

1-プロモ-3-クロロプロバンのマウスを用いた
吸入によるがん原性試験報告書

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TABLE 1 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1-BROMO-3-CHLOROPROPANE

Weeks on Study	Control		25 ppm			100 ppm			400 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	23.0	(50) 50/50	23.0	(50) 100	50/50	23.0	(50) 100	50/50	23.0	(50) 100	50/50
1	24.0	(50) 50/50	24.2	(50) 101	50/50	23.8	(50) 99	50/50	23.0	(50) 96	50/50
2	24.9	(50) 50/50	25.0	(50) 100	50/50	24.7	(50) 99	50/50	23.6	(50) 95	50/50
3	25.6	(50) 50/50	25.5	(50) 100	50/50	24.9	(50) 97	50/50	24.1	(50) 94	50/50
4	26.2	(50) 50/50	25.8	(50) 98	50/50	26.9	(50) 103	50/50	25.3	(50) 97	50/50
5	26.7	(50) 50/50	26.3	(50) 99	50/50	26.5	(50) 99	50/50	24.9	(50) 93	50/50
6	27.3	(50) 50/50	27.1	(50) 99	50/50	26.8	(50) 98	50/50	25.6	(50) 94	50/50
7	27.9	(50) 50/50	27.5	(50) 99	50/50	27.1	(50) 97	50/50	26.0	(50) 93	50/50
8	28.3	(50) 50/50	28.1	(50) 99	50/50	27.6	(50) 98	50/50	26.6	(50) 94	50/50
9	29.0	(50) 50/50	28.5	(50) 98	50/50	28.0	(50) 97	50/50	27.1	(50) 93	50/50
10	29.5	(50) 50/50	29.1	(50) 99	50/50	28.4	(50) 96	50/50	27.5	(50) 93	50/50
11	30.0	(50) 50/50	29.7	(50) 99	50/50	29.0	(50) 97	50/50	27.9	(50) 93	50/50
12	30.6	(50) 50/50	30.3	(50) 99	50/50	29.6	(50) 97	50/50	28.1	(50) 92	50/50
13	31.1	(50) 50/50	30.7	(50) 99	50/50	30.1	(50) 97	50/50	28.6	(50) 92	50/50
14	31.7	(50) 50/50	31.4	(50) 99	50/50	30.6	(50) 97	50/50	29.4	(50) 93	50/50
18	33.8	(50) 50/50	33.7	(50) 100	50/50	32.9	(50) 97	50/50	31.4	(50) 93	50/50
22	36.1	(50) 50/50	35.9	(50) 99	50/50	35.1	(50) 97	50/50	33.0	(50) 91	50/50
26	38.0	(50) 50/50	37.9	(50) 100	50/50	36.4	(50) 96	50/50	34.5	(50) 91	50/50
30	39.4	(50) 50/50	39.1	(50) 99	50/50	37.7	(50) 96	50/50	35.5	(50) 90	50/50
34	41.0	(50) 50/50	40.7	(50) 99	50/50	39.2	(49) 96	49/50	36.4	(50) 89	50/50
38	42.2	(50) 50/50	42.0	(50) 100	50/50	40.0	(49) 95	49/50	37.9	(50) 90	50/50
42	43.0	(50) 50/50	42.8	(50) 100	50/50	40.7	(49) 95	49/50	37.3	(50) 87	50/50
46	43.3	(50) 50/50	43.5	(50) 100	50/50	40.9	(49) 94	49/50	38.0	(50) 88	50/50
50	44.0	(49) 49/50	44.8	(50) 102	50/50	41.7	(49) 95	49/50	39.2	(50) 89	50/50
54	45.4	(48) 48/50	45.4	(50) 100	50/50	42.0	(48) 93	48/50	39.8	(50) 88	50/50
58	45.7	(48) 48/50	46.2	(50) 101	50/50	42.2	(48) 92	48/50	40.1	(49) 88	49/50
62	45.9	(46) 46/50	47.1	(49) 103	49/50	43.2	(48) 94	48/50	40.6	(48) 88	48/50
66	47.2	(45) 45/50	47.9	(49) 101	49/50	44.3	(48) 94	48/50	41.3	(48) 88	48/50
70	47.1	(45) 45/50	48.3	(47) 103	47/50	44.6	(48) 95	48/50	41.4	(48) 88	48/50
74	47.5	(45) 45/50	48.4	(47) 102	47/50	45.1	(47) 95	47/50	41.3	(48) 87	48/50
78	47.7	(44) 44/50	48.6	(47) 102	47/50	44.8	(45) 94	45/50	41.6	(48) 87	48/50
82	48.1	(43) 43/50	49.0	(45) 102	45/50	45.3	(44) 94	44/50	42.1	(48) 88	48/50
86	49.2	(42) 42/50	50.0	(44) 102	44/50	46.3	(42) 94	42/50	43.1	(47) 88	47/50
90	48.8	(40) 40/50	49.6	(44) 102	44/50	46.3	(42) 95	42/50	43.5	(45) 89	45/50
94	48.5	(40) 40/50	49.1	(41) 101	41/50	45.6	(41) 94	41/50	42.8	(42) 88	42/50
98	48.3	(40) 40/50	48.3	(40) 100	40/50	45.4	(39) 94	39/50	43.2	(39) 89	39/50
102	47.0	(38) 38/50	45.9	(36) 98	36/50	42.9	(37) 91	37/50	40.8	(38) 87	38/50
104	46.8	(38) 38/50	45.5	(33) 97	33/50	42.2	(37) 90	37/50	40.0	(36) 85	36/50

