

Summary of Drinking Water Carcinogenicity Study  
of 2-Phenoxyethanol  
in B6D2F1 Mice

June 2007

Japan Bioassay Research Center

Japan Industrial Safety and Health Association

## PREFACE

The tests were contracted and supported by the Ministry of Health, Labour and Welfare of Japan. The tests were conducted by Japan Bioassay Research Center (JBRC) and the report was prepared by JBRC and peer reviewed by outside expert pathologist. Complete report was submitted to Ministry of Health, Labour and Welfare of Japan on June 26, 2007.

This English Summary was translated by JBRC from Japanese complete report.

## Summary of Drinking Water Carcinogenicity Study of 2-Phenoxyethanol in B6D2F1 Mice

### **Purpose, materials and methods**

2-Phenoxyethanol (CAS No. 122-99-6) is a colorless clear liquid with a melting point of 10-12°C and a boiling point of 244.7°C, and is soluble in water (2.7 wt%).

The carcinogenicity and chronic toxicity of 2-phenoxyethanol were examined in groups of 50 B6D2F1/Crlj mice of both sexes administered 2-phenoxyethanol in drinking water for 2 years (104 weeks). The drinking water concentration of 2-phenoxyethanol was 0, 5000, 10000 or 20000 ppm (w/w). The highest dose level was chosen so as not to exceed the maximum tolerated dose (MTD), based on both growth rate and toxicity in the previous 13-week toxicity study. 2-Phenoxyethanol was analyzed for purity and stability by both infrared spectrometry and high performance liquid chromatography before and after its use. The concentrations of 2-phenoxyethanol in drinking water were determined by high performance liquid chromatography at the time of preparation, and on the 5th day after preparation, while stored at room temperature. The animals were observed daily for clinical signs and mortality. Body weight, water consumption and food consumption were measured once a week for the first 14 weeks and every 4 weeks thereafter. Animals found dead, in a moribund state, or surviving to the end of the 2-year administration period underwent complete necropsy. Urinalysis was performed near the end of the administration period. For hematology and blood biochemistry, the surviving animals were bled under ether anesthesia, after they were fasted overnight, for the terminal necropsy. Organs and tissues were removed, weighed and examined for macroscopic lesions at necropsy. The organs and tissues were fixed and embedded in paraffin. Tissue sections of 5 µm thick were prepared and stained with hematoxylin and eosin and examined for histopathology. Incidences of neoplastic lesions were statistically analyzed by Fisher's exact test. A positive trend of the dose-response relationship for the neoplastic incidence was analyzed by Peto's test. Incidences of non-neoplastic lesions and urinalysis were analyzed by Chi-square test. Changes in body weight, water consumption, food consumption, hematological and blood biochemical parameters, and organ weights were analyzed by Dunnett's test. The present studies were conducted in accordance with the Organisation for Economic Co-operation and Development (OECD) Good Laboratory Practice and with reference to the OECD Guideline for Testing of Chemicals 451 "Carcinogenicity Studies".

## **Results**

There was no significant difference in survival rate between any 2-phenoxyethanol-administered group of either sex and respective control. No clinical sign was observed in any 2-phenoxyethanol-administered group of either sex. Growth rates of the males and females administered 10,000 ppm and above were suppressed in a dose-related manner. Terminal body weights of the 5000, 10000 and 20000 ppm-administered groups were 98%, 84% and 73% for males, and 100%, 92% and 79% for females, as compared with the respective controls. Food consumption was decreased in both the males and females administered 10,000 ppm and above. A dose-dependent decrease in water consumption was noted in all the 2-phenoxyethanol-administered groups of both sexes.

No significant increase in the incidence of neoplastic lesions was found in any 2-phenoxyethanol-administered group of either sex as compared with the respective control.

Hematological and biochemical parameters were slightly changed in the 2-phenoxyethanol-administered male and females, but these changes were considered not to be clearly related to the administration of phenoxyethanol. Lowered urinary pH was observed in both the males and females administered 10,000 ppm and above, and might be caused by phenoxyacetic acid, a urinary metabolite of 2-phenoxyethanol.

## **Conclusions**

In mice, there was no evidence of carcinogenic activity of 2-phenoxyethanol in males or females.

## TABLES

TABLE 1	SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL
TABLE 2	SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL
TABLE 3	FOOD CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL
TABLE 4	FOOD CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL
TABLE 5	WATER CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL
TABLE 6	WATER CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL
TABLE 7	HEMATOLOGY OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL
TABLE 8	HEMATOLOGY OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL
TABLE 9	BIOCHEMISTRY OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL
TABLE 10	BIOCHEMISTRY OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL
TABLE 11	URINALYSIS OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL
TABLE 12	URINALYSIS OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL

## TABLES (CONTINUED)

- TABLE 13 ORGAN WEIGHTS OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL
- TABLE 14 ORGAN WEIGHTS OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL
- TABLE 15 INCIDENCES OF SELECTED NEOPLASTIC LESIONS OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL
- TABLE 16 INCIDENCES OF SELECTED NON-NEOPLASTIC LESIONS OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL
- TABLE 17 INCIDENCES OF SELECTED NON-NEOPLASTIC LESIONS OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL
- TABLE 18 HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER : B6D2F1/CrIj MALE MICE
- TABLE 19 CAUSE OF DEATH OF MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL

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

Week on Study	Control		5000 ppm			10000 ppm			20000 ppm		
	Av. Wt. <50>	No. of Surviv.	Av. Wt.	% of cont. <50>	No. of Surviv.	Av. Wt.	% of cont. <50>	No. of Surviv.	Av. Wt.	% of cont. <50>	No. of Surviv.
0	23.8 ( 50 )	50 / 50	23.8 ( 50 )	100	50 / 50	23.8 ( 50 )	100	50 / 50	23.8 ( 50 )	100	50 / 50
1	24.4 ( 50 )	50 / 50	24.4 ( 50 )	100	50 / 50	24.0 ( 50 )	98	50 / 50	23.0 ( 50 )	94	50 / 50
2	25.3 ( 50 )	50 / 50	25.4 ( 50 )	100	50 / 50	24.9 ( 50 )	98	50 / 50	24.0 ( 50 )	95	50 / 50
3	26.2 ( 50 )	50 / 50	26.2 ( 50 )	100	50 / 50	25.7 ( 50 )	98	50 / 50	24.8 ( 50 )	95	50 / 50
4	27.2 ( 50 )	50 / 50	27.1 ( 50 )	100	50 / 50	26.4 ( 50 )	97	50 / 50	25.7 ( 50 )	94	50 / 50
5	27.8 ( 50 )	50 / 50	27.7 ( 50 )	100	50 / 50	27.0 ( 50 )	97	50 / 50	26.1 ( 50 )	94	50 / 50
6	28.6 ( 50 )	50 / 50	28.5 ( 50 )	100	50 / 50	27.5 ( 50 )	96	50 / 50	26.6 ( 50 )	93	50 / 50
7	29.4 ( 50 )	50 / 50	29.0 ( 50 )	99	50 / 50	27.9 ( 50 )	95	50 / 50	27.0 ( 50 )	92	50 / 50
8	30.2 ( 50 )	50 / 50	30.0 ( 50 )	99	50 / 50	28.6 ( 50 )	95	50 / 50	27.3 ( 50 )	90	50 / 50
9	30.8 ( 50 )	50 / 50	30.4 ( 50 )	99	50 / 50	29.1 ( 50 )	94	50 / 50	27.6 ( 50 )	90	50 / 50
10	31.5 ( 50 )	50 / 50	31.4 ( 50 )	100	50 / 50	29.9 ( 50 )	95	50 / 50	28.1 ( 50 )	89	50 / 50
11	32.2 ( 50 )	50 / 50	31.9 ( 50 )	99	50 / 50	30.3 ( 50 )	94	50 / 50	28.2 ( 50 )	88	50 / 50
12	32.7 ( 50 )	50 / 50	32.5 ( 50 )	99	50 / 50	30.9 ( 50 )	94	50 / 50	28.6 ( 50 )	87	50 / 50
13	33.7 ( 50 )	50 / 50	33.2 ( 50 )	99	50 / 50	31.5 ( 50 )	93	50 / 50	29.1 ( 50 )	86	50 / 50
17	35.5 ( 50 )	50 / 50	35.9 ( 50 )	101	50 / 50	33.4 ( 50 )	94	50 / 50	30.4 ( 50 )	86	50 / 50
21	37.6 ( 50 )	50 / 50	37.4 ( 50 )	99	50 / 50	34.8 ( 50 )	93	50 / 50	30.6 ( 50 )	81	50 / 50
25	39.1 ( 50 )	50 / 50	39.7 ( 49 )	102	49 / 50	36.3 ( 50 )	93	50 / 50	31.3 ( 49 )	80	49 / 50
29	41.3 ( 50 )	50 / 50	41.6 ( 49 )	101	49 / 50	37.7 ( 50 )	91	50 / 50	32.8 ( 49 )	79	49 / 50
33	42.6 ( 50 )	50 / 50	43.1 ( 49 )	101	49 / 50	38.6 ( 50 )	91	50 / 50	33.9 ( 48 )	80	48 / 50
37	44.2 ( 50 )	50 / 50	44.2 ( 49 )	100	49 / 50	39.4 ( 50 )	89	50 / 50	34.5 ( 48 )	78	48 / 50
41	45.4 ( 50 )	50 / 50	45.6 ( 49 )	100	49 / 50	40.4 ( 50 )	89	50 / 50	35.4 ( 48 )	78	48 / 50
45	46.4 ( 50 )	50 / 50	46.6 ( 49 )	100	49 / 50	41.0 ( 50 )	88	50 / 50	35.4 ( 48 )	76	48 / 50
49	47.2 ( 50 )	50 / 50	47.6 ( 49 )	101	49 / 50	41.6 ( 50 )	88	50 / 50	36.1 ( 48 )	76	48 / 50
53	47.6 ( 49 )	49 / 50	48.3 ( 49 )	101	49 / 50	42.1 ( 50 )	88	50 / 50	36.1 ( 48 )	76	48 / 50
57	47.9 ( 48 )	48 / 50	49.0 ( 49 )	102	49 / 50	42.5 ( 50 )	89	50 / 50	36.5 ( 48 )	76	48 / 50
61	48.4 ( 48 )	48 / 50	49.6 ( 49 )	102	49 / 50	43.1 ( 50 )	89	50 / 50	36.6 ( 48 )	76	48 / 50
65	48.7 ( 48 )	48 / 50	50.2 ( 49 )	103	49 / 50	43.1 ( 50 )	89	50 / 50	36.6 ( 48 )	75	48 / 50
69	49.3 ( 48 )	48 / 50	50.8 ( 49 )	103	49 / 50	43.7 ( 50 )	89	50 / 50	36.7 ( 48 )	74	48 / 50
73	48.9 ( 46 )	46 / 50	50.8 ( 49 )	104	49 / 50	43.7 ( 50 )	89	50 / 50	36.6 ( 48 )	75	48 / 50
77	48.4 ( 45 )	45 / 50	50.9 ( 49 )	105	49 / 50	43.5 ( 50 )	90	50 / 50	35.9 ( 48 )	74	48 / 50
78	49.8 ( 42 )	42 / 50	51.0 ( 49 )	102	49 / 50	43.7 ( 50 )	88	50 / 50	36.5 ( 47 )	73	47 / 50
82	49.8 ( 42 )	42 / 50	51.0 ( 48 )	102	48 / 50	43.6 ( 50 )	88	50 / 50	36.3 ( 47 )	73	47 / 50
86	50.1 ( 40 )	40 / 50	51.5 ( 46 )	103	46 / 50	43.5 ( 48 )	87	48 / 50	35.8 ( 45 )	71	45 / 50
90	50.6 ( 38 )	38 / 50	51.4 ( 44 )	102	44 / 50	43.7 ( 47 )	86	47 / 50	36.2 ( 43 )	72	43 / 50
94	50.4 ( 38 )	38 / 50	50.9 ( 42 )	101	42 / 50	43.7 ( 46 )	87	46 / 50	36.5 ( 42 )	72	42 / 50
98	50.0 ( 38 )	38 / 50	49.5 ( 41 )	99	41 / 50	42.9 ( 43 )	86	43 / 50	35.9 ( 42 )	72	42 / 50
102	48.1 ( 38 )	38 / 50	48.9 ( 35 )	102	35 / 50	42.0 ( 42 )	87	42 / 50	35.1 ( 41 )	73	41 / 50
104	48.5 ( 35 )	35 / 50	47.7 ( 35 )	98	35 / 50	40.9 ( 42 )	84	42 / 50	35.2 ( 41 )	73	41 / 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 2-PHENOXYETHANOL

