1,4 - ジクロロ - 2 - ニトロベンゼンのマウスを用いた
経口投与による 2 週間毒性試験(混餌試験)報告書

試験番号：０２９９

APPENDIX

APPENDIXES

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 1-1	1-4	1-7	2-4	2-7
DEATH	Control	0	0	0	0	0
	625 ppm	0	0	0	0	0
	1250 ppm	0	0	0	0	0
	2500 ppm	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	1	2
LOCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0
	625 ppm	0	0	0	0	0
	1250 ppm	0	0	0	0	0
	2500 ppm	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	0	1
PRONE	Control	0	0	0	0	0
	625 ppm	0	0	0	0	0
	1250 ppm	0	0	0	0	0
	2500 ppm	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	0	1
PILOERECTION	Control	0	0	0	0	0
	625 ppm	0	0	0	0	0
	1250 ppm	0	0	0	0	0
	2500 ppm	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	9	8
YELLOW URINE	Control	0	0	0	0	0
	625 ppm	0	0	0	0	0
	1250 ppm	4	5	10	10	10
	2500 ppm	6	6	10	10	10
	5000 ppm	10	10	10	10	10
	10000 ppm	10	10	10	9	8
SMALL STOOL	Control	0	0	0	0	0
	625 ppm	0	0	0	0	0
	1250 ppm	0	0	0	0	0
	2500 ppm	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	0	2

Clinical sign	Group Name	Administration Week-day 1-1	1-4	1-7	2-4	2-7
OLIGO-STOOL	Control	0	0	0	0	0
	625 ppm	0	0	0	0	0
	1250 ppm	0	0	0	0	0
	2500 ppm	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	0	2

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day 1-1	1-4	1-7	2-4	2-7
DEATH	Control	0	0	0	0	0
	625 ppm	0	0	0	0	0
	1250 ppm	0	0	0	0	0
	2500 ppm	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	0	6
LOCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0
	625 ppm	0	0	0	0	0
	1250 ppm	0	0	0	0	0
	2500 ppm	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	2	0
HUNCHBACK POSITION	Control	0	0	0	0	0
	625 ppm	0	0	0	0	0
	1250 ppm	0	0	0	0	0
	2500 ppm	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	0	3
PILOERECTION	Control	0	0	0	0	0
	625 ppm	0	0	0	0	0
	1250 ppm	0	0	0	0	0
	2500 ppm	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	10	4
IRREGULAR BREATHING	Control	0	0	0	0	0
	625 ppm	0	0	0	0	0
	1250 ppm	0	0	0	0	0
	2500 ppm	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	1	0
ABNORMAL RESPIRATION	Control	0	0	0	0	0
	625 ppm	0	0	0	0	0
	1250 ppm	0	0	0	0	0
	2500 ppm	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	1	0

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day 1-1	1-4	1-7	2-4	2-7
YELLOW URINE	Control	0	0	0	0	0
	625 ppm	1	4	4	1	1
	1250 ppm	3	3	5	7	10
	2500 ppm	3	10	10	10	10
	5000 ppm	9	10	10	10	10
	10000 ppm	10	10	10	10	4
SMALL STOOL	Control	0	0	0	0	0
	625 ppm	0	0	0	0	0
	1250 ppm	0	0	0	0	0
	2500 ppm	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	0	1
OLIGO-STOOL	Control	0	0	0	0	0
	625 ppm	0	0	0	0	0
	1250 ppm	0	0	0	0	0
	2500 ppm	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	0	1

APPENDIX B 1

BODY WEIGHT CHANGES :SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-1	1-4	1-7	2-4	2-7
Control	20.0± 0.8	22.4± 0.7	20.3± 1.0	23.3± 0.7	23.7± 0.9	24.1± 1.2
625 ppm	20.0± 0.8	22.5± 0.4	20.6± 0.8	23.3± 1.0	23.5± 0.9	24.3± 0.6
1250 ppm	20.0± 0.8	22.2± 1.0	20.1± 0.9	23.6± 1.0	23.7± 0.7	24.3± 0.8
2500 ppm	20.1± 0.7	21.3± 1.8	20.6± 1.1	23.3± 1.1	23.8± 1.1	24.4± 1.3
5000 ppm	20.1± 0.8	19.5± 0.9**	19.8± 2.0	21.7± 0.8**	22.7± 0.5*	23.5± 0.4
10000 ppm	20.0± 0.8	18.2± 0.7**	16.7± 1.2**	16.1± 0.9**	14.6± 0.5**	13.7± 0.6**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX B 2

BODY WEIGHT CHANGES : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-1	1-4	1-7	2-4	2-7
Control	17.3± 0.6	17.7± 0.6	17.2± 0.7	18.6± 0.5	18.9± 0.7	19.3± 0.5
625 ppm	17.3± 0.6	17.6± 0.7	17.3± 0.5	18.5± 0.7	18.6± 0.6	19.0± 0.6
1250 ppm	17.4± 0.5	17.6± 0.5	17.3± 0.8	18.8± 0.8	19.0± 0.6	19.2± 0.8
2500 ppm	17.3± 0.6	16.8± 0.7*	17.2± 0.9	18.0± 1.0	18.7± 0.8	19.1± 0.7
5000 ppm	17.4± 0.5	16.4± 0.6**	16.5± 1.0	18.4± 0.8	19.0± 0.8	19.7± 1.0
10000 ppm	17.3± 0.6	15.2± 0.5**	14.4± 0.4**	13.8± 0.6**	12.0± 0.7**	11.2± 0.5**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX C 1

FOOD CONSUMPTION CHANGES : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-4(4)	1-7(3)	2-4(4)	2-7(3)
Control	3.7± 0.5	5.3± 0.8	4.2± 0.4	3.9± 0.5
625 ppm	3.9± 0.3	5.2± 1.1	4.3± 0.7	4.1± 0.7
1250 ppm	3.6± 0.2	5.9± 0.8	4.4± 0.6	4.1± 0.6
2500 ppm	3.6± 0.2	5.5± 0.6	4.3± 0.4	4.3± 0.5
5000 ppm	3.3± 0.4*	5.0± 0.5	4.5± 0.6	3.9± 0.4
10000 ppm	2.6± 0.6**	2.7± 0.4**	1.7± 0.6**	1.8± 1.2**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX C 2

FOOD CONSUMPTION CHANGES : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-4(4)	1-7(3)	2-4(4)	2-7(3)
Control	3.6± 0.4	4.5± 0.6	4.3± 0.5	3.7± 0.5
625 ppm	3.4± 0.2	4.0± 0.4	3.8± 0.3	3.5± 0.4
1250 ppm	3.3± 0.2	4.2± 0.9	3.8± 0.7	3.4± 0.5
2500 ppm	3.1± 0.5*	3.9± 0.7	3.8± 0.4	3.3± 0.4
5000 ppm	3.4± 0.4	5.1± 1.3	4.1± 0.7	3.7± 0.6
10000 ppm	2.7± 0.4**	3.0± 0.6**	2.3± 0.9**	1.4± 0.4**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX D 1

CHEMICAL INTAKE CHANGES : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0299
ANIMAL : MOUSE BDF_1
UNIT : g/kgBW/day
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week			
	1(1-4)	1(1-7)	2(2-4)	2(2-7)
Control	0.000	0.000	0.000	0.000
625ppm	0.118	0.139	0.114	0.105
1250ppm	0.224	0.313	0.232	0.211
2500ppm	0.437	0.590	0.452	0.441
5000ppm	0.833	1.152	1.023	0.830
10000ppm	1.557	1.677	1.164	1.314

APPENDIX D 2

CHEMICAL INTAKE CHANGES : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0299
ANIMAL : MOUSE BDF_1
UNIT : g/kgBW/day
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week			
	1(1-4)	1(1-7)	2(2-4)	2(2-7)
Control	0.000	0.000	0.000	0.000
625ppm	0.123	0.135	0.128	0.115
1250ppm	0.238	0.279	0.250	0.221
2500ppm	0.451	0.542	0.508	0.432
5000ppm	1.030	1.386	1.079	0.939
10000ppm	1.875	2.174	1.917	1.250

