プロピオノニトリルのマウスを用いた
吸入による１３週間毒性試験報告書

試験番号：0456

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(13-WEEK STUDY)
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APPENDIX A 1

BODY WEIGHT CHANGES : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0456
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	23.4± 0.7	24.7± 1.0	26.0± 0.8	26.2± 1.3	26.9± 1.2	27.7± 1.1	27.8± 0.9
3ppm	23.4± 0.8	24.8± 1.1	25.7± 1.1	25.7± 1.4	26.0± 1.5	26.9± 1.7	27.2± 1.6
6ppm	23.4± 0.8	24.7± 0.9	25.8± 0.9	26.1± 1.4	26.6± 1.5	27.2± 1.5	27.3± 1.5
12ppm	23.4± 0.8	25.0± 0.7	26.1± 0.8	26.4± 0.8	26.2± 1.0	27.4± 1.2	27.3± 1.1
25ppm	23.4± 0.8	25.1± 0.8	25.7± 0.7	25.9± 0.8	26.4± 1.0	26.6± 1.0	27.2± 1.1
50ppm	23.4± 0.8	24.8± 0.6	25.7± 1.0	26.0± 1.0	26.2± 0.9	26.8± 0.7	27.0± 0.7

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

STUDY NO. : 0456
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-7
Control	28.6± 0.9	28.8± 1.4	29.1± 1.4	29.9± 1.5	30.5± 1.6	31.2± 1.5	31.7± 1.6
3ppm	27.6± 1.8	27.9± 1.6	28.2± 1.6	29.0± 2.2	29.4± 2.0	30.0± 2.2	30.3± 2.2
6ppm	27.7± 1.3	28.2± 1.3	28.4± 1.4	28.8± 1.5	29.8± 1.5	30.1± 1.4	30.5± 1.6
12ppm	27.9± 1.1	28.2± 1.1	28.7± 1.3	29.2± 1.5	30.0± 1.6	30.6± 1.8	31.3± 2.1
25ppm	27.6± 1.3	28.0± 1.5	28.1± 1.4	28.7± 1.5	29.2± 1.9	30.1± 1.8	30.8± 1.9
50ppm	27.6± 1.0	27.9± 1.4	28.1± 1.2	28.5± 1.5	29.2± 1.5	29.6± 1.6	30.1± 1.5

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

APPENDIX A 2

BODY WEIGHT CHANGES : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0456
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	18.9± 0.7	19.8± 0.5	20.9± 0.9	21.6± 0.8	22.3± 0.9	22.5± 0.7	23.0± 1.0
3ppm	18.9± 0.7	20.4± 1.0	21.4± 1.2	21.8± 0.9	22.5± 0.9	23.2± 0.9	23.8± 0.8
6ppm	18.9± 0.7	20.1± 0.8	20.9± 0.7	21.9± 0.8	22.3± 1.2	22.8± 1.2	23.2± 1.3
12ppm	18.9± 0.7	20.2± 0.6	20.8± 0.9	21.6± 0.9	22.0± 0.7	22.9± 1.1	23.5± 0.6
25ppm	18.9± 0.8	20.1± 0.8	21.1± 0.9	21.5± 1.0	21.8± 0.9	22.1± 1.0	23.3± 0.9
50ppm	18.9± 0.8	20.1± 1.0	21.0± 0.9	21.3± 1.2	21.8± 1.2	22.2± 1.2	23.1± 1.3

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

STUDY NO. : 0456
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-7
Control	23.2± 1.0	23.9± 1.0	23.4± 1.0	24.1± 1.7	24.1± 1.4	24.8± 1.4	24.8± 1.2
3ppm	24.1± 0.9	24.2± 1.3	24.7± 1.2	25.0± 1.4	25.6± 1.5	25.6± 1.4	26.1± 1.4
6ppm	23.9± 1.0	24.0± 1.6	23.7± 1.0	24.1± 1.3	24.9± 1.6	25.2± 1.5	25.3± 1.5
12ppm	23.6± 1.0	23.9± 0.7	23.8± 0.8	24.5± 0.7	24.5± 0.9	25.3± 1.3	25.6± 1.3
25ppm	23.1± 1.0	23.5± 1.3	23.7± 1.1	24.2± 1.1	24.5± 1.0	25.5± 1.8	25.1± 1.2
50ppm	23.8± 1.8	23.7± 1.0	24.1± 1.2	24.6± 1.3	24.6± 1.0	24.9± 1.6	25.5± 1.5

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

APPENDIX B 1

FOOD CONSUMPTION CHANGES : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0456
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(6)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	4.3± 0.3	4.2± 0.2	4.0± 0.4	4.3± 0.4	4.2± 0.3	4.3± 0.3	4.3± 0.2
3ppm	4.3± 0.3	4.3± 0.4	4.1± 0.4	4.3± 0.4	4.4± 0.4	4.4± 0.4	4.5± 0.5
6ppm	4.4± 0.2	4.3± 0.2	4.1± 0.4	4.3± 0.4	4.4± 0.4	4.5± 0.3	4.6± 0.3
12ppm	4.4± 0.1	4.4± 0.2	4.3± 0.3	4.3± 0.2	4.4± 0.2	4.4± 0.2	4.5± 0.2
25ppm	4.4± 0.1	4.1± 0.2	3.9± 0.2	4.1± 0.3	4.1± 0.3	4.2± 0.3	4.3± 0.2
50ppm	4.3± 0.1	4.2± 0.2	4.0± 0.2	4.4± 1.0	4.3± 0.7	4.3± 0.2	4.3± 0.3

