1 - ブロモブタンのマウスを用いた
吸入による2週間毒性試験報告書

試験番号：0481

APPENDICES

APPENDICES

APPENDICES (CONTINUED)

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APPENDIX A 1

IDENTITY OF 1-BROMOBUTANE IN THE 2-WEEK INHALATION STUDY

IDENTITY OF 1-BROMOBUTANE IN THE 2-WEEK INHALATION STUDY

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

Lot No. : ASQ0017

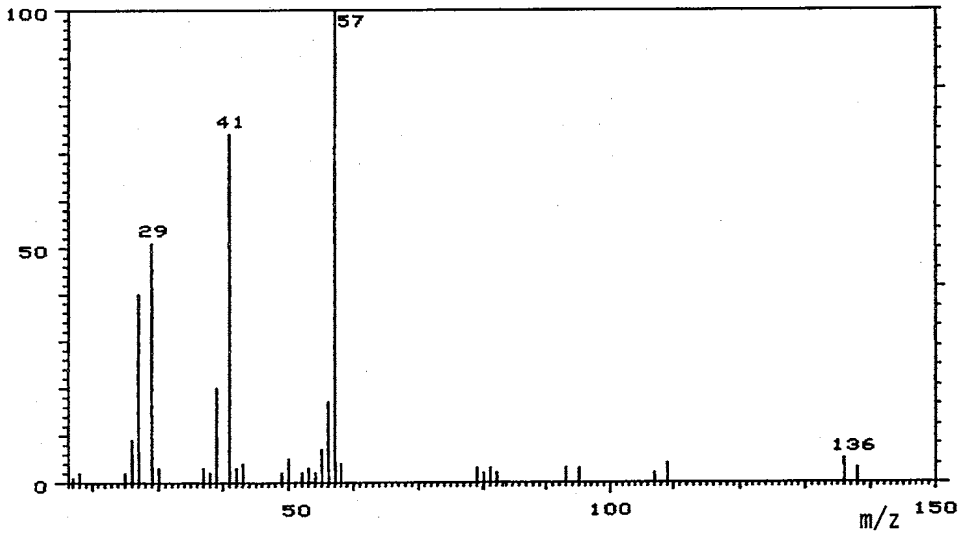
1. Spectral Data

Mass Spectrometry

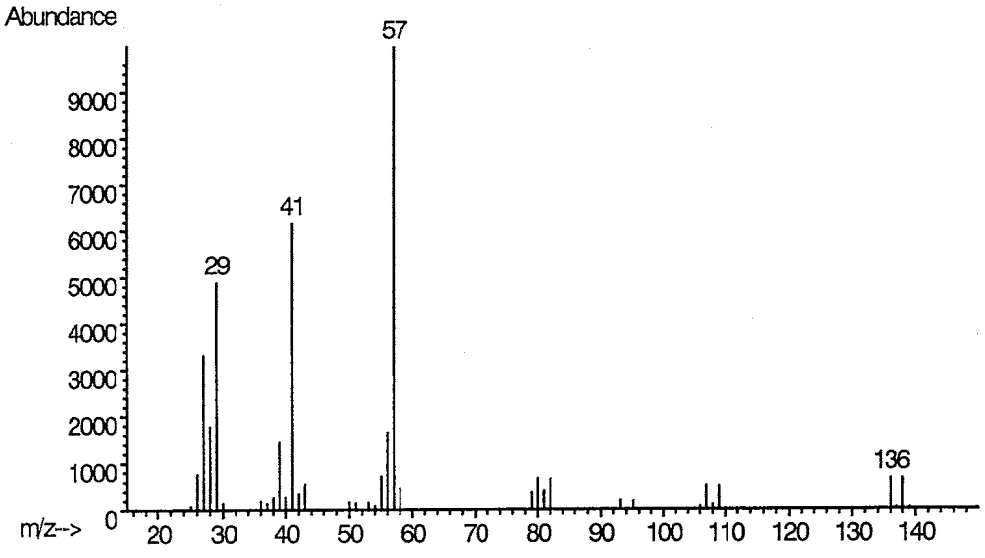
Instrument : Hitachi M-80B Mass Spectrometer

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.

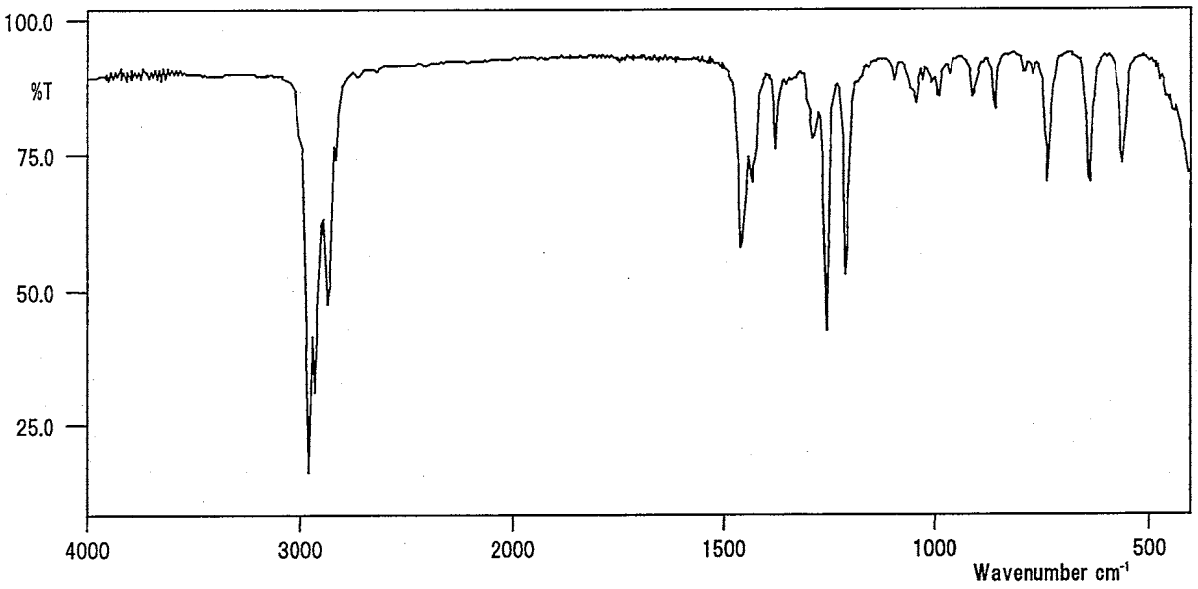
(*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed. New York, NY:John Wiley and Sons.)

