アセト酢酸メチルのマウスを用いた
経口投与によるがん原性試験（混水試験）報告書

試験番号：0449

TABLES

TABLES

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

Week on Study	Control		2000 ppm			6325 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	23.5 (50)	50 / 50	23.5 (50)	100	50 / 50	23.5 (50)	100	50 / 50	23.5 (50)	100	50 / 50
1	24.8 (50)	50 / 50	24.7 (50)	100	50 / 50	24.5 (50)	99	50 / 50	24.6 (50)	99	50 / 50
2	25.5 (50)	50 / 50	25.5 (50)	100	50 / 50	25.4 (50)	100	50 / 50	25.4 (50)	100	50 / 50
3	26.0 (50)	50 / 50	26.1 (50)	100	50 / 50	25.9 (50)	100	50 / 50	26.1 (50)	100	50 / 50
4	27.0 (50)	50 / 50	27.0 (50)	100	50 / 50	26.7 (50)	99	50 / 50	27.1 (50)	100	50 / 50
5	27.7 (50)	50 / 50	27.8 (50)	100	50 / 50	27.5 (50)	99	50 / 50	27.7 (50)	100	50 / 50
6	28.2 (50)	50 / 50	28.6 (50)	101	50 / 50	28.2 (50)	100	50 / 50	28.5 (50)	101	50 / 50
7	28.9 (50)	50 / 50	29.1 (50)	101	50 / 50	28.5 (50)	99	50 / 50	28.9 (50)	100	50 / 50
8	29.4 (50)	50 / 50	29.8 (50)	101	50 / 50	29.2 (50)	99	50 / 50	29.5 (50)	100	50 / 50
9	30.4 (50)	50 / 50	30.8 (50)	101	50 / 50	29.9 (50)	98	50 / 50	30.3 (50)	100	50 / 50
10	31.0 (50)	50 / 50	31.5 (50)	102	50 / 50	30.7 (50)	99	50 / 50	31.1 (50)	100	50 / 50
11	31.8 (50)	50 / 50	32.2 (50)	101	50 / 50	31.6 (50)	99	50 / 50	31.8 (50)	100	50 / 50
12	32.8 (50)	50 / 50	33.1 (50)	101	50 / 50	32.3 (50)	98	50 / 50	32.7 (50)	100	50 / 50
13	33.2 (50)	50 / 50	33.5 (50)	101	50 / 50	32.9 (50)	99	50 / 50	32.8 (50)	99	50 / 50
14	33.9 (50)	50 / 50	34.6 (50)	102	50 / 50	33.6 (50)	99	50 / 50	33.7 (50)	99	50 / 50
18	35.9 (50)	50 / 50	36.7 (50)	102	50 / 50	35.7 (50)	99	50 / 50	35.7 (50)	99	50 / 50
22	38.3 (50)	50 / 50	39.3 (50)	103	50 / 50	38.2 (50)	100	50 / 50	38.5 (50)	101	50 / 50
26	39.8 (50)	50 / 50	40.8 (50)	103	50 / 50	39.9 (50)	100	50 / 50	39.8 (50)	100	50 / 50