APPENDIX E 1

HEMATOLOGY : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	9	10.31± 0.30	15.9± 0.5	49.3± 0.9	47.8± 1.3	15.4± 0.3	32.3± 0.8	1090± 87
625 ppm	10	10.42± 0.34	15.9± 0.4	50.0± 1.2	48.0± 0.5	15.2± 0.2	31.7± 0.4	1061± 72
1250 ppm	10	10.31± 0.27	15.7± 0.6	49.3± 1.4	47.8± 0.4	15.3± 0.2	31.9± 0.5	1080± 97
2500 ppm	10	9.77± 0.32	14.9± 0.5*	46.6± 1.9*	47.6± 0.8	15.3± 0.3	32.0± 0.4	1188± 86
5000 ppm	10	9.03± 0.33**	14.2± 0.4**	42.8± 2.0**	47.3± 1.1	15.7± 0.2	33.1± 0.6	1214± 149
10000 ppm	5	9.47± 0.37**	14.0± 0.5**	38.5± 1.3**	40.7± 0.6**	14.8± 0.1**	36.4± 0.4**	1713± 135**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	METHEMOGLOBIN %
Control	9	0.3± 0.0
625 ppm	10	0.3± 0.1
1250 ppm	10	0.2± 0.1
2500 ppm	10	0.3± 0.1
5000 ppm	10	0.6± 0.3
10000 ppm	5	-

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
Control	9	2.52± 1.09	0± 0	12± 5	1± 1	0± 0	3± 1	84± 7	0± 0
625 ppm	10	2.86± 0.71	0± 0	14± 6	2± 1	0± 0	2± 1	82± 6	0± 0
1250 ppm	10	2.85± 1.02	0± 1	9± 3	1± 1	0± 0	2± 1	87± 2	0± 0
2500 ppm	10	2.31± 0.98	1± 1	12± 4	1± 1	0± 0	2± 1	84± 4	0± 0
5000 ppm	10	2.45± 0.43	1± 1	16± 4	1± 2	0± 0	2± 0	80± 6	0± 0
10000 ppm	5	0.27± 0.04	3± 2	64± 10**	0± 0	0± 0	4± 2	29± 11**	0± 0

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX E 2

HEMATOLOGY : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$		HEMOGLOBIN g/dℓ		HEMATOCRIT %		MCV f ℓ		MCH p g		MCHC g/dℓ		PLATELET $10^3/\mu\ell$	
Control	10	10.18±	0.15	15.5±	0.4	47.9±	1.2	47.1±	0.5	15.3±	0.2	32.5±	0.2	970±	43
625 ppm	10	10.32±	0.38	16.0±	0.7	49.4±	2.1	47.8±	0.4	15.5±	0.2	32.3±	0.4	884±	87
1250 ppm	9	10.05±	0.26	15.4±	0.2	47.4±	1.5	47.2±	0.5	15.4±	0.2	32.6±	0.7	945±	40
2500 ppm	9	9.70±	0.32	15.0±	0.3	46.5±	0.9	48.0±	1.0	15.5±	0.3	32.3±	0.3	995±	86
5000 ppm	10	8.63±	0.44**	14.0±	0.5**	42.8±	1.9**	49.7±	0.7**	16.2±	0.3**	32.7±	0.7	1133±	39
10000 ppm	3	9.71±	0.51	14.5±	0.9	41.1±	2.6**	42.2±	0.4**	15.0±	0.2	35.5±	0.3**	1684±	227

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

Group Name	NO. of Animals	METHEMOGLOBIN %
Control	10	0.3± 0.0
625 ppm	10	0.3± 0.0
1250 ppm	9	0.3± 0.0
2500 ppm	9	0.2± 0.2
5000 ppm	10	0.7± 0.4
10000 ppm	3	-

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$		Differential WBC (%) N-BAND		N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHERS	
Control	10	2.66±	1.25	0±	0	12±	5	2±	1	0±	0	3±	1	82±	5	0±	0
625 ppm	10	3.48±	1.81	1±	1	10±	1	2±	1	0±	0	2±	0	85±	2	0±	0
1250 ppm	9	2.95±	0.77	0±	0	10±	1	3±	1	0±	0	2±	1	84±	2	0±	0
2500 ppm	9	4.15±	1.40	0±	1	11±	3	1±	1	0±	0	3±	1	85±	4	0±	0
5000 ppm	10	2.97±	0.70	1±	1	11±	1	1±	1	0±	0	2±	2	85±	3	0±	0
10000 ppm	3	0.96±	1.40	3±	1	75±	4	0±	1	0±	0	3±	2	19±	1**	0±	0

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX F 1

BIOCHEMISTRY : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	TOTAL PROTEIN g/dl	ALBUMIN g/dl	A/G RATIO	T-BILIRUBIN mg/dl	GLUCOSE mg/dl	T-CHOLESTEROL mg/dl	PHOSPHOLIPID mg/dl
Control	5	4.9± 0.1	2.7± 0.0	1.2± 0.0	0.22± 0.07	279± 17	91± 3	178± 19
625 ppm	4	4.9± 0.1	2.8± 0.1	1.3± 0.0	0.19± 0.02	285± 26	108± 1	211± 5
1250 ppm	5	4.8± 0.2	2.8± 0.1	1.4± 0.1	0.21± 0.02	269± 12	108± 6	206± 9
2500 ppm	5	5.0± 0.2	2.9± 0.1*	1.3± 0.1	0.23± 0.06	265± 21	135± 5*	237± 8**
5000 ppm	5	5.4± 0.2**	3.1± 0.1**	1.3± 0.0	0.23± 0.03	245± 24	159± 18**	263± 31**
10000 ppm	4	6.0± 0.1**	3.7± 0.1**	1.7± 0.1	0.36± 0.04**	139± 45**	142± 22**	193± 20

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	GOT IU/ℓ		GPT IU/ℓ		LDH IU/ℓ		G-GTP IU/ℓ		CPK IU/ℓ		UREA NITROGEN mg/dℓ		SODIUM mEq/ℓ	
Control	5	33±	4	19±	3	199±	83	3±	4	89±	44	19.3±	6.0	149±	1
625 ppm	4	34±	3	22±	2	182±	25	1±	1	74±	39	23.3±	7.1	150±	1
1250 ppm	5	34±	2	30±	2	216±	23	2±	3	87±	35	24.0±	4.0	150±	2
2500 ppm	5	34±	6	46±	15*	195±	30	2±	2	73±	31	23.9±	4.2	149±	2
5000 ppm	5	48±	10	95±	25**	295±	48	1±	1	113±	46	20.4±	3.8	151±	2
10000 ppm	4	109±	28**	96±	43**	624±	238**	8±	5	924±	692*	37.7±	7.0**	153±	3**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	POTASSIUM mEq／ℓ		CHLORIDE mEq／ℓ		CALCIUM mg／dℓ		INORGANIC PHOSPHORUS mg／dℓ	
Control	5	5.2±	0.4	119±	1	9.4±	0.3	9.1±	1.2
625 ppm	4	5.1±	0.4	118±	1	9.8±	0.1	8.8±	1.1
1250 ppm	5	5.0±	0.2	118±	2	9.6±	0.3	9.0±	0.8
2500 ppm	5	4.9±	0.5	118±	2	9.6±	0.4	8.8±	1.4
5000 ppm	5	5.2±	0.4	117±	2	10.1±	0.4**	10.0±	0.4
10000 ppm	4	5.9±	0.9	122±	3	9.5±	0.3	7.5±	2.6