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

STUDY NO. : 0456
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)
Control	4.3± 0.3	4.3± 0.3	4.4± 0.3	4.5± 0.3	4.6± 0.3	4.6± 0.2
3ppm	4.5± 0.4	4.5± 0.3	4.7± 0.4	4.7± 0.4	4.6± 0.4	4.6± 0.4
6ppm	4.6± 0.4	4.6± 0.4	4.6± 0.4	4.8± 0.3	4.6± 0.4	4.7± 0.4
12ppm	4.5± 0.2	4.6± 0.3	4.7± 0.2	4.6± 0.3	4.8± 0.2	4.8± 0.3
25ppm	4.3± 0.2	4.2± 0.3	4.4± 0.2	4.3± 0.3	4.4± 0.3	4.5± 0.3
50ppm	4.2± 0.3	4.2± 0.2	4.4± 0.3	4.4± 0.3	4.4± 0.3	4.4± 0.3

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

APPENDIX B 2

FOOD CONSUMPTION CHANGES : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0456
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(6)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	3.8± 0.2	3.7± 0.2	3.7± 0.2	4.0± 0.3	3.9± 0.3	4.0± 0.2	4.1± 0.2
3ppm	3.9± 0.3	3.8± 0.3	3.7± 0.3	4.0± 0.3	4.2± 0.2	4.7± 1.5*	4.3± 0.3
6ppm	3.8± 0.2	3.8± 0.2	4.0± 0.3	4.1± 0.2	4.2± 0.2*	4.4± 0.3**	4.4± 0.2
12ppm	3.8± 0.2	3.7± 0.2	3.8± 0.2	4.0± 0.2	4.2± 0.3*	4.3± 0.2*	4.4± 0.3
25ppm	3.8± 0.2	3.8± 0.4	3.7± 0.3	4.0± 0.3	3.9± 0.3	4.2± 0.3	4.1± 0.2
50ppm	3.9± 0.3	3.7± 0.2	3.5± 0.3	3.8± 0.2	3.8± 0.3	4.2± 0.2	4.2± 0.3

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

STUDY NO. : 0456
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)
Control	4.2± 0.2	4.0± 0.2	4.2± 0.2	4.1± 0.2	4.4± 0.3	4.2± 0.2
3ppm	4.4± 0.4	4.4± 0.3*	4.4± 0.3	4.5± 0.4*	4.5± 0.3	4.7± 0.2**
6ppm	4.4± 0.3	4.3± 0.3	4.4± 0.2	4.4± 0.3	4.5± 0.3	4.5± 0.4
12ppm	4.5± 0.8	4.4± 0.5*	4.4± 0.2	4.3± 0.5	4.5± 0.3	4.5± 0.5
25ppm	4.3± 0.2	4.2± 0.2	4.3± 0.3	4.2± 0.2	4.5± 0.4	4.2± 0.3
50ppm	4.1± 0.3	4.2± 0.2	4.2± 0.2	4.2± 0.3	4.3± 0.3	4.3± 0.2

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

APPENDIX C 1

URINALYSIS : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0456 URINALYSIS
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Occult blood −	±	+	2+	3+	CHI
Control	10	0	0	0	0	2	7	1		0	0	6	4	0	0		10	0	0	0	0	0		0	5	5	0	0	0		10	0	0	0	0	
3ppm	10	0	0	0	0	1	7	2		0	0	4	6	0	0		10	0	0	0	0	0		0	8	1	1	0	0		10	0	0	0	0	
6ppm	10	0	0	0	0	4	4	2		0	0	9	1	0	0		10	0	0	0	0	0		0	8	2	0	0	0		10	0	0	0	0	
12ppm	10	0	0	0	0	1	8	1		0	0	6	4	0	0		10	0	0	0	0	0		0	6	4	0	0	0		10	0	0	0	0	
25ppm	10	0	0	1	1	0	7	1		0	0	6	4	0	0		10	0	0	0	0	0		0	8	2	0	0	0		10	0	0	0	0	
50ppm	10	0	0	0	1	2	4	3		0	1	6	3	0	0		10	0	0	0	0	0		0	5	5	0	0	0		10	0	0	0	0	

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

STUDY NO. : 0456 URINALYSIS
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

Group Name	NO. of Animals	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0	
3ppm	10	10	0	0	0	0	
6ppm	10	10	0	0	0	0	
12ppm	10	10	0	0	0	0	
25ppm	10	10	0	0	0	0	
50ppm	10	10	0	0	0	0	

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

APPENDIX C 2

URINALYSIS : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0456 URINALYSIS
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Occult blood −	±	+	2+	3+	CHI
Control	10	0	0	1	1	1	6	1		0	6	4	0	0	0		10	0	0	0	0	0		1	8	1	0	0	0		10	0	0	0	0	
3ppm	10	0	0	0	0	3	7	0		0	1	9	0	0	0	*	10	0	0	0	0	0		0	9	1	0	0	0		10	0	0	0	0	
6ppm	10	0	0	0	0	4	5	1		0	4	6	0	0	0		10	0	0	0	0	0		0	8	2	0	0	0		10	0	0	0	0	
12ppm	10	0	0	0	2	1	6	1		0	6	4	0	0	0		10	0	0	0	0	0		0	10	0	0	0	0		10	0	0	0	0	
25ppm	10	0	0	0	0	0	10	0		0	1	8	1	0	0		10	0	0	0	0	0		0	9	1	0	0	0		10	0	0	0	0	
50ppm	10	0	0	0	3	1	6	0		0	8	2	0	0	0		10	0	0	0	0	0		1	9	0	0	0	0		10	0	0	0	0	

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

STUDY NO. : 0456 URINALYSIS
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

