グリオキサルのマウスを用いた経口投与による
が ん 原 性 試 験（混 水 試 験）報 告 書

試験番号：0268

TABLES

TABLES

TABLE 1 EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE DRINKING WATER STUDY OF GLYOXAL

2-year study

<Method of Administration>
drinking water
<Number of Groups>
Male 4, Female 4
<Size of Groups>
50 males and 50 females of each group[*1]
<Animals>
Strain and Species
Crj:BDF_1 mouse
Animal Source
Charles River Japan, Inc.
Duration Held Before Study
2 wk
Age When Placed on Study
6 wk
Age When Killed
111 wk
<Doses>
Male: 0, 333, 1000, or 3000ppm
Female: 0, 1500, 3000, or 6000ppm
<Duration of Dosing>
7 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 in duration of quarantine
Glass bottle in duration of acclimation and administration
Available *ad libitum*
Animal per Cage
Single (stainless steel wire)
Animal Room Environment
Barrier system
Temperature : 24±2℃
Humidity : 55±10%
Fluorescent light 12 h/d
15~17 room air changes /h
<Type and Frequency of Observation>
Clinical Sign
Observed 1 per d
Body Weight
Weighed 1 per wk for 14wk
Weighed 1 per 4wks thereafter
Water Consumption
Weighed 1 per wk for 14wk
Weighed 1 per 4wks thereafter
Food Consumption
Weighed 1 per wk for 14wk
Weighed 1 per 4wks thereafter

*1 1 animal accidentally dead in 6000ppm female group

TABLE 1 (Continued) EXPERIMENTAL DESIGN AND MATERIALS AND METHODS IN THE 2-YEAR DRINKING WATER STUDY OF GLYOXAL

2-year study
<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 concentrate (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, Glutamic oxaloacetic transaminase (GOT), Glutamic pyruvic transaminase (GPT), Alkaline phosphatase(ALP), Lactate dehydrogenase (LDH), Creatine phosphokinase (CPK), Urea nitrogen, 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, Occult blood, Urobilinogen.
<Necropsy> Necropsy performed on all animals.
<Organ Weight> Organ weight measurement performed on scheduled sacrificed animals. The following organs were weighed; brain, lung, liver, spleen, heart, kidney, adrenal, testis, ovary.
<Histopathologic Examination> Histopathologic examination performed on all animals per sex per groups. 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, gall bladder, 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.

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

Week on Study	Control Av.Wt. <50>	Control No. of Surviv.	333ppm Av.Wt. <50>	333ppm % of cont.	333ppm No. of Surviv.	1000ppm Av.Wt. <50>	1000ppm % of cont.	1000ppm No. of Surviv.	3000ppm Av.Wt. <50>	3000ppm % of cont.	3000ppm No. of Surviv.
0	23.1 (50)	50/50	23.1 (50)	100	50/50	23.1 (50)	100	50/50	23.1 (50)	100	50/50
1	23.9 (50)	50/50	23.9 (50)	100	50/50	23.8 (50)	100	50/50	23.2 (50)	97	50/50
2	24.9 (50)	50/50	24.7 (50)	99	50/50	24.7 (50)	99	50/50	24.0 (50)	96	50/50
3	25.4 (50)	50/50	25.2 (50)	99	50/50	25.4 (50)	100	50/50	24.5 (50)	96	50/50
4	26.2 (50)	50/50	25.9 (50)	99	49/50	25.8 (50)	98	50/50	25.1 (50)	96	50/50
5	26.6 (50)	50/50	26.8 (49)	101	49/50	26.5 (50)	100	50/50	25.9 (50)	97	50/50
6	27.2 (50)	50/50	27.3 (49)	100	49/50	27.1 (50)	100	50/50	26.0 (50)	96	50/50
7	28.1 (50)	50/50	28.2 (49)	100	49/50	27.7 (50)	99	50/50	26.5 (50)	94	50/50
8	28.3 (50)	50/50	28.7 (49)	101	49/50	28.4 (50)	100	50/50	26.8 (50)	95	50/50
9	28.8 (50)	50/50	29.2 (49)	101	49/50	28.8 (50)	100	50/50	27.1 (50)	94	50/50
10	29.3 (50)	50/50	29.6 (49)	101	49/50	29.2 (50)	100	50/50	27.3 (50)	93	50/50
11	30.2 (50)	50/50	30.5 (49)	101	49/50	30.1 (50)	100	50/50	27.9 (50)	92	50/50
12	30.8 (50)	50/50	31.1 (49)	101	49/50	30.5 (50)	99	50/50	28.5 (49)	93	49/50
13	31.8 (50)	50/50	31.8 (49)	100	49/50	31.3 (50)	98	50/50	28.8 (49)	91	49/50
14	32.3 (50)	50/50	32.4 (49)	100	49/50	31.8 (50)	98	50/50	29.1 (49)	90	49/50
18	35.4 (50)	50/50	35.4 (49)	100	49/50	34.8 (50)	98	50/50	31.1 (49)	88	49/50
22	38.2 (49)	49/50	37.6 (49)	98	49/50	36.8 (50)	96	50/50	32.3 (49)	85	49/50
26	39.7 (49)	49/50	38.8 (49)	98	49/50	38.1 (50)	96	50/50	33.1 (49)	83	49/50
30	42.2 (49)	49/50	41.6 (49)	99	49/50	40.3 (50)	95	50/50	34.6 (49)	82	49/50
34	44.6 (49)	49/50	43.4 (49)	97	49/50	41.9 (50)	94	50/50	35.8 (49)	80	49/50
38	46.1 (49)	49/50	44.9 (49)	97	49/50	43.4 (50)	94	50/50	36.8 (49)	80	49/50
42	47.3 (49)	49/50	45.8 (49)	97	49/50	43.9 (50)	93	50/50	37.3 (49)	79	49/50
46	48.1 (49)	49/50	47.0 (49)	98	49/50	44.6 (50)	93	50/50	38.1 (49)	79	49/50
50	48.7 (49)	49/50	47.5 (49)	98	49/50	45.4 (50)	93	50/50	38.5 (49)	79	49/50
54	49.0 (48)	48/50	47.5 (49)	97	49/50	45.1 (50)	92	50/50	38.4 (49)	78	49/50
58	49.5 (48)	48/50	47.9 (49)	97	49/50	45.5 (50)	92	50/50	38.3 (49)	77	49/50
62	50.1 (48)	48/50	48.7 (49)	97	49/50	46.6 (50)	93	50/50	39.0 (49)	78	49/50
66	50.8 (48)	48/50	49.1 (48)	97	48/50	46.9 (50)	92	50/50	39.7 (48)	78	48/50
70	51.4 (48)	48/50	50.2 (48)	98	48/50	48.2 (49)	94	49/50	41.2 (47)	80	47/50
74	51.6 (48)	48/50	50.9 (48)	99	48/50	50.1 (47)	97	47/50	41.8 (47)	81	47/50
78	52.5 (47)	47/50	51.8 (47)	99	47/50	50.5 (47)	96	47/50	42.5 (46)	81	46/50
82	53.2 (46)	46/50	52.1 (47)	98	47/50	50.2 (46)	94	46/50	42.5 (46)	80	46/50
86	52.5 (45)	45/50	51.7 (47)	98	47/50	49.7 (45)	95	45/50	41.8 (45)	80	45/50
90	52.9 (41)	41/50	51.6 (47)	98	47/50	49.4 (45)	93	45/50	41.5 (43)	78	43/50
94	53.8 (36)	36/50	52.1 (46)	97	46/50	50.0 (44)	93	44/50	42.1 (42)	78	42/50
98	52.3 (36)	36/50	51.1 (44)	98	44/50	49.4 (41)	94	41/50	40.9 (42)	78	42/50
102	51.1 (34)	34/50	50.2 (43)	98	43/50	48.8 (40)	95	40/50	40.8 (41)	80	41/50
104	49.6 (33)	33/50	49.0 (41)	99	41/50	48.2 (38)	97	38/50	40.3 (40)	81	40/50

