1-ブロモ-3-クロロプロバンのラットを用いた
吸 入 に よ る が ん 原 性 試 験 報 告 書

試験番号：０４１７

TABLES

TABLES

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

Weeks on Study	Control Av.Wt.	Control No.of Surviv. <50>	25 ppm Av.Wt.	25 ppm % of cont.	25 ppm No.of Surviv. <50>	100 ppm Av.Wt.	100 ppm % of cont.	100 ppm No.of Surviv. <50>	400 ppm Av.Wt.	400 ppm % of cont.	400 ppm No.of Surviv. <50>
0	112 (50)	50/50	112 (50)	100	50/50	112 (50)	100	50/50	112 (50)	100	50/50
1	142 (50)	50/50	141 (50)	99	50/50	140 (50)	99	50/50	131 (50)	92	50/50
2	176 (50)	50/50	176 (50)	100	50/50	175 (50)	99	50/50	158 (50)	90	50/50
3	202 (50)	50/50	204 (50)	101	50/50	203 (50)	100	50/50	179 (50)	89	50/50
4	227 (50)	50/50	228 (50)	100	50/50	227 (50)	100	50/50	195 (50)	86	50/50
5	245 (50)	50/50	246 (50)	100	50/50	246 (50)	100	50/50	209 (50)	85	50/50
6	260 (50)	50/50	262 (50)	101	50/50	262 (50)	101	50/50	221 (50)	85	50/50
7	273 (50)	50/50	275 (50)	101	50/50	276 (50)	101	50/50	230 (50)	84	50/50
8	284 (50)	50/50	286 (50)	101	50/50	288 (50)	101	50/50	239 (50)	84	50/50
9	294 (50)	50/50	296 (50)	101	50/50	299 (50)	102	50/50	251 (50)	85	50/50
10	301 (50)	50/50	306 (50)	102	50/50	307 (50)	102	50/50	257 (50)	85	50/50
11	309 (50)	50/50	312 (50)	101	50/50	314 (50)	102	50/50	260 (50)	84	50/50
12	315 (50)	50/50	318 (50)	101	50/50	322 (50)	102	50/50	266 (50)	84	50/50
13	322 (50)	50/50	325 (50)	101	50/50	328 (50)	102	50/50	272 (50)	84	50/50
14	327 (50)	50/50	331 (50)	101	50/50	335 (50)	102	50/50	277 (50)	85	50/50
18	344 (50)	50/50	348 (50)	101	50/50	352 (50)	102	50/50	292 (50)	85	50/50
22	359 (50)	50/50	365 (50)	102	50/50	369 (50)	103	50/50	305 (50)	85	50/50
26	372 (50)	50/50	376 (50)	101	50/50	381 (50)	102	50/50	320 (50)	86	50/50
30	377 (50)	50/50	382 (49)	101	49/50	390 (49)	103	49/50	327 (50)	87	50/50
34	389 (50)	50/50	395 (49)	102	49/50	401 (49)	103	49/50	342 (49)	88	49/50
38	397 (50)	50/50	401 (49)	101	49/50	407 (49)	103	49/50	351 (49)	88	49/50
42	403 (50)	50/50	407 (49)	101	49/50	415 (48)	103	48/50	349 (49)	87	49/50
46	412 (50)	50/50	418 (49)	101	49/50	422 (48)	102	48/50	339 (48)	82	48/50
50	415 (50)	50/50	421 (49)	101	49/50	425 (48)	102	48/50	345 (48)	83	48/50
54	414 (50)	50/50	423 (49)	102	49/50	425 (48)	103	48/50	347 (48)	84	48/50
58	421 (48)	48/50	427 (49)	101	49/50	431 (48)	102	48/50	351 (48)	83	48/50
62	425 (48)	48/50	429 (49)	101	49/50	433 (48)	102	48/50	355 (48)	84	48/50
66	426 (47)	47/50	432 (48)	101	48/50	435 (48)	102	48/50	351 (47)	82	47/50
70	428 (47)	47/50	434 (48)	101	48/50	439 (48)	103	48/50	352 (47)	82	47/50
74	424 (46)	46/50	432 (47)	102	47/50	436 (48)	103	48/50	349 (46)	82	46/50
78	427 (46)	46/50	435 (45)	102	45/50	436 (48)	102	48/50	347 (45)	81	45/50
82	424 (45)	45/50	436 (45)	103	45/50	434 (48)	102	48/50	339 (45)	80	45/50
86	427 (43)	43/50	428 (44)	100	44/50	435 (46)	102	46/50	338 (43)	79	43/50
90	429 (43)	43/50	430 (40)	100	40/50	435 (46)	101	46/50	334 (42)	78	42/50
94	425 (43)	43/50	424 (40)	100	40/50	431 (46)	101	46/50	329 (41)	77	41/50
98	420 (42)	42/50	416 (39)	99	39/50	414 (44)	99	44/50	324 (38)	77	38/50
102	414 (40)	40/50	412 (35)	100	35/50	420 (39)	101	39/50	313 (35)	76	35/50
104	408 (40)	40/50	405 (35)	99	35/50	412 (38)	101	38/50	305 (30)	75	30/50

< > : 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 RATS IN THE 2-YEAR INHALATION STUDY OF 1-BROMO-3-CHLOROPROPANE