Group Name	NO. of Animals	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0	
3ppm	10	10	0	0	0	0	
6ppm	10	10	0	0	0	0	
12ppm	10	10	0	0	0	0	
25ppm	10	10	0	0	0	0	
50ppm	10	10	0	0	0	0	

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

APPENDIX D 1

HEMATOLOGY : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0456
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RED BLOOD CELL $10^5/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV fℓ	MCH pg	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	10	11.12± 0.43	15.7± 0.5	49.1± 1.1	44.2± 0.8	14.2± 0.1	32.1± 0.5	1483± 70
3ppm	10	10.41± 1.62	14.9± 2.3	46.6± 6.4	45.0± 1.4	14.3± 0.3	31.7± 1.0	1449± 85
6ppm	10	11.04± 0.28	15.8± 0.4	48.9± 1.1	44.3± 0.5	14.3± 0.2	32.3± 0.5	1463± 75
12ppm	10	10.87± 0.41	15.6± 0.6	48.5± 1.6	44.6± 0.4	14.3± 0.2	32.2± 0.3	1417± 84
25ppm	9	10.93± 0.26	15.6± 0.3	48.7± 1.0	44.5± 0.3	14.3± 0.1	32.1± 0.3	1426± 82
50ppm	10	10.80± 0.50	15.4± 0.5	48.0± 1.7	44.4± 0.7	14.3± 0.2	32.2± 0.4	1417± 118

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

STUDY NO. : 0456
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$		Differential WBC (%) N-BAND		N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHER	
Control	10	1.83±	1.23	0±	0	13±	3	2±	2	0±	0	2±	1	83±	3	0±	0
3ppm	10	1.38±	0.80	0±	0	11±	5	2±	2	0±	0	2±	1	85±	4	0±	0
6ppm	10	1.46±	0.78	0±	1	14±	3	1±	1	0±	0	1±	1	83±	3	0±	0
12ppm	10	1.17±	0.74	0±	1	18±	10	1±	1	0±	0	1±	1	80±	10	0±	0
25ppm	9	1.48±	0.80	0±	0	13±	2	1±	1	0±	0	2±	1	84±	3	0±	0
50ppm	10	1.23±	0.71	0±	1	13±	5	1±	1	0±	0	1±	2	84±	4	0±	0

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

APPENDIX D 2

HEMATOLOGY : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0456
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$		HEMOGLOBIN g/dℓ		HEMATOCRIT %		MCV fℓ		MCH pg		MCHC g/dℓ		PLATELET $10^3/\mu\ell$	
Control	10	10.86±	0.23	15.9±	0.3	48.4±	0.9	44.6±	0.4	14.6±	0.2	32.7±	0.3	1314±	94
3ppm	10	10.90±	0.24	15.9±	0.4	48.7±	1.0	44.7±	0.4	14.6±	0.1	32.6±	0.4	1326±	60
6ppm	10	10.91±	0.25	15.7±	0.3	48.2±	0.6	44.2±	1.0	14.4±	0.3	32.6±	0.5	1305±	48
12ppm	10	10.95±	0.31	15.7±	0.5	48.5±	1.1	44.3±	0.6	14.4±	0.3	32.5±	0.5	1346±	105
25ppm	10	10.85±	0.23	15.7±	0.4	48.5±	0.7	44.7±	0.8	14.4±	0.4	32.3±	0.6	1315±	50
50ppm	10	10.72±	0.27	15.7±	0.4	48.1±	1.2	44.9±	0.5	14.7±	0.1	32.7±	0.3	1375±	102

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

STUDY NO. : 0456
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHER
Control	10	1.18± 0.66	0± 0	18± 5	0± 1	0± 0	1± 1	81± 6	0± 0
3ppm	10	1.10± 1.47	0± 0	22± 11	1± 1	0± 0	1± 1	77± 10	0± 0
6ppm	10	0.75± 0.61	0± 1	21± 10	0± 1	0± 0	0± 0	78± 10	0± 0
12ppm	10	0.77± 0.51	0± 1	19± 8	1± 2	0± 0	1± 1	79± 8	0± 0
25ppm	10	0.98± 0.44	0± 0	15± 6	1± 1	0± 0	1± 1	84± 7	0± 0
50ppm	10	1.06± 0.63	0± 0	17± 7	1± 1	0± 0	1± 2	81± 7	0± 0

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

APPENDIX E 1

BIOCHEMISTRY : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0456
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

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	TRIGLYCERIDE mg/dℓ
Control	10	5.1± 0.2	3.0± 0.1	1.4± 0.1	0.15± 0.02	190± 29	88± 11	28± 10
3ppm	10	5.0± 0.2	2.9± 0.1	1.5± 0.1	0.14± 0.01	186± 32	75± 13*	25± 17
6ppm	10	4.9± 0.1	3.0± 0.1	1.5± 0.1*	0.13± 0.01	186± 37	72± 8**	17± 5
12ppm	10	5.0± 0.2	2.9± 0.1	1.5± 0.1	0.15± 0.01	199± 30	75± 10*	20± 10
25ppm	10	5.0± 0.2	3.0± 0.1	1.5± 0.1*	0.15± 0.01	189± 26	80± 9	21± 6
50ppm	10	5.1± 0.2	3.0± 0.1	1.5± 0.1	0.14± 0.01	188± 26	81± 9	19± 7

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

STUDY NO. : 0456
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dℓ	GOT IU/ℓ	GPT IU/ℓ	LDH IU/ℓ	ALP IU/ℓ	G-GTP IU/ℓ	CPK IU/ℓ
Control	10	180± 19	39± 4	17± 3	189± 42	144± 14	1± 0	48± 18
3ppm	10	159± 26	43± 4	18± 2	180± 22	142± 22	1± 1	63± 34
6ppm	10	155± 14	41± 5	16± 2	167± 22	149± 7	1± 0	49± 16
12ppm	10	157± 21	41± 4	17± 2	198± 16	151± 12	1± 1	66± 27
25ppm	10	166± 20	40± 4	17± 2	206± 50	145± 7	1± 1	55± 15
50ppm	10	169± 19	40± 7	17± 2	182± 27	144± 9	1± 0	50± 12

