クロトンアルデヒドのラットを用いた
吸入によるがん原性試験報告書

試験番号　0318

TABLES

TABLES

TABLE 1 EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE 2-YEAR INHALATION STUDY OF CROTONALDEHYDE

<Method of Administration>
Inhalation
<Number of Groups>
Male 4, Female 4
<Size of Groups>
50 males and 50 females of each group
<Animals>
Strain and Species
F344/DuCrj(Fischer)rat
Animal Source
Charles River Japan, Inc.
Duration Held Before Study
2 wk
Age When Placed on Study
6 wk
Age When Killed
110～111 wk
<Doses>
Male and Female
0, 3, 6, 12ppm
<Duration of Dosing>
6 h/d, 5 d/wk for 104 wk
<Animal Maintenance>
Feed
CRF-1 (Oriental Yeast Co., Ltd.)
Sterilized by γ-ray
Available *ad libitum*
Water
Filtrated and sterilized by ultraviolet ray
Automatic watering system
Available *ad libitum*
Animal per Cage
Single (stainless steel wire)
Animal Room Environment
Barrier system
Temperature : 22±2℃
Fluorescent light : 12 h/d
Air changes : 15～17 time/h
Chamber Environment
Temperature : 22±2℃
Humidity : 55±15%
Air changes : 12±1 time/h
Pressure : 0～-15mmAq
<Type and Frequency of Observation>
Clinical Sign
Observed 1 per day for mortality, Detailed clinical observation performed on once weekly before exposure.
Body Weight
Weighed 1 per wk for 14wk
Weighed 1 per 4wks thereafter
Food Consumption
Weighed 1 per wk for 14wk
Weighed 1 per 4wks thereafter

TABLE 1 (Continued) EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE 2-YEAR INHALATION STUDY OF CROTONALDEHYDE

<Hematology>
Hematological examination performed on scheduled sacrificed animals.
The following measurement parameters were examined;
Red blood cell (RBC), Hemoglobin, Hematocrit,
Mean Corpuscular Volume (MCV),
Mean Corpuscular hemoglobin (MCH),
Mean Corpuscular hemoglobin concentration (MCHC),
Platelet, White blood cell (WBC), Differential WBC.

<Biochemistry>
Biochemistrical examination performed on scheduled sacrificed animals.
The following measurement parameters were examined;
Total protein, Albumin, A/G ratio,
Total bilirubin, Glucose, Total cholesterol,
Triglyceride, Phospholipid,
Glutamic oxaloacetic transaminase (GOT),
Glutamic pyruvic transaminase (GPT),
Lactate dehydrogenase (LDH),
Alkaline phosphatase (ALP),
γ -Glutamyl transpeptidase (γ -GTP),
Creatine phosphokinase (CPK),
Urea nitrogen, Creatinine,
Sodium, Potassium, Chloride,
Calcium, Inorganic phosphorus.

<Urinalysis>
Urinalysis performed on all animals that survived to end of dosing period using fresh urine collection.
The following measurement parameters were examined;
pH, Protein, Glucose, Ketone body, Bilirubin,
Occult blood, Urobilinogen.

<Necropsy>
Necropsy performed on all animals.

<Organ Weight>
Organ weight measurement performed on scheduled sacrificed animals.
The following organs were weighed;
adrenal, testis, ovary, heart, lung, kidney, spleen, liver, brain.

<Histopathologic Examination>
Histopathologic examination performed on all animals.
The following organs were examined;
skin, nasal cavity, nasopharynx, larynx, trachea, lung,
bone marrow, lymph node, thymus, spleen, heart, tongue,
salivary gland, esophagus, stomach, small intestine,
large intestine, liver, pancreas, kidney, urinary bladder,
pituitary, thyroid, parathyroid, adrenal, testis, epididymis, seminal vesicle,
prostate, ovary, uterus, vagina, mammary gland,
brain, spinal cord, peripheral nerve, eye, Harderian gland, muscle, bone,
other organs/tissues with gross lesions.

