p-ニトロアニソールのマウスを用いた
経口投与によるがん原性試験(混餌試験)報告書

試験番号：０４０２

TABLES

TABLES

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

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

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

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

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

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

TABLE 7 HEMATOLOGY OF MALE MICE IN THE 2-YEAR FEED STUDY OF *p*-NITROANISOLE

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

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

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

TABLES (Continued)

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

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

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

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

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

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

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

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

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

TABLE 20 HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER : Crj/BDF1 MALE MICE

TABLE 21 HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER : Crj/BDF1 FEMALE MICE

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

Week on Study	Control		5000 ppm			10000 ppm			20000 ppm		
	Av. Wt.	No. of Surviv. < 50 >	Av. Wt.	% of cont.	No. of Surviv. < 50 >	Av. Wt.	% of cont.	No. of Surviv. < 50 >	Av. Wt.	% of cont.	No. of Surviv. < 50 >
0	23.3 (50)	50 / 50	23.2 (50)	100	50 / 50	23.3 (50)	100	50 / 50	23.3 (50)	100	50 / 50
1	23.8 (50)	50 / 50	23.5 (50)	99	50 / 50	22.9 (50)	96	50 / 50	21.2 (50)	89	50 / 50
2	24.7 (50)	50 / 50	24.5 (50)	99	50 / 50	24.2 (50)	98	50 / 50	23.2 (50)	94	50 / 50
3	25.5 (50)	50 / 50	25.5 (50)	100	50 / 50	25.1 (50)	98	50 / 50	24.6 (50)	96	50 / 50
4	26.6 (50)	50 / 50	26.3 (50)	99	50 / 50	25.9 (50)	97	50 / 50	25.7 (50)	97	50 / 50
5	27.1 (50)	50 / 50	26.8 (50)	99	50 / 50	26.2 (50)	97	50 / 50	26.0 (50)	96	50 / 50
6	27.7 (50)	50 / 50	27.4 (50)	99	50 / 50	27.0 (50)	97	50 / 50	26.6 (50)	96	50 / 50
7	28.8 (50)	50 / 50	28.3 (50)	98	50 / 50	27.0 (50)	94	50 / 50	26.7 (50)	93	50 / 50
8	29.1 (50)	50 / 50	28.8 (50)	99	50 / 50	27.7 (50)	95	50 / 50	27.3 (50)	94	50 / 50
9	29.8 (50)	50 / 50	29.0 (50)	97	50 / 50	28.0 (50)	94	50 / 50	27.6 (50)	93	50 / 50
10	30.9 (50)	50 / 50	29.9 (50)	97	50 / 50	28.7 (50)	93	50 / 50	27.7 (50)	90	50 / 50
11	31.7 (50)	50 / 50	30.5 (50)	96	50 / 50	28.7 (50)	91	50 / 50	27.8 (50)	88	50 / 50
12	32.0 (50)	50 / 50	30.8 (50)	96	50 / 50	28.8 (50)	90	50 / 50	27.8 (50)	87	50 / 50
13	32.7 (50)	50 / 50	31.4 (50)	96	50 / 50	29.4 (50)	90	50 / 50	28.5 (50)	87	50 / 50
14	33.6 (50)	50 / 50	32.1 (50)	96	50 / 50	29.9 (50)	89	50 / 50	28.8 (50)	86	50 / 50
18	36.2 (50)	50 / 50	34.4 (50)	95	50 / 50	31.3 (50)	86	50 / 50	29.7 (50)	82	50 / 50
22	38.7 (50)	50 / 50	36.4 (50)	94	50 / 50	32.6 (50)	84	50 / 50	30.2 (49)	78	49 / 50
26	41.1 (50)	50 / 50	37.8 (50)	92	50 / 50	33.4 (49)	81	49 / 50	30.7 (49)	75	49 / 50
30	43.5 (50)	50 / 50	40.2 (50)	92	50 / 50	34.9 (49)	80	49 / 50	31.1 (49)	71	49 / 50
34	44.7 (50)	50 / 50	41.2 (50)	92	50 / 50	35.0 (48)	78	48 / 50	31.2 (49)	70	49 / 50
38	47.0 (50)	50 / 50	43.4 (50)	92	50 / 50	36.5 (47)	78	47 / 50	31.2 (49)	66	49 / 50
42	48.2 (50)	50 / 50	44.9 (50)	93	50 / 50	37.4 (46)	78	46 / 50	31.9 (49)	66	49 / 50
46	49.9 (50)	50 / 50	46.0 (50)	92	50 / 50	38.2 (45)	77	45 / 50	32.1 (48)	64	48 / 50
50	50.6 (50)	50 / 50	47.4 (50)	94	50 / 50	38.7 (45)	76	45 / 50	32.1 (47)	63	47 / 50
54	51.4 (49)	49 / 50	48.2 (49)	94	49 / 50	39.2 (44)	76	44 / 50	32.4 (47)	63	47 / 50
58	51.6 (49)	49 / 50	48.7 (49)	94	49 / 50	39.5 (44)	77	44 / 50	32.3 (47)	63	47 / 50
62	53.0 (47)	47 / 50	49.8 (49)	94	49 / 50	40.0 (44)	75	44 / 50	32.3 (47)	61	47 / 50
66	53.9 (46)	46 / 50	50.6 (49)	94	49 / 50	41.0 (44)	76	44 / 50	32.3 (44)	60	44 / 50
70	53.7 (46)	46 / 50	51.4 (48)	96	48 / 50	40.4 (44)	75	44 / 50	32.0 (41)	60	41 / 50
74	54.4 (46)	46 / 50	51.6 (48)	95	48 / 50	40.2 (44)	74	44 / 50	31.3 (41)	58	41 / 50
78	54.9 (46)	46 / 50	52.6 (47)	96	47 / 50	40.2 (42)	73	42 / 50	31.4 (39)	57	39 / 50
82	55.4 (44)	44 / 50	52.7 (46)	95	46 / 50	40.7 (40)	73	40 / 50	30.7 (37)	55	37 / 50
86	55.2 (43)	43 / 50	52.1 (46)	94	46 / 50	40.3 (39)	73	39 / 50	30.5 (33)	55	33 / 50
90	55.4 (42)	42 / 50	52.2 (45)	94	45 / 50	40.0 (37)	72	37 / 50	30.0 (31)	54	31 / 50
94	54.1 (41)	41 / 50	51.3 (42)	95	42 / 50	40.0 (36)	74	36 / 50	30.0 (28)	55	28 / 50
98	52.2 (40)	40 / 50	49.2 (40)	94	40 / 50	37.7 (32)	72	32 / 50	30.4 (24)	58	24 / 50
102	50.8 (37)	37 / 50	48.7 (37)	96	37 / 50	37.1 (30)	73	30 / 50	29.8 (16)	59	16 / 50
104	49.6 (36)	36 / 50	47.9 (35)	97	35 / 50	37.4 (27)	75	27 / 50	29.6 (16)	60	16 / 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 MICE IN THE 2-YEAR FEED STUDY OF *p*-NITROANISOLE

