1 - ブロモブタンのマウスを用いた
吸入による13週間毒性試験報告書

試験番号：0504

APPENDICES

APPENDICES

APPENDICES (CONTINUED)

APPENDIX A 1

IDENTITY OF 1-BROMOBUTANE IN THE 13-WEEK INHALATION STUDY

IDENTITY OF 1-BROMOBUTANE IN THE 13-WEEK INHALATION STUDY

Test Substance : 1-Bromobutane (Wako Pure Chemical Industries, Ltd.)

Lot No. : ASQ0017

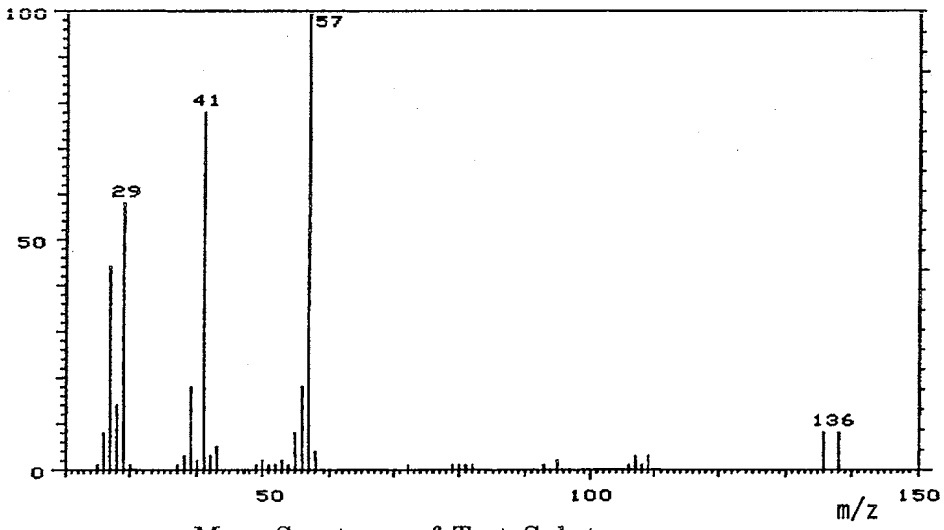
1. Spectral Data

Mass Spectrometry

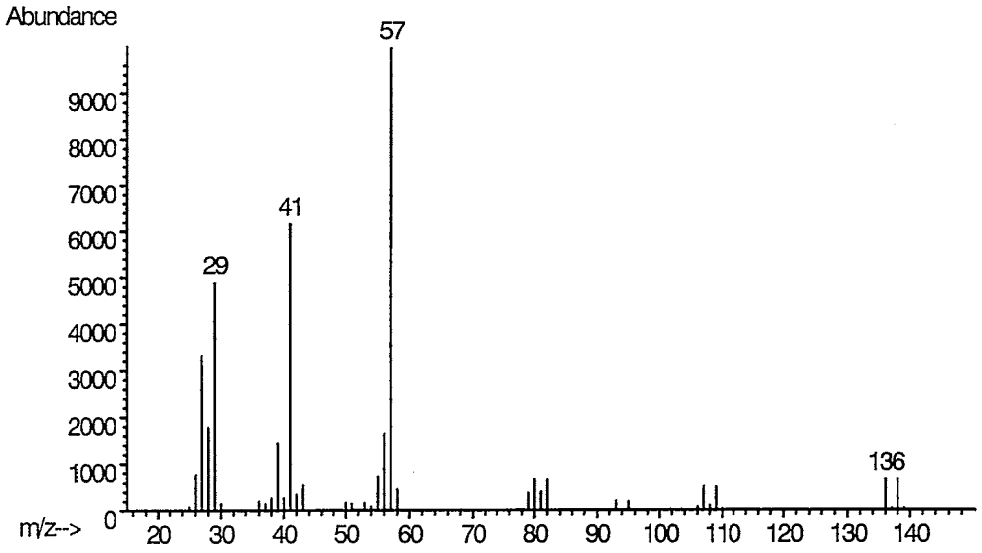
Instrument : Hitachi M-80B Mass Spectrometer

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.

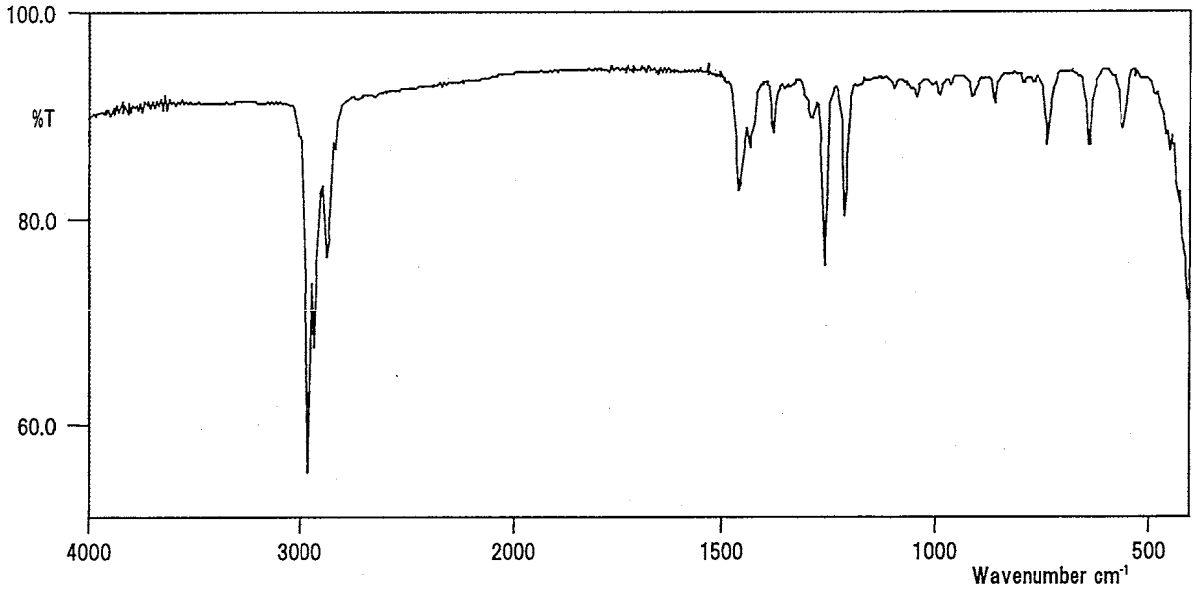
(*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed. New York, NY:John Wiley and Sons.)