Infrared Spectrometry

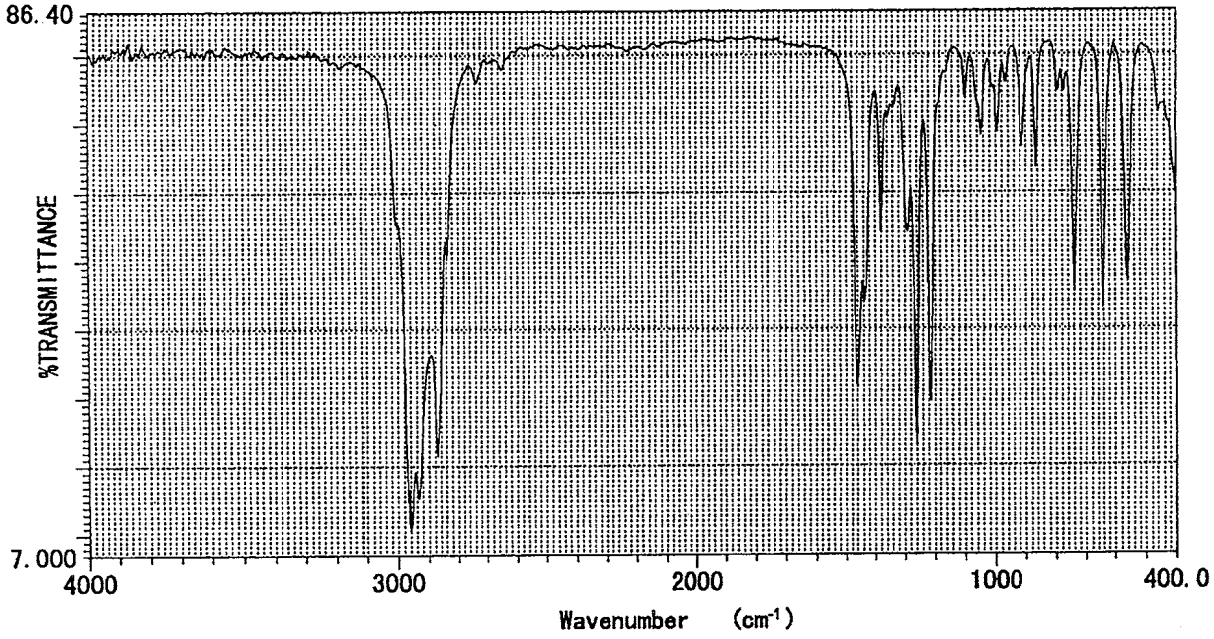
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

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 2-WEEK INHALATION STUDY

STABILITY OF 1-BROMOBUTANE IN THE 2-WEEK INHALATION STUDY

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

Lot No. : ASQ0017

1. Sample : This lot was used from 2003.4.9 to 2003.4.22. 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 (%)
2003.03.19	1	4.139	100
2003.04.25	1	4.127	100

Result: Gas chromatography indicated one major peak (peak No. 1) analyzed on 2003.3.19 and one major peak(peak No. 1) analyzed on 2003.4.25. No new trace impurity peak in the test substance analyzed on 2003.4.25 was detected.

3. Conclusion: The test substance was stable for about 1 month in a dark place at room temperature.

APPENDIX B 1

CONCENTRATION OF 1-BROMOBUTANE IN THE INHALATION CHAMBER OF THE 2-WEEK INHALATION STUDY

CONCENTRATION OF 1-BROMOBUTANE IN THE INHALATION CHAMBER OF THE 2-WEEK INHALATION STUDY

Group Name	Concentration(ppm) Mean ± S.D.
Control	0.0 ± 0.0
500ppm	500.3 ± 2.5
1000ppm	1000.5 ± 3.6
2000ppm	2000.6
4000ppm	4003.7
8000ppm	8034.9

APPENDIX B 2

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 2-WEEK INHALATION STUDY OF 1-BROMOBUTANE

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 2-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	22.6 ± 0.1	59.1 ± 0.6	104.6 ± 0.3	12.1
500ppm	22.3 ± 0.1	60.5 ± 0.4	104.2 ± 0.4	12.0
1000ppm	22.2 ± 0.1	60.7 ± 0.5	104.6 ± 1.5	12.1
2000ppm	22.2 ± 0.4	61.1 ± 0.6	104.5 ± 0.8	12.1
4000ppm	22.3	58.6	106.0	12.2
8000ppm	22.5	53.8	106.5	12.3