Week on Study	Control		5000 ppm			10000 ppm			20000 ppm		
	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	19.1 (50)	50 / 50	19.1 (50)	100	50 / 50	19.1 (50)	100	50 / 50	19.1 (50)	100	50 / 50
1	19.5 (50)	50 / 50	18.8 (50)	96	50 / 50	19.0 (50)	97	50 / 50	17.4 (50)	89	50 / 50
2	19.8 (50)	50 / 50	19.6 (50)	99	50 / 50	19.5 (50)	98	50 / 50	19.6 (50)	99	50 / 50
3	20.2 (50)	50 / 50	19.8 (50)	98	50 / 50	20.2 (50)	100	50 / 50	20.4 (50)	101	50 / 50
4	20.7 (50)	50 / 50	20.6 (49)	100	50 / 50	20.6 (50)	100	50 / 50	20.9 (50)	101	50 / 50
5	21.3 (50)	50 / 50	21.2 (50)	100	50 / 50	21.3 (50)	100	50 / 50	21.3 (50)	100	50 / 50
6	21.7 (50)	50 / 50	21.5 (50)	99	50 / 50	21.4 (50)	99	50 / 50	21.5 (50)	99	50 / 50
7	22.3 (50)	50 / 50	22.0 (50)	99	50 / 50	22.0 (50)	99	50 / 50	22.0 (50)	99	50 / 50
8	22.6 (50)	50 / 50	22.5 (50)	100	50 / 50	22.3 (50)	99	50 / 50	22.1 (50)	98	50 / 50
9	22.9 (50)	50 / 50	22.7 (50)	99	50 / 50	22.8 (50)	100	50 / 50	22.4 (50)	98	50 / 50
10	23.4 (50)	50 / 50	23.1 (50)	99	50 / 50	23.1 (50)	99	50 / 50	22.8 (50)	97	50 / 50
11	23.7 (50)	50 / 50	23.3 (50)	98	50 / 50	23.3 (50)	98	50 / 50	23.2 (50)	98	50 / 50
12	23.7 (50)	50 / 50	23.3 (50)	98	50 / 50	23.3 (50)	98	50 / 50	23.1 (50)	97	50 / 50
13	24.3 (50)	50 / 50	24.3 (50)	100	50 / 50	23.6 (50)	97	50 / 50	23.3 (50)	96	50 / 50
14	24.7 (50)	50 / 50	24.2 (50)	98	50 / 50	23.6 (50)	96	50 / 50	23.5 (50)	95	50 / 50
18	26.2 (50)	50 / 50	24.9 (50)	95	50 / 50	24.6 (50)	94	50 / 50	24.3 (50)	93	50 / 50
22	27.7 (50)	50 / 50	26.8 (50)	97	50 / 50	25.9 (50)	94	50 / 50	25.1 (50)	91	50 / 50
26	29.7 (50)	50 / 50	27.9 (50)	94	50 / 50	26.7 (50)	90	50 / 50	25.5 (50)	86	50 / 50
30	31.3 (50)	50 / 50	29.2 (50)	93	50 / 50	27.2 (50)	87	50 / 50	26.1 (50)	83	50 / 50
34	32.6 (50)	50 / 50	30.1 (50)	92	50 / 50	27.8 (50)	85	50 / 50	26.8 (50)	82	50 / 50
38	33.9 (50)	50 / 50	31.9 (50)	94	50 / 50	28.7 (50)	85	50 / 50	26.8 (50)	79	50 / 50
42	34.5 (50)	50 / 50	32.4 (50)	94	50 / 50	29.8 (50)	86	50 / 50	27.9 (50)	81	50 / 50
46	35.7 (50)	50 / 50	33.3 (50)	93	50 / 50	30.2 (50)	85	50 / 50	28.3 (49)	79	49 / 50
50	35.8 (50)	50 / 50	33.6 (50)	94	50 / 50	30.4 (50)	85	50 / 50	28.0 (49)	78	49 / 50
54	36.3 (49)	49 / 50	34.2 (49)	94	49 / 50	30.9 (50)	85	50 / 50	28.4 (49)	78	49 / 50
58	37.1 (49)	49 / 50	34.8 (48)	94	48 / 50	31.2 (50)	84	50 / 50	28.6 (49)	77	49 / 50
62	38.0 (49)	49 / 50	35.2 (48)	93	48 / 50	31.1 (50)	82	50 / 50	28.2 (49)	74	49 / 50
66	38.6 (45)	45 / 50	35.7 (48)	92	48 / 50	31.8 (50)	82	50 / 50	28.1 (48)	73	48 / 50
70	38.2 (43)	43 / 50	36.1 (48)	95	48 / 50	31.6 (50)	83	50 / 50	28.0 (47)	73	47 / 50
74	38.7 (43)	43 / 50	36.3 (46)	94	46 / 50	31.5 (49)	81	49 / 50	27.4 (43)	71	43 / 50
78	38.8 (40)	40 / 50	36.2 (46)	93	46 / 50	31.1 (49)	80	49 / 50	27.3 (39)	70	39 / 50
82	37.8 (39)	39 / 50	36.6 (44)	97	44 / 50	31.2 (44)	83	44 / 50	26.9 (38)	71	38 / 50
86	39.7 (34)	34 / 50	36.2 (42)	91	42 / 50	31.0 (42)	78	42 / 50	27.2 (38)	69	38 / 50
90	40.4 (29)	29 / 50	35.6 (42)	88	42 / 50	30.6 (36)	76	36 / 50	26.7 (31)	66	31 / 50
94	40.8 (27)	27 / 50	35.5 (38)	87	38 / 50	30.6 (34)	75	34 / 50	27.0 (28)	66	28 / 50
98	40.4 (25)	25 / 50	35.3 (36)	87	36 / 50	29.7 (33)	74	33 / 50	27.1 (20)	67	20 / 50
102	39.5 (24)	24 / 50	34.7 (30)	88	30 / 50	29.6 (30)	75	30 / 50	27.4 (14)	69	14 / 50
104	38.8 (23)	23 / 50	34.9 (27)	90	27 / 50	29.7 (30)	77	30 / 50	27.1 (13)	70	13 / 50