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

TABLE 3 SURVIVAL ANIMAL NUMBERS AND BODY WEIGHT CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF GLYOXAL

Week on Study	Control Av.Wt.	Control No. of Surviv. <50>	1500ppm Av.Wt.	1500ppm % of cont.	1500ppm No. of Surviv. <50>	3000ppm Av.Wt.	3000ppm % of cont.	3000ppm No. of Surviv. <50>	6000ppm Av.Wt.	6000ppm % of cont.	6000ppm No. of Surviv. <50>
0	18.6 (50)	50/50	18.6 (50)	100	50/50	18.6 (50)	100	50/50	18.6 (50)	100	50/50
1	19.4 (50)	50/50	19.5 (50)	101	50/50	18.9 (50)	97	50/50	18.4 (49)	95	49/49
2	19.9 (50)	50/50	20.1 (50)	101	50/50	19.4 (50)	97	50/50	18.5 (49)	93	49/49
3	20.6 (50)	50/50	20.7 (50)	100	50/50	20.2 (50)	98	50/50	19.1 (49)	93	49/49
4	21.1 (50)	50/50	21.3 (50)	101	50/50	20.5 (50)	97	50/50	19.5 (49)	92	49/49
5	21.5 (50)	50/50	21.5 (50)	100	50/50	20.8 (50)	97	50/50	19.9 (49)	93	49/49
6	21.7 (50)	50/50	21.7 (50)	100	50/50	21.0 (50)	97	50/50	20.4 (49)	94	49/49
7	22.3 (50)	50/50	22.3 (50)	100	50/50	21.4 (50)	96	50/50	20.7 (49)	93	49/49
8	22.8 (50)	50/50	22.4 (50)	98	50/50	21.5 (50)	94	50/50	20.7 (49)	91	49/49
9	23.1 (50)	50/50	23.1 (50)	100	50/50	22.0 (50)	95	50/50	21.2 (49)	92	49/49
10	23.5 (50)	50/50	23.3 (50)	99	50/50	22.0 (50)	94	50/50	21.3 (49)	91	49/49
11	23.7 (50)	50/50	23.3 (50)	98	50/50	22.5 (50)	95	50/50	21.6 (49)	91	49/49
12	24.2 (50)	50/50	23.7 (50)	98	50/50	22.3 (50)	92	50/50	22.0 (49)	91	49/49
13	24.3 (50)	50/50	24.2 (50)	100	50/50	22.6 (50)	93	50/50	22.2 (49)	91	49/49
14	24.2 (50)	50/50	24.0 (50)	99	50/50	22.8 (50)	94	50/50	22.0 (49)	91	49/49
18	25.9 (50)	50/50	25.2 (50)	97	50/50	23.6 (50)	91	50/50	22.9 (49)	88	49/49
22	27.5 (50)	50/50	26.2 (50)	95	50/50	24.1 (50)	88	50/50	23.2 (49)	84	49/49
26	27.8 (50)	50/50	26.9 (50)	97	50/50	24.9 (50)	90	50/50	23.7 (49)	85	49/49
30	29.0 (50)	50/50	28.0 (50)	97	50/50	25.3 (50)	87	50/50	23.7 (49)	82	49/49
34	30.2 (50)	50/50	29.2 (50)	97	50/50	25.7 (50)	85	50/50	24.3 (49)	80	49/49
38	31.3 (50)	50/50	29.5 (50)	94	50/50	26.0 (50)	83	50/50	24.4 (49)	78	49/49
42	32.5 (50)	50/50	30.5 (50)	94	50/50	26.9 (50)	83	50/50	24.4 (49)	75	49/49
46	33.3 (48)	48/50	30.9 (50)	93	50/50	26.9 (50)	81	50/50	25.0 (48)	75	48/49
50	33.6 (48)	48/50	31.1 (50)	93	50/50	26.9 (50)	80	50/50	25.2 (48)	75	48/49
54	34.1 (47)	47/50	31.0 (50)	91	50/50	27.0 (50)	79	50/50	24.7 (47)	72	47/49
58	34.1 (47)	47/50	31.2 (50)	91	50/50	27.3 (50)	80	50/50	25.0 (47)	73	47/49
62	34.2 (47)	47/50	31.5 (50)	92	50/50	27.2 (50)	80	50/50	25.1 (47)	73	47/49
66	35.6 (44)	44/50	32.2 (50)	90	50/50	27.5 (49)	77	49/50	25.1 (46)	71	46/49
70	36.2 (43)	43/50	33.0 (49)	91	49/50	27.8 (49)	77	49/50	25.4 (46)	70	46/49
74	36.7 (42)	42/50	33.0 (47)	90	47/50	28.1 (49)	77	49/50	25.5 (46)	69	46/49
78	37.7 (42)	42/50	33.8 (45)	90	45/50	28.7 (48)	76	48/50	26.1 (46)	69	46/49
82	37.8 (41)	41/50	34.2 (45)	90	45/50	28.9 (44)	76	44/50	26.1 (45)	69	45/49
86	37.8 (38)	38/50	34.0 (44)	90	44/50	28.6 (44)	76	44/50	25.7 (43)	68	43/49
90	37.7 (36)	36/50	33.2 (40)	88	40/50	28.9 (44)	77	44/50	25.9 (42)	69	42/49
94	38.1 (35)	35/50	33.7 (38)	88	38/50	28.7 (40)	75	40/50	25.8 (40)	68	40/49
98	36.9 (34)	34/50	32.8 (34)	89	34/50	28.5 (39)	77	39/50	25.2 (39)	68	39/49
102	36.6 (31)	31/50	32.8 (31	90	31/50	27.8 (36)	76	36/50	25.2 (39)	69	39/49
104	36.1 (30)	30/50	32.4 (29)	90	29/50	28.0 (32)	78	32/50	25.7 (39)	71	39/49

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

TABLE 4 INCIDENCE OF EXTERNAL AND INTERNAL MASS IN CLINICAL OBSERVATION OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF GLYOXAL