APPENDIX C 1

CLINICAL OBSERVATION : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0481
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 1-1	1-2	1-4	1-7	2-3	2-7
LOCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0	0
	500ppm	0	0	0	0	0	0
	1000ppm	5	0	1	-	-	-
	2000ppm	4	-	-	-	-	-
	4000ppm	-	-	-	-	-	-
	8000ppm	-	-	-	-	-	-
HUNCHBACK POSITION	Control	0	0	0	0	0	0
	500ppm	0	0	0	0	0	0
	1000ppm	0	1	1	-	-	-
	2000ppm	0	-	-	-	-	-
	4000ppm	-	-	-	-	-	-
	8000ppm	-	-	-	-	-	-
PILOERECTION	Control	0	0	0	0	0	0
	500ppm	0	0	0	0	0	0
	1000ppm	5	1	1	-	-	-
	2000ppm	4	-	-	-	-	-
	4000ppm	-	-	-	-	-	-
	8000ppm	-	-	-	-	-	-
SOILED PERI-GENITALIA	Control	0	0	0	0	0	0
	500ppm	0	0	0	0	0	0
	1000ppm	0	0	1	-	-	-
	2000ppm	0	-	-	-	-	-
	4000ppm	-	-	-	-	-	-
	8000ppm	-	-	-	-	-	-
IRREGULAR BREATHING	Control	0	0	0	0	0	0
	500ppm	0	0	0	0	0	0
	1000ppm	5	0	0	-	-	-
	2000ppm	4	-	-	-	-	-
	4000ppm	-	-	-	-	-	-
	8000ppm	-	-	-	-	-	-
BRADYPNEA	Control	0	0	0	0	0	0
	500ppm	0	0	0	0	0	0
	1000ppm	0	0	1	-	-	-
	2000ppm	4	-	-	-	-	-
	4000ppm	-	-	-	-	-	-
	8000ppm	-	-	-	-	-	-

STUDY NO. : 0481
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 1-1	1-2	1-4	1-7	2-3	2-7
SUBNORMAL TEMP	Control	0	0	0	0	0	0
	500ppm	0	0	0	0	0	0
	1000ppm	0	0	0	-	-	-
	2000ppm	4	-	-	-	-	-
	4000ppm	-	-	-	-	-	-
	8000ppm	-	-	-	-	-	-

APPENDIX C 2

CLINICAL OBSERVATION : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

Clinical sign	Group Name	Administration Week-day 1-1	1-2	1-4	1-7	2-3	2-7
LOCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0	0
	500ppm	0	0	0	0	0	0
	1000ppm	0	0	0	0	0	0
	2000ppm	5	-	-	-	-	-
	4000ppm	-	-	-	-	-	-
	8000ppm	-	-	-	-	-	-
HUNCHBACK POSITION	Control	0	0	0	0	0	0
	500ppm	0	0	0	0	0	0
	1000ppm	0	0	0	0	2	2
	2000ppm	0	-	-	-	-	-
	4000ppm	-	-	-	-	-	-
	8000ppm	-	-	-	-	-	-
PILOERECTION	Control	0	0	0	0	0	0
	500ppm	0	0	0	0	0	0
	1000ppm	0	0	0	0	1	0
	2000ppm	5	-	-	-	-	-
	4000ppm	-	-	-	-	-	-
	8000ppm	-	-	-	-	-	-
IRREGULAR BREATHING	Control	0	0	0	0	0	0
	500ppm	0	0	0	0	0	0
	1000ppm	0	0	0	0	0	2
	2000ppm	5	-	-	-	-	-
	4000ppm	-	-	-	-	-	-
	8000ppm	-	-	-	-	-	-
BRADYPNEA	Control	0	0	0	0	0	0
	500ppm	0	0	0	0	0	0
	1000ppm	0	0	0	0	0	0
	2000ppm	5	-	-	-	-	-
	4000ppm	-	-	-	-	-	-
	8000ppm	-	-	-	-	-	-
SUBNORMAL TEMP	Control	0	0	0	0	0	0
	500ppm	0	0	0	0	0	0
	1000ppm	0	0	0	0	0	0
	2000ppm	5	-	-	-	-	-
	4000ppm	-	-	-	-	-	-
	8000ppm	-	-	-	-	-	-

APPENDIX D 1

BODY WEIGHT CHANGES : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0481
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	1-2	1-4	1-7	2-3	2-7
Control	23.1± 1.2	23.5± 1.0	23.8± 1.0	24.4± 1.2	24.8± 1.3	25.3± 1.3
500ppm	23.1± 1.3	22.6± 1.1	23.2± 0.9	23.5± 1.2	25.0± 1.3	24.8± 1.0
1000ppm !	23.1± 1.2	19.7	17.2	-	-	-
2000ppm	23.1± 1.3	-	-	-	-	-
4000ppm	23.1± 0.9	-	-	-	-	-
8000ppm	23.1± 0.8	-	-	-	-	-

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

! : Significant test is not applied to this group.

APPENDIX D 2

BODY WEIGHT CHANGES : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0481
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	1-2	1-4	1-7	2-3	2-7
Control	19.2± 0.8	19.2± 0.8	19.4± 0.3	19.6± 0.8	20.7± 0.8	20.8± 0.6
500ppm	19.1± 0.9	18.5± 1.3	19.3± 0.8	19.3± 1.2	20.4± 0.9	19.6± 1.0
1000ppm	19.1± 0.9	18.2± 0.3	19.0± 0.5	19.1± 0.3	18.6± 1.4*	17.5± 1.3**
2000ppm	19.2± 0.8	-	-	-	-	-
4000ppm	19.2± 0.9	-	-	-	-	-
8000ppm	19.2± 0.8	-	-	-	-	-

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

APPENDIX E 1

FOOD CONSUMPTION CHANGES : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0481
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration 1-7(6)	week-day(effective) 2-7(7)
Control	4.4± 0.4	4.2± 0.4
500ppm	4.1± 0.3	4.5± 0.2
1000ppm	-	-
2000ppm	-	-
4000ppm	-	-
8000ppm	-	-

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

APPENDIX E 2

FOOD CONSUMPTION CHANGES : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0481
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration 1-7(6)	week-day(effective) 2-7(7)
Control	3.5± 0.3	3.7± 0.3
500ppm	3.7± 0.2	3.9± 0.1
1000ppm	3.7± 0.2	3.3± 0.5
2000ppm	-	-
4000ppm	-	-
8000ppm	-	-