TABLE 2 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF MALE RATS IN THE 2-YEAR INHALATION STUDY OF CROTONALDEHYDE

Weeks on Study	Control Av.Wt.	Control No.of Surviv. <50>	3ppm Av.Wt.	3ppm % of cont.	3ppm No.of Surviv. <50>	6ppm Av.Wt.	6ppm % of cont.	6ppm No.of Surviv. <50>	12ppm Av.Wt.	12ppm % of cont.	12ppm No.of Surviv. <50>
0	114 (50)	50/50	114 (50)	100	50/50	114 (50)	100	50/50	114 (50)	100	50/50
1	142 (50)	50/50	140 (50)	99	50/50	141 (50)	99	50/50	137 (50)	96	50/50
2	172 (50)	50/50	170 (50)	99	50/50	171 (50)	99	50/50	165 (50)	96	50/50
3	199 (50)	50/50	195 (50)	98	50/50	196 (50)	98	50/50	190 (50)	95	50/50
4	222 (50)	50/50	218 (50)	98	50/50	218 (50)	98	50/50	211 (50)	95	50/50
5	238 (50)	50/50	235 (50)	99	50/50	236 (50)	99	50/50	228 (50)	96	50/50
6	252 (50)	50/50	247 (50)	98	50/50	250 (50)	99	50/50	241 (50)	96	50/50
7	266 (50)	50/50	262 (50)	98	50/50	263 (50)	99	50/50	253 (50)	95	50/50
8	278 (50)	50/50	276 (50)	99	50/50	276 (50)	99	50/50	263 (50)	95	50/50
9	290 (50)	50/50	285 (50)	98	50/50	287 (50)	99	50/50	273 (50)	94	50/50
10	299 (50)	50/50	294 (50)	98	50/50	295 (50)	99	50/50	280 (50)	94	50/50
11	305 (50)	50/50	300 (50)	98	50/50	302 (50)	99	50/50	285 (50)	93	50/50
12	313 (50)	50/50	307 (50)	98	50/50	309 (50)	99	50/50	292 (50)	93	50/50
13	320 (50)	50/50	314 (50)	98	50/50	316 (50)	99	50/50	296 (50)	93	50/50
14	323 (50)	50/50	317 (50)	98	50/50	318 (50)	98	50/50	300 (50)	93	50/50
18	340 (50)	50/50	336 (50)	99	50/50	333 (50)	98	50/50	314 (50)	92	50/50
22	354 (50)	50/50	350 (50)	99	50/50	346 (50)	98	50/50	328 (50)	93	50/50
26	365 (50)	50/50	363 (50)	99	50/50	362 (50)	99	50/50	340 (50)	93	50/50
30	376 (50)	50/50	372 (50)	99	50/50	371 (50)	99	50/50	348 (50)	93	50/50
34	385 (50)	50/50	380 (50)	99	50/50	380 (50)	99	50/50	353 (50)	92	50/50
38	393 (50)	50/50	390 (50)	99	50/50	386 (50)	98	50/50	359 (50)	91	50/50
42	398 (50)	50/50	397 (50)	100	50/50	392 (50)	98	50/50	365 (50)	92	50/50
46	404 (50)	50/50	403 (50)	100	50/50	397 (50)	98	50/50	372 (50)	92	50/50
50	409 (50)	50/50	408 (50)	100	50/50	401 (50)	98	50/50	376 (50)	92	50/50
54	409 (50)	50/50	411 (50)	100	50/50	405 (50)	99	50/50	379 (50)	93	50/50
58	414 (50)	50/50	417 (50)	101	50/50	409 (50)	99	50/50	382 (50)	92	50/50
62	419 (50)	50/50	420 (50)	100	50/50	412 (50)	98	50/50	387 (50)	92	50/50
66	419 (50)	50/50	419 (50)	100	50/50	414 (50)	99	50/50	386 (50)	92	50/50
70	424 (49)	49/50	423 (50)	100	50/50	417 (50)	98	50/50	391 (50)	92	50/50
74	424 (49)	49/50	424 (50)	100	50/50	418 (50)	99	50/50	394 (50)	93	50/50
78	423 (49)	49/50	424 (50)	100	50/50	418 (50)	99	50/50	392 (47)	93	47/50
82	421 (49)	49/50	424 (49)	101	49/50	417 (50)	99	50/50	388 (47)	92	46/50
86	420 (48)	48/50	424 (48)	101	48/50	413 (49)	98	49/50	387 (46)	92	46/50
90	414 (48)	47/50	421 (47)	102	47/50	412 (49)	100	49/50	384 (45)	93	45/50
94	412 (47)	47/50	417 (46)	101	46/50	409 (49)	99	49/50	381 (44)	92	44/50
98	404 (46)	46/50	409 (45)	101	45/50	400 (48)	99	48/50	376 (43)	93	43/50
102	403 (42)	42/50	407 (40)	101	40/50	395 (45)	98	45/50	373 (39)	93	39/50
104	405 (39)	39/50	401 (39)	99	39/50	388 (45)	96	45/50	369 (38)	91	38/50