Week on Study	Control		5000 ppm			10000 ppm			20000 ppm		
	Av. Wt. <50>	No. of Surviv.	Av. Wt.	% of cont. <50>	No. of Surviv.	Av. Wt.	% of cont. <50>	No. of Surviv.	Av. Wt.	% of cont. <50>	No. of Surviv.
0	19.5 ( 50 )	50 / 50	19.5 ( 50 )	100	50 / 50	19.5 ( 50 )	100	50 / 50	19.5 ( 50 )	100	50 / 50
1	19.9 ( 50 )	50 / 50	19.8 ( 50 )	99	50 / 50	19.8 ( 50 )	99	50 / 50	18.4 ( 50 )	92	50 / 50
2	20.4 ( 50 )	50 / 50	20.4 ( 50 )	100	50 / 50	20.3 ( 50 )	100	50 / 50	19.6 ( 50 )	96	50 / 50
3	21.0 ( 50 )	50 / 50	21.0 ( 50 )	100	50 / 50	21.0 ( 50 )	100	50 / 50	20.5 ( 50 )	98	50 / 50
4	21.7 ( 50 )	50 / 50	21.6 ( 50 )	100	50 / 50	21.6 ( 50 )	100	50 / 50	21.2 ( 50 )	98	50 / 50
5	22.3 ( 50 )	50 / 50	22.0 ( 50 )	99	50 / 50	22.0 ( 50 )	99	50 / 50	21.4 ( 50 )	96	50 / 50
6	22.7 ( 50 )	50 / 50	22.6 ( 50 )	100	50 / 50	22.5 ( 50 )	99	50 / 50	21.9 ( 50 )	96	50 / 50
7	23.3 ( 50 )	50 / 50	23.2 ( 50 )	100	50 / 50	23.0 ( 50 )	99	50 / 50	22.4 ( 50 )	96	50 / 50
8	23.7 ( 50 )	50 / 50	23.6 ( 50 )	100	50 / 50	23.3 ( 50 )	98	50 / 50	22.7 ( 50 )	96	50 / 50
9	24.3 ( 50 )	50 / 50	24.1 ( 50 )	99	50 / 50	24.1 ( 50 )	99	50 / 50	23.2 ( 50 )	95	50 / 50
10	24.4 ( 50 )	50 / 50	24.5 ( 50 )	100	50 / 50	24.2 ( 50 )	99	50 / 50	23.2 ( 50 )	95	50 / 50
11	24.7 ( 50 )	50 / 50	24.5 ( 50 )	99	50 / 50	24.5 ( 50 )	99	50 / 50	23.5 ( 50 )	95	50 / 50
12	24.9 ( 50 )	50 / 50	24.7 ( 50 )	99	50 / 50	24.5 ( 50 )	98	50 / 50	23.7 ( 50 )	95	50 / 50
13	25.6 ( 50 )	50 / 50	25.3 ( 50 )	99	50 / 50	24.7 ( 50 )	96	50 / 50	23.9 ( 50 )	93	50 / 50
17	26.6 ( 50 )	50 / 50	26.6 ( 50 )	100	50 / 50	25.7 ( 50 )	97	50 / 50	24.7 ( 50 )	93	50 / 50
21	27.8 ( 50 )	50 / 50	27.8 ( 50 )	100	50 / 50	26.8 ( 50 )	96	50 / 50	24.9 ( 50 )	90	50 / 50
25	28.7 ( 50 )	50 / 50	28.1 ( 50 )	98	50 / 50	27.4 ( 50 )	95	50 / 50	25.2 ( 50 )	88	50 / 50
29	29.7 ( 50 )	50 / 50	29.4 ( 50 )	99	50 / 50	28.3 ( 50 )	95	50 / 50	26.1 ( 50 )	88	50 / 50
33	31.1 ( 50 )	50 / 50	30.1 ( 50 )	97	50 / 50	28.7 ( 50 )	92	50 / 50	25.9 ( 50 )	83	50 / 50
37	31.3 ( 50 )	50 / 50	31.2 ( 50 )	100	50 / 50	29.4 ( 50 )	94	50 / 50	26.3 ( 50 )	84	50 / 50
41	32.7 ( 49 )	49 / 50	31.8 ( 50 )	97	50 / 50	29.9 ( 49 )	91	49 / 50	26.2 ( 50 )	80	50 / 50
45	33.2 ( 47 )	47 / 50	32.6 ( 50 )	98	50 / 50	30.5 ( 49 )	92	49 / 50	26.3 ( 50 )	79	50 / 50
49	33.7 ( 47 )	47 / 50	33.3 ( 50 )	99	50 / 50	30.9 ( 49 )	92	49 / 50	26.8 ( 48 )	80	48 / 50
53	34.1 ( 47 )	47 / 50	33.6 ( 50 )	99	50 / 50	31.7 ( 48 )	93	48 / 50	26.8 ( 48 )	79	48 / 50
57	34.5 ( 47 )	47 / 50	34.3 ( 48 )	99	48 / 50	31.8 ( 48 )	92	48 / 50	27.3 ( 47 )	79	47 / 50
61	34.7 ( 47 )	47 / 50	34.3 ( 48 )	99	48 / 50	32.1 ( 48 )	93	48 / 50	27.2 ( 47 )	78	47 / 50
65	35.1 ( 46 )	46 / 50	34.8 ( 48 )	99	48 / 50	32.4 ( 48 )	92	48 / 50	27.2 ( 46 )	77	46 / 50
69	35.4 ( 46 )	46 / 50	35.2 ( 48 )	99	48 / 50	32.8 ( 48 )	93	48 / 50	27.7 ( 45 )	78	45 / 50
73	35.5 ( 45 )	45 / 50	35.0 ( 48 )	99	48 / 50	32.7 ( 48 )	92	48 / 50	27.5 ( 45 )	77	45 / 50
77	35.7 ( 44 )	44 / 50	35.1 ( 47 )	98	47 / 50	33.0 ( 47 )	92	47 / 50	27.3 ( 44 )	76	44 / 50
78	35.9 ( 44 )	44 / 50	35.2 ( 47 )	98	47 / 50	32.8 ( 45 )	91	45 / 50	27.3 ( 44 )	76	44 / 50
82	35.6 ( 43 )	43 / 50	35.5 ( 47 )	100	47 / 50	33.1 ( 44 )	93	44 / 50	28.0 ( 43 )	79	43 / 50
86	36.4 ( 39 )	39 / 50	35.7 ( 45 )	98	45 / 50	33.1 ( 43 )	91	43 / 50	27.9 ( 43 )	77	43 / 50
90	36.5 ( 37 )	37 / 50	36.4 ( 44 )	100	44 / 50	33.4 ( 41 )	92	41 / 50	27.9 ( 40 )	76	40 / 50
94	36.1 ( 33 )	33 / 50	35.4 ( 39 )	98	39 / 50	33.5 ( 40 )	93	40 / 50	27.8 ( 38 )	77	38 / 50
98	35.5 ( 29 )	29 / 50	35.1 ( 37 )	99	37 / 50	32.7 ( 35 )	92	35 / 50	27.8 ( 37 )	78	37 / 50
102	34.4 ( 25 )	25 / 50	34.6 ( 36 )	101	36 / 50	32.5 ( 33 )	94	33 / 50	27.2 ( 35 )	79	35 / 50
104	34.7 ( 24 )	24 / 50	34.7 ( 34 )	100	34 / 50	32.0 ( 32 )	92	32 / 50	27.4 ( 34 )	79	34 / 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 DRINKING WATER STUDY OF 2-PHENOXYETHANOL