30	41.4 (50)	50 / 50	42.8 (50)	103	50 / 50	41.5 (50)	100	50 / 50	41.3 (50)	100	50 / 50
34	42.2 (50)	50 / 50	43.7 (50)	104	50 / 50	42.5 (50)	101	50 / 50	42.2 (50)	100	50 / 50
38	43.6 (50)	50 / 50	45.2 (50)	104	50 / 50	43.9 (50)	101	50 / 50	43.6 (50)	100	50 / 50
42	44.9 (50)	50 / 50	46.6 (50)	104	50 / 50	45.1 (50)	100	50 / 50	44.9 (50)	100	50 / 50
46	45.7 (50)	50 / 50	47.5 (50)	104	50 / 50	46.3 (50)	101	50 / 50	45.8 (50)	100	50 / 50
50	46.5 (50)	50 / 50	48.5 (50)	104	50 / 50	47.4 (50)	102	50 / 50	46.7 (50)	100	50 / 50
54	47.9 (49)	49 / 50	49.3 (50)	103	50 / 50	48.0 (50)	100	50 / 50	47.9 (50)	100	50 / 50
58	49.3 (48)	48 / 50	50.5 (50)	102	50 / 50	49.0 (50)	99	50 / 50	48.8 (50)	99	50 / 50
62	49.5 (48)	48 / 50	50.8 (50)	103	50 / 50	49.2 (50)	99	50 / 50	49.2 (50)	99	50 / 50
66	50.1 (48)	48 / 50	50.9 (49)	102	49 / 50	49.9 (50)	100	50 / 50	49.7 (50)	99	50 / 50
70	50.2 (48)	48 / 50	50.8 (49)	101	49 / 50	49.7 (50)	99	50 / 50	49.8 (50)	99	50 / 50
74	50.9 (47)	47 / 50	52.3 (47)	103	47 / 50	50.5 (49)	99	49 / 50	49.9 (49)	98	49 / 50
78	52.0 (45)	45 / 50	53.1 (47)	102	47 / 50	51.0 (48)	98	48 / 50	51.3 (48)	99	48 / 50
82	52.1 (43)	43 / 50	53.1 (47)	102	47 / 50	51.7 (46)	99	46 / 50	51.2 (48)	98	48 / 50
86	50.7 (42)	42 / 50	52.9 (46)	104	46 / 50	51.3 (45)	101	45 / 50	51.0 (46)	101	46 / 50
90	50.7 (35)	35 / 50	52.3 (45)	103	45 / 50	51.4 (43)	101	43 / 50	51.4 (44)	101	44 / 50
94	48.9 (35)	35 / 50	51.7 (43)	106	43 / 50	50.3 (42)	103	42 / 50	50.3 (43)	103	43 / 50
98	49.9 (29)	29 / 50	51.7 (41)	104	41 / 50	49.5 (42)	99	42 / 50	50.8 (39)	102	39 / 50
102	50.1 (28)	28 / 50	50.3 (40)	100	40 / 50	48.6 (39)	97	39 / 50	50.1 (38)	100	38 / 50
104	51.4 (25)	25 / 50	50.0 (37)	97	37 / 50	47.2 (37)	92	37 / 50	49.7 (37)	97	37 / 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 METHYL ACETOACETATE