Infrared Spectrometry

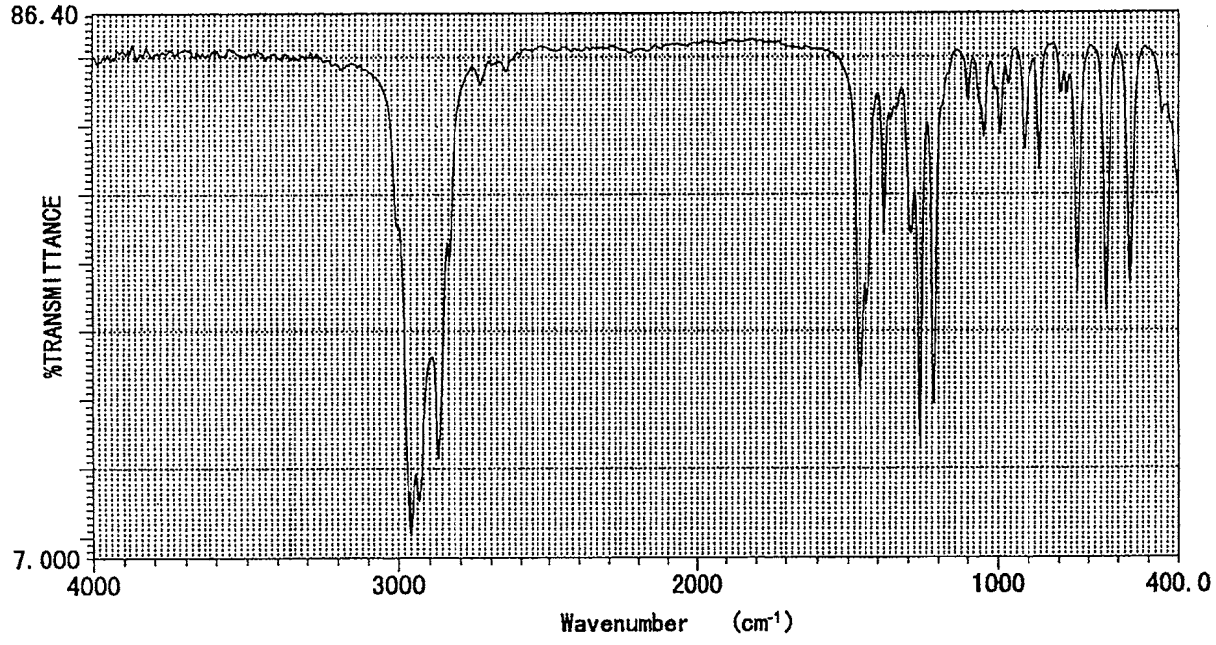
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

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 1-bromobutane by mass spectrum and infrared spectrum.

APPENDIX A 2

STABILITY OF 1-BROMOBUTANE IN THE 13-WEEK INHALATION STUDY

STABILITY OF 1-BROMOBUTANE IN THE 13-WEEK INHALATION STUDY

Test Substance : 1-Bromobutane (Wako Pure Chemical Industries, Ltd.)

Lot No. : ASQ0017

1. Sample : This lot was used from 2003.9.25 to 2003.12.24. 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 : 100° C

Flow Rate : 15 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μL

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
2003.09.11	1	4.096	100
2003.12.26	1	4.096	100

Result: Gas chromatography indicated one major peak (peak No. 1) analyzed on 2003.9.11 and one major peak(peak No. 1) analyzed on 2003.12.26. No new trace impurity peak in the test substance analyzed on 2003.12.26 was detected.

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

APPENDIX B 1

CONCENTRATION OF 1-BROMOBUTANE IN THE INHALATION CHAMBER OF THE 13-WEEK INHALATION STUDY

CONCENTRATION OF 1-BROMOBUTANE IN THE INHALATION CHAMBER OF THE 13-WEEK INHALATION STUDY

Group Name	Concentration(ppm) Mean ± S.D.
Control	0.0 ± 0.0
31ppm	31.1 ± 0.2
63ppm	63.2 ± 0.4
125ppm	125.3 ± 0.7
250ppm	250.6 ± 1.5
500ppm	500.8 ± 3.0

APPENDIX B 2

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 13-WEEK INHALATION STUDY OF 1-BROMOBUTANE

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 13-WEEK INHALATION STUDY OF 1-BROMOBUTANE

Group Name	Temperature (℃) Mean ± S.D.	Humidity (%) Mean ± S.D.	Ventilation Rate (L/min) Mean ± S.D.	Air Change (time/h) Mean
Control	22.4 ± 0.2	58.8 ± 0.8	104.5 ± 0.6	12.1
31ppm	22.3 ± 0.2	58.1 ± 0.8	104.1 ± 0.7	12.0
63ppm	22.3 ± 0.2	57.6 ± 1.0	104.5 ± 0.7	12.1
125ppm	22.2 ± 0.2	59.8 ± 1.2	104.2 ± 0.6	12.0
250ppm	22.3 ± 0.2	57.2 ± 1.0	104.3 ± 0.5	12.0
500ppm	22.2 ± 0.2	57.5 ± 1.8	104.1 ± 0.6	12.0

APPENDIX C

CLINICAL OBSERVATION : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0504
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7
		1	1	1	1	1	1	1	1	1	1	1	1	1
HUNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	31ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	63ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	125ppm	0	0	1	0	0	0	0	0	0	0	0	0	0
	250ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	500ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
WASTING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	31ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	63ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	125ppm	1	0	0	0	0	0	0	0	0	0	0	0	0
	250ppm	1	0	0	0	0	0	0	0	0	0	0	0	0
	500ppm	0	0	0	0	0	0	0	0	0	0	0	0	0