Week on Study	Control		5000 ppm			10000 ppm			20000 ppm		
	Av. FC. <50>	No. of Surviv.	Av. FC.	% of cont. <50>	No. of Surviv.	Av. FC.	% of cont. <50>	No. of Surviv.	Av. FC.	% of cont. <50>	No. of Surviv.
1	4.1 ( 50 )	50 / 50	4.0 ( 50 )	98	50 / 50	3.8 ( 50 )	93	50 / 50	3.3 ( 50 )	80	50 / 50
2	3.9 ( 50 )	50 / 50	3.9 ( 50 )	100	50 / 50	3.8 ( 50 )	97	50 / 50	3.6 ( 50 )	92	50 / 50
3	4.0 ( 50 )	50 / 50	3.9 ( 50 )	98	50 / 50	3.8 ( 50 )	95	50 / 50	3.7 ( 50 )	93	50 / 50
4	4.1 ( 50 )	50 / 50	4.0 ( 50 )	98	50 / 50	3.9 ( 50 )	95	50 / 50	3.8 ( 50 )	93	50 / 50
5	4.1 ( 50 )	50 / 50	4.0 ( 50 )	98	50 / 50	4.0 ( 50 )	98	50 / 50	3.8 ( 50 )	93	50 / 50
6	4.1 ( 50 )	50 / 50	4.0 ( 50 )	98	50 / 50	3.9 ( 50 )	95	50 / 50	3.7 ( 50 )	90	50 / 50
7	4.1 ( 50 )	50 / 50	4.0 ( 50 )	98	50 / 50	3.9 ( 50 )	95	50 / 50	3.7 ( 50 )	90	50 / 50
8	4.2 ( 50 )	50 / 50	4.2 ( 50 )	100	50 / 50	4.0 ( 50 )	95	50 / 50	3.7 ( 50 )	88	50 / 50
9	4.1 ( 50 )	50 / 50	4.1 ( 50 )	100	50 / 50	4.1 ( 50 )	100	50 / 50	3.7 ( 50 )	90	50 / 50
10	4.1 ( 50 )	50 / 50	4.1 ( 50 )	100	50 / 50	4.1 ( 50 )	100	50 / 50	3.8 ( 50 )	93	50 / 50
11	4.2 ( 50 )	50 / 50	4.2 ( 50 )	100	50 / 50	4.2 ( 50 )	100	50 / 50	4.0 ( 50 )	95	50 / 50
12	4.3 ( 50 )	50 / 50	4.4 ( 50 )	102	50 / 50	4.3 ( 50 )	100	50 / 50	4.0 ( 50 )	93	50 / 50
13	4.3 ( 50 )	50 / 50	4.3 ( 50 )	100	50 / 50	4.3 ( 50 )	100	50 / 50	3.9 ( 50 )	91	50 / 50
17	4.1 ( 50 )	50 / 50	4.2 ( 50 )	102	50 / 50	4.2 ( 50 )	102	50 / 50	3.8 ( 50 )	93	50 / 50
21	4.2 ( 50 )	50 / 50	4.2 ( 50 )	100	50 / 50	4.1 ( 50 )	98	50 / 50	3.7 ( 50 )	88	50 / 50
25	4.1 ( 50 )	50 / 50	4.2 ( 49 )	102	49 / 50	4.0 ( 50 )	98	50 / 50	3.7 ( 49 )	90	49 / 50
29	4.3 ( 50 )	50 / 50	4.3 ( 49 )	100	49 / 50	4.0 ( 50 )	93	50 / 50	3.8 ( 49 )	88	49 / 50
33	4.2 ( 50 )	50 / 50	4.2 ( 49 )	100	49 / 50	3.9 ( 50 )	93	50 / 50	3.6 ( 48 )	86	48 / 50
37	4.3 ( 50 )	50 / 50	4.2 ( 49 )	98	49 / 50	4.0 ( 50 )	93	50 / 50	3.7 ( 48 )	86	48 / 50
41	4.5 ( 50 )	50 / 50	4.4 ( 49 )	98	49 / 50	4.2 ( 50 )	93	50 / 50	3.9 ( 48 )	87	48 / 50
45	4.5 ( 50 )	50 / 50	4.5 ( 49 )	100	49 / 50	4.2 ( 50 )	93	50 / 50	3.8 ( 48 )	84	48 / 50
49	4.5 ( 50 )	50 / 50	4.5 ( 49 )	100	49 / 50	4.2 ( 50 )	93	50 / 50	3.8 ( 48 )	84	48 / 50
53	4.5 ( 49 )	49 / 50	4.6 ( 49 )	102	49 / 50	4.3 ( 50 )	96	50 / 50	3.9 ( 48 )	87	48 / 50
57	4.6 ( 48 )	48 / 50	4.7 ( 49 )	102	49 / 50	4.4 ( 50 )	96	50 / 50	4.0 ( 48 )	87	48 / 50
61	4.6 ( 48 )	48 / 50	4.7 ( 49 )	102	49 / 50	4.4 ( 50 )	96	50 / 50	3.9 ( 48 )	85	48 / 50
65	4.7 ( 48 )	48 / 50	4.7 ( 49 )	100	49 / 50	4.3 ( 50 )	91	50 / 50	3.9 ( 48 )	83	48 / 50
69	4.6 ( 48 )	48 / 50	4.6 ( 49 )	100	49 / 50	4.3 ( 50 )	93	50 / 50	3.8 ( 48 )	83	48 / 50
73	4.6 ( 46 )	46 / 50	4.6 ( 49 )	100	49 / 50	4.3 ( 50 )	93	50 / 50	3.9 ( 48 )	85	48 / 50
77	4.5 ( 45 )	45 / 50	4.6 ( 49 )	102	49 / 50	4.3 ( 50 )	96	50 / 50	3.8 ( 48 )	84	48 / 50
78	4.7 ( 42 )	42 / 50	4.7 ( 49 )	100	49 / 50	4.3 ( 50 )	91	50 / 50	3.8 ( 47 )	81	47 / 50
82	4.8 ( 42 )	42 / 50	4.7 ( 48 )	98	48 / 50	4.3 ( 50 )	90	50 / 50	3.9 ( 47 )	81	47 / 50
86	4.8 ( 40 )	40 / 50	4.9 ( 46 )	102	46 / 50	4.4 ( 48 )	92	48 / 50	3.9 ( 45 )	81	45 / 50
90	5.0 ( 38 )	38 / 50	5.0 ( 44 )	100	44 / 50	4.5 ( 47 )	90	47 / 50	3.9 ( 43 )	78	43 / 50
94	4.8 ( 38 )	38 / 50	4.7 ( 42 )	98	42 / 50	4.3 ( 46 )	90	46 / 50	4.1 ( 42 )	85	42 / 50
98	4.8 ( 38 )	38 / 50	4.7 ( 41 )	98	41 / 50	4.3 ( 43 )	90	43 / 50	3.9 ( 42 )	81	42 / 50
102	4.8 ( 38 )	38 / 50	4.8 ( 35 )	100	35 / 50	4.3 ( 42 )	90	42 / 50	4.0 ( 41 )	83	41 / 50
104	4.7 ( 35 )	35 / 50	4.5 ( 35 )	96	35 / 50	4.2 ( 42 )	89	42 / 50	4.0 ( 41 )	85	41 / 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 DRINKING WATER STUDY OF 2-PHENOXYETHANOL

Week on Study	Control		5000 ppm			10000 ppm			20000 ppm		
	Av. FC. <50>	No. of Surviv.	Av. FC.	% of cont. <50>	No. of Surviv.	Av. FC.	% of cont. <50>	No. of Surviv.	Av. FC.	% of cont. <50>	No. of Surviv.
1	3.4 ( 50 )	50 / 50	3.3 ( 50 )	97	50 / 50	3.2 ( 50 )	94	50 / 50	2.6 ( 50 )	76	50 / 50
2	3.3 ( 50 )	50 / 50	3.3 ( 50 )	100	50 / 50	3.3 ( 50 )	100	50 / 50	3.2 ( 50 )	97	50 / 50
3	3.3 ( 50 )	50 / 50	3.3 ( 50 )	100	50 / 50	3.3 ( 50 )	100	50 / 50	3.1 ( 50 )	94	50 / 50
4	3.4 ( 50 )	50 / 50	3.4 ( 50 )	100	50 / 50	3.4 ( 50 )	100	50 / 50	3.3 ( 50 )	97	50 / 50
5	3.5 ( 50 )	50 / 50	3.5 ( 50 )	100	50 / 50	3.5 ( 50 )	100	50 / 50	3.3 ( 50 )	94	50 / 50
6	3.5 ( 50 )	50 / 50	3.5 ( 50 )	100	50 / 50	3.5 ( 50 )	100	50 / 50	3.3 ( 50 )	94	50 / 50
7	3.6 ( 50 )	50 / 50	3.6 ( 50 )	100	50 / 50	3.6 ( 50 )	100	50 / 50	3.4 ( 50 )	94	50 / 50
8	3.6 ( 50 )	50 / 50	3.6 ( 50 )	100	50 / 50	3.7 ( 50 )	103	50 / 50	3.4 ( 50 )	94	50 / 50
9	3.7 ( 50 )	50 / 50	3.7 ( 50 )	100	50 / 50	3.8 ( 50 )	103	50 / 50	3.5 ( 50 )	95	50 / 50
10	3.7 ( 50 )	50 / 50	3.8 ( 50 )	103	50 / 50	3.7 ( 50 )	100	50 / 50	3.5 ( 50 )	95	50 / 50
11	3.8 ( 50 )	50 / 50	3.7 ( 50 )	97	50 / 50	3.8 ( 50 )	100	50 / 50	3.6 ( 50 )	95	50 / 50
12	3.9 ( 50 )	50 / 50	3.9 ( 50 )	100	50 / 50	3.9 ( 50 )	100	50 / 50	3.7 ( 50 )	95	50 / 50
13	3.8 ( 50 )	50 / 50	3.9 ( 50 )	103	50 / 50	3.9 ( 50 )	103	50 / 50	3.7 ( 50 )	97	50 / 50
17	3.7 ( 50 )	50 / 50	3.8 ( 50 )	103	50 / 50	3.7 ( 50 )	100	50 / 50	3.5 ( 50 )	95	50 / 50
21	3.8 ( 50 )	50 / 50	3.9 ( 50 )	103	50 / 50	3.8 ( 50 )	100	50 / 50	3.5 ( 50 )	92	50 / 50
25	3.7 ( 50 )	50 / 50	3.6 ( 50 )	97	50 / 50	3.6 ( 50 )	97	50 / 50	3.2 ( 50 )	86	50 / 50
29	3.8 ( 50 )	50 / 50	3.8 ( 50 )	100	50 / 50	3.7 ( 50 )	97	50 / 50	3.5 ( 50 )	92	50 / 50
33	3.7 ( 50 )	50 / 50	3.6 ( 50 )	97	50 / 50	3.5 ( 50 )	95	50 / 50	3.3 ( 50 )	89	50 / 50
37	3.6 ( 50 )	50 / 50	3.7 ( 50 )	103	50 / 50	3.7 ( 50 )	103	50 / 50	3.4 ( 50 )	94	50 / 50
41	4.0 ( 49 )	49 / 50	3.9 ( 50 )	98	50 / 50	3.7 ( 49 )	93	49 / 50	3.4 ( 50 )	85	50 / 50
45	4.0 ( 47 )	47 / 50	4.0 ( 50 )	100	50 / 50	3.7 ( 49 )	93	49 / 50	3.5 ( 50 )	88	50 / 50
49	3.9 ( 47 )	47 / 50	3.9 ( 50 )	100	50 / 50	3.8 ( 49 )	97	49 / 50	3.5 ( 48 )	90	48 / 50
53	4.1 ( 47 )	47 / 50	3.9 ( 50 )	95	50 / 50	4.0 ( 48 )	98	48 / 50	3.6 ( 48 )	88	48 / 50
57	4.2 ( 47 )	47 / 50	4.1 ( 48 )	98	48 / 50	4.0 ( 48 )	95	48 / 50	3.7 ( 47 )	88	47 / 50
61	4.0 ( 47 )	47 / 50	4.0 ( 48 )	100	48 / 50	3.9 ( 48 )	98	48 / 50	3.5 ( 47 )	88	47 / 50
65	4.2 ( 46 )	46 / 50	4.2 ( 48 )	100	48 / 50	3.9 ( 48 )	93	48 / 50	3.6 ( 46 )	86	46 / 50
69	4.0 ( 46 )	46 / 50	4.1 ( 47 )	103	48 / 50	3.9 ( 48 )	98	48 / 50	3.5 ( 45 )	88	45 / 50
73	3.9 ( 45 )	45 / 50	4.0 ( 48 )	103	48 / 50	3.9 ( 48 )	100	48 / 50	3.5 ( 45 )	90	45 / 50
77	4.2 ( 44 )	44 / 50	4.0 ( 47 )	95	47 / 50	3.9 ( 47 )	93	47 / 50	3.6 ( 44 )	86	44 / 50
78	4.1 ( 44 )	44 / 50	3.9 ( 47 )	95	47 / 50	3.7 ( 45 )	90	45 / 50	3.5 ( 44 )	85	44 / 50
82	4.2 ( 43 )	43 / 50	4.1 ( 47 )	98	47 / 50	4.0 ( 44 )	95	44 / 50	3.8 ( 43 )	90	43 / 50
86	4.4 ( 39 )	39 / 50	4.1 ( 45 )	93	45 / 50	4.0 ( 43 )	91	43 / 50	3.9 ( 43 )	89	43 / 50
90	4.4 ( 37 )	37 / 50	4.4 ( 44 )	100	44 / 50	4.1 ( 41 )	93	41 / 50	3.8 ( 40 )	86	40 / 50
94	4.3 ( 33 )	33 / 50	4.1 ( 39 )	95	39 / 50	4.1 ( 40 )	95	40 / 50	3.8 ( 38 )	88	38 / 50
98	4.3 ( 29 )	29 / 50	4.3 ( 37 )	100	37 / 50	4.0 ( 35 )	93	35 / 50	3.9 ( 37 )	91	37 / 50
102	4.4 ( 25 )	25 / 50	4.3 ( 36 )	98	36 / 50	4.1 ( 33 )	93	33 / 50	3.8 ( 35 )	86	35 / 50
104	4.5 ( 24 )	24 / 50	4.2 ( 34 )	93	34 / 50	3.8 ( 32 )	84	32 / 50	3.8 ( 34 )	84	34 / 50