Week on Study	Control		2000 ppm			6325 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	19.8 (50)	50 / 50	19.8 (50)	100	50 / 50	19.8 (50)	100	50 / 50	19.8 (50)	100	50 / 50
1	20.3 (50)	50 / 50	20.4 (50)	100	50 / 50	20.3 (50)	100	50 / 50	20.1 (50)	99	50 / 50
2	20.4 (50)	50 / 50	20.7 (50)	101	50 / 50	20.7 (50)	101	50 / 50	20.7 (50)	101	50 / 50
3	20.8 (50)	50 / 50	21.0 (50)	101	50 / 50	20.9 (50)	100	50 / 50	20.9 (50)	100	50 / 50
4	21.3 (50)	50 / 50	21.4 (50)	100	50 / 50	21.7 (50)	102	50 / 50	21.6 (50)	101	50 / 50
5	21.9 (50)	50 / 50	21.9 (50)	100	50 / 50	22.0 (50)	100	50 / 50	21.8 (50)	100	50 / 50
6	22.4 (50)	50 / 50	22.9 (50)	102	50 / 50	22.7 (50)	101	50 / 50	22.2 (50)	99	50 / 50
7	22.6 (50)	50 / 50	22.7 (50)	100	50 / 50	22.6 (50)	100	50 / 50	22.5 (50)	100	50 / 50
8	23.0 (50)	50 / 50	23.2 (50)	101	50 / 50	23.0 (50)	100	50 / 50	23.2 (50)	101	50 / 50
9	23.5 (50)	50 / 50	23.7 (50)	101	50 / 50	23.6 (50)	100	50 / 50	23.6 (50)	100	50 / 50
10	24.0 (50)	50 / 50	24.1 (50)	100	50 / 50	24.0 (50)	100	50 / 50	23.8 (50)	99	50 / 50
11	24.1 (50)	50 / 50	24.1 (50)	100	50 / 50	24.3 (50)	101	50 / 50	24.1 (50)	100	50 / 50
12	24.3 (50)	50 / 50	24.7 (50)	102	50 / 50	24.5 (50)	101	50 / 50	24.0 (50)	99	50 / 50
13	24.4 (50)	50 / 50	24.8 (50)	102	50 / 50	24.7 (50)	101	50 / 50	24.3 (50)	100	50 / 50
14	24.8 (50)	50 / 50	24.9 (50)	100	50 / 50	24.9 (50)	100	50 / 50	24.6 (50)	99	50 / 50
18	25.6 (50)	50 / 50	25.7 (50)	100	50 / 50	25.8 (50)	101	50 / 50	25.7 (50)	100	50 / 50
22	27.0 (50)	50 / 50	27.2 (50)	101	50 / 50	27.0 (50)	100	50 / 50	26.5 (50)	98	50 / 50
26	27.3 (50)	50 / 50	27.8 (50)	102	50 / 50	28.1 (50)	103	50 / 50	27.4 (50)	100	50 / 50
30	27.9 (50)	50 / 50	28.7 (50)	103	50 / 50	28.8 (50)	103	50 / 50	28.3 (50)	101	50 / 50
34	28.5 (50)	50 / 50	29.2 (50)	102	50 / 50	29.3 (50)	103	50 / 50	28.6 (50)	100	50 / 50
38	29.2 (50)	50 / 50	30.1 (50)	103	50 / 50	30.2 (49)	103	49 / 50	29.3 (50)	100	50 / 50
42	29.8 (50)	50 / 50	30.8 (50)	103	50 / 50	30.8 (49)	103	49 / 50	30.0 (50)	101	50 / 50
46	30.6 (50)	50 / 50	31.4 (50)	103	50 / 50	32.0 (49)	105	49 / 50	30.5 (50)	100	50 / 50
50	31.2 (50)	50 / 50	32.3 (49)	104	49 / 50	32.5 (49)	104	49 / 50	31.3 (50)	100	50 / 50
54	31.9 (50)	50 / 50	32.9 (49)	103	49 / 50	33.0 (49)	103	49 / 50	31.4 (49)	98	49 / 50
58	32.3 (50)	50 / 50	33.9 (49)	105	49 / 50	33.7 (49)	104	49 / 50	32.1 (49)	99	49 / 50
62	32.8 (48)	48 / 50	33.8 (49)	103	49 / 50	34.7 (49)	106	49 / 50	32.6 (47)	99	47 / 50
66	33.6 (46)	46 / 50	34.4 (49)	102	49 / 50	34.9 (49)	104	49 / 50	33.3 (47)	99	47 / 50
70	33.0 (44)	44 / 50	34.1 (49)	103	49 / 50	34.9 (49)	106	49 / 50	33.4 (47)	101	47 / 50
74	33.6 (43)	43 / 50	34.3 (47)	102	47 / 50	35.1 (49)	104	49 / 50	33.2 (44)	99	44 / 50
78	34.2 (43)	43 / 50	35.4 (47)	104	47 / 50	35.8 (48)	105	48 / 50	33.8 (42)	99	42 / 50
82	34.8 (40)	40 / 50	35.4 (43)	102	43 / 50	35.9 (48)	103	48 / 50	33.7 (40)	97	40 / 50
86	34.7 (39)	39 / 50	35.2 (40)	101	40 / 50	36.1 (47)	104	47 / 50	33.7 (38)	97	38 / 50
90	34.7 (38)	38 / 50	34.5 (35)	99	35 / 50	35.9 (46)	103	46 / 50	33.6 (34)	97	34 / 50
94	34.6 (38)	38 / 50	35.0 (34)	101	34 / 50	36.0 (44)	104	44 / 50	34.1 (32)	99	32 / 50
98	34.4 (37)	37 / 50	34.6 (27)	101	27 / 50	35.9 (41)	104	41 / 50	33.6 (31)	98	31 / 50
102	33.9 (36)	36 / 50	34.5 (25)	102	25 / 50	35.6 (38)	105	38 / 50	32.8 (28)	97	28 / 50
104	33.9 (36)	36 / 50	33.5 (23)	99	23 / 50	35.7 (31)	105	31 / 50	32.3 (26)	95	26 / 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 METHYL ACETOACETATE