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

APPENDIX F 1

HEMATOLOGY : SUMMARY,
MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0481
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (3W)

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	5	11.08± 0.34	16.4± 0.5	51.1± 2.0	46.1± 0.9	14.8± 0.2	32.1± 0.3	1242± 56
500ppm	4	10.40± 0.21**	15.3± 0.3**	48.2± 0.8*	46.4± 0.2	14.8± 0.2	31.8± 0.2	1262± 59
1000ppm	0	-	-	-	-	-	-	-
2000ppm	0	-	-	-	-	-	-	-
4000ppm	0	-	-	-	-	-	-	-
8000ppm	0	-	-	-	-	-	-	-

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

STUDY NO. : 0481
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (3W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHER
Control	5	1.50± 0.71	0± 1	16± 7	2± 1	0± 0	1± 1	80± 5	0± 0
500ppm	4	2.74± 1.03	1± 1	7± 1*	2± 1	0± 0	1± 1	89± 1*	0± 0
1000ppm	0	-	-	-	-	-	-	-	-
2000ppm	0	-	-	-	-	-	-	-	-
4000ppm	0	-	-	-	-	-	-	-	-
8000ppm	0	-	-	-	-	-	-	-	-

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

APPENDIX F 2

HEMATOLOGY : SUMMARY,
MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0481
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (3W)

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	5	11.14± 0.19	16.5± 0.2	51.0± 0.8	45.8± 0.2	14.8± 0.1	32.4± 0.3	1115± 50
500ppm	5	10.46± 0.23**	15.7± 0.4*	48.4± 0.9**	46.3± 0.7	15.0± 0.1*	32.5± 0.4	1112± 98
1000ppm	5	10.49± 0.29**	15.5± 0.5**	47.4± 1.4**	45.2± 0.7	14.7± 0.1	32.6± 0.6	1218± 69
2000ppm	0	-	-	-	-	-	-	-
4000ppm	0	-	-	-	-	-	-	-
8000ppm	0	-	-	-	-	-	-	-

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

STUDY NO. : 0481
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (3W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHER
Control	5	1.84± 0.79	1± 1	11± 4	1± 1	0± 0	1± 1	87± 4	0± 0
500ppm	5	1.33± 0.23	0± 1	13± 5	3± 2	0± 0	1± 1	83± 6	0± 0
1000ppm	5	0.78± 0.45*	0± 0	15± 4	3± 3	0± 0	2± 2	80± 4	0± 0
2000ppm	0	-	-	-	-	-	-	-	-
4000ppm	0	-	-	-	-	-	-	-	-
8000ppm	0	-	-	-	-	-	-	-	-

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

APPENDIX G 1

BIOCHEMISTRY : SUMMARY,
MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0481
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (3W)

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	5	5.2± 0.3	3.0± 0.0	1.4± 0.1	0.16± 0.04	224± 27	75± 10	32± 16
500ppm	5	4.9± 0.1*	2.9± 0.2	1.4± 0.2	0.16± 0.02	252± 21	100± 15*	24± 7
1000ppm	0	-	-	-	-	-	-	-
2000ppm	0	-	-	-	-	-	-	-
4000ppm	0	-	-	-	-	-	-	-
8000ppm	0	-	-	-	-	-	-	-

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

STUDY NO. : 0481
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (3W)

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	5	165± 21	42± 6	20± 6	265± 146	280± 16	1± 1	161± 127
500ppm	5	177± 20	37± 4	20± 6	178± 63	249± 12**	2± 1	56± 21
1000ppm	0	-	-	-	-	-	-	-
2000ppm	0	-	-	-	-	-	-	-
4000ppm	0	-	-	-	-	-	-	-
8000ppm	0	-	-	-	-	-	-	-

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

STUDY NO. : 0481
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (3W)

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	5	28.3± 3.8	149± 1	5.1± 0.6	118± 2	8.7± 0.1	5.9± 1.2
500ppm	5	14.7± 1.4**	148± 1	4.9± 0.4	121± 2*	8.7± 0.2	7.1± 1.0
1000ppm	0	-	-	-	-	-	-
2000ppm	0	-	-	-	-	-	-
4000ppm	0	-	-	-	-	-	-
8000ppm	0	-	-	-	-	-	-

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

APPENDIX G 2

BIOCHEMISTRY : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0481
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (3W)

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	5	5.3± 0.2	3.5± 0.2	2.0± 0.3	0.15± 0.03	172± 28	75± 9	19± 7
500ppm	5	5.1± 0.1	3.3± 0.0	1.8± 0.1	0.15± 0.02	223± 16	92± 10	21± 7
1000ppm	5	5.4± 0.2	3.6± 0.2	2.0± 0.3	0.18± 0.02	188± 67	109± 23**	17± 12
2000ppm	0	-	-	-	-	-	-	-
4000ppm	0	-	-	-	-	-	-	-
8000ppm	0	-	-	-	-	-	-	-

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

STUDY NO. : 0481
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (3W)

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	5	153± 10	49± 7	22± 5	259± 82	413± 46	1± 1	123± 72
500ppm	5	154± 14	41± 3	21± 4	190± 71	328± 12**	1± 1	65± 52
1000ppm	5	160± 43	56± 11	24± 6	253± 60	340± 46*	1± 1	53± 32
2000ppm	0	-	-	-	-	-	-	-
4000ppm	0	-	-	-	-	-	-	-
8000ppm	0	-	-	-	-	-	-	-

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

STUDY NO. : 0481
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (3W)