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

TABLE 3 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF FEMALE RATS IN THE 2-YEAR INHALATION STUDY OF CROTONALDEHYDE

Weeks on Study	Control Av.Wt.	Control No.of Surviv. <50>	3ppm Av.Wt.	3ppm % of cont.	3ppm No.of Surviv. <50>	6ppm Av.Wt.	6ppm % of cont.	6ppm No.of Surviv. <50>	12ppm Av.Wt.	12ppm % of cont.	12ppm No.of Surviv. <50>
0	94 (50)	50/50	94 (50)	100	50/50	94 (50)	100	50/50	94 (50)	100	50/50
1	108 (50)	50/50	108 (50)	100	50/50	109 (50)	101	50/50	107 (50)	99	50/50
2	121 (50)	50/50	121 (50)	100	50/50	121 (50)	100	50/50	118 (50)	98	50/50
3	133 (50)	50/50	131 (50)	98	50/50	132 (50)	99	50/50	128 (50)	96	50/50
4	140 (50)	50/50	140 (50)	100	50/50	139 (50)	99	50/50	135 (50)	96	50/50
5	148 (50)	50/50	147 (50)	99	50/50	146 (50)	99	50/50	142 (50)	96	50/50
6	154 (50)	50/50	152 (50)	99	50/50	150 (50)	97	50/50	146 (50)	95	50/50
7	158 (50)	50/50	157 (50)	99	50/50	155 (50)	98	50/50	151 (50)	96	50/50
8	162 (50)	50/50	162 (50)	100	50/50	159 (50)	98	50/50	155 (50)	96	50/50
9	167 (50)	50/50	167 (50)	100	50/50	164 (50)	98	50/50	159 (50)	95	50/50
10	172 (50)	50/50	171 (50)	99	50/50	168 (50)	98	50/50	163 (50)	95	50/50
11	175 (50)	50/50	174 (50)	99	50/50	171 (50)	98	50/50	166 (50)	95	50/50
12	178 (50)	50/50	176 (50)	99	50/50	173 (50)	97	50/50	168 (50)	94	50/50
13	183 (50)	50/50	181 (50)	99	50/50	177 (50)	97	50/50	172 (50)	94	50/50
14	181 (50)	50/50	181 (50)	100	50/50	176 (50)	97	50/50	172 (50)	95	50/50
18	190 (50)	50/50	188 (50)	99	50/50	184 (50)	97	50/50	177 (50)	93	50/50
22	193 (50)	50/50	192 (50)	99	50/50	190 (50)	98	50/50	182 (50)	94	50/50
26	201 (50)	50/50	199 (50)	99	50/50	196 (50)	98	50/50	187 (50)	93	50/50
30	203 (50)	50/50	202 (50)	100	50/50	200 (50)	99	50/50	191 (50)	94	50/50
34	207 (50)	50/50	207 (50)	100	50/50	205 (50)	99	50/50	193 (50)	93	50/50
38	214 (49)	49/50	212 (50)	99	50/50	212 (50)	99	50/50	199 (50)	93	50/50
42	217 (49)	49/50	215 (50)	99	50/50	214 (50)	99	50/50	202 (50)	93	50/50
46	219 (49)	49/50	218 (50)	100	50/50	218 (50)	100	50/50	206 (49)	94	49/50
50	224 (49)	49/50	223 (50)	100	50/50	224 (50)	100	50/50	211 (49)	94	49/50
54	227 (49)	49/50	225 (50)	99	50/50	228 (50)	100	50/50	215 (49)	95	49/50
58	232 (49)	49/50	230 (50)	99	50/50	231 (50)	100	50/50	215 (49)	93	49/50
62	236 (49)	49/50	234 (50)	99	50/50	237 (50)	100	50/50	222 (49)	94	49/50
66	236 (49)	49/50	238 (49)	101	49/50	240 (50)	102	50/50	221 (49)	94	49/50
70	246 (48)	48/50	245 (49)	100	49/50	247 (50)	100	50/50	227 (49)	92	49/50
74	252 (47)	47/50	250 (49)	99	49/50	251 (50)	100	50/50	231 (49)	92	49/50
78	257 (47)	47/50	255 (48)	99	48/50	255 (49)	99	49/50	235 (49)	91	49/50
82	262 (47)	47/50	259 (48)	99	48/50	260 (49)	99	49/50	238 (48)	91	48/50
86	262 (46)	46/50	261 (48)	100	48/50	263 (49)	100	49/50	239 (47)	91	47/50
90	266 (44)	44/50	264 (47)	99	47/50	264 (49)	99	48/50	242 (47)	91	47/50
94	265 (44)	44/50	264 (44)	100	44/50	268 (47)	101	47/50	244 (47)	92	47/50
98	269 (41)	40/50	268 (41)	100	41/50	268 (44)	100	44/50	245 (45)	91	44/50
102	275 (39)	39/50	272 (38)	99	38/50	270 (40)	98	40/50	250 (40)	91	40/50
104	272 (39)	39/50	272 (38)	100	38/50	269 (40)	99	40/50	248 (40)	91	40/50

