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

試験番号：０３７１

TABLES

TABLES

TABLES (CONTINUED)

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

Week on Study	Control		500 ppm			1000 ppm			2000 ppm		
	Av. Wt.	No. of Surviv.	Av. Wt.	% of cont.	No. of Surviv.	Av. Wt.	% of cont.	No. of Surviv.	Av. Wt.	% of cont.	No. of Surviv.
	<50>		<50>			<50>			<50>		
0	118 (50)	50 / 50	118 (50)	100	50 / 50	118 (50)	100	50 / 50	118 (50)	100	50 / 50
1	147 (50)	50 / 50	143 (50)	97	50 / 50	139 (50)	95	50 / 50	129 (50)	88	50 / 50
2	176 (50)	50 / 50	171 (50)	97	50 / 50	166 (50)	94	50 / 50	154 (50)	88	50 / 50
3	202 (50)	50 / 50	194 (50)	96	50 / 50	192 (50)	95	50 / 50	178 (50)	88	50 / 50
4	223 (50)	50 / 50	214 (50)	96	50 / 50	212 (50)	95	50 / 50	196 (50)	88	50 / 50
5	239 (50)	50 / 50	229 (50)	96	50 / 50	228 (50)	95	50 / 50	211 (50)	88	50 / 50
6	251 (50)	50 / 50	239 (50)	95	50 / 50	238 (50)	95	50 / 50	219 (50)	87	50 / 50
7	261 (50)	50 / 50	250 (50)	96	50 / 50	248 (50)	95	50 / 50	227 (50)	87	50 / 50
8	273 (50)	50 / 50	259 (50)	95	50 / 50	257 (50)	94	50 / 50	235 (50)	86	50 / 50
9	282 (50)	50 / 50	268 (50)	95	50 / 50	266 (50)	94	50 / 50	241 (50)	85	50 / 50
10	289 (50)	50 / 50	276 (50)	96	50 / 50	274 (50)	95	50 / 50	247 (50)	85	50 / 50
11	296 (50)	50 / 50	282 (50)	95	50 / 50	281 (50)	95	50 / 50	251 (50)	85	50 / 50
12	303 (50)	50 / 50	288 (50)	95	50 / 50	287 (50)	95	50 / 50	257 (50)	85	50 / 50
13	310 (50)	50 / 50	296 (50)	95	50 / 50	294 (50)	95	50 / 50	263 (50)	85	50 / 50
14	315 (50)	50 / 50	300 (50)	95	50 / 50	297 (50)	94	50 / 50	267 (50)	85	50 / 50
18	330 (50)	50 / 50	319 (50)	97	50 / 50	313 (50)	95	50 / 50	279 (50)	85	50 / 50
22	344 (50)	50 / 50	332 (50)	97	50 / 50	326 (50)	95	50 / 50	289 (50)	84	50 / 50
26	358 (50)	50 / 50	345 (50)	96	50 / 50	338 (50)	94	50 / 50	301 (50)	84	50 / 50
30	368 (50)	50 / 50	354 (50)	96	50 / 50	346 (50)	94	50 / 50	306 (50)	83	50 / 50
34	376 (50)	50 / 50	360 (50)	96	50 / 50	353 (50)	94	50 / 50	313 (50)	83	50 / 50
38	382 (50)	50 / 50	369 (50)	97	50 / 50	361 (50)	95	50 / 50	316 (50)	83	50 / 50
42	388 (50)	50 / 50	375 (50)	97	50 / 50	365 (50)	94	50 / 50	319 (50)	82	50 / 50
46	396 (50)	50 / 50	380 (50)	96	50 / 50	369 (50)	93	50 / 50	322 (50)	81	50 / 50
50	398 (50)	50 / 50	383 (50)	96	50 / 50	373 (50)	94	50 / 50	325 (50)	82	50 / 50
54	404 (50)	50 / 50	387 (50)	96	50 / 50	376 (50)	93	50 / 50	325 (50)	80	50 / 50
58	410 (50)	50 / 50	389 (50)	95	50 / 50	377 (50)	92	50 / 50	327 (49)	80	49 / 50
62	413 (50)	50 / 50	392 (50)	95	50 / 50	379 (50)	92	50 / 50	328 (49)	79	49 / 50
66	420 (50)	50 / 50	394 (50)	94	50 / 50	380 (50)	90	50 / 50	327 (48)	78	48 / 50
70	425 (50)	50 / 50	396 (50)	93	50 / 50	382 (49)	90	49 / 50	330 (48)	78	48 / 50
74	426 (50)	50 / 50	394 (49)	92	49 / 50	384 (49)	90	49 / 50	329 (48)	77	48 / 50
78	426 (50)	50 / 50	400 (47)	94	47 / 50	382 (47)	90	47 / 50	327 (48)	77	48 / 50
82	426 (49)	49 / 50	401 (47)	94	47 / 50	383 (46)	90	46 / 50	327 (48)	77	48 / 50
86	430 (47)	47 / 50	403 (46)	94	46 / 50	381 (46)	89	46 / 50	323 (48)	75	48 / 50
90	430 (46)	46 / 50	399 (46)	93	46 / 50	376 (46)	87	46 / 50	317 (47)	74	47 / 50
94	426 (45)	45 / 50	387 (42)	91	42 / 50	370 (45)	87	45 / 50	309 (46)	73	46 / 50
98	419 (44)	44 / 50	383 (40)	91	40 / 50	362 (43)	86	43 / 50	302 (44)	72	44 / 50
102	413 (42)	42 / 50	377 (39)	91	39 / 50	355 (43)	86	43 / 50	294 (43)	71	43 / 50
104	406 (41)	41 / 50	377 (36)	93	36 / 50	349 (42)	86	42 / 50	287 (42)	71	42 / 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 DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