Weeks on Study	Control Av.Wt.	Control No.of Surviv. <50>	25 ppm Av.Wt.	25 ppm % of cont.	25 ppm No.of Surviv. <50>	100 ppm Av.Wt.	100 ppm % of cont.	100 ppm No.of Surviv. <50>	400 ppm Av.Wt.	400 ppm % of cont.	400 ppm No.of Surviv. <50>
0	91 (50)	50/50	91 (50)	100	50/50	91 (50)	100	50/50	91 (50)	100	50/50
1	106 (50)	50/50	107 (50)	101	50/50	107 (50)	101	50/50	103 (50)	97	50/50
2	121 (50)	50/50	121 (50)	100	50/50	123 (50)	102	50/50	115 (50)	95	50/50
3	133 (50)	50/50	132 (50)	99	50/50	133 (50)	100	50/50	124 (50)	93	50/50
4	142 (50)	50/50	143 (50)	101	50/50	145 (50)	102	50/50	133 (50)	94	50/50
5	148 (50)	50/50	150 (50)	101	50/50	153 (50)	103	50/50	140 (50)	95	50/50
6	155 (50)	50/50	157 (50)	101	50/50	159 (50)	103	50/50	146 (50)	94	50/50
7	160 (50)	50/50	162 (50)	101	50/50	165 (50)	103	50/50	151 (50)	94	50/50
8	164 (50)	50/50	166 (50)	101	50/50	169 (50)	103	50/50	155 (50)	95	50/50
9	169 (50)	50/50	170 (50)	101	50/50	173 (50)	102	50/50	158 (50)	93	50/50
10	173 (50)	50/50	175 (50)	101	50/50	177 (50)	102	50/50	163 (50)	94	50/50
11	176 (50)	50/50	179 (50)	102	50/50	182 (50)	103	50/50	166 (50)	94	50/50
12	178 (50)	50/50	180 (50)	101	50/50	185 (50)	104	50/50	168 (50)	94	50/50
13	181 (50)	50/50	183 (50)	101	50/50	187 (50)	103	50/50	171 (50)	94	50/50
14	183 (50)	50/50	185 (50)	101	50/50	190 (50)	104	50/50	173 (50)	95	50/50
18	189 (50)	50/50	191 (50)	101	50/50	196 (50)	104	50/50	180 (50)	95	50/50
22	197 (50)	50/50	199 (50)	101	50/50	204 (50)	104	50/50	187 (50)	95	50/50
26	203 (50)	50/50	205 (50)	101	50/50	208 (50)	102	50/50	194 (50)	96	50/50
30	206 (50)	50/50	209 (50)	101	50/50	214 (49)	104	49/50	199 (50)	97	50/50
34	212 (50)	50/50	215 (50)	101	50/50	221 (49)	104	49/50	206 (50)	97	50/50
38	217 (50)	50/50	218 (50)	100	50/50	225 (49)	104	49/50	213 (50)	98	50/50
42	220 (50)	50/50	222 (50)	101	50/50	231 (49)	105	49/50	213 (50)	97	50/50
46	227 (50)	50/50	228 (50)	100	50/50	238 (49)	105	49/50	209 (50)	92	50/50
50	227 (50)	50/50	231 (50)	102	50/50	239 (49)	105	49/50	210 (50)	93	50/50
54	230 (50)	50/50	236 (50)	103	50/50	245 (49)	107	49/50	215 (50)	93	50/50
58	234 (50)	50/50	243 (49)	104	49/50	251 (49)	107	49/50	220 (49)	94	49/50
62	236 (50)	50/50	244 (49)	103	49/50	253 (48)	107	48/50	220 (49)	93	49/50
66	242 (50)	50/50	250 (49)	103	49/50	261 (48)	108	48/50	225 (49)	93	49/50
70	247 (48)	48/50	256 (49)	104	49/50	265 (48)	107	48/50	227 (49)	92	49/50
74	252 (47)	47/50	259 (49)	103	49/50	270 (48)	107	48/50	229 (48)	91	48/50
78	255 (47)	47/50	266 (49)	104	49/50	275 (48)	108	48/50	230 (47)	90	47/50
82	259 (44)	44/50	268 (49)	103	49/50	279 (48)	108	48/50	229 (45)	88	45/50
86	259 (43)	43/50	270 (48)	104	48/50	281 (47)	108	47/50	229 (43)	88	43/50
90	269 (42)	42/50	278 (47)	103	47/50	290 (46)	108	46/50	230 (42)	86	42/50
94	269 (42)	42/50	283 (45)	105	45/50	295 (45)	110	45/50	231 (38)	86	38/50
98	273 (40)	40/50	284 (45)	104	45/50	293 (45)	107	45/50	228 (33)	84	33/50
102	274 (38)	38/50	282 (45)	103	45/50	289 (43)	105	43/50	218 (28)	80	28/50
104	272 (38)	38/50	280 (45)	103	45/50	295 (39)	108	39/50	218 (26)	80	26/50

< > : 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 RATS 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	3/50	3/50	5/47	8/46	11/43	11/50 (0/10)
	25 ppm	0/50	0/50	2/50	4/49	6/49	9/48	8/45	12/40	17/50 (7/15)
	100 ppm	0/50	0/50	0/50	1/48	2/48	6/48	9/48	11/46	12/50 (1/12)
	400 ppm	0/50	0/50	0/50	1/49	2/48	3/47	4/45	7/42	7/50 (3/20)
Internal mass										
	Control	0/50	0/50	0/50	0/50	0/50	0/47	1/46	2/43	3/50 (1/10)
	25 ppm	0/50	0/50	1/50	0/49	0/49	1/48	0/45	0/40	2/50 (2/15)
	100 ppm	0/50	0/50	0/50	0/48	0/48	0/48	0/48	0/46	0/50 (0/12)
	400 ppm	0/50	0/50	0/50	0/49	0/48	0/47	0/45	0/42	0/50 (0/20)

