o-フェニレンジアミン二塩酸塩のマウスを用いた
経口投与によるがん原性試験(混水試験)報告書

試験番号：０３７２

TABLES

TABLES

TABLES (CONTINUED)

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TABLE 1 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

Week on Study	Control		500 ppm			1000 ppm			2000 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	22.8 (50)	50 / 50	22.8 (50)	100	50 / 50	22.8 (50)	100	50 / 50	22.8 (50)	100	50 / 50
1	23.5 (50)	50 / 50	23.4 (50)	100	50 / 50	22.9 (50)	97	50 / 50	22.2 (50)	94	50 / 50
2	24.8 (50)	50 / 50	24.5 (50)	99	50 / 50	24.3 (50)	98	50 / 50	23.5 (50)	95	50 / 50
3	25.4 (50)	50 / 50	25.3 (50)	100	50 / 50	24.9 (50)	98	50 / 50	23.8 (50)	94	50 / 50
4	25.9 (50)	50 / 50	26.0 (50)	100	50 / 50	25.7 (50)	99	50 / 50	24.9 (50)	96	50 / 50
5	26.9 (50)	50 / 50	26.3 (50)	98	50 / 50	26.1 (50)	97	50 / 50	25.1 (50)	93	50 / 50
6	27.6 (50)	50 / 50	27.2 (50)	99	50 / 50	26.7 (50)	97	50 / 50	26.2 (50)	95	50 / 50
7	28.2 (50)	50 / 50	27.5 (50)	98	50 / 50	26.7 (50)	95	50 / 50	26.5 (50)	94	50 / 50
8	29.6 (50)	50 / 50	28.9 (50)	98	50 / 50	28.0 (50)	95	50 / 50	27.3 (50)	92	50 / 50
9	29.9 (50)	50 / 50	29.2 (50)	98	50 / 50	27.8 (50)	93	50 / 50	27.2 (50)	91	50 / 50
10	30.8 (50)	50 / 50	29.5 (50)	96	50 / 50	28.8 (50)	94	50 / 50	28.1 (50)	91	50 / 50
11	31.1 (50)	50 / 50	29.9 (50)	96	50 / 50	29.0 (50)	93	50 / 50	28.0 (50)	90	50 / 50
12	32.0 (50)	50 / 50	30.9 (50)	97	50 / 50	29.6 (50)	93	50 / 50	28.6 (50)	89	50 / 50
13	32.7 (50)	50 / 50	31.3 (50)	96	50 / 50	30.1 (50)	92	50 / 50	28.7 (50)	88	50 / 50
14	33.7 (50)	50 / 50	32.3 (50)	96	50 / 50	30.8 (50)	91	50 / 50	29.4 (50)	87	50 / 50
18	36.2 (50)	50 / 50	34.0 (50)	94	50 / 50	32.4 (50)	90	50 / 50	30.8 (50)	85	50 / 50
22	38.5 (50)	50 / 50	35.9 (50)	93	50 / 50	33.6 (50)	87	50 / 50	31.8 (50)	83	50 / 50
26	40.8 (50)	50 / 50	37.1 (50)	91	50 / 50	35.1 (50)	86	50 / 50	33.2 (50)	81	50 / 50
30	42.9 (50)	50 / 50	38.3 (50)	89	50 / 50	36.1 (50)	84	50 / 50	33.9 (50)	79	50 / 50
34	44.4 (50)	50 / 50	39.0 (50)	88	50 / 50	36.5 (50)	82	50 / 50	34.5 (50)	78	50 / 50
38	45.7 (50)	50 / 50	39.7 (50)	87	50 / 50	37.4 (50)	82	50 / 50	35.1 (50)	77	50 / 50
42	46.8 (50)	50 / 50	41.0 (49)	88	49 / 50	38.2 (50)	82	50 / 50	35.9 (49)	77	49 / 50
46	47.8 (50)	50 / 50	41.9 (49)	88	49 / 50	38.9 (50)	81	50 / 50	36.4 (49)	76	49 / 50
50	48.7 (50)	50 / 50	42.7 (49)	88	49 / 50	39.5 (50)	81	50 / 50	37.2 (49)	76	49 / 50
54	49.5 (50)	50 / 50	43.9 (49)	89	49 / 50	40.3 (50)	81	50 / 50	37.4 (49)	76	49 / 50
58	49.8 (50)	50 / 50	43.4 (48)	87	48 / 50	40.1 (50)	81	50 / 50	37.0 (49)	74	49 / 50
62	50.5 (50)	50 / 50	43.3 (48)	86	48 / 50	40.0 (49)	79	49 / 50	36.7 (49)	73	49 / 50
66	51.6 (50)	50 / 50	45.0 (47)	87	47 / 50	41.0 (49)	79	49 / 50	38.0 (49)	74	49 / 50
70	52.1 (50)	50 / 50	45.1 (46)	87	46 / 50	41.4 (49)	79	49 / 50	38.4 (49)	74	49 / 50
74	52.0 (50)	50 / 50	45.6 (46)	88	46 / 50	41.5 (49)	80	49 / 50	37.6 (49)	72	49 / 50
78	52.1 (50)	50 / 50	45.3 (45)	87	45 / 50	41.7 (49)	80	49 / 50	38.1 (48)	73	48 / 50
82	52.6 (48)	48 / 50	46.0 (44)	87	44 / 50	41.4 (49)	79	49 / 50	37.7 (48)	72	48 / 50
86	52.4 (48)	48 / 50	46.1 (43)	88	43 / 50	41.1 (49)	78	49 / 50	36.5 (47)	70	47 / 50
90	51.6 (47)	47 / 50	44.9 (43)	87	43 / 50	39.4 (48)	76	48 / 50	35.9 (43)	70	43 / 50
94	50.5 (45)	45 / 50	44.6 (41)	88	41 / 50	39.1 (47)	77	47 / 50	35.7 (41)	71	41 / 50
98	51.2 (41)	41 / 50	44.1 (40)	86	40 / 50	38.6 (46)	75	46 / 50	35.2 (40)	69	40 / 50
102	51.8 (39)	39 / 50	43.5 (39)	84	39 / 50	38.5 (42)	74	42 / 50	34.2 (40)	66	40 / 50
104	52.6 (38)	38 / 50	44.4 (38)	84	38 / 50	38.8 (42)	74	42 / 50	34.5 (39)	66	39 / 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 DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