APPENDIX D 1

BODY WEIGHT CHANGES : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0504
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	24.2± 0.9	25.3± 1.0	26.5± 1.0	27.4± 1.2	28.5± 1.0	29.0± 1.1	29.6± 1.4
31ppm	24.2± 0.9	25.2± 1.1	26.0± 1.2	26.2± 1.4	26.6± 1.5**	27.1± 1.7**	27.6± 1.6**
63ppm	24.2± 1.0	25.2± 0.8	26.2± 1.0	26.4± 0.8	27.0± 1.0*	27.7± 1.3	28.0± 1.4*
125ppm	24.2± 0.9	24.0± 3.0	25.7± 0.6	25.5± 2.0*	26.5± 1.2**	27.2± 1.4*	27.3± 1.5**
250ppm	24.2± 0.9	24.1± 2.6	24.5± 2.4*	25.7± 0.6**	26.5± 1.1**	26.7± 1.1**	27.5± 1.2**
500ppm	24.2± 1.0	24.4± 0.6	25.0± 0.5**	25.3± 0.8**	25.8± 0.7**	26.6± 1.3**	27.2± 1.2**

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

STUDY NO. : 0504
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	30.1± 1.4	30.7± 1.4	31.2± 1.5	31.7± 1.4	32.3± 1.9	32.7± 2.1	33.3± 1.9
31ppm	28.4± 1.7*	29.0± 2.0	29.2± 1.8*	29.9± 2.0	30.7± 2.1	30.8± 2.2	31.6± 2.4
63ppm	28.7± 1.1	29.3± 1.3	29.5± 1.3	29.6± 1.6*	30.2± 1.5*	30.5± 1.5*	31.2± 1.5*
125ppm	28.4± 1.7*	28.8± 1.7*	28.9± 1.7*	29.4± 1.6**	29.9± 1.7*	30.3± 1.7*	30.7± 1.6**
250ppm	27.9± 1.2**	28.2± 1.4**	28.7± 1.2**	29.0± 1.2**	29.4± 1.4**	29.5± 1.4**	30.0± 1.4**
500ppm	27.8± 1.4**	28.4± 1.4**	28.4± 1.9**	29.3± 1.5**	29.7± 1.6**	30.4± 1.8*	30.4± 1.9**

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

APPENDIX D 2

BODY WEIGHT CHANGES : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0504
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	19.4± 0.8	20.4± 0.8	21.2± 0.9	21.8± 1.0	22.2± 0.9	23.1± 0.7	23.7± 1.0
31ppm	19.4± 0.8	20.2± 1.2	21.5± 1.0	21.9± 0.9	22.8± 1.2	23.5± 1.3	23.9± 1.5
63ppm	19.4± 0.8	20.4± 0.8	21.6± 1.0	21.9± 0.9	22.6± 1.2	23.4± 0.9	23.7± 0.9
125ppm	19.4± 0.8	20.3± 0.7	21.2± 0.8	21.5± 0.6	22.4± 0.8	23.1± 0.6	23.4± 0.8
250ppm	19.4± 0.8	20.0± 1.3	21.5± 0.5	21.0± 0.7	22.8± 0.7	23.1± 1.0	23.4± 1.3
500ppm	19.4± 0.8	20.3± 1.1	20.9± 0.9	21.0± 1.0	22.0± 1.2	22.5± 0.6	22.7± 1.0

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

STUDY NO. : 0504
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	23.6± 1.0	24.1± 0.9	24.7± 1.1	24.6± 1.1	24.9± 1.2	25.4± 1.1	25.9± 1.2
31ppm	24.4± 1.2	24.4± 1.4	24.8± 1.3	24.9± 1.1	26.4± 1.9	25.9± 1.9	26.6± 1.8
63ppm	24.1± 1.0	24.6± 0.9	24.6± 1.2	24.8± 1.0	25.3± 0.8	25.9± 1.0	26.1± 1.3
125ppm	24.0± 1.0	24.5± 1.0	24.4± 0.6	25.1± 0.8	25.3± 0.9	25.4± 0.8	25.7± 0.7
250ppm	23.9± 1.4	23.8± 1.0	24.1± 1.1	24.9± 0.9	25.4± 1.2	25.6± 1.2	25.9± 1.3
500ppm	23.4± 1.3	23.5± 1.0	23.7± 1.4	24.5± 0.7	25.1± 1.1	24.6± 1.2	25.1± 1.2

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

APPENDIX E 1

FOOD CONSUMPTION CHANGES : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0504
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	4.6± 0.3	4.5± 0.3	4.7± 0.4	4.7± 0.4	4.7± 0.5	4.4± 0.4	4.7± 0.4
31ppm	4.6± 0.2	4.4± 0.5	4.5± 0.5	4.5± 0.4	4.6± 0.5	4.7± 0.4	4.7± 0.5
63ppm	4.7± 0.4	4.7± 0.3	4.8± 0.4	4.8± 0.5	5.0± 0.5	5.0± 0.4**	5.0± 0.4
125ppm	4.2± 0.9	4.8± 0.7	5.0± 0.8	4.8± 0.5	5.1± 0.6	5.1± 0.6**	4.9± 0.5
250ppm	4.1± 0.7	4.4± 1.0	4.8± 0.5	4.6± 0.4	4.7± 0.4	4.9± 0.5	4.8± 0.5
500ppm	4.1± 0.3*	4.3± 0.2	4.4± 0.3	4.4± 0.3	4.6± 0.3	4.8± 0.3	4.8± 0.4

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

STUDY NO. : 0504
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	4.8± 0.5	4.6± 0.4	4.6± 0.4	4.8± 0.5	4.7± 0.4	4.7± 0.4
31ppm	4.8± 0.5	4.4± 0.4	4.7± 0.5	4.8± 0.4	4.7± 0.5	4.7± 0.4
63ppm	5.0± 0.3	4.8± 0.4	4.7± 0.4	4.9± 0.2	4.9± 0.3	4.7± 0.4
125ppm	5.0± 0.5	4.8± 0.5	4.7± 0.4	4.9± 0.4	4.9± 0.5	4.7± 0.4
250ppm	4.8± 0.4	4.7± 0.3	4.6± 0.3	4.7± 0.3	4.6± 0.4	4.6± 0.3
500ppm	4.9± 0.3	4.7± 0.4	4.8± 0.3	5.0± 0.4	5.0± 0.4	4.7± 0.4