< > : 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 INHALATION STUDY OF 1-BROMO-3-CHLOROPROPANE

Weeks on Study	Control		25 ppm			100 ppm			400 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>		<49>			<50>			<50>		
0	18.6 (50)	50/50	18.6 (49)	100	49/49	18.6 (50)	100	50/50	18.6 (50)	100	50/50
1	19.1 (50)	50/50	19.3 (49)	101	49/49	19.2 (50)	101	50/50	18.6 (50)	97	50/50
2	20.0 (50)	50/50	20.2 (49)	101	49/49	19.9 (50)	100	50/50	19.1 (50)	96	50/50
3	20.5 (50)	50/50	20.4 (49)	100	49/49	20.3 (50)	99	50/50	19.6 (50)	96	50/50
4	21.0 (50)	50/50	20.9 (49)	100	49/49	21.6 (50)	103	50/50	20.4 (50)	97	50/50
5	21.5 (50)	50/50	21.4 (49)	100	49/49	21.5 (50)	100	50/50	20.6 (50)	96	50/50
6	22.1 (50)	50/50	22.1 (49)	100	49/49	22.1 (50)	100	50/50	21.1 (50)	95	50/50
7	22.4 (50)	50/50	22.3 (49)	100	49/49	22.2 (50)	99	50/50	21.6 (50)	96	50/50
8	22.7 (50)	50/50	22.8 (49)	100	49/49	22.5 (50)	99	50/50	21.9 (50)	96	50/50
9	23.1 (50)	50/50	23.0 (49)	100	49/49	23.2 (50)	100	50/50	21.9 (50)	95	50/50
10	23.2 (50)	50/50	23.2 (49)	100	49/49	23.0 (50)	99	50/50	22.3 (50)	96	50/50
11	23.5 (50)	50/50	23.6 (49)	100	49/49	23.3 (50)	99	50/50	22.7 (50)	97	50/50
12	23.7 (50)	50/50	23.8 (49)	100	49/49	23.8 (50)	100	50/50	23.0 (50)	97	50/50
13	24.0 (50)	50/50	23.7 (49)	99	49/49	23.7 (50)	99	50/50	23.3 (50)	97	50/50
14	24.3 (50)	50/50	24.2 (49)	100	49/49	24.1 (50)	99	50/50	23.5 (50)	97	50/50
18	25.3 (50)	50/50	25.4 (49)	100	49/49	25.1 (50)	99	50/50	24.3 (50)	96	50/50
22	26.2 (50)	50/50	26.2 (49)	100	49/49	25.6 (50)	98	50/50	24.8 (50)	95	50/50
26	26.7 (50)	50/50	27.0 (49)	101	49/49	26.4 (50)	99	50/50	25.4 (50)	95	50/50
30	27.4 (50)	50/50	27.8 (49)	101	49/49	26.8 (50)	98	50/50	25.8 (50)	94	50/50
34	27.9 (50)	50/50	28.5 (49)	102	49/49	27.4 (50)	98	50/50	26.1 (50)	94	50/50
38	28.4 (49)	49/50	28.7 (49)	101	49/49	27.9 (50)	98	50/50	26.6 (50)	94	50/50
42	29.1 (49)	49/51	29.4 (49)	101	49/49	27.9 (50)	96	50/50	26.4 (50)	91	50/50
46	28.8 (49)	49/52	29.4 (49)	102	49/49	27.9 (50)	97	50/50	26.7 (50)	93	50/50
50	29.7 (49)	49/53	29.7 (49)	100	49/49	28.4 (49)	96	49/50	26.9 (50)	91	50/50
54	29.8 (49)	49/54	30.2 (48)	101	48/49	28.6 (49)	96	49/50	27.0 (50)	91	50/50
58	30.0 (49)	49/55	30.7 (48)	102	48/49	28.7 (49)	96	49/50	27.2 (50)	91	50/50
62	30.4 (49)	49/56	31.4 (47)	103	47/49	29.3 (49)	96	49/50	27.0 (49)	89	49/50
66	30.6 (49)	49/57	32.2 (47)	105	47/49	29.6 (49)	97	49/50	27.2 (48)	89	48/50
70	30.7 (49)	49/58	31.5 (46)	103	46/49	29.3 (49)	95	49/50	27.3 (48)	89	48/50
74	31.4 (49)	49/59	32.5 (46)	104	46/49	30.0 (49)	96	49/50	27.2 (47)	87	47/50
78	31.8 (48)	48/50	32.3 (45)	102	45/49	29.7 (46)	93	46/50	27.3 (46)	86	46/50
82	32.0 (45)	45/50	32.2 (41)	101	41/49	29.6 (45)	93	45/50	27.6 (46)	86	46/50
86	31.6 (44)	44/50	33.0 (39)	104	39/49	29.6 (44)	94	44/50	28.3 (44)	90	44/50
90	31.6 (40)	40/50	33.7 (37)	107	37/49	29.4 (44)	93	44/50	28.4 (42)	90	42/50
94	31.5 (38)	38/50	33.2 (32)	105	32/49	30.2 (40)	96	40/50	28.6 (39)	91	39/50
98	32.0 (36)	36/50	33.1 (29)	103	29/49	30.2 (38)	94	38/50	28.8 (36)	90	36/50
102	31.4 (32)	32/50	32.0 (25)	102	25/49	30.5 (33)	97	33/50	28.1 (35)	89	35/50
104	31.6 (30)	30/50	31.9 (24)	101	24/49	30.4 (32)	96	32/50	28.1 (33)	89	33/50