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

TABLE 5 WATER CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL

Week on Study	Control		5000 ppm			10000 ppm			20000 ppm		
	Av. WC. <50>	No. of Surviv.	Av. WC.	% of cont. <50>	No. of Surviv.	Av. WC.	% of cont. <50>	No. of Surviv.	Av. WC.	% of cont. <50>	No. of Surviv.
1	5.1 ( 50 )	50 / 50	4.5 ( 50 )	88	50 / 50	3.6 ( 50 )	71	50 / 50	3.0 ( 50 )	59	50 / 50
2	5.0 ( 49 )	50 / 50	4.5 ( 49 )	90	50 / 50	3.7 ( 50 )	74	50 / 50	2.7 ( 50 )	54	50 / 50
3	5.2 ( 49 )	50 / 50	4.6 ( 50 )	88	50 / 50	3.9 ( 50 )	75	50 / 50	3.0 ( 50 )	58	50 / 50
4	5.0 ( 50 )	50 / 50	4.5 ( 50 )	90	50 / 50	3.7 ( 50 )	74	50 / 50	2.8 ( 50 )	56	50 / 50
5	4.8 ( 49 )	50 / 50	4.5 ( 50 )	94	50 / 50	3.9 ( 50 )	81	50 / 50	2.9 ( 50 )	60	50 / 50
6	4.6 ( 48 )	50 / 50	4.5 ( 50 )	98	50 / 50	3.9 ( 50 )	85	50 / 50	2.8 ( 50 )	61	50 / 50
7	4.6 ( 50 )	50 / 50	4.3 ( 50 )	93	50 / 50	3.7 ( 50 )	80	50 / 50	2.8 ( 50 )	61	50 / 50
8	4.5 ( 49 )	50 / 50	4.3 ( 50 )	96	50 / 50	3.6 ( 50 )	80	50 / 50	2.7 ( 50 )	60	50 / 50
9	4.5 ( 50 )	50 / 50	4.3 ( 50 )	96	50 / 50	3.7 ( 50 )	82	50 / 50	2.7 ( 50 )	60	50 / 50
10	4.6 ( 50 )	50 / 50	4.3 ( 50 )	93	50 / 50	3.7 ( 50 )	80	50 / 50	2.8 ( 50 )	61	50 / 50
11	4.4 ( 50 )	50 / 50	4.4 ( 50 )	100	50 / 50	3.6 ( 50 )	82	50 / 50	2.8 ( 50 )	64	50 / 50
12	4.3 ( 50 )	50 / 50	4.1 ( 50 )	95	50 / 50	3.5 ( 50 )	81	50 / 50	2.7 ( 50 )	63	50 / 50
13	4.0 ( 50 )	50 / 50	4.0 ( 50 )	100	50 / 50	3.4 ( 50 )	85	50 / 50	2.7 ( 50 )	68	50 / 50
17	4.0 ( 50 )	50 / 50	3.8 ( 50 )	95	50 / 50	3.2 ( 50 )	80	50 / 50	2.6 ( 50 )	65	50 / 50
21	4.2 ( 50 )	50 / 50	4.0 ( 50 )	95	50 / 50	3.4 ( 49 )	81	50 / 50	2.9 ( 50 )	69	50 / 50
25	3.9 ( 50 )	50 / 50	3.8 ( 49 )	97	49 / 50	3.2 ( 50 )	82	50 / 50	2.7 ( 49 )	69	49 / 50
29	3.9 ( 50 )	50 / 50	3.6 ( 49 )	92	49 / 50	3.0 ( 50 )	77	50 / 50	2.5 ( 49 )	64	49 / 50
33	3.9 ( 50 )	50 / 50	3.6 ( 49 )	92	49 / 50	3.1 ( 50 )	79	50 / 50	2.7 ( 48 )	69	48 / 50
37	3.8 ( 50 )	50 / 50	3.6 ( 49 )	95	49 / 50	2.9 ( 50 )	76	50 / 50	2.5 ( 48 )	66	48 / 50
41	3.8 ( 50 )	50 / 50	3.7 ( 49 )	97	49 / 50	3.0 ( 50 )	79	50 / 50	2.6 ( 48 )	68	48 / 50
45	4.0 ( 50 )	50 / 50	3.7 ( 49 )	93	49 / 50	3.1 ( 50 )	78	50 / 50	2.7 ( 48 )	68	48 / 50
49	4.1 ( 50 )	50 / 50	3.8 ( 49 )	93	49 / 50	3.2 ( 50 )	78	50 / 50	2.8 ( 48 )	68	48 / 50
53	4.1 ( 49 )	49 / 50	3.8 ( 49 )	93	49 / 50	3.2 ( 50 )	78	50 / 50	2.7 ( 48 )	66	48 / 50
57	4.2 ( 48 )	48 / 50	3.9 ( 49 )	93	49 / 50	3.2 ( 50 )	76	50 / 50	2.8 ( 48 )	67	48 / 50
61	4.2 ( 48 )	48 / 50	3.8 ( 49 )	90	49 / 50	3.3 ( 50 )	79	50 / 50	2.6 ( 48 )	62	48 / 50
65	4.4 ( 48 )	48 / 50	4.0 ( 49 )	91	49 / 50	3.5 ( 50 )	80	50 / 50	2.9 ( 48 )	66	48 / 50
69	4.4 ( 48 )	48 / 50	4.1 ( 49 )	93	49 / 50	3.5 ( 50 )	80	50 / 50	2.8 ( 48 )	64	48 / 50
73	4.5 ( 46 )	46 / 50	4.0 ( 49 )	89	49 / 50	3.5 ( 50 )	78	50 / 50	3.0 ( 48 )	67	48 / 50
77	4.6 ( 45 )	45 / 50	4.2 ( 49 )	91	49 / 50	3.6 ( 50 )	78	50 / 50	3.1 ( 48 )	67	48 / 50
78	4.7 ( 42 )	42 / 50	4.3 ( 49 )	91	49 / 50	3.7 ( 50 )	79	50 / 50	3.2 ( 47 )	68	47 / 50
82	4.5 ( 41 )	42 / 50	4.0 ( 48 )	89	48 / 50	3.5 ( 50 )	78	50 / 50	2.9 ( 47 )	64	47 / 50
86	4.6 ( 40 )	40 / 50	4.3 ( 46 )	93	46 / 50	3.8 ( 48 )	83	48 / 50	3.0 ( 45 )	65	45 / 50
90	4.5 ( 36 )	38 / 50	4.1 ( 43 )	91	44 / 50	3.8 ( 47 )	84	47 / 50	3.0 ( 43 )	67	43 / 50
94	4.5 ( 36 )	38 / 50	4.0 ( 41 )	89	42 / 50	3.6 ( 46 )	80	46 / 50	3.2 ( 42 )	71	42 / 50
98	4.8 ( 37 )	38 / 50	4.2 ( 39 )	88	41 / 50	3.8 ( 42 )	79	43 / 50	3.2 ( 42 )	67	42 / 50
102	4.7 ( 34 )	38 / 50	4.2 ( 35 )	89	35 / 50	3.7 ( 42 )	79	42 / 50	3.1 ( 41 )	66	41 / 50
104	4.8 ( 32 )	35 / 50	4.1 ( 35 )	85	35 / 50	3.8 ( 42 )	79	42 / 50	3.3 ( 41 )	69	41 / 50