Week on Study	Control		1000 ppm			2000 ppm			4000 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	18.9 (50)	50 / 50	18.9 (50)	100	50 / 50	18.9 (50)	100	50 / 50	18.9 (50)	100	50 / 50
1	18.7 (50)	50 / 50	18.9 (50)	101	50 / 50	18.3 (50)	98	50 / 50	16.3 (50)	87	50 / 50
2	19.9 (50)	50 / 50	19.8 (50)	99	50 / 50	19.3 (50)	97	50 / 50	18.1 (50)	91	50 / 50
3	20.5 (50)	50 / 50	20.5 (50)	100	50 / 50	19.8 (50)	97	50 / 50	19.1 (50)	93	50 / 50
4	21.2 (50)	50 / 50	20.8 (50)	98	50 / 50	20.0 (50)	94	50 / 50	19.3 (50)	91	50 / 50
5	21.6 (50)	50 / 50	20.7 (50)	96	50 / 50	20.0 (50)	93	50 / 50	19.7 (50)	91	50 / 50
6	22.2 (50)	50 / 50	22.3 (50)	100	50 / 50	21.0 (50)	95	50 / 50	20.2 (50)	91	50 / 50
7	22.7 (50)	50 / 50	22.2 (50)	98	50 / 50	21.5 (50)	95	50 / 50	20.6 (50)	91	50 / 50
8	23.2 (50)	50 / 50	22.4 (50)	97	50 / 50	21.5 (50)	93	50 / 50	21.1 (50)	91	50 / 50
9	23.3 (50)	50 / 50	23.0 (50)	99	50 / 50	22.2 (50)	95	50 / 50	21.4 (50)	92	50 / 50
10	23.9 (50)	50 / 50	23.5 (50)	98	50 / 50	22.5 (50)	94	50 / 50	21.8 (50)	91	50 / 50
11	24.1 (50)	50 / 50	23.4 (50)	97	50 / 50	22.6 (50)	94	50 / 50	21.8 (50)	90	50 / 50
12	24.1 (50)	50 / 50	23.5 (50)	98	50 / 50	22.8 (50)	95	50 / 50	22.0 (50)	91	50 / 50
13	24.7 (50)	50 / 50	23.8 (50)	96	50 / 50	23.3 (50)	94	50 / 50	22.3 (50)	90	50 / 50
14	24.9 (50)	50 / 50	24.0 (50)	96	50 / 50	23.2 (50)	93	50 / 50	22.4 (50)	90	50 / 50
18	26.0 (50)	50 / 50	25.1 (50)	97	50 / 50	24.2 (50)	93	50 / 50	23.3 (50)	90	50 / 50
22	27.3 (50)	50 / 50	25.8 (50)	95	50 / 50	24.7 (50)	90	50 / 50	23.7 (50)	87	50 / 50
26	28.6 (50)	50 / 50	26.5 (50)	93	50 / 50	25.5 (50)	89	50 / 50	24.4 (50)	85	50 / 50
30	29.7 (50)	50 / 50	27.1 (50)	91	50 / 50	25.5 (50)	86	50 / 50	24.5 (50)	82	50 / 50
34	30.5 (50)	50 / 50	27.6 (50)	90	50 / 50	26.1 (50)	86	50 / 50	24.6 (50)	81	50 / 50
38	31.3 (50)	50 / 50	28.3 (50)	90	50 / 50	26.7 (50)	85	50 / 50	25.1 (50)	80	50 / 50
42	31.8 (50)	50 / 50	28.6 (50)	90	50 / 50	27.1 (50)	85	50 / 50	25.3 (50)	80	50 / 50
46	32.6 (49)	49 / 50	29.6 (50)	91	50 / 50	26.8 (50)	82	50 / 50	25.7 (50)	79	50 / 50
50	33.2 (49)	49 / 50	29.7 (49)	89	49 / 50	27.6 (50)	83	50 / 50	25.9 (49)	78	49 / 50
54	33.8 (48)	48 / 50	30.0 (49)	89	49 / 50	27.4 (50)	81	50 / 50	26.0 (49)	77	49 / 50
58	33.8 (48)	48 / 50	29.7 (49)	88	49 / 50	27.3 (49)	81	49 / 50	25.7 (49)	76	49 / 50
62	33.4 (48)	48 / 50	30.4 (49)	91	49 / 50	27.2 (49)	81	49 / 50	25.6 (49)	77	49 / 50
66	34.5 (48)	48 / 50	31.3 (48)	91	48 / 50	27.9 (49)	81	49 / 50	26.1 (48)	76	48 / 50
70	35.1 (48)	48 / 50	31.8 (48)	91	48 / 50	28.3 (49)	81	49 / 50	25.7 (48)	73	48 / 50
74	35.5 (48)	48 / 50	32.1 (46)	90	46 / 50	28.3 (48)	80	48 / 50	25.5 (47)	72	47 / 50
78	35.4 (47)	47 / 50	32.1 (45)	91	45 / 50	28.4 (46)	80	46 / 50	25.4 (46)	72	46 / 50
82	35.7 (41)	41 / 50	32.5 (43)	91	43 / 50	29.1 (45)	82	45 / 50	24.7 (45)	69	45 / 50
86	35.6 (39)	39 / 50	32.0 (42)	90	42 / 50	28.7 (42)	81	42 / 50	24.0 (44)	67	44 / 50
90	34.7 (39)	39 / 50	31.6 (40)	91	40 / 50	28.7 (39)	83	39 / 50	23.7 (43)	68	43 / 50
94	34.2 (36)	36 / 50	31.3 (36)	92	36 / 50	28.6 (34)	84	34 / 50	23.6 (40)	69	40 / 50
98	34.0 (35)	35 / 50	31.3 (33)	92	33 / 50	28.4 (33)	84	33 / 50	23.5 (40)	69	40 / 50
102	33.4 (30)	30 / 50	32.0 (30)	96	30 / 50	28.5 (28)	85	28 / 50	23.5 (35)	70	35 / 50
104	35.8 (24)	24 / 50	31.5 (29)	88	29 / 50	29.3 (28)	82	28 / 50	23.9 (34)	67	34 / 50