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 RATS 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	0/50	0/50	1/47	10/42	10/50 (1/12)
	25 ppm	0/50	0/50	0/50	0/50	0/50	1/49	3/49	9/46	9/50 (0/5)
	100 ppm	0/50	1/50	0/49	1/49	2/49	2/48	6/48	10/45	12/50 (3/11)
	400 ppm	0/50	0/50	0/50	0/50	2/50	3/49	10/46	11/40	14/50 (7/24)
Internal mass										
	Control	0/50	0/50	0/50	0/50	0/50	1/50	1/47	1/42	2/50 (2/12)
	25 ppm	0/50	0/50	0/50	0/50	0/50	0/49	0/49	0/46	0/50 (0/5)
	100 ppm	0/50	0/50	0/49	0/49	0/49	0/48	1/48	1/45	2/50 (1/11)
	400 ppm	0/50	0/50	0/50	0/50	0/50	0/49	3/46	4/40	5/50 (8/24)

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 RATS IN THE 2-YEAR INHALATION STUDY OF 1-BROMO-3-CHLOROPROPANE

Weeks on Study	Control Av.FC. <50>	25 ppm Av.FC. <50>	25 ppm % of cont.	100 ppm Av.FC. <50>	100 ppm % of cont.	400 ppm Av.FC. <50>	400 ppm % of cont.
1	14.5 (50)	14.3 (50)	99	14.1 (50)	97	12.6 (50)	87
2	15.9 (50)	16.1 (50)	101	16.2 (50)	102	15.0 (50)	94
3	17.3 (50)	17.5 (50)	101	18.1 (50)	105	16.7 (50)	97
4	17.5 (50)	17.6 (50)	101	18.2 (50)	104	17.2 (50)	98
5	17.5 (50)	17.5 (50)	100	17.9 (50)	102	17.3 (50)	99
6	17.1 (50)	17.4 (50)	102	18.1 (50)	106	17.6 (50)	103
7	17.2 (50)	17.3 (50)	101	17.8 (50)	103	17.4 (50)	101
8	16.6 (50)	16.8 (50)	101	17.5 (50)	105	17.5 (50)	105
9	17.2 (50)	17.4 (50)	101	17.7 (50)	103	17.6 (50)	102
10	16.9 (50)	17.3 (50)	102	17.7 (50)	105	17.4 (50)	103
11	16.8 (50)	17.1 (50)	102	17.4 (50)	104	17.4 (50)	104
12	16.9 (50)	17.0 (50)	101	17.4 (50)	103	17.7 (50)	105
13	16.8 (50)	16.9 (50)	101	17.3 (50)	103	17.8 (50)	106
14	16.8 (50)	16.9 (50)	101	17.4 (50)	104	17.9 (50)	107
18	16.4 (50)	16.6 (50)	101	16.9 (50)	103	17.5 (50)	107
22	17.0 (50)	17.0 (50)	100	17.3 (50)	102	18.0 (50)	106
26	16.8 (50)	16.7 (50)	99	16.8 (50)	100	17.6 (50)	105
30	16.2 (50)	16.2 (49)	100	16.7 (49)	103	17.3 (50)	107
34	17.1 (50)	17.5 (49)	102	17.4 (49)	102	17.9 (49)	105
38	16.6 (50)	16.3 (49)	98	16.7 (49)	101	17.1 (49)	103
42	16.6 (50)	16.6 (49)	100	17.0 (48)	102	16.2 (49)	98
46	17.2 (50)	17.2 (49)	100	17.1 (48)	99	17.8 (48)	103
50	17.1 (50)	17.2 (49)	101	17.2 (48)	101	17.7 (48)	104
54	16.5 (50)	17.0 (49)	103	17.2 (48)	104	17.6 (48)	107
58	17.1 (48)	16.9 (49)	99	17.2 (48)	101	17.4 (48)	102
62	17.5 (48)	17.1 (49)	98	17.2 (48)	98	17.0 (48)	97
66	17.4 (47)	17.4 (48)	100	17.4 (48)	100	16.9 (47)	97
70	17.0 (47)	17.0 (48)	100	17.3 (48)	102	17.2 (47)	101
74	17.2 (46)	17.0 (47)	99	17.2 (48)	100	17.0 (46)	99
78	17.6 (46)	17.4 (45)	99	17.5 (48)	99	17.2 (45)	98
82	16.8 (45)	17.3 (45)	103	17.5 (48)	104	16.9 (44)	101
86	17.2 (43)	16.9 (44)	98	17.1 (46)	99	16.6 (43)	97
90	17.5 (43)	17.1 (40)	98	17.4 (46)	99	16.7 (42)	95
94	16.8 (43)	16.7 (40)	99	17.0 (46)	101	16.5 (41)	98
98	17.2 (42)	16.8 (39)	98	16.1 (44)	94	17.2 (38)	100
102	17.6 (40)	16.8 (35)	95	17.3 (39)	98	16.8 (34)	95
104	17.2 (40)	16.3 (35)	95	17.0 (38)	99	16.7 (30)	97