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	0/49	0/49	1/49	1/48	2/47	1/38	2/50(1/17)
	333ppm	0/50	0/49	0/49	0/49	1/49	0/48	0/47	0/47	1/50(1/ 9)
	1000ppm	0/50	0/50	0/50	0/50	0/50	1/50	1/46	1/44	1/50(0/12)
	3000ppm	0/50	0/49	0/49	0/49	0/49	0/48	0/46	0/42	0/50(0/10)
Internal mass										
	Control	0/50	0/50	0/49	0/49	0/49	1/48	5/47	5/38	8/50(5/17)
	333ppm	0/50	0/49	1/49	2/49	2/49	2/48	6/47	9/47	11/50(3/ 9)
	1000ppm	0/50	0/50	1/50	1/50	2/50	2/50	2/46	2/44	6/50(2/12)
	3000ppm	0/50	0/50	0/49	1/49	1/49	2/48	2/46	1/42	3/50(2/10)

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 5 INCIDENCE OF EXTERNAL AND INTERNAL MASS IN CLINICAL OBSERVATION OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF GLYOXAL

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	0/47	1/47	1/44	0/42	3/35	4/50(2/20)
	1500ppm	0/50	0/50	0/50	0/50	0/50	0/50	0/45	4/38	4/50(2/21)
	3000ppm	0/50	0/50	0/50	0/50	0/50	1/49	0/47	1/43	2/50(1/18)
	6000ppm	0/49	0/49	0/49	1/48	1/47	1/46	2/46	1/41	2/49(1/11)
Internal mass										
	Control	0/50	0/50	0/50	0/47	0/47	2/44	4/42	3/35	7/50(5/20)
	1500ppm	0/50	0/50	0/50	0/50	1/50	4/50	6/45	5/38	11/50(7/21)
	3000ppm	0/50	0/50	0/50	0/50	1/50	1/49	6/47	4/43	8/50(4/18)
	6000ppm	0/49	0/49	0/49	2/48	4/47	3/46	7/46	3/41	8/49(5/11)

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 WATER CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF GLYOXAL

Week on Study	Control		333ppm			1000ppm			3000ppm		
	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>		
1	4.3 (50)	50/50	4.0 (50)	93	50/50	3.5 (49)	81	50/50	2.9 (50)	67	50/50
2	4.4 (50)	50/50	3.9 (50)	89	50/50	3.4 (50)	77	50/50	2.6 (50)	59	50/50
3	4.2 (50)	50/50	3.9 (50)	93	50/50	3.4 (50)	81	50/50	2.6 (50)	62	50/50
4	4.3 (50)	50/50	4.0 (50)	93	49/50	3.5 (50)	81	50/50	2.4 (50)	56	50/50
5	4.2 (50)	50/50	3.8 (49)	90	49/50	3.4 (50)	81	50/50	2.6 (50)	62	50/50
6	4.3 (50)	50/50	3.7 (49)	86	49/50	3.4 (50)	79	50/50	2.4 (50)	56	50/50
7	4.1 (50)	50/50	3.5 (49)	85	49/50	3.3 (50)	80	50/50	2.3 (50)	56	50/50
8	4.0 (50)	50/50	3.5 (49)	88	49/50	3.2 (50)	80	50/50	2.2 (50)	55	50/50
9	4.1 (50)	50/50	3.5 (49)	85	49/50	3.2 (50)	78	50/50	2.3 (50)	56	50/50
10	4.0 (50)	50/50	3.5 (49)	88	49/50	3.1 (50)	78	50/50	1.9 (50)	47	50/50
11	4.1 (49)	50/50	3.6 (49)	88	49/50	3.3 (50)	80	50/50	2.3 (50)	56	50/50
12	4.0 (48)	50/50	3.5 (49)	88	49/50	3.1 (50)	78	50/50	2.3 (49)	58	49/50
13	3.7 (48)	50/50	3.4 (49)	92	49/50	3.1 (50)	84	50/50	2.1 (49)	57	49/50
14	3.8 (49)	50/50	3.4 (49)	89	49/50	3.1 (50)	82	50/50	2.2 (49)	58	49/50
18	3.7 (50)	50/50	3.4 (49)	92	49/50	3.1 (50)	84	50/50	2.1 (49)	57	49/50
22	3.2 (49)	49/50	3.1 (49)	97	49/50	2.7 (50)	84	50/50	2.0 (49)	63	49/50
26	3.4 (48)	49/50	3.4 (49)	100	49/50	2.9 (50)	85	50/50	2.1 (49)	62	49/50
30	3.3 (49)	49/50	3.4 (49)	103	49/50	2.9 (50)	88	50/50	2.0 (49)	61	49/50
34	3.6 (49)	49/50	3.3 (49)	92	49/50	2.9 (50)	81	50/50	2.2 (49)	61	49/50
38	3.6 (49)	49/50	3.4 (49)	94	49/50	2.9 (50)	81	50/50	2.1 (49)	58	49/50
42	3.5 (49)	49/50	3.4 (49)	97	49/50	2.9 (50)	83	50/50	2.2 (49)	63	49/50
46	3.6 (49)	49/50	3.5 (49)	97	49/50	3.0 (50)	83	50/50	2.2 (49)	61	49/50
50	3.5 (49)	49/50	3.4 (49)	97	49/50	3.0 (50)	86	50/50	2.2 (49)	63	49/50
54	3.7 (48)	48/50	3.7 (49)	100	49/50	3.3 (50)	89	50/50	2.4 (49)	65	49/50
58	3.8 (48)	48/50	3.7 (49)	97	49/50	3.2 (50)	84	50/50	2.4 (49)	63	49/50
62	3.8 (48)	48/50	3.8 (49)	100	49/50	3.2 (50)	84	50/50	2.4 (49)	63	49/50
66	4.1 (48)	48/50	3.9 (47)	95	48/50	3.3 (50)	80	50/50	2.3 (48)	56	48/50
70	4.0 (48)	48/50	3.8 (48)	95	48/50	3.3 (49)	83	49/50	2.4 (47)	60	47/50
74	3.9 (47)	48/50	3.7 (47)	95	48/50	3.3 (47)	85	47/50	2.4 (47)	62	47/50
78	4.3 (47)	47/50	4.0 (47)	93	47/50	3.3 (47)	77	47/50	2.6 (46)	60	46/50
82	4.4 (46)	46/50	4.0 (47)	91	47/50	3.5 (46)	80	46/50	2.6 (46)	59	46/50
86	4.3 (45)	45/50	4.0 (47)	93	47/50	3.5 (45)	81	45/50	2.6 (45)	60	45/50
90	4.3 (41)	41/50	4.0 (47)	93	47/50	3.5 (45)	81	45/50	2.6 (43)	60	43/50
94	4.3 (36)	36/50	4.1 (46)	95	46/50	3.6 (44)	84	44/50	2.7 (42)	63	42/50
98	4.4 (36)	36/50	3.9 (44)	89	44/50	3.5 (41)	80	41/50	2.4 (42)	55	42/50
102	4.8 (34)	34/50	4.0 (43)	83	43/50	3.5 (40)	73	40/50	2.4 (41)	50	41/50
104	5.0 (32)	33/50	4.1 (41)	82	41/50	3.8 (38)	76	38/50	2.4 (40)	48	40/50