Week on Study	Control		250 ppm			500 ppm			1000 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	95 (50)	50 / 50	95 (50)	100	50 / 50	95 (50)	100	50 / 50	95 (50)	100	50 / 50
1	110 (50)	50 / 50	110 (50)	100	50 / 50	108 (50)	98	50 / 50	105 (50)	95	50 / 50
2	123 (50)	50 / 50	123 (50)	100	50 / 50	121 (50)	98	50 / 50	118 (50)	96	50 / 50
3	133 (50)	50 / 50	133 (50)	100	50 / 50	130 (50)	98	50 / 50	126 (50)	95	50 / 50
4	141 (50)	50 / 50	140 (50)	99	50 / 50	138 (50)	98	50 / 50	132 (50)	94	50 / 50
5	148 (50)	50 / 50	147 (50)	99	50 / 50	144 (50)	97	50 / 50	137 (50)	93	50 / 50
6	153 (50)	50 / 50	151 (50)	99	50 / 50	149 (50)	97	50 / 50	140 (50)	92	50 / 50
7	157 (50)	50 / 50	156 (50)	99	50 / 50	153 (50)	97	50 / 50	145 (50)	92	50 / 50
8	161 (50)	50 / 50	160 (50)	99	50 / 50	157 (50)	98	50 / 50	149 (50)	93	50 / 50
9	165 (50)	50 / 50	164 (50)	99	50 / 50	160 (50)	97	50 / 50	151 (50)	92	50 / 50
10	167 (50)	50 / 50	166 (50)	99	50 / 50	164 (50)	98	50 / 50	155 (50)	93	50 / 50
11	171 (50)	50 / 50	172 (50)	101	50 / 50	167 (50)	98	50 / 50	158 (50)	92	50 / 50
12	173 (50)	50 / 50	174 (50)	101	50 / 50	170 (50)	98	50 / 50	160 (50)	92	50 / 50
13	175 (50)	50 / 50	176 (50)	101	50 / 50	172 (50)	98	50 / 50	161 (50)	92	50 / 50
14	176 (50)	50 / 50	178 (50)	101	50 / 50	174 (50)	99	50 / 50	163 (50)	93	50 / 50
18	184 (50)	50 / 50	185 (50)	101	50 / 50	181 (50)	98	50 / 50	169 (50)	92	50 / 50
22	189 (50)	50 / 50	188 (50)	99	50 / 50	185 (50)	98	50 / 50	173 (50)	92	50 / 50
26	193 (50)	50 / 50	194 (50)	101	50 / 50	190 (50)	98	50 / 50	178 (50)	92	50 / 50
30	199 (50)	50 / 50	198 (50)	99	50 / 50	196 (50)	98	50 / 50	182 (50)	91	50 / 50
34	204 (50)	50 / 50	204 (50)	100	50 / 50	200 (50)	98	50 / 50	185 (50)	91	50 / 50
38	206 (50)	50 / 50	205 (50)	100	50 / 50	202 (50)	98	50 / 50	187 (50)	91	50 / 50
42	211 (50)	50 / 50	210 (50)	100	50 / 50	205 (50)	97	50 / 50	189 (50)	90	50 / 50
46	215 (50)	50 / 50	213 (50)	99	50 / 50	208 (49)	97	49 / 50	191 (50)	89	50 / 50
50	219 (50)	50 / 50	216 (50)	99	50 / 50	212 (49)	97	49 / 50	196 (50)	89	50 / 50
54	223 (50)	50 / 50	220 (50)	99	50 / 50	216 (49)	97	49 / 50	199 (50)	89	50 / 50
58	227 (50)	50 / 50	223 (50)	98	50 / 50	220 (49)	97	49 / 50	202 (50)	89	50 / 50
62	232 (50)	50 / 50	227 (49)	98	49 / 50	224 (49)	97	49 / 50	204 (50)	88	50 / 50
66	237 (50)	50 / 50	232 (49)	98	49 / 50	228 (49)	96	49 / 50	206 (50)	87	50 / 50
70	243 (49)	49 / 50	236 (49)	97	49 / 50	232 (49)	95	49 / 50	209 (49)	86	49 / 50
74	250 (48)	48 / 50	244 (47)	98	47 / 50	237 (49)	95	49 / 50	214 (49)	86	49 / 50
78	255 (48)	48 / 50	248 (47)	97	47 / 50	240 (49)	94	49 / 50	217 (48)	85	48 / 50
82	263 (47)	47 / 50	252 (46)	96	46 / 50	245 (49)	93	49 / 50	221 (48)	84	48 / 50
86	264 (47)	47 / 50	255 (45)	97	45 / 50	249 (49)	94	49 / 50	219 (48)	83	48 / 50
90	264 (45)	45 / 50	256 (45)	97	45 / 50	251 (49)	95	49 / 50	221 (46)	84	46 / 50
94	265 (45)	45 / 50	253 (45)	95	45 / 50	249 (48)	94	48 / 50	220 (45)	83	45 / 50
98	267 (44)	44 / 50	256 (43)	96	43 / 50	251 (45)	94	45 / 50	219 (44)	82	44 / 50
102	271 (41)	41 / 50	259 (40)	96	40 / 50	250 (44)	92	44 / 50	218 (42)	80	42 / 50
104	269 (41)	41 / 50	253 (38)	94	38 / 50	248 (44)	92	44 / 50	217 (41)	81	41 / 50

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

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

Week on Study	Control		500 ppm			1000 ppm			2000 ppm		
	Av. WC.	No. of Surviv. <50>	Av. WC.	% of cont.	No. of Surviv. <50>	Av. WC.	% of cont.	No. of Surviv. <50>	Av. WC.	% of cont.	No. of Surviv. <50>
1	17.1 (50)	50 / 50	15.7 (50)	92	50 / 50	13.7 (50)	80	50 / 50	11.7 (50)	68	50 / 50
2	18.0 (50)	50 / 50	16.0 (49)	89	50 / 50	14.3 (50)	79	50 / 50	12.3 (50)	68	50 / 50
3	19.1 (49)	50 / 50	17.4 (50)	91	50 / 50	15.3 (50)	80	50 / 50	13.4 (50)	70	50 / 50
4	19.5 (50)	50 / 50	17.2 (50)	88	50 / 50	15.8 (50)	81	50 / 50	13.4 (50)	69	50 / 50
5	19.5 (50)	50 / 50	17.4 (50)	89	50 / 50	16.4 (50)	84	50 / 50	13.2 (50)	68	50 / 50
6	19.8 (50)	50 / 50	16.9 (50)	85	50 / 50	16.2 (50)	82	50 / 50	13.3 (50)	67	50 / 50
7	19.1 (50)	50 / 50	16.8 (50)	88	50 / 50	15.5 (50)	81	50 / 50	12.7 (50)	66	50 / 50
8	19.0 (50)	50 / 50	16.9 (50)	89	50 / 50	15.4 (50)	81	50 / 50	12.7 (50)	67	50 / 50
9	18.7 (50)	50 / 50	17.4 (50)	93	50 / 50	15.8 (50)	84	50 / 50	13.1 (50)	70	50 / 50
10	18.6 (50)	50 / 50	17.5 (50)	94	50 / 50	16.2 (50)	87	50 / 50	13.2 (50)	71	50 / 50
11	18.0 (50)	50 / 50	16.4 (50)	91	50 / 50	15.2 (50)	84	50 / 50	12.9 (50)	72	50 / 50
12	18.1 (49)	50 / 50	16.2 (50)	90	50 / 50	14.9 (50)	82	50 / 50	12.4 (50)	69	50 / 50
13	18.0 (50)	50 / 50	16.1 (50)	89	50 / 50	15.0 (50)	83	50 / 50	12.3 (50)	68	50 / 50
14	18.1 (50)	50 / 50	16.1 (50)	89	50 / 50	14.4 (50)	80	50 / 50	12.4 (50)	69	50 / 50
18	18.0 (50)	50 / 50	16.6 (50)	92	50 / 50	15.2 (50)	84	50 / 50	12.7 (50)	71	50 / 50
22	17.3 (50)	50 / 50	15.5 (50)	90	50 / 50	14.8 (50)	86	50 / 50	12.4 (50)	72	50 / 50
26	17.2 (50)	50 / 50	15.7 (50)	91	50 / 50	14.3 (50)	83	50 / 50	12.2 (50)	71	50 / 50
30	16.1 (50)	50 / 50	14.8 (50)	92	50 / 50	13.7 (50)	85	50 / 50	11.6 (50)	72	50 / 50
34	16.5 (50)	50 / 50	15.1 (50)	92	50 / 50	14.3 (50)	87	50 / 50	12.1 (50)	73	50 / 50
38	16.7 (50)	50 / 50	15.2 (49)	91	50 / 50	14.6 (50)	87	50 / 50	12.5 (50)	75	50 / 50
42	16.5 (50)	50 / 50	15.4 (50)	93	50 / 50	14.4 (50)	87	50 / 50	12.8 (49)	78	50 / 50
46	16.9 (50)	50 / 50	15.3 (50)	91	50 / 50	14.3 (50)	85	50 / 50	12.6 (50)	75	50 / 50
50	16.9 (50)	50 / 50	15.6 (50)	92	50 / 50	14.8 (50)	88	50 / 50	13.4 (50)	79	50 / 50
54	17.0 (50)	50 / 50	15.7 (50)	92	50 / 50	14.8 (50)	87	50 / 50	13.6 (50)	80	50 / 50
58	17.2 (50)	50 / 50	15.1 (50)	88	50 / 50	14.4 (50)	84	50 / 50	13.0 (49)	76	49 / 50
62	17.1 (50)	50 / 50	15.6 (50)	91	50 / 50	14.8 (50)	87	50 / 50	13.5 (49)	79	49 / 50
66	16.6 (50)	50 / 50	14.8 (50)	89	50 / 50	14.2 (50)	86	50 / 50	13.3 (48)	80	48 / 50
70	17.9 (50)	50 / 50	15.5 (50)	87	50 / 50	14.6 (49)	82	49 / 50	13.8 (48)	77	48 / 50
74	17.6 (50)	50 / 50	15.9 (49)	90	49 / 50	14.5 (49)	82	49 / 50	13.0 (48)	74	48 / 50
78	17.7 (50)	50 / 50	16.4 (47)	93	47 / 50	14.8 (47)	84	47 / 50	13.7 (48)	77	48 / 50
82	17.6 (49)	49 / 50	16.3 (47)	93	47 / 50	14.4 (46)	82	46 / 50	13.8 (48)	78	48 / 50
86	18.6 (47)	47 / 50	15.5 (46)	83	46 / 50	14.6 (46)	78	46 / 50	13.9 (48)	75	48 / 50
90	18.6 (46)	46 / 50	15.7 (46)	84	46 / 50	14.5 (46)	78	46 / 50	14.2 (47)	76	47 / 50
94	19.5 (44)	45 / 50	16.7 (42)	86	42 / 50	14.7 (45)	75	45 / 50	14.2 (46)	73	46 / 50
98	20.7 (44)	44 / 50	17.3 (40)	84	40 / 50	15.6 (43)	75	43 / 50	15.1 (44)	73	44 / 50
102	19.5 (42)	42 / 50	17.4 (39)	89	39 / 50	15.3 (42)	78	43 / 50	15.5 (43)	79	43 / 50
104	20.0 (41)	41 / 50	18.2 (36)	91	36 / 50	15.2 (42)	76	42 / 50	15.3 (42)	77	42 / 50