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX F 2

BIOCHEMISTRY : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	TOTAL PROTEIN g/dℓ		ALBUMIN g/dℓ		A/G RATIO		T-BILIRUBIN mg/dℓ		GLUCOSE mg/dℓ		T-CHOLESTEROL mg/dℓ		PHOSPHOLIPID mg/dℓ	
Control	5	4.8±	0.1	2.9±	0.1	1.5±	0.0	0.22±	0.06	252±	12	74±	6	137±	9
625 ppm	5	4.9±	0.2	3.0±	0.2	1.6±	0.0	0.27±	0.14	244±	13	94±	6**	167±	6**
1250 ppm	5	4.7±	0.1	2.9±	0.1	1.7±	0.1	0.23±	0.08	241±	14	92±	6**	162±	17*
2500 ppm	5	4.9±	0.1	3.0±	0.0	1.6±	0.1	0.22±	0.02	229±	15*	106±	4**	189±	13**
5000 ppm	5	5.1±	0.1*	3.1±	0.1	1.5±	0.1	0.27±	0.06	236±	13	140±	10**	233±	17**
10000 ppm	3	5.5±	0.6*	3.8±	0.2	2.2±	0.3	0.50±	0.10**	156±	16**	112±	15**	161±	21

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	GOT IU/ℓ		GPT IU/ℓ		LDH IU/ℓ		G-GTP IU/ℓ		CPK IU/ℓ		UREA NITROGEN mg/dℓ		SODIUM mEq/ℓ	
Control	5	40±	6	19±	4	204±	75	1±	1	66±	37	17.8±	2.5	148±	1
625 ppm	5	38±	4	20±	2	192±	32	1±	1	75±	18	18.0±	0.7	149±	2
1250 ppm	5	42±	3	24±	2	200±	41	1±	1	72±	25	17.1±	2.3	148±	1
2500 ppm	5	40±	3	33±	6	187±	30	0±	0	76±	17	20.1±	4.8	148±	2
5000 ppm	5	70±	16*	122±	36**	254±	110	3±	2	113±	69	16.3±	1.7	149±	1
10000 ppm	3	133±	98*	140±	128**	725±	658	19±	8*	519±	679	45.9±	16.8	152±	1**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dℓ	INORGANIC PHOSPHORUS mg/dℓ
Control	5	5.1± 0.6	119± 2	9.2± 0.3	8.0± 1.0
625 ppm	5	4.8± 0.6	118± 2	9.5± 0.4	8.0± 1.0
1250 ppm	5	4.3± 0.5	118± 1	9.2± 0.1	7.8± 0.6
2500 ppm	5	4.3± 0.4	117± 1	9.4± 0.2	7.8± 0.7
5000 ppm	5	4.6± 0.7	116± 2	9.3± 0.5	8.6± 2.0
10000 ppm	3	5.7± 0.3	117± 3	8.9± 0.9	7.5± 2.2

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX G 1

GROSS FINDINGS : SUMMARY, MOUSE : MALE ALL ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
ALL ANIMALS (0- 2W)

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	625 ppm 10 (%)	1250 ppm 10 (%)	2500 ppm 10 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
spleen	black zone		0 (0)	1 (10)	0 (0)	0 (0)
kidney	white zone		0 (0)	0 (0)	1 (10)	0 (0)
	hydronephrosis		0 (0)	1 (10)	0 (0)	0 (0)

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
ALL ANIMALS (0- 2W)

Organ	Findings	Group Name / NO. of Animals	5000 ppm 10 (%)	10000 ppm 10 (%)
thymus	atrophic		0 (0)	10 (100)
spleen	black zone		0 (0)	0 (0)
kidney	white zone		0 (0)	0 (0)
	hydronephrosis		0 (0)	0 (0)

APPENDIX G 2

GROSS FINDINGS : SUMMARY, MOUSE : FEMALE ALL ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
ALL ANIMALS (0- 2W)

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	625 ppm 10 (%)	1250 ppm 10 (%)	2500 ppm 10 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
spleen	black zone		0 (0)	0 (0)	1 (10)	2 (20)
kidney	enlarged		0 (0)	0 (0)	0 (0)	1 (10)

Organ	Findings	Group Name / NO. of Animals	5000 ppm 10 (%)	10000 ppm 10 (%)
thymus	atrophic		0 (0)	10 (100)
spleen	black zone		0 (0)	0 (0)
kidney	enlarged		0 (0)	0 (0)

APPENDIX G 3

GROSS FINDINGS : SUMMARY, MOUSE : MALE

DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name	Control	625 ppm	1250 ppm	2500 ppm
		NO. of Animals	0 (%)	0 (%)	0 (%)	0 (%)
thymus	atrophic		- (-)	- (-)	- (-)	- (-)

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name	5000 ppm	10000 ppm
		NO. of Animals	0 (%)	2 (%)
thymus	atrophic		- (-)	2 (100)

APPENDIX G 4

GROSS FINDINGS : SUMMARY, MOUSE : FEMALE

DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name / NO. of Animals	Control 0 (%)	625 ppm 0 (%)	1250 ppm 0 (%)	2500 ppm 0 (%)
thymus	atrophic		- (-)	- (-)	- (-)	- (-)

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name	5000 ppm	10000 ppm
		NO. of Animals	0 (%)	6 (%)
thymus	atrophic		- (-)	6 (100)

APPENDIX G 5

GROSS FINDINGS : SUMMARY, MOUSE : MALE

SACRIFICED ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	625 ppm 10 (%)	1250 ppm 10 (%)	2500 ppm 10 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
spleen	black zone		0 (0)	1 (10)	0 (0)	0 (0)
kidney	white zone		0 (0)	0 (0)	1 (10)	0 (0)
	hydronephrosis		0 (0)	1 (10)	0 (0)	0 (0)

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name / NO. of Animals	5000 ppm 10 (%)	10000 ppm 8 (%)
thymus	atrophic		0 (0)	8 (100)
spleen	black zone		0 (0)	0 (0)
kidney	white zone		0 (0)	0 (0)
	hydronephrosis		0 (0)	0 (0)

APPENDIX G 6

GROSS FINDINGS : SUMMARY, MOUSE : FEMALE

SACRIFICED ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	625 ppm 10 (%)	1250 ppm 10 (%)	2500 ppm 10 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
spleen	black zone		0 (0)	0 (0)	1 (10)	2 (20)
kidney	enlarged		0 (0)	0 (0)	0 (0)	1 (10)

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name NO. of Animals	5000 ppm 10 (%)	10000 ppm 4 (%)
thymus	atrophic		0 (0)	4 (100)
spleen	black zone		0 (0)	0 (0)
kidney	enlarged		0 (0)	0 (0)

APPENDIX H 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	5	24.0± 1.1	0.054± 0.003	0.008± 0.003	0.186± 0.014	0.120± 0.007	0.141± 0.017
625 ppm	5	24.4± 0.5	0.051± 0.009	0.008± 0.002	0.181± 0.018	0.130± 0.009	0.141± 0.012
1250 ppm	5	23.9± 0.8	0.050± 0.008	0.008± 0.002	0.160± 0.030	0.124± 0.011	0.142± 0.016
2500 ppm	4	25.3± 1.0	0.054± 0.005	0.008± 0.002	0.167± 0.027	0.134± 0.010	0.150± 0.005
5000 ppm	4	23.3± 0.3	0.051± 0.010	0.009± 0.001	0.151± 0.049	0.125± 0.011	0.142± 0.012
10000 ppm	5	13.8± 0.5**	0.004± 0.001**	0.005± 0.002*	0.040± 0.008**	0.081± 0.007**	0.100± 0.024**

