	0	0	0	0
	oral cavity	1	0	0	0	0	0	0	0
	kidney	0	0	1	0	0	0	0	0
	pituitary	2	1	3	0	2	0	1	1
	thyroid	0	0	1	0	0	0	0	0
	uterus	—	—	—	—	1	5	7	3
	mammary gland	0	0	0	0	0	0	1	0
	brain	0	1	1	0	0	0	1	0
	spinal cord	0	1	0	0	0	0	0	0
	Zymbal gland	0	1	0	0	0	0	1	0
	bone	0	1	1	1	0	0	1	0
	retroperit	0	0	0	0	0	0	1	0
	peritoneum	1	0	1	0	0	0	0	0
	abdominal cavity	1	0	0	0	0	0	0	0

TABLE 20 HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER : F344/DuCrj MALE RATS

Organs	Tumors	No. of animals examined	No. of animals bearing tumor	Incidence (%)	Min. - Max. (%)
Spleen		<1599>			
	Mononuclear cell leukemia		190	11.9	4 - 22
Liver		<1599>			
	Hepatocellular adenoma		26	1.6	0 - 6
Testis		<1598>			
	Interstitial cell tumor		1368	85.6	56 - 98

32 carcinogenicity studies examined in Japan Bioassay Research Center were used.
Study No. : 0043, 0059, 0061, 0063, 0065, 0067, 0095, 0104, 0115, 0130, 0141, 0158, 0162, 0189, 0205, 0210, 0224, 0242, 0267, 0269, 0278, 0284, 0288, 0294, 0296, 0318, 0328, 0342, 0347, 0365, 0371, 0399

TABLE 21 HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER : F344/DuCrj FEMALE RATS

Organs	Tumors	No. of animals examined	No. of animals bearing tumor	Incidence (%)	Min. - Max. (%)
Spleen		<1547>			
	Mononuclear cell leukemia		201	13.0	2 - 26
Liver		<1547>			
	Hepatocellular adenoma		20	1.3	0 - 6
Uterus		<1547>			
	Adenocarcinoma		6	0.4	0 - 4
	Endometrial stromal polyp		221	14.3	2 - 28

31 carcinogenicity studies examined in Japan Bioassay Research Center were used.
Study No. : 0043, 0059, 0061, 0063, 0065, 0067, 0095, 0104, 0115, 0130, 0141, 0158, 0162, 0189, 0205, 0210, 0224, 0242, 0267, 0269, 0278, 0284, 0296, 0303, 0318, 0328, 0342, 0347, 0365, 0371, 0399