Week on Study	Control		2000 ppm			6325 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	3.8 (50)	50 / 50	3.7 (50)	97	50 / 50	3.8 (50)	100	50 / 50	3.8 (50)	100	50 / 50
2	3.7 (50)	50 / 50	3.7 (50)	100	50 / 50	4.2 (50)	114	50 / 50	4.2 (50)	114	50 / 50
3	3.7 (50)	50 / 50	3.7 (50)	100	50 / 50	3.7 (50)	100	50 / 50	3.7 (50)	100	50 / 50
4	3.7 (50)	50 / 50	3.7 (50)	100	50 / 50	3.8 (50)	103	50 / 50	3.8 (50)	103	50 / 50
5	3.8 (50)	50 / 50	3.9 (50)	103	50 / 50	3.9 (50)	103	50 / 50	3.8 (50)	100	50 / 50
6	3.8 (50)	50 / 50	3.9 (50)	103	50 / 50	3.9 (50)	103	50 / 50	3.9 (50)	103	50 / 50
7	3.9 (50)	50 / 50	3.9 (50)	100	50 / 50	3.9 (50)	100	50 / 50	3.9 (50)	100	50 / 50
8	3.9 (50)	50 / 50	4.0 (50)	103	50 / 50	4.0 (50)	103	50 / 50	4.0 (50)	103	50 / 50
9	3.9 (50)	50 / 50	3.9 (50)	100	50 / 50	3.9 (50)	100	50 / 50	3.8 (50)	97	50 / 50
10	3.9 (50)	50 / 50	4.0 (50)	103	50 / 50	4.0 (50)	103	50 / 50	4.0 (50)	103	50 / 50
11	3.9 (50)	50 / 50	4.0 (50)	103	50 / 50	4.0 (50)	103	50 / 50	4.0 (50)	103	50 / 50
12	4.0 (50)	50 / 50	4.0 (50)	100	50 / 50	4.0 (50)	100	50 / 50	4.0 (50)	100	50 / 50
13	4.0 (50)	50 / 50	3.9 (50)	98	50 / 50	4.0 (50)	100	50 / 50	3.9 (50)	98	50 / 50
14	4.1 (50)	50 / 50	4.1 (50)	100	50 / 50	4.1 (50)	100	50 / 50	4.1 (50)	100	50 / 50
18	4.1 (50)	50 / 50	4.2 (50)	102	50 / 50	4.1 (50)	100	50 / 50	4.0 (50)	98	50 / 50
22	4.2 (50)	50 / 50	4.2 (50)	100	50 / 50	4.1 (50)	98	50 / 50	4.0 (50)	95	50 / 50
26	4.1 (50)	50 / 50	4.4 (50)	107	50 / 50	4.4 (50)	107	50 / 50	4.3 (50)	105	50 / 50
30	4.2 (50)	50 / 50	4.3 (50)	102	50 / 50	4.3 (50)	102	50 / 50	4.2 (50)	100	50 / 50
34	4.2 (50)	50 / 50	4.3 (50)	102	50 / 50	4.3 (50)	102	50 / 50	4.2 (50)	100	50 / 50
38	4.3 (50)	50 / 50	4.4 (50)	102	50 / 50	4.3 (50)	100	50 / 50	4.2 (50)	98	50 / 50
42	4.4 (50)	50 / 50	4.5 (50)	102	50 / 50	4.4 (50)	100	50 / 50	4.3 (50)	98	50 / 50
46	4.5 (50)	50 / 50	4.5 (50)	100	50 / 50	4.5 (50)	100	50 / 50	4.4 (50)	98	50 / 50
50	4.4 (50)	50 / 50	4.4 (50)	100	50 / 50	4.4 (50)	100	50 / 50	4.2 (50)	95	50 / 50
54	4.4 (49)	49 / 50	4.5 (50)	102	50 / 50	4.4 (50)	100	50 / 50	4.3 (50)	98	50 / 50
58	4.5 (48)	48 / 50	4.5 (47)	100	50 / 50	4.5 (50)	100	50 / 50	4.3 (50)	96	50 / 50
62	4.5 (48)	48 / 50	4.6 (50)	102	50 / 50	4.6 (50)	102	50 / 50	4.4 (50)	98	50 / 50
66	4.5 (48)	48 / 50	4.6 (49)	102	49 / 50	4.6 (50)	102	50 / 50	4.4 (50)	98	50 / 50
70	4.7 (48)	48 / 50	4.7 (49)	100	49 / 50	4.6 (50)	98	50 / 50	4.5 (50)	96	50 / 50
74	4.5 (47)	47 / 50	4.7 (47)	104	47 / 50	4.6 (49)	102	49 / 50	4.4 (49)	98	49 / 50
78	4.6 (45)	45 / 50	4.8 (47)	104	47 / 50	4.7 (48)	102	48 / 50	4.5 (48)	98	48 / 50
82	4.7 (43)	43 / 50	4.7 (47)	100	47 / 50	4.7 (46)	100	46 / 50	4.6 (48)	98	48 / 50
86	4.5 (42)	42 / 50	4.8 (46)	107	46 / 50	4.7 (45)	104	45 / 50	4.5 (46)	100	46 / 50
90	4.6 (35)	35 / 50	4.8 (45)	104	45 / 50	4.7 (43)	102	43 / 50	4.5 (44)	98	44 / 50
94	4.6 (35)	35 / 50	4.8 (43)	104	43 / 50	4.7 (42)	102	42 / 50	4.3 (43)	93	43 / 50
98	4.6 (29)	29 / 50	4.6 (41)	100	41 / 50	4.5 (42)	98	42 / 50	4.4 (39)	96	39 / 50
102	4.5 (28)	28 / 50	4.6 (40)	102	40 / 50	4.5 (39)	100	39 / 50	4.4 (38)	98	38 / 50
104	4.9 (24)	25 / 50	4.7 (35)	96	37 / 50	4.5 (37)	92	37 / 50	4.6 (37)	94	37 / 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 METHYL ACETOACETATE