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

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

Week on Study	Control		250 ppm			500 ppm			1000 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	15.0 (50)	50 / 50	15.2 (50)	101	50 / 50	13.9 (50)	93	50 / 50	11.6 (49)	77	50 / 50
2	17.2 (49)	50 / 50	16.0 (48)	93	50 / 50	15.4 (49)	90	50 / 50	11.8 (50)	69	50 / 50
3	17.4 (49)	50 / 50	16.5 (49)	95	50 / 50	14.3 (50)	82	50 / 50	11.8 (48)	68	50 / 50
4	17.8 (50)	50 / 50	17.1 (49)	96	50 / 50	14.5 (50)	81	50 / 50	11.5 (50)	65	50 / 50
5	17.7 (47)	50 / 50	17.2 (46)	97	50 / 50	15.3 (49)	86	50 / 50	11.4 (50)	64	50 / 50
6	17.1 (46)	50 / 50	19.1 (47)	112	50 / 50	15.9 (50)	93	50 / 50	11.4 (48)	67	50 / 50
7	16.3 (49)	50 / 50	15.3 (48)	94	50 / 50	13.0 (50)	80	50 / 50	10.4 (50)	64	50 / 50
8	18.0 (48)	50 / 50	17.3 (48)	96	50 / 50	13.7 (49)	76	50 / 50	11.2 (50)	62	50 / 50
9	18.2 (49)	50 / 50	18.5 (49)	102	50 / 50	15.5 (50)	85	50 / 50	11.6 (50)	64	50 / 50
10	18.0 (48)	50 / 50	17.7 (48)	98	50 / 50	15.2 (48)	84	50 / 50	11.3 (50)	63	50 / 50
11	17.0 (50)	50 / 50	17.0 (50)	100	50 / 50	14.5 (50)	85	50 / 50	11.0 (50)	65	50 / 50
12	16.7 (49)	50 / 50	16.9 (49)	101	50 / 50	14.5 (50)	87	50 / 50	10.9 (50)	65	50 / 50
13	18.1 (47)	50 / 50	18.0 (46)	99	50 / 50	14.4 (49)	80	50 / 50	10.8 (50)	60	50 / 50
14	20.4 (50)	50 / 50	19.6 (50)	96	50 / 50	14.6 (49)	72	50 / 50	10.9 (50)	53	50 / 50
18	19.2 (47)	50 / 50	17.3 (47)	90	50 / 50	15.4 (49)	80	50 / 50	11.7 (50)	61	50 / 50
22	16.6 (48)	50 / 50	16.5 (50)	99	50 / 50	14.8 (50)	89	50 / 50	11.0 (50)	66	50 / 50
26	16.5 (49)	50 / 50	17.1 (50)	104	50 / 50	14.7 (50)	89	50 / 50	10.8 (50)	65	50 / 50
30	17.8 (50)	50 / 50	15.7 (50)	88	50 / 50	14.0 (50)	79	50 / 50	10.7 (50)	60	50 / 50
34	15.8 (50)	50 / 50	15.4 (50)	97	50 / 50	13.3 (50)	84	50 / 50	10.4 (49)	66	50 / 50
38	15.7 (50)	50 / 50	14.4 (49)	92	50 / 50	13.0 (50)	83	50 / 50	10.6 (48)	68	50 / 50
42	15.4 (50)	50 / 50	14.5 (49)	94	50 / 50	13.6 (50)	88	50 / 50	10.8 (49)	70	50 / 50
46	14.9 (50)	50 / 50	14.3 (49)	96	50 / 50	13.3 (49)	89	49 / 50	10.8 (50)	72	50 / 50
50	14.6 (50)	50 / 50	13.9 (50)	95	50 / 50	12.7 (49)	87	49 / 50	11.1 (50)	76	50 / 50
54	15.2 (50)	50 / 50	14.4 (50)	95	50 / 50	13.5 (49)	89	49 / 50	11.4 (50)	75	50 / 50
58	14.7 (50)	50 / 50	14.1 (50)	96	50 / 50	12.9 (49)	88	49 / 50	11.1 (50)	76	50 / 50
62	14.9 (50)	50 / 50	14.4 (49)	97	49 / 50	12.9 (49)	87	49 / 50	11.3 (50)	76	50 / 50
66	14.6 (50)	50 / 50	13.8 (49)	95	49 / 50	12.9 (49)	88	49 / 50	12.0 (50)	82	50 / 50
70	15.1 (49)	49 / 50	14.0 (49)	93	49 / 50	12.8 (49)	85	49 / 50	11.6 (48)	77	49 / 50
74	14.3 (48)	48 / 50	13.9 (47)	97	47 / 50	12.4 (49)	87	49 / 50	11.3 (49)	79	49 / 50
78	15.8 (48)	48 / 50	14.2 (47)	90	47 / 50	13.1 (49)	83	49 / 50	11.3 (48)	72	48 / 50
82	16.0 (47)	47 / 50	13.9 (46)	87	46 / 50	12.9 (49)	81	49 / 50	11.5 (48)	72	48 / 50
86	15.3 (47)	47 / 50	14.4 (45)	94	45 / 50	13.2 (49)	86	49 / 50	11.2 (47)	73	48 / 50
90	15.6 (45)	45 / 50	14.0 (45)	90	45 / 50	13.2 (49)	85	49 / 50	11.8 (46)	76	46 / 50
94	16.3 (44)	45 / 50	15.1 (45)	93	45 / 50	13.7 (48)	84	48 / 50	12.3 (45)	75	45 / 50
98	16.9 (44)	44 / 50	16.2 (43)	96	43 / 50	13.8 (44)	82	45 / 50	12.3 (42)	73	44 / 50
102	17.7 (40)	41 / 50	15.7 (40)	89	40 / 50	13.7 (44)	77	44 / 50	12.6 (42)	71	42 / 50
104	18.1 (40)	41 / 50	15.8 (38)	87	38 / 50	14.4 (44)	80	44 / 50	12.6 (41)	70	41 / 50