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

TABLE 3 INCIDENCES OF EXTERNAL AND INTERNAL MASSES IN CLINICAL OBSERVATION OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1-BROMO-3-CHLOROPROPANE

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	0/48	1/45	2/43	2/40	4/50 (1/12)
25 ppm	0/50	0/50	0/50	0/50	0/50	0/49	1/47	1/43	1/50 (1/17)
100 ppm	0/50	0/50	0/50	0/49	0/48	0/48	1/45	2/42	3/50 (0/13)
400 ppm	0/50	0/50	0/50	0/50	0/50	0/48	2/48	5/44	6/50 (1/14)
Internal mass									
Control	0/50	0/50	0/50	2/50	4/48	2/45	3/43	8/40	12/50 (5/12)
25 ppm	0/50	0/50	0/50	0/50	0/50	1/49	3/47	8/43	9/50 (6/17)
100 ppm	0/50	2/50	2/50	3/49	1/48	1/48	3/45	2/42	7/50 (5/13)
400 ppm	3/50	5/50	5/50	6/50	5/50	3/48	3/48	3/44	7/50 (4/14)

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 4 INCIDENCES OF EXTERNAL AND INTERNAL MASSES IN CLINICAL OBSERVATION OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 1-BROMO-3-CHLOROPROPANE

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	0/49	0/49	1/49	2/48	5/39	6/50 (3/20)
25 ppm	0/49	0/49	0/49	0/49	0/49	0/47	0/44	0/35	0/49 (0/26)
100 ppm	0/50	0/50	0/50	0/50	0/49	1/49	1/46	2/42	3/50 (1/18)
400 ppm	0/50	0/50	0/50	0/50	0/50	0/48	5/46	5/42	6/50 (1/17)
Internal mass									
Control	0/50	0/50	2/50	1/49	1/49	2/49	5/48	7/39	11/50 (9/20)
25 ppm	0/49	0/49	0/49	3/49	5/49	2/47	13/44	14/35	23/49 (17/26)
100 ppm	0/50	0/50	2/50	2/50	3/49	6/49	6/46	11/42	14/50 (8/18)
400 ppm	1/50	1/50	1/50	1/50	4/50	3/48	6/46	10/42	16/50 (12/17)

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 5 FOOD CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR
INHALATION STUDY OF 1-BROMO-3-CHLOROPROPANE

Weeks on Study	Control		25 ppm		100 ppm		400 ppm				
	Av.FC.		Av.FC. % of		Av.FC. % of		Av.FC. % of				
	<50>		<50>		<50>		<50>				
1	3.8	(50)	3.8	(50)	100	3.7	(50)	97	3.5	(50)	92
2	3.8	(50)	3.7	(50)	97	3.8	(50)	100	3.5	(50)	92
3	3.7	(50)	3.8	(50)	103	3.7	(50)	100	3.6	(50)	97
4	3.9	(50)	3.9	(50)	100	3.9	(50)	100	3.7	(50)	95
5	4.0	(50)	3.9	(50)	98	4.0	(50)	100	3.8	(50)	95
6	4.1	(50)	4.1	(50)	100	3.8	(50)	93	3.8	(50)	93
7	4.1	(50)	4.0	(50)	98	4.0	(50)	98	3.9	(50)	95
8	4.1	(50)	4.2	(50)	102	4.0	(50)	98	4.0	(50)	98
9	4.1	(50)	4.1	(50)	100	4.0	(50)	98	4.0	(50)	98
10	4.2	(50)	4.2	(50)	100	4.1	(50)	98	4.0	(50)	95
11	4.2	(50)	4.3	(50)	102	4.2	(50)	100	4.1	(50)	98
12	4.3	(50)	4.3	(50)	100	4.3	(50)	100	4.1	(50)	95
13	4.3	(50)	4.3	(50)	100	4.2	(50)	98	4.1	(50)	95
14	4.3	(50)	4.3	(50)	100	4.3	(50)	100	4.2	(50)	98
18	4.4	(50)	4.3	(50)	98	4.3	(50)	98	4.2	(50)	95
22	4.5	(50)	4.5	(50)	100	4.4	(50)	98	4.2	(50)	93
26	4.5	(50)	4.5	(50)	100	4.4	(50)	98	4.4	(50)	98
30	4.6	(50)	4.6	(50)	100	4.5	(50)	98	4.4	(50)	96
34	4.7	(50)	4.7	(50)	100	4.6	(49)	98	4.4	(50)	94
38	4.7	(50)	4.7	(50)	100	4.7	(49)	100	4.5	(50)	96
42	4.7	(50)	4.7	(50)	100	4.6	(49)	98	4.3	(50)	91
46	4.7	(50)	4.7	(50)	100	4.6	(49)	98	4.5	(50)	96
50	4.8	(49)	4.8	(50)	100	4.6	(49)	96	4.6	(50)	96
54	4.8	(48)	4.7	(50)	98	4.7	(48)	98	4.5	(50)	94
58	4.9	(48)	4.9	(50)	100	4.6	(48)	94	4.4	(49)	90
62	4.8	(46)	4.7	(49)	98	4.6	(48)	96	4.5	(48)	94
66	4.9	(45)	4.8	(49)	98	4.7	(48)	96	4.6	(48)	94
70	4.8	(45)	4.8	(47)	100	4.6	(48)	96	4.4	(48)	92
74	4.7	(45)	4.6	(47)	98	4.7	(47)	100	4.4	(48)	94
78	4.9	(44)	4.8	(47)	98	4.7	(45)	96	4.6	(48)	94
82	5.0	(43)	5.0	(45)	100	4.9	(44)	98	4.6	(48)	92
86	5.1	(42)	4.9	(44)	96	4.9	(42)	96	4.7	(47)	92
90	4.9	(40)	4.9	(44)	100	4.8	(42)	98	4.7	(45)	96
94	5.0	(40)	4.9	(41)	98	4.8	(41)	96	4.6	(42)	92
98	4.9	(40)	4.8	(40)	98	4.8	(39)	98	4.6	(39)	94
102	4.8	(38)	4.6	(36)	96	4.6	(37)	96	4.4	(38)	92
104	4.8	(38)	4.7	(33)	98	4.6	(37)	96	4.3	(36)	90