Week on Study	Control		2000 ppm			6325 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	3.3 (50)	50 / 50	3.3 (50)	100	50 / 50	3.3 (50)	100	50 / 50	3.2 (50)	97	50 / 50
2	3.3 (50)	50 / 50	3.4 (50)	103	50 / 50	3.4 (50)	103	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	3.2 (50)	97	50 / 50
4	3.4 (50)	50 / 50	3.5 (50)	103	50 / 50	3.5 (50)	103	50 / 50	3.4 (50)	100	50 / 50
5	3.4 (50)	50 / 50	3.5 (50)	103	50 / 50	3.5 (50)	103	50 / 50	3.3 (50)	97	50 / 50
6	3.7 (50)	50 / 50	3.7 (50)	100	50 / 50	3.7 (50)	100	50 / 50	3.6 (50)	97	50 / 50
7	3.7 (50)	50 / 50	3.7 (50)	100	50 / 50	3.7 (50)	100	50 / 50	3.5 (49)	95	50 / 50
8	3.8 (50)	50 / 50	3.8 (50)	100	50 / 50	3.8 (50)	100	50 / 50	3.7 (50)	97	50 / 50
9	3.7 (50)	50 / 50	3.8 (50)	103	50 / 50	3.8 (50)	103	50 / 50	3.7 (50)	100	50 / 50
10	3.8 (50)	50 / 50	3.9 (50)	103	50 / 50	3.8 (50)	100	50 / 50	3.7 (50)	97	50 / 50
11	3.7 (50)	50 / 50	3.8 (50)	103	50 / 50	3.8 (50)	103	50 / 50	3.7 (50)	100	50 / 50
12	3.7 (50)	50 / 50	3.8 (50)	103	50 / 50	3.8 (50)	103	50 / 50	3.6 (50)	97	50 / 50
13	3.5 (50)	50 / 50	3.5 (50)	100	50 / 50	3.6 (50)	103	50 / 50	3.4 (50)	97	50 / 50
14	3.7 (50)	50 / 50	3.6 (50)	97	50 / 50	3.6 (50)	97	50 / 50	3.6 (50)	97	50 / 50
18	3.5 (50)	50 / 50	3.6 (50)	103	50 / 50	3.6 (50)	103	50 / 50	3.5 (50)	100	50 / 50
22	3.8 (50)	50 / 50	3.9 (50)	103	50 / 50	3.9 (36)	103	50 / 50	3.6 (50)	95	50 / 50
26	3.7 (50)	50 / 50	3.8 (50)	103	50 / 50	3.8 (50)	103	50 / 50	3.7 (50)	100	50 / 50
30	3.6 (50)	50 / 50	3.7 (50)	103	50 / 50	3.7 (50)	103	50 / 50	3.6 (50)	100	50 / 50
34	3.7 (50)	50 / 50	3.6 (50)	97	50 / 50	3.6 (50)	97	50 / 50	3.6 (50)	97	50 / 50
38	3.8 (50)	50 / 50	3.7 (50)	97	50 / 50	3.7 (49)	97	49 / 50	3.6 (50)	95	50 / 50
42	3.8 (50)	50 / 50	3.8 (50)	100	50 / 50	3.8 (49)	100	49 / 50	3.8 (50)	100	50 / 50
46	3.9 (50)	50 / 50	3.7 (50)	95	50 / 50	3.9 (49)	100	49 / 50	3.6 (50)	92	50 / 50
50	3.8 (50)	50 / 50	3.7 (49)	97	49 / 50	3.7 (49)	97	49 / 50	3.6 (50)	95	50 / 50
54	3.8 (50)	50 / 50	3.8 (49)	100	49 / 50	3.8 (49)	100	49 / 50	3.7 (49)	97	49 / 50
58	3.9 (50)	50 / 50	4.0 (49)	103	49 / 50	3.8 (49)	97	49 / 50	3.7 (49)	95	49 / 50
62	3.9 (48)	48 / 50	4.0 (49)	103	49 / 50	4.0 (49)	103	49 / 50	3.8 (47)	97	47 / 50
66	4.0 (46)	46 / 50	3.9 (49)	98	49 / 50	3.9 (49)	98	49 / 50	3.8 (47)	95	47 / 50
70	4.1 (44)	44 / 50	4.0 (49)	98	49 / 50	4.0 (49)	98	49 / 50	3.9 (47)	95	47 / 50
74	3.8 (43)	43 / 50	3.9 (47)	103	47 / 50	4.0 (49)	105	49 / 50	3.7 (44)	97	44 / 50
78	4.0 (43)	43 / 50	4.0 (47)	100	47 / 50	4.1 (48)	103	48 / 50	3.8 (42)	95	42 / 50
82	4.2 (40)	40 / 50	4.1 (43)	98	43 / 50	4.2 (48)	100	48 / 50	4.0 (40)	95	40 / 50
86	4.0 (39)	39 / 50	4.0 (40)	100	40 / 50	4.1 (47)	103	47 / 50	3.8 (38)	95	38 / 50
90	4.1 (38)	38 / 50	4.1 (35)	100	35 / 50	4.2 (46)	102	46 / 50	3.8 (34)	93	34 / 50
94	3.9 (38)	38 / 50	4.2 (34)	108	34 / 50	4.1 (44)	105	44 / 50	3.8 (32)	97	32 / 50
98	4.0 (37)	37 / 50	4.1 (27)	103	27 / 50	4.1 (41)	103	41 / 50	3.8 (31)	95	31 / 50
102	4.0 (36)	36 / 50	4.1 (25)	103	25 / 50	4.1 (38)	103	38 / 50	3.7 (28)	93	28 / 50
104	4.0 (36)	36 / 50	4.0 (23)	100	23 / 50	4.2 (31)	105	31 / 50	3.9 (26)	98	26 / 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 METHYL ACETOACETATE