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

APPENDIX E 2

FOOD CONSUMPTION CHANGES : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0504
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± 0.3	3.9± 0.1	4.0± 0.3	4.2± 0.2	4.2± 0.2	4.8± 0.5	4.3± 0.2
31ppm	3.9± 0.2	4.0± 0.3	4.2± 0.2	4.4± 0.3	4.6± 0.3**	4.7± 0.3	4.7± 0.3**
63ppm	3.9± 0.2	4.1± 0.2	4.2± 0.2	4.3± 0.2	4.5± 0.2*	4.5± 0.2	4.5± 0.3
125ppm	3.8± 0.3	4.1± 0.2	4.2± 0.2	4.2± 0.3	4.5± 0.3*	4.5± 0.3	4.7± 0.2**
250ppm	3.5± 0.6	3.9± 0.4	3.9± 0.2	4.1± 0.2	4.3± 0.2	4.4± 0.2	4.5± 0.3
500ppm	3.6± 0.4	3.8± 0.4	4.0± 0.3	4.0± 0.2	4.3± 0.2	4.4± 0.1	4.5± 0.3

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

STUDY NO. : 0504
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	4.5± 0.3	4.3± 0.2	4.2± 0.2	4.3± 0.3	4.3± 0.2	4.2± 0.3
31ppm	4.7± 0.3	4.5± 0.3	4.5± 0.3**	4.9± 0.4**	4.7± 0.3**	4.8± 0.3**
63ppm	4.7± 0.3	4.3± 0.3	4.4± 0.2	4.5± 0.2	4.5± 0.2	4.6± 0.2
125ppm	4.7± 0.3	4.6± 0.3	4.6± 0.2**	4.6± 0.2*	4.6± 0.2*	4.6± 0.3
250ppm	4.5± 0.2	4.5± 0.3	4.5± 0.1*	4.6± 0.2*	4.5± 0.2	4.6± 0.3
500ppm	4.5± 0.1	4.6± 0.3	4.6± 0.3**	4.6± 0.3*	4.6± 0.3	4.9± 1.0*

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

APPENDIX F 1

URINALYSIS : SUMMARY,
MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0504
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

URINALYSIS

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	2	0	0	3	2	3		0	2	7	1	0	0		10	0	0	0	0	0		1	2	4	3	0	0		9	1	0	0	0	
31ppm	8	0	0	0	0	2	4	2		0	0	7	1	0	0		8	0	0	0	0	0		1	3	4	0	0	0		8	0	0	0	0	
63ppm	8	0	0	0	1	3	3	1		0	0	4	4	0	0		8	0	0	0	0	0		0	0	6	2	0	0		8	0	0	0	0	
125ppm	10	0	2	0	1	4	2	1		0	0	8	2	0	0		10	0	0	0	0	0		1	0	8	1	0	0		10	0	0	0	0	
250ppm	9	0	0	1	0	2	3	3		0	2	5	2	0	0		9	0	0	0	0	0		1	2	5	1	0	0		9	0	0	0	0	
500ppm	10	0	1	0	1	4	3	1		0	5	4	1	0	0		10	0	0	0	0	0		3	4	2	1	0	0		10	0	0	0	0	

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

STUDY NO. : 0504 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	
31ppm	8	8	0	0	0	0	
63ppm	8	8	0	0	0	0	
125ppm	10	10	0	0	0	0	
250ppm	9	9	0	0	0	0	
500ppm	10	10	0	0	0	0	

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

APPENDIX F 2

URINALYSIS : SUMMARY,
MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0504 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	0	1	1	8	0		0	3	6	1	0	0		10	0	0	0	0	0		1	9	0	0	0	0		10	0	0	0	0	
31ppm	10	0	0	0	0	2	7	1		0	4	6	0	0	0		10	0	0	0	0	0		4	6	0	0	0	0		10	0	0	0	0	
63ppm	10	0	0	1	0	2	7	0		0	5	5	0	0	0		10	0	0	0	0	0		5	5	0	0	0	0		10	0	0	0	0	
125ppm	10	0	0	0	0	2	6	2		0	4	6	0	0	0		10	0	0	0	0	0		2	8	0	0	0	0		10	0	0	0	0	
250ppm	10	0	0	0	0	3	6	1		0	2	7	1	0	0		10	0	0	0	0	0		0	9	1	0	0	0		10	0	0	0	0	
500ppm	10	0	0	0	0	3	7	0		0	3	7	0	0	0		10	0	0	0	0	0		2	8	0	0	0	0		10	0	0	0	0	

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

STUDY NO. : 0504
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0	
31ppm	10	10	0	0	0	0	
63ppm	10	10	0	0	0	0	
125ppm	10	10	0	0	0	0	
250ppm	10	10	0	0	0	0	
500ppm	10	10	0	0	0	0	

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

APPENDIX G 1

HEMATOLOGY : SUMMARY,
MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0504
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 $10^6/\mu\ell$		HEMOGLOBIN g/dℓ		HEMATOCRIT %		MCV fℓ		MCH pg		MCHC g/dℓ		PLATELET $10^3/\mu\ell$	
Control	9	11.01±	0.24	16.1±	0.6	52.2±	1.3	47.4±	0.9	14.6±	0.4	30.8±	1.1	1313±	94
31ppm	10	11.02±	0.28	15.8±	0.4	52.0±	1.0	47.2±	0.5	14.4±	0.1	30.5±	0.3	1336±	93
63ppm	9	10.89±	0.21	15.8±	0.3	51.8±	1.3	47.5±	0.5	14.5±	0.2	30.5±	0.3	1276±	84
125ppm	9	10.86±	0.33	15.8±	0.5	51.8±	1.5	47.7±	0.4	14.5±	0.2	30.4±	0.4	1262±	96
250ppm	10	10.43±	0.47**	15.0±	0.7**	49.8±	2.0*	47.8±	0.5	14.5±	0.1	30.2±	0.3	1293±	151
500ppm	10	10.14±	0.45**	14.9±	0.7**	49.3±	2.3**	48.6±	0.6**	14.7±	0.2	30.2±	0.4	1408±	114