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

TABLE 3 WATER CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

Week on Study	Control		500 ppm			1000 ppm			2000 ppm		
	Av. WC.	No. of Surviv. <50>	Av. WC.	% of cont.	No. of Surviv. <50>	Av. WC.	% of cont.	No. of Surviv. <50>	Av. WC.	% of cont.	No. of Surviv. <50>
1	4.7 (47)	50 / 50	4.4 (50)	94	50 / 50	3.4 (50)	72	50 / 50	2.3 (50)	49	50 / 50
2	4.7 (43)	50 / 50	4.8 (44)	102	50 / 50	3.7 (50)	79	50 / 50	2.7 (50)	57	50 / 50
3	4.4 (44)	50 / 50	4.9 (48)	111	50 / 50	3.8 (50)	86	50 / 50	2.7 (50)	61	50 / 50
4	4.6 (47)	50 / 50	4.5 (48)	98	50 / 50	3.5 (50)	76	50 / 50	2.8 (50)	61	50 / 50
5	4.5 (48)	50 / 50	4.0 (50)	89	50 / 50	3.4 (50)	76	50 / 50	2.7 (50)	60	50 / 50
6	4.8 (46)	50 / 50	4.6 (49)	96	50 / 50	3.8 (50)	79	50 / 50	3.2 (50)	67	50 / 50
7	4.4 (49)	50 / 50	4.1 (50)	93	50 / 50	3.5 (50)	80	50 / 50	3.0 (50)	68	50 / 50
8	4.5 (44)	50 / 50	4.3 (47)	96	50 / 50	3.6 (49)	80	50 / 50	3.0 (50)	67	50 / 50
9	4.6 (46)	50 / 50	4.2 (48)	91	50 / 50	3.4 (48)	74	50 / 50	3.2 (50)	70	50 / 50
10	4.8 (50)	50 / 50	4.5 (48)	94	50 / 50	3.6 (50)	75	50 / 50	3.1 (50)	65	50 / 50
11	4.3 (49)	50 / 50	4.0 (49)	93	50 / 50	3.5 (50)	81	50 / 50	2.9 (50)	67	50 / 50
12	4.2 (50)	50 / 50	4.1 (50)	98	50 / 50	3.4 (50)	81	50 / 50	2.9 (50)	69	50 / 50
13	4.4 (49)	50 / 50	4.1 (50)	93	50 / 50	3.6 (49)	82	50 / 50	3.0 (50)	68	50 / 50
14	4.3 (43)	50 / 50	4.1 (49)	95	50 / 50	3.3 (49)	77	50 / 50	3.0 (50)	70	50 / 50
18	3.8 (50)	50 / 50	3.6 (50)	95	50 / 50	3.2 (50)	84	50 / 50	2.8 (50)	74	50 / 50
22	3.7 (50)	50 / 50	3.4 (50)	92	50 / 50	3.0 (50)	81	50 / 50	2.7 (50)	73	50 / 50
26	3.7 (50)	50 / 50	3.5 (50)	95	50 / 50	3.1 (50)	84	50 / 50	2.7 (50)	73	50 / 50
30	3.7 (50)	50 / 50	3.5 (50)	95	50 / 50	3.0 (50)	81	50 / 50	2.8 (50)	76	50 / 50
34	4.0 (50)	50 / 50	3.6 (50)	90	50 / 50	3.2 (50)	80	50 / 50	2.9 (50)	73	50 / 50
38	4.1 (50)	50 / 50	3.9 (50)	95	50 / 50	3.3 (50)	80	50 / 50	3.0 (50)	73	50 / 50
42	4.1 (50)	50 / 50	3.7 (49)	90	49 / 50	3.3 (50)	80	50 / 50	3.1 (49)	76	49 / 50
46	4.1 (50)	50 / 50	3.7 (49)	90	49 / 50	3.4 (50)	83	50 / 50	3.2 (49)	78	49 / 50
50	3.9 (50)	50 / 50	3.7 (49)	95	49 / 50	3.3 (50)	85	50 / 50	3.0 (49)	77	49 / 50
54	4.0 (50)	50 / 50	3.6 (49)	90	49 / 50	3.3 (50)	83	50 / 50	3.1 (49)	78	49 / 50
58	4.0 (50)	50 / 50	3.9 (48)	97	48 / 50	3.5 (50)	88	50 / 50	3.1 (49)	78	49 / 50
62	4.1 (50)	50 / 50	3.4 (48)	83	48 / 50	3.4 (49)	83	49 / 50	3.1 (49)	76	49 / 50
66	4.2 (50)	50 / 50	3.7 (47)	88	47 / 50	3.5 (49)	83	49 / 50	3.4 (49)	81	49 / 50
70	4.4 (50)	50 / 50	3.9 (46)	89	46 / 50	3.6 (49)	82	49 / 50	3.5 (49)	80	49 / 50
74	4.4 (50)	50 / 50	3.8 (46)	86	46 / 50	3.6 (49)	82	49 / 50	3.4 (49)	77	49 / 50
78	4.5 (50)	50 / 50	4.0 (45)	89	45 / 50	3.7 (49)	82	49 / 50	3.4 (47)	76	48 / 50
82	4.6 (48)	48 / 50	4.0 (44)	87	44 / 50	3.7 (49)	80	49 / 50	3.5 (48)	76	48 / 50
86	4.4 (47)	48 / 50	3.9 (43)	89	43 / 50	3.6 (49)	82	49 / 50	3.3 (47)	75	47 / 50
90	4.5 (45)	47 / 50	4.2 (42)	93	43 / 50	3.9 (48)	87	48 / 50	3.6 (43)	80	43 / 50
94	4.2 (43)	45 / 50	4.0 (40)	95	41 / 50	3.9 (47)	93	47 / 50	3.8 (41)	90	41 / 50
98	4.7 (39)	41 / 50	4.0 (40)	85	40 / 50	3.9 (46)	83	46 / 50	3.9 (40)	83	40 / 50
102	4.8 (38)	39 / 50	4.0 (39)	83	39 / 50	4.1 (42)	85	42 / 50	4.0 (40)	83	40 / 50
104	4.6 (36)	38 / 50	4.0 (38)	87	38 / 50	4.0 (41)	87	42 / 50	4.1 (38)	89	39 / 50

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

TABLE 4 WATER CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

Week on Study	Control		1000 ppm			2000 ppm			4000 ppm		
	Av. WC.	No. of Surviv. <50>	Av. WC.	% of cont.	No. of Surviv. <50>	Av. WC.	% of cont.	No. of Surviv. <50>	Av. WC.	% of cont.	No. of Surviv. <50>
1	4.2 (50)	50 / 50	3.3 (50)	79	50 / 50	2.2 (50)	52	50 / 50	1.6 (50)	38	50 / 50
2	4.4 (49)	50 / 50	3.3 (49)	75	50 / 50	2.4 (50)	55	50 / 50	1.8 (50)	41	50 / 50
3	4.2 (50)	50 / 50	3.3 (50)	79	50 / 50	2.3 (50)	55	50 / 50	1.8 (50)	43	50 / 50
4	4.3 (50)	50 / 50	3.2 (50)	74	50 / 50	2.4 (50)	56	50 / 50	1.9 (50)	44	50 / 50
5	4.2 (50)	50 / 50	3.1 (50)	74	50 / 50	2.3 (50)	55	50 / 50	1.9 (50)	45	50 / 50
6	4.4 (50)	50 / 50	3.5 (50)	80	50 / 50	2.7 (50)	61	50 / 50	2.1 (50)	48	50 / 50
7	4.2 (50)	50 / 50	3.4 (50)	81	50 / 50	2.6 (50)	62	50 / 50	2.0 (50)	48	50 / 50
8	4.3 (50)	50 / 50	3.5 (49)	81	50 / 50	2.6 (50)	60	50 / 50	2.0 (50)	47	50 / 50
9	4.3 (50)	50 / 50	3.6 (50)	84	50 / 50	2.7 (50)	63	50 / 50	2.1 (50)	49	50 / 50
10	4.2 (50)	50 / 50	3.5 (49)	83	50 / 50	2.7 (50)	64	50 / 50	2.0 (50)	48	50 / 50
11	4.2 (50)	50 / 50	3.5 (50)	83	50 / 50	2.7 (50)	64	50 / 50	2.2 (50)	52	50 / 50
12	4.3 (50)	50 / 50	3.5 (50)	81	50 / 50	2.7 (49)	63	50 / 50	2.2 (50)	51	50 / 50
13	4.3 (48)	50 / 50	3.8 (48)	88	50 / 50	2.9 (50)	67	50 / 50	2.3 (50)	53	50 / 50
14	4.3 (50)	50 / 50	3.6 (50)	84	50 / 50	3.0 (49)	70	50 / 50	2.2 (50)	51	50 / 50
18	4.1 (50)	50 / 50	3.4 (50)	83	50 / 50	2.7 (50)	66	50 / 50	2.2 (50)	54	50 / 50
22	4.1 (50)	50 / 50	3.3 (50)	80	50 / 50	2.7 (49)	66	50 / 50	2.0 (50)	49	50 / 50
26	4.0 (50)	50 / 50	3.1 (50)	78	50 / 50	2.6 (50)	65	50 / 50	2.0 (50)	50	50 / 50
30	4.0 (50)	50 / 50	3.2 (50)	80	50 / 50	2.7 (50)	68	50 / 50	2.2 (50)	55	50 / 50
34	4.0 (50)	50 / 50	3.2 (50)	80	50 / 50	2.8 (50)	70	50 / 50	2.2 (50)	55	50 / 50
38	3.9 (49)	50 / 50	3.2 (50)	82	50 / 50	2.6 (50)	67	50 / 50	2.2 (50)	56	50 / 50
42	3.9 (50)	50 / 50	3.2 (49)	82	50 / 50	2.6 (50)	67	50 / 50	2.2 (50)	56	50 / 50
46	4.0 (49)	49 / 50	3.1 (50)	78	50 / 50	2.7 (50)	68	50 / 50	2.3 (50)	58	50 / 50
50	4.0 (49)	49 / 50	3.2 (49)	80	49 / 50	2.7 (50)	68	50 / 50	2.3 (49)	58	49 / 50
54	3.9 (48)	48 / 50	3.0 (49)	77	49 / 50	2.7 (50)	69	50 / 50	2.2 (49)	56	49 / 50
58	3.8 (48)	48 / 50	3.1 (49)	82	49 / 50	2.6 (49)	68	49 / 50	2.2 (49)	58	49 / 50
62	3.9 (48)	48 / 50	3.0 (49)	77	49 / 50	2.6 (49)	67	49 / 50	2.3 (49)	59	49 / 50
66	3.9 (48)	48 / 50	3.0 (48)	77	48 / 50	2.8 (48)	72	49 / 50	2.4 (48)	62	48 / 50
70	3.7 (48)	48 / 50	3.0 (48)	81	48 / 50	2.7 (49)	73	49 / 50	2.3 (48)	62	48 / 50
74	3.9 (48)	48 / 50	3.0 (46)	77	46 / 50	2.7 (48)	69	48 / 50	2.5 (47)	64	47 / 50
78	3.9 (47)	47 / 50	3.1 (45)	79	45 / 50	2.8 (46)	72	46 / 50	2.8 (46)	72	46 / 50
82	4.1 (41)	41 / 50	3.2 (43)	78	43 / 50	3.0 (45)	73	45 / 50	3.1 (45)	76	45 / 50
86	3.9 (39)	39 / 50	3.1 (42)	79	42 / 50	2.9 (42)	74	42 / 50	3.3 (44)	85	44 / 50
90	4.0 (39)	39 / 50	3.1 (40)	78	40 / 50	3.1 (39)	78	39 / 50	3.4 (43)	85	43 / 50
94	4.1 (36)	36 / 50	3.5 (36)	85	36 / 50	3.5 (34)	85	34 / 50	4.0 (40)	98	40 / 50
98	4.2 (35)	35 / 50	3.3 (33)	79	33 / 50	3.7 (33)	88	33 / 50	3.7 (40)	88	40 / 50
102	4.1 (28)	30 / 50	3.5 (30)	85	30 / 50	3.8 (28)	93	28 / 50	3.8 (35)	93	35 / 50
104	4.3 (21)	24 / 50	3.3 (29)	77	29 / 50	4.1 (28)	95	28 / 50	3.8 (33)	88	34 / 50