Week on Study	Control		2000 ppm			6325 ppm			20000 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	4.6 (50)	50 / 50	4.6 (50)	100	50 / 50	4.8 (50)	104	50 / 50	4.6 (50)	100	50 / 50
2	4.5 (50)	50 / 50	4.5 (50)	100	50 / 50	4.6 (50)	102	50 / 50	4.3 (50)	96	50 / 50
3	4.3 (50)	50 / 50	4.4 (50)	102	50 / 50	4.6 (49)	107	50 / 50	4.2 (50)	98	50 / 50
4	4.3 (50)	50 / 50	4.2 (50)	98	50 / 50	4.5 (49)	105	50 / 50	4.3 (50)	100	50 / 50
5	4.2 (50)	50 / 50	4.2 (50)	100	50 / 50	4.5 (50)	107	50 / 50	4.3 (50)	102	50 / 50
6	4.2 (49)	50 / 50	4.4 (50)	105	50 / 50	4.5 (49)	107	50 / 50	4.3 (50)	102	50 / 50
7	4.1 (50)	50 / 50	4.2 (50)	102	50 / 50	4.4 (50)	107	50 / 50	4.1 (50)	100	50 / 50
8	4.1 (50)	50 / 50	4.4 (50)	107	50 / 50	4.5 (50)	110	50 / 50	4.3 (50)	105	50 / 50
9	4.1 (50)	50 / 50	4.2 (50)	102	50 / 50	4.5 (50)	110	50 / 50	4.2 (50)	102	50 / 50
10	4.1 (50)	50 / 50	4.2 (50)	102	50 / 50	4.4 (50)	107	50 / 50	4.1 (50)	100	50 / 50
11	3.9 (50)	50 / 50	4.1 (50)	105	50 / 50	4.2 (50)	108	50 / 50	4.1 (50)	105	50 / 50
12	3.9 (50)	50 / 50	4.0 (50)	103	50 / 50	4.1 (50)	105	50 / 50	3.9 (50)	100	50 / 50
13	3.9 (50)	50 / 50	3.9 (50)	100	50 / 50	4.2 (50)	108	50 / 50	3.9 (50)	100	50 / 50
14	3.9 (50)	50 / 50	3.9 (50)	100	50 / 50	4.2 (50)	108	50 / 50	3.8 (50)	97	50 / 50
18	3.6 (50)	50 / 50	3.7 (50)	103	50 / 50	3.8 (50)	106	50 / 50	3.6 (50)	100	50 / 50
22	3.3 (50)	50 / 50	3.4 (50)	103	50 / 50	3.5 (50)	106	50 / 50	3.3 (50)	100	50 / 50
26	3.6 (50)	50 / 50	3.6 (50)	100	50 / 50	3.7 (50)	103	50 / 50	3.4 (50)	94	50 / 50
30	3.6 (50)	50 / 50	3.6 (50)	100	50 / 50	3.6 (50)	100	50 / 50	3.4 (50)	94	50 / 50
34	3.7 (50)	50 / 50	3.6 (50)	97	50 / 50	3.7 (50)	100	50 / 50	3.4 (50)	92	50 / 50
38	3.7 (50)	50 / 50	3.6 (50)	97	50 / 50	3.7 (50)	100	50 / 50	3.5 (50)	95	50 / 50
42	3.8 (50)	50 / 50	3.7 (50)	97	50 / 50	3.7 (50)	97	50 / 50	3.4 (50)	89	50 / 50
46	4.0 (50)	50 / 50	3.9 (50)	98	50 / 50	4.0 (50)	100	50 / 50	3.6 (50)	90	50 / 50
50	3.7 (50)	50 / 50	3.7 (50)	100	50 / 50	3.7 (50)	100	50 / 50	3.4 (50)	92	50 / 50
54	3.9 (49)	49 / 50	3.9 (50)	100	50 / 50	3.9 (50)	100	50 / 50	3.6 (50)	92	50 / 50
58	3.7 (48)	48 / 50	3.8 (50)	103	50 / 50	3.8 (50)	103	50 / 50	3.3 (50)	89	50 / 50
62	3.9 (48)	48 / 50	4.0 (50)	103	50 / 50	4.0 (50)	103	50 / 50	3.5 (50)	90	50 / 50
66	3.9 (48)	48 / 50	4.1 (49)	105	49 / 50	4.1 (49)	105	50 / 50	3.5 (50)	90	50 / 50
70	4.1 (48)	48 / 50	4.1 (49)	100	49 / 50	4.1 (49)	100	50 / 50	3.6 (50)	88	50 / 50
74	4.1 (47)	47 / 50	4.3 (47)	105	47 / 50	4.3 (48)	105	49 / 50	3.8 (49)	93	49 / 50
78	4.3 (45)	45 / 50	4.4 (47)	102	47 / 50	4.3 (47)	100	48 / 50	3.9 (48)	91	48 / 50
82	4.4 (43)	43 / 50	4.3 (47)	98	47 / 50	4.4 (46)	100	46 / 50	3.7 (48)	84	48 / 50
86	4.4 (42)	42 / 50	4.6 (46)	105	46 / 50	4.5 (45)	102	45 / 50	3.9 (46)	89	46 / 50
90	4.4 (33)	35 / 50	4.5 (43)	102	45 / 50	4.4 (43)	100	43 / 50	3.9 (44)	89	44 / 50
94	4.4 (34)	35 / 50	4.8 (42)	109	43 / 50	4.6 (42)	105	42 / 50	3.9 (43)	89	43 / 50
98	4.6 (26)	29 / 50	4.5 (38)	98	41 / 50	4.4 (42)	96	42 / 50	3.9 (39)	85	39 / 50
102	4.4 (27)	28 / 50	4.8 (39)	109	40 / 50	4.4 (38)	100	39 / 50	4.1 (38)	93	38 / 50
104	4.9 (25)	25 / 50	4.4 (36)	90	37 / 50	4.3 (36)	88	37 / 50	4.2 (37)	86	37 / 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 METHYL ACETOACETATE