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

STUDY NO. : 0504
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RETICULOCYTE %
Control	9	2.5± 0.2
31ppm	10	2.6± 0.1
63ppm	9	2.5± 0.2
125ppm	9	2.5± 0.1
250ppm	10	2.3± 0.4
500ppm	10	2.7± 0.8

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

STUDY NO. : 0504
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	9	2.67± 1.45	0± 1	12± 4	2± 2	0± 0	3± 2	83± 5	0± 0
31ppm	10	2.62± 1.23	0± 1	11± 4	1± 1	0± 0	3± 2	85± 5	0± 0
63ppm	9	1.88± 1.32	1± 1	13± 4	1± 1	0± 0	4± 3	81± 6	0± 0
125ppm	9	1.61± 1.36	0± 0	14± 6	2± 1	0± 0	2± 1	82± 7	0± 0
250ppm	10	2.27± 1.72	1± 1	14± 5	1± 2	0± 0	2± 1	83± 4	0± 0
500ppm	10	2.33± 1.13	1± 1	12± 4	3± 2	0± 0	3± 1	81± 3	0± 0

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

(HCL070)

APPENDIX G 2

HEMATOLOGY : SUMMARY,
MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0504
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 f ℓ		MCH p g		MCHC g/dℓ		PLATELET $10^3/\mu\ell$	
Control	9	10.81±	0.46	15.9±	0.7	51.2±	2.1	47.3±	0.3	14.7±	0.4	31.2±	0.8	1243±	67
31ppm	10	10.93±	0.29	15.9±	0.5	51.9±	1.3	47.5±	0.5	14.6±	0.1	30.7±	0.4	1236±	80
63ppm	10	10.81±	0.35	15.8±	0.5	51.8±	1.3	47.9±	0.8	14.6±	0.2	30.4±	0.4*	1212±	60
125ppm	9	10.91±	0.35	15.9±	0.6	52.2±	1.5	47.9±	0.5	14.6±	0.1	30.5±	0.4*	1224±	62
250ppm	9	10.60±	0.48	15.7±	0.7	51.3±	2.2	48.4±	0.4**	14.8±	0.1	30.7±	0.1	1245±	94
500ppm	10	10.27±	0.30*	15.3±	0.5	50.1±	1.4	48.9±	0.3**	14.9±	0.1**	30.5±	0.2*	1241±	63

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

Group Name	NO. of Animals	RETICULOCYTE %
Control	9	2.6± 0.2
31ppm	10	2.7± 0.4
63ppm	10	2.5± 0.3
125ppm	9	2.5± 0.4
250ppm	9	2.2± 0.5
500ppm	10	2.3± 0.5

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

STUDY NO. : 0504
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	9	1.86±	1.01	0±	0	13±	5	1±	1	0±	0	2±	1	83±	6	0±	0
31ppm	10	1.77±	1.17	0±	0	17±	6	2±	2	0±	0	1±	1	80±	5	0±	0
63ppm	10	1.41±	1.00	0±	0	14±	6	1±	2	0±	0	1±	1	83±	6	0±	0
125ppm	9	2.10±	1.30	0±	1	20±	7	1±	1	0±	0	2±	1	77±	7	0±	0
250ppm	9	2.11±	1.74	0±	1	20±	7	2±	2	0±	0	2±	2	76±	6*	0±	0
500ppm	10	1.50±	0.72	1±	1	18±	7	2±	1	0±	0	2±	1	78±	6	0±	0

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

APPENDIX H 1

BIOCHEMISTRY : SUMMARY,
MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0504
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	5.0± 0.3	2.8± 0.1	1.3± 0.0	0.14± 0.01	211± 37	81± 14	42± 23
31ppm	10	5.1± 0.2	2.9± 0.1	1.4± 0.0	0.14± 0.02	235± 43	77± 10	30± 9
63ppm	9	5.0± 0.2	2.9± 0.1	1.4± 0.1	0.15± 0.03	191± 43	74± 12	29± 16
125ppm	9	4.9± 0.1	2.8± 0.1	1.4± 0.1	0.14± 0.01	198± 54	75± 7	25± 11
250ppm	10	5.3± 0.2*	3.1± 0.2**	1.4± 0.1	0.16± 0.01	217± 30	97± 14*	29± 12
500ppm	10	5.2± 0.3	3.0± 0.2	1.3± 0.1	0.15± 0.02	241± 73	101± 15**	37± 20

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

STUDY NO. : 0504
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	168± 29	45± 5	20± 4	186± 43	147± 11	1± 1	71± 34
31ppm	10	160± 19	41± 4	18± 2	164± 17	152± 6	1± 1	53± 15
63ppm	9	157± 25	50± 16	21± 6	206± 81	156± 7	1± 1	73± 51
125ppm	9	154± 9	46± 9	20± 4	177± 34	144± 8	0± 1	51± 15
250ppm	10	192± 22	51± 14	74± 42**	196± 31	162± 15**	1± 1	45± 17
500ppm	10	188± 26	42± 12	22± 6	167± 19	145± 12	1± 0	34± 11**

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

STUDY NO. : 0504
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	25.8± 3.0	153± 2	4.3± 0.4	121± 4	8.5± 0.4	8.3± 2.1
31ppm	10	27.9± 2.8	152± 2	4.1± 0.5	121± 2	8.5± 0.3	7.4± 1.4
63ppm	9	26.9± 1.4	152± 1	4.2± 0.5	122± 2	8.6± 0.2	8.0± 1.6
125ppm	9	24.7± 3.4	153± 1	3.9± 0.3	122± 2	8.5± 0.1	7.6± 1.5
250ppm	10	25.9± 3.3	152± 1	4.1± 0.3	121± 2	8.8± 0.2*	7.2± 1.1
500ppm	10	22.7± 2.6	151± 1	4.3± 0.3	122± 2	8.7± 0.2	7.4± 1.1