< >:No. of effective animals, ( ):No. of measurement animals Av.WC.: g

TABLE 7 WATER CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF GLYOXAL

Week on Study	Control Av.Wt.	Control No. of Surviv. <50>	1500ppm Av.Wt.	1500ppm % of cont.	1500ppm No. of Surviv. <50>	3000ppm Av.Wt.	3000ppm % of cont.	3000ppm No. of Surviv. <50>	6000ppm Av.Wt.	6000ppm % of cont.	6000ppm No. of Surviv. <50>
1	3.8 (50)	50/50	3.1 (50)	82	50/50	2.5 (50)	66	50/50	2.0 (49)	53	49/49
2	4.1 (50)	50/50	3.2 (50)	78	50/50	2.4 (50)	59	50/50	1.7 (49)	41	49/49
3	4.3 (50)	50/50	3.2 (50)	74	50/50	2.6 (50)	60	50/50	1.9 (49)	44	49/49
4	4.4 (49)	50/50	3.1 (50)	70	50/50	2.4 (50)	55	50/50	1.7 (49)	39	49/49
5	4.5 (50)	50/50	3.2 (50)	71	50/50	2.5 (50)	56	50/50	1.8 (49)	40	49/49
6	4.6 (49)	50/50	3.3 (50)	72	50/50	2.5 (50)	54	50/50	1.7 (49)	37	49/49
7	4.5 (50)	50/50	3.3 (50)	73	50/50	2.5 (50)	56	50/50	1.8 (49)	40	49/49
8	4.8 (50)	50/50	3.1 (50)	65	50/50	2.5 (50)	52	50/50	1.8 (49)	38	49/49
9	4.3 (48)	50/50	3.3 (50)	77	50/50	2.4 (50)	56	50/50	2.0 (49)	47	49/49
10	4.4 (50)	50/50	3.2 (50)	73	50/50	2.4 (50)	55	50/50	1.8 (49)	41	49/49
11	4.0 (48)	50/50	3.1 (50)	78	50/50	2.4 (50)	60	50/50	1.8 (49)	45	49/49
12	4.3 (50)	50/50	3.1 (50)	72	50/50	2.4 (50)	56	50/50	1.9 (49)	44	49/49
13	4.1 (50)	50/50	3.0 (50)	73	50/50	2.4 (50)	59	50/50	1.9 (49)	46	49/49
14	4.4 (49)	50/50	3.1 (50)	70	50/50	2.5 (50)	57	50/50	1.9 (49)	43	49/49
18	4.0 (48)	50/50	3.0 (50)	75	50/50	2.4 (50)	60	50/50	1.8 (49)	45	49/49
22	4.2 (50)	50/50	2.8 (50)	67	50/50	2.2 (50)	52	50/50	1.7 (49)	40	49/49
26	3.9 (50)	50/50	2.8 (50)	72	50/50	2.3 (50)	59	50/50	1.7 (49)	44	49/49
30	3.8 (49)	50/50	2.8 (50)	74	50/50	2.2 (50)	58	50/50	1.8 (49)	47	49/49
34	4.3 (50)	50/50	2.8 (50)	65	50/50	2.4 (50)	56	50/50	1.9 (49)	44	49/49
38	3.8 (49)	50/50	2.9 (50)	76	50/50	2.3 (50)	61	50/50	1.8 (49)	47	49/49
42	3.8 (50)	50/50	2.7 (50)	71	50/50	2.3 (50)	61	50/50	1.7 (49)	45	49/49
46	3.6 (47)	48/50	2.7 (50)	75	50/50	2.3 (50)	64	50/50	1.7 (48)	47	48/49
50	3.9 (48)	48/50	2.9 (50)	74	50/50	2.3 (50)	59	50/50	1.8 (48)	46	48/49
54	4.0 (47)	47/50	2.8 (50)	70	50/50	2.4 (50)	60	50/50	1.9 (47)	47	47/49
58	3.9 (47)	47/50	2.8 (50)	72	50/50	2.4 (50)	62	50/50	1.9 (47)	49	47/49
62	3.9 (47)	47/50	2.8 (50)	72	50/50	2.4 (50)	62	50/50	1.8 (47)	46	47/49
66	4.4 (44)	44/50	3.1 (50)	70	50/50	2.4 (49)	55	49/50	1.8 (46)	41	46/49
70	3.9 (43)	43/50	2.8 (49)	72	49/50	2.4 (49)	62	49/50	1.8 (46)	46	46/49
74	4.2 (42)	42/50	2.8 (47)	67	47/50	2.5 (49)	60	49/50	1.9 (46)	45	46/49
78	4.0 (42)	42/50	2.8 (45)	70	45/50	2.4 (48)	60	48/50	1.9 (46)	47	46/49
82	3.9 (41)	41/50	3.0 (45)	77	45/50	2.5 (44)	64	44/50	1.9 (45)	49	45/49
86	3.8 (38)	38/50	2.9 (44)	76	44/50	2.5 (44)	66	44/50	1.9 (43)	50	43/49
90	3.9 (36)	36/50	2.8 (40)	72	40/50	2.5 (44)	64	44/50	1.9 (42)	49	42/49
94	4.0 (35)	35/50	2.8 (38)	70	38/50	2.5 (40)	63	40/50	1.8 (40)	45	40/49
98	3.9 (34)	34/50	2.8 (34)	72	34/50	2.5 (39)	64	39/50	1.8 (39)	46	39/49
102	3.9 (31)	31/50	2.9 (31)	74	31/50	2.7 (36)	69	36/50	1.8 (39)	46	39/49
104	4.1 (30)	30/50	3.1 (29)	76	29/50	2.7 (32)	66	32/50	2.0 (39)	49	39/49