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

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

Week on Study	Control		5000 ppm			10000 ppm			20000 ppm		
	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	4.0 (50)	50 / 50	3.8 (50)	95	50 / 50	3.7 (50)	93	50 / 50	3.5 (50)	88	50 / 50
2	3.9 (50)	50 / 50	4.0 (50)	103	50 / 50	4.1 (50)	105	50 / 50	4.3 (50)	110	50 / 50
3	4.0 (50)	50 / 50	4.2 (50)	105	50 / 50	4.1 (49)	103	50 / 50	4.2 (50)	105	50 / 50
4	4.1 (50)	50 / 50	4.2 (49)	102	50 / 50	4.0 (50)	98	50 / 50	4.1 (50)	100	50 / 50
5	4.0 (50)	50 / 50	4.1 (50)	103	50 / 50	4.1 (50)	103	50 / 50	4.2 (50)	105	50 / 50
6	3.9 (50)	50 / 50	4.1 (50)	105	50 / 50	4.1 (50)	105	50 / 50	4.1 (49)	105	50 / 50
7	4.1 (50)	50 / 50	4.1 (50)	100	50 / 50	4.0 (50)	98	50 / 50	4.1 (48)	100	50 / 50
8	4.0 (50)	50 / 50	4.2 (50)	105	50 / 50	4.1 (50)	103	50 / 50	4.3 (49)	108	50 / 50
9	4.0 (50)	50 / 50	4.0 (50)	100	50 / 50	3.9 (50)	98	50 / 50	4.0 (49)	100	50 / 50
10	4.1 (50)	50 / 50	4.2 (50)	102	50 / 50	4.0 (50)	98	50 / 50	4.0 (49)	98	50 / 50
11	4.0 (50)	50 / 50	4.0 (50)	100	50 / 50	3.9 (50)	98	50 / 50	4.1 (49)	103	50 / 50
12	4.0 (50)	50 / 50	4.0 (50)	100	50 / 50	3.9 (50)	98	50 / 50	4.2 (50)	105	50 / 50
13	3.9 (50)	50 / 50	3.9 (50)	100	50 / 50	3.9 (50)	100	50 / 50	4.0 (50)	103	50 / 50
14	4.1 (50)	50 / 50	4.1 (50)	100	50 / 50	4.0 (50)	98	50 / 50	4.1 (50)	100	50 / 50
18	4.2 (50)	50 / 50	4.2 (50)	100	50 / 50	4.1 (50)	98	50 / 50	4.3 (50)	102	50 / 50
22	4.2 (50)	50 / 50	4.2 (50)	100	50 / 50	4.2 (50)	100	50 / 50	4.5 (49)	107	49 / 50
26	4.5 (50)	50 / 50	4.3 (50)	96	50 / 50	4.3 (49)	96	49 / 50	4.6 (46)	102	49 / 50
30	4.3 (50)	50 / 50	4.5 (50)	105	50 / 50	4.3 (49)	100	49 / 50	4.5 (47)	105	49 / 50
34	4.4 (50)	50 / 50	4.6 (50)	105	50 / 50	4.5 (48)	102	48 / 50	5.0 (47)	114	49 / 50
38	4.6 (50)	50 / 50	4.6 (48)	100	50 / 50	4.5 (46)	98	47 / 50	5.0 (47)	109	49 / 50
42	4.5 (50)	50 / 50	4.7 (50)	104	50 / 50	4.5 (46)	100	46 / 50	4.6 (49)	102	49 / 50
46	4.6 (50)	50 / 50	4.6 (48)	100	50 / 50	4.6 (44)	100	45 / 50	4.8 (44)	104	48 / 50
50	4.5 (50)	50 / 50	4.7 (49)	104	50 / 50	4.4 (45)	98	45 / 50	4.6 (46)	102	47 / 50
54	4.6 (49)	49 / 50	4.8 (47)	104	49 / 50	4.4 (44)	96	44 / 50	4.9 (45)	107	47 / 50
58	4.8 (49)	49 / 50	4.9 (47)	102	49 / 50	4.9 (44)	102	44 / 50	5.0 (44)	104	47 / 50
62	4.7 (47)	47 / 50	4.9 (49)	104	49 / 50	4.8 (44)	102	44 / 50	5.0 (45)	106	47 / 50
66	4.9 (46)	46 / 50	5.0 (48)	102	49 / 50	4.9 (44)	100	44 / 50	5.0 (39)	102	44 / 50
70	4.9 (46)	46 / 50	5.0 (47)	102	48 / 50	4.8 (44)	98	44 / 50	5.4 (30)	110	41 / 50
74	4.9 (42)	46 / 50	5.0 (39)	102	48 / 50	4.8 (39)	98	44 / 50	5.2 (20)	106	41 / 50
78	5.0 (46)	46 / 50	5.4 (45)	108	47 / 50	5.0 (41)	100	42 / 50	5.5 (20)	110	39 / 50
82	4.8 (44)	44 / 50	5.0 (46)	104	46 / 50	4.8 (39)	100	40 / 50	5.7 (23)	119	37 / 50
86	4.9 (43)	43 / 50	5.2 (46)	106	46 / 50	4.9 (39)	100	39 / 50	6.0 (20)	122	33 / 50
90	4.9 (41)	42 / 50	5.2 (45)	106	45 / 50	4.8 (34)	98	37 / 50	5.3 (11)	108	31 / 50
94	4.8 (40)	41 / 50	5.1 (42)	106	42 / 50	4.9 (33)	102	36 / 50	6.1 (12)	127	28 / 50
98	4.7 (40)	40 / 50	5.2 (40)	111	40 / 50	4.9 (29)	104	32 / 50	6.5 (6)	138	24 / 50
102	4.8 (36)	37 / 50	5.0 (36)	104	37 / 50	4.6 (25)	96	30 / 50	6.5 (3)	135	16 / 50
104	4.6 (35)	36 / 50	4.8 (34)	104	35 / 50	4.8 (23)	104	27 / 50	6.5 (2)	141	16 / 50