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

TABLE 4 INCIDENCE OF EXTERNAL AND INTERNAL MASS IN CLINICAL OBSERVATION OF MALE RATS IN THE 2-YEAR INHALATION STUDY OF CROTONALDEHYDE

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										
	0ppm	0/50	0/50	0/50	0/50	2/50	6/50	7/49	10/47	12/50(5/11)
	3ppm	0/50	0/50	1/50	2/50	3/50	2/50	1/49	9/46	9/50(4/11)
	6ppm	0/50	0/50	0/50	0/50	2/50	4/50	5/50	7/49	8/50(3/ 5)
	12ppm	0/50	0/50	0/50	0/50	2/50	5/50	4/47	8/45	10/50(2/12)
Internal mass										
	0ppm	0/50	0/50	0/50	0/50	0/50	0/50	1/49	0/47	1/50(1/11)
	3ppm	0/50	0/50	0/50	0/50	0/50	0/50	0/49	3/46	3/50(1/11)
	6ppm	0/50	0/50	0/50	0/50	0/50	0/50	0/50	2/49	2/50(2/ 5)
	12ppm	0/50	0/50	0/50	0/50	0/50	1/50	1/47	4/45	4/50(3/12)

No. of animals with mass / No. of survival animals at first week on each period.
(No. of dead and moribund animals with mass / No. of dead and moribund animals)

TABLE 5 INCIDENCE OF EXTERNAL AND INTERNAL MASS IN CLINICAL OBSERVATION OF FEMALE RATS IN THE 2-YEAR INHALATION STUDY OF CROTONALDEHYDE

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										
	0ppm	0/50	0/50	0/50	0/49	1/49	1/49	5/47	5/44	7/50(2/11)
	3ppm	0/50	0/50	0/50	0/50	2/50	4/49	11/48	15/45	17/50(6/12)
	6ppm	0/50	0/50	1/50	1/50	1/50	4/50	5/49	7/47	9/50(4/10)
	12ppm	0/50	0/50	0/50	0/50	0/49	1/49	3/49	7/47	7/50(1/10)
Internal mass										
	0ppm	0/50	0/50	0/50	0/49	0/49	0/49	0/47	3/44	3/50(2/12)
	3ppm	0/50	0/50	0/50	0/50	0/50	1/49	1/48	3/45	5/50(2/12)
	6ppm	0/50	0/50	0/50	0/50	0/50	0/50	0/49	4/47	4/50(4/10)
	12ppm	0/50	0/50	0/50	0/50	0/49	0/49	1/49	6/47	7/50(6/10)

No. of animals with mass / No. of survival animals at first week on each period.
(No. of dead and moribund animals with mass / No. of dead and moribund animals)