Week on Study	Control			2000 ppm			6325 ppm			20000 ppm		
	Av. WC.		No. of Surviv.	Av. WC.	% of cont.	No. of Surviv.	Av. WC.	% of cont.	No. of Surviv.	Av. WC.	% of cont.	No. of Surviv.
	<50>			<50>			<50>			<50>		
1	4.2 (50)		50 / 50	4.3 (50)	102	50 / 50	4.3 (50)	102	50 / 50	4.0 (50)	95	50 / 50
2	4.1 (50)		50 / 50	4.3 (50)	105	50 / 50	4.4 (50)	107	50 / 50	4.1 (50)	100	50 / 50
3	4.2 (50)		50 / 50	4.2 (49)	100	50 / 50	4.3 (50)	102	50 / 50	4.1 (49)	98	50 / 50
4	4.3 (49)		50 / 50	4.8 (49)	112	50 / 50	4.6 (50)	107	50 / 50	4.2 (50)	98	50 / 50
5	4.4 (50)		50 / 50	4.5 (49)	102	50 / 50	4.6 (50)	105	50 / 50	4.3 (50)	98	50 / 50
6	4.5 (50)		50 / 50	4.5 (48)	100	50 / 50	4.7 (50)	104	50 / 50	4.3 (50)	96	50 / 50
7	4.4 (49)		50 / 50	4.7 (50)	107	50 / 50	4.6 (49)	105	50 / 50	4.1 (50)	93	50 / 50
8	4.5 (49)		50 / 50	4.8 (50)	107	50 / 50	4.9 (48)	109	50 / 50	4.3 (50)	96	50 / 50
9	4.7 (50)		50 / 50	4.7 (50)	100	50 / 50	4.8 (49)	102	50 / 50	4.2 (50)	89	50 / 50
10	4.6 (50)		50 / 50	5.0 (48)	109	50 / 50	4.7 (48)	102	50 / 50	4.3 (50)	93	50 / 50
11	4.4 (50)		50 / 50	4.8 (50)	109	50 / 50	4.6 (50)	105	50 / 50	4.1 (50)	93	50 / 50
12	4.6 (50)		50 / 50	4.7 (49)	102	50 / 50	4.8 (50)	104	50 / 50	4.3 (49)	93	50 / 50
13	4.5 (50)		50 / 50	4.7 (50)	104	50 / 50	4.5 (48)	100	50 / 50	4.2 (50)	93	50 / 50
14	4.3 (50)		50 / 50	4.3 (48)	100	50 / 50	4.3 (48)	100	50 / 50	4.0 (50)	93	50 / 50
18	4.1 (50)		50 / 50	4.4 (50)	107	50 / 50	4.6 (49)	112	50 / 50	4.0 (50)	98	50 / 50
22	4.2 (50)		50 / 50	4.3 (50)	102	50 / 50	4.3 (50)	102	50 / 50	3.9 (50)	93	50 / 50
26	4.4 (50)		50 / 50	4.4 (50)	100	50 / 50	4.5 (49)	102	50 / 50	4.0 (50)	91	50 / 50
30	4.1 (49)		50 / 50	4.1 (50)	100	50 / 50	4.3 (50)	105	50 / 50	3.8 (50)	93	50 / 50
34	4.2 (50)		50 / 50	4.2 (49)	100	50 / 50	4.0 (50)	95	50 / 50	3.7 (50)	88	50 / 50
38	4.0 (50)		50 / 50	4.2 (50)	105	50 / 50	4.1 (49)	103	49 / 50	3.8 (50)	95	50 / 50
42	4.0 (50)		50 / 50	4.1 (50)	103	50 / 50	4.0 (49)	100	49 / 50	3.7 (50)	93	50 / 50
46	4.2 (50)		50 / 50	4.2 (50)	100	50 / 50	4.2 (49)	100	49 / 50	3.9 (50)	93	50 / 50
50	4.0 (50)		50 / 50	3.7 (49)	93	49 / 50	3.9 (49)	98	49 / 50	3.7 (50)	93	50 / 50
54	3.9 (49)		50 / 50	4.0 (49)	103	49 / 50	4.0 (49)	103	49 / 50	3.8 (49)	97	49 / 50
58	4.0 (49)		50 / 50	3.9 (49)	98	49 / 50	4.0 (49)	100	49 / 50	3.6 (49)	90	49 / 50
62	3.9 (48)		48 / 50	4.0 (49)	103	49 / 50	4.0 (49)	103	49 / 50	3.8 (47)	97	47 / 50
66	4.0 (46)		46 / 50	3.8 (49)	95	49 / 50	3.9 (49)	98	49 / 50	3.8 (47)	95	47 / 50
70	3.9 (43)		44 / 50	4.0 (49)	103	49 / 50	4.0 (49)	103	49 / 50	3.7 (47)	95	47 / 50
74	4.1 (43)		43 / 50	4.2 (47)	102	47 / 50	4.1 (49)	100	49 / 50	3.7 (44)	90	44 / 50
78	4.1 (42)		43 / 50	4.2 (47)	102	47 / 50	4.2 (48)	102	48 / 50	3.7 (42)	90	42 / 50
82	4.3 (40)		40 / 50	4.1 (43)	95	43 / 50	4.3 (48)	100	48 / 50	3.8 (40)	88	40 / 50
86	4.2 (39)		39 / 50	4.3 (40)	102	40 / 50	4.1 (47)	98	47 / 50	3.8 (38)	90	38 / 50
90	4.1 (38)		38 / 50	4.2 (35)	102	35 / 50	4.2 (46)	102	46 / 50	3.7 (34)	90	34 / 50
94	4.2 (38)		38 / 50	4.5 (33)	107	34 / 50	4.3 (44)	102	44 / 50	3.9 (32)	93	32 / 50
98	4.2 (37)		37 / 50	4.2 (26)	100	27 / 50	4.1 (41)	98	41 / 50	4.1 (31)	98	31 / 50
102	4.1 (35)		36 / 50	4.4 (24)	107	25 / 50	4.3 (38)	105	38 / 50	3.9 (28)	95	28 / 50
104	4.3 (36)		36 / 50	4.5 (23)	105	23 / 50	4.3 (31)	100	31 / 50	4.0 (25)	93	26 / 50