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	5	24.7± 2.8	150± 2	4.6± 0.3	119± 1	8.7± 0.2	6.3± 1.6
500ppm	5	13.4± 3.0**	147± 1	4.4± 0.4	118± 1	8.4± 0.4	6.4± 1.3
1000ppm	5	14.3± 7.1**	147± 3	4.1± 0.3	119± 4	8.6± 0.3	6.5± 1.0
2000ppm	0	-	-	-	-	-	-
4000ppm	0	-	-	-	-	-	-
8000ppm	0	-	-	-	-	-	-

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

APPENDIX H 1

GROSS FINDINGS : SUMMARY, MOUSE : MALE : DEAD AND MORIBUND ANIMALS (2-WEEK STUDY)

STUDY NO. : 0481
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 3W)

Organ	Findings	Group Name / NO. of Animals	Control 0	(%)	500ppm 0	(%)	1000ppm 5	(%)	2000ppm 5	(%)
lung	red		-	(-)	-	(-)	0	(0)	1	(20)
	red zone		-	(-)	-	(-)	1	(20)	3	(60)
liver	white zone		-	(-)	-	(-)	1	(20)	0	(0)
	red zone		-	(-)	-	(-)	1	(20)	0	(0)
	accentuation of lobular structure		-	(-)	-	(-)	2	(40)	0	(0)

Organ	Findings	Group Name / NO. of Animals	4000ppm 5	(%)	8000ppm 5	(%)
lung	red		0	(0)	0	(0)
	red zone		2	(40)	3	(60)
liver	white zone		0	(0)	0	(0)
	red zone		0	(0)	0	(0)
	accentuation of lobular structure		0	(0)	0	(0)

APPENDIX H 2

GROSS FINDINGS : SUMMARY,
MOUSE : MALE :
SACRIFICED ANIMALS
(2-WEEK STUDY)

STUDY NO. : 0481
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (3W)

Organ	Findings	Group Name / NO. of Animals	Control 5	(%)	500ppm 5	(%)	1000ppm 0	(%)	2000ppm 0	(%)
spleen	black zone		0	(0)	1	(20)	-	(-)	-	(-)
forestomach	thick		0	(0)	1	(20)	-	(-)	-	(-)
liver	white zone		0	(0)	1	(20)	-	(-)	-	(-)

STUDY NO. : 0481
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (3W)

Organ	Findings	Group Name / NO. of Animals	0 (%)	4000ppm 0 (%)	8000ppm 0 (%)
spleen	black zone		- (-)	- (-)	
forestomach	thick		- (-)	- (-)	
liver	white zone		- (-)	- (-)	

APPENDIX H 3

GROSS FINDINGS : SUMMARY, MOUSE : FEMALE : DEAD AND MORIBUND ANIMALS (2-WEEK STUDY)

STUDY NO. : 0481
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 3W)

Organ	Findings	Group Name / NO. of Animals	Control 0	(%)	500ppm 0	(%)	1000ppm 0	(%)	2000ppm 5	(%)
lung	red		-	(-)	-	(-)	-	(-)	1	(20)
	red zone		-	(-)	-	(-)	-	(-)	3	(60)
spleen	black zone		-	(-)	-	(-)	-	(-)	1	(20)
liver	accentuation of lobular structure		-	(-)	-	(-)	-	(-)	5	(100)
thoracic ca	pleural fluid		-	(-)	-	(-)	-	(-)	3	(60)

STUDY NO. : 0481
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 3W)

Organ	Findings	Group Name / NO. of Animals	4000ppm 5 (%)	8000ppm 5 (%)
lung	red		0 (0)	0 (0)
	red zone		0 (0)	3 (60)
spleen	black zone		0 (0)	0 (0)
liver	accentuation of lobular structure		0 (0)	0 (0)
thoracic ca	pleural fluid		0 (0)	0 (0)

APPENDIX H 4

GROSS FINDINGS : SUMMARY, MOUSE : FEMALE : SACRIFICED ANIMALS (2-WEEK STUDY)

Organ	Findings	Group Name / NO. of Animals	Control 5 (%)	500ppm 5 (%)	1000ppm 5 (%)	2000ppm 0 (%)
thymus	atrophic		0 (0)	0 (0)	1 (20)	- (-)
spleen	black zone		1 (20)	0 (0)	0 (0)	- (-)
forestomach	thick		0 (0)	1 (20)	1 (20)	- (-)
ovary	cyst		1 (20)	0 (0)	0 (0)	- (-)

STUDY NO. : 0481
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (3W)

Organ	Findings	Group Name / NO. of Animals	0	4000ppm (%)	0	8000ppm (%)
thymus	atrophic		-	(-)	-	(-)
spleen	black zone		-	(-)	-	(-)
forestomach	thick		-	(-)	-	(-)
ovary	cyst		-	(-)	-	(-)

APPENDIX I 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0481
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (3W)

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	5	21.4± 0.9	0.049± 0.006	0.011± 0.002	0.186± 0.021	0.126± 0.024	0.141± 0.017
500ppm	5	21.6± 1.0	0.028± 0.005**	0.010± 0.003	0.177± 0.020	0.123± 0.013	0.150± 0.010
1000ppm	0	-	-	-	-	-	-
2000ppm	0	-	-	-	-	-	-
4000ppm	0	-	-	-	-	-	-
8000ppm	0	-	-	-	-	-	-

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

STUDY NO. : 0481
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (3W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.330± 0.027	0.037± 0.007	0.962± 0.032	0.431± 0.035
500ppm	5	0.351± 0.039	0.032± 0.004	1.077± 0.084*	0.420± 0.016
1000ppm	0	-	-	-	-
2000ppm	0	-	-	-	-
4000ppm	0	-	-	-	-
8000ppm	0	-	-	-	-

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

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PPENDIX I 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0481
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (3W)