< > : 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 INHALATION STUDY OF 1-BROMO-3-CHLOROPROPANE

Weeks on Study	Control		25 ppm		100 ppm		400 ppm	
	Av.FC.		Av.FC. % of		Av.FC. % of		Av.FC. % of	
	<50>		<49>		<50>		<50>	
1	3.3	(50)	3.3	(49) 100	3.2	(50) 97	3.1	(50) 94
2	3.2	(50)	3.3	(49) 103	3.3	(50) 103	3.1	(50) 97
3	3.4	(50)	3.4	(49) 100	3.3	(50) 97	3.2	(50) 94
4	3.6	(50)	3.6	(49) 100	3.6	(50) 100	3.4	(50) 94
5	3.7	(50)	3.7	(49) 100	3.7	(50) 100	3.4	(50) 92
6	3.9	(50)	3.8	(49) 97	3.7	(50) 95	3.6	(50) 92
7	3.9	(50)	3.8	(49) 97	3.9	(50) 100	3.7	(50) 95
8	3.9	(50)	3.9	(49) 100	3.9	(50) 100	3.7	(50) 95
9	4.0	(50)	3.9	(49) 98	4.1	(50) 103	3.7	(50) 93
10	4.0	(50)	4.0	(49) 100	4.0	(50) 100	3.7	(50) 93
11	4.0	(50)	4.0	(49) 100	4.2	(50) 105	3.8	(50) 95
12	4.1	(50)	4.0	(49) 98	4.1	(50) 100	3.9	(50) 95
13	4.0	(50)	4.0	(49) 100	4.0	(50) 100	3.9	(50) 98
14	4.1	(50)	4.0	(49) 98	4.1	(50) 100	3.9	(50) 95
18	4.1	(50)	4.0	(49) 98	4.2	(50) 102	3.9	(50) 95
22	4.1	(50)	4.1	(49) 100	4.2	(50) 102	3.9	(50) 95
26	4.2	(50)	4.1	(49) 98	4.3	(50) 102	4.0	(50) 95
30	4.3	(50)	4.3	(49) 100	4.5	(50) 105	4.2	(50) 98
34	4.5	(50)	4.4	(49) 98	4.5	(50) 100	4.3	(50) 96
38	4.3	(49)	4.3	(49) 100	4.5	(50) 105	4.3	(50) 100
42	4.4	(49)	4.2	(49) 95	4.5	(50) 102	4.1	(50) 93
46	4.2	(49)	4.3	(49) 102	4.4	(50) 105	4.1	(50) 98
50	4.4	(49)	4.3	(49) 98	4.4	(49) 100	4.0	(50) 91
54	4.3	(49)	4.2	(48) 98	4.3	(49) 100	4.0	(50) 93
58	4.4	(49)	4.4	(48) 100	4.3	(49) 98	3.9	(50) 89
62	4.4	(49)	4.2	(47) 95	4.3	(49) 98	3.9	(49) 89
66	4.2	(49)	4.4	(47) 105	4.3	(49) 102	3.8	(48) 90
70	4.3	(49)	4.1	(46) 95	4.1	(49) 95	3.8	(48) 88
74	4.1	(49)	4.1	(46) 100	4.3	(49) 105	3.8	(47) 93
78	4.4	(48)	4.3	(45) 98	4.3	(46) 98	3.9	(46) 89
82	4.5	(45)	4.3	(41) 96	4.2	(45) 93	3.9	(46) 87
86	4.4	(44)	4.4	(39) 100	4.2	(44) 95	4.0	(44) 91
90	4.5	(40)	4.3	(37) 96	4.1	(44) 91	4.0	(42) 89
94	4.4	(38)	4.5	(32) 102	4.3	(40) 98	3.9	(39) 89
98	4.5	(36)	4.4	(29) 98	4.2	(38) 93	3.8	(36) 84
102	4.4	(32)	4.3	(25) 98	4.2	(33) 95	3.8	(35) 86
104	4.5	(30)	4.3	(24) 96	4.2	(32) 93	3.8	(33) 84