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

STUDY NO. : 0456
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	UREA NITROGEN mg/dl	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dl	INORGANIC PHOSPHORUS mg/dl
Control	10	27.5± 3.4	149± 1	4.6± 0.3	120± 3	8.6± 0.3	6.6± 0.9
3ppm	10	28.3± 5.0	150± 1*	4.5± 0.1	121± 2	8.5± 0.2	6.8± 0.8
6ppm	10	25.5± 4.4	150± 1*	4.3± 0.3	121± 1	8.3± 0.2*	6.5± 1.0
12ppm	10	26.6± 3.3	150± 1	4.5± 0.3	121± 2	8.4± 0.2	6.5± 1.0
25ppm	10	30.5± 4.4	150± 1	4.5± 0.3	121± 2	8.5± 0.2	7.0± 1.1
50ppm	10	31.3± 4.8	150± 1	4.6± 0.3	121± 2	8.6± 0.1	6.5± 0.8

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

APPENDIX E 2

BIOCHEMISTRY : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0456
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

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	TRIGLYCERIDE mg/dℓ
Control	10	5.2± 0.1	3.4± 0.1	1.9± 0.2	0.14± 0.01	158± 22	71± 8	13± 6
3ppm	10	5.3± 0.2	3.4± 0.1	1.9± 0.2	0.14± 0.01	162± 23	72± 12	13± 7
6ppm	10	5.3± 0.1	3.4± 0.1	1.8± 0.1	0.14± 0.01	162± 15	66± 12	12± 11
12ppm	10	5.2± 0.1	3.4± 0.1	1.8± 0.1	0.14± 0.01	177± 20	69± 11	11± 5
25ppm	10	5.2± 0.1	3.4± 0.1	1.8± 0.1	0.13± 0.01	165± 32	70± 6	11± 5
50ppm	10	5.3± 0.2	3.4± 0.2	1.9± 0.1	0.14± 0.01	174± 23	76± 11	13± 6

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

STUDY NO. : 0456
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dℓ	GOT IU/ℓ	GPT IU/ℓ	LDH IU/ℓ	ALP IU/ℓ	G-GTP IU/ℓ	CPK IU/ℓ
Control	10	143± 21	64± 15	25± 4	242± 71	251± 26	1± 1	122± 53
3ppm	10	142± 26	73± 28	27± 7	297± 116	250± 36	1± 1	136± 107
6ppm	10	131± 25	67± 14	25± 5	269± 90	247± 17	1± 0	124± 69
12ppm	10	134± 19	58± 11	23± 3	216± 44	251± 40	1± 1	89± 34
25ppm	10	141± 18	90± 111	42± 61	279± 227	238± 20	1± 0	78± 23
50ppm	10	149± 23	57± 14	22± 4	225± 40	232± 31	1± 0	98± 38

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

STUDY NO. : 0456
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	UREA NITROGEN mg/dl	SODIUM mEq/l	POTASSIUM mEq/l	CHLORIDE mEq/l	CALCIUM mg/dl	INORGANIC PHOSPHORUS mg/dl
Control	10	24.2± 3.3	150± 1	4.5± 0.4	121± 2	8.7± 0.2	6.8± 0.5
3ppm	10	22.9± 4.3	150± 2	4.4± 0.4	121± 2	8.6± 0.2	6.3± 0.8
6ppm	10	22.9± 1.4	150± 1	4.3± 0.3	121± 2	8.6± 0.1	6.5± 0.5
12ppm	10	22.4± 3.2	150± 1	4.4± 0.2	120± 2	8.7± 0.2	6.8± 0.8
25ppm	10	23.3± 2.8	150± 1	4.6± 0.4	121± 2	8.7± 0.2	6.2± 1.0
50ppm	10	23.2± 2.7	150± 1	4.5± 0.3	121± 1	8.7± 0.2	5.9± 0.8

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

APPENDIX F 1

GROSS FINDINGS : SUMMARY, MOUSE : MALE : SACRIFICED ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0456
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
ALL ANIMALS (0- 14W)

Organ	Findings	Group Name / NO. of Animals	Control 10	(%)	3ppm 10	(%)	6ppm 10	(%)	12ppm 10	(%)
spleen	black zone		0	(0)	0	(0)	0	(0)	0	(0)
kidney	nodule		0	(0)	0	(0)	0	(0)	0	(0)
	hydronephrosis		1	(10)	1	(10)	0	(0)	0	(0)

Organ	Findings	Group Name / NO. of Animals	25ppm 10	(%)	50ppm 10	(%)
spleen	black zone		0	(0)	2	(20)
kidney	nodule		1	(10)	0	(0)
	hydronephrosis		0	(0)	1	(10)

APPENDIX F 2

GROSS FINDINGS : SUMMARY, MOUSE : FEMALE : SACRIFICED ANIMALS

(13-WEEK STUDY)

Organ	Findings	Group Name / NO. of Animals	Control 10	(%)	3ppm 10	(%)	6ppm 10	(%)	12ppm 10	(%)
spleen	black zone		2	(20)	1	(10)	1	(10)	0	(0)
ovary	cyst		1	(10)	1	(10)	1	(10)	0	(0)

STUDY NO. : 0456
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
ALL ANIMALS (0- 14W)