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

APPENDIX H 2

BIOCHEMISTRY : SUMMARY,
MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0504
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± 0.3	3.2± 0.1	1.7± 0.2	0.15± 0.04	182± 17	86± 11	34± 12
31ppm	10	5.2± 0.2	3.3± 0.2	1.8± 0.2	0.14± 0.03	198± 15	79± 10	27± 18
63ppm	10	5.3± 0.2	3.4± 0.2	1.8± 0.1	0.14± 0.02	198± 22	81± 11	23± 8
125ppm	9	5.3± 0.2	3.4± 0.1	1.8± 0.2	0.14± 0.02	197± 21	77± 12	21± 10
250ppm	9	5.2± 0.3	3.2± 0.2	1.7± 0.1	0.14± 0.02	208± 11	90± 24	25± 20
500ppm	10	5.0± 0.1	3.3± 0.1	1.8± 0.2	0.13± 0.01	205± 34	91± 16	22± 6

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

STUDY NO. : 0504
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	176± 20	64± 21	25± 8	252± 70	224± 21	1± 0	103± 60
31ppm	10	154± 24	62± 23	27± 8	251± 116	233± 29	1± 1	98± 66
63ppm	10	162± 21	66± 22	31± 16	250± 60	243± 30	1± 1	107± 43
125ppm	9	157± 24	59± 17	25± 6	229± 77	238± 19	1± 1	73± 28
250ppm	9	163± 35	51± 15	23± 5	209± 81	223± 18	1± 1	64± 30
500ppm	10	166± 27	55± 22	23± 9	211± 63	230± 21	1± 1	44± 25**

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

STUDY NO. : 0504
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	22.6± 2.3	152± 2	4.2± 0.6	121± 2	8.7± 0.2	6.9± 1.1
31ppm	10	23.6± 3.6	151± 2	3.9± 0.2	120± 3	8.7± 0.2	6.7± 1.2
63ppm	10	24.9± 3.0	152± 2	4.3± 0.3	121± 2	8.7± 0.3	7.2± 1.5
125ppm	9	24.2± 3.2	152± 1	3.8± 0.4	122± 2	8.8± 0.3	6.8± 0.9
250ppm	9	23.2± 2.5	151± 2	4.1± 0.2	123± 2	8.6± 0.2	5.9± 1.1
500ppm	10	21.1± 2.9	150± 2	4.2± 0.2	123± 3	8.6± 0.2	6.2± 1.4

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

APPENDIX I 1

GROSS FINDINGS : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0504
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 (%)	31ppm 10 (%)	63ppm 10 (%)	125ppm 10 (%)
spleen	black zone		0 (0)	1 (10)	0 (0)	0 (0)

STUDY NO. : 0504
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	250ppm		500ppm	
		NO. of Animals	10	(%)	10	(%)
spleen	black zone		0	(0)	1	(10)

APPENDIX I 2

GROSS FINDINGS : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0504
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name / NO. of Animals	Control 10	(%)	31ppm 10	(%)	63ppm 10	(%)	125ppm 10	(%)
spleen	black zone		0	(0)	0	(0)	1	(10)	2	(20)
ovary	cyst		0	(0)	0	(0)	1	(10)	0	(0)

STUDY NO. : 0504
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name / NO. of Animals	250ppm 10	(%)	500ppm 10	(%)
spleen	black zone		0	(0)	0	(0)
ovary	cyst		0	(0)	0	(0)

APPENDIX J 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0504
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	29.7± 2.1	0.036± 0.004	0.010± 0.002	0.232± 0.015	0.175± 0.018	0.176± 0.014
31ppm	10	27.8± 2.2	0.036± 0.004	0.010± 0.002	0.228± 0.023	0.168± 0.012	0.171± 0.011
63ppm	10	27.3± 1.7*	0.036± 0.003	0.010± 0.002	0.241± 0.022	0.176± 0.012	0.168± 0.008
125ppm	10	26.6± 1.5**	0.036± 0.003	0.011± 0.002	0.228± 0.028	0.171± 0.013	0.173± 0.013
250ppm	10	26.0± 1.3**	0.035± 0.005	0.010± 0.001	0.225± 0.014	0.160± 0.010	0.166± 0.010
500ppm	10	26.8± 1.9**	0.035± 0.003	0.009± 0.002	0.222± 0.027	0.166± 0.010	0.181± 0.009

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

STUDY NO. : 0504
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	0.465± 0.026	0.053± 0.006	1.211± 0.061	0.451± 0.012
31ppm	10	0.465± 0.032	0.049± 0.004	1.181± 0.085	0.455± 0.012
63ppm	10	0.476± 0.033	0.051± 0.005	1.216± 0.085	0.451± 0.016
125ppm	10	0.479± 0.029	0.046± 0.007**	1.226± 0.092	0.457± 0.010
250ppm	10	0.488± 0.026	0.049± 0.003	1.236± 0.088	0.454± 0.010
500ppm	10	0.492± 0.027	0.047± 0.004*	1.356± 0.159**	0.443± 0.006

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

APPENDIX J 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0504
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	22.0± 0.9	0.048± 0.006	0.013± 0.002	0.024± 0.003	0.139± 0.005	0.162± 0.013
31ppm	10	22.0± 1.9	0.043± 0.009	0.013± 0.001	0.026± 0.005	0.145± 0.008	0.164± 0.012
63ppm	10	21.7± 1.1	0.047± 0.007	0.012± 0.001	0.029± 0.007	0.140± 0.008	0.164± 0.013
125ppm	10	21.4± 0.7	0.043± 0.006	0.015± 0.003	0.028± 0.005	0.143± 0.006	0.169± 0.008
250ppm	10	21.5± 1.1	0.042± 0.005	0.012± 0.002	0.026± 0.003	0.139± 0.007	0.169± 0.007
500ppm	10	20.9± 1.2	0.041± 0.005	0.011± 0.001*	0.025± 0.004	0.136± 0.008	0.174± 0.007