< >:No. of effective animals, ( ):No. of measurement animals Av.WC.: g

TABLE 8 FOOD CONSUMPTION CHANGES OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF GLYOXAL

Week on Study	Control		333ppm			1000ppm			3000ppm		
	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>		
1	3.4 (50)	50/50	3.4 (50)	100	50/50	3.4 (50)	100	50/50	3.1 (50)	91	50/50
2	3.5 (50)	50/50	3.4 (50)	97	50/50	3.4 (50)	97	50/50	3.3 (50)	94	50/50
3	3.4 (50)	50/50	3.3 (50)	97	50/50	3.4 (50)	100	50/50	3.3 (50)	97	50/50
4	3.5 (50)	50/50	3.5 (50)	100	49/50	3.5 (50)	100	50/50	3.4 (50)	97	50/50
5	3.5 (50)	50/50	3.5 (49)	100	49/50	3.5 (50)	100	50/50	3.3 (50)	94	50/50
6	3.5 (50)	50/50	3.5 (49)	100	49/50	3.5 (50)	100	50/50	3.3 (50)	94	50/50
7	3.6 (50)	50/50	3.6 (49)	100	49/50	3.6 (50)	100	50/50	3.4 (50)	94	50/50
8	3.5 (50)	50/50	3.5 (49)	100	49/50	3.6 (50)	103	50/50	3.3 (50)	94	50/50
9	3.6 (50)	50/50	3.6 (49)	100	49/50	3.6 (50)	100	50/50	3.4 (50)	94	50/50
10	3.6 (50)	50/50	3.6 (49)	100	49/50	3.6 (50)	100	50/50	3.3 (50)	92	50/50
11	3.8 (50)	50/50	3.7 (49)	97	49/50	3.6 (50)	95	50/50	3.4 (50)	89	50/50
12	3.8 (50)	50/50	3.7 (49)	97	49/50	3.7 (50)	97	50/50	3.5 (49)	92	49/50
13	3.9 (50)	50/50	3.8 (49)	97	49/50	3.7 (50)	95	50/50	3.4 (49)	87	49/50
14	3.8 (50)	50/50	3.8 (49)	100	49/50	3.7 (50)	97	50/50	3.4 (49)	89	49/50
18	3.9 (50)	50/50	3.9 (49)	100	49/50	3.8 (50)	97	50/50	3.5 (49)	90	49/50
22	3.9 (49)	49/50	3.8 (49)	97	49/50	3.8 (50)	97	50/50	3.5 (49)	90	49/50
26	4.0 (49)	49/50	3.9 (49)	97	49/50	3.8 (50)	95	50/50	3.5 (49)	88	49/50
30	4.1 (49)	49/50	4.0 (49)	98	49/50	3.9 (50)	95	50/50	3.6 (49)	88	49/50
34	4.2 (49)	49/50	4.0 (49)	95	49/50	4.0 (50)	95	50/50	3.6 (49)	86	49/50
38	4.3 (49)	49/50	4.2 (49)	98	49/50	4.0 (50)	93	50/50	3.7 (49)	86	49/50
42	4.3 (49)	49/50	4.1 (49)	95	49/50	4.0 (50)	93	50/50	3.6 (49)	84	49/50
46	4.2 (49)	49/50	4.1 (49)	98	49/50	4.1 (50)	98	50/50	3.7 (49)	88	49/50
50	4.4 (49)	49/50	4.3 (49)	98	49/50	4.3 (50)	98	50/50	3.8 (49)	86	49/50
54	4.4 (48)	48/50	4.2 (49)	95	49/50	4.2 (50)	95	50/50	3.8 (49)	86	49/50
58	4.5 (48)	48/50	4.4 (49)	98	49/50	4.4 (50)	98	50/50	3.9 (49)	87	49/50
62	4.6 (48)	48/50	4.4 (49)	96	49/50	4.3 (50)	93	50/50	3.9 (49)	85	49/50
66	4.5 (48)	48/50	4.3 (48)	96	48/50	4.1 (50)	91	50/50	3.8 (48)	84	48/50
70	4.4 (48)	48/50	4.2 (48)	95	48/50	4.1 (49)	93	49/50	3.8 (47)	86	47/50
74	4.4 (48)	48/50	4.3 (48)	98	48/50	4.4 (47)	100	47/50	3.9 (47)	89	47/50
78	4.8 (47)	47/50	4.6 (46)	96	47/50	4.5 (47)	94	47/50	4.0 (46)	83	46/50
82	4.7 (46)	46/50	4.6 (46)	98	47/50	4.6 (46)	98	46/50	4.2 (46)	89	46/50
86	4.7 (45)	45/50	4.5 (47)	96	47/50	3.7 (45)	79	45/50	4.1 (45)	87	45/50
90	4.7 (41)	41/50	4.5 (47)	96	47/50	4.6 (45)	98	45/50	4.3 (43)	91	43/50
94	4.8 (36)	36/50	4.5 (46)	94	46/50	4.6 (44)	96	44/50	4.2 (42)	87	42/50
98	4.4 (35)	36/50	4.3 (44)	98	44/50	4.4 (41)	100	41/50	4.0 (42)	91	42/50
102	4.5 (34)	34/50	4.3 (43)	96	43/50	4.4 (40)	98	40/50	3.9 (41)	87	41/50
104	4.6 (33)	33/50	4.4 (41)	96	41/50	4.4 (38)	96	38/50	4.0 (40)	87	40/50

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

TABLE 9 FOOD CONSUMPTION CHANGES OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF GLYOXAL

Week on Study	Control Av.Wt.	Control No. of Surviv. <50>	1500ppm Av.Wt.	1500ppm % of cont.	1500ppm No. of Surviv. <50>	3000ppm Av.Wt.	3000ppm % of cont.	3000ppm No. of Surviv. <50>	6000ppm Av.Wt.	6000ppm % of cont.	6000ppm No. of Surviv. <50>
1	2.8 (50)	50/50	2.8 (50)	100	50/50	2.6 (50)	93	50/50	2.4 (49)	86	49/49
2	2.9 (50)	50/50	2.8 (50)	97	50/50	2.7 (50)	93	50/50	2.5 (49)	86	49/49
3	3.1 (50)	50/50	3.0 (50)	97	50/50	2.9 (50)	94	50/50	2.7 (49)	87	49/49
4	3.1 (50)	50/50	3.1 (50)	100	50/50	2.9 (50)	94	50/50	2.7 (49)	87	49/49
5	3.2 (50)	50/50	3.1 (50)	97	50/50	3.0 (50)	94	50/50	2.8 (49)	88	49/49
6	3.2 (50)	50/50	3.2 (50)	100	50/50	3.0 (50)	94	50/50	2.9 (49)	91	49/49
7	3.3 (50)	50/50	3.2 (50)	97	50/50	3.1 (50)	94	50/50	2.9 (49)	88	49/49
8	3.3 (50)	50/50	3.2 (50)	97	50/50	3.0 (50)	91	50/50	2.9 (49)	88	49/49
9	3.4 (50)	50/50	3.3 (50)	97	50/50	3.1 (50)	91	50/50	3.0 (49)	88	49/49
10	3.4 (50)	50/50	3.3 (50)	97	50/50	3.0 (50)	88	50/50	2.9 (49)	85	49/49
11	3.2 (50)	50/50	2.8 (50)	88	50/50	3.1 (50)	97	50/50	3.0 (49)	94	49/49
12	3.5 (50)	50/50	3.4 (50)	97	50/50	3.1 (50)	89	50/50	3.1 (49)	89	49/49
13	3.4 (50)	50/50	3.3 (50)	97	50/50	3.1 (50)	91	50/50	3.1 (49)	91	49/49
14	3.4 (50)	50/50	3.4 (50)	100	50/50	3.3 (50)	97	50/50	3.1 (49)	91	49/49
18	3.6 (50)	50/50	3.4 (50)	94	50/50	3.2 (50)	89	50/50	3.1 (49)	86	49/49
22	3.7 (50)	50/50	3.5 (50)	95	50/50	3.3 (50)	89	50/50	3.1 (49)	84	49/49
26	3.7 (50)	50/50	3.7 (50)	100	50/50	3.4 (50)	92	50/50	3.2 (49)	86	49/49
30	3.8 (50)	50/50	3.7 (50)	97	50/50	3.4 (50)	89	50/50	3.2 (49)	84	49/49
34	4.0 (50)	50/50	3.8 (50)	95	50/50	3.5 (50)	88	50/50	3.5 (49)	88	49/49
38	4.1 (50)	50/50	3.8 (50)	93	50/50	3.7 (50)	90	50/50	3.5 (49)	85	49/49
42	4.2 (50)	50/50	3.9 (50)	93	50/50	3.7 (50)	88	50/50	3.4 (49)	81	49/49
46	4.2 (48)	48/50	4.1 (50)	98	50/50	3.7 (50)	88	50/50	3.6 (48)	86	48/49
50	4.1 (48)	48/50	4.0 (50)	98	50/50	3.6 (50)	88	50/50	3.6 (48)	88	48/49
54	4.0 (47)	47/50	3.7 (50)	92	50/50	3.5 (50)	88	50/50	3.4 (47)	85	47/49
58	4.0 (47)	47/50	3.8 (50)	95	50/50	3.7 (50)	92	50/50	3.5 (47)	88	47/49
62	4.0 (47)	47/50	3.8 (50)	95	50/50	3.6 (50)	90	50/50	3.5 (47)	88	47/49
66	4.1 (44)	44/50	3.7 (50)	90	50/50	3.4 (49)	83	49/50	3.2 (46)	78	46/49
70	4.4 (43)	43/50	3.9 (49)	89	49/50	3.7 (49)	84	49/50	3.5 (46)	80	46/49
74	4.4 (42)	42/50	3.9 (47)	89	47/50	3.8 (49)	86	49/50	3.7 (46)	84	46/49
78	4.2 (42)	42/50	3.8 (45)	90	45/50	3.6 (48)	86	48/50	3.7 (45)	88	46/49
82	4.2 (41)	41/50	4.1 (45)	98	45/50	3.9 (44)	93	44/50	3.7 (45)	88	45/49
86	4.1 (38)	38/50	3.9 (44)	95	44/50	3.8 (44)	93	44/50	3.9 (43)	95	43/49
90	4.2 (36)	36/50	4.0 (40)	95	40/50	3.9 (44)	93	44/50	3.7 (42)	88	42/49
94	4.3 (35)	35/50	4.0 (38)	93	38/50	3.9 (40)	91	40/50	3.6 (40)	84	40/49
98	3.9 (31)	34/50	3.9 (34)	100	34/50	3.7 (39)	95	39/50	3.4 (39)	87	39/49
102	4.1 (31)	31/50	3.9 (31)	95	31/50	3.7 (36)	90	36/50	3.3 (39)	80	39/49
104	4.3 (30)	30/50	3.8 (29)	88	29/50	3.8 (32)	88	32/50	3.7 (39)	86	39/49