TABLE 6 FOOD CONSUMPTION CHANGES OF MALE RATS
IN THE 2-YEAR INHALATION STUDY OF CROTONALDEHYDE

Weeks on Study	Control Av.FC.	<50>	3ppm Av.FC.	<50>	% of cont.	6ppm Av.FC.	<50>	% of cont.	12ppm Av.FC.	<50>	% of cont.
1	14.5	(50)	14.1	(50)	97	14.3	(50)	99	13.6	(50)	94
2	15.5	(50)	15.3	(50)	99	15.4	(50)	99	14.9	(50)	96
3	16.9	(50)	16.7	(50)	99	16.4	(50)	97	16.0	(50)	95
4	17.3	(50)	17.2	(50)	99	17.2	(50)	99	16.9	(50)	98
5	17.3	(50)	17.1	(50)	99	17.2	(50)	99	17.0	(50)	98
6	16.7	(50)	16.4	(50)	98	16.8	(50)	101	16.3	(50)	98
7	16.9	(50)	16.7	(50)	99	16.5	(50)	98	16.1	(50)	95
8	16.9	(50)	16.5	(50)	98	16.9	(50)	100	16.2	(50)	96
9	17.2	(50)	16.5	(50)	96	16.7	(50)	97	16.0	(50)	93
10	17.5	(50)	16.9	(50)	97	17.2	(50)	98	16.5	(50)	94
11	16.9	(50)	16.4	(50)	97	16.5	(50)	98	16.0	(50)	95
12	16.8	(50)	16.3	(50)	97	16.7	(50)	99	16.0	(50)	95
13	17.4	(50)	16.9	(50)	97	17.3	(50)	99	16.5	(50)	95
14	16.7	(50)	16.5	(50)	99	16.3	(50)	98	15.5	(50)	93
18	16.8	(50)	16.5	(50)	98	16.2	(50)	96	16.2	(50)	96
22	16.9	(50)	16.7	(50)	99	16.9	(50)	100	16.3	(50)	96
26	16.8	(50)	17.0	(50)	101	17.7	(50)	105	16.6	(50)	99
30	17.0	(50)	16.8	(50)	99	17.0	(50)	100	16.3	(50)	96
34	17.1	(50)	17.1	(50)	100	17.2	(50)	101	16.4	(50)	96
38	17.0	(50)	17.1	(50)	101	17.0	(50)	100	16.4	(50)	96
42	16.9	(50)	17.0	(50)	101	17.2	(50)	102	16.6	(50)	98
46	16.9	(50)	17.1	(50)	101	17.1	(50)	101	16.8	(50)	99
50	17.7	(50)	17.3	(50)	98	17.3	(50)	98	16.9	(50)	95
54	17.3	(50)	17.4	(50)	101	17.7	(50)	102	17.2	(50)	99
58	17.7	(50)	17.8	(50)	101	17.6	(50)	99	16.9	(50)	95
62	17.6	(50)	17.6	(50)	100	17.7	(50)	101	17.2	(50)	98
66	17.3	(50)	17.3	(50)	100	17.5	(50)	101	16.7	(50)	97
70	17.3	(49)	17.5	(50)	101	16.9	(50)	98	16.2	(50)	94
74	17.4	(49)	17.7	(50)	102	17.3	(50)	99	17.2	(50)	99
78	17.6	(49)	17.3	(50)	98	17.6	(50)	100	17.1	(47)	97
82	17.2	(49)	16.9	(49)	98	16.7	(50)	97	15.9	(47)	92
86	17.3	(48)	17.3	(48)	100	17.1	(49)	99	16.7	(46)	97
90	16.9	(48)	17.6	(47)	104	17.3	(49)	102	16.8	(45)	99
94	16.6	(47)	16.8	(46)	101	16.8	(49)	101	16.0	(44)	96
98	16.5	(45)	16.5	(45)	100	16.6	(48)	101	16.2	(43)	98
102	16.5	(41)	16.8	(40)	102	17.3	(45)	105	16.6	(39)	101
104	17.2	(39)	17.2	(39)	100	17.2	(45)	100	17.2	(38)	100