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

TABLE 6 WATER CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL

Week on Study	Control		5000 ppm			10000 ppm			20000 ppm		
	Av. WC. <50>	No. of Surviv.	Av. WC.	% of cont. <50>	No. of Surviv.	Av. WC.	% of cont. <50>	No. of Surviv.	Av. WC.	% of cont. <50>	No. of Surviv.
1	4.2 ( 50 )	50 / 50	3.8 ( 50 )	90	50 / 50	2.9 ( 49 )	69	50 / 50	2.5 ( 50 )	60	50 / 50
2	4.2 ( 50 )	50 / 50	3.7 ( 50 )	88	50 / 50	3.1 ( 50 )	74	50 / 50	2.3 ( 49 )	55	50 / 50
3	4.2 ( 50 )	50 / 50	3.8 ( 50 )	90	50 / 50	3.2 ( 50 )	76	50 / 50	2.5 ( 50 )	60	50 / 50
4	4.3 ( 50 )	50 / 50	3.9 ( 50 )	91	50 / 50	3.3 ( 50 )	77	50 / 50	2.6 ( 50 )	60	50 / 50
5	4.2 ( 50 )	50 / 50	3.8 ( 50 )	90	50 / 50	3.4 ( 50 )	81	50 / 50	2.6 ( 50 )	62	50 / 50
6	4.2 ( 50 )	50 / 50	3.9 ( 50 )	93	50 / 50	3.3 ( 50 )	79	50 / 50	2.6 ( 50 )	62	50 / 50
7	4.2 ( 50 )	50 / 50	3.7 ( 50 )	88	50 / 50	3.3 ( 50 )	79	50 / 50	2.6 ( 50 )	62	50 / 50
8	4.3 ( 50 )	50 / 50	3.8 ( 50 )	88	50 / 50	3.3 ( 50 )	77	50 / 50	2.6 ( 50 )	60	50 / 50
9	4.4 ( 50 )	50 / 50	4.0 ( 50 )	91	50 / 50	3.5 ( 50 )	80	50 / 50	2.8 ( 50 )	64	50 / 50
10	4.4 ( 50 )	50 / 50	4.0 ( 50 )	91	50 / 50	3.4 ( 50 )	77	50 / 50	2.7 ( 49 )	61	50 / 50
11	4.2 ( 50 )	50 / 50	3.8 ( 50 )	90	50 / 50	3.4 ( 50 )	81	50 / 50	2.7 ( 50 )	64	50 / 50
12	4.3 ( 50 )	50 / 50	3.9 ( 50 )	91	50 / 50	3.5 ( 50 )	81	50 / 50	2.8 ( 50 )	65	50 / 50
13	4.2 ( 50 )	50 / 50	3.8 ( 50 )	90	50 / 50	3.2 ( 50 )	76	50 / 50	2.7 ( 50 )	64	50 / 50
17	4.2 ( 50 )	50 / 50	3.7 ( 50 )	88	50 / 50	3.2 ( 50 )	76	50 / 50	2.8 ( 50 )	67	50 / 50
21	4.3 ( 50 )	50 / 50	3.7 ( 50 )	86	50 / 50	3.3 ( 50 )	77	50 / 50	3.0 ( 50 )	70	50 / 50
25	4.2 ( 50 )	50 / 50	3.5 ( 50 )	83	50 / 50	3.0 ( 50 )	71	50 / 50	2.7 ( 50 )	64	50 / 50
29	4.0 ( 49 )	50 / 50	3.4 ( 50 )	85	50 / 50	3.0 ( 50 )	75	50 / 50	2.6 ( 50 )	65	50 / 50
33	4.1 ( 50 )	50 / 50	3.5 ( 50 )	85	50 / 50	2.9 ( 50 )	71	50 / 50	2.6 ( 50 )	63	50 / 50
37	3.9 ( 49 )	50 / 50	3.5 ( 50 )	90	50 / 50	3.0 ( 50 )	77	50 / 50	2.6 ( 50 )	67	50 / 50
41	4.2 ( 49 )	49 / 50	3.5 ( 50 )	83	50 / 50	3.0 ( 49 )	71	49 / 50	2.4 ( 50 )	57	50 / 50
45	4.2 ( 47 )	47 / 50	3.6 ( 50 )	86	50 / 50	3.1 ( 49 )	74	49 / 50	2.5 ( 50 )	60	50 / 50
49	4.2 ( 47 )	47 / 50	3.5 ( 50 )	83	50 / 50	3.0 ( 49 )	71	49 / 50	2.5 ( 48 )	60	48 / 50
53	4.3 ( 47 )	47 / 50	3.5 ( 50 )	81	50 / 50	3.1 ( 48 )	72	48 / 50	2.6 ( 48 )	60	48 / 50
57	4.4 ( 47 )	47 / 50	3.6 ( 48 )	82	48 / 50	3.1 ( 48 )	70	48 / 50	2.6 ( 47 )	59	47 / 50
61	4.3 ( 47 )	47 / 50	3.5 ( 48 )	81	48 / 50	3.0 ( 48 )	70	48 / 50	2.5 ( 47 )	58	47 / 50
65	4.4 ( 46 )	46 / 50	3.6 ( 48 )	82	48 / 50	3.1 ( 48 )	70	48 / 50	2.7 ( 46 )	61	46 / 50
69	4.4 ( 46 )	46 / 50	3.5 ( 48 )	80	48 / 50	3.2 ( 48 )	73	48 / 50	2.7 ( 45 )	61	45 / 50
73	4.3 ( 45 )	45 / 50	3.5 ( 48 )	81	48 / 50	3.0 ( 48 )	70	48 / 50	2.6 ( 45 )	60	45 / 50
77	4.3 ( 44 )	44 / 50	3.4 ( 47 )	79	47 / 50	3.0 ( 47 )	70	47 / 50	2.7 ( 44 )	63	44 / 50
78	4.2 ( 44 )	44 / 50	3.5 ( 47 )	83	47 / 50	2.9 ( 45 )	69	45 / 50	2.7 ( 44 )	64	44 / 50
82	4.3 ( 43 )	43 / 50	3.4 ( 47 )	79	47 / 50	3.2 ( 44 )	74	44 / 50	2.8 ( 43 )	65	43 / 50
86	4.2 ( 38 )	39 / 50	3.4 ( 45 )	81	45 / 50	3.1 ( 42 )	74	43 / 50	2.7 ( 43 )	64	43 / 50
90	4.2 ( 37 )	37 / 50	3.4 ( 44 )	81	44 / 50	3.1 ( 41 )	74	41 / 50	2.7 ( 40 )	64	40 / 50
94	4.4 ( 33 )	33 / 50	3.4 ( 39 )	77	39 / 50	3.3 ( 40 )	75	40 / 50	2.8 ( 38 )	64	38 / 50
98	4.9 ( 29 )	29 / 50	3.6 ( 37 )	73	37 / 50	3.1 ( 35 )	63	35 / 50	2.9 ( 37 )	59	37 / 50
102	4.6 ( 24 )	25 / 50	3.7 ( 36 )	80	36 / 50	3.3 ( 33 )	72	33 / 50	2.9 ( 35 )	63	35 / 50
104	4.6 ( 23 )	24 / 50	3.8 ( 34 )	83	34 / 50	3.2 ( 32 )	70	32 / 50	2.9 ( 34 )	63	34 / 50

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

TABLE 7 HEMATOLOGY OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL

Group Name	Control	5000 ppm	10000 ppm	20000 ppm
No. of examined animals	35	34	41	40
WBC ( $10^3/\mu\text{L}$ )	3.09 $\pm$ 1.56	3.53 $\pm$ 3.25	2.95 $\pm$ 1.55	2.28 $\pm$ 1.14 *
Mean $\pm$ S.D.				
Significant difference: * : $p \leq 0.05$ ** : $p \leq 0.01$ Test of Dunnett				

TABLE 8 HEMATOLOGY OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL

Group Name	Control	5000 ppm	10000 ppm	20000 ppm
No. of examined animals	22	34	32	34
HEMATOCRIT (%)	40.0 $\pm$ 6.4	41.9 $\pm$ 4.8	42.6 $\pm$ 2.9	43.8 $\pm$ 2.8 *
Mean $\pm$ S.D.				
Significant difference: * : $p \leq 0.05$ ** : $p \leq 0.01$ Test of Dunnett				

TABLE 9 BIOCHEMISTRY OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL

Group Name	Control	5000 ppm	10000 ppm	20000 ppm
No. of examined animals	35	34	41	40
A/G RATIO	1.1 ± 0.2	1.2 ± 0.2	1.2 ± 0.1 *	1.2 ± 0.2 **
T-CHOLESTEROL (mg/dL)	112 ± 44	108 ± 33	97 ± 24 *	100 ± 29 *
TRIGLYCERIDE (mg/dL)	39 ± 20	44 ± 34	34 ± 19	25 ± 14 **
PHOSPHOLIPID (mg/dL)	197 ± 68	191 ± 50	175 ± 35 *	181 ± 44 *
ALT (IU/L)	56 ± 78	49 ± 60	36 ± 45 **	30 ± 34 **
POTASSIUM (mEq/L)	4.2 ± 0.3	4.3 ± 0.6	4.1 ± 0.3	4.0 ± 0.4 *

Mean ± S.D.  
Significant difference: \* :  $p \leq 0.05$  \*\* :  $p \leq 0.01$  Test of Dunnett

TABLE 10 BIOCHEMISTRY OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL

Group Name	Control	5000 ppm	10000 ppm	20000 ppm
No. of examined animals	22	34	31	33
A/G RATIO	1.2 ± 0.3	1.3 ± 0.2	1.3 ± 0.2	1.4 ± 0.2 *
TRIGLYCERIDE (mg/dL)	34 ± 27	36 ± 33	29 ± 17	18 ± 10 *
AST (IU/L)	125 ± 110	90 ± 40	109 ± 83	81 ± 58 **
ALT (IU/L)	48 ± 46	34 ± 19	49 ± 60	25 ± 15 **
LDH (IU/L)	809 ± 1860	484 ± 584	424 ± 641	245 ± 149 **
ALP (IU/L)	215 ± 112	168 ± 61	218 ± 67	239 ± 81 *
SODIUM (mEq/L)	152 ± 2	153 ± 2	153 ± 2	155 ± 2 **
CHLORIDE (mEq/L)	121 ± 4	121 ± 3	122 ± 2	123 ± 4 *
CALCIUM (mg/dL)	9.1 ± 0.7	9.0 ± 0.5	9.0 ± 0.4	8.8 ± 0.5 **