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

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

TABLE 6 FOOD CONSUMPTION CHANGES OF FEMALE RATS IN THE 2-YEAR INHALATION STUDY OF 1-BROMO-3-CHLOROPROPANE

Weeks on Study	Control Av.FC. <50>	25 ppm Av.FC. <50>	% of cont.	100 ppm Av.FC. <50>	% of cont.	400 ppm Av.FC. <50>	% of cont.
1	10.8 (50)	10.7 (50)	99	10.9 (50)	101	9.8 (50)	91
2	11.0 (50)	11.4 (50)	104	11.9 (50)	108	11.2 (50)	102
3	11.4 (50)	11.6 (50)	102	12.3 (50)	108	11.5 (50)	101
4	11.5 (50)	11.7 (50)	102	12.4 (50)	108	11.9 (49)	103
5	11.3 (50)	11.6 (50)	103	12.7 (50)	112	12.2 (50)	108
6	11.2 (50)	11.5 (50)	103	12.1 (50)	108	12.1 (50)	108
7	11.1 (50)	11.4 (50)	103	11.9 (50)	107	12.2 (50)	110
8	10.8 (50)	10.8 (50)	100	11.4 (50)	106	12.2 (50)	113
9	11.2 (50)	11.2 (50)	100	11.4 (50)	102	12.0 (50)	107
10	11.0 (50)	11.0 (50)	100	11.4 (50)	104	12.0 (50)	109
11	11.0 (50)	11.5 (50)	105	12.0 (50)	109	12.4 (50)	113
12	11.3 (50)	11.3 (50)	100	12.1 (50)	107	12.6 (50)	112
13	11.1 (50)	11.3 (50)	102	11.9 (50)	107	12.7 (50)	114
14	11.3 (50)	11.5 (50)	102	12.2 (50)	108	12.8 (50)	113
18	10.8 (50)	11.2 (50)	104	11.4 (50)	106	12.6 (50)	117
22	11.3 (50)	11.6 (50)	103	11.7 (50)	104	12.6 (50)	112
26	11.0 (50)	11.0 (50)	100	11.1 (50)	101	12.3 (50)	112
30	10.9 (50)	10.9 (50)	100	11.4 (49)	105	12.4 (50)	114
34	10.9 (50)	11.5 (50)	106	12.0 (49)	110	12.6 (50)	116
38	11.3 (50)	11.3 (50)	100	11.8 (49)	104	12.3 (50)	109
42	11.2 (50)	11.2 (50)	100	12.2 (49)	109	11.7 (50)	104
46	11.7 (50)	11.5 (50)	98	12.0 (49)	103	12.4 (50)	106
50	10.9 (50)	11.4 (50)	105	11.7 (49)	107	12.5 (50)	115
54	11.6 (50)	11.9 (50)	103	12.6 (49)	109	13.0 (50)	112
58	11.5 (50)	11.7 (49)	102	12.2 (49)	106	12.7 (49)	110
62	11.6 (50)	11.5 (49)	99	11.9 (48)	103	12.1 (49)	104
66	12.0 (50)	12.0 (49)	100	12.7 (48)	106	12.9 (49)	108
70	12.0 (48)	12.0 (49)	100	12.6 (48)	105	12.6 (49)	105
74	12.1 (47)	12.0 (49)	99	12.5 (48)	103	12.4 (48)	102
78	12.3 (47)	12.6 (49)	102	13.0 (48)	106	12.7 (47)	103
82	12.2 (44)	12.2 (49)	100	12.9 (48)	106	12.8 (45)	105
86	12.0 (43)	12.4 (48)	103	12.8 (47)	107	13.1 (42)	109
90	12.8 (42)	12.5 (47)	98	13.5 (46)	105	13.1 (42)	102
94	12.1 (42)	12.7 (45)	105	13.2 (45)	109	12.8 (38)	106
98	12.6 (40)	13.0 (45)	103	13.2 (45)	105	13.8 (33)	110
102	12.4 (38)	12.6 (45)	102	12.8 (42)	103	13.2 (28)	106
104	12.2 (38)	12.7 (45)	104	12.9 (39)	106	13.3 (26)	109

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

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

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

Group Name	Control	25 ppm	100 ppm	400 ppm
No. of examined animals	40	35	38	29
MCH (pg)	16.5 ± 1.2	16.3 ± 1.1	16.5 ± 0.9	15.8 ± 0.9 *
PLATELET ($10^3/\mu$ L)	929 ± 241	1004 ± 326	1117 ± 241 **	1045 ± 204

Mean ± S.D.

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

TABLE 8 HEMATOLOGY OF FEMALE RATS 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	45	37	26
MCV (fL)	53.9 ± 3.3	53.1 ± 3.0	54.9 ± 8.7	52.1 ± 4.2 **
MCH (pg)	18.2 ± 0.8	17.8 ± 1.0	18.3 ± 1.9	16.9 ± 1.3 **
MCHC (g/dL)	33.9 ± 1.9	33.5 ± 2.0	33.6 ± 1.7	32.4 ± 1.1 **
PLATELET ($10^3/\mu$ L)	658 ± 92	716 ± 208	721 ± 168	1041 ± 284 **
WBC ($10^3/\mu$ L)	12.46 ± 57.20	2.98 ± 1.48	3.21 ± 3.38	11.62 ± 20.13 **

Mean ± S.D.