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

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

Week on Study	Control		500 ppm			1000 ppm			2000 ppm		
	Av. FC.	No. of Surviv. <50>	Av. FC.	% of cont.	No. of Surviv. <50>	Av. FC.	% of cont.	No. of Surviv. <50>	Av. FC.	% of cont.	No. of Surviv. <50>
1	13.3 (50)	50 / 50	12.7 (50)	95	50 / 50	12.0 (50)	90	50 / 50	10.3 (50)	77	50 / 50
2	14.4 (50)	50 / 50	13.9 (50)	97	50 / 50	13.5 (50)	94	50 / 50	12.2 (50)	85	50 / 50
3	15.7 (50)	50 / 50	14.7 (50)	94	50 / 50	14.6 (50)	93	50 / 50	13.4 (50)	85	50 / 50
4	16.1 (50)	50 / 50	15.4 (50)	96	50 / 50	15.3 (50)	95	50 / 50	14.1 (50)	88	50 / 50
5	15.8 (50)	50 / 50	15.3 (50)	97	50 / 50	15.2 (50)	96	50 / 50	14.2 (50)	90	50 / 50
6	15.9 (50)	50 / 50	15.1 (50)	95	50 / 50	15.1 (50)	95	50 / 50	13.9 (50)	87	50 / 50
7	15.5 (50)	50 / 50	14.8 (50)	95	50 / 50	14.8 (49)	95	50 / 50	13.5 (50)	87	50 / 50
8	15.6 (50)	50 / 50	14.7 (49)	94	50 / 50	14.9 (50)	96	50 / 50	13.6 (50)	87	50 / 50
9	15.5 (50)	50 / 50	14.9 (50)	96	50 / 50	14.8 (50)	95	50 / 50	13.6 (50)	88	50 / 50
10	15.5 (50)	50 / 50	15.1 (50)	97	50 / 50	15.4 (49)	99	50 / 50	13.8 (50)	89	50 / 50
11	15.6 (50)	50 / 50	15.0 (50)	96	50 / 50	15.4 (50)	99	50 / 50	14.0 (50)	90	50 / 50
12	15.6 (50)	50 / 50	15.0 (50)	96	50 / 50	15.6 (50)	100	50 / 50	14.3 (50)	92	50 / 50
13	15.3 (50)	50 / 50	14.8 (50)	97	50 / 50	15.1 (50)	99	50 / 50	13.9 (50)	91	50 / 50
14	15.2 (50)	50 / 50	14.6 (50)	96	50 / 50	14.8 (50)	97	50 / 50	13.7 (50)	90	50 / 50
18	15.0 (50)	50 / 50	14.9 (50)	99	50 / 50	14.6 (50)	97	50 / 50	13.7 (50)	91	50 / 50
22	15.3 (50)	50 / 50	14.9 (50)	97	50 / 50	15.4 (50)	101	50 / 50	14.3 (50)	93	50 / 50
26	15.5 (50)	50 / 50	15.3 (50)	99	50 / 50	15.2 (50)	98	50 / 50	14.4 (50)	93	50 / 50
30	15.1 (50)	50 / 50	14.9 (50)	99	50 / 50	14.9 (50)	99	50 / 50	14.0 (50)	93	50 / 50
34	15.2 (50)	50 / 50	15.3 (50)	101	50 / 50	15.3 (50)	101	50 / 50	14.7 (50)	97	50 / 50
38	15.5 (50)	50 / 50	15.5 (50)	100	50 / 50	15.6 (50)	101	50 / 50	14.6 (50)	94	50 / 50
42	15.5 (50)	50 / 50	15.8 (50)	102	50 / 50	15.7 (50)	101	50 / 50	15.0 (50)	97	50 / 50
46	15.7 (50)	50 / 50	15.7 (50)	100	50 / 50	15.8 (50)	101	50 / 50	14.9 (50)	95	50 / 50
50	15.8 (50)	50 / 50	15.7 (50)	99	50 / 50	15.9 (50)	101	50 / 50	15.0 (50)	95	50 / 50
54	16.2 (50)	50 / 50	16.1 (50)	99	50 / 50	16.2 (50)	100	50 / 50	15.3 (50)	94	50 / 50
58	16.1 (50)	50 / 50	15.8 (50)	98	50 / 50	15.8 (50)	98	50 / 50	15.2 (49)	94	49 / 50
62	15.9 (50)	50 / 50	15.8 (50)	99	50 / 50	15.8 (50)	99	50 / 50	14.7 (49)	92	49 / 50
66	15.9 (50)	50 / 50	15.2 (50)	96	50 / 50	15.1 (50)	95	50 / 50	13.8 (48)	87	48 / 50
70	15.9 (50)	50 / 50	15.3 (50)	96	50 / 50	15.3 (49)	96	49 / 50	14.5 (48)	91	48 / 50
74	16.1 (50)	50 / 50	15.2 (49)	94	49 / 50	15.8 (49)	98	49 / 50	14.5 (48)	90	48 / 50
78	16.1 (50)	50 / 50	16.0 (47)	99	47 / 50	15.8 (47)	98	47 / 50	14.6 (48)	91	48 / 50
82	15.8 (49)	49 / 50	15.7 (47)	99	47 / 50	15.5 (46)	98	46 / 50	14.5 (48)	92	48 / 50
86	15.8 (47)	47 / 50	15.3 (46)	97	46 / 50	15.3 (46)	97	46 / 50	14.0 (48)	89	48 / 50
90	16.3 (46)	46 / 50	15.5 (46)	95	46 / 50	15.3 (46)	94	46 / 50	14.1 (47)	87	47 / 50
94	16.0 (45)	45 / 50	15.3 (42)	96	42 / 50	15.1 (45)	94	45 / 50	13.8 (46)	86	46 / 50
98	15.9 (44)	44 / 50	15.6 (40)	98	40 / 50	15.0 (43)	94	43 / 50	14.0 (44)	88	44 / 50
102	15.7 (42)	42 / 50	15.5 (37)	99	39 / 50	14.9 (43)	95	43 / 50	13.9 (43)	89	43 / 50
104	15.5 (41)	41 / 50	16.2 (36)	105	36 / 50	14.7 (42)	95	42 / 50	13.4 (42)	86	42 / 50