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

TABLE 5 FOOD CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

Week on Study	Control		500 ppm			1000 ppm			2000 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	3.7 (50)	50 / 50	3.6 (50)	97	50 / 50	3.6 (50)	97	50 / 50	3.4 (50)	92	50 / 50
2	3.9 (50)	50 / 50	3.8 (50)	97	50 / 50	3.8 (50)	97	50 / 50	3.7 (50)	95	50 / 50
3	3.9 (50)	50 / 50	3.9 (50)	100	50 / 50	3.9 (50)	100	50 / 50	3.7 (50)	95	50 / 50
4	4.0 (50)	50 / 50	4.0 (50)	100	50 / 50	3.9 (50)	98	50 / 50	3.8 (50)	95	50 / 50
5	4.0 (50)	50 / 50	3.9 (50)	97	50 / 50	3.9 (50)	98	50 / 50	3.8 (50)	95	50 / 50
6	4.1 (50)	50 / 50	4.1 (50)	100	50 / 50	3.9 (50)	95	50 / 50	4.0 (50)	98	50 / 50
7	4.1 (50)	50 / 50	4.0 (50)	98	50 / 50	3.9 (50)	95	50 / 50	4.1 (50)	100	50 / 50
8	4.2 (50)	50 / 50	4.1 (50)	98	50 / 50	4.1 (50)	98	50 / 50	4.0 (50)	95	50 / 50
9	4.2 (50)	50 / 50	4.0 (50)	95	50 / 50	3.9 (50)	93	50 / 50	4.0 (50)	95	50 / 50
10	4.3 (50)	50 / 50	4.1 (50)	95	50 / 50	4.1 (50)	95	50 / 50	4.1 (50)	95	50 / 50
11	4.2 (50)	50 / 50	4.3 (49)	102	50 / 50	4.1 (50)	98	50 / 50	4.1 (50)	98	50 / 50
12	4.3 (50)	50 / 50	4.3 (50)	100	50 / 50	4.2 (50)	98	50 / 50	4.1 (50)	95	50 / 50
13	4.2 (50)	50 / 50	4.1 (50)	98	50 / 50	4.0 (50)	95	50 / 50	4.0 (50)	95	50 / 50
14	4.4 (50)	50 / 50	4.3 (50)	98	50 / 50	4.2 (50)	95	50 / 50	4.1 (50)	93	50 / 50
18	4.4 (50)	50 / 50	4.3 (50)	98	50 / 50	4.2 (50)	95	50 / 50	4.1 (50)	93	50 / 50
22	4.5 (50)	50 / 50	4.2 (50)	93	50 / 50	4.2 (50)	93	50 / 50	4.1 (50)	91	50 / 50
26	4.5 (50)	50 / 50	4.3 (50)	96	50 / 50	4.2 (50)	93	50 / 50	4.0 (50)	89	50 / 50
30	4.7 (50)	50 / 50	4.3 (50)	91	50 / 50	4.2 (50)	89	50 / 50	3.9 (50)	83	50 / 50
34	4.9 (50)	50 / 50	4.6 (50)	94	50 / 50	4.5 (50)	92	50 / 50	4.3 (50)	88	50 / 50
38	5.0 (50)	50 / 50	4.7 (50)	94	50 / 50	4.6 (50)	92	50 / 50	4.3 (50)	86	50 / 50
42	4.9 (50)	50 / 50	4.6 (49)	94	49 / 50	4.6 (50)	94	50 / 50	4.4 (49)	90	49 / 50
46	5.0 (50)	50 / 50	4.6 (49)	92	49 / 50	4.5 (50)	90	50 / 50	4.3 (49)	86	49 / 50
50	4.9 (50)	50 / 50	4.8 (49)	98	49 / 50	4.5 (50)	92	50 / 50	4.5 (49)	92	49 / 50
54	5.0 (50)	50 / 50	4.6 (49)	92	49 / 50	4.5 (50)	90	50 / 50	4.3 (49)	86	49 / 50
58	4.7 (50)	50 / 50	4.3 (48)	91	48 / 50	4.2 (50)	89	50 / 50	4.0 (49)	85	49 / 50
62	4.6 (50)	50 / 50	3.9 (48)	85	48 / 50	4.2 (48)	91	49 / 50	4.0 (49)	87	49 / 50
66	5.0 (50)	50 / 50	4.6 (47)	92	47 / 50	4.5 (49)	90	49 / 50	4.4 (49)	88	49 / 50
70	5.1 (50)	50 / 50	4.8 (46)	94	46 / 50	4.7 (49)	92	49 / 50	4.5 (49)	88	49 / 50
74	5.1 (50)	50 / 50	4.7 (46)	92	46 / 50	4.8 (49)	94	49 / 50	4.6 (49)	90	49 / 50
78	5.1 (50)	50 / 50	4.6 (45)	90	45 / 50	4.6 (49)	90	49 / 50	4.3 (48)	84	48 / 50
82	5.2 (48)	48 / 50	4.8 (44)	92	44 / 50	4.7 (49)	90	49 / 50	4.5 (48)	87	48 / 50
86	4.9 (48)	48 / 50	4.7 (43)	96	43 / 50	4.5 (49)	92	49 / 50	4.2 (47)	86	47 / 50
90	5.1 (47)	47 / 50	4.8 (43)	94	43 / 50	4.6 (48)	90	48 / 50	4.3 (43)	84	43 / 50
94	5.0 (45)	45 / 50	4.6 (41)	92	41 / 50	4.5 (47)	90	47 / 50	3.9 (41)	78	41 / 50
98	4.9 (41)	41 / 50	4.5 (40)	92	40 / 50	4.4 (46)	90	46 / 50	4.2 (40)	86	40 / 50
102	5.0 (39)	39 / 50	4.4 (39)	88	39 / 50	4.4 (42)	88	42 / 50	4.1 (40)	82	40 / 50
104	4.8 (37)	38 / 50	4.4 (38)	92	38 / 50	4.4 (42)	92	42 / 50	4.1 (39)	85	39 / 50