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

TABLE 10 NEOPLASTIC LESIONS INCIDENCE AND STATISTICAL ANALYSIS OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF GLYOXAL

Group Name	Control	333ppm	1000ppm	3000ppm
SITE : lymph node				
TUMOR : malignant lymphoma				
Tumor rate				
Overall rates(a)	7/50(14.0)	9/50(18.0)	4/50(8.0)	2/50(4.0)
Adjusted rates(b)	15.15	9.76	10.53	2.50
Terminal rates(c)	5/33(15.2)	4/41(9.8)	4/38(10.5)	1/40(2.5)
Statistical analysis				
Peto test				
Standard method(d)	P=0.8988			
Prevalence method(d)	P=0.9694			
Combined analysis (d)	P=0.9887			
Cochran-Amitage test(e)	P=0.0354*			
Fisher Exact test(e)		P=0.3932	P=0.2624	P=0.0798
SITE : spleen				
TUMOR : hemangiosarcoma				
Tumor rate				
Overall rates(a)	5/50(10.0)	4/50(8.0)	1/50(2.0)	0/50(0.0)
Adjusted rates(b)	5.26	8.70	2.38	0.0
Terminal rates(c)	1/33(3.0)	2/41(4.9)	0/38(0.0)	0/40(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P=0.9818			
Prevalence method(d)	P=0.9751			
Combined analysis (d)	P=0.9973			
Cochran-Amitage test(e)	P=0.0178*			
Fisher Exact test(e)		P=0.4998	P=0.1022	P=0.0281*
SITE : spleen				
TUMOR : hemangioma, hemangiosarcoma				
Tumor rate				
Overall rates(a)	5/50(10.0)	4/50(8.0)	2/50(4.0)	0/50(0.0)
Adjusted rates(b)	5.26	8.70	4.76	0.0
Terminal rates(c)	1/33(3.0)	2/41(4.9)	1/38(2.6)	0/40(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P=0.9818			
Prevalence method(d)	P=0.9660			
Combined analysis (d)	P=0.9956			
Cochran-Amitage test(e)	P=0.0222*			
Fisher Exact test(e)		P=0.4998	P=0.2181	P=0.0281*
SITE : liver				
TUMOR : hepatocellular adenoma				
Tumor rate				
Overall rates(a)	10/50(20.0)	11/50(22.0)	10/50(20.0)	3/50(6.0)
Adjusted rates(b)	20.45	25.00	22.22	7.50
Terminal rates(c)	6/33(18.2)	10/41(24.4)	8/38(21.1)	3/40(7.5)
Statistical analysis				
Peto test				
Standard method(d)	P=1.0000 ?			
Prevalence method(d)	P=0.9855			
Combined analysis (d)	P=0.9903			
Cochran-Amitage test(e)	P=0.0219*			
Fisher Exact test(e)		P=0.4992	P=0.4007	P=0.0357*

TABLE 10 NEOPLASTIC LESIONS INCIDENCE AND STATISTICAL ANALYSIS OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF GLYOXAL(CONTINUED)

Group Name	Control	333ppm	1000ppm	3000ppm
SITE : liver				
TUMOR : hepatocellular carcinoma				
Tumor rate				
Overall rates(a)	8/50(16.0)	11/50(22.0)	6/50(12.0)	2/50(4.0)
Adjusted rates(b)	15.15	23.91	15.79	0.0
Terminal rates(c)	5/33(15.2)	9/41(22.0)	6/38(15.8)	0/40(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P=0.2333			
Prevalence method(d)	P=0.9995			
Combined analysis (d)	P=0.9948			
Cochran-Amitage test(e)	P=0.0157*			
Fisher Exact test(e)		P=0.3059	P=0.3875	P=0.0458*
SITE : liver				
TUMOR : hepatocellular adenoma, hepatocellular carcinoma				
Tumor rate				
Overall rates(a)	17/50(34.0)	20/50(40.0)	13/50(26.0)	5/50(10.0)
Adjusted rates(b)	33.33	43.48	28.95	7.50
Terminal rates(c)	11/33(33.3)	17/41(41.5)	11/38(28.9)	3/40(7.5)
Statistical analysis				
Peto test				
Standard method(d)	P=0.3865			
Prevalence method(d)	P=0.9999			
Combined analysis (d)	P=0.9997			
Cochran-Amitage test(e)	P=0.0007**			
Fisher Exact test(e)		P=0.3401	P=0.2570	P=0.0035**
SITE : Harderian gland				
TUMOR : adenoma				
Tumor rate				
Overall rates(a)	4/50(8.0)	4/50(8.0)	4/50(8.0)	0/50(0.0)
Adjusted rates(b)	12.12	9.76	10.53	0.0
Terminal rates(c)	4/33(12.1)	4/41(9.8)	4/38(10.5)	0/40(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P=------			
Prevalence method(d)	P=0.9889			
Combined analysis (d)	P=------			
Cochran-Amitage test(e)	P=0.0498*			
Fisher Exact test(e)		P=0.3573	P=0.3573	P=0.0587
SITE : ALL SITE				
TUMOR : histiocytic sarcoma				
Tumor rate				
Overall rates(a)	7/50(14.0)	1/50(2.0)	6/50(12.0)	3/50(6.0)
Adjusted rates(b)	9.09	0.0	7.89	2.33
Terminal rates(c)	3/33(9.1)	0/41(0.0)	3/38(7.9)	0/40(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P=0.6548			
Prevalence method(d)	P=0.7088			
Combined analysis (d)	P=0.7595			
Cochran-Amitage test(e)	P=0.5019			
Fisher Exact test(e)		P=0.0297*	P=0.4997	P=0.1590