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.352± 0.025	0.050± 0.006	1.180± 0.107	0.427± 0.011
625 ppm	5	0.372± 0.030	0.051± 0.004	1.331± 0.081	0.425± 0.017
1250 ppm	5	0.379± 0.026	0.054± 0.010	1.421± 0.084**	0.421± 0.012
2500 ppm	4	0.393± 0.029	0.085± 0.021	1.709± 0.143**	0.427± 0.014
5000 ppm	4	0.372± 0.014	0.130± 0.010*	1.908± 0.076**	0.448± 0.023
10000 ppm	5	0.222± 0.019**	0.012± 0.003	0.994± 0.056*	0.380± 0.017**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX H 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	5	19.3± 0.6	0.069± 0.005	0.009± 0.001	0.018± 0.004	0.103± 0.007	0.129± 0.020
625 ppm	5	19.0± 0.4	0.066± 0.010	0.010± 0.001	0.016± 0.005	0.092± 0.009	0.134± 0.015
1250 ppm	5	19.3± 0.6	0.066± 0.004	0.010± 0.002	0.016± 0.004	0.101± 0.005	0.132± 0.012
2500 ppm	5	19.4± 0.6	0.072± 0.013	0.010± 0.001	0.017± 0.004	0.101± 0.003	0.128± 0.011
5000 ppm	5	19.2± 1.0	0.067± 0.009	0.011± 0.004	0.016± 0.009	0.096± 0.005	0.126± 0.017
10000 ppm	4	11.2± 0.5**	0.008± 0.006**	0.006± 0.003	0.007± 0.001	0.086± 0.007**	0.118± 0.021

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.241± 0.013	0.052± 0.005	0.929± 0.077	0.442± 0.007
625 ppm	5	0.240± 0.017	0.055± 0.002	1.000± 0.054	0.425± 0.013
1250 ppm	5	0.252± 0.014	0.060± 0.015	1.064± 0.057*	0.429± 0.012
2500 ppm	5	0.258± 0.017	0.080± 0.011	1.231± 0.100**	0.423± 0.020
5000 ppm	5	0.248± 0.010	0.133± 0.018**	1.444± 0.044**	0.421± 0.016
10000 ppm	4	0.184± 0.008**	0.016± 0.003	0.802± 0.042*	0.395± 0.013**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX I 1

ORGAN WEIGHT, RELATIVE : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	5	24.0± 1.1	0.226± 0.014	0.035± 0.012	0.776± 0.066	0.499± 0.019	0.592± 0.084
625 ppm	5	24.4± 0.5	0.207± 0.035	0.031± 0.010	0.743± 0.067	0.532± 0.044	0.579± 0.050
1250 ppm	5	23.9± 0.8	0.208± 0.037	0.032± 0.008	0.666± 0.113	0.519± 0.048	0.595± 0.069
2500 ppm	4	25.3± 1.0	0.213± 0.020	0.032± 0.005	0.659± 0.090	0.528± 0.039	0.595± 0.023
5000 ppm	4	23.3± 0.3	0.218± 0.043	0.040± 0.004	0.647± 0.215	0.534± 0.044	0.610± 0.047
10000 ppm	5	13.8± 0.5**	0.031± 0.010**	0.035± 0.013	0.291± 0.059**	0.587± 0.063	0.729± 0.179

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	1.471± 0.080	0.208± 0.020	4.929± 0.461	1.782± 0.048
625 ppm	5	1.525± 0.121	0.207± 0.017	5.454± 0.263	1.744± 0.092
1250 ppm	5	1.583± 0.103	0.227± 0.048	5.945± 0.365**	1.761± 0.067
2500 ppm	4	1.554± 0.080	0.335± 0.075**	6.758± 0.539**	1.688± 0.056
5000 ppm	4	1.596± 0.070	0.557± 0.042**	8.185± 0.231**	1.923± 0.119
10000 ppm	5	1.618± 0.175	0.086± 0.026**	7.235± 0.562**	2.766± 0.190**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX I 2

ORGAN WEIGHT, RELATIVE : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	5	19.3± 0.6	0.356± 0.025	0.049± 0.006	0.093± 0.025	0.532± 0.037	0.666± 0.103
625 ppm	5	19.0± 0.4	0.348± 0.047	0.053± 0.008	0.083± 0.028	0.488± 0.052	0.704± 0.079
1250 ppm	5	19.3± 0.6	0.345± 0.027	0.050± 0.010	0.083± 0.020	0.527± 0.037	0.685± 0.080
2500 ppm	5	19.4± 0.6	0.371± 0.065	0.051± 0.005	0.089± 0.023	0.520± 0.010	0.663± 0.052
5000 ppm	5	19.2± 1.0	0.348± 0.057	0.057± 0.019	0.084± 0.049	0.502± 0.019	0.657± 0.103
10000 ppm	4	11.2± 0.5**	0.069± 0.048**	0.052± 0.023	0.063± 0.005	0.771± 0.103	1.059± 0.235**

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	1.249± 0.070	0.271± 0.025	4.804± 0.340	2.285± 0.049
625 ppm	5	1.265± 0.086	0.291± 0.010	5.270± 0.289	2.241± 0.051
1250 ppm	5	1.310± 0.097	0.312± 0.087	5.526± 0.371**	2.223± 0.037
2500 ppm	5	1.332± 0.056	0.412± 0.059	6.354± 0.410**	2.189± 0.148
5000 ppm	5	1.291± 0.070	0.689± 0.062**	7.520± 0.244**	2.193± 0.069
10000 ppm	4	1.652± 0.124**	0.138± 0.022	7.177± 0.175**	3.537± 0.093**

Significant difference : * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX J 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : MALE : ALL ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0- 2W)

Organ	Findings	Group Name	Control				625 ppm				1250 ppm				2500 ppm			
		No. of Animals on Study	2				2				2				2			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
{Respiratory system}																		
lung			< 2>				< 2>				< 2>				< 2>			
	congestion		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}																		
thymus			< 2>				< 2>				< 2>				< 2>			
	atrophy		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			< 2>				< 2>				< 2>				< 2>			
	atrophy		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	deposit of melanin		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	extramedullary hematopoiesis		0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Digestive system}																		
stomach			< 2>				< 2>				< 2>				< 2>			
	erosion:forestomach		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	5000 ppm				10000 ppm			
		No. of Animals on Study	2				3			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
lung			< 2>				< 3>			
	congestion		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(33)	(0)	(0)	(0)
{Hematopoietic system}										
thymus			< 2>				< 3>			
	atrophy		0	0	0	0	0	0	3	0
			(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)
spleen			< 2>				< 3>			
	atrophy		0	0	0	0	0	3	0	0
			(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
	deposit of melanin		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	extramedullary hematopoiesis		0	2	0	0	0	0	0	0
			(0)	(100)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}										
stomach			< 2>				< 3>			
	erosion:forestomach		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(67)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	Control				625 ppm				1250 ppm				2500 ppm			
		No. of Animals on Study	2				2				2				2			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
(Digestive system)																		
stomach			< 2>				< 2>				< 2>				< 2>			
	hyperplasia:forestomach		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
liver			< 2>				< 2>				< 2>				< 2>			
	increase in mitosis		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
	granulation		2	0	0	0	1	0	0	0	2	0	0	0	1	0	0	0
			(100)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
	hepatocellular hypertrophy:central		0	0	0	0	2	0	0	0	2	0	0	0	0	2	0	0
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
(Reproductive system)																		
testis			< 2>				< 2>				< 2>				< 2>			
	germ cell necrosis		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
epididymis			< 2>				< 2>				< 2>				< 2>			
	spermatogenic granuloma		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	5000 ppm				10000 ppm			
		No. of Animals on Study	2				3			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
stomach			< 2>				< 3>			
	hyperplasia:forestomach		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(33)	(0)	(0)	(0)
liver			< 2>				< 3>			
	increase in mitosis		2	0	0	0	0	0	0	0
			(100)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hepatocellular hypertrophy:central		0	0	2	0	0	1	1	0
			(0)	(0)	(100)	(0)	(0)	(33)	(33)	(0)
{Reproductive system}										
testis			< 2>				< 3>			
	germ cell necrosis		2	0	0	0	0	1	1	0
			(100)	(0)	(0)	(0)	(0)	(33)	(33)	(0)
epididymis			< 2>				< 3>			
	spermatogenic granuloma		0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(33)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	Control				625 ppm				1250 ppm				2500 ppm			
		No. of Animals on Study	2				2				2				2			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Reproductive system}																		
epididymis			< 2>				< 2>				< 2>				< 2>			
	decreased:sperma		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	debris of spermatic elements		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	5000 ppm				10000 ppm			
		No. of Animals on Study	2				3			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Reproductive system}										
epididymis			< 2>				< 3>			
	decreased:sperma		1	1	0	0	1	1	0	0
			(50)	(50)	(0)	(0)	(33)	(33)	(0)	(0)
	debris of spermatic elements		2	0	0	0	0	0	0	0
			(100)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