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

TABLE 6 FOOD CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

Week on Study	Control		1000 ppm			2000 ppm			4000 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	3.0 (50)	50 / 50	3.1 (50)	103	50 / 50	2.8 (50)	93	50 / 50	2.2 (50)	73	50 / 50
2	3.4 (50)	50 / 50	3.3 (50)	97	50 / 50	3.1 (50)	91	50 / 50	3.1 (50)	91	50 / 50
3	3.4 (50)	50 / 50	3.4 (49)	100	50 / 50	3.2 (50)	94	50 / 50	3.1 (50)	91	50 / 50
4	3.5 (50)	50 / 50	3.4 (50)	97	50 / 50	3.2 (50)	91	50 / 50	2.9 (50)	83	50 / 50
5	3.4 (50)	50 / 50	3.3 (50)	97	50 / 50	3.2 (50)	94	50 / 50	3.0 (50)	88	50 / 50
6	3.5 (50)	50 / 50	3.5 (50)	100	50 / 50	3.4 (50)	97	50 / 50	3.1 (50)	89	50 / 50
7	3.7 (50)	50 / 50	3.5 (50)	95	50 / 50	3.4 (50)	92	50 / 50	3.2 (50)	86	50 / 50
8	3.7 (49)	50 / 50	3.6 (50)	97	50 / 50	3.3 (50)	89	50 / 50	3.2 (50)	86	50 / 50
9	3.7 (50)	50 / 50	3.7 (50)	100	50 / 50	3.5 (50)	95	50 / 50	3.3 (50)	89	50 / 50
10	3.7 (50)	50 / 50	3.7 (50)	100	50 / 50	3.5 (50)	95	50 / 50	3.2 (50)	86	50 / 50
11	3.7 (50)	50 / 50	3.7 (50)	100	50 / 50	3.6 (50)	97	50 / 50	3.3 (50)	89	50 / 50
12	3.7 (50)	50 / 50	3.7 (49)	100	50 / 50	3.6 (50)	97	50 / 50	3.3 (50)	89	50 / 50
13	3.8 (50)	50 / 50	3.8 (50)	100	50 / 50	3.7 (50)	97	50 / 50	3.4 (50)	89	50 / 50
14	3.9 (50)	50 / 50	3.8 (50)	97	50 / 50	3.8 (50)	97	50 / 50	3.5 (50)	90	50 / 50
18	4.0 (50)	50 / 50	3.9 (50)	98	50 / 50	3.8 (50)	95	50 / 50	3.5 (50)	88	50 / 50
22	4.0 (50)	50 / 50	3.8 (50)	95	50 / 50	3.7 (50)	93	50 / 50	3.4 (50)	85	50 / 50
26	4.1 (50)	50 / 50	4.0 (50)	98	50 / 50	3.8 (50)	93	50 / 50	3.6 (50)	88	50 / 50
30	4.0 (50)	50 / 50	3.8 (50)	95	50 / 50	3.6 (50)	90	50 / 50	3.4 (50)	85	50 / 50
34	4.1 (50)	50 / 50	3.9 (50)	95	50 / 50	3.8 (50)	93	50 / 50	3.6 (50)	88	50 / 50
38	4.2 (50)	50 / 50	4.0 (50)	95	50 / 50	3.9 (50)	93	50 / 50	3.6 (50)	86	50 / 50
42	4.0 (50)	50 / 50	3.9 (50)	98	50 / 50	3.7 (50)	93	50 / 50	3.5 (50)	88	50 / 50
46	4.0 (49)	49 / 50	4.0 (50)	100	50 / 50	3.7 (50)	93	50 / 50	3.5 (50)	88	50 / 50
50	4.1 (49)	49 / 50	3.8 (49)	93	49 / 50	3.6 (50)	88	50 / 50	3.4 (49)	83	49 / 50
54	4.1 (48)	48 / 50	3.7 (49)	90	49 / 50	3.5 (50)	85	50 / 50	3.3 (49)	80	49 / 50
58	3.8 (48)	48 / 50	3.4 (49)	89	49 / 50	3.2 (49)	84	49 / 50	3.1 (49)	82	49 / 50
62	3.8 (48)	48 / 50	3.5 (49)	92	49 / 50	3.3 (49)	87	49 / 50	3.1 (49)	82	49 / 50
66	4.1 (48)	48 / 50	3.7 (48)	90	48 / 50	3.5 (49)	85	49 / 50	3.4 (48)	83	48 / 50
70	4.2 (48)	48 / 50	3.9 (48)	93	48 / 50	3.7 (49)	88	49 / 50	3.4 (48)	81	48 / 50
74	4.1 (48)	48 / 50	3.9 (46)	95	46 / 50	3.6 (48)	88	48 / 50	3.4 (47)	83	47 / 50
78	4.0 (47)	47 / 50	3.8 (45)	95	45 / 50	3.5 (46)	88	46 / 50	3.3 (46)	83	46 / 50
82	4.0 (41)	41 / 50	3.8 (43)	95	43 / 50	3.6 (45)	90	45 / 50	3.3 (45)	83	45 / 50
86	4.2 (39)	39 / 50	3.7 (42)	88	42 / 50	3.6 (42)	86	42 / 50	3.3 (44)	79	44 / 50
90	4.1 (39)	39 / 50	3.7 (40)	90	40 / 50	4.0 (39)	98	39 / 50	3.7 (43)	90	43 / 50
94	4.1 (36)	36 / 50	3.8 (36)	93	36 / 50	3.7 (34)	90	34 / 50	3.3 (40)	80	40 / 50
98	4.0 (35)	35 / 50	3.7 (33)	92	33 / 50	3.6 (33)	90	33 / 50	3.2 (40)	80	40 / 50
102	4.0 (30)	30 / 50	3.7 (30)	92	30 / 50	3.7 (28)	92	28 / 50	3.2 (35)	80	35 / 50
104	4.4 (24)	24 / 50	3.6 (29)	82	29 / 50	3.7 (28)	84	28 / 50	3.1 (34)	70	34 / 50

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

TABLE 7 INCIDENCES OF EXTERNAL AND INTERNAL MASSES IN CLINICAL OBSERVATION OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