Mean ± S.D.  
Significant difference: \* :  $p \leq 0.05$  \*\* :  $p \leq 0.01$  Test of Dunnett

TABLE 11 URINALYSIS OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL

Group Name		Control	5000 ppm	10000 ppm	20000 ppm
No. of examined animals		35	35	42	41
pH	Grade				
	5.0	0	0	0	0
	6.0	3	7	11	10
	6.5	8	13	26	22
	7.0	13	11	5	9
	7.5	8	4	0	0
	8.0	2	0	0	0
	8.5	1	0	0	0
	Chi square test			**	**

Significant difference: \* :  $p \leq 0.05$  \*\* :  $p \leq 0.01$

TABLE 12 URINALYSIS OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL

Group Name		Control	5000 ppm	10000 ppm	20000 ppm
No. of examined animals		25	35	33	34
pH	Grade				
	5.0	0	0	0	0
	6.0	0	1	2	4
	6.5	4	6	10	12
	7.0	3	9	10	14
	7.5	3	10	10	4
	8.0	13	9	1	0
	8.5	2	0	0	0
	Chi square test			**	**
Ketone body	—	6	0	3	1
	±	10	14	5	13
	+	6	14	17	10
	2+	3	7	7	10
	3+	0	0	1	0
	4+	0	0	0	0
		Chi square test		*	*

Significant difference: \* :  $p \leq 0.05$  \*\* :  $p \leq 0.01$

TABLE 13 ORGAN WEIGHTS OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL

Group Name	Control	5000 ppm	10000 ppm	20000 ppm
No. of examined animals	35	35	42	41
Body weight (g)	45.0 ± 7.8	44.5 ± 8.0	37.9 ± 5.6	32.3 ± 4.3
Adrenals (g)	0.011 ± 0.002	0.011 ± 0.002	0.011 ± 0.002	0.011 ± 0.003
Adrenals (%)	0.026 ± 0.007	0.025 ± 0.007	0.029 ± 0.007	0.035 ± 0.010
Testes (g)	0.233 ± 0.028	0.228 ± 0.025	0.256 ± 0.213	0.217 ± 0.027
Testes (%)	0.532 ± 0.112	0.529 ± 0.117	0.699 ± 0.655	0.681 ± 0.123
Heart (g)	0.227 ± 0.021	0.221 ± 0.029	0.202 ± 0.020	0.185 ± 0.016
Heart (%)	0.520 ± 0.112	0.512 ± 0.111	0.542 ± 0.071	0.580 ± 0.066
Lungs (g)	0.200 ± 0.026	0.244 ± 0.126	0.212 ± 0.089	0.202 ± 0.078
Lungs (%)	0.456 ± 0.093	0.580 ± 0.431	0.571 ± 0.273	0.631 ± 0.240
Kidneys (g)	0.646 ± 0.044	0.668 ± 0.078	0.638 ± 0.059	0.840 ± 1.256
Kidneys (%)	1.476 ± 0.280	1.538 ± 0.274	1.707 ± 0.201	2.623 ± 3.835
Liver (g)	1.661 ± 0.458	1.985 ± 1.090	1.524 ± 0.381	1.379 ± 0.281
Liver (%)	3.826 ± 1.610	4.603 ± 2.639	4.095 ± 1.194	4.315 ± 1.005
Brain (g)	0.449 ± 0.015	0.445 ± 0.015	0.443 ± 0.017	0.436 ± 0.013
Brain (%)	1.027 ± 0.191	1.035 ± 0.212	1.192 ± 0.172	1.368 ± 0.169

Mean ± S.D.  
Significant difference: \* :  $p \leq 0.05$  \*\* :  $p \leq 0.01$  Test of Dunnett

TABLE 14 ORGAN WEIGHTS OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL

Group Name	Control	5000 ppm	10000 ppm	20000 ppm
No. of examined animals	24	34	32	34
Body weight (g)	31.3 ± 5.3	31.9 ± 4.0	29.4 ± 4.1	24.8 ± 2.5
Heart (g)	0.182 ± 0.031	0.172 ± 0.020	0.163 ± 0.017	0.153 ± 0.018
Heart (%)	0.595 ± 0.136	0.542 ± 0.053	0.565 ± 0.090	0.621 ± 0.073
Lungs (g)	0.219 ± 0.079	0.200 ± 0.026	0.190 ± 0.019	0.188 ± 0.019
Lungs (%)	0.717 ± 0.286	0.635 ± 0.109	0.658 ± 0.110	0.763 ± 0.087
Kidneys (g)	0.569 ± 0.356	0.461 ± 0.064	0.457 ± 0.042	0.444 ± 0.057
Kidneys (%)	1.926 ± 1.548	1.461 ± 0.226	1.581 ± 0.222	1.807 ± 0.282
Spleen (g)	0.419 ± 0.967	0.210 ± 0.127	0.169 ± 0.165	0.118 ± 0.109
Spleen (%)	1.391 ± 3.281	0.657 ± 0.380	0.581 ± 0.564	0.486 ± 0.478
Liver (g)	1.514 ± 0.365	1.659 ± 0.786	1.864 ± 2.509	1.190 ± 0.176
Liver (%)	4.906 ± 1.265	5.171 ± 2.049	6.144 ± 7.081	4.804 ± 0.529
Brain (g)	0.466 ± 0.016	0.465 ± 0.016	0.461 ± 0.016	0.455 ± 0.017
Brain (%)	1.522 ± 0.234	1.483 ± 0.210	1.599 ± 0.229	1.854 ± 0.166

Mean ± S.D.  
Significant difference: \* :  $p \leq 0.05$  \*\* :  $p \leq 0.01$  Test of Dunnett



TABLE 15 INCIDENCES OF SELECTED NEOPLASTIC LESIONS OF MALE MICE  
IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL

Group Name	Control	5000 ppm	10000 ppm	20000 ppm	Peto test	Cochran- Armitage test
Number of examined animals	50	50	50	50		
liver	<50>	<50>	<50>	<50>		
hepatocellular adenoma 1)	17 (34 %)	14 (28 %)	7 (14 %) *	6 (12 %) **		↓ ↓
hepatocellular carcinoma 2)	3 ( 6 %)	3 ( 6 %)	1 ( 2 %)	1 ( 2 %)		
hepatoblastoma 3)	0 ( 0 %)	1 ( 2 %)	0 ( 0 %)	0 ( 0 %)		
1) + 2)	19 (38 %)	16 (32 %)	8 (16 %) *	7 (14 %) **		↓ ↓
1) + 2) + 3)	19 (38 %)	17 (34 %)	8 (16 %) *	7 (14 %) **		↓ ↓
all site	<50>	<50>	<50>	<50>		
malignant lymphoma	2 ( 4 %)	8 (16 %) *	8 (16 %) *	4 ( 8 %)		
Significant difference: * : $p \leq 0.05$ ** : $p \leq 0.01$			Fisher's exact test for neoplastic lesion			
↑(↓) : $p \leq 0.05$ ↑↑(↓↓) : $p \leq 0.01$			Peto or Cochran-Armitage test for neoplastic lesion			
< > : Number of animals examined at the site						

TABLE 16 INCIDENCES OF SELECTED NON-NEOPLASTIC LESIONS OF MALE MICE  
IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL

Group Name	Control				5000 ppm				10000 ppm				20000 ppm			
Number of examined animals	50				50				50				50			
Grade of non-neoplastic lesion	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>
adrenal spindle-cell hyperplasia	<50>				<50>				<50>				<50>			
	8	0	0	0	7	0	0	0	6	1	0	0	0	0	0	0**

Grade 1: Slight 2: Moderate 3: Marked 4: Severe  
 < > : Number of animals examined at the site  
 Significant difference: \* :  $p \leq 0.05$  \*\* :  $p \leq 0.01$  Test of Chi Square

TABLE 17 INCIDENCES OF SELECTED NON-NEOPLASTIC LESIONS OF FEMALE MICE  
IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL

Group Name	Control				5000 ppm				10000 ppm				20000 ppm			
Number of examined animals	50				50				50				50			
Grade of non-neoplastic lesion	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>
adrenal spindle-cell hyperplasia	<50>				<50>				<50>				<50>			
	23	0	0	0	26	0	0	0	34	0	0	0*	29	0	0	0

Grade 1: Slight 2: Moderate 3: Marked 4: Severe  
 < > : Number of animals examined at the site  
 Significant difference: \* :  $p \leq 0.05$  \*\* :  $p \leq 0.01$  Test of Chi Square

TABLE 18 HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS  
IN JAPAN BIOASSAY RESEARCH CENTER : B6D2F1/Crlj MALE MICE

Organs Tumors	No. of animals examined	No. of animals bearing tumor	Incidence (%)	Min. - Max. (%)
Lymph node Malignant lymphoma	1796	212	11.8	2 - 28
Thymus Malignant lymphoma	1796	2	0.1	0 - 2
Spleen Malignant lymphoma	1795	64	3.6	0 - 10
All site Malignant lymphoma	1796	278	15.5	2 - 28

36 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,  
0402, 0406, 0418, 0422, 0438, 0449, 0458, 0462

TABLE 19 CAUSE OF DEATH OF MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL

Group name	Male				Female			
	Control	5000 ppm	10000 ppm	20000 ppm	Control	5000 ppm	10000 ppm	20000 ppm
Number of dead or moribund animals	15	15	8	9	26	16	18	16
No microscopical confirmation	0	1	1	1	0	0	1	0
integumentary system lesion	1	1	0	0	0	0	0	0
hepatic lesion	0	0	0	0	1	0	0	0
renal lesion	1	1	0	0	1	0	1	0
hemorrhage	0	0	0	0	0	1	0	0
urinary retention	1	0	1	0	0	0	0	0
arteritis	0	0	0	1	0	0	2	1
tooth lesion	0	0	0	0	0	0	1	0
hydronephrosis	1	0	0	1	1	0	0	0
peritonitis	0	1	0	0	0	0	0	1
Tumor death : leukemia	1	3	1	2	9	8	3	3
subcutis	1	0	0	0	1	0	1	1
nasal cavity	1	0	0	0	0	0	0	0
lung	1	1	0	0	0	0	0	0
spleen	1	0	0	0	1	0	0	1
salivary gland	1	0	0	0	0	0	0	0
stomach	0	1	0	0	0	0	0	0
small intestine	0	0	0	0	0	0	0	1
liver	4	5	4	2	1	1	2	1
urinary bladder	0	1	0	0	0	0	0	0
urethra	0	0	0	1	0	0	0	0
pituitary gland	0	0	0	0	1	0	0	0
epididymis	0	0	1	0	—	—	—	—
ovary	—	—	—	—	0	1	0	0
uterus	—	—	—	—	10	5	6	7
brain	0	0	0	0	0	0	1	0
peripheral nerves	0	0	0	1	0	0	0	0
retroperitoneum	1	0	0	0	0	0	0	0