Organ	Findings	Group Name / NO. of Animals	25ppm 10	(%)	50ppm 10	(%)
spleen	black zone		1	(10)	1	(10)
ovary	cyst		0	(0)	0	(0)

APPENDIX G 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0456
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (14W)

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	28.2± 1.5	0.038± 0.004	0.009± 0.001	0.224± 0.026	0.155± 0.012	0.158± 0.014
3ppm	10	26.7± 2.2	0.033± 0.004	0.009± 0.003	0.222± 0.010	0.152± 0.010	0.160± 0.012
6ppm	10	26.7± 1.4	0.033± 0.006	0.009± 0.002	0.232± 0.017	0.155± 0.011	0.164± 0.012
12ppm	10	27.6± 2.0	0.034± 0.011	0.010± 0.002	0.219± 0.020	0.155± 0.010	0.160± 0.007
25ppm	10	27.1± 1.8	0.032± 0.008	0.009± 0.002	0.212± 0.026	0.153± 0.012	0.161± 0.009
50ppm	10	26.4± 1.7	0.034± 0.005	0.009± 0.002	0.231± 0.016	0.152± 0.012	0.157± 0.009

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

STUDY NO. : 0456
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (14W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.561± 0.310	0.051± 0.007	1.173± 0.061	0.432± 0.015
3ppm	10	0.463± 0.027	0.061± 0.041	1.150± 0.052	0.429± 0.016
6ppm	10	0.465± 0.025	0.045± 0.004	1.145± 0.054	0.431± 0.018
12ppm	10	0.471± 0.020	0.047± 0.005	1.172± 0.063	0.430± 0.015
25ppm	10	0.450± 0.016	0.045± 0.004	1.153± 0.068	0.428± 0.012
50ppm	10	0.493± 0.128	0.050± 0.004	1.139± 0.071	0.430± 0.021

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

APPENDIX G 2

ORGAN WEIGHT, ABSOLUTE: SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0456
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (14W)

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	20.6± 1.0	0.039± 0.007	0.013± 0.002	0.026± 0.005	0.125± 0.006	0.151± 0.009
3ppm	10	21.5± 1.3	0.039± 0.009	0.014± 0.002	0.028± 0.005	0.132± 0.010	0.157± 0.011
6ppm	10	20.9± 1.0	0.040± 0.006	0.014± 0.001	0.029± 0.014	0.130± 0.007	0.152± 0.009
12ppm	10	21.4± 1.1	0.042± 0.008	0.015± 0.002	0.026± 0.002	0.134± 0.009	0.151± 0.009
25ppm	10	21.3± 1.2	0.040± 0.007	0.014± 0.001	0.026± 0.004	0.127± 0.008	0.155± 0.012
50ppm	10	21.4± 1.2	0.043± 0.006	0.014± 0.002	0.027± 0.003	0.124± 0.008	0.152± 0.010

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

STUDY NO. : 0456
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (14W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.309± 0.013	0.054± 0.006	0.920± 0.071	0.441± 0.015
3ppm	10	0.319± 0.018	0.052± 0.009	0.984± 0.078	0.450± 0.018
6ppm	10	0.311± 0.016	0.053± 0.008	0.945± 0.057	0.439± 0.012
12ppm	10	0.316± 0.013	0.051± 0.009	0.977± 0.079	0.439± 0.020
25ppm	10	0.314± 0.019	0.055± 0.006	0.952± 0.040	0.454± 0.023
50ppm	10	0.300± 0.017	0.054± 0.010	0.962± 0.080	0.447± 0.017

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

APPENDIX H 1

ORGAN WEIGHT, RELATIVE : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0456
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (14W)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	28.2± 1.5	0.134± 0.018	0.030± 0.003	0.794± 0.088	0.548± 0.043	0.560± 0.049
3ppm	10	26.7± 2.2	0.121± 0.011	0.035± 0.014	0.837± 0.081	0.569± 0.046	0.601± 0.035
6ppm	10	26.7± 1.4	0.122± 0.019	0.034± 0.007	0.869± 0.062	0.579± 0.027	0.616± 0.061
12ppm	10	27.6± 2.0	0.120± 0.033	0.035± 0.007	0.800± 0.105	0.564± 0.050	0.583± 0.038
25ppm	10	27.1± 1.8	0.120± 0.029	0.034± 0.007	0.785± 0.101	0.568± 0.054	0.596± 0.055
50ppm	10	26.4± 1.7	0.127± 0.017	0.034± 0.010	0.877± 0.071	0.575± 0.036	0.597± 0.047

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

STUDY NO. : 0456
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (14W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	2.018± 1.234	0.181± 0.033	4.158± 0.133	1.533± 0.071
3ppm	10	1.738± 0.087	0.233± 0.171	4.319± 0.262	1.618± 0.171
6ppm	10	1.744± 0.085	0.169± 0.013	4.292± 0.177	1.618± 0.112
12ppm	10	1.715± 0.121	0.171± 0.013	4.256± 0.174	1.563± 0.097
25ppm	10	1.664± 0.090	0.166± 0.009	4.259± 0.131	1.586± 0.108
50ppm	10	1.876± 0.535	0.190± 0.020	4.313± 0.145	1.632± 0.110

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

APPENDIX H 2

ORGAN WEIGHT, RELATIVE : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0456
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (14W)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	20.6± 1.0	0.190± 0.032	0.065± 0.007	0.124± 0.023	0.609± 0.026	0.731± 0.022
3ppm	10	21.5± 1.3	0.182± 0.037	0.065± 0.009	0.131± 0.026	0.615± 0.055	0.727± 0.034
6ppm	10	20.9± 1.0	0.191± 0.030	0.067± 0.006	0.137± 0.069	0.621± 0.027	0.725± 0.028
12ppm	10	21.4± 1.1	0.194± 0.032	0.070± 0.007	0.122± 0.014	0.627± 0.055	0.706± 0.036
25ppm	10	21.3± 1.2	0.188± 0.029	0.067± 0.007	0.124± 0.021	0.597± 0.027	0.730± 0.072
50ppm	10	21.4± 1.2	0.200± 0.021	0.066± 0.008	0.126± 0.017	0.583± 0.032	0.713± 0.049