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

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

Group Name	Control	25 ppm	100 ppm	400 ppm
No. of examined animals	40	35	38	29
ALBUMIN (g/dL)	2.9 ± 0.4	2.9 ± 0.2	2.8 ± 0.2	2.7 ± 0.2 **
A/G RATIO	0.8 ± 0.1	0.8 ± 0.1	0.7 ± 0.1 **	0.7 ± 0.1 *
T-CHOLESTEROL (mg/dL)	200 ± 78	189 ± 61	241 ± 65 *	249 ± 56 **
TRIGLYCERIDE (mg/dL)	144 ± 150	108 ± 62	190 ± 132 *	205 ± 130 **
PHOSPHOLIPID (mg/dL)	284 ± 108	271 ± 73	333 ± 81 **	352 ± 66 **
GPT (IU/L)	39 ± 15	35 ± 10	34 ± 20 *	58 ± 54
ALP (IU/L)	214 ± 93	194 ± 43	176 ± 82 **	175 ± 66 **
G-GTP (IU/L)	6 ± 4	5 ± 3	7 ± 4	11 ± 8 *
CPK (IU/L)	109 ± 86	92 ± 11	93 ± 18	99 ± 55 **
UREA NITROGEN (mg/dL)	24.2 ± 12.8	21.0 ± 4.4	26.8 ± 12.2 *	38.8 ± 70.5 **
POTASSIUM (mEq/L)	3.8 ± 0.4	3.5 ± 0.3 *	3.6 ± 0.3	3.8 ± 0.7
CHLORIDE (mEq/L)	106 ± 2	106 ± 1	107 ± 2	111 ± 4 **
CALCIUM (mg/dL)	10.4 ± 0.5	10.4 ± 0.4	10.8 ± 0.7 **	10.7 ± 0.8

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

TABLE 10 BIOCHEMISTRY OF FEMALE RATS 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	45	38	26
ALBUMIN (g/dL)	3.6 ± 0.3	3.6 ± 0.2	3.5 ± 0.3	3.1 ± 0.4 **
A/G RATIO	1.1 ± 0.1	1.1 ± 0.1	1.0 ± 0.1 *	0.9 ± 0.1 **
T-BILIRUBIN (mg/dL)	0.14 ± 0.07	0.14 ± 0.04	0.23 ± 0.60	0.20 ± 0.07 **
GLUCOSE (mg/dL)	155 ± 15	159 ± 18	163 ± 20	136 ± 22 **
T-CHOLESTEROL (mg/dL)	124 ± 25	162 ± 67 **	187 ± 55 **	288 ± 85 **
TRIGLYCERIDE (mg/dL)	53 ± 56	114 ± 146 **	118 ± 104 **	159 ± 107 **
PHOSPHOLIPID (mg/dL)	227 ± 46	287 ± 110 **	321 ± 86 **	437 ± 116 **
GOT (IU/L)	186 ± 194	138 ± 68	143 ± 191	1015 ± 1144 **
GPT (IU/L)	75 ± 38	67 ± 35	63 ± 35	421 ± 622 **
LDH (IU/L)	361 ± 667	243 ± 104	236 ± 110	618 ± 759 **
ALP (IU/L)	144 ± 61	116 ± 53 **	109 ± 64 **	384 ± 284 **
G-GTP (IU/L)	2 ± 1	2 ± 1	2 ± 2	26 ± 27 **
UREA NITROGEN (mg/dL)	20.0 ± 13.7	18.1 ± 2.6	17.7 ± 2.8	22.2 ± 5.2 **
CREATININE (mg/dL)	0.5 ± 0.0	0.5 ± 0.1	0.5 ± 0.1	0.4 ± 0.1 **
CHLORIDE (mEq/L)	104 ± 2	104 ± 3	106 ± 2	109 ± 5 **
CALCIUM (mg/dL)	10.3 ± 0.4	10.4 ± 0.3	10.5 ± 0.4	10.6 ± 0.5 **

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

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

Group Name		Control	25 ppm	100 ppm	400 ppm
No. of examined animals		40	35	38	31
	Grade				
pH	5.0	0	0	0	0
	6.0	0	0	0	0
	6.5	4	2	3	8
	7.0	7	3	5	11
	7.5	17	18	16	11
	8.0	12	12	14	1
	8.5	0	0	0	0
	Chi square test				**
Protein	−	0	0	0	0
	±	0	0	0	0
	+	0	0	0	0
	2+	0	1	0	0
	3+	12	15	4	5
	4+	28	19	34	26
	Chi square test			*	

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

TABLE 12 URINALYSIS OF FEMALE RATS 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	45	41	27
	Grade				
pH	5.0	0	0	0	0
	6.0	0	0	2	0
	6.5	2	4	1	6
	7.0	7	7	5	11
	7.5	8	11	10	5
	8.0	17	19	19	4
	8.5	4	4	4	1
	Chi square test				*
Protein	−	1	0	0	0
	±	2	1	0	0
	+	7	13	1	0
	2+	13	10	6	1
	3+	9	10	18	8
	4+	6	11	16	18
	Chi square test			**	**