TABLE 10 NEOPLASTIC LESIONS INCIDENCE AND STATISTICAL ANALYSIS OF MALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF GLYOXAL(CONTINUED)

Group Name	Control	333ppm	1000ppm	3000ppm
SITE : ALL SITE				
TUMOR : malignant lymphoma				
Tumor rate				
Overall rates(a)	7/50(14.0)	12/50(24.0)	5/50(10.0)	3/50(6.0)
Adjusted rates(b)	15.15	17.07	13.16	5.00
Terminal rates(c)	5/33(15.2)	7/41(17.1)	5/38(13.2)	2/40(5.0)
Statistical analysis				
Peto test				
Standard method(d)	P=0.8988			
Prevalence method(d)	P=0.9599			
Combined analysis (d)	P=0.9864			
Cochran-Amitage test(e)	P=0.0454*			
Fisher Exact test(e)		P=0.1542	P=0.3800	P=0.1590
SITE : ALL SITE				
TUMOR : hemangiosarcoma				
Tumor rate				
Overall rates(a)	5/50(10.0)	7/50(14.0)	3/50(6.0)	1/50(2.0)
Adjusted rates(b)	5.26	13.04	5.26	2.50
Terminal rates(c)	1/33(3.0)	4/41(9.8)	2/38(5.3)	1/40(2.5)
Statistical analysis				
Peto test				
Standard method(d)	P=0.9627			
Prevalence method(d)	P=0.9164			
Combined analysis (d)	P=0.9850			
Cochran-Amitage test(e)	P=0.0438*			
Fisher Exact test(e)		P=0.3800	P=0.3576	P=0.1022

(a):Number of tumor-bearing animals/number of animals examined at the site.
(b):Kaplan-Meire estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.
(c):Observed tumor incidence at terminal kill.
(d):Beneath the control incidence are the P-values associated with the trend test.
Standard method :Death analysis
Prevalence method :Incidental tumor test
Combined analysis :Death analysis + Incidental tumor test
(e):The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.
?: The conditional probabilities of the largest and smallest possible out comes can not be estimated or this P-value is beyond the estimated P-value.
------:There is no data which should be statistical analysis.
Significant difference; *:P≦0.05 **:P≦0.01

TABLE 11 NEOPLASTIC LESIONS INCIDENCE AND STATISTICAL ANALYSIS OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF GLYOXAL

Group Name	Control	1500ppm	3000ppm	6000ppm
SITE : lymph node				
TUMOR : malignant lymphoma				
Tumor rate				
Overall rates(a)	18/50(36.0)	23/50(46.0)	19/50(38.0)	10/49(20.4)
Adjusted rates(b)	30.00	34.48	18.75	20.51
Terminal rates(c)	9/30(30.0)	10/29(34.5)	6/32(18.8)	8/39(20.5)
Statistical analysis				
Peto test				
Standard method(d)	P=0.9902			
Prevalence method(d)	P=0.8864			
Combined analysis (d)	P=0.9947			
Cochran-Amitage test(e)	P=0.0370*			
Fisher Exact test(e)		P=0.2085	P=0.4991	P=0.0666
SITE : liver				
TUMOR : hepatocellular adenoma, hepatocellular carcinoma				
Tumor rate				
Overall rates(a)	3/50(6.0)	2/50(4.0)	0/50(0.0)	0/49(0.0)
Adjusted rates(b)	6.82	6.90	0.0	0.0
Terminal rates(c)	2/30(6.7)	2/29(6.9)	0/32(0.0)	0/39(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P=------			
Prevalence method(d)	P=0.9913			
Combined analysis (d)	P=------			
Cochran-Amitage test(e)	P=0.0397*			
Fisher Exact test(e)		P=0.4999	P=0.1212	P=0.1250
SITE : pituitary gland				
TUMOR : adenoma				
Tumor rate				
Overall rates(a)	6/49(12.2)	4/49(8.2)	4/50(8.0)	0/49(0.0)
Adjusted rates(b)	16.67	13.79	11.43	0.0
Terminal rates(c)	5/30(16.7)	4/29(13.8)	3/32(9.4)	0/39(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P=0.9250 ?			
Prevalence method(d)	P=0.9942			
Combined analysis (d)	P=0.9974			
Cochran-Amitage test(e)	P=0.0186*			
Fisher Exact test(e)		P=0.3704	P=0.3575	P=0.0133*
SITE : pituitary gland				
TUMOR : adenoma, adenocarcinoma				
Tumor rate				
Overall rates(a)	6/49(12.2)	4/49(8.2)	5/50(10.0)	0/49(0.0)
Adjusted rates(b)	16.67	13.79	14.29	0.0
Terminal rates(c)	5/30(16.7)	4/29(13.8)	3/32(9.4)	0/39(0.0)
Statistical analysis				
Peto test				
Standard method(d)	P=0.9250 ?			
Prevalence method(d)	P=0.9919			
Combined analysis (d)	P=0.9962			
Cochran-Amitage test(e)	P=0.0255*			
Fisher Exact test(e)		P=0.3704	P=0.4859	P=0.0133*

TABLE 11 NEOPLASTIC LESIONS INCIDENCE AND STATISTICAL ANALYSIS OF FEMALE MICE IN THE 2-YEAR DRINKING WATER STUDY OF GLYOXAL(CONTINUED)

Group Name	Control	1500ppm	3000ppm	6000ppm
SITE : ALL SITE				
TUMOR : malignant lymphoma				
Tumor rate				
Overall rates(a)	18/50(36.0)	24/50(48.0)	20/50(40.0)	10/49(20.4)
Adjusted rates(b)	30.00	37.93	21.88	20.51
Terminal rates(c)	9/30(30.0)	11/29(37.9)	7/32(21.9)	8/39(20.5)
Statistical analysis				
Peto test				
Standard method(d)	P=0.9902			
Prevalence method(d)	P=0.9020			
Combined analysis (d)	P=0.9955			
Cochran-Amitage test(e)	P=0.0340*			
Fisher Exact test(e)		P=0.1558	P=0.4103	P=0.0666