< > : 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 DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

Week on Study	Control		250 ppm			500 ppm			1000 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	10.5 (50)	50 / 50	10.5 (50)	100	50 / 50	10.0 (50)	95	50 / 50	9.3 (50)	89	50 / 50
2	10.7 (50)	50 / 50	10.9 (50)	102	50 / 50	10.6 (50)	99	50 / 50	10.1 (50)	94	50 / 50
3	10.9 (50)	50 / 50	11.0 (50)	101	50 / 50	10.9 (50)	100	50 / 50	10.3 (50)	94	50 / 50
4	11.0 (50)	50 / 50	11.1 (50)	101	50 / 50	10.9 (50)	99	50 / 50	10.1 (50)	92	50 / 50
5	10.9 (50)	50 / 50	10.8 (50)	99	50 / 50	10.6 (50)	97	50 / 50	10.0 (50)	92	50 / 50
6	10.6 (50)	50 / 50	10.6 (50)	100	50 / 50	10.4 (50)	98	50 / 50	9.5 (50)	90	50 / 50
7	10.3 (50)	50 / 50	10.4 (50)	101	50 / 50	10.2 (50)	99	50 / 50	9.5 (50)	92	50 / 50
8	10.5 (50)	50 / 50	10.5 (50)	100	50 / 50	10.3 (50)	98	50 / 50	9.8 (50)	93	50 / 50
9	10.5 (50)	50 / 50	10.7 (50)	102	50 / 50	10.3 (50)	98	50 / 50	9.8 (50)	93	50 / 50
10	10.3 (50)	50 / 50	10.6 (50)	103	50 / 50	10.5 (50)	102	50 / 50	9.8 (50)	95	50 / 50
11	10.5 (50)	50 / 50	10.8 (50)	103	50 / 50	10.5 (50)	100	50 / 50	9.8 (50)	93	50 / 50
12	10.5 (50)	50 / 50	10.8 (50)	103	50 / 50	10.5 (50)	100	50 / 50	9.9 (50)	94	50 / 50
13	10.2 (50)	50 / 50	10.5 (50)	103	50 / 50	10.4 (50)	102	50 / 50	9.7 (50)	95	50 / 50
14	10.1 (50)	50 / 50	10.5 (50)	104	50 / 50	10.2 (50)	101	50 / 50	9.4 (50)	93	50 / 50
18	10.3 (50)	50 / 50	10.5 (50)	102	50 / 50	10.3 (50)	100	50 / 50	9.6 (50)	93	50 / 50
22	10.5 (50)	50 / 50	10.7 (50)	102	50 / 50	10.6 (49)	101	50 / 50	9.9 (50)	94	50 / 50
26	10.5 (50)	50 / 50	10.9 (50)	104	50 / 50	10.8 (50)	103	50 / 50	10.1 (50)	96	50 / 50
30	10.8 (50)	50 / 50	10.9 (50)	101	50 / 50	10.7 (50)	99	50 / 50	10.0 (49)	93	50 / 50
34	10.7 (50)	50 / 50	10.9 (50)	102	50 / 50	10.6 (49)	99	50 / 50	10.0 (50)	93	50 / 50
38	10.7 (50)	50 / 50	10.8 (50)	101	50 / 50	10.5 (49)	98	50 / 50	10.0 (50)	93	50 / 50
42	11.1 (50)	50 / 50	11.2 (50)	101	50 / 50	10.9 (50)	98	50 / 50	10.4 (50)	94	50 / 50
46	11.1 (50)	50 / 50	11.2 (50)	101	50 / 50	10.9 (49)	98	49 / 50	10.4 (50)	94	50 / 50
50	11.2 (50)	50 / 50	11.1 (50)	99	50 / 50	11.0 (49)	98	49 / 50	10.6 (50)	95	50 / 50
54	11.4 (50)	50 / 50	11.3 (50)	99	50 / 50	10.9 (49)	96	49 / 50	10.6 (50)	93	50 / 50
58	11.1 (50)	50 / 50	11.2 (50)	101	50 / 50	11.2 (49)	101	49 / 50	10.6 (50)	95	50 / 50
62	11.2 (50)	50 / 50	11.2 (48)	100	49 / 50	11.0 (49)	98	49 / 50	10.3 (50)	92	50 / 50
66	11.1 (50)	50 / 50	11.0 (49)	99	49 / 50	10.9 (49)	98	49 / 50	10.3 (50)	93	50 / 50
70	11.3 (49)	49 / 50	11.4 (49)	101	49 / 50	11.1 (49)	98	49 / 50	10.4 (49)	92	49 / 50
74	11.3 (48)	48 / 50	11.4 (47)	101	47 / 50	11.1 (49)	98	49 / 50	10.6 (49)	94	49 / 50
78	11.9 (48)	48 / 50	11.7 (46)	98	47 / 50	11.3 (49)	95	49 / 50	10.6 (48)	89	48 / 50
82	12.2 (47)	47 / 50	11.7 (46)	96	46 / 50	11.5 (49)	94	49 / 50	10.9 (48)	89	48 / 50
86	11.7 (47)	47 / 50	11.6 (45)	99	45 / 50	11.3 (49)	97	49 / 50	10.4 (48)	89	48 / 50
90	11.9 (45)	45 / 50	11.9 (45)	100	45 / 50	11.5 (49)	97	49 / 50	10.9 (46)	92	46 / 50
94	11.9 (45)	45 / 50	11.7 (45)	98	45 / 50	11.2 (48)	94	48 / 50	10.7 (45)	90	45 / 50
98	11.9 (44)	44 / 50	12.1 (43)	102	43 / 50	11.4 (45)	96	45 / 50	10.6 (44)	89	44 / 50
102	12.1 (41)	41 / 50	11.8 (40)	98	40 / 50	11.1 (44)	92	44 / 50	10.6 (42)	88	42 / 50
104	11.6 (41)	41 / 50	11.2 (38)	97	38 / 50	11.2 (44)	97	44 / 50	10.5 (40)	91	41 / 50