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

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

Week on Study	Control		5000 ppm			10000 ppm			20000 ppm		
	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	3.6 (50)	50 / 50	3.3 (49)	92	50 / 50	3.5 (49)	97	50 / 50	2.8 (49)	78	50 / 50
2	3.5 (50)	50 / 50	3.4 (50)	97	50 / 50	3.5 (50)	100	50 / 50	3.6 (49)	103	50 / 50
3	3.5 (50)	50 / 50	3.4 (50)	97	50 / 50	3.4 (50)	97	50 / 50	3.4 (49)	97	50 / 50
4	3.8 (50)	50 / 50	3.6 (50)	95	50 / 50	3.6 (50)	95	50 / 50	3.4 (50)	89	50 / 50
5	3.8 (50)	50 / 50	3.7 (50)	97	50 / 50	3.7 (50)	97	50 / 50	3.3 (50)	87	50 / 50
6	3.6 (50)	50 / 50	3.6 (50)	100	50 / 50	3.5 (50)	97	50 / 50	3.2 (50)	89	50 / 50
7	3.8 (50)	50 / 50	3.7 (50)	97	50 / 50	3.6 (50)	95	50 / 50	3.6 (50)	95	50 / 50
8	3.7 (50)	50 / 50	3.8 (50)	103	50 / 50	3.7 (50)	100	50 / 50	3.5 (50)	95	50 / 50
9	3.8 (50)	50 / 50	3.6 (50)	95	50 / 50	3.7 (50)	97	50 / 50	3.5 (50)	92	50 / 50
10	3.8 (50)	50 / 50	3.6 (50)	95	50 / 50	3.6 (50)	95	50 / 50	3.5 (50)	92	50 / 50
11	3.8 (50)	50 / 50	3.7 (50)	97	50 / 50	3.7 (50)	97	50 / 50	3.8 (50)	100	50 / 50
12	3.8 (50)	50 / 50	3.7 (50)	97	50 / 50	3.6 (50)	95	50 / 50	3.6 (50)	95	50 / 50
13	3.9 (50)	50 / 50	3.7 (50)	95	50 / 50	3.7 (50)	95	50 / 50	3.8 (50)	97	50 / 50
14	4.0 (50)	50 / 50	3.7 (50)	93	50 / 50	3.7 (50)	93	50 / 50	3.8 (50)	95	50 / 50
18	3.8 (50)	50 / 50	3.7 (50)	97	50 / 50	4.0 (50)	105	50 / 50	3.8 (50)	100	50 / 50
22	4.0 (50)	50 / 50	3.9 (50)	98	50 / 50	4.2 (50)	105	50 / 50	4.0 (50)	100	50 / 50
26	4.3 (50)	50 / 50	4.1 (50)	95	50 / 50	4.4 (50)	102	50 / 50	4.1 (50)	95	50 / 50
30	4.2 (50)	50 / 50	4.0 (50)	95	50 / 50	4.1 (50)	98	50 / 50	4.1 (50)	98	50 / 50
34	4.5 (50)	50 / 50	4.3 (50)	96	50 / 50	4.4 (50)	98	50 / 50	4.3 (49)	96	50 / 50
38	4.4 (49)	50 / 50	4.4 (50)	100	50 / 50	4.5 (50)	102	50 / 50	4.3 (48)	98	50 / 50
42	4.6 (49)	50 / 50	4.7 (50)	102	50 / 50	4.8 (49)	104	50 / 50	4.7 (47)	102	50 / 50
46	4.7 (50)	50 / 50	4.6 (50)	98	50 / 50	4.9 (50)	104	50 / 50	4.9 (47)	104	49 / 50
50	4.5 (50)	50 / 50	4.3 (50)	96	50 / 50	4.6 (50)	102	50 / 50	4.5 (47)	100	49 / 50
54	4.6 (49)	49 / 50	4.3 (49)	93	49 / 50	4.6 (50)	100	50 / 50	4.8 (47)	104	49 / 50
58	4.8 (47)	49 / 50	4.8 (48)	100	48 / 50	5.2 (48)	108	50 / 50	5.2 (49)	108	49 / 50
62	4.9 (48)	49 / 50	4.8 (47)	98	48 / 50	5.0 (50)	102	50 / 50	4.9 (43)	100	49 / 50
66	4.7 (45)	45 / 50	4.6 (48)	98	48 / 50	5.0 (49)	106	50 / 50	5.2 (45)	111	48 / 50
70	4.7 (42)	43 / 50	4.9 (48)	104	48 / 50	5.0 (48)	106	50 / 50	5.1 (35)	109	47 / 50
74	4.4 (36)	43 / 50	4.6 (41)	105	46 / 50	5.0 (43)	114	49 / 50	4.7 (31)	107	43 / 50
78	4.7 (36)	40 / 50	4.9 (45)	104	46 / 50	5.0 (43)	106	49 / 50	5.1 (24)	109	39 / 50
82	4.6 (38)	39 / 50	4.9 (44)	107	44 / 50	5.2 (41)	113	44 / 50	5.2 (27)	113	38 / 50
86	4.9 (33)	34 / 50	5.0 (42)	102	42 / 50	5.5 (41)	112	42 / 50	5.6 (21)	114	38 / 50
90	5.1 (29)	29 / 50	4.7 (41)	92	42 / 50	5.4 (34)	106	36 / 50	5.4 (15)	106	31 / 50
94	5.1 (27)	27 / 50	4.9 (38)	96	38 / 50	5.6 (29)	110	34 / 50	5.9 (15)	116	28 / 50
98	4.9 (23)	25 / 50	5.0 (35)	102	36 / 50	5.6 (30)	114	33 / 50	6.5 (8)	133	20 / 50
102	4.9 (23)	24 / 50	4.8 (30)	98	30 / 50	5.7 (27)	116	30 / 50	5.7 (5)	116	14 / 50
104	4.9 (21)	23 / 50	5.2 (25)	106	27 / 50	5.7 (25)	116	30 / 50	6.2 (5)	127	13 / 50