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

STUDY NO. : 0504
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	0.312± 0.017	0.062± 0.006	0.980± 0.043	0.471± 0.019
31ppm	10	0.313± 0.016	0.058± 0.012	0.986± 0.117	0.474± 0.015
63ppm	10	0.314± 0.012	0.059± 0.006	0.999± 0.070	0.469± 0.015
125ppm	10	0.318± 0.015	0.056± 0.007	1.030± 0.083	0.465± 0.006
250ppm	10	0.316± 0.019	0.053± 0.007*	1.000± 0.071	0.462± 0.008
500ppm	10	0.325± 0.014	0.047± 0.005**	0.982± 0.060	0.453± 0.012*

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

APPENDIX K 1

ORGAN WEIGHT, RELATIVE : SUMMARY, MOUSE : MALE

(13-WEEK STUDY)

STUDY NO. : 0504
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	29.7± 2.1	0.120± 0.015	0.034± 0.007	0.782± 0.064	0.589± 0.044	0.593± 0.057
31ppm	10	27.8± 2.2	0.130± 0.014	0.037± 0.007	0.825± 0.095	0.606± 0.036	0.619± 0.059
63ppm	10	27.3± 1.7*	0.131± 0.014	0.035± 0.007	0.884± 0.092	0.646± 0.053*	0.616± 0.027
125ppm	10	26.6± 1.5**	0.134± 0.015	0.039± 0.006	0.861± 0.122	0.644± 0.041*	0.652± 0.043*
250ppm	10	26.0± 1.3**	0.135± 0.014	0.039± 0.007	0.868± 0.073	0.615± 0.042	0.639± 0.041
500ppm	10	26.8± 1.9**	0.133± 0.013	0.035± 0.006	0.830± 0.096	0.619± 0.050	0.678± 0.035**

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

STUDY NO. : 0504
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	1.569± 0.089	0.179± 0.019	4.082± 0.196	1.525± 0.118
31ppm	10	1.678± 0.062	0.176± 0.015	4.256± 0.116	1.646± 0.096*
63ppm	10	1.744± 0.093**	0.185± 0.012	4.457± 0.232	1.658± 0.110*
125ppm	10	1.803± 0.086**	0.172± 0.020	4.606± 0.205**	1.722± 0.098**
250ppm	10	1.882± 0.132**	0.189± 0.010	4.758± 0.257**	1.750± 0.087**
500ppm	10	1.840± 0.104**	0.175± 0.009	5.054± 0.408**	1.657± 0.106*

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

APPENDIX K 2

ORGAN WEIGHT, RELATIVE : SUMMARY, MOUSE : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0504
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	22.0± 0.9	0.218± 0.025	0.061± 0.007	0.111± 0.015	0.633± 0.020	0.737± 0.043
31ppm	10	22.0± 1.9	0.197± 0.035	0.059± 0.004	0.119± 0.026	0.662± 0.046	0.748± 0.040
63ppm	10	21.7± 1.1	0.218± 0.022	0.057± 0.007	0.132± 0.038	0.647± 0.043	0.756± 0.045
125ppm	10	21.4± 0.7	0.201± 0.021	0.068± 0.013	0.130± 0.020	0.669± 0.019	0.791± 0.037*
250ppm	10	21.5± 1.1	0.194± 0.019	0.058± 0.008	0.119± 0.011	0.648± 0.030	0.787± 0.044*
500ppm	10	20.9± 1.2	0.194± 0.017	0.054± 0.007	0.118± 0.019	0.653± 0.035	0.834± 0.035**

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

STUDY NO. : 0504
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	1.419± 0.061	0.281± 0.019	4.458± 0.177	2.141± 0.090
31ppm	10	1.433± 0.097	0.263± 0.035	4.488± 0.338	2.173± 0.201
63ppm	10	1.449± 0.068	0.271± 0.026	4.605± 0.168	2.166± 0.118
125ppm	10	1.484± 0.049	0.262± 0.028	4.806± 0.278*	2.173± 0.080
250ppm	10	1.473± 0.098	0.246± 0.027*	4.657± 0.288	2.154± 0.116
500ppm	10	1.556± 0.049**	0.226± 0.014**	4.695± 0.207	2.170± 0.101

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

APPENDIX L 1

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

(13-WEEK STUDY)

Organ	Findings	Group Name	Control				31ppm				63ppm				125ppm			
		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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}																		
nasal cavit			<10>				<10>				<10>				<10>			
	eosinophilic change:olfactory epithelium		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	disarrangement:olfactory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lung			<10>				<10>				<10>				<10>			
	basophilic change:bronchiole		0	0	0	0	10	0	0	0 **	10	0	0	0 **	10	0	0	0 **
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Hematopoietic system}																		
spleen			<10>				<10>				<10>				<10>			
	deposit of melanin		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}																		
stomach			<10>				<10>				<10>				<10>			
	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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	250ppm				500ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			<10>				<10>			
	eosinophilic change:olfactory epithelium		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	disarrangement:olfactory epithelium		0	0	0	0	7	0	0	0 **
			(0)	(0)	(0)	(0)	(70)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
lung			<10>				<10>			
	basophilic change:bronchiole		10	0	0	0 **	10	0	0	0 **
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Hematopoietic system}										
spleen			<10>				<10>			
	deposit of melanin		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Digestive system}										
stomach			<10>				<10>			
	erosion:forestomach		3	0	0	0	1	0	0	0
			(30)	(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	Control				31ppm				63ppm				125ppm			
		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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
stomach			<10>				<10>				<10>				<10>			
	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			<10>				<10>				<10>				<10>			
	necrosis:central		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	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		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	nuclear enlargement:central		0	0	0	0	0	0	0	0	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}																		
epididymis			<10>				<10>				<10>				<10>			
	spermatogenic granuloma		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(10)	(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	250ppm				500ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
stomach			<10>				<10>			
	hyperplasia:forestomach		3	7	0	0 **	3	5	0	0 **
			(30)	(70)	(0)	(0)	(30)	(50)	(0)	(0)
liver			<10>				<10>			
	necrosis:central		3	7	0	0 **	2	0	0	0
			(30)	(70)	(0)	(0)	(20)	(0)	(0)	(0)
	necrosis:focal		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	granulation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	nuclear enlargement:central		10	0	0	0 **	1	0	0	0
			(100)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Reproductive system}										
epididymis			<10>				<10>			
	spermatogenic granuloma		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	Control				31ppm				63ppm				125ppm			
		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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Body cavities}																		
adipose			<10>				<10>				<10>				<10>			
	mineralization		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(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	250ppm				500ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Body cavities}										
adipose			<10>				<10>			
	mineralization		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 L 2