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	5	17.2± 0.8	0.061± 0.006	0.009± 0.002	0.022± 0.005	0.102± 0.013	0.124± 0.005
500ppm	5	16.9± 1.0	0.032± 0.002**	0.010± 0.001	0.016± 0.004	0.096± 0.005	0.136± 0.012
1000ppm	5	15.3± 1.1*	0.022± 0.009**	0.011± 0.002	0.014± 0.002*	0.097± 0.015	0.137± 0.005*
2000ppm	0	-	-	-	-	-	-
4000ppm	0	-	-	-	-	-	-
8000ppm	0	-	-	-	-	-	-

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

STUDY NO. : 0481
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (3W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.231± 0.009	0.036± 0.005	0.753± 0.047	0.428± 0.013
500ppm	5	0.248± 0.016	0.029± 0.002	0.814± 0.045	0.422± 0.010
1000ppm	5	0.236± 0.010	0.026± 0.006**	0.806± 0.060	0.414± 0.008
2000ppm	0	-	-	-	-
4000ppm	0	-	-	-	-
8000ppm	0	-	-	-	-

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

APPENDIX J 1

ORGAN WEIGHT, RELATIVE : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0481
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (3W)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	5	21.4± 0.9	0.227± 0.027	0.050± 0.008	0.866± 0.077	0.585± 0.099	0.655± 0.068
500ppm	5	21.6± 1.0	0.130± 0.023**	0.045± 0.013	0.820± 0.084	0.566± 0.047	0.694± 0.019
1000ppm	0	-	-	-	-	-	-
2000ppm	0	-	-	-	-	-	-
4000ppm	0	-	-	-	-	-	-
8000ppm	0	-	-	-	-	-	-

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

STUDY NO. : 0481
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (3W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	1.538± 0.105	0.170± 0.025	4.490± 0.215	2.009± 0.110
500ppm	5	1.619± 0.133	0.147± 0.012	4.974± 0.224**	1.944± 0.080
1000ppm	0	-	-	-	-
2000ppm	0	-	-	-	-
4000ppm	0	-	-	-	-
8000ppm	0	-	-	-	-

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

APPENDIX J 2

ORGAN WEIGHT, RELATIVE : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0481
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (3W)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	5	17.2± 0.8	0.356± 0.043	0.050± 0.011	0.129± 0.027	0.594± 0.050	0.719± 0.025
500ppm	5	16.9± 1.0	0.192± 0.018**	0.057± 0.007	0.095± 0.025	0.570± 0.037	0.802± 0.037
1000ppm	5	15.3± 1.1*	0.141± 0.054**	0.071± 0.011*	0.092± 0.008*	0.629± 0.054	0.899± 0.085**
2000ppm	0	-	-	-	-	-	-
4000ppm	0	-	-	-	-	-	-
8000ppm	0	-	-	-	-	-	-

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

STUDY NO. : 0481
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (3W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	1.346± 0.012	0.208± 0.020	4.380± 0.171	2.495± 0.170
500ppm	5	1.470± 0.096*	0.172± 0.007*	4.825± 0.104*	2.504± 0.105
1000ppm	5	1.546± 0.105**	0.166± 0.027*	5.267± 0.310**	2.710± 0.161
2000ppm	0	-	-	-	-
4000ppm	0	-	-	-	-
8000ppm	0	-	-	-	-

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

APPENDIX K 1

HISTOPATHOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY, MOUSE : MALE : DEAD AND MORIBUND ANIMALS (2-WEEK STUDY)