< > : 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 OF MALE MICE 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	0/50	0/46	0/46	3/41	3/50(1/14)
5000 ppm	0/50	0/50	0/50	1/50	1/50	0/49	0/47	2/42	3/50(3/15)
10000 ppm	0/50	0/50	0/49	0/47	0/45	0/44	0/42	2/36	2/50(1/23)
20000 ppm	0/50	0/50	0/49	1/49	1/47	1/44	1/38	1/29	1/50(1/34)
Internal mass									
Control	1/50	1/50	2/50	1/50	3/50	4/46	7/46	13/41	22/50(7/14)
5000 ppm	2/50	1/50	1/50	3/50	3/50	4/49	8/47	16/42	20/50(9/15)
10000 ppm	1/50	1/50	2/49	2/47	2/45	4/44	8/42	12/36	17/50(10/23)
20000 ppm	1/50	2/50	0/49	1/49	2/47	18/44	28/38	28/29	39/50(24/34)

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 OF FEMALE MICE 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	1/49	3/45	4/40	4/28	6/50(3/27)
5000 ppm	0/50	0/50	0/50	0/50	0/49	0/48	2/46	5/39	5/50(3/23)
10000 ppm	0/50	0/50	0/50	0/50	0/50	0/50	4/48	4/35	6/50(5/20)
20000 ppm	0/50	0/50	0/50	0/50	0/49	0/48	1/38	1/29	1/50(1/37)
Internal mass									
Control	0/50	0/50	0/50	0/50	6/49	4/45	8/40	7/28	18/50(16/27)
5000 ppm	0/50	0/50	0/50	2/50	4/49	5/48	12/46	14/39	24/50(16/23)
10000 ppm	0/50	0/50	0/50	1/50	1/50	11/50	13/48	20/35	34/50(16/20)
20000 ppm	0/50	1/50	1/50	1/50	3/49	18/48	30/38	29/29	49/50(36/37)

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 MICE IN THE 2-YEAR FEED STUDY OF *p*-NITROANISOLE

Group name	Control	5000 ppm	10000 ppm	20000 ppm
No. of examined animals	32	33	26	16
Red blood cell ($10^6/\mu$ L)	9.06 ± 2.12	9.27 ± 1.28	8.77 ± 1.80	7.94 ± 2.48 *
Hemoglobin (g/dL)	12.4 ± 2.7	13.0 ± 1.7	12.6 ± 2.4	10.4 ± 3.2 *
Hematocrit (%)	40.4 ± 8.1	42.2 ± 4.9	40.8 ± 6.3	36.0 ± 9.1 *
MCV (fL)	45.2 ± 4.2	45.7 ± 1.9	47.6 ± 6.3 **	47.2 ± 7.6
MCH (pg)	13.8 ± 1.0	14.0 ± 0.6	14.4 ± 0.6 **	13.3 ± 0.9
MCHC (g/dL)	30.6 ± 1.8	30.7 ± 1.0	30.6 ± 2.5	28.5 ± 2.5 **
Differential WBC (%)				
Eosino	1 ± 1	2 ± 1	2 ± 1	0 ± 0 **

Mean ± S.D.

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

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

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

Group name	Control	5000 ppm	10000 ppm	20000 ppm
No. of examined animals	23	24	29	13
MCH (pg)	14.4 ± 0.3	14.4 ± 0.6	14.0 ± 0.7	13.8 ± 1.4 **
MCHC (g/dL)	31.3 ± 1.0	31.3 ± 0.8	30.7 ± 1.3	28.5 ± 3.5 **
Platelet ($10^3/\mu$ L)	1073 ± 375	1275 ± 344	1321 ± 349	1517 ± 695 *
Differential WBC (%)				
N-band	1 ± 1	1 ± 2	1 ± 2	4 ± 5 **
N-seg	23 ± 13	22 ± 12	26 ± 15	37 ± 19 *

Mean ± S.D.

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

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

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

Group name	Control	5000 ppm	10000 ppm	20000 ppm
No. of examined animals	34	34	27	16
Total protein (g/dL)	5.4 ± 0.9	5.3 ± 0.8	5.1 ± 0.5	6.0 ± 0.7 **
Albumin (g/dL)	2.9 ± 0.5	3.0 ± 0.4	2.9 ± 0.3	3.2 ± 0.3 **
Total bilirubin (mg/dL)	0.17 ± 0.10	0.17 ± 0.08	0.18 ± 0.16	0.38 ± 0.37 **
Glucose (mg/dL)	169 ± 56	199 ± 50	212 ± 62 **	177 ± 32
T-cholesterol (mg/dL)	120 ± 64	128 ± 47	124 ± 32	250 ± 59 **
Phospholipid (mg/dL)	215 ± 99	235 ± 73	225 ± 63	450 ± 119 **
GOT (IU/L)	208 ± 302	114 ± 145	162 ± 263	1250 ± 1590 **
GPT (IU/L)	110 ± 134	95 ± 143	134 ± 181	1157 ± 1198 **
LDH (IU/L)	1056 ± 2228	754 ± ####	2087 ± ####	9029 ± 7690 **
ALP (IU/L)	163 ± 111	160 ± 99	296 ± 312 *	923 ± 691 **
γ-GTP (IU/L)	3 ± 4	4 ± 5	2 ± 1	14 ± 15 **
CPK (IU/L)	64 ± 66	51 ± 24	76 ± 85	133 ± 46 **
Urea nitrogen (mg/dL)	24.0 ± 13.9	25.6 ± 5.6 *	28.0 ± 8.6 **	27.6 ± 3.6 **
Chloride (mEq/L)	122 ± 4	123 ± 4	125 ± 4 *	121 ± 3
Calcium (mg/dL)	9.3 ± 0.7	9.3 ± 0.6	9.1 ± 0.5	9.9 ± 0.5 **