< > : No. of effective animals, () : No. of measured animals

Av.FC. : Averaged food consumption (Unit:g)

TABLE 7 HEMATOLOGY OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1-BROMO-3-CHLOROPROPANE

Group Name	Control	25 ppm	100 ppm	400 ppm
No. of examined animals	36	31	34	32
RED BLOOD CELL ($10^6/\mu\text{L}$)	9.66 \pm 0.96	10.21 \pm 1.25	9.68 \pm 0.75	8.55 \pm 1.44 **
HEMOGLOBIN (g/dL)	13.6 \pm 1.4	13.8 \pm 1.7	13.4 \pm 1.0	12.3 \pm 1.9 **
HEMATOCRIT (%)	44.0 \pm 4.4	45.0 \pm 6.0	44.0 \pm 3.1	40.7 \pm 5.6 **
MCV (fL)	45.6 \pm 1.5	44.1 \pm 2.1 *	45.4 \pm 1.3	48.0 \pm 3.8 **
MCH (pg)	14.1 \pm 0.3	13.5 \pm 0.6 **	13.9 \pm 0.5	14.5 \pm 0.9
MCHC (g/dL)	30.9 \pm 0.8	30.6 \pm 0.5	30.5 \pm 0.6 **	30.2 \pm 0.9 **
PLATELET ($10^3/\mu\text{L}$)	1910 \pm 287	2034 \pm 408	1923 \pm 286	1518 \pm 539 **
Differential WBC (%)				
EOSINO	2 \pm 1	1 \pm 1 **	2 \pm 2	2 \pm 2
OTHER	0 \pm 1	0 \pm 0	0 \pm 1	3 \pm 11 **

Mean \pm S.D.
Significant difference: * : p<0.05 ** : p<0.01 Test of Dunnett

TABLE 8 HEMATOLOGY OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 1-BROMO-3-CHLOROPROPANE

Group Name	Control	25 ppm	100 ppm	400 ppm
No. of examined animals	30	23	31	31
MCV (fL)	45.0 \pm 1.4	45.2 \pm 2.3	47.1 \pm 5.0 *	47.0 \pm 2.1 **
MCHC (g/dL)	31.0 \pm 0.8	30.8 \pm 1.1	30.7 \pm 1.5	30.6 \pm 1.1 *
PLATELET ($10^3/\mu\text{L}$)	1296 \pm 259	1142 \pm 362	1042 \pm 384 **	1073 \pm 323 *

Mean \pm S.D.
Significant difference: * : p<0.05 ** : p<0.01 Test of Dunnett

TABLE 9 BIOCHEMISTRY OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1-BROMO-3-CHLOROPROPANE

Group Name	Control	25 ppm	100 ppm	400 ppm	
No. of examined animals	37	31	34	34	
A/G RATIO	1.3 ± 0.2	1.2 ± 0.2	1.3 ± 0.2	1.4 ± 0.2	**
T-CHOLESTEROL (mg/dL)	103 ± 39	118 ± 41	100 ± 34	87 ± 25	*
PHOSPHOLIPID (mg/dL)	194 ± 45	219 ± 61	188 ± 43	163 ± 36	**
GPT (IU/L)	34 ± 59	57 ± 62 *	39 ± 42 *	62 ± 87	**
ALP (IU/L)	141 ± 53	159 ± 120	140 ± 33	187 ± 77	**
G-GTP (IU/L)	1 ± 1	1 ± 1	1 ± 1	2 ± 1	*
UREA NITROGEN (mg/dL)	25.7 ± 9.9	24.1 ± 5.9	21.6 ± 3.2 *	19.1 ± 3.4	**
CHLORIDE (mEq/L)	122 ± 2	122 ± 3	124 ± 3	130 ± 4	**

Mean ± S.D.

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

TABLE 10 BIOCHEMISTRY OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 1-BROMO-3-CHLOROPROPANE

Group Name	Control	25 ppm	100 ppm	400 ppm	
No. of examined animals	30	23	31	32	
TOTAL PROTEIN (g/dL)	5.2 ± 0.6	5.3 ± 0.6	4.8 ± 0.8 **	5.0 ± 0.4	
A/G RATIO	1.3 ± 0.2	1.5 ± 0.4	1.6 ± 0.3 **	1.6 ± 0.3	**
CPK (IU/L)	104 ± 62	191 ± 425	136 ± 123	73 ± 44	*
CHLORIDE (mEq/L)	122 ± 3	123 ± 3	124 ± 3	127 ± 4	**

Mean ± S.D.