APPENDIX J 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : FEMALE: ALL ANIMALS

(2-WEEK STUDY)

Organ	Findings	Group Name	Control				625 ppm				1250 ppm				2500 ppm			
		No. of Animals on Study	2				2				2				2			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Respiratory system)																		
lung			< 2>				< 2>				< 2>				< 2>			
	congestion		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
(Hematopoietic system)																		
thymus			< 2>				< 2>				< 2>				< 2>			
	atrophy		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			< 2>				< 2>				< 2>				< 2>			
	atrophy		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	extramedullary hematopoiesis		0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
(Digestive system)																		
stomach			< 2>				< 2>				< 2>				< 2>			
	erosion:forestomach		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	5000 ppm				10000 ppm			
		No. of Animals on Study	2				3			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
lung			< 2>				< 3>			
	congestion		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(33)	(0)	(0)	(0)
{Hematopoietic system}										
thymus			< 2>				< 3>			
	atrophy		0	0	0	0	0	0	3	0
			(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)
spleen			< 2>				< 3>			
	atrophy		0	0	0	0	0	3	0	0
			(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
	extramedullary hematopoiesis		0	2	0	0	0	0	0	0
			(0)	(100)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}										
stomach			< 2>				< 3>			
	erosion:forestomach		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(33)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	Control				625 ppm				1250 ppm				2500 ppm			
		No. of Animals on Study	2				2				2				2			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Digestive system)																		
stomach			< 2>				< 2>				< 2>				< 2>			
	hyperplasia:forestomach		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
liver			< 2>				< 2>				< 2>				< 2>			
	increase in mitosis		0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	granulation		2	0	0	0	2	0	0	0	2	0	0	0	2	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	hepatocellular hypertrophy:central		0	0	0	0	1	0	0	0	2	0	0	0	0	2	0	0
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
(Nervous system)																		
brain			< 2>				< 2>				< 2>				< 2>			
	hemorrhage		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	5000 ppm				10000 ppm			
		No. of Animals on Study	2				3			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Digestive system)										
stomach			< 2>				< 3>			
	hyperplasia:forestomach		2	0	0	0	1	0	0	0
			(100)	(0)	(0)	(0)	(33)	(0)	(0)	(0)
liver			< 2>				< 3>			
	increase in mitosis		2	0	0	0	0	0	0	0
			(100)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hepatocellular hypertrophy:central		0	0	2	0	0	1	2	0
			(0)	(0)	(100)	(0)	(0)	(33)	(67)	(0)
(Nervous system)										
brain			< 2>				< 3>			
	hemorrhage		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(33)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

APPENDIX J 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : MALE : DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name	Control				625 ppm				1250 ppm				2500 ppm			
		No. of Animals on Study	0				0				0				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Respiratory system)																		
lung			< 0>				< 0>				< 0>				< 0>			
	congestion		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
(Hematopoietic system)																		
thymus			< 0>				< 0>				< 0>				< 0>			
	atrophy		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
spleen			< 0>				< 0>				< 0>				< 0>			
	atrophy		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	5000 ppm				10000 ppm			
		No. of Animals on Study	0				1			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Respiratory system)										
lung			< 0>				< 1>			
	congestion		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
(Hematopoietic system)										
thymus			< 0>				< 1>			
	atrophy		-	-	-	-	0	0	1	0
			(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)
spleen			< 0>				< 1>			
	atrophy		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

APPENDIX J 4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : FEMALE: DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 0				625 ppm 0				1250 ppm 0				2500 ppm 0			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
(Respiratory system)																		
lung		< 0>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	congestion		(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
(Hematopoietic system)																		
thymus		< 0>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	atrophy		(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
spleen		< 0>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	atrophy		(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
(Digestive system)																		
liver		< 0>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	hepatocellular hypertrophy:central		(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	5000 ppm				10000 ppm			
		No. of Animals on Study	0				1			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
lung			< 0>				< 1>			
	congestion		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
{Hematopoietic system}										
thymus			< 0>				< 1>			
	atrophy		-	-	-	-	0	0	1	0
			(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)
spleen			< 0>				< 1>			
	atrophy		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
{Digestive system}										
liver			< 0>				< 1>			
	hepatocellular hypertrophy:central		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

APPENDIX J 5

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : MALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name	Control				625 ppm				1250 ppm				2500 ppm			
		No. of Animals on Study	2				2				2				2			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}																		
thymus			< 2>				< 2>				< 2>				< 2>			
	atrophy		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			< 2>				< 2>				< 2>				< 2>			
	atrophy		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	deposit of melanin		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	extramedullary hematopoiesis		0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Digestive system}																		
stomach			< 2>				< 2>				< 2>				< 2>			
	erosion:forestomach		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia:forestomach		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	5000 ppm				10000 ppm			
		No. of Animals on Study	2				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
thymus			< 2>				< 2>			
	atrophy		0	0	0	0	0	0	2	0
			(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)
spleen			< 2>				< 2>			
	atrophy		0	0	0	0	0	2	0	0
			(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
	deposit of melanin		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	extramedullary hematopoiesis		0	2	0	0	0	0	0	0
			(0)	(100)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}										
stomach			< 2>				< 2>			
	erosion:forestomach		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	hyperplasia:forestomach		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	Control				625 ppm				1250 ppm				2500 ppm			
		No. of Animals on Study	2				2				2				2			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
liver			< 2>				< 2>				< 2>				< 2>			
	increase in mitosis		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
	granulation		2	0	0	0	1	0	0	0	2	0	0	0	1	0	0	0
			(100)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
	hepatocellular hypertrophy:central		0	0	0	0	2	0	0	0	2	0	0	0	0	2	0	0
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
{Reproductive system}																		
testis			< 2>				< 2>				< 2>				< 2>			
	germ cell necrosis		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
epididymis			< 2>				< 2>				< 2>				< 2>			
	spermatogenic granuloma		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	decreased:sperma		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	5000 ppm				10000 ppm			
		No. of Animals on Study	2				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]										
liver			< 2>				< 2>			
	increase in mitosis		2	0	0	0	0	0	0	0
			(100)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hepatocellular hypertrophy:central		0	0	2	0	0	1	1	0
			(0)	(0)	(100)	(0)	(0)	(50)	(50)	(0)
[Reproductive system]										
testis			< 2>				< 2>			
	germ cell necrosis		2	0	0	0	0	1	1	0
			(100)	(0)	(0)	(0)	(0)	(50)	(50)	(0)
epididymis			< 2>				< 2>			
	spermatogenic granuloma		0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(50)	(0)	(0)
	decreased:sperma		1	1	0	0	1	1	0	0
			(50)	(50)	(0)	(0)	(50)	(50)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	Control				625 ppm				1250 ppm				2500 ppm			
		No. of Animals on Study	2				2				2				2			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Reproductive system)																		
epididymis			< 2>				< 2>				< 2>				< 2>			
	debris of spermatic elements		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	5000 ppm				10000 ppm			
		No. of Animals on Study	2				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Reproductive system}										
epididymis				< 2>				< 2>		
	debris of spermatic elements		2	0	0	0	0	0	0	0
			(100)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

APPENDIX J 6

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : FEMALE: SACRIFICED ANIMALS