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	0/50	0/49	2/47	2/50(1/12)
500 ppm	0/50	0/50	0/50	0/49	0/49	1/47	3/45	1/43	4/50(3/12)
1000 ppm	0/50	0/50	0/50	0/50	1/50	1/49	2/49	2/48	3/50(1/ 8)
2000 ppm	0/50	0/50	0/50	0/49	0/49	1/49	0/48	2/42	3/50(1/11)
Internal mass									
Control	0/50	1/50	1/50	1/50	1/50	6/50	10/49	10/47	15/50(5/12)
500 ppm	0/50	1/50	1/50	1/49	2/49	2/47	1/45	8/43	11/50(5/12)
1000 ppm	0/50	1/50	3/50	3/50	4/50	5/49	5/49	13/48	16/50(2/ 8)
2000 ppm	0/50	1/50	1/50	0/49	0/49	0/49	4/48	6/42	10/50(6/11)

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

TABLE 8 INCIDENCES OF EXTERNAL AND INTERNAL MASSES IN CLINICAL OBSERVATION OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

Time of mass occurrence (week)	0～13	14～26	27～39	40～52	53～65	66～78	79～91	92～104	0～104
External mass									
Control	0/50	0/50	0/50	1/50	2/48	2/48	3/46	3/37	3/50(1/26)
1000 ppm	0/50	0/50	0/50	0/50	0/49	0/48	0/45	0/37	0/50(0/21)
2000 ppm	0/50	0/50	0/50	0/50	0/50	0/49	0/46	2/38	2/50(1/22)
4000 ppm	0/50	0/50	0/50	0/50	1/49	2/48	2/46	2/41	4/50(4/16)
Internal mass									
Control	0/50	0/50	0/50	0/50	0/48	4/48	6/46	6/37	11/50(8/26)
1000 ppm	0/50	1/50	1/50	3/50	5/49	11/48	14/45	14/37	26/50(19/21)
2000 ppm	0/50	0/50	0/50	0/50	3/50	10/49	17/46	20/38	31/50(18/22)
4000 ppm	0/50	0/50	1/50	2/50	2/49	6/48	11/46	21/41	27/50(13/16)

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

TABLE 9 HEMATOLOGY OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

Group name	Control	500 ppm	1000 ppm	2000 ppm	
No. of examined animals	36	38	42	39	
Red blood cell ($10^6/\mu$ L)	9.60 ± 0.91	9.59 ± 1.28	9.43 ± 1.92	9.10 ± 0.84	**
Hemoglobin (g/dL)	13.8 ± 1.1	13.6 ± 1.5	13.5 ± 2.3	13.3 ± 1.2	**
MCV (fL)	45.8 ± 1.9	45.3 ± 2.9	46.9 ± 6.3	46.9 ± 1.2	**
MCHC (g/dL)	31.5 ± 0.7	31.4 ± 1.0	31.1 ± 1.3	31.1 ± 0.6	**
Platelet ($10^3/\mu$ L)	1911 ± 411	1985 ± 418	2084 ± 470	2279 ± 303	**
WBC ($10^3/\mu$ L)	4.47 ± 8.86	2.96 ± 1.61	3.05 ± 2.90	2.00 ± 1.31	**
Differential WBC (%)					
N-Seg	30 ± 17	29 ± 13	36 ± 14	42 ± 17	**
Eosino	2 ± 1	2 ± 3	1 ± 1	1 ± 3	**
Mono	5 ± 3	5 ± 2	4 ± 2	3 ± 1	**

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

TABLE 10 HEMATOLOGY OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

Group name	Control	1000 ppm	2000 ppm		4000 ppm	
No. of examined animals	22	27	25		28	
Hemoglobin (g/dL)	14.1 ± 2.3	13.6 ± 1.7	12.9 ± 2.7		13.4 ± 1.2	**
MCV (fL)	45.7 ± 2.3	46.7 ± 2.8	47.4 ± 5.1		46.7 ± 2.1	**
MCHC (g/dL)	31.6 ± 1.1	31.5 ± 1.1	30.9 ± 1.6	*	30.7 ± 0.6	**
Platelet ($10^3/\mu$L)	1210 ± 273	1329 ± 374	1399 ± 453		1641 ± 454	**
Differential WBC (%)						
Eosino	3 ± 4	1 ± 1	1 ± 1	**	1 ± 1	**

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

TABLE 11 BIOCHEMISTRY OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

Group name	Control	500 ppm		1000 ppm		2000 ppm	
No. of examined animals	37	38		42		39	
Total protein (g/dL)	5.1 ± 0.6	5.3 ± 0.7		5.3 ± 0.9		5.6 ± 0.8	**
Albumin (g/dL)	2.9 ± 0.4	3.0 ± 0.4		3.0 ± 0.5	*	3.2 ± 0.3	**
Triglyceride (mg/dL)	47 ± 27	41 ± 24		41 ± 16		31 ± 11	**
GPT (IU/L)	49 ± 77	135 ± 355		178 ± 514	**	119 ± 300	**
ALP (IU/L)	124 ± 28	220 ± 244	**	337 ± 396	**	279 ± 182	**
CPK (IU/L)	42 ± 13	47 ± 20		120 ± 337	*	84 ± 129	**
Urea nitrogen (mg/dL)	23.4 ± 9.4	22.8 ± 3.3		28.4 ± 12.1	**	30.9 ± 11.3	**
Sodium (mEq/L)	152 ± 1	152 ± 1		152 ± 3		153 ± 2	**
Potassium (mEq/L)	4.3 ± 0.4	4.1 ± 0.3		4.2 ± 0.4		4.0 ± 0.4	**

Mean ± S.D.

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

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

TABLE 12 BIOCHEMISTRY OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

Group name	Control	1000 ppm		2000 ppm		4000 ppm	
No. of examined animals	23	27		26		31	
Total protein (g/dL)	5.5 ± 1.1	5.3 ± 0.5		5.4 ± 0.9		5.7 ± 0.7	*
Albumin (g/dL)	2.9 ± 0.3	3.1 ± 0.3		3.2 ± 0.5	**	3.5 ± 0.4	**
A/G Ratio	1.3 ± 0.3	1.4 ± 0.2		1.5 ± 0.2		1.6 ± 0.2	**
T-cholesterol (mg/dL)	85 ± 37	93 ± 37		133 ± 81	**	169 ± 74	**
Phospholipid (mg/dL)	163 ± 61	177 ± 53		244 ± 116	**	286 ± 104	**
GPT (IU/L)	40 ± 23	74 ± 123		120 ± 189		207 ± 316	**
ALP (IU/L)	171 ± 53	254 ± 88	*	443 ± 468	**	598 ± 559	**
CPK (IU/L)	73 ± 65	64 ± 43		117 ± 184		112 ± 88	**
Urea nitrogen (mg/dL)	23.6 ± 24.3	24.5 ± 10.6		27.5 ± 11.9	**	30.7 ± 13.9	**
Sodium (mEq/L)	151 ± 2	151 ± 2		152 ± 3		155 ± 4	**
Chloride (mEq/L)	123 ± 3	123 ± 4		124 ± 5		126 ± 4	**

Mean ± S.D.