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

TABLE 7 FOOD CONSUMPTION CHANGES OF FEMALE RATS IN THE 2-YEAR INHALATION STUDY OF CROTONALDEHYDE

Weeks on Study	Control Av.FC. <50>	3ppm Av.FC. <50>	3ppm % of cont.	6ppm Av.FC. <50>	6ppm % of cont.	12ppm Av.FC. <50>	12ppm % of cont.
1	10.8 (50)	10.6 (50)	98	10.7 (50)	99	10.4 (50)	96
2	11.0 (50)	11.0 (50)	100	10.8 (50)	98	10.7 (50)	97
3	11.6 (50)	11.4 (50)	98	11.4 (50)	98	11.0 (50)	95
4	11.6 (50)	11.6 (50)	100	11.4 (50)	98	11.4 (50)	98
5	11.8 (50)	11.5 (50)	97	11.6 (50)	98	11.1 (50)	94
6	11.4 (50)	11.3 (50)	99	10.9 (50)	96	10.8 (50)	95
7	11.3 (50)	11.0 (50)	97	10.9 (50)	96	10.9 (50)	96
8	11.2 (50)	11.0 (50)	98	10.5 (50)	94	10.5 (50)	94
9	11.3 (50)	11.3 (50)	100	11.4 (50)	101	11.1 (50)	98
10	11.6 (50)	11.1 (50)	96	10.8 (50)	93	10.8 (50)	93
11	11.7 (50)	11.4 (50)	97	11.1 (50)	95	11.3 (50)	97
12	11.5 (50)	11.3 (50)	98	10.8 (50)	94	10.5 (50)	91
13	12.5 (50)	12.0 (50)	96	12.2 (50)	98	12.5 (50)	100
14	11.4 (50)	11.3 (50)	99	10.3 (50)	90	10.3 (50)	90
18	11.5 (50)	11.2 (50)	97	10.9 (50)	95	10.9 (50)	95
22	11.5 (50)	11.5 (50)	100	11.3 (50)	98	10.9 (50)	95
26	11.9 (50)	11.3 (50)	95	11.1 (50)	93	10.7 (50)	90
30	11.1 (50)	11.3 (50)	102	11.2 (50)	101	11.0 (50)	99
34	11.6 (50)	12.0 (50)	103	11.3 (50)	97	10.8 (50)	93
38	11.7 (49)	11.3 (50)	97	11.3 (50)	97	10.6 (50)	91
42	11.5 (49)	11.5 (50)	100	11.1 (50)	97	11.1 (50)	97
46	11.3 (49)	11.3 (50)	100	11.3 (50)	100	11.1 (49)	98
50	12.1 (49)	11.8 (50)	98	11.6 (50)	96	11.6 (49)	96
54	11.8 (49)	11.6 (50)	98	11.8 (50)	100	11.4 (49)	97
58	12.6 (49)	12.3 (50)	98	11.7 (50)	93	11.3 (49)	90
62	12.1 (49)	12.1 (50)	100	12.2 (50)	101	11.7 (49)	97
66	11.6 (49)	11.9 (49)	103	11.6 (50)	100	11.2 (49)	97
70	12.3 (48)	12.3 (49)	100	11.9 (50)	97	11.5 (49)	93
74	12.4 (47)	12.4 (49)	100	12.5 (50)	101	11.9 (49)	96
78	12.5 (47)	12.5 (48)	100	12.3 (49)	98	12.2 (49)	98
82	12.6 (47)	12.7 (48)	101	12.4 (49)	98	11.4 (48)	90
86	12.2 (46)	12.6 (48)	103	12.6 (49)	103	11.7 (47)	96
90	12.6 (44)	12.6 (47)	100	12.2 (49)	97	12.3 (47)	98
94	11.7 (44)	12.0 (44)	103	12.1 (47)	103	11.6 (47)	99
98	12.5 (41)	12.8 (41)	102	12.7 (44)	102	12.0 (45)	96
102	12.7 (39)	12.7 (38)	100	12.7 (40)	100	12.1 (40)	95
104	12.4 (39)	12.9 (38)	104	12.7 (40)	102	12.1 (40)	98