## FIGURES

- FIGURE 1 SURVIVAL ANIMAL RATE OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL
- FIGURE 2 SURVIVAL ANIMAL RATE OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL
- FIGURE 3 BODY WEIGHT CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL
- FIGURE 4 BODY WEIGHT CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL
- FIGURE 5 FOOD CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL
- FIGURE 6 FOOD CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL
- FIGURE 7 WATER CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL
- FIGURE 8 WATER CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL

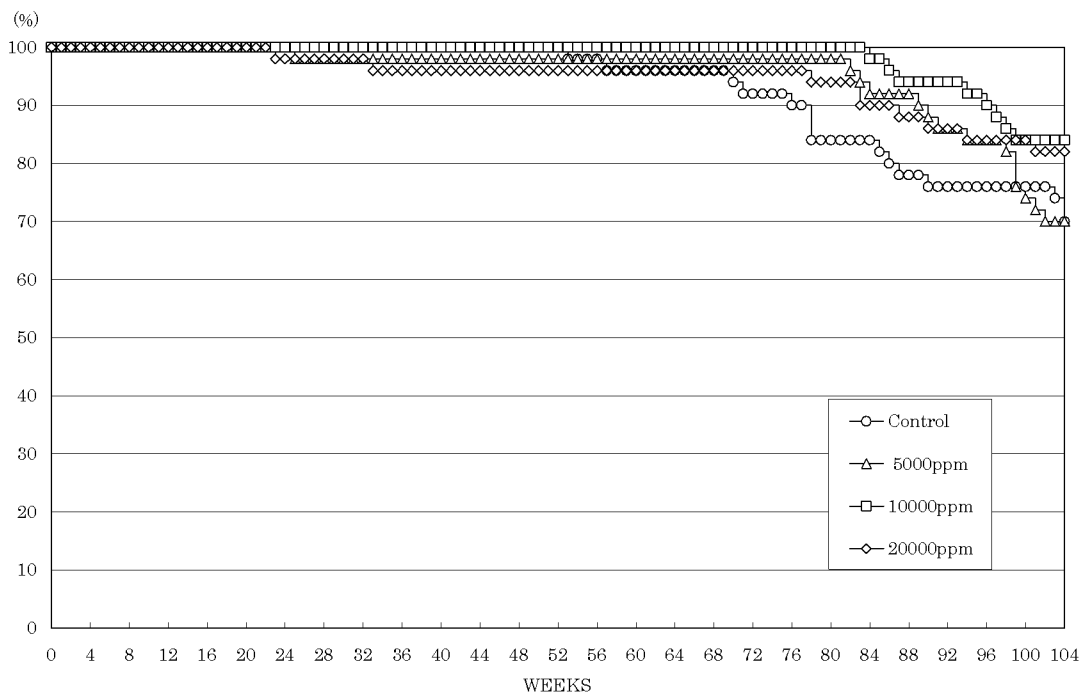


FIGURE 1 SURVIVAL ANIMAL RATE OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL

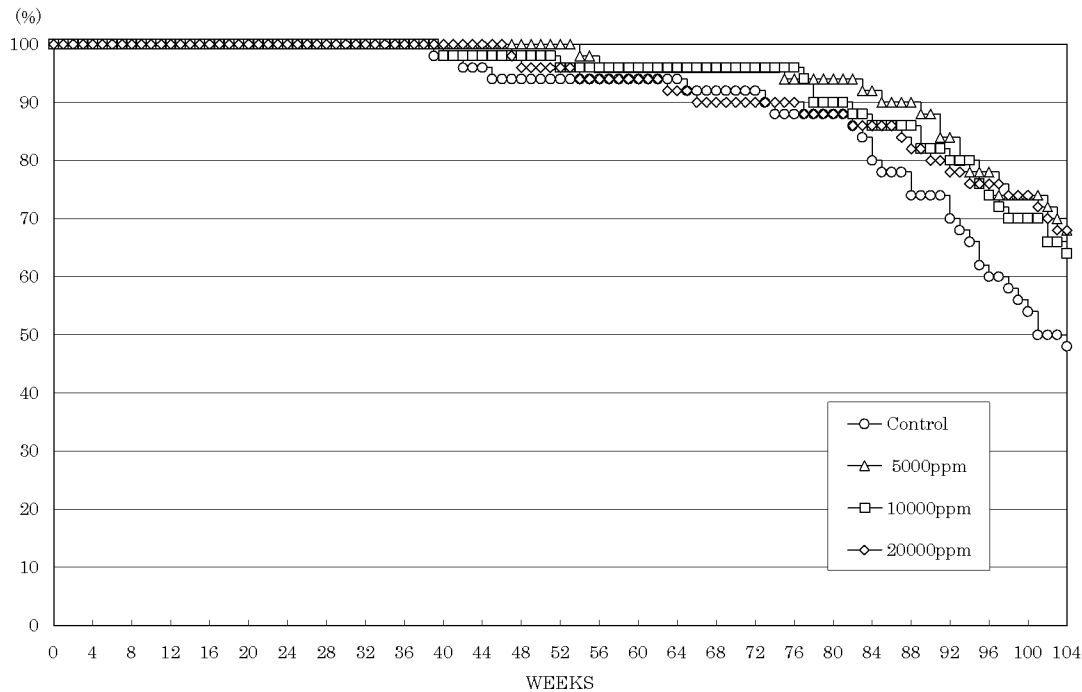


FIGURE 2 SURVIVAL ANIMAL RATE OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL