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

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

TABLE 13 URINALYSIS OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

Group	Grade	Control	500 ppm	1000 ppm	2000 ppm
Number of examined animals		38	38	42	39
pH	6.0	1	1	7	6
	6.5	6	19	28	25
	7.0	16	12	7	8
	7.5	14	6	0	0
	8.0	1	0	0	0
	8.5	0	0	0	0
	Chi square test		*	**	**

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

TABLE 14 URINALYSIS OF FEMALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

Group	Grade	Control	1000 ppm	2000 ppm	4000 ppm
Number of examined animals		27	29	28	34
pH	6.0	1	2	9	25
	6.5	3	14	16	9
	7.0	6	8	3	0
	7.5	5	4	0	0
	8.0	10	1	0	0
	8.5	2	0	0	0
	Chi square test		**	**	**
Protein	±	0	2	6	13
	+	9	9	10	16
	2+	16	16	11	4
	3+	2	2	1	1
	4+	0	0	0	0
	Chi square test				**
Ketone body	−	3	2	3	13
	±	20	18	22	20
	+	4	7	1	1
	2+	0	2	2	0
	Chi square test				**

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

TABLE 15 ORGAN WEIGHTS OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

Group name	Control	500 ppm	1000 ppm	2000 ppm
No. of examined animals	37	38	42	39
Body weight (g)	48.1 ± 7.0	40.3 ± 5.3 **	35.1 ± 4.1 **	31.0 ± 2.6 **
Adrenals (g)	0.011 ± 0.003	0.010 ± 0.003	0.010 ± 0.003	0.009 ± 0.003
Adrenals (%)	0.023 ± 0.009	0.025 ± 0.008	0.030 ± 0.009 **	0.031 ± 0.011 **
Testes (g)	0.219 ± 0.044	0.221 ± 0.051	0.204 ± 0.033	0.209 ± 0.030
Testes (%)	0.461 ± 0.094	0.557 ± 0.156 *	0.586 ± 0.102 **	0.679 ± 0.109 **
Heart (g)	0.232 ± 0.026	0.216 ± 0.018 **	0.210 ± 0.019 **	0.197 ± 0.021 **
Heart (%)	0.495 ± 0.111	0.547 ± 0.094 *	0.602 ± 0.065 **	0.639 ± 0.068 **
Lungs (g)	0.238 ± 0.091	0.222 ± 0.046	0.208 ± 0.037 *	0.195 ± 0.027 **
Lungs (%)	0.504 ± 0.196	0.556 ± 0.114 *	0.600 ± 0.127 **	0.637 ± 0.128 **
Kidneys (g)	0.964 ± 1.964	0.757 ± 0.893	0.675 ± 0.447 *	0.765 ± 0.918
Kidneys (%)	2.119 ± 4.555	1.925 ± 2.408 *	1.932 ± 1.234 **	2.473 ± 2.930 **
Spleen (g)	0.092 ± 0.080	0.143 ± 0.210	0.169 ± 0.271	0.092 ± 0.112
Spleen (%)	0.199 ± 0.171	0.373 ± 0.584 *	0.506 ± 0.867 **	0.298 ± 0.365 *
Liver (g)	1.792 ± 0.601	1.902 ± 0.633	2.092 ± 0.964	1.872 ± 0.504
Liver (%)	3.919 ± 2.259	4.945 ± 2.625 **	6.162 ± 3.224 **	6.115 ± 1.984 **
Brain (g)	0.453 ± 0.017	0.456 ± 0.017	0.453 ± 0.020	0.453 ± 0.018
Brain (%)	0.967 ± 0.173	1.151 ± 0.157 **	1.308 ± 0.156 **	1.470 ± 0.127 **

Mean ± S.D.

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

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

TABLE 16 ORGAN WEIGHTS OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

Group name	Control	1000 ppm	2000 ppm	4000 ppm
No. of examined animals	24	29	28	34
Body weight (g)	31.1 ± 3.4	28.4 ± 4.4	26.4 ± 5.6 **	21.5 ± 2.1 **
Adrenals (g)	0.013 ± 0.003	0.013 ± 0.004	0.012 ± 0.002	0.010 ± 0.002 **
Adrenals (%)	0.040 ± 0.009	0.045 ± 0.018	0.046 ± 0.009	0.049 ± 0.015 *
Ovaries (g)	0.097 ± 0.113	0.268 ± 0.866	0.052 ± 0.077	0.041 ± 0.037
Ovaries (%)	0.310 ± 0.383	0.893 ± 2.780	0.201 ± 0.268	0.193 ± 0.198
Heart (g)	0.183 ± 0.026	0.169 ± 0.031	0.158 ± 0.032 **	0.139 ± 0.025 **
Heart (%)	0.600 ± 0.129	0.597 ± 0.086	0.612 ± 0.136	0.649 ± 0.122
Lungs (g)	0.249 ± 0.243	0.197 ± 0.053	0.191 ± 0.028	0.173 ± 0.024 **
Lungs (%)	0.831 ± 0.904	0.700 ± 0.187	0.745 ± 0.157 *	0.810 ± 0.100 **
Kidneys (g)	0.501 ± 0.273	1.056 ± 2.744	2.107 ± 6.004	0.442 ± 0.338 **
Kidneys (%)	1.655 ± 0.992	3.077 ± 6.025 *	5.634 ± 12.482 **	2.070 ± 1.574 **
Spleen (g)	0.169 ± 0.159	0.298 ± 0.672	0.168 ± 0.128	0.115 ± 0.178 **
Spleen (%)	0.576 ± 0.598	1.048 ± 2.384	0.642 ± 0.487	0.510 ± 0.734
Liver (g)	1.490 ± 0.300	1.580 ± 0.437	1.993 ± 1.208	2.024 ± 0.976
Liver (%)	4.891 ± 1.346	5.611 ± 1.529	7.834 ± 5.039 **	9.451 ± 4.632 **
Brain (g)	0.471 ± 0.021	0.466 ± 0.017	0.455 ± 0.025 *	0.443 ± 0.021 **
Brain (%)	1.533 ± 0.186	1.674 ± 0.231	1.775 ± 0.254 **	2.081 ± 0.225 **

Mean ± S.D.

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

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

TABLE 17 INCIDENCES OF SELECTED LESIONS OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

Group		Control	500 ppm	1000 ppm	2000 ppm	Peto	Cochran-
Number of examined animals		50	50	50	50	test	Armitage test
Organ / Findings	Grade of nonneoplastic finding						
Nasal cavity							
Eosinophilic change: respiratory epithelium	1+	31	25	25	36		
	2+	0	1	3	6		
	3+	1	1	0	3		
	Chi square test				**		
Respiratoty metaplasia: olfactory epithelium	1+	18	7	12	11		
	2+	0	0	1	0		
	Chi square test		*				
Lung							
Bronchiolar-alveolar adenoma		5	4	5	2		
Bronchiolar-alveolar carcinoma		9	4	5	5		
Stomach							
Hyperplasia:glandular stomach	1+	6	1	0	1		
	3+	1	0	0	0		
	Chi square test			*			
Liver							
Acidophilic cell focus	1+	1	9	5	5		
	2+	1	1	4	0		
	Chi square test		*				
Basophilic cell focus	1+	2	5	6	7		
	2+	0	0	3	1		
	3+	0	0	0	1		
	Chi square test						
Hemangioma		6	4	1	0 *		↓ ↓
Hepatocellular adenoma 1)		12	25 **	34 **	35 **	↑ ↑	↑ ↑
Hepatocellular carcinoma 2)		6	9	12	10		
1)+2)		18	29 *	39 **	38 **	↑ ↑	↑ ↑
Gall bladder							
Hyperplasia	1+	0 a)	13	8 b)	8 c)		
	Chi square test		**	*	*		
Papillary adenoma		0	2	4	5 *	↑	↑
Kidney							
Hydronephrosis	1+	0	0	0	0		
	2+	2	0	0	0		
	3+	1	1	2	3		
	4+	0	1	0	1		
	Chi square test						
Brain							
Mineralization	1+	21	8	20	16		
	Chi square test		**				
All site							
Hemangioma		7	5	3	1 *		↓

Grade 1+: Slight 2+: Moderate 3+: Marked 4+: Severe

Significant difference * : $p<0.05$ ** : $p<0.01$ Chi square test for non-neoplastic lesion

Fisher's exact test for neoplastic lesion

↑(↓) : $p<0$ ↑ ↑(↓ ↓) : $p<0.01$ Peto or Cochran-Armitage test for neoplastic lesion

a): No. of examined animal is 46. b): No. of examined animal is 49. c): No. of examined animal is 47.