(2-WEEK STUDY)

Organ	Findings	Group Name	Control				625 ppm				1250 ppm				2500 ppm			
		No. of Animals on Study	2				2				2				2			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}																		
thymus			< 2>				< 2>				< 2>				< 2>			
	atrophy		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			< 2>				< 2>				< 2>				< 2>			
	atrophy		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	extramedullary hematopoiesis		0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Digestive system}																		
stomach			< 2>				< 2>				< 2>				< 2>			
	erosion:forestomach		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia:forestomach		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
liver			< 2>				< 2>				< 2>				< 2>			
	increase in mitosis		0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	5000 ppm				10000 ppm			
		No. of Animals on Study	2				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
thymus			< 2>				< 2>			
	atrophy		0	0	0	0	0	0	2	0
			(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)
spleen			< 2>				< 2>			
	atrophy		0	0	0	0	0	2	0	0
			(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
	extramedullary hematopoiesis		0	2	0	0	0	0	0	0
			(0)	(100)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}										
stomach			< 2>				< 2>			
	erosion:forestomach		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
	hyperplasia:forestomach		2	0	0	0	1	0	0	0
			(100)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
liver			< 2>				< 2>			
	increase in mitosis		2	0	0	0	0	0	0	0
			(100)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

STUDY NO. : 0299
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name	Control				625 ppm				1250 ppm				2500 ppm			
		No. of Animals on Study	2				2				2				2			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
liver			< 2>				< 2>				< 2>				< 2>			
	granulation		2	0	0	0	2	0	0	0	2	0	0	0	2	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	hepatocellular hypertrophy:central		0	0	0	0	1	0	0	0	2	0	0	0	0	2	0	0
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
{Nervous system}																		
brain			< 2>				< 2>				< 2>				< 2>			
	hemorrhage		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	5000 ppm				10000 ppm			
		No. of Animals on Study	2				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Digestive system)										
liver			< 2>				< 2>			
	granulation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hepatocellular hypertrophy:central		0	0	2	0	0	0	2	0
			(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)
(Nervous system)										
brain			< 2>				< 2>			
	hemorrhage		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

APPENDIX K 1

IDENTITY OF 1,4-DICHLORO-2-NITROBENZENE

IN THE 2-WEEK FEED STUDY

IDENTITY OF 1,4-DICHLORO-2-NITROBENZENE IN THE 2-WEEK FEED STUDY

Test Substance : 1,4-Dichloro-2-nitrobenzene (Wako Pure Chemical Industries, Ltd.)

Lot No. : CAN1112

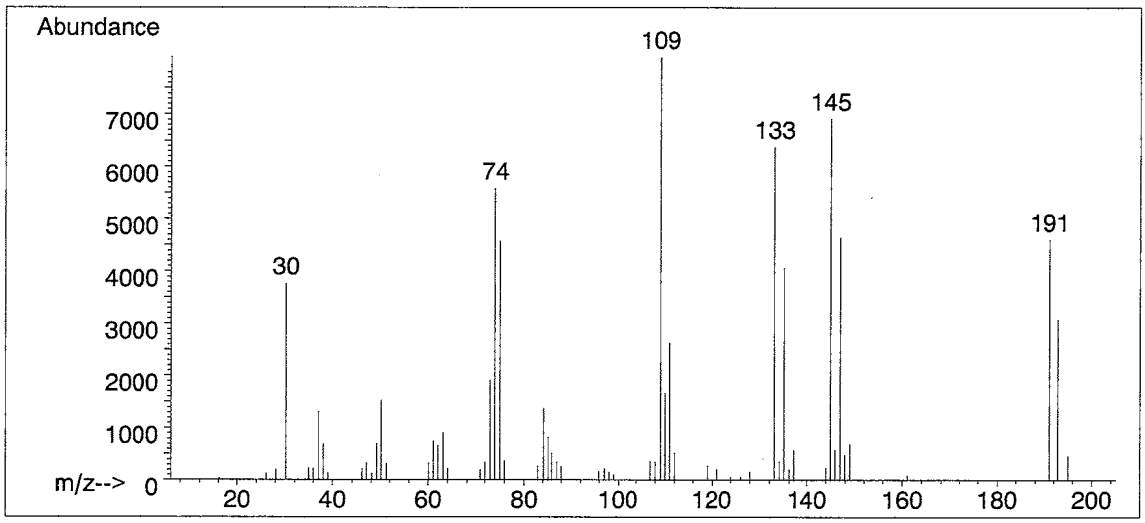
1. Spectral Data

Mass Spectrometry

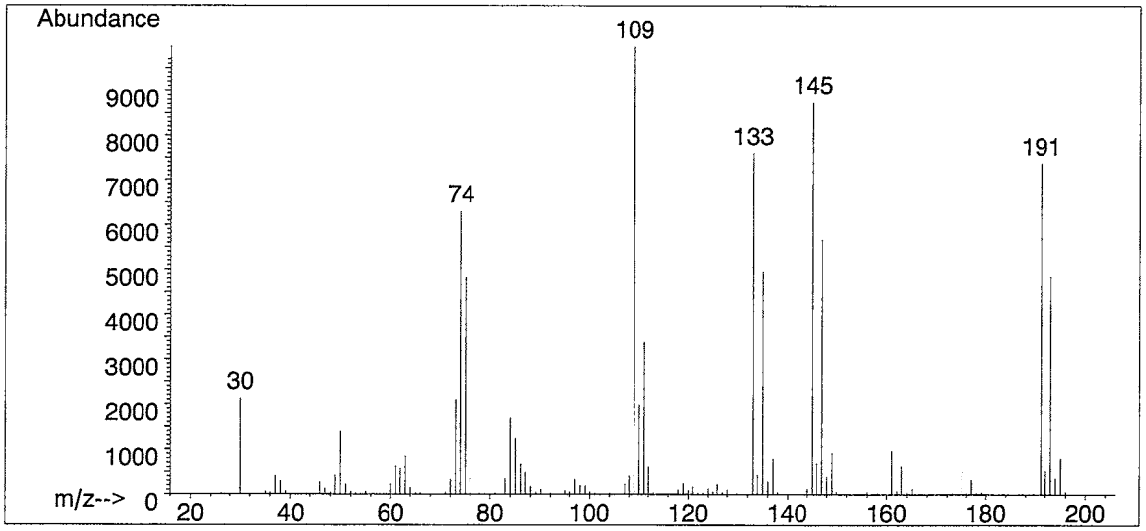
Instrument : Hewlett Packard 5989B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance



Mass Spectrum of Literature Data*

Results: The mass spectrum was consistent with literature spectrum.

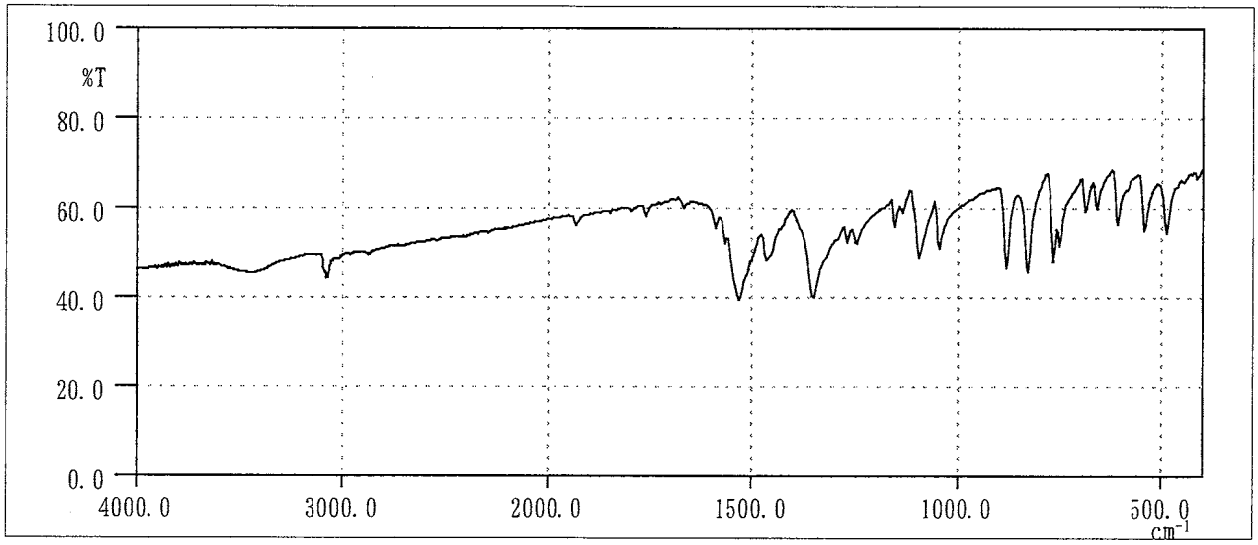
(*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition. John Wiley and Sons, Inc. (U.S.), Entry Number 74222)