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

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

Group Name	Control	25 ppm	100 ppm	400 ppm
No. of examined animals	40	35	38	30
Body weight (g)	381 ± 30	378 ± 31	384 ± 45	279 ± 32 **
Adrenals (g)	0.103 ± 0.154	0.106 ± 0.188	0.163 ± 0.528	0.065 ± 0.010 **
Adrenals (%)	0.030 ± 0.056	0.029 ± 0.051	0.041 ± 0.129	0.024 ± 0.006 **
Testes (g)	3.787 ± 1.532	3.685 ± 1.441	3.437 ± 1.460	4.229 ± 1.223
Testes (%)	0.992 ± 0.395	0.979 ± 0.401	0.895 ± 0.367	1.527 ± 0.416 **
Heart (g)	1.251 ± 0.114	1.227 ± 0.099	1.282 ± 0.103	1.148 ± 0.100 **
Heart (%)	0.331 ± 0.040	0.327 ± 0.049	0.337 ± 0.033	0.416 ± 0.050 **
Lungs (g)	1.421 ± 0.102	1.405 ± 0.128	1.462 ± 0.272	1.375 ± 0.146 *
Lungs (%)	0.375 ± 0.037	0.373 ± 0.035	0.387 ± 0.101	0.498 ± 0.069 **
Kidneys (g)	2.772 ± 0.284	2.732 ± 0.235	2.991 ± 0.321 **	2.834 ± 0.261
Kidneys (%)	0.731 ± 0.086	0.729 ± 0.107	0.789 ± 0.130 *	1.023 ± 0.100 **
Spleen (g)	1.271 ± 2.224	0.930 ± 0.230	0.989 ± 0.250	0.968 ± 0.625
Spleen (%)	0.332 ± 0.575	0.247 ± 0.066	0.262 ± 0.083	0.342 ± 0.207 **
Liver (g)	11.401 ± 2.455	11.149 ± 1.059	13.099 ± 1.687 **	13.581 ± 2.917 **
Liver (%)	2.993 ± 0.600	2.965 ± 0.361	3.442 ± 0.509 **	4.877 ± 1.039 **
Brain (g)	2.056 ± 0.058	2.060 ± 0.045	2.050 ± 0.052	1.958 ± 0.054 **
Brain (%)	0.543 ± 0.044	0.549 ± 0.050	0.540 ± 0.051	0.711 ± 0.092 **

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

TABLE 14 ORGAN WEIGHTS OF FEMALE RATS 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	45	39		26	
Body weight (g)	253 ± 26	260 ± 29	275 ± 24	**	199 ± 28	**
Adrenals (g)	0.076 ± 0.015	0.076 ± 0.021	0.073 ± 0.008		0.094 ± 0.090	
Adrenals (%)	0.030 ± 0.007	0.030 ± 0.014	0.027 ± 0.003		0.047 ± 0.040	**
Ovaries (g)	0.131 ± 0.027	0.199 ± 0.494	0.131 ± 0.026		0.104 ± 0.035	**
Ovaries (%)	0.052 ± 0.011	0.077 ± 0.189	0.048 ± 0.010		0.052 ± 0.016	
Heart (g)	0.890 ± 0.084	0.888 ± 0.099	0.936 ± 0.119		0.880 ± 0.081	
Heart (%)	0.355 ± 0.052	0.346 ± 0.065	0.342 ± 0.040		0.448 ± 0.060	**
Lungs (g)	1.034 ± 0.205	0.991 ± 0.072	1.059 ± 0.326		1.156 ± 0.387	*
Lungs (%)	0.415 ± 0.111	0.386 ± 0.058	0.390 ± 0.147		0.601 ± 0.281	**
Kidneys (g)	1.738 ± 0.174	1.776 ± 0.229	1.862 ± 0.204	*	2.071 ± 0.167	**
Kidneys (%)	0.694 ± 0.107	0.692 ± 0.149	0.682 ± 0.093		1.055 ± 0.151	**
Spleen (g)	0.798 ± 1.043	0.646 ± 0.608	0.869 ± 1.957		0.943 ± 1.020	
Spleen (%)	0.336 ± 0.506	0.263 ± 0.304	0.337 ± 0.839		0.481 ± 0.522	**
Liver (g)	6.543 ± 1.056	7.019 ± 0.902	7.937 ± 1.032	**	15.357 ± 4.930	**
Liver (%)	2.612 ± 0.541	2.714 ± 0.342	2.899 ± 0.378	**	7.969 ± 3.238	**
Brain (g)	1.866 ± 0.053	1.855 ± 0.054	1.848 ± 0.048		1.798 ± 0.049	**
Brain (%)	0.745 ± 0.079	0.722 ± 0.089	0.678 ± 0.064	**	0.918 ± 0.127	**

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

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

Group Name	Control	25ppm	100ppm	400ppm	Peto	Cochran-
Number of examined animals	50	50	50	50	test	Armitage test
Integumentary system/appandage						
skin/appendage	<50>	<50>	<50>	<50>		
trichoepithelioma	0 (0 %)	1 (2 %)	0 (0 %)	3 (6 %)	↑	↑
Respiratory system						
lung	<50>	<50>	<50>	<50>		
bronchiolar-alveolar adenoma	2 (4 %)	1 (2 %)	1 (2 %)	7 (14 %)	↑↑	↑↑
bronchiolar-alveolar carcinoma	0 (0 %)	2 (4 %)	0 (0 %)	0 (0 %)		
Digestive system						
large intestine	<50>	<50>	<50>	<50>		
adenoma	0 (0 %)	0 (0 %)	0 (0 %)	3 (6 %)	↑↑	↑↑
adenocarcinoma	0 (0 %)	0 (0 %)	0 (0 %)	1 (2 %)		
liver	<50>	<50>	<50>	<50>		
hepatocellular adenoma	1 (2 %)	1 (2 %)	2 (4 %)	10 (20 %)**	↑↑	↑↑
hepatocellular carcinoma	0 (0 %)	0 (0 %)	1 (2 %)	6 (12 %)*	↑↑	↑↑
hemangiosarcoma	1 (2 %)	0 (0 %)	0 (0 %)	2 (4 %)		