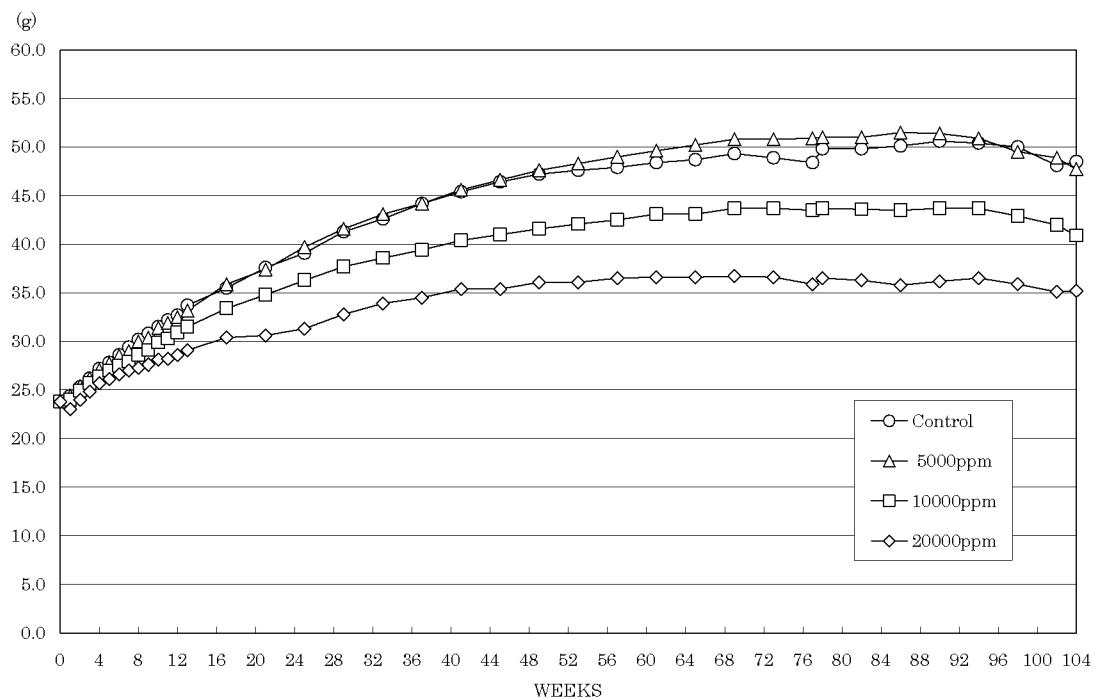


FIGURE 3 BODY WEIGHT CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL

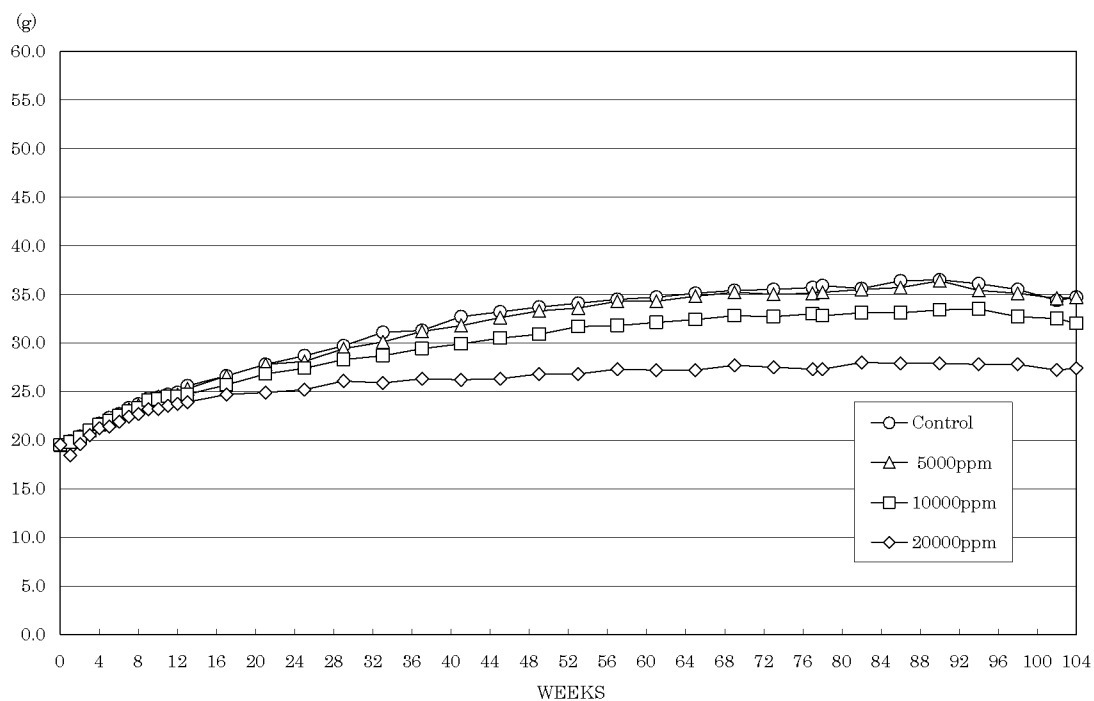


FIGURE 4 BODY WEIGHT CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL

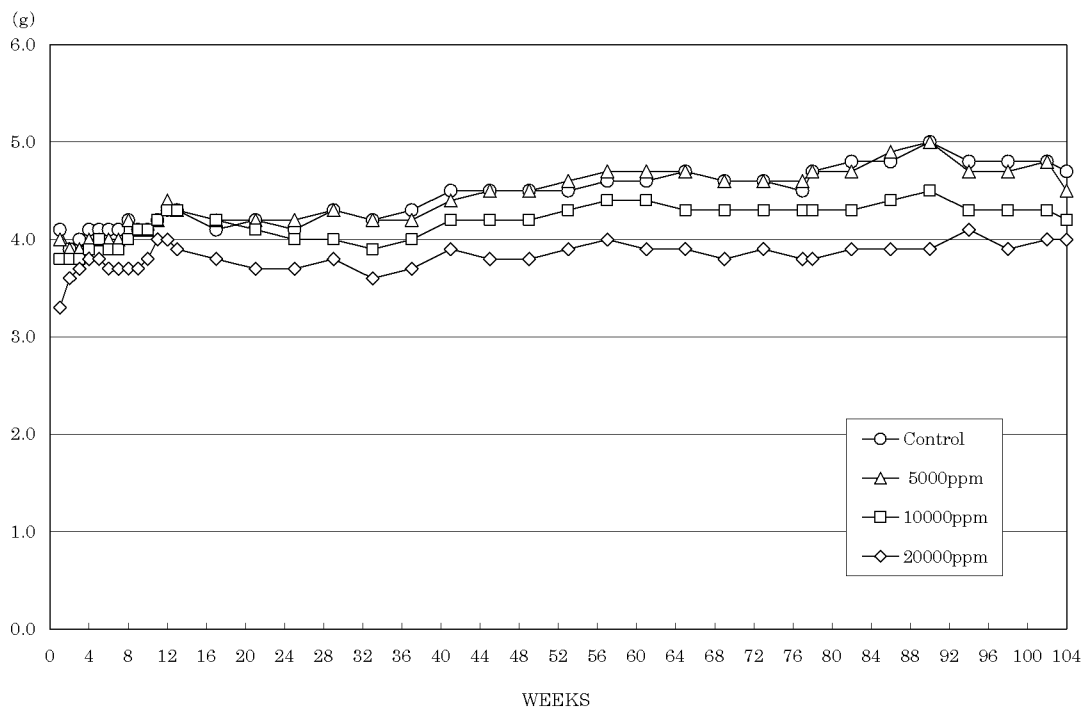


FIGURE 5 FOOD CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL

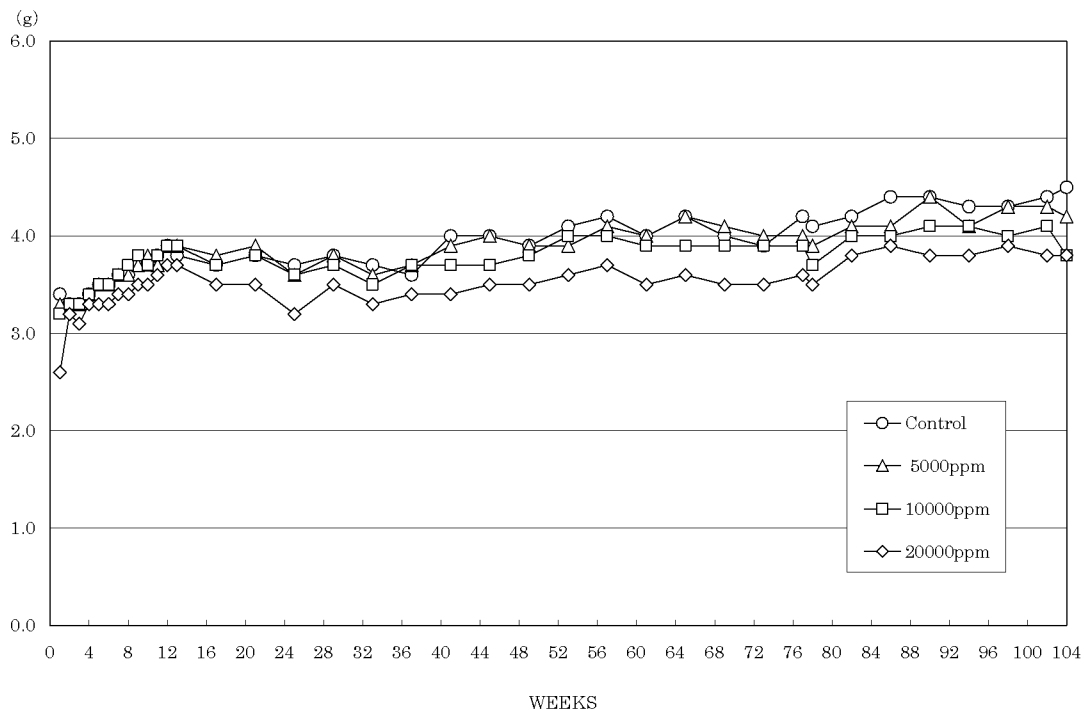


FIGURE 6 FOOD CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL



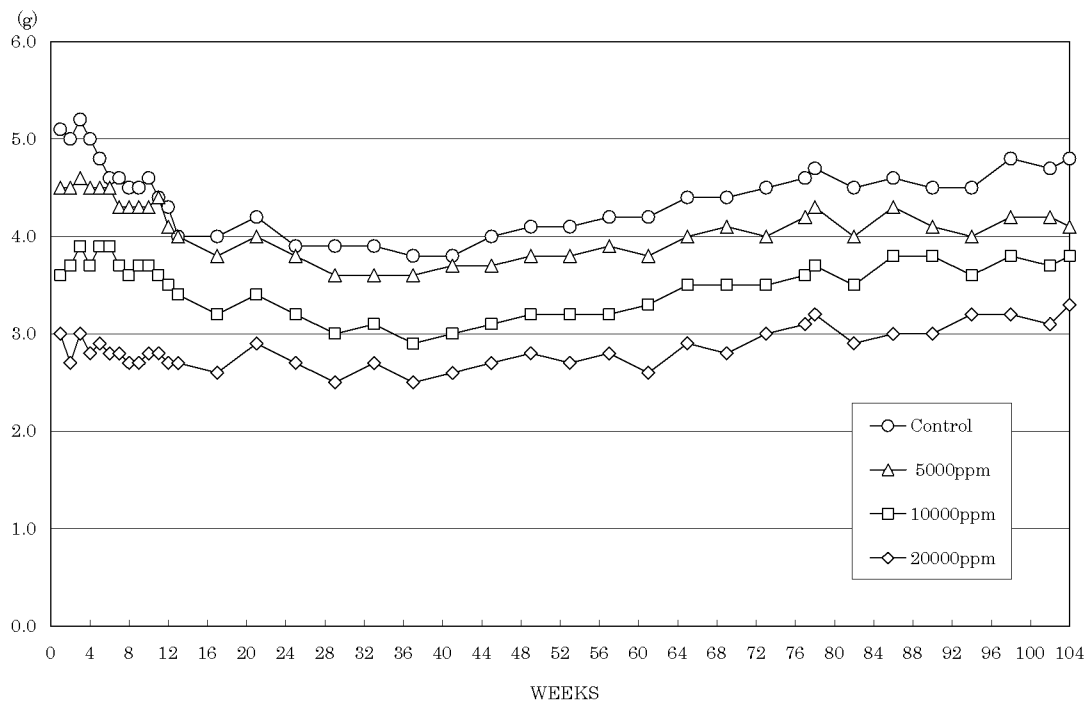


FIGURE 7 WATER CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL

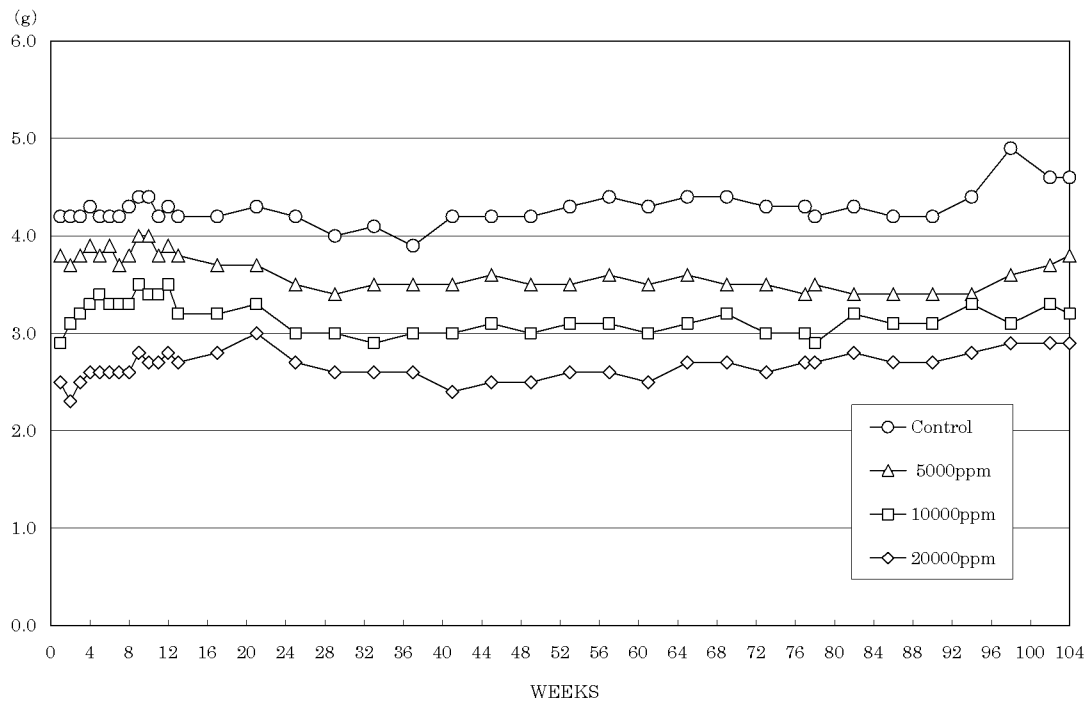


FIGURE 8 WATER CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF 2-PHENOXYETHANOL