Infrared Spectrometry

Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr

Resolution : 2 cm^{-1}



Infrared Spectrum of Test Substance

Determined Values Wave Number (cm^{-1})	Literature Values* Wave Number (cm^{-1})
460～ 510	460～ 510
510～ 560	510～ 560
560～ 620	560～ 620
620～ 670	620～ 670
670～ 690	670～ 690
690～ 790	690～ 790
790～ 850	790～ 850
850～ 900	850～ 900
900～1060	900～1060
1060～1120	1060～1120
1120～1170	1120～1170
1170～1180	1170～1180
1180～1260	1180～1260
1260～1280	1260～1280
1280～1400	1280～1400
1400～1470	1400～1470
1470～1580	1470～1580
1580～1600	1580～1600
1650～1690	1650～1690
1750～1780	1750～1780
1780～1810	1780～1810
1900～1950	1900～1950
3000～3100	3000～3100

Results: The infrared spectrum was consistent with literature spectrum.
(*Performed by Wako Pure Chemical Industries, Ltd.)

2. Conclusions: The test substance was identified as 1,4-dichloro-2-nitrobenzene by the mass spectrum and the infrared spectrum.

APPENDIX K 2

STABILITY OF 1,4-DICHLORO-2-NITROBENZENE

IN THE 2-WEEK FEED STUDY

STABILITY OF 1,4-DICHLORO-2-NITROBENZENE IN THE 2-WEEK FEED STUDY

Test Substance : 1,4-Dichloro-2-nitrobenzene (Wako Pure Chemical Industries, Ltd.)

Lot No. : CAN1112

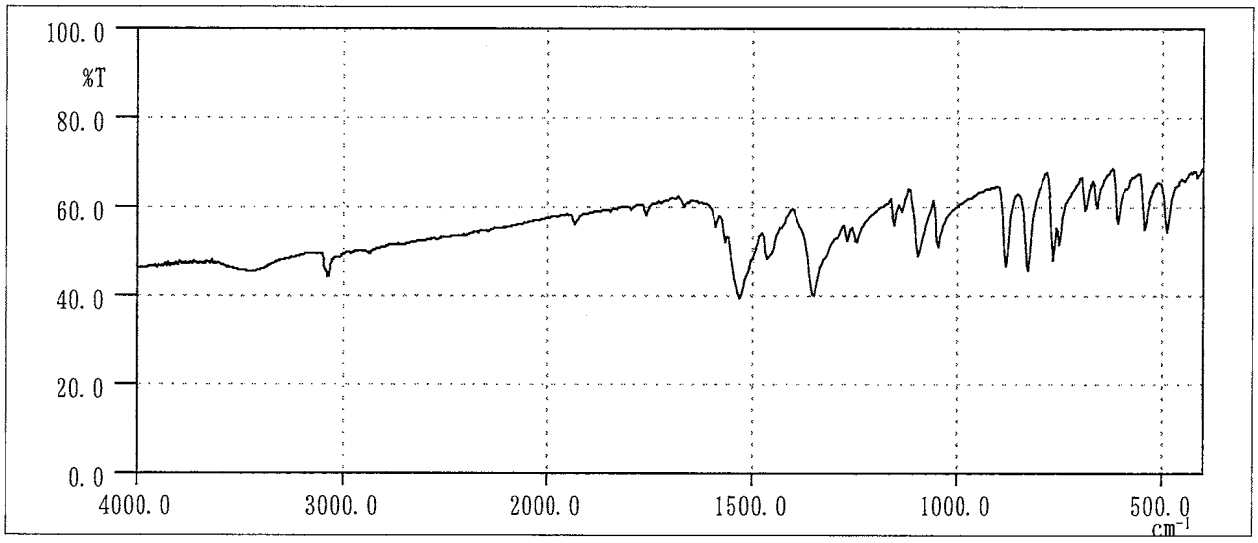
1. Sample : This lot was used from 1995.11.2 to 1995.11.16. Test substance was stored in a dark place at room temperature.

2. Infrared Spectrometry

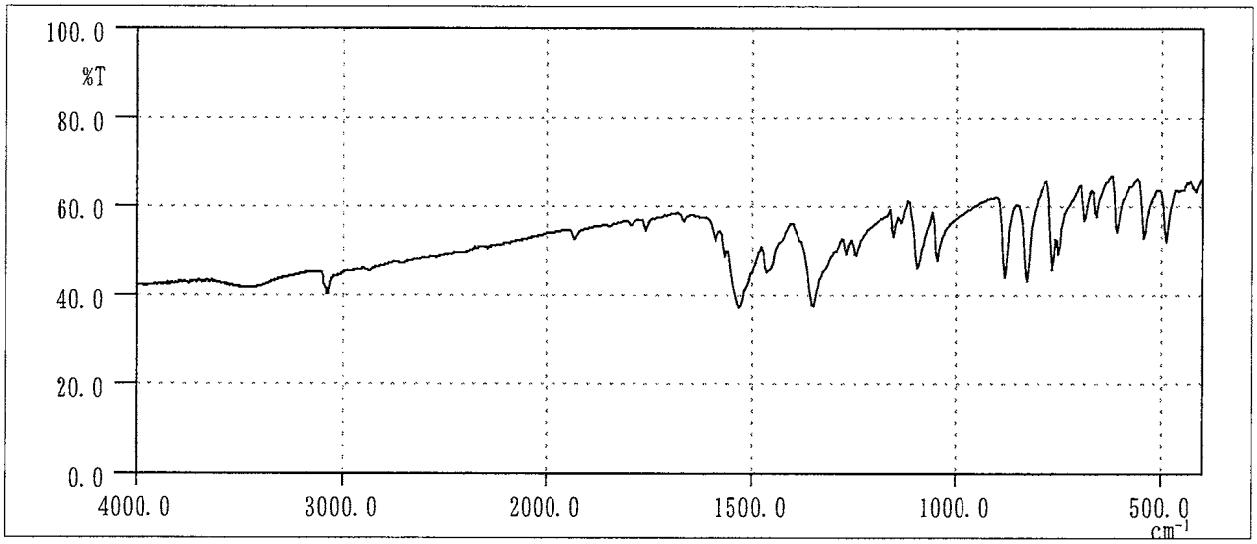
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr

Resolution : 2 cm^{-1}



Infrared Spectrum of Test Substance (date analyzed : 1995.09.21)



Infrared Spectrum of Test Substance (date analyzed : 1995.11.28)

Results: The results of infrared spectrum did not change before and after the study.