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

Group Name	Control	25ppm	100ppm	400ppm	Peto	Cochran-
Number of examined animals	50	50	50	50	test	Armitage test
Integumentary system/appandage						
skin/appendage	<50>	<50>	<50>	<50>		
trichoepithelioma	0 (0 %)	0 (0 %)	1 (2 %)	2 (4 %)		
Respiratory system						
lung	<50>	<50>	<50>	<50>		
bronchiolar-alveolar adenoma	1 (2 %)	0 (0 %)	1 (2 %)	5 (10 %)	↑ ↑	↑ ↑
Hematopoietic system						
spleen	<50>	<50>	<50>	<50>		
mononuclear cell leukemia	5 (10 %)	3 (6 %)	5 (10 %)	13 (26 %)*	↑ ↑	↑ ↑
Digestive system						
large intestine	<50>	<50>	<50>	<50>		
adenoma	0 (0 %)	0 (0 %)	0 (0 %)	2 (4 %)		
liver	<50>	<50>	<50>	<50>		
hepatocellular adenoma	1 (2 %)	0 (0 %)	2 (4 %)	32 (64 %)**	↑ ↑	↑ ↑
hepatocellular carcinoma	0 (0 %)	0 (0 %)	0 (0 %)	38 (76 %)**	↑ ↑	↑ ↑
hemangioma	0 (0 %)	0 (0 %)	0 (0 %)	1 (2 %)		
hemangiosarcoma	0 (0 %)	0 (0 %)	0 (0 %)	6 (12 %)*	↑ ↑	↑ ↑

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 RATS IN THE 2-YEAR INHALATION STUDY OF 1-BROMO-3-CHLOROPROPANE

Group Name	Control				25ppm				100ppm				400ppm			
Number of examined animals	50				50				50				50			
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>			
inflammation:respiratory epithelium	0	0	0	0	6	2	0	0 *	5	2	0	0 *	13	13	0	0 **
squamous cell metaplasia:respiratory epithelium	0	0	0	0	2	0	0	0	1	0	0	0	16	7	0	0 **
hyperplasia with atypia:transitional epithelium	0	0	0	0	0	0	0	0	0	0	0	0	1	3	0	0
respiratory metaplasia:gland	15	15	0	0	14	21	0	0	16	22	0	0	2	37	0	0 **
atrophy:olfactory epithelium	0	0	0	0	0	0	0	0	2	0	0	0	11	18	1	0 **
necrosis:olfactory epithelium	0	0	0	0	0	0	0	0	1	0	0	0	5	3	0	0 *
respiratory metaplasia:olfactory epithelium	2	2	0	0	4	1	0	0	0	0	0	0	7	9	0	0 *
lung	<50>				<50>				<50>				<50>			
bronchiolar-alveolar cell hyperplasia	0	0	0	0	1	0	0	0	2	0	0	0	3	0	0	0
Hematopoietic system																
spleen	<50>				<50>				<50>				<50>			
deposit of hemosiderin	10	22	0	0	8	25	2	0	5	30	0	0	7	32	3	0 *
Digestive system																
liver	<50>				<50>				<50>				<50>			
clear cell focus	7	9	0	0	9	4	0	0	17	12	0	0 *	0	13	27	0 **
acidophilic cell focus	0	1	0	0	0	0	0	0	2	1	0	0	7	13	0	0 **
basophilic cell focus	2	1	0	0	0	1	0	0	2	5	0	0	1	8	0	0 *
Urinary system																
kidney	<50>				<50>				<50>				<50>			
chronic nephropathy	6	28	6	2	5	35	3	1	1	27	13	5	2	28	14	2

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

TABLE 18 INCIDENCES OF SELECTED NON-NEOPLASTIC LESIONS OF FEMALE RATS IN THE 2-YEAR INHALATION STUDY OF 1-BROMO-3-CHLOROPROPANE