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

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

Group name	Control	5000 ppm	10000 ppm	20000 ppm
No. of examined animals	23	25	29	13
Total protein (g/dL)	5.0 ± 0.4	5.0 ± 0.8	5.2 ± 0.8	5.9 ± 0.5 **
Albumin (g/dL)	2.9 ± 0.2	2.8 ± 0.2	2.9 ± 0.3	3.4 ± 0.3 **
Total bilirubin (mg/dL)	0.15 ± 0.03	0.15 ± 0.05	0.16 ± 0.03	0.48 ± 0.59 **
T-cholesterol (mg/dL)	69 ± 22	86 ± 19	127 ± 38 **	225 ± 43 **
Phospholipid (mg/dL)	138 ± 35	165 ± 38	245 ± 68 **	398 ± 77 **
GOT (IU/L)	112 ± 84	85 ± 37	294 ± 366 **	1213 ± 1411 **
GPT (IU/L)	37 ± 23	47 ± 31	324 ± 386 **	1007 ± 1037 **
LDH (IU/L)	685 ± 950	442 ± 573	1387 ± #### *	9917 ± ##### **
ALP (IU/L)	176 ± 70	227 ± 114	495 ± 313 **	943 ± 469 **
γ-GTP (IU/L)	2 ± 1	3 ± 4	5 ± 5 **	14 ± 8 **
CPK (IU/L)	95 ± 85	110 ± 144	108 ± 87	222 ± 200 **
Urea nitrogen (mg/dL)	19.0 ± 5.1	21.8 ± 14.2	31.8 ± 30.1 **	33.5 ± 18.0 **
Chloride (mEq/L)	123 ± 3	124 ± 2	123 ± 4	120 ± 4 *
Calcium (mg/dL)	9.1 ± 0.5	9.0 ± 0.4	9.6 ± 0.5 **	10.1 ± 0.3 **

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

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

Group name	Grade	Control	5000 ppm	10000 ppm	20000 ppm
Number of examined animals		36	35	29	16
pH	6.0	6	3	3	10
	6.5	15	10	11	4
	7.0	7	11	4	1
	7.5	6	9	9	1
	8.0	2	2	2	0
	8.5	0	0	0	0
	Chi square test				*
Protein	−	0	0	0	0
	±	4	6	9	10
	+	23	24	19	6
	2+	8	5	1	0
	3+	1	0	0	0
	Chi square test			*	**

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

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

Group name	Grade	Control	5000 ppm	10000 ppm	20000 ppm
Number of examined animals		24	30	30	13
pH	6.0	1	1	2	7
	6.5	4	6	8	6
	7.0	8	7	12	0
	7.5	8	10	5	0
	8.0	2	6	3	0
	8.5	1	0	0	0
	Chi square test				**

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

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

Group name	Control	5000 ppm	10000 ppm	20000 ppm
No. of examined animals	36	35	27	16
Body weight (g)	45.8 ± 8.0	45.2 ± 7.5	34.7 ± 4.7 **	27.3 ± 2.8 **
Adrenals (g)	0.012 ± 0.003	0.010 ± 0.002 *	0.010 ± 0.002 **	0.009 ± 0.002 *
Adrenals (%)	0.026 ± 0.009	0.023 ± 0.006	0.029 ± 0.008	0.035 ± 0.007 **
Testes (g)	0.218 ± 0.026	0.219 ± 0.028	0.203 ± 0.041	0.202 ± 0.027
Testes (%)	0.492 ± 0.111	0.498 ± 0.099	0.590 ± 0.126 **	0.743 ± 0.101 **
Heart (g)	0.232 ± 0.042	0.225 ± 0.025	0.196 ± 0.020 **	0.167 ± 0.013 **
Heart (%)	0.532 ± 0.207	0.513 ± 0.112	0.573 ± 0.081 *	0.617 ± 0.063 **
Lungs (g)	0.257 ± 0.104	0.265 ± 0.087	0.252 ± 0.047	0.227 ± 0.025
Lungs (%)	0.590 ± 0.299	0.597 ± 0.177	0.742 ± 0.188 **	0.839 ± 0.120 **
Kidneys (g)	0.649 ± 0.360	0.605 ± 0.163	0.542 ± 0.044 **	0.457 ± 0.068 **
Kidneys (%)	1.463 ± 0.874	1.385 ± 0.524	1.580 ± 0.168 **	1.676 ± 0.187 **
Spleen (g)	0.161 ± 0.399	0.243 ± 0.489	0.103 ± 0.127	0.142 ± 0.118
Spleen (%)	0.375 ± 0.933	0.575 ± 1.141	0.301 ± 0.357	0.525 ± 0.454 **
Liver (g)	2.001 ± 0.931	2.248 ± 0.653 *	2.607 ± 2.501	5.750 ± 2.701 **
Liver (%)	4.529 ± 2.425	5.251 ± 2.298	7.575 ± 7.066 **	20.673 ± 7.440 **
Brain (g)	0.446 ± 0.016	0.450 ± 0.016	0.451 ± 0.020	0.435 ± 0.015
Brain (%)	1.010 ± 0.224	1.024 ± 0.178	1.324 ± 0.176 **	1.607 ± 0.126 **

Mean ± S.D.

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

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

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

Group name	Control	5000 ppm	10000 ppm	20000 ppm
No. of examined animals	23	27	30	13
Body weight (g)	35.8 ± 6.2	32.6 ± 5.1	27.3 ± 5.3 **	25.2 ± 4.1 **
Adrenals (g)	0.013 ± 0.002	0.012 ± 0.002	0.011 ± 0.002 **	0.010 ± 0.002 **
Adrenals (%)	0.036 ± 0.007	0.039 ± 0.010	0.041 ± 0.007	0.039 ± 0.009
Heart (g)	0.173 ± 0.031	0.174 ± 0.033	0.152 ± 0.016 *	0.145 ± 0.025 **
Heart (%)	0.493 ± 0.102	0.541 ± 0.094	0.570 ± 0.086 **	0.580 ± 0.061 *
Lungs (g)	0.218 ± 0.070	0.230 ± 0.028 *	0.253 ± 0.151	0.210 ± 0.043
Lungs (%)	0.642 ± 0.314	0.718 ± 0.103 *	0.963 ± 0.702 **	0.850 ± 0.206 **
Kidneys (g)	0.410 ± 0.043	0.617 ± 1.011	0.490 ± 0.524	0.373 ± 0.082 **
Kidneys (%)	1.170 ± 0.190	1.875 ± 2.845 *	1.885 ± 2.336 **	1.478 ± 0.160 **
Liver (g)	1.499 ± 0.341	1.567 ± 0.413	2.645 ± 0.954 **	6.056 ± 4.245 **
Liver (%)	4.268 ± 1.135	4.867 ± 1.219	9.909 ± 3.902 **	22.727 ± 10.532 **
Brain (g)	0.463 ± 0.014	0.466 ± 0.018	0.458 ± 0.020	0.436 ± 0.021 **
Brain (%)	1.330 ± 0.237	1.467 ± 0.245	1.713 ± 0.204 **	1.775 ± 0.283 **