3. Gas Chromatography

Instrument	: Hewlett Packard 5890A Gas Chromatograph
Column	: Methyl Silicone (0.2 mmϕ × 50m)
Column Temperature	: 180 °C → (10 °C/min) → 215 °C → (20 °C/min) → 250 °C (2 min)
Flow Rate	: 1 mL/min
Detector	: FID (Flame Ionization Detector)
Injection Volume	: 1 μL

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
1995.09.21	1	3.636	100
1995.11.28	1	3.636	100

Results: Gas chromatography indicated one major peak (peak No.1) analyzed on 1995.9.21 and one major peak (peak No.1) analyzed on 1995.11.28. No new trace impurity peak in the test substance analyzed on 1995.11.28 was detected.

4. Conclusions: The test substance was stable for about 2 months in a dark place at room temperature.

APPENDIX K 3

CONCENTMOUSEION OF 1,4-DICHLORO-2-NITROBENZENE

IN FORMULATED DIETS IN THE 2-WEEK FEED STUDY

CONCENTRATION OF 1,4-DICHLORO-2-NITROBENZENE IN FORMULATED DIETS IN THE 2-WEEK FEED STUDY

	Target Concentration				
Date Analyzed	625[a]	1250	2500	5000	10000
1995.10.26	601.5 (96.2)[b]	1162.5 (93.0)	2365.5 (94.6)	4945.3 (98.9)	9673.7 (96.7)

[a] ppm
[b] %

Analytical Method : The samples were analyzed by gas chromatography.

Instrument : Hewlett Packard 5890A Gas Chromatograph
Column : Methyl Silicone (0.2 mmϕ × 50m)
Column Temperature : 180 °C → (10 °C/min) → 215 °C → (20 °C/min) → 250 °C (2 min)
Flow Rate : 1 mL/min
Detector : FID (Flame Ionization Detector)
Injection Volume : 1 µL

HOMOGENEITY OF 1,4-DICHLORO-2-NITROBENZENE IN FORMULATED DIETS IN THE 2-WEEK FEED STUDY

	Target Concentration				
	625[a]	1250	2500	5000	10000
Coefficient Variation	1.23[b]	0.47	1.80	6.22	1.70

[a] ppm
[b] % (n=7)

Analytical Method : The samples were analyzed by gas chromatography.

Instrument : Hewlett Packard 5890A Gas Chromatograph
Column : Methyl Silicone (0.2 mmϕ × 50m)
Column Temperature : 180 °C → (10 °C/min) → 215 °C → (20 °C/min) → 250 °C (2 min)
Flow Rate : 1 mL/min
Detector : FID (Flame Ionization Detector)
Injection Volume : 1 µL

APPENDIX K 4

STABILITY OF 1,4-DICHLORO-2-NITROBENZENE

IN FORMULATED DIETSIN THE 2-WEEK FEED STUDY

STABILITY OF 1,4-DICHLORO-2-NITROBENZENE IN FORMULATED DIETS IN THE 2-WEEK FEED STUDY

		Target Concentration				
Date Prepared	Date Analyzed	625[a]	1250	2500	5000	10000
1995.10.25	1995.10.26	601.5 (100)[b]	1162.5 (100)	2365.5 (100)	4945.3 (100)	9673.7 (100)
	1995.10.30[c]	548.3 (91.2)	1079.2 (92.8)	2140.5 (90.5)	4248.9 (85.9)	9141.0 (94.5)
	1995.11.20[d]	620.0 (103)	1331.0 (114)	2269.3 (95.9)	4615.5 (93.3)	9324.0 (96.4)

[a] ppm
[b] % (Percentage was based on the concentration on date of preparation.)
[c] Animal room samples
[d] Cold storage samples

Analytical Method : The samples were analyzed by gas chromatography.

Instrument : Hewlett Packard 5890A Gas Chromatograph
Column : Methyl Silicone (0.2 mmϕ × 50m)
Column Temperature : 180 °C → (10 °C/min) → 215 °C → (20 °C/min) → 250 °C (2 min)
Flow Rate : 1 mL/min
Detector : FID (Flame Ionization Detector)
Injection Volume : 1 μL

APPENDIX L 1

METHODS FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK FEED STUDY OF 1,4-DICHLORO-2-NITROBENZENE

METHODS FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK FEED STUDY OF 1,4-DICHLORO-2-NITROBENZENE

Item	Method
Hematology	
Red blood cell (RBC)	Light scattering method [1]
Hemoglobin (Hgb)	Cyanmethemoglobin method [1]
Methemoglobin	Multiple-wavelength Spectrophotometric method [4]
Hematocrit (Hct)	Calculated as RBC×MCV/10 [1]
Mean corpuscular volume (MCV)	Light scattering method [1]
Mean corpuscular hemoglobin (MCH)	Calculated as Hgb/RBC×10 [1]
Mean corpuscular hemoglobin concentration (MCHC)	Calculated as Hgb/Hct×100 [1]
Platelet	Light scattering method [1]
White blood cell (WBC)	Light scattering method [1]
Differential WBC	Pattern recognition method [2] (May-Grunwald-Giemsa staining)
Biochemistry	
Total protein (TP)	Biuret method [3]
Albumin (Alb)	BCG method [3]
A/G ratio	Calculated as Alb/(TP−Alb) [3]
T-bilirubin	Alkaline azobilirubin method [3]
Glucose	Enzymatic method (GLK・G-6-PDH) [3]
T-cholesterol	Enzymatic method (CE・COD・POD) [3]
Phospholipid	Enzymatic method (PLD・COD・POD) [3]
Glutamic oxaloacetic transaminase (GOT)	IFCC method [3]
Glutamic pyruvic transaminase (GPT)	IFCC method [3]
Lactate dehydrogenase (LDH)	Wroblewski-LaDue method [3]
γ-Glutamyl transpeptidase (γ-GTP)	L-γ-Glutamyl-p-nitroanilide method [3]
Creatine phosphokinase (CPK)	GSCC method [3]
Urea nitrogen	Enzymatic method (Urease・GLDH) [3]
Sodium	Ion selective electrode method [3]
Potassium	Ion selective electrode method [3]
Chloride	Ion selective electrode method [3]
Calcium	OCPC method [3]
Inorganic phosphorus	Enzymatic method (PNP・XOD・POD) [3]

1) Automatic blood cell analyzer (Technicon H・1 : Technicon Instruments Corporation)

2) Automatic blood cell differential analyzer (Hitachi 8200 : Hitachi,Ltd.)

3) Automatic analyzer (Hitachi 7070 : Hitachi,Ltd.)

4) CO-oximeter (CIBA・CORNING 270 : Ciba Corning Diagnostics Corp)

APPENDIX M 1

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK FEED STUDY OF 1,4-DICHLORO-2-NITROBENZENE

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY
IN THE 2-WEEK FEED STUDY OF 1,4-DICHLORO-2-NITROBENZENE

Item	Unit	Decimal Place
Hematology		
Red blood cell (RBC)	$\times 10^6/\mu L$	2
Hemoglobin	g/dL	1
Methemoglobin	%	1
Hematocrit	%	1
Mean corpuscular volume (MCV)	fL	1
Mean corpuscular hemoglobin (MCH)	pg	1
Mean corpuscular hemoglobin concentration (MCHC)	g/dL	1
Platelet	$\times 10^3/\mu L$	0
White blood cell (WBC)	$\times 10^3/\mu L$	2
Differential WBC	%	0
Biochemistry		
Total protein	g/dL	1
Albumin	g/dL	1
A/G ratio	–	1
T-bilirubin	mg/dL	2
Glucose	mg/dL	0
T-cholesterol	mg/dL	0
Phospholipid	mg/dL	0
Glutamic oxaloacetic transaminase (GOT)	IU/L	0
Glutamic pyruvic transaminase (GPT)	IU/L	0
Lactate dehydrogenase (LDH)	IU/L	0
γ-Glutamyl transpeptidase (γ-GTP)	IU/L	0
Creatine phosphokinase (CPK)	IU/L	0
Urea nitrogen	mg/dL	1
Sodium	mEq/L	0
Potassium	mEq/L	1
Chloride	mEq/L	0
Calcium	mg/dL	1
Inorganic phosphorus	mg/dL	1