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

(13-WEEK STUDY)

Organ	Findings	Grade	Control 1	Control 2	Control 3	Control 4	31ppm 1	31ppm 2	31ppm 3	31ppm 4	63ppm 1	63ppm 2	63ppm 3	63ppm 4	125ppm 1	125ppm 2	125ppm 3	125ppm 4
		No. of Animals on Study	10				10				10				10			
{Respiratory system}																		
nasal cavit			<10>				<10>				<10>				<10>			
	eosinophilic change:olfactory epithelium		0	0	0	0	1	0	0	0	1	1	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(10)	(0)	(0)	(20)	(0)	(0)	(0)
	eosinophilic change:respiratory epithelium		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)
	disarrangement:olfactory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
nasopharynx			<10>				<10>				<10>				<10>			
	eosinophilic change		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)	(0)	(0)	(0)
lung			<10>				<10>				<10>				<10>			
	basophilic change:bronchiole		0	0	0	0	10	0	0	0 **	10	0	0	0 **	10	0	0	0 **
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Hematopoietic system}																		
spleen			<10>				<10>				<10>				<10>			
	deposit of melanin		0	0	0	0	0	0	0	0	1	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(20)	(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	250ppm				500ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			<10>				<10>			
	eosinophilic change:olfactory epithelium		6	0	0	0 *	8	0	0	0 **
			(60)	(0)	(0)	(0)	(80)	(0)	(0)	(0)
	eosinophilic change:respiratory epithelium		7	0	0	0 **	8	0	0	0 **
			(70)	(0)	(0)	(0)	(80)	(0)	(0)	(0)
	disarrangement:olfactory epithelium		1	0	0	0	3	0	0	0
			(10)	(0)	(0)	(0)	(30)	(0)	(0)	(0)
nasopharynx			<10>				<10>			
	eosinophilic change		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lung			<10>				<10>			
	basophilic change:bronchiole		10	0	0	0 **	10	0	0	0 **
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Hematopoietic system}										
spleen			<10>				<10>			
	deposit of melanin		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 / No. of Animals on Study / Grade	Control 10 1 (%)	Control 10 2 (%)	Control 10 3 (%)	Control 10 4 (%)	31ppm 10 1 (%)	31ppm 10 2 (%)	31ppm 10 3 (%)	31ppm 10 4 (%)	63ppm 10 1 (%)	63ppm 10 2 (%)	63ppm 10 3 (%)	63ppm 10 4 (%)	125ppm 10 1 (%)	125ppm 10 2 (%)	125ppm 10 3 (%)	125ppm 10 4 (%)
{Digestive system}																		
stomach			<10>				<10>				<10>				<10>			
	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			<10>				<10>				<10>				<10>			
	necrosis:focal		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	granulation		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)	0 (0)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	hyaline cast		0 (0)	0 (0)	0 (0)	0 (0)	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>			
	cyst		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)

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	250ppm				500ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
stomach			<10>				<10>			
	erosion:forestomach		1	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	hyperplasia:forestomach		6	3	0	0 **	4	6	0	0 **
			(60)	(30)	(0)	(0)	(40)	(60)	(0)	(0)
liver			<10>				<10>			
	necrosis:focal		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Urinary system}										
kidney			<10>				<10>			
	hyaline cast		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(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 M

METHODS, UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK INHALATION STUDY OF 1-BROMOBUTANE

METHODS,UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK INHALATION STUDY OF 1-BROMOBUTANE

Item	Method	Unit	Decimal place
Hematology			
Red blood cell (RBC)	Light scattering method [1]	$\times 10^6/\mu L$	2
Hemoglobin (Hgb)	Cyanmethemoglobin method [1]	g/dL	1
Hematocrit (Hct)	Calculated as RBC×MCV/10 [1]	%	1
Mean corpuscular volume (MCV)	Light scattering method [1]	fL	1
Mean corpuscular hemoglobin (MCH)	Calculated as Hgb/RBC×10 [1]	pg	1
Mean corpuscular hemoglobin concentration (MCHC)	Calculated as Hgb/Hct×100 [1]	g/dL	1
Platelet	Light scattering method [1]	$\times 10^3/\mu L$	0
Reticulocyte	Light scattering method [1]	%	1
White blood cell (WBC)	Light scattering method [1]	$\times 10^3/\mu L$	2
Differential WBC	Pattern recognition method [2] (Wright staining)	%	0
Biochemistry			
Total protein (TP)	Biuret method [3]	g/dL	1
Albumin (Alb)	BCG method [3]	g/dL	1
A/G ratio	Calculated as Alb/(TP−Alb) [3]	−	1
T-bilirubin	Alkaline azobilirubin method [3]	mg/dL	2
Glucose	GlcK·G-6-PDH method [3]	mg/dL	0
T-cholesterol	CE·COD·POD method [3]	mg/dL	0
Triglyceride	LPL·GK·GPO·POD method [3]	mg/dL	0
Phospholipid	PLD·ChOD·POD method [3]	mg/dL	0
Glutamic oxaloacetic transaminase (GOT)	JSCC method [3]	IU/L	0
Glutamic pyruvic transaminase (GPT)	JSCC method [3]	IU/L	0
Lactate dehydrogenase (LDH)	SFBC method [3]	IU/L	0
Alkaline phosphatase (ALP)	GSCC method [3]	IU/L	0
γ-Glutamyl transpeptidase (γ-GTP)	JSCC method [3]	IU/L	0
Creatine phosphokinase (CPK)	JSCC method [3]	IU/L	0
Urea nitrogen	Urease·GLDH method [3]	mg/dL	1
Sodium	Ion selective electrode method [3]	mEq/L	0
Potassium	Ion selective electrode method [3]	mEq/L	1
Chloride	Ion selective electrode method [3]	mEq/L	0
Calcium	OCPC method [3]	mg/dL	1
Inorganic phosphorus	PNP·XOD·POD method [3]	mg/dL	1

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.)