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

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

Time of mass occurrence (week)	0～13	14～26	27～39	40～52	53～65	66～78	79～91	92～104	0～104
External mass									
Control	0/50	0/50	0/50	1/50	2/50	3/50	2/50	7/46	10/50(2/ 9)
500 ppm	1/50	0/50	0/50	2/50	6/50	12/50	15/47	19/45	22/50(7/14)
1000 ppm	0/50	0/50	0/50	0/50	2/50	3/50	7/46	10/46	14/50(2/ 8)
2000 ppm	0/50	0/50	0/50	0/50	5/50	4/48	7/48	8/47	11/50(1/ 8)
Internal mass									
Control	0/50	0/50	0/50	0/50	0/50	0/50	0/50	1/46	1/50(1/ 9)
500 ppm	0/50	0/50	0/50	0/50	0/50	0/50	0/47	0/45	0/50(0/14)
1000 ppm	0/50	0/50	0/50	0/50	0/50	0/50	0/46	2/46	2/50(1/ 8)
2000 ppm	0/50	0/50	0/50	0/50	0/50	0/48	0/48	2/47	2/50(0/ 8)

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

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

Time of mass occurrence (week)	0～13	14～26	27～39	40～52	53～65	66～78	79～91	92～104	0～104
External mass									
Control	0/50	0/50	0/50	0/50	1/50	2/50	5/48	8/45	9/50(3/ 9)
250 ppm	0/50	0/50	0/50	0/50	1/50	3/49	4/46	6/45	9/50(4/12)
500 ppm	0/50	0/50	0/50	0/50	0/49	1/49	4/49	10/49	11/50(2/ 6)
1000 ppm	0/50	0/50	1/50	1/50	2/50	1/50	3/48	4/46	6/50(4/ 9)
Internal mass									
Control	0/50	0/50	0/50	0/50	0/50	0/50	0/48	0/45	0/50(0/ 9)
250 ppm	0/50	0/50	0/50	0/50	0/50	2/49	0/46	3/45	5/50(2/12)
500 ppm	0/50	0/50	0/50	0/50	0/49	0/49	0/49	0/49	0/50(0/ 6)
1000 ppm	0/50	0/50	0/50	0/50	0/50	0/50	2/48	3/46	4/50(3/ 9)

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

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

Group name	Control	500 ppm	1000 ppm	2000 ppm
No. of examined animals	40	36	42	42
MCV (fL)	50.1 ± 7.7	48.4 ± 2.3	48.8 ± 4.4 *	50.0 ± 3.7
MCH (pg)	16.8 ± 2.0	16.2 ± 1.5 *	16.4 ± 1.3 *	16.8 ± 1.2

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

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

Group name	Control	250 ppm	500 ppm	1000 ppm
No. of examined animals	39	38	43	41
Hemoglobin (g/dL)	14.5 ± 1.8	14.1 ± 3.2	13.9 ± 2.8	14.0 ± 1.8 *
MCV (fL)	53.2 ± 3.4	55.5 ± 14.1	54.4 ± 10.0	52.1 ± 5.8 **
MCH (pg)	18.4 ± 0.8	18.8 ± 2.7	18.5 ± 2.5	17.9 ± 1.9 **
MCHC (g/dL)	34.7 ± 1.0	34.3 ± 2.2	34.2 ± 1.9	34.4 ± 0.8 **
Platelet(10^3/μL)	644 ± 115	578 ± 154	661 ± 156	777 ± 168 **

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

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

Group name	Control	500 ppm		1000 ppm		2000 ppm	
No. of examined animals	40	36		42		42	
Total protein(g/dL)	6.8 ± 0.4	6.6 ± 0.4		6.7 ± 0.3		6.5 ± 0.4	**
A/G ratio	1.1 ± 0.1	1.1 ± 0.1		1.1 ± 0.1		1.2 ± 0.1	**
T-cholesterol (mg/dL)	185 ± 72	172 ± 77		155 ± 52		123 ± 39	**
Phospholipid (mg/dL)	272 ± 98	265 ± 103		237 ± 69		201 ± 51	**
GOT (IU/L)	97 ± 49	76 ± 25		167 ± 270		1887 ± 10973	*
GPT (IU/L)	45 ± 23	41 ± 17		90 ± 168		256 ± 1059	*
γ-GTP (IU/L)	12 ± 6	14 ± 6		23 ± 36	*	16 ± 12	
CPK (IU/L)	92 ± 26	82 ± 14		87 ± 31	*	97 ± 88	
Urea nitrogen (mg/L)	19.1 ± 2.0	20.0 ± 2.8		19.6 ± 3.7		26.0 ± 19.2	**
Sodium (mEq/L)	142 ± 2	141 ± 2		141 ± 1	*	141 ± 2	*
Potassium (mEq/L)	3.9 ± 0.3	4.0 ± 0.3		4.1 ± 0.3		4.3 ± 1.0	**
Calcium (mg/dL)	10.3 ± 0.4	10.1 ± 0.3	*	10.2 ± 0.3		10.0 ± 0.4	**

Mean ± S.D.

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

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

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

Group name	Control	250 ppm		500 ppm	1000 ppm	
No. of examined animals	39	38		43	41	
Total protein (g/dL)	7.1 ± 0.4	6.8 ± 0.5	**	6.9 ± 0.5	7.0 ± 0.4	
T-cholesterol (mg/dL)	139 ± 36	132 ± 34		139 ± 32	165 ± 36	**
Phospholipid (mg/dL)	257 ± 64	247 ± 64		254 ± 48	290 ± 51	*
GOT (IU/L)	127 ± 82	179 ± 263		179 ± 325	596 ± 928	**
GPT (IU/L)	54 ± 26	62 ± 54		78 ± 218	254 ± 322	**
ALP (IU/L)	139 ± 81	193 ± 313		141 ± 128	206 ± 128	**
γ-GTP (IU/L)	6 ± 5	7 ± 6		9 ± 13	42 ± 56	**
Urea Nitrogen (mg/dL)	17.2 ± 5.3	17.1 ± 2.7		18.8 ± 11.6	18.7 ± 3.2	**
Calcium (mg/dL)	10.3 ± 0.3	10.2 ± 0.3		10.4 ± 0.4	10.5 ± 0.4	*

Mean ± S.D.