Organ	Findings	Group Name	Control				500ppm				1000ppm				2000ppm			
		No. of Animals on Study	0				0				5				5			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}																		
nasal cavit			< 0>				< 0>				< 5>				< 5>			
	necrosis:olfactory epithelium		-	-	-	-	-	-	-	-	3	2	0	0	0	2	0	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(60)	(40)	(0)	(0)	(0)	(40)	(0)	(0)
lung			< 0>				< 0>				< 5>				< 5>			
	congestion		-	-	-	-	-	-	-	-	1	0	0	0	0	4	1	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(20)	(0)	(0)	(0)	(0)	(80)	(20)	(0)
	hemorrhage		-	-	-	-	-	-	-	-	0	0	0	0	0	1	0	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)
	edema		-	-	-	-	-	-	-	-	0	0	0	0	0	1	0	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)
	edema:perivascular		-	-	-	-	-	-	-	-	3	2	0	0	4	1	0	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(60)	(40)	(0)	(0)	(80)	(20)	(0)	(0)
{Hematopoietic system}																		
thymus			< 0>				< 0>				< 5>				< 5>			
	atrophy		-	-	-	-	-	-	-	-	0	0	1	0	0	0	0	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(0)	(0)	(20)	(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	4000ppm				8000ppm			
		No. of Animals on Study	5				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			< 5>				< 5>			
	necrosis:olfactory epithelium		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lung			< 5>				< 5>			
	congestion		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hemorrhage		0	2	0	0	3	0	0	0
			(0)	(40)	(0)	(0)	(60)	(0)	(0)	(0)
	edema		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	edema:perivascular		4	0	0	0	0	0	0	0
			(80)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}										
thymus			< 5>				< 5>			
	atrophy		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	Control				500ppm				1000ppm				2000ppm			
		No. of Animals on Study	0				0				5				5			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}																		
spleen			< 0>				< 0>				< 5>				< 5>			
	atrophy		-	-	-	-	-	-	-	-	1	0	0	0	0	0	0	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Circulatory system}																		
heart			< 0>				< 0>				< 5>				< 5>			
	hemorrhage		-	-	-	-	-	-	-	-	0	0	0	0	3	0	0	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(0)	(0)	(0)	(0)	(60)	(0)	(0)	(0)
	ground glass appearance		-	-	-	-	-	-	-	-	0	4	0	0	0	0	0	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(0)	(80)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}																		
liver			< 0>				< 0>				< 5>				< 5>			
	necrosis:central		-	-	-	-	-	-	-	-	0	0	1	0	5	0	0	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(0)	(0)	(20)	(0)	(100)	(0)	(0)	(0)
	vacuolic change		-	-	-	-	-	-	-	-	5	0	0	0	4	1	0	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)	(80)	(20)	(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	4000ppm				8000ppm			
		No. of Animals on Study	5				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
spleen			< 5>				< 5>			
	atrophy		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Circulatory system}										
heart			< 5>				< 5>			
	hemorrhage		3	2	0	0	0	0	0	0
			(60)	(40)	(0)	(0)	(0)	(0)	(0)	(0)
	ground glass appearance		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}										
liver			< 5>				< 5>			
	necrosis:central		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	vacuolic change		5	0	0	0	1	4	0	0
			(100)	(0)	(0)	(0)	(20)	(80)	(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 / No. of Animals on Study / Grade	Control 0 1 (%)	Control 0 2 (%)	Control 0 3 (%)	Control 0 4 (%)	500ppm 0 1 (%)	500ppm 0 2 (%)	500ppm 0 3 (%)	500ppm 0 4 (%)	1000ppm 5 1 (%)	1000ppm 5 2 (%)	1000ppm 5 3 (%)	1000ppm 5 4 (%)	2000ppm 5 1 (%)	2000ppm 5 2 (%)	2000ppm 5 3 (%)	2000ppm 5 4 (%)
{Digestive system}																		
liver			< 0>				< 0>				< 5>				< 5>			
	hydropic change		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	1 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hemorrhage:central		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	0 (0)	0 (0)	5 (100)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hemorrhage:portal		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)
{Urinary system}																		
kidney			< 0>				< 0>				< 5>				< 5>			
	tubular necrosis:proximale tubule		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
{Reproductive system}																		
testis			< 0>				< 0>				< 5>				< 5>			
	germ cell necrosis		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	0 (0)	1 (20)	0 (0)	0 (0)	1 (20)	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	4000ppm				8000ppm			
		No. of Animals on Study	5				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
liver			< 5>				< 5>			
	hydropic change		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hemorrhage:central		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hemorrhage:portal		0	2	3	0	0	0	0	0
			(0)	(40)	(60)	(0)	(0)	(0)	(0)	(0)
{Urinary system}										
kidney			< 5>				< 5>			
	tubular necrosis:proximale tubule		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Reproductive system}										
testis			< 5>				< 5>			
	germ cell necrosis		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

APPENDIX K 2

HISTOPATHOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY, MOUSE : MALE : SACRIFICED ANIMALS (2-WEEK STUDY)

STUDY NO. : 0481
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (3W)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 5				500ppm 5				1000ppm 0				2000ppm 0			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Respiratory system}																		
nasal cavit			< 5>				< 5>				< 0>				< 0>			
	atrophy:olfactory epithelium		0	0	0	0	5	0	0	0	-	-	-	-	-	-	-	-
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
lung			< 5>				< 5>				< 0>				< 0>			
	basophilic change:bronchiole		0	0	0	0	5	0	0	0	-	-	-	-	-	-	-	-
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{Hematopoietic system}																		
thymus			< 5>				< 5>				< 0>				< 0>			
	atrophy		0	0	0	0	2	0	0	0	-	-	-	-	-	-	-	-
			(0)	(0)	(0)	(0)	(40)	(0)	(0)	(0)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
spleen			< 5>				< 5>				< 0>				< 0>			
	deposit of melanin		0	0	0	0	1	0	0	0	-	-	-	-	-	-	-	-
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{Digestive system}																		
stomach			< 5>				< 5>				< 0>				< 0>			
	erosion:forestomach		0	0	0	0	1	0	0	0	-	-	-	-	-	-	-	-
			(0)	(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

Organ	Findings	Group Name	4000ppm				8000ppm			
		No. of Animals on Study	0				0			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			< 0>				< 0>			
	atrophy:olfactory epithelium		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
lung			< 0>				< 0>			
	basophilic change:bronchiole		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{Hematopoietic system}										
thymus			< 0>				< 0>			
	atrophy		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
spleen			< 0>				< 0>			
	deposit of melanin		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{Digestive system}										
stomach			< 0>				< 0>			
	erosion:forestomach		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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				500ppm				1000ppm				2000ppm			
		No. of Animals on Study	5				5				0				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
stomach			< 5>				< 5>				< 0>				< 0>			
	hyperplasia:forestomach		0	0	0	0	0	2	0	0	-	-	-	-	-	-	-	-
			(0)	(0)	(0)	(0)	(0)	(40)	(0)	(0)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
liver			< 5>				< 5>				< 0>				< 0>			
	necrosis:focal		0	0	0	0	0	1	0	0	-	-	-	-	-	-	-	-
			(0)	(0)	(0)	(0)	(0)	(20)	(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	4000ppm				8000ppm			
		No. of Animals on Study	0				0			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
stomach			< 0>				< 0>			
	hyperplasia:forestomach		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
liver			< 0>				< 0>			
	necrosis:focal		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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 3

HISTOPATHOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY, MOUSE : FEMALE : DEAD AND MORIBUND ANIMALS (2-WEEK STUDY)