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

TABLE 11 URINALYSIS OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1-BROMO-3-CHLOROPROPANE

Group Name		Control	25 ppm	100 ppm	400 ppm
No. of examined animals		38	34	36	36
pH	Grade				
	5.0	0	0	0	0
	6.0	0	5	5	8
	6.5	4	4	11	22
	7.0	4	5	10	4
	7.5	19	12	5	1
	8.0	7	8	2	0
	8.5	4	0	3	1
	Chi square test			**	**
Protein	—	1	0	0	0
	±	10	8	4	0
	+	25	22	23	17
	2+	2	3	8	17
	3+	0	1	1	2
	4+	0	0	0	0
	Chi square test				**
Ketone body	—	16	22	8	4
	±	20	10	14	9
	+	2	2	12	17
	2+	0	0	2	6
	3+	0	0	0	0
	4+	0	0	0	0
Chi square test			**	**	

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

TABLE 12 URINALYSIS OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 1-BROMO-3-CHLOROPROPANE

Group Name		Control	25 ppm	100 ppm	400 ppm
No. of examined animals		30	24	32	33
pH	Grade				
	5.0	0	1	0	0
	6.0	1	1	3	3
	6.5	2	4	3	15
	7.0	2	0	2	3
	7.5	4	3	3	6
	8.0	19	15	18	6
	8.5	2	0	3	0
	Chi square test				**
Protein	—	0	1	0	0
	±	7	4	0	2
	+	13	13	14	12
	2+	7	6	16	16
	3+	3	0	2	3
	4+	0	0	0	0
		Chi square test			*
Ketone body	—	9	8	0	0
	±	14	13	13	13
	+	6	3	15	9
	2+	1	0	4	11
	3+	0	0	0	0
	4+	0	0	0	0
	Chi square test			**	**

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

TABLE 13 ORGAN WEIGHTS OF MALE MICE IN THE 2-YEAR INHALATION STUDY OF 1-BROMO-3-CHLOROPROPANE

Group Name	Control	25 ppm	100 ppm	400 ppm
No. of examined animals	38	33	37	36
Body weight (g)	42.5 ± 7.0	41.4 ± 7.7	38.3 ± 7.4 *	36.1 ± 7.3 **
Testes (g)	0.220 ± 0.038	0.213 ± 0.038	0.206 ± 0.031	0.183 ± 0.033 **
Testes (%)	0.525 ± 0.098	0.532 ± 0.123	0.558 ± 0.133	0.522 ± 0.125
Heart (g)	0.218 ± 0.020	0.220 ± 0.020	0.213 ± 0.024	0.203 ± 0.023 *
Heart (%)	0.521 ± 0.068	0.545 ± 0.084	0.576 ± 0.133	0.576 ± 0.082 **
Lungs (g)	0.231 ± 0.171	0.335 ± 0.250	0.309 ± 0.219	0.304 ± 0.169
Lungs (%)	0.604 ± 0.747	0.891 ± 0.876 **	0.879 ± 0.917 **	0.880 ± 0.550 **
Kidneys (g)	0.640 ± 0.186	0.620 ± 0.063	0.624 ± 0.062	1.006 ± 2.200
Kidneys (%)	1.524 ± 0.415	1.529 ± 0.202	1.672 ± 0.258 **	2.598 ± 4.628 **
Spleen (g)	0.144 ± 0.257	0.077 ± 0.032	0.065 ± 0.027	0.102 ± 0.141 *
Spleen (%)	0.354 ± 0.651	0.187 ± 0.072	0.175 ± 0.080	0.312 ± 0.489
Liver (g)	1.543 ± 0.267	1.838 ± 0.737	1.580 ± 0.315	1.729 ± 0.587
Liver (%)	3.679 ± 0.616	4.564 ± 1.937 *	4.246 ± 1.124 **	4.956 ± 2.176 **
Brain (g)	0.455 ± 0.016	0.457 ± 0.018	0.463 ± 0.022	0.442 ± 0.014 **
Brain (%)	1.102 ± 0.198	1.141 ± 0.217	1.268 ± 0.343 *	1.268 ± 0.232 **

Mean ± S.D.
Significant difference: * : p<0.05 ** : p<0.01 Test of Dunnett

TABLE 14 ORGAN WEIGHTS OF FEMALE MICE IN THE 2-YEAR INHALATION STUDY OF 1-BROMO-3-CHLOROPROPANE

Group Name	Control	25 ppm	100 ppm	400 ppm
No. of examined animals	30	24	32	33
Body weight (g)	27.5 ± 4.5	27.9 ± 4.2	26.3 ± 2.8	25.0 ± 2.4
Heart (g)	0.172 ± 0.022	0.185 ± 0.038	0.171 ± 0.017	0.157 ± 0.015 *
Heart (%)	0.639 ± 0.106	0.668 ± 0.125	0.652 ± 0.071	0.635 ± 0.081
Lungs (g)	0.195 ± 0.023	0.272 ± 0.175 **	0.263 ± 0.191 **	0.266 ± 0.157 **
Lungs (%)	0.721 ± 0.086	1.042 ± 0.940	1.024 ± 0.861 **	1.071 ± 0.626 **
Kidneys (g)	0.576 ± 0.855	0.496 ± 0.309	0.518 ± 0.471	0.441 ± 0.053
Kidneys (%)	2.108 ± 3.014	1.802 ± 1.163	1.926 ± 1.486 *	1.779 ± 0.246 **
Brain (g)	0.494 ± 0.055	0.472 ± 0.023	0.468 ± 0.020 *	0.445 ± 0.016 **
Brain (%)	1.848 ± 0.396	1.727 ± 0.253	1.797 ± 0.188	1.801 ± 0.187