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

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

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

Group	Grade	Control	500 ppm	1000 ppm	2000 ppm
Number of examined animals		40	36	42	43
pH	6.0	2	0	2	7
	6.5	4	6	12	12
	7.0	10	11	12	12
	7.5	23	18	12	10
	8.0	1	1	4	2
	8.5	0	0	0	0
	Chi square test				*
Occult blood	−	37	30	33	8
	±	2	2	2	1
	+	1	1	0	1
	2+	0	1	3	4
	3+	0	2	4	29
	Chi square test				**

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

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

Group	Grade	Control	250 ppm	500 ppm	1000 ppm
Number of examined animals		41	39	44	41
pH	6.0	0	3	2	6
	6.5	4	2	13	20
	7.0	10	9	15	11
	7.5	12	10	9	3
	8.0	14	14	5	1
	8.5	1	1	0	0
	Chi square test			*	**
Protein	±	3	1	1	0
	+	12	6	9	4
	2+	13	15	14	15
	3+	6	10	13	17
	4+	7	7	7	5
	Chi square test				*
Ketone body	-	22	11	11	9
	±	18	27	33	32
	+	1	1	0	0
	Chi square test			*	**
Occult blood	−	39	35	39	21
	±	1	0	1	4
	+	0	0	1	0
	2+	0	0	1	3
	3+	1	4	2	13
	Chi square test				**

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

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

Group name	Control	500 ppm	1000 ppm	2000 ppm
No. of examined animals	41	36	42	42
Body weight (g)	382 ± 33	355 ± 47 *	330 ± 22 **	269 ± 29 **
Adrenals (g)	0.082 ± 0.072	0.064 ± 0.009	0.058 ± 0.008 **	0.069 ± 0.108 **
Adrenals (%)	0.022 ± 0.022	0.018 ± 0.003	0.018 ± 0.002	0.026 ± 0.043
Testes (g)	2.751 ± 1.358	3.444 ± 0.946 *	3.796 ± 1.093 **	3.334 ± 1.356
Testes (%)	0.721 ± 0.346	0.983 ± 0.278 **	1.155 ± 0.347 **	1.247 ± 0.483 **
Heart (g)	1.283 ± 0.203	1.195 ± 0.128	1.104 ± 0.084 **	0.975 ± 0.097 **
Heart (%)	0.338 ± 0.065	0.342 ± 0.057	0.336 ± 0.034	0.364 ± 0.027 **
Lungs (g)	1.448 ± 0.319	1.360 ± 0.098	1.383 ± 0.466 **	1.192 ± 0.095 **
Lungs (%)	0.381 ± 0.091	0.388 ± 0.047	0.421 ± 0.157 **	0.447 ± 0.054 **
Kidneys (g)	2.633 ± 0.322	2.564 ± 0.179	2.490 ± 0.171	2.255 ± 0.220 **
Kidneys (%)	0.692 ± 0.093	0.732 ± 0.090 *	0.756 ± 0.049 **	0.845 ± 0.095 **
Spleen (g)	1.290 ± 1.941	0.942 ± 0.396	0.918 ± 0.609	0.589 ± 0.486 **
Spleen (%)	0.342 ± 0.536	0.271 ± 0.128	0.276 ± 0.169	0.223 ± 0.212 **
Liver (g)	11.367 ± 2.693	10.606 ± 1.290	10.651 ± 2.410	9.269 ± 3.410 **
Liver (%)	2.986 ± 0.753	3.009 ± 0.344	3.241 ± 0.818 **	3.461 ± 1.344 **
Brain (g)	2.043 ± 0.060	2.007 ± 0.049 **	1.988 ± 0.046 **	1.929 ± 0.048 **
Brain (%)	0.538 ± 0.045	0.573 ± 0.056 *	0.605 ± 0.043 **	0.726 ± 0.083 **

Mean ± S.D.

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

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

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

Group name	Control	250 ppm	500 ppm	1000 ppm
No. of examined animals	41	38	44	41
Body weight (g)	253 ± 23	237 ± 30	234 ± 24 **	204 ± 19 **
Adrenals (g)	0.076 ± 0.053	0.070 ± 0.013	0.065 ± 0.012	0.081 ± 0.135 **
Adrenals (%)	0.030 ± 0.020	0.030 ± 0.007	0.028 ± 0.006	0.040 ± 0.069
Ovaries (g)	0.135 ± 0.019	0.125 ± 0.020	0.127 ± 0.024	0.124 ± 0.021
Ovaries (%)	0.053 ± 0.007	0.053 ± 0.008	0.054 ± 0.009	0.061 ± 0.011 **
Heart (g)	0.874 ± 0.063	0.878 ± 0.096	0.870 ± 0.081	0.791 ± 0.079 **
Heart (%)	0.348 ± 0.031	0.377 ± 0.073	0.376 ± 0.054 *	0.389 ± 0.037 **
Lungs (g)	1.015 ± 0.094	1.084 ± 0.303	1.051 ± 0.315	0.957 ± 0.146 **
Lungs (%)	0.404 ± 0.048	0.473 ± 0.190	0.454 ± 0.152	0.474 ± 0.093 **
Kidneys (g)	1.729 ± 0.140	1.715 ± 0.133	1.712 ± 0.126	1.691 ± 0.153
Kidneys (%)	0.688 ± 0.071	0.739 ± 0.139	0.738 ± 0.087 *	0.833 ± 0.085 **
Spleen (g)	0.660 ± 0.566	1.312 ± 2.723	0.697 ± 0.707	0.716 ± 1.332
Spleen (%)	0.264 ± 0.230	0.616 ± 1.402	0.307 ± 0.353	0.363 ± 0.734
Liver (g)	6.694 ± 0.951	6.580 ± 1.098	6.814 ± 1.323	9.406 ± 3.630 **
Liver (%)	2.653 ± 0.338	2.809 ± 0.538	2.934 ± 0.626	4.649 ± 1.846 **
Brain (g)	1.862 ± 0.049	1.854 ± 0.044	1.833 ± 0.043 *	1.826 ± 0.050 **
Brain (%)	0.743 ± 0.071	0.797 ± 0.119	0.792 ± 0.088 *	0.904 ± 0.097 **

Mean ± S.D.

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

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

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

Group		Control	500 ppm	1000 ppm	2000 ppm	Peto	Cochran-
Number of examined animals		50	50	50	50	test	Armitage test
Organ / Findings	Grade of nonneoplastic finding						
Nasal cavity							
Mineralization	1+	20	24	22	9		
	Chi square test				*		
Inflammation:foreign body	1+	15	10	10	3		
	2+	1	2	3	2		
	3+	0	1	0	1		
	Chi square test				*		
Eosinophilic change: olfactory epithelium	1+	27	25	21	20		
	2+	4	7	16	22		
	3+	2	1	2	6		
	Chi square test			*	**		
Heart							
Myocardial fibrosis	1+	19	20	16	9		
	Chi square test				*		
Tooth							
Inflammation	1+	11	0	1	8		
	2+	1	0	0	0		
	Chi square test		**	**			
Liver							
Clear cell focus	1+	2	9	8	3		
	2+	0	0	3	0		
	3+	0	0	1	0		
	Chi square test			*			
Basophilic cell focus	1+	18	22	15	25		
	2+	1	9	17	12		
	3+	0	0	4	1		
	4+	0	0	1	0		
	Chi square test		**	**	**		
Hepatocellular adenoma 1)		3	2	12 *	15 **	↑ ↑	↑ ↑
Hepatocellular carcinoma 2)		1	1	6	10 **	↑ ↑	↑ ↑
1)+2)		4	3	16 **	22 **	↑ ↑	↑ ↑
Pancreas							
Islet cell adenoma		7	3	1 *	1 *		↓

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

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

Fisher's exact test for neoplastic lesion

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

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

TABLE 17 INCIDENCES OF SELECTED LESIONS OF MALE RATS IN THE 2-YEAR DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE (Continued)