Organ	Findings	Group Name	Control				500ppm				1000ppm				2000ppm			
		No. of Animals on Study	0				0				0				5			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
{Respiratory system}																		
nasal cavit			< 0>				< 0>				< 0>				< 5>			
	necrosis:olfactory epithelium		-	-	-	-	-	-	-	-	-	-	-	-	4	0	0	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(80)	(0)	(0)	(0)
lung			< 0>				< 0>				< 0>				< 5>			
	congestion		-	-	-	-	-	-	-	-	-	-	-	-	1	1	0	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(20)	(20)	(0)	(0)
	hemorrhage		-	-	-	-	-	-	-	-	-	-	-	-	0	0	0	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(0)	(0)	(0)	(0)
	edema:perivascular		-	-	-	-	-	-	-	-	-	-	-	-	4	1	0	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(80)	(20)	(0)	(0)
{Hematopoietic system}																		
spleen			< 0>				< 0>				< 0>				< 5>			
	deposit of melanin		-	-	-	-	-	-	-	-	-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(20)	(0)	(0)	(0)
{Circulatory system}																		
heart			< 0>				< 0>				< 0>				< 5>			
	hemorrhage		-	-	-	-	-	-	-	-	-	-	-	-	2	0	0	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(40)	(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	4000ppm				8000ppm			
		No. of Animals on Study	5				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			< 5>				< 5>			
	necrosis:olfactory epithelium		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lung			< 5>				< 5>			
	congestion		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hemorrhage		1	0	0	0	3	0	0	0
			(20)	(0)	(0)	(0)	(60)	(0)	(0)	(0)
	edema:perivascular		1	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}										
spleen			< 5>				< 5>			
	deposit of melanin		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Circulatory system}										
heart			< 5>				< 5>			
	hemorrhage		1	0	0	0	0	0	0	0
			(20)	(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	Control				500ppm				1000ppm				2000ppm			
		No. of Animals on Study	0				0				0				5			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Circulatory system}																		
heart			< 0>				< 0>				< 0>				< 5>			
	ground glass appearance		-	-	-	-	-	-	-	-	-	-	-	-	0	3	2	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(0)	(60)	(40)	(0)
{Digestive system}																		
liver			< 0>				< 0>				< 0>				< 5>			
	vacuolic change		-	-	-	-	-	-	-	-	-	-	-	-	4	0	0	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(80)	(0)	(0)	(0)
	hemorrhage:central		-	-	-	-	-	-	-	-	-	-	-	-	0	0	5	0
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)
	hemorrhage:portal		-	-	-	-	-	-	-	-	-	-	-	-	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	4000ppm				8000ppm			
		No. of Animals on Study	5				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Circulatory system}										
heart			< 5>				< 5>			
	ground glass appearance		0	3	1	0	0	0	0	0
			(0)	(60)	(20)	(0)	(0)	(0)	(0)	(0)
{Digestive system}										
liver			< 5>				< 5>			
	vacuolic change		0	5	0	0	0	5	0	0
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
	hemorrhage:central		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hemorrhage:portal		0	3	1	0	0	0	0	0
			(0)	(60)	(20)	(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 K 4

HISTOPATHOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY, MOUSE : FEMALE : SACRIFICED ANIMALS (2-WEEK STUDY)

Organ	Findings	Group Name	Control				500ppm				1000ppm				2000ppm			
		No. of Animals on Study	5				5				5				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}																		
nasal cavit			< 5>				< 5>				< 5>				< 0>			
	atrophy:olfactory epithelium		0	0	0	0	5	0	0	0	5	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
lung			< 5>				< 5>				< 5>				< 0>			
	basophilic change:bronchiole		0	0	0	0	5	0	0	0	5	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
{Hematopoietic system}																		
thymus			< 5>				< 5>				< 5>				< 0>			
	atrophy		0	0	0	0	4	0	0	0	5	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(80)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
spleen			< 5>				< 5>				< 5>				< 0>			
	deposit of melanin		1	0	0	0	0	0	0	0	0	0	0	0	-	-	-	-
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
{Digestive system}																		
stomach			< 5>				< 5>				< 5>				< 0>			
	erosion:forestomach		0	0	0	0	1	0	0	0	0	1	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(20)	(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	4000ppm				8000ppm			
		No. of Animals on Study	0				0			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			< 0>				< 0>			
	atrophy:olfactory epithelium		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
lung			< 0>				< 0>			
	basophilic change:bronchiole		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{Hematopoietic system}										
thymus			< 0>				< 0>			
	atrophy		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
spleen			< 0>				< 0>			
	deposit of melanin		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{Digestive system}										
stomach			< 0>				< 0>			
	erosion:forestomach		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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 / No. of Animals on Study / Grade	Control				500ppm				1000ppm				2000ppm			
			5				5				5				0			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Digestive system}																		
stomach			< 5>				< 5>				< 5>				< 0>			
	ulcer:forestomach		0	0	0	0	1	0	0	0	0	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
	hyperplasia:forestomach		0	0	0	0	0	3	0	0	1	0	1	0	-	-	-	-
			(0)	(0)	(0)	(0)	(0)	(60)	(0)	(0)	(20)	(0)	(20)	(0)	(-)	(-)	(-)	(-)
{Endocrine system}																		
parathyroid			< 4>				< 5>				< 5>				< 0>			
	cyst		1	0	0	0	0	0	0	0	0	0	0	0	-	-	-	-
			(25)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
adrenal			< 5>				< 5>				< 5>				< 0>			
	necrosis:cortex		0	0	0	0	0	0	0	0	0	2	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(40)	(0)	(0)	(-)	(-)	(-)	(-)
{Reproductive system}																		
ovary			< 5>				< 5>				< 5>				< 0>			
	cyst		1	0	0	0	0	0	0	0	0	0	0	0	-	-	-	-
			(20)	(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	4000ppm				8000ppm			
		No. of Animals on Study	0				0			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
stomach			< 0>				< 0>			
	ulcer:forestomach		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	hyperplasia:forestomach		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{Endocrine system}										
parathyroid			< 0>				< 0>			
	cyst		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
adrenal			< 0>				< 0>			
	necrosis:cortex		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{Reproductive system}										
ovary			< 0>				< 0>			
	cyst		-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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 L

METHODS, UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK INHALATION STUDY OF 1-BROMOBUTANE

METHODS,UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-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
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.)