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 MICE IN THE 2-YEAR FEED STUDY OF *p*-NITROANISOLE

Group name Number of examined animals	Control <50>	5000 ppm <50>	10000 ppm <50>	20000 ppm <50>		
Liver						
Hepatocellular adenoma[1]	12 (24%) [a]	17 (34%)	18 (36%)	3 (6%) *		⇩
Hepatocellular carcinoma[2]	16 (32%)	11 (22%)	14 (28%)	39 (78%) **	⬆⬆	⇧⇧
Hepatoblastoma[3]	1 (2%)	12 (24%) **	18 (36%) **	38 (76%) **	⬆⬆	⇧⇧
1)+2)	22 (44%)	26 (52%)	25 (50%)	40 (80%) **	⬆⬆	⇧⇧
2)+3)	16 (32%)	19 (38%)	28 (56%) *	43 (86%) **	⬆⬆	⇧⇧
1)+2)+3)	22 (44%)	27 (54%)	33 (66%) *	43 (86%) **	⬆⬆	⇧⇧
Hemangioma[4]	7 (14%)	2 (4%)	1 (2%) *	0 (0%) **		⇩⇩
Hemangiosarcoma[5]	1 (2%)	1 (2%)	0 (0%)	0 (0%)		
4)+5)	8 (16%)	3 (6%)	1 (2%) *	0 (0%) **		⇩⇩
Spleen						
Mastcytoma:malignant	0 (0%)	0 (0%)	6 (12%) *	0 (0%)		
Hemangioma[6]	4 (8%)	1 (2%)	0 (0%)	0 (0%)		⇩
Hemangiosarcoma[7]	0 (0%)	1 (2%)	0 (0%)	0 (0%)		
6)+7)	4 (8%)	2 (4%)	0 (0%)	0 (0%)		⇩
Lung						
Bronchiolar-alveolar adenoma[8]	6 (12%)	2 (4%)	1 (2%)	1 (2%)		⇩
Bronchiolar-alveolar carcinoma[9]	3 (6%)	1 (2%)	2 (4%)	1 (2%)		
8)+9)	9 (18%)	3 (6%)	3 (6%)	2 (4%) *		⇩
Lymph node						
Malignant lymphoma	8 (16%)	13 (26%)	6 (12%)	3 (6%)		⇩

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

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

Group name Number of examined animals	Control <50>	5000 ppm <50>	10000 ppm <50>	20000 ppm <50>		
Liver						
Hepatocellular adenoma[1)]	5 (10%) [a)]	18 (36%) **	13 (26%) *	4 (8%)		
Hepatocellular carcinoma[2)]	2 (4%)	12 (24%) **	41 (82%) **	46 (92%) **	⬆⬆	⇧⇧
Hepatoblastoma[3)]	0 (0%)	0 (0%)	8 (16%) **	38 (76%) **	⬆⬆	⇧⇧
1)+2)	7 (14%)	24 (48%) **	44 (88%) **	47 (94%) **	⬆⬆	⇧⇧
2)+3)	2 (4%)	12 (24%) **	42 (84%) **	48 (96%) **	⬆⬆	⇧⇧
1)+2)+3)	7 (14%)	24 (48%) **	45 (90%) **	48 (96%) **	⬆⬆	⇧⇧
Histiocytic sarcoma	1 (2%)	0 (0%)	0 (0%)	3 (6%)	⬆	
Hemangioma	3 (6%)	1 (2%)	0 (0%)	0 (0%)		⇩
Spleen						
Malignant lymphoma	7 (14%)	7 (14%)	4 (8%)	1 (2%) *		⇩
Lymph node						
Malignant lymphoma	16 (32%)	16 (32%)	14 (28%)	3 (6%) **		⇩⇩
Uterus						
Endometrial stromal polyp	5 (10%)	1 (2%)	0 (0%) *	0 (0%) *		⇩⇩
All site						
Histiocytic sarcoma	18 (36%)	17 (34%)	15 (30%)	15 (30%)		

[a)] : No. of animals with bearing tumor (incidence ; %)
* : Significant difference, $p<0.05$ (Fisher's exact test for neoplastic lesion)
** : Significant difference, $p<0.01$ (Fisher's exact test for neoplastic lesion)
⬆⬆ : Significant difference, $p<0.01$ (Peto test for neoplastic lesion)
⬆ : Significant difference, $p<0.05$ (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 MICE IN THE 2-YEAR FEED STUDY OF *p*-NITROANISOLE

Group name	Control				5000 ppm				10000 ppm				20000 ppm			
Number 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 : respiratory epithelium	12	1	0	0	20	4	0	0	19	7	0	0 *	29	10	0	0 **
Atrophy: olfactory epithelium	0	0	0	0	2	0	0	0	3	3	0	0 *	1	0	0	0
Lung																
Bronchiolar-alveolar cell hyperplasia	3	0	0	0	44	3	0	0 **	40	2	0	0 **	36	5	0	0 **
Bone marrow																
Erythropoiesis:increased	0	0	0	0	3	0	0	0	6	0	0	0 *	14	0	0	0 **
Spleen																
Deposit of hemosiderin	0	0	0	0	0	0	0	0	8	0	0	0 **	13	1	0	0 **
Extramedullary hematopoiesis	9	4	3	0	4	6	6	0	4	4	5	0	5	6	19	2 **
Tooth																
Dysplasia	8	10	8	0	26	11	2	0 **	18	13	6	0	23	5	1	0 **
Liver																
Granulation	13	0	0	0	15	0	0	0	6	1	0	0	0	0	0	0 **
Hepatocellular hypertrophy: central	0	0	0	0	0	15	0	0 **	0	34	1	0 **	0	35	0	0 **
Nuclear atypia:central	0	0	0	0	0	0	0	0	11	2	0	0 **	17	21	0	0 **
Acidophilic cell focus	5	2	0	0	5	2	1	0	3	3	0	0	9	4	0	0
Kidney																
Basophilic change	16	1	0	0	20	0	0	0	14	0	0	0	1	0	0	0 **
Deposit of hemosiderin	0	0	0	0	1	2	1	0	0	2	7	0 **	2	4	17	2 **
Testis																
Mineralization	27	18	2	0	32	9	4	0	23	3	0	0 **	5	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 MICE IN THE 2-YEAR FEED STUDY OF *p*-NITROANISOLE