(a):Number of tumor-bearing animals/number of animals examined at the site.
(b):Kaplan-Meire estimated tumor incidence at the end of the study after adjusting for intercurrent mortality.
(c):Observed tumor incidence at terminal kill.
(d):Beneath the control incidence are the P-values associated with the trend test.
Standard method :Death analysis
Prevalence method :Incidental tumor test
Combined analysis :Death analysis + Incidental tumor test
(e):The Cochran-Armitage and Fisher exact test compare directly the overall incidence rates.
?: The conditional probabilities of the largest and smallest possible out comes can not be estimated or this P-value is beyond the estimated P-value.
------:There is no data which should be statistical analysis.
Significant difference; *:P≦0.05 **:P≦0.01

TABLE 12 NUMBER OF MICE WITH SELECTED NON-NEOPLASTIC LESIONS IN THE 2-YEAR DRINKING WATER STUDY OF GLYOXAL

Group name		Male				Female			
		Control	333ppm	1000ppm	3000ppm	Control	1500ppm	3000ppm	6000ppm
<all animal No.>(sacrificed animal No.)		<50> (33)	<50> (41)	<50> (38)	<50> (40)	<50> (30)	<50> (29)	<50> (32)	<49> (39)
Nasal cavity		23 (18)	28 (22)	35* (28)	35* (30)	8 (6)	3 (3)	3 (2)	2 (2)
eosinophilic change	+	22 (17)	28 (22)	35 (28)	35 (30)	8 (6)	3 (3)	3 (2)	2 (2)
:olfactory epithelium	2+	1 (1)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	3+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	4+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
respiratory metaplasia		7 (7)	5 (4)	18* (15)	17* (16)	8 (4)	4 (3)	1* (1)	2 (2)
:olfactory epithelium	+	7 (7)	5 (4)	18 (15)	17 (16)	8 (4)	4 (3)	1 (1)	2 (2)
	2+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	3+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	4+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
respiratory metaplasia		22 (16)	18 (18)	32 (26)	23 (19)	7 (7)	8 (6)	24* (18)*	37* (32)**
:gland	+	22 (16)	18 (18)	32 (26)	23 (19)	7 (7)	8 (6)	24 (18)	37 (32)
	2+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	3+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	4+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Liver		27 (26)	34 (34)	33 (32)	39* (38)	23 (23)	18 (18)	23 (23)	28 (28)
granulation	+	27 (26)	34 (34)	33 (32)	39 (38)	23 (23)	18 (18)	22 (22)	27 (27)
	2+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)	1 (1)
	3+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	4+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
Kidney		13 (12)	37** (35)**	33** (28)**	32** (30)**	2 (2)	7 (3)	3 (1)	1 (1)
basophilic change	+	13 (12)	37 (35)	33 (28)	32 (30)	2 (2)	6 (3)	3 (1)	1 (1)
	2+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (0)	0 (0)	0 (0)
	3+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	4+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade +:Slight 2+:Moderate 3+:Marked 4+:Severe
< >:Number of animals examined at the site
( ):Sacrificed animals

TABLE 12 NUMBER OF MICE WITH SELECTED NON-NEOPLASTIC LESIONS IN THE 2-YEAR DRINKING WATER STUDY OF GLYOXAL(Continued)

Group name		Male				Female			
		Control	333ppm	1000ppm	3000ppm	Control	1500ppm	3000ppm	6000ppm
<all animal No.>(sacrificed animal No.)		<50> (33)	<50> (41)	<50> (38)	<50> (40)	<50> (30)	<50> (29)	<50> (32)	<49> (39)
Kidney									
mineralization		27 (24)	36 (32)	26 (19)	17 (15)**	0 (0)	0 (0)	1 (1)	0 (0)
:cortex	+	27 (24)	36 (32)	26 (19)	17 (15)	0 (0)	0 (0)	0 (0)	0 (0)
	2+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)	0 (0)
	3+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	4+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
mineralization		2 (2)	5 (4)	3 (2)	0 (0)	7 (6)	0* (0)*	0* (0)*	0* (0)*
:papillary	+	2 (2)	5 (4)	3 (2)	0 (0)	7 (6)	0 (0)	0 (0)	0 (0)
	2+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	3+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	4+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
desquamation		0 (0)	1 (1)	0 (0)	8** (8)*	4 (4)	20** (11)*	12 (9)	21** (15)*
:pelvis	+	0 (0)	1 (1)	0 (0)	8 (8)	4 (4)	14 (5)	12 (9)	21 (15)
	2+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	6 (6)	0 (0)	0 (0)
	3+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	4+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
hydronephrosis		3 (0)	3 (2)	3 (1)	5 (3)	0 (0)	3 (2)	8* (7)*	6* (4)
	+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (1)	2 (1)	1 (1)
	2+	1 (0)	1 (1)	1 (1)	2 (2)	0 (0)	2 (1)	6 (6)	5 (3)
	3+	2 (0)	2 (1)	2 (0)	3 (1)	0 (0)	0 (0)	0 (0)	0 (0)
	4+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
papillary necrosis		2 (2)	0 (0)	2 (1)	4 (4)	1 (0)	1 (1)	7 (6)*	8* (8)*
	+	2 (2)	0 (0)	2 (1)	4 (4)	1 (0)	1 (1)	7 (6)	8 (8)
	2+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	3+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	4+	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Grade +:Slight 2+:Moderate 3+:Marked 4+:Severe
< >:Number of animals examined at the site
( ):Sacrificed animals

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

Group		Male				Female			
		Control	333ppm	1000ppm	3000ppm	Control	1500ppm	3000ppm	6000ppm
Number of dead or moribund animals		17	9	12	10	20	21	18	10
No microscopical confirmation		2	0	0	0	2	0	0	0
Cardiovascular lesion		0	0	0	1	1	0	0	0
Reproductive system lesion		0	0	0	0	1	1	0	0
Renal lesion		0	0	0	1	0	0	0	0
Body cavity lesion		0	0	0	0	0	1	0	0
Thrombosis		0	0	0	0	0	0	0	1
Hydronephrosis		2	1	2	2	0	0	0	0
Tumor death	leukemia	2	5	0	1	8	13	13	2
	subcutis	0	0	1	0	1	0	0	0
	lymph node	0	0	0	0	1	0	0	0
	lung	0	1	3	0	0	0	0	0
	bone marrow	0	0	1	0	0	0	0	0
	spleen	3	0	0	0	0	0	0	0
	small intestine	1	0	0	0	0	0	0	0
	liver	7	2	4	4	2	0	0	2
	pituitary	0	0	0	0	1	0	0	0
	uterus	-	-	-	-	2	5	5	3
	bone	0	0	0	1	0	0	0	0
	peritoneum	0	0	0	0	1	0	0	0
	mediastinum	0	0	1	0	0	0	0	0