Mean ± S.D.
Significant difference: * : p<0.05 ** : p<0.01 Test of Dunnett

TABLE 15 INCIDENCES OF SELECTED NEOPLASTIC LESIONS OF MALE MICE
IN THE 2-YEAR INHALATION STUDY OF 1-BROMO-3-CHLOROPROPANE

Group Name	Control	25ppm	100ppm	400ppm	Peto test	Cochran- Armitage test
Respiratory system						
lung	<50>	<50>	<50>	<50>		
bronchiolar-alveolar adenoma	5 (10 %)	21 (42 %)**	20 (40 %)**	26 (52 %)**	↑ ↑	↑ ↑
bronchiolar-alveolar carcinoma	3 (6 %)	29 (58 %)**	26 (52 %)**	26 (52 %)**	↑	↑
adenosquamous carcinoma	0 (0 %)	0 (0 %)	0 (0 %)	1 (2 %)		
squamous cell carcinoma	0 (0 %)	0 (0 %)	1 (2 %)	0 (0 %)		
Digestive system						
stomach	<50>	<50>	<50>	<50>		
squamous cell papilloma	1 (2 %)	1 (2 %)	2 (4 %)	8 (16 %)*	↑ ↑	↑ ↑
liver	<50>	<50>	<50>	<50>		
hepatocellular adenoma	4 (8 %)	10 (20 %)	8 (16 %)	14 (28 %)**	↑ ↑	↑
hepatocellular carcinoma	3 (6 %)	5 (10 %)	3 (6 %)	3 (6 %)		
hepatoblastoma	0 (0 %)	0 (0 %)	1 (2 %)	1 (2 %)		
Special sense organs/appendage						
Harderian gland	<50>	<50>	<50>	<50>		
adenoma	4 (8 %)	4 (8 %)	4 (8 %)	13 (26 %)*	↑ ↑	↑ ↑
Significant difference * : p<0.05 ** : p<0.01						
↑(↓) : p<0.05 ↑↑(↓↓) : p<0.01						
Fisher's exact test for neoplastic lesion						
Peto or Cochran-Armitage test for neoplastic lesion						
< > : Number of animals examined at the site						

TABLE 16 INCIDENCES OF SELECTED NEOPLASTIC LESIONS OF FEMALE MICE
IN THE 2-YEAR INHALATION STUDY OF 1-BROMO-3-CHLOROPROPANE

Group Name	Control	25ppm	100ppm	400ppm	Peto test	Cochran- Armitage test
Respiratory system						
lung	<50>	<49>	<50>	<50>		
bronchiolar-alveolar adenoma	2 (4 %)	19 (39 %) **	25 (50 %) **	30 (60 %) **	↑ ↑	↑ ↑
bronchiolar-alveolar carcinoma	2 (4 %)	12 (24 %) **	20 (40 %) **	13 (26 %) **		
Digestive system						
stomach	<50>	<49>	<50>	<50>		
squamous cell papilloma	0 (0 %)	0 (0 %)	1 (2 %)	8 (16 %) **	↑ ↑	↑ ↑
squamous cell carcinoma	0 (0 %)	1 (2 %)	0 (0 %)	1 (2 %)		
Special sense organs/appendage						
Harderian gland	<50>	<49>	<50>	<50>		
adenoma	3 (6 %)	0 (0 %)	2 (4 %)	14 (28 %) **	↑ ↑	↑ ↑
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 17 INCIDENCES OF SELECTED NON-NEOPLASTIC LESIONS OF MALE MICE
IN THE 2-YEAR INHALATION STUDY OF 1-BROMO-3-CHLOROPROPANE

Group Name	Control				25ppm				100ppm				400ppm			
	50				50				50				50			
Number of examined animals																
Grade of non-neoplastic lesion	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
Respiratory system																
nasal cavity	<50>				<50>				<50>				<50>			
respiratory metaplasia:olfactory epithelium	4	1	0	0	3	1	0	0	5	0	0	0	29	19	0	0 **
atrophy:olfactory epithelium	0	1	0	0	0	1	0	0	0	0	0	0	37	0	0	0 **
eosinophilic change:olfactory epithelium	10	1	0	0	14	0	0	0	18	0	0	0	17	5	0	0 *
exudate	0	1	0	0	0	1	0	0	0	1	0	0	3	0	0	0
respiratory metaplasia:gland	8	0	0	0	9	0	0	0	9	0	0	0	23	23	1	0 **
nasopharynx	<50>				<50>				<50>				<50>			
eosinophilic change	5	0	0	0	3	0	0	0	6	1	0	0	34	3	0	0 **
lung	<50>				<50>				<50>				<50>			
bronchiolar-alveolar cell hyperplasia	3	1	0	0	20	4	0	0 **	23	3	0	0 **	27	6	0	0 **
Digestive system																
stomach	<50>				<50>				<50>				<50>			
squamous cell hyperplasia:forestomach	2	0	0	0	1	2	0	0	4	0	0	0	17	1	0	0 **
Special sense organs/appendage																
Harderian gland	<50>				<50>				<50>				<50>			
hyperplasia	0	0	0	0	0	0	0	0	0	0	0	0	4	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 INCIDENCES OF SELECTED NON-NEOPLASTIC LESIONS OF FEMALE MICE
IN THE 2-YEAR INHALATION STUDY OF 1-BROMO-3-CHLOROPROPANE