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

TABLE 8 SELECTED NASAL CAVITY LESIONS OF MALE RATS IN THE 2-YEAR INHALATION STUDY OF CROTONALDEHYDE

Group Name	0ppm				3 ppm				6 ppm				12 ppm			
No. of Animals	50				50				50				50			
Findings Grade [a)]	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
non-neoplastic lesions																
respiratory epithelium																
inflammation	1	0	0	0	7	1	0	0*	24	1	0	0**	19	23	0	0**
hyperplasia	0	0	0	0	2	0	1	0	24	6	2	0**	10	24	6	0**
squamous cell metaplasia	1	0	0	0	11	3	1	0**	29	17	2	0**	8	21	19	0**
squamous cell hyperplasia	0	0	0	0	0	1	0	0	2	1	0	0	6	0	0	0*
olfactory epithelium																
necrosis	0	0	0	0	0	0	0	0	3	1	0	0	1	1	0	0
atrophy	0	0	0	0	0	0	0	0	2	0	0	0	1	6	0	0*
respiratory metaplasia	0	0	0	0	8	0	0	0**	5	3	0	0*	5	2	1	0*
others																
inflammation : foreign body	19	5	0	0	16	4	2	0	11	1	4	0*	20	15	7	0**
neoplastic lesions																
adenoma	0				1				1				2			
rhabdomyosarcoma	0				0				0				1			

a) 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

Significant difference ; * : $P \leqq 0.05$ ** : $P \leqq 0.01$ Test of Chi Square

TABLE 9 SELECTED NASAL CAVITY LESIONS OF FEMALE RATS IN THE 2-YEAR INHALATION STUDY OF CROTONALDEHYDE

Group Name	0ppm				3 ppm				6 ppm				12 ppm			
No. of Animals	50				50				50				50			
Findings Grade [a]	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
non-neoplastic lesions																
respiratory epithelium																
inflammation	0	0	0	0	0	0	0	0	17	0	0	0**	24	9	3	0**
hyperplasia	0	0	0	0	0	0	0	0	8	3	0	0**	13	18	5	0**
squamous cell metaplasia	0	0	0	0	18	0	0	0**	27	14	1	0**	19	17	9	0**
squamous cell hyperplasia	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0
olfactory epithelium																
necrosis	0	0	0	0	0	0	0	0	1	0	0	0	3	1	0	0
atrophy	0	0	0	0	0	0	0	0	1	0	0	0	2	5	0	0*
respiratory metaplasia	0	0	0	0	0	0	0	0	0	0	0	0	13	0	0	0**
eosinophilic change	0	10	36	1	3	14	33	0	0	13	34	0	5	16	24	0*
others																
inflammation : foreign body	0	0	0	0	3	0	0	0	1	1	0	0	31	3	0	0**
neoplastic lesions																
adenoma	0				0				0				1			

[a] 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

Significant difference ; * : $P \leqq 0.05$ ** : $P \leqq 0.01$ Test of Chi Square

TABLE 10 CAUSE OF DEATH OF RATS IN THE 2-YEAR INHALATION STUDY OF CROTONALDEHYDE

	Male				Female			
Group	0ppm	3ppm	6ppm	12ppm	0ppm	3ppm	6ppm	12ppm
Number of dead or moribund animals	11	11	5	12	11	12	10	10
No microscopical confirmation	1	0	0	0	2	0	0	0
CNS disorders	0	0	0	0	0	1	0	1
Nervous system disorders	0	0	0	1	0	0	1	0
Urinary retention	0	0	1	0	0	0	0	0
Chronic nephropathy	1	1	0	0	0	0	0	0
Tumor death : leukemia	1	3	2	4	4	4	1	3
subcutis	0	1	2	1	0	1	1	0
nasal cavity	0	0	0	1	0	0	0	0
lung	2	0	0	0	1	0	0	0
small intestine	0	1	0	0	0	0	0	0
liver	0	1	0	0	0	0	1	0
pituitary gland	4	2	0	4	3	2	4	3
thyroid	1	0	0	0	0	0	0	0
adrenal gland	0	0	0	1	0	0	0	0
uterus	-	-	-	-	0	1	2	2
mammary gland	0	0	0	0	1	1	0	0
preputial/clitoral gland	0	1	0	0	0	2	0	0
brain	0	0	0	0	0	0	0	1
Zymbal gland	1	0	0	0	0	0	0	0
peritoneum	0	1	0	0	0	0	0	0