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

STUDY NO. : 0456
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (14W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.505± 0.079	0.263± 0.024	4.463± 0.150	2.147± 0.124
3ppm	10	1.483± 0.051	0.240± 0.033	4.568± 0.224	2.094± 0.122
6ppm	10	1.489± 0.032	0.254± 0.032	4.518± 0.105	2.101± 0.079
12ppm	10	1.483± 0.084	0.237± 0.034	4.568± 0.211	2.056± 0.086
25ppm	10	1.474± 0.063	0.256± 0.023	4.474± 0.112	2.136± 0.131
50ppm	10	1.408± 0.080*	0.254± 0.042	4.505± 0.248	2.095± 0.121

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

APPENDIX I 1

HISTOPATHOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS :
SUMMARY, MOUSE : MALE : SACRIFICED ANIMALS

(13-WEEK STUDY)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 10				3ppm 10				6ppm 10				12ppm 10			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Hematopoietic system}																		
spleen			<10>				<10>				<10>				<10>			
	deposit of melanin		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)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	necrosis:focal		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)
	granulation		3 (30)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)
	mobilization of Kuppfer cell		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)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	inflammatory polyp		0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	25ppm				50ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
spleen			<10>				<10>			
	deposit of melanin		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	extramedullary hematopoiesis		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}										
liver			<10>				<10>			
	necrosis:focal		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		2	0	0	0	2	0	0	0
			(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	mobilization of Kuppfer cell		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Urinary system}										
kidney			<10>				<10>			
	inflammatory polyp		0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(10)	(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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				3ppm				6ppm				12ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	hydronephrosis		0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0
			(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Endocrine system}																		
pituitary			< 9>				<10>				< 9>				<10>			
	Rathke pouch		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)	(10)	(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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	25ppm				50ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}										
kidney			<10>				<10>			
	hydronephrosis		0	0	0	0	0	0	1	0
			(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)
{Endocrine system}										
pituitary			< 9>				<10>			
	Rathke pouch		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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

APPENDIX I 2

HISTOPATHOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS :
SUMMARY, MOUSE : FEMALE : SACRIFICED ANIMALS

(13-WEEK STUDY)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 10 1 (%)	Control 10 2 (%)	Control 10 3 (%)	Control 10 4 (%)	3ppm 10 1 (%)	3ppm 10 2 (%)	3ppm 10 3 (%)	3ppm 10 4 (%)	6ppm 10 1 (%)	6ppm 10 2 (%)	6ppm 10 3 (%)	6ppm 10 4 (%)	12ppm 10 1 (%)	12ppm 10 2 (%)	12ppm 10 3 (%)	12ppm 10 4 (%)
{Hematopoietic system}																		
spleen		<10>	<10>				<10>				<10>				<10>			
	deposit of melanin		2 (20)	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)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
{Digestive system}																		
liver		<10>	<10>				<10>				<10>				<10>			
	granulation		3 (30)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	3 (30)	0 (0)	0 (0)	0 (0)	3 (30)	0 (0)	0 (0)	0 (0)
{Urinary system}																		
kidney		<10>	<10>				<10>				<10>				<10>			
	cyst		0 (0)	1 (10)	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)
{Reproductive system}																		
ovary		<10>	<10>				<10>				<10>				<10>			
	cyst		1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	25ppm				50ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
spleen			<10>				<10>			
	deposit of melanin		1	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	extramedullary hematopoiesis		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}										
liver			<10>				<10>			
	granulation		2	0	0	0	1	0	0	0
			(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Urinary system}										
kidney			<10>				<10>			
	cyst		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Reproductive system}										
ovary			<10>				<10>			
	cyst		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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

APPENDIX J 1

IDENTITY OF PROPIONONITRILE IN THE 13-WEEK INHALATION STUDY

IDENTITY OF PROPIONONITRILE IN THE 13-WEEK INHALATION STUDY

Test Substance : Propiononitrile (Wako Pure Chemical Industries, Ltd.)