The combined incidences indicate the tumor-bearing animals but not the tumors.

TABLE 18 INCIDENCES OF SELECTED LESIONS OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

Group		Control	1000 ppm	2000 ppm	4000 ppm	Peto	Cochran-Armitage
Number of examined animals		50	50	50	50	test	test
Organ / Findings	Grade of nonneoplastic finding						
Nasal cavity							
Eosinophilic change: olfactory epithelium	1+	7	1	11	18		
	Chi square test				*		
Eosinophilic change: respiratory epithelium	1+	30	26	15	9		
	2+	5	18	32	28		
	3+	2	1	1	11		
	Chi square test		**	**	**		
Respiratory metaplasia : gland	1+	14	19	22	31		
	2+	0	0	5	3		
	Chi square test			**	**		
Nasopharynx							
Eosinophilic change	1+	2	5	3	13		
	2+	1	0	0	0		
	Chi square test				**		
Lung							
Metastasis : liver tumor		2	3	5	2		
Lymph node							
Malignant lymphoma		22	16	6 **	3 **		↓ ↓
Spleen							
Extramedullary hematopoiesis	1+	14	5	10	9		
	2+	5	1	7	2		
	3+	1	1	2	4		
	Chi square test		*				
Liver							
Clear cell focus	1+	0	4	3	6		
	2+	0	0	0	0		
	3+	0	0	0	2		
	Chi square test				*		
Acidophilic cell focus	1+	1	3	3	12		
	2+	0	1	0	5		
	3+	0	0	0	1		
	4+	1	0	0	0		
	Chi square test				**		
Basophilic cell focus	1+	0	5	4	9		
	2+	1	2	0	1		
	Chi square test				**		
Hepatocellular adenoma 1)		6	22 **	23 **	34 **	↑ ↑	↑ ↑
Hepatocellular carcinoma 2)		1	4	11 **	17 **	↑ ↑	↑ ↑
1)+2)		6	23 **	31 **	41 **	↑ ↑	↑ ↑
Gall bladder							
Hyperplasia	1+	0	2	14	10		
	Chi square test			**	**		
Papillary adenoma		0	1	5 *	3		

Grade 1+: Slight 2+: Moderate 3+: Marked 4+: Severe

Significant difference * : $p<0.05$ ** : $p<0.01$ Chi square test for non-neoplastic lesion

Fisher's exact test for neoplastic lesion

↑(↓) : $p<0.05$ ↑↑(↓↓) : $p<0.01$ Peto or Cochran-Armitage test for neoplastic lesion

The combined incidences indicate the tumor-bearing animals but not the tumors.

TABLE 18 INCIDENCES OF SELECTED LESIONS OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE (Continued)

Group		Control	1000 ppm	2000 ppm	4000 ppm	Peto	Cochran-
Number of examined animals		50	50	50	50	test	Armitage test
Organ / Findings	Grade of nonneoplastic finding						
Kidney							
Inflammatory polyp	1+	0	2	0	1		
	2+	2	2	2	2		
	3+	0	5	8	3		
	Chi square test			*			
Hydronephrosis	1+	1	4	0	4		
	2+	0	1	2	0		
	3+	1	7	11	7		
	Chi square test		*	**	*		
Pituitary							
Hyperplasia	1+	5	8	3	4		
	2+	6	2	1	0		
	3+	1	0	0	0		
	Chi square test				*		
Adenoma		6	3	1	1		↓
Adrenal							
Spindle-cell hyperplasia	1+	23	18	17	36		
	2+	24	29	32	11		
	3+	0	0	1	0		
	Chi square test				*		
Uterus							
Endometrial stromal polyp		3	0	0	0		↓
Histiocytic sarcoma		9	18	* 10	10		
All site							
Malignant lymphoma		23	17	7 **	4 **		↓↓

Grade 1+: Slight 2+: Moderate 3+: Marked 4+: Severe

Significant difference * : $p<0.05$ ** : $p<0.01$ Chi square test for non-neoplastic lesion

Fisher's exact test for neoplastic lesion

↑(↓) : $p<0.05$ ↑↑(↓↓) : $p<0.01$ Peto or Cochran-Armitage test for neoplastic lesion

The combined incidences indicate the tumor-bearing animals but not the tumors.

TABLE 19 HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER : Crj:BDF_1 MALE MICE

Organs	Tumors	No. of animals examined	No. of animals with bearing tumors	Incidence (%)	Min. - Max. (%)
Liver		<1296>			
	Hepatocellular adenoma 1)		231	17.8	4 - 34
	Hepatocellular carcinoma 2)		265	20.4	2 - 42
	Hepatoblastoma 3)		7	0.5	0 - 6
	2)+3)		267	20.6	2 - 46
	1)+2)+3)		456	35.2	8 - 72

27 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

TABLE 20 HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER : Crj:BDF_1 FEMALE MICE

Organs	Tumors	No. of animals examined	No. of animals with bearing tumors	Incidence (%)	Min. - Max. (%)
Liver		<1298>			
	Hepatocellular adenoma 1)		66	5.1	0 - 10
	Hepatocellular carcinoma 2)		32	2.5	0 - 8
	Hepatoblastoma 3)		0	0.0	0 - 0
	2)+3)		33	2.4	0 - 8
	1)+2)+3)		95	7.3	4 - 14

27 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

TABLE 21 CAUSE OF DEATH OF MICE IN THE 2-YEAR DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

	Male				Female			
Group	Control	500 ppm	1000 ppm	2000 ppm	Control	1000 ppm	2000 ppm	4000 ppm
Number of dead or moribund animals	12	12	8	11	26	21	22	16
No microscopical confirmation	0	1	1	0	0	0	1	0
Integumentary system lesion	0	0	0	1	0	0	0	0
Renal lesion	0	0	0	0	1	0	0	1
Urinary retention	1	1	0	1	0	0	0	0
Hydronephrosis	1	1	1	2	0	2	6	4
Tumor death : leukemia	3	4	1	3	14	8	1	1
subcutis	0	0	1	0	0	0	0	0
lung	0	0	0	0	0	0	1	0
spleen	1	1	0	0	1	1	0	0
salivary gland	0	0	1	0	0	0	0	0
small intestine	0	0	0	1	0	0	0	0
large intestine	0	0	0	0	0	1	0	0
liver	4	3	2	2	2	1	3	2
pancreas	1	0	0	0	0	0	0	0
pituitary	0	0	0	0	1	0	0	1
ovary	—	—	—	—	0	0	0	1
uterus	—	—	—	—	6	8	9	6
spinal cord	0	0	0	1	0	0	0	0
peripheral nerves	0	1	1	0	1	0	0	0
bone	1	0	0	0	0	0	0	0
peritoneum	0	0	0	0	0	0	1	0