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

TABLE 7 BIOCHEMISTRY OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF METHYL ACETOACETATE

Group Name	Control	2000 ppm	6325 ppm	20000 ppm
No. of examined animals	36	23	30	26
ALP (IU/L)	210 ± 74	192 ± 62	179 ± 66	257 ± 99 *
CK (IU/L)	118 ± 124	76 ± 52 *	287 ± 1030	131 ± 221

Mean ± S.D.

Significant difference: * : p≦0.05 ** : p≦0.01 Test of Dunnett

TABLE 8 URINALYSIS OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF METHYL ACETOACETATE

Group Name		Control	2000 ppm	6325 ppm	20000 ppm
No. of examined animals		36	25	37	28
	Grade				
pH	5.0	0	0	0	0
	6.0	0	1	1	2
	6.5	1	0	4	6
	7.0	4	4	10	6
	7.5	5	2	5	5
	8.0	17	15	14	8
	8.5	9	3	3	1
	Chi square test				*
Ketone body	−	5	2	5	0
	±	24	20	28	12
	+	6	1	3	9
	2+	1	2	1	5
	3+	0	0	0	2
	4+	0	0	0	0
	Chi square test				**

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

TABLE 9 ORGAN WEIGHTS OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF METHYL ACETOACETATE

Group Name	Control	2000 ppm	6325 ppm	20000 ppm
No. of examined animals	25	37	37	37
Body weight (g)	48.0 ± 5.0	46.5 ± 8.3	44.0 ± 7.2	46.4 ± 6.8
Heart (g)	0.211 ± 0.018	0.218 ± 0.023	0.213 ± 0.024	0.215 ± 0.034
Heart (%)	0.445 ± 0.051	0.489 ± 0.154	0.493 ± 0.074 *	0.469 ± 0.077
Kidneys (g)	0.630 ± 0.048	0.656 ± 0.087	0.728 ± 0.462	0.925 ± 1.289
Kidneys (%)	1.328 ± 0.190	1.482 ± 0.613	1.737 ± 1.373 **	2.036 ± 2.849
Liver (g)	1.633 ± 0.188	1.716 ± 0.427	2.000 ± 0.951	1.838 ± 0.678
Liver (%)	3.433 ± 0.497	3.778 ± 1.042	4.678 ± 2.487 *	4.118 ± 2.058

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

TABLE 10 ORGAN WEIGHTS OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF METHYL ACETOACETATE

Group Name	Control	2000 ppm	6325 ppm	20000 ppm
No. of examined animals	36	23	31	26
Body weight (g)	30.9 ± 3.9	30.8 ± 3.4	32.4 ± 4.1	29.4 ± 4.0
Kidneys (g)	0.420 ± 0.040	0.438 ± 0.048	0.471 ± 0.144	0.454 ± 0.085
Kidneys (%)	1.373 ± 0.166	1.426 ± 0.122	1.485 ± 0.562	1.573 ± 0.416 *

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

TABLE 11 INCIDENCES OF SELECTED NEOPLASTIC LESIONS OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF METHYL ACETOACETATE

Group Name	Control	2000 ppm	6325 ppm	20000 ppm	Peto	Cochran-
Number of examined animals	50	50	50	50	test	Armitage test
lung	<50>	<50>	<50>	<50>		
bronchiolar-alveolar carcinoma	0 (0 %)	1 (2 %)	2 (4 %)	4 (8 %)	↑	↑

Significant difference * : p≦0.05 ** : p≦0.01 Fisher's exact test for neoplastic lesion
↑(↓) : p≦0.05 ↑↑(↓↓) : p≦0.01 Peto or Cochran-Armitage test for neoplastic lesion
< > : Number of animals examined at the site

TABLE 12 HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER : BDF1 FEMALE MICE

Organs Tumors	No. of animals examined	No. of animals bearing tumor	Incidence (%)	Min. - Max. (%)
Lung	1597			
Bronchiolar-alveolar adenoma		56	3.5	0 - 10
Bronchiolar-alveolar carcinoma		47	2.9	0 - 8

32 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

TABLE 13 CAUSE OF DEATH OF MICE IN THE 2-YEAR DRINKING WATER STUDY OF METHYL ACETOACETATE

	Male				Female			
Group name	Control	2000 ppm	6325 ppm	20000 ppm	Control	2000 ppm	6325 ppm	20000 ppm
Number of dead or moribund animals	25	13	13	13	14	27	19	24
No microscopical confirmation	1	0	0	0	1	1	0	0
Cardiovascular lesion	0	0	0	2	0	0	0	0
Renal lesion	0	0	1	0	0	0	0	0
Reproductive system lesion	0	0	1	0	0	0	0	1
Central nervous system lesion	0	0	0	0	1	0	0	0
Urinary retention	2	3	0	0	0	1	1	0
Hydronephrosis	0	1	0	0	0	0	0	0
Tumor death : leukemia	6	2	5	1	2	7	7	8
subcutis	1	0	1	0	0	0	0	0
nasal cavity	1	0	0	0	0	0	0	0
lung	1	1	0	1	0	1	0	1
lymph node	0	0	0	1	0	0	0	0
spleen	0	1	0	1	0	2	1	0
heart	0	0	0	1	0	0	0	0
liver	12	4	5	4	1	2	1	1
urinary bladder	0	1	0	0	0	0	0	0
epididymis	1	0	0	0	—	—	—	—
pituitary gland	0	0	0	0	0	2	2	1
uterus	—	—	—	—	8	10	7	12
mammary gland	0	0	0	0	0	1	0	0
peripheral nerves	0	0	0	1	1	0	0	0
retroperitoneum	0	0	0	1	0	0	0	0