Lot No. : LDG4790

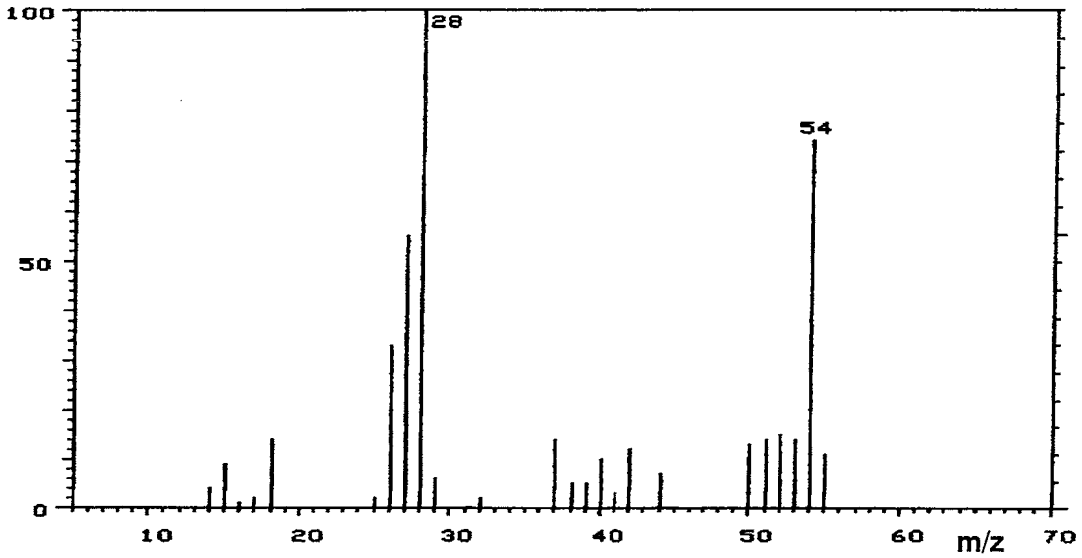
1. Spectral Data

Mass Spectrometry

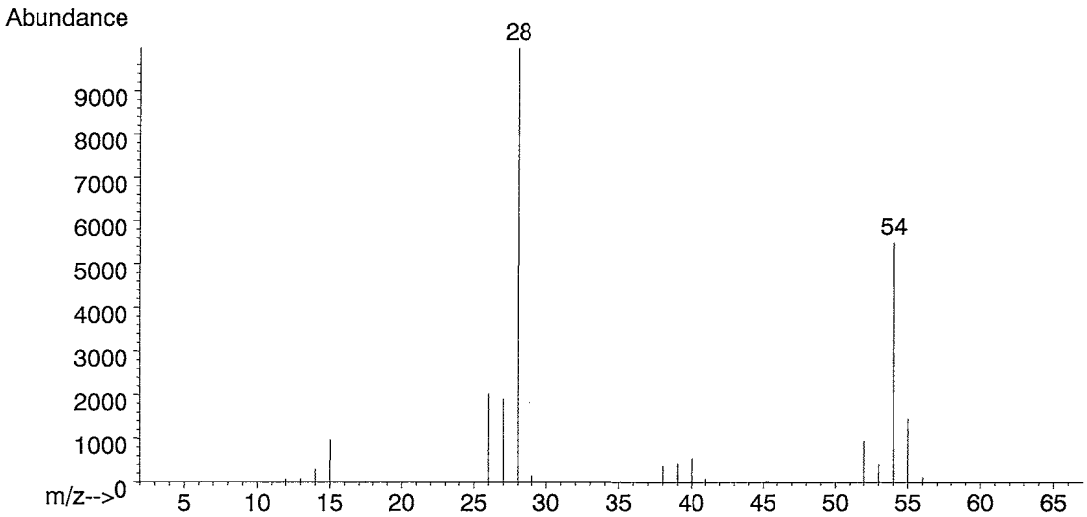
Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance



Mass Spectrum of Literature Data*

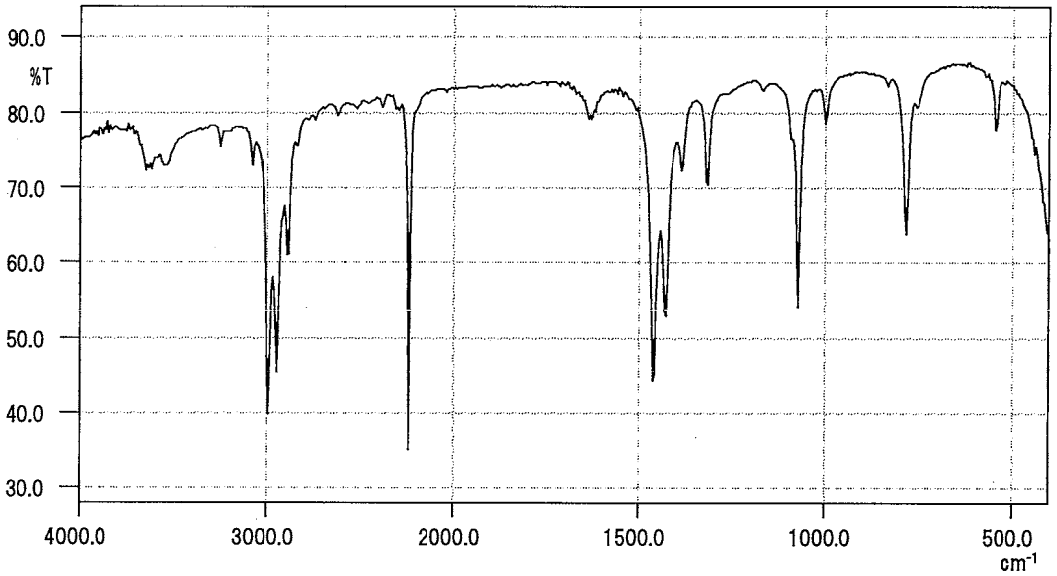
Result: The mass spectrum was consistent with literature spectrum.
(*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed. New York, NY : John Wiley and Sons.)