Group Name	Control				25ppm				100ppm				400ppm			
Number of examined animals	50				50				50				50			
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>			
inflammation:respiratory epithelium	0	0	0	0	3	0	0	0	4	0	0	0	12	1	0	0 **
squamous cell metaplasia:respiratory epithelium	0	0	0	0	0	1	0	0	2	0	0	0	16	9	0	0 **
hyperplasia with atypia:transitional epithelium	0	0	0	0	0	0	0	0	0	1	0	0	1	1	0	0
respiratory metaplasia:gland	17	15	0	0	22	16	0	0	25	18	0	0 *	3	30	0	0 **
atrophy:olfactory epithelium	0	0	0	0	0	0	0	0	0	0	0	0	21	16	2	0 **
necrosis:olfactory epithelium	0	0	0	0	0	0	0	0	0	0	0	0	8	0	0	0 **
Hematopoietic system																
bone marrow	<50>				<50>				<50>				<50>			
increased hematopoiesis	2	0	0	0	3	0	0	0	2	0	0	0	11	0	0	0 *
spleen	<50>				<50>				<50>				<50>			
deposit of hemosiderin	2	38	4	0	1	43	1	0	1	38	2	0	1	28	0	0 **
Digestive system																
liver	<50>				<50>				<50>				<50>			
clear cell focus	3	1	0	0	0	0	0	0	7	0	0	0	1	12	20	1 **
acidophilic cell focus	0	0	0	0	0	0	0	0	1	0	0	0	4	9	0	0 **
basophilic cell focus	15	8	0	0	9	5	0	0	11	9	0	0	1	5	0	0 **
bile duct hyperplasia	1	3	0	0	4	7	0	0	17	12	0	0 **	13	9	0	0 **
granulation	7	13	1	0	5	5	0	0	0	3	0	0 **	1	2	0	0 **
Urinary system																
kidney	<50>				<50>				<50>				<50>			
chronic nephropathy	20	2	0	0	11	12	1	0 *	19	17	1	1 **	9	31	5	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 RATS IN THE 2-YEAR INHALATION STUDY OF 1-BROMO-3-CHLOROPROPANE

	Male				Female			
Group name	Control	25 ppm	100 ppm	400 ppm	Control	25 ppm	100 ppm	400 ppm
Number of dead or moribund animals	10	15	12	20	12	5	11	24
No microscopical confirmation	1	0	1	3	2	3	1	0
Respiratory system lesion	0	0	0	1	0	0	0	0
Chronic nephropathy	0	0	2	0	0	0	1	0
Renal lesion	0	0	0	0	1	0	0	0
Urinary retention	0	0	0	1	0	0	0	0
Central nervous system lesion	0	0	0	1	0	0	0	0
Hemorrhage	0	0	0	0	1	0	0	0
Tumor death : leukemia	2	2	2	1	3	1	3	8
skin/appendage	0	0	1	1	0	0	0	0
subcutis	0	2	0	0	0	0	1	0
brown fat	0	1	0	0	0	0	0	0
nasal cavity	0	0	0	1	0	0	1	0
spleen	1	1	0	0	0	0	0	0
heart	0	0	0	1	0	0	0	0
oral cavity	0	0	0	2	0	0	0	0
stomach	0	0	0	0	0	0	0	1
small intestine	0	0	1	0	0	0	0	0
large intestine	0	0	0	1	0	0	0	0
liver	0	0	0	3	0	0	0	8
pituitary gland	3	4	2	1	5	0	3	1
thyroid	0	0	0	0	0	0	0	1
adrenal gland	2	1	0	0	0	0	0	0
epididymis	0	0	0	1	0	0	0	0
uterus	—	—	—	—	0	1	0	2
mammary gland	0	1	0	0	0	0	0	0
preputial/clitoral gland	0	0	0	1	0	0	0	1
brain	0	1	1	0	0	0	1	1
Zymbal gland	0	1	0	0	0	0	0	1
bone	1	1	1	0	0	0	0	0
peritoneum	0	0	1	1	0	0	0	0

TABLE 20
HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER : F344/DuCrj MALE RATS

Organs Tumors	No. of animals examined	No. of animals bearing tumor	Incidence (%)	Min. - Max. (%)
Liver	1749			
Hepatocellular adenoma		30	1.7	0 - 8
Hepatocellular carcinoma		6	0.3	0 - 2
Hemangiosarcoma		0	0.0	0 - 0
Lung	1749			
Bronchiolar-alveolar adenoma		62	3.5	0 - 10
Large intestine	1749			
Adenoma		0	0.0	0 - 0
Adenocarcinoma		0	0.0	0 - 0
Skin/appendage	1747			
Trichoepithelioma		14	0.8	0 - 4

35 carcinogenicity studies examined in Japan Bioassay Research Center were used.
Study No. : 0043, 0059, 0061, 0063, 0065, 0067, 0095, 0104, 0115, 0130, 0141, 0158, 0162, 0189, 0205, 0210, 0224, 0242, 0267, 0269, 0278, 0284, 0288, 0294, 0296, 0318, 0328, 0342, 0347, 0365, 0371, 0396, 0399, 0401, 0407

TABLE 21
HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER : F344/DuCrj FEMALE RATS

Organs Tumors	No. of animals examined	No. of animals bearing tumor	Incidence (%)	Min. - Max. (%)
Liver	1597			
Hepatocellular adenoma		20	1.3	0 - 6
Hepatocellular carcinoma		2	0.1	0 - 2
Hemangiosarcoma		1	0.1	0 - 2
Lung	1597			
Bronchiolar-alveolar adenoma		30	1.9	0 - 10
Spleen	1597			
Mononuclear cell leukemia		209	13.1	2 - 26
Large intestine	1597			
Adenoma		0	0.0	0 - 0
Skin/appendage	1597			
Trichoepithelioma		3	0.2	0 - 2

32 carcinogenicity studies examined in Japan Bioassay Research Center were used.
Study No. : 0043, 0059, 0061, 0063, 0065, 0067, 0095, 0104, 0115, 0130, 0141, 0158, 0162, 0189, 0205, 0210, 0224, 0242, 0267, 0269, 0278, 0284, 0296, 0303, 0318, 0328, 0342, 0347, 0365, 0371, 0399, 0401