Group		Control	500 ppm	1000 ppm	2000 ppm	Peto	Cochran-Armitage
Number of examined animals		50	50	50	50	test	test
Organ / Findings	Grade of Nonneoplastic finding						
Kidney							
Infract	1+	0	2	2	6		
	2+	0	0	0	1		
	Chi square test				*		
Chronic nephropathy	1+	3	10	8	16		
	2+	25	18	18	19		
	3+	20	13	20	5		
	4+	2	3	0	0		
	Chi square test		*		**		
Papillary necrosis	1+	0	0	0	10		
	2+	0	0	0	5		
	Chi square test				**		
Mineralization:papilla	1+	7	18	16	24		
	2+	0	0	0	2		
	Chi square test		*		**		
Urothelial hyperplasia:pelvis	1+	8	10	17	19		
	2+	0	0	1	3		
	Chi square test				**		
Urinary bladder							
Simple hyperplasia:	1+	1	0	3	6		
transitional epithelium	3+	0	1	0	0		
	Chi square test						
Nodular hyperplasia:	1+	0	1	1	6		
transitional epithelium	Chi square test				*		
Transitional cell papilloma 3)		1	0	0	6	↑↑	↑↑
Transitional cell carcinoma 4)		1	0	0	4	↑	↑
3)+4)		2	0	0	10 *	↑↑	↑↑
Pituitary							
Adenoma		25	20	10 **	13 *		↓↓
Thyroid							
Follicular adenoma 5)		0	1	0	4	↑↑	↑
Follicular adenocarcinoma 6)		1	0	1	1		
5)+6)		1	1	1	5	↑	↑
Testis							
Atrophy	1+	47	46	43	35		
	Chi square test				**		
Intrestitial cell tumor		37	39	45 *	43	↑	

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

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

Fisher's exact test for neoplastic lesion

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

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

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

Group		Control	250 ppm	500 ppm	1000 ppm	Peto	Cochran-Armitage
Number of examined animals		50	50	50	50	test	test
Organ / Findings	Grade of nonneoplastic finding						
Nasal cavity							
Mineralization	1+	24	16	16	12		
	Chi square test				*		
Eosinophilic change: olfactory epithelium	1+	20	13	8	6		
	2+	23	17	28	12		
	3+	5	15	11	29		
	4+	0	0	0	1		
	Chi square test		*	*	**		
Lung							
Metastasis :liver tumor		0	0	0	5		
Liver							
Basophilic cell focus	1+	7	15	21	17		
	2+	1	6	13	8		
	3+	0	0	5	8		
	Chi square test		*	**	**		
Bile duct hyperplasia	1+	13	10	10	3		
	Chi square test				*		
Hepatocellular adenoma 1)		1	3	15 **	36 **	↑ ↑	↑ ↑
Hepatocellular carcinoma 2)		0	0	4	18 **	↑ ↑	↑ ↑
1)+2)		1	3	19 **	44 **	↑ ↑	↑ ↑
Pancreas							
Atrophy	1+	0	6	1	4		
	Chi square test		*				
Kidney							
Papillary necrosis	1+	2	1	1	6		
	2+	0	0	0	5		
	Chi square test				*		
Mineralization:papilla	1+	7	8	12	22		
	2+	0	1	0	2		
	Chi square test				**		
Urothelial hyperplasia:pelvis	1+	2	12	10	17		
	Chi square test		**	*	**		
Urinary bladder							
Simple hyperplasia: transitional epithelium	1+	0	1	0	0		
	2+	0	0	0	2		
	Chi square test						
Nodular hyperplasia: transitional epithelium	1+	0	0	0	1		
	Chi square test						
Transitional cell papilloma		1	0	1	1		
Pituitary							
Cyst	1+	12	24	21	15		
	2+	0	2	1	0		
	Chi square test		*				
Adenoma		23	9 **	14 *	11 **		↓

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

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

Fisher's exact test for neoplastic lesion

↑(↓) : $p<0.0$ ↑ ↑(↓ ↓) : $p<0.01$ Peto or Cochran-Armitage test for neoplastic lesion

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

TABLE 19 HISTORICAL CONTROL DATA OF SELECTED NEOPLASTIC LESIONS IN JAPAN BIOASSAY RESEARCH CENTER : F344/DuCrj MALE RATS

Organs / Tumors	No. of animals examined	No. of animals with bearing tumors	Incidence (%)	Min. - Max. (%)
Liver	<1499>			
Hepatocellular adenoma 1)		21	1.4	0 - 6
Hepatocellular carcinoma 2)		4	0.3	0 - 2
1)+2)		25	1.7	0 - 6
Pancreas				
Islet cell adenoma	<1499>	46	2.7	0 - 12
Urinary bladder	<1498>			
Transitional cell papilloma		6	0.4	0 - 2
Pituitary gland	<1494>			
Adenoma		523	35.0	18 - 66
Thyroid	<1493>			
Follicular adenoma 1)		13	0.8	0 - 4
Follicular adenocarcinoma 2)		29	1.9	0 - 8
1)+2)		41	2.7	0 - 8
Peritoneum	<1499>			
Mesothelioma		41	2.7	0 - 8

30 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

TABLE 20 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 with bearing tumors	Incidence (%)	Min. - Max. (%)
Liver	<1447>			
Hepatocellular adenoma 1)		18	1.2	0 - 6
Hepatocellular carcinoma 2)		1	0.1	0 - 2
1)+2)		19	1.3	0 - 8
Urinary bladder	<1445>			
Transtional cell papilloma		8	0.6	0 - 2
Pituitary	<1445>			
Adenoma		570	39.4	16 - 71
Uterus	<1447>			
Endometrial stromal polyp		209	14.4	2 - 28
Mammary gland	<1447>			
Fibroadenoma		162	11.2	0 - 20

29 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

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

		Male				Female			
Group		Control	500 ppm	1000 ppm	2000 ppm	Control	250 ppm	500 ppm	1000 ppm
Number of dead or moribund animals		9	14	8	8	9	12	6	9
No microscopical confirmation		0	1	1	2	0	0	0	0
Digestive system lesion		1	0	0	0	0	0	0	0
Chronic nephropathy		1	0	0	0	0	0	0	0
Urinary retension		0	1	0	0	0	0	0	0
Pneumonia		0	0	0	0	1	0	0	0
Arteritis		0	0	0	0	1	0	0	0
Tumor death	leukemia	1	1	3	0	2	5	2	2
	skin/app	0	1	0	0	0	0	0	1
	subcutis	0	4	1	0	0	0	0	0
	nasopharynx	0	0	0	0	0	0	0	1
	thymus	0	0	0	0	1	0	0	0
	liver	0	0	1	1	0	0	0	3
	kidney	0	0	1	0	0	0	0	0
	urinary bladder	0	0	0	3	0	0	0	0
	pituitary	3	3	0	0	3	3	2	0
	thyroid	1	0	0	1	0	0	0	0
	uterus	—	—	—	—	0	1	1	0
	mammary gland	0	0	0	0	1	0	0	0
	brain	1	1	0	1	0	1	0	0
	spinal cord	1	0	0	0	0	0	0	0
	Zymbal gland	0	0	0	0	0	0	1	1
	bone	0	1	1	0	0	1	0	1
	mediastium	0	1	0	0	0	1	0	0