Infrared Spectrometry

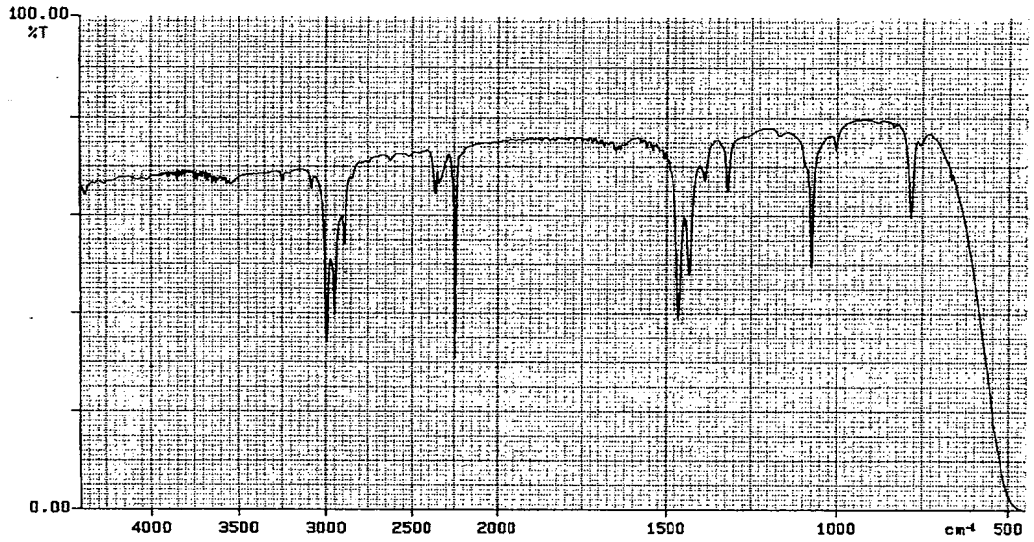
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 4 cm^{-1}



Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data*

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

2. Conclusion: The test substance was identified as propiononitrile by mass spectrum and infrared spectrum.

APPENDIX J 2

STABILITY OF PROPIONONITRILE IN THE 13-WEEK INHALATION STUDY

STABILITY OF PROPIONONITRILE IN THE 13-WEEK INHALATION STUDY

Test Substance : Propiononitrile (Wako Pure Chemical Industries, Ltd.)

Lot No. : LDG4790

1. Sample : This lot was used from 2002.9.24 to 2002.12.20. Test substance was stored in a dark place at room temperature.

2. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : Methyl Silicone (0.53 mmϕ × 60 m)

Column Temperature: 80° C

Flow Rate : 10 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μL

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
2002.09.13	1	3.822	100
2002.12.27	1	3.817	100

Result: Gas chromatography indicated one major peak (peak No.1) analyzed on 2002.9.13 and one major peak (peak No.1) analyzed on 2002.12.27. No new trace impurity peak in the test substance analyzed on 2002.12.27 was detected.

3. Conclusion: The test substance was stable for about 3 months in a dark place at room temperature.

APPENDIX K 1

CONCENTRATION OF PROPIONONITRILE IN THE INHALATION CHAMBER OF THE 13-WEEK INHALATION STUDY

CONCENTRATION OF PROPIONONITRILE IN THE INHALATION CHAMBER
OF THE 13-WEEK INHALATION STUDY

Group Name	Concentration(ppm) Mean ± S.D.
Control	0.0 ± 0.0
3 ppm	3.0 ± 0.0
6 ppm	6.0 ± 0.1
12 ppm	12.0 ± 0.1
25 ppm	25.1 ± 0.2
50 ppm	50.0 ± 0.3

APPENDIX K 2

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 13-WEEK INHALATION STUDY OF PROPIONONITRILE

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 13-WEEK INHALATION STUDY OF PROPIONONITRILE

Group Name	Temperature(℃) Mean ± S.D.	Humidity(%) Mean ± S.D.	Ventilation Rate(L/min) Mean ± S.D.	Air Change(time/h) Mean
Control	22.0 ± 0.2	57.0 ± 0.5	104.6 ± 0.7	12.1
3ppm	22.1 ± 0.1	58.1 ± 0.5	104.4 ± 0.4	12.0
6ppm	22.1 ± 0.1	58.4 ± 0.6	104.6 ± 0.3	12.1
12ppm	22.2 ± 0.2	57.9 ± 0.6	104.5 ± 0.3	12.1
25ppm	22.4 ± 0.1	56.8 ± 0.4	104.6 ± 0.3	12.1
50ppm	22.3 ± 0.1	57.3 ± 0.5	104.6 ± 0.4	12.1

APPENDIX L 1

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS IN THE 13-WEEK INHALATION STUDY OF PROPIONONITRILE

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS IN THE 13-WEEK INHALATION STUDY OF PROPIONONITRILE

Item	Method
Hematology	
Red blood cell (RBC)	Light scattering method [1]
Hemoglobin (Hgb)	Cyanmethemoglobin method [1]
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] (Wright 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	GlcK·G-6-PDH method [3]
T-cholesterol	CE·COD·POD method [3]
Triglyceride	LPL·GK·GPO·POD method [3]
Phospholipid	PLD·ChOD·POD method [3]
Glutamic oxaloacetic transaminase (GOT)	JSCC method [3]
Glutamic pyruvic transaminase (GPT)	JSCC method [3]
Lactate dehydrogenase (LDH)	SFBC method [3]
Alkaline phosphatase (ALP)	GSCC method [3]
γ-Glutamyl transpeptidase (γ-GTP)	JSCC method [3]
Creatine phosphokinase (CPK)	JSCC method [3]
Urea nitrogen	Urease·GLDH method [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	PNP·XOD·POD method [3]
Urinalysis	
pH, Protein, Glucose, Ketone body, Occult blood, Urobilinogen	Urinalysis reagent paper method [4]

1) Automatic blood cell analyzer (ADVIA120 : Bayer Corporation)
2) Automatic blood cell differential analyzer (MICROX HEG-120NA : OMRON Corporation)
3) Automatic analyzer (Hitachi 7070 : Hitachi,Ltd.)
4) Ames reagent strips for urinalysis (Uro-Labstix : Bayer Corporation)

APPENDIX L 2

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK INHALATION STUDY OF PROPIONONITRILE

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK INHALATION STUDY OF PROPIONONITRILE

Item	Unit	Decimal place
Hematology		
Red blood cell (RBC)	$\times 10^6/\mu L$	2
Hemoglobin	g/dL	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
Triglyceride	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
Alkaline phosphatase (ALP)	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