Group Name	Control				25ppm				100ppm				400ppm			
	50				49				50				50			
Number of examined animals																
Grade of non-neoplastic lesion	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
Respiratory system																
nasal cavity	<50>				<49>				<50>				<50>			
respiratory metaplasia:olfactory epithelium	5	0	0	0	6	0	0	0	9	0	0	0	4	42	3	0 **
atrophy:olfactory epithelium	0	0	0	0	0	0	0	0	0	0	0	0	25	0	0	0 **
eosinophilic change:olfactory epithelium	23	3	1	0	16	4	4	0	22	3	0	0	9	32	8	1 **
exudate	0	0	0	0	0	0	0	0	2	0	0	0	20	0	0	0 **
respiratory metaplasia:gland	8	0	0	0	9	0	0	0	11	0	0	0	13	32	1	0 **
nasopharynx	<50>				<49>				<50>				<50>			
eosinophilic change	10	1	0	0	11	3	0	0	22	2	0	0 *	38	5	0	0 **
exudate	0	0	0	0	0	0	0	0	1	0	0	0	17	0	0	0 **
lung	<50>				<49>				<50>				<50>			
bronchiolar-alveolar cell hyperplasia	7	0	0	0	20	1	0	0 **	28	3	0	0 **	20	7	0	0 **
Digestive system																
stomach	<50>				<49>				<50>				<50>			
squamous cell hyperplasia:forestomach	2	2	0	0	2	0	0	0	10	1	0	0 *	18	3	0	0 **
Nervous system																
brain	<50>				<49>				<50>				<50>			
mineralization	21	0	0	0	10	0	0	0 *	16	0	0	0	4	0	0	0 **
Special sense organs/appendage																
Harderian gland	<50>				<49>				<50>				<50>			
hyperplasia	0	0	0	0	0	0	0	0	2	0	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 19 CAUSE OF DEATH OF MALE AND FEMALE MICE IN THE 2-YEAR
INHALATION STUDY OF 1-BROMO-3-CHLOROPROPANE

Group name	Male				Female			
	Control	25 ppm	100 ppm	400 ppm	Control	25 ppm	100 ppm	400 ppm
Number of dead or moribund animals	12	17	13	14	20	25	18	17
No microscopical confirmation	0	0	1	0	0	0	1	0
Hydronephrosis	0	0	1	4	1	1	0	0
Urinary retention	3	0	0	0	1	0	0	0
Hemorrhage	1	0	0	0	0	0	0	1
Tumor death :leukemia	4	4	4	4	9	13	5	7
subcutis	0	0	0	0	0	1	0	0
lung	0	6	1	4	1	0	3	0
spleen	0	0	1	0	0	0	0	1
large intestine	0	0	0	0	0	0	1	0
liver	3	7	4	2	1	1	0	0
urinary bladder	1	0	0	0	0	0	0	0
pituitary gland	0	0	0	0	2	3	0	0
adrenal gland	0	0	0	0	0	0	0	1
uterus	—	—	—	—	4	6	7	7
mammary gland	0	0	0	0	1	0	0	0
peripheral nerves	0	0	1	0	0	0	1	0

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

Organs Tumors	No. of animals examined	No. of animals bearing tumor	Incidence (%)	Min. - Max. (%)
Lung	1495			
Bronchiolar-alveolar adenoma		120	8.0	2 - 18
Bronchiolar-alveolar carcinoma		162	10.8	0 - 24
Adenosquamous carcinoma		0	0.0	0 - 0
Squamous cell carcinoma		0	0.0	0 - 0
Stomach	1495			
Squamous cell papilloma		3	0.2	0 - 2
Liver	1496			
Hepatocellular adenoma		273	18.2	4 - 34
Harderian gland	1495			
Adenoma		69	4.6	0 - 10

30 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

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

Organs Tumors	No. of animals examined	No. of animals bearing tumor	Incidence (%)	Min. - Max. (%)
Lung	1498			
Bronchiolar-alveolar adenoma		54	3.6	0 - 10
Bronchiolar-alveolar carcinoma		43	2.9	0 - 8
Stomach	1497			
Squamous cell papilloma		4	0.3	0 - 2
Squamous cell carcinoma		2	0.1	0 - 2
Harderian gland	1498			
Adenoma		47	3.1	0 - 12

30 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