Group name	Control				5000 ppm				10000 ppm				20000 ppm			
Number 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	4	0	0	0	7	3	0	0	15	2	0	0 **	26	2	0	0 **
Eosinophilic change : respiratory epithelium	26	6	0	0	30	13	1	1 *	29	13	0	0 *	20	24	1	0 **
Respiratory metaplasia:gland	6	0	0	0	4	0	0	0	6	0	0	0	15	0	0	0 *
Nasopharynx																
Eosinophilic change : respiratory epithelium	3	0	0	0	5	0	3	1	7	3	1	0	11	0	0	0 *
Lung																
Bronchiolar-alveolar cell hyperplasia	0	0	0	0	40	2	0	0 **	40	0	0	0 **	41	2	0	0 **
Bone marrow																
Erythropoiesis:increased	2	0	0	0	0	0	0	0	2	0	0	0	17	0	0	0 **
Spleen																
Deposit of hemosiderin	3	0	0	0	13	0	0	0 *	22	0	0	0 **	13	0	0	0 *
Extramedullary hematopoiesis	5	6	9	0	8	1	4	0	11	5	3	1	9	3	29	0 **
Heart																
Mineralization	4	0	0	0	3	0	0	0	6	1	0	0	13	1	0	0 *
Liver																
Hepatocellular hypertrophy: central	0	0	0	0	0	0	0	0	0	1	0	0	0	9	0	0 **
Acidophilic cell focus	2	0	0	0	4	0	0	0	9	0	0	0	7	0	0	0
Kidney																
Deposit of hemosiderin	0	0	0	0	1	0	0	0	1	1	2	0	0	5	24	5 **
Adrenal																
Spindle-cell hyperplasia	5	43	2	0	4	40	6	0	1	41	4	0	21	28	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 MICE IN THE 2-YEAR FEED STUDY OF *p*-NITROANISOLE

	Male				Female			
Group	Control	5000ppm	10000ppm	20000ppm	Control	5000ppm	10000ppm	20000ppm
Number of dead or moribund animals	14	15	23	34	27	23	20	37
No microscopical confirmation	1	0	2	2	1	0	0	0
Urinary retention	2	0	0	2	0	0	0	0
Endocrine system lesion	0	0	0	0	1	0	0	0
Tooth lesion	0	0	2	0	1	0	0	0
Hydronephrosis	2	2	2	0	0	0	1	0
Tumor death : leukemia	4	5	2	1	8	11	7	0
subcutis	0	1	1	1	1	0	1	1
lung	0	0	2	0	0	0	1	0
spleen	1	0	2	0	1	0	0	0
liver	3	7	10	26	2	0	2	31
epididymis	0	0	0	1	—	—	—	—
ovary	—	—	—	—	0	1	0	0
uterus	—	—	—	—	10	11	8	5
brain	0	0	0	1	0	0	0	0
muscle	1	0	0	0	1	0	0	0
peritoneum	0	0	0	0	1	0	0	0

TABLE 20 HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER : Crj:BDF1 MALE MICE

Organs / Tumors	No. of animals examined	No. of animals bearing tumor	Incidence (%)	Min. - Max. (%)
Liver	<1446>			
Hepatocellular adenoma 1)		261	18.0	4 - 34
Hepatocellular carcinoma 2)		291	20.1	2 - 42
Hepatoblastoma 3)		9	0.6	0 - 6
1)+2)		508	35.1	8 - 68
2)+3)		295	20.4	2 - 46
1)+2)+3)		513	35.5	8 - 72
Hemangioma 4)		32	2.2	0 - 12
Hemangiosarcoma 5)		67	4.6	0 - 14
4)+5)				
Spleen	<1445>			
Mastocytoma: malignant		3	0.2	0 - 4
Hemangioma 6)		33	2.3	0 - 10
Hemangiosarcoma 7)		47	3.3	0 - 10
6)+7)				
Lung	<1445>			
Bronchio-alveolar adenoma 8)		113	7.8	2 - 18
Bronchio-alveolar carcinoma 9)		160	11.1	0 - 24
8)+9)		271	18.8	2 - 30
Lymph node	<1446>			
Malignant lymphoma		170	11.8	2 - 28

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

Study No. : 0044, 0060, 0062, 0064, 0066, 0068, 0096, 0105, 0116, 0140, 0159, 0163, 0190, 0206, 0211, 0225, 0243, 0268, 0270, 0279, 0285, 0297, 0319, 0329, 0343, 0348, 0366, 0372, 0406

(Study No. 0402)

TABLE 21 HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER : Crj:BDF1 FEMALE MICE

Organs / Tumors	No. of animals examined	No. of animals bearing tumor	Incidence (%)	Min. - Max. (%)
Liver	<1448>			
Hepatocellular adenoma 1)		77	5.3	0 - 10
Hepatocellular carcinoma 2)		35	2.4	0 - 12
Hepatoblastoma 3)		0	0.0	0 - 0
1)+2)		108	7.5	4 - 14
2)+3)		35	2.4	0 - 12
1)+2)+3)		108	7.5	2 - 14
Histiocytic sarcoma		19	1.3	0 - 4
Hemangioma		15	1.0	0 - 6
Lung	<1448>			
Bronchio-alveolar adenoma 4)		52	3.6	0 - 10
Bronchio-alveolar carcinoma 5)		43	3.0	0 - 8
4)+5)		94	6.5	0 - 14
Spleen	<1447>			
Malignant lymphoma		94	6.5	0 - 26
Lymph node	<1448>			
Malignant lymphoma		426	29.4	12 - 46
Uterus	<1446>			
Endometrial stromal polyp		44	3.0	0 - 10

29 carcinogenicity studies examined in Japan Bioassay Research Center were used.
Study No. : 0044, 0060, 0062, 0064, 0066, 0068, 0096, 0105, 0116, 0140, 0159, 0163, 0190, 0206, 0211, 0225, 0243, 0268, 0270, 0279, 0285, 0297, 0319, 0329, 0343, 0348, 0366, 0372, 0406