酢酸イソプロピ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：0559

APPENDICES

APPENDICES

APPENDICES (CONTINUED)

APPENDIX A 1

IDENTITY AND IMPURITY OF ISOPROPYL ACETATE IN THE 13-WEEK INHALATION STUDY

IDENTITY AND IMPURITY OF ISOPROPYL ACETATE IN THE 13-WEEK INHALATION STUDY

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

Lot No. : KLL5209

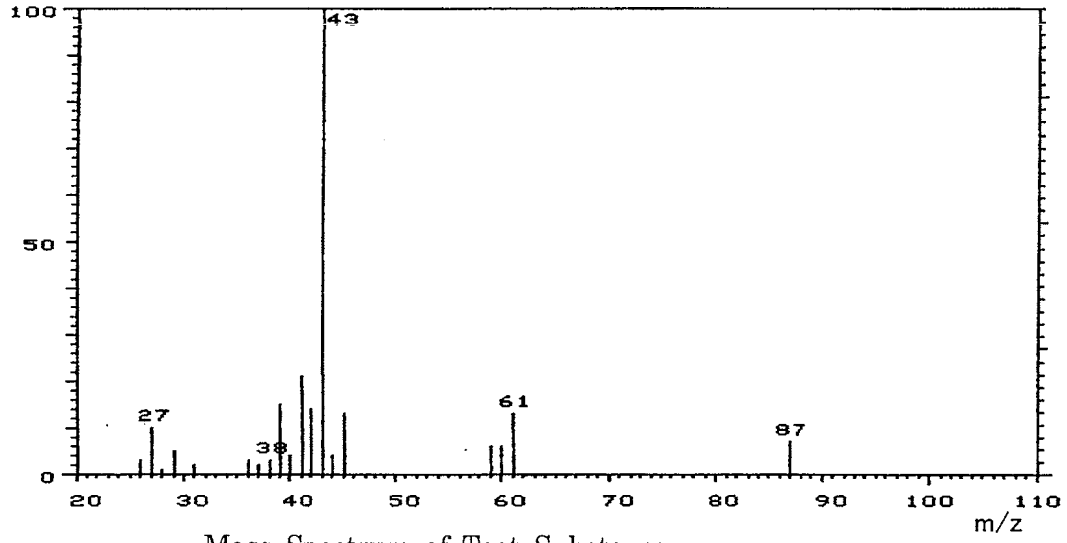
1. Spectral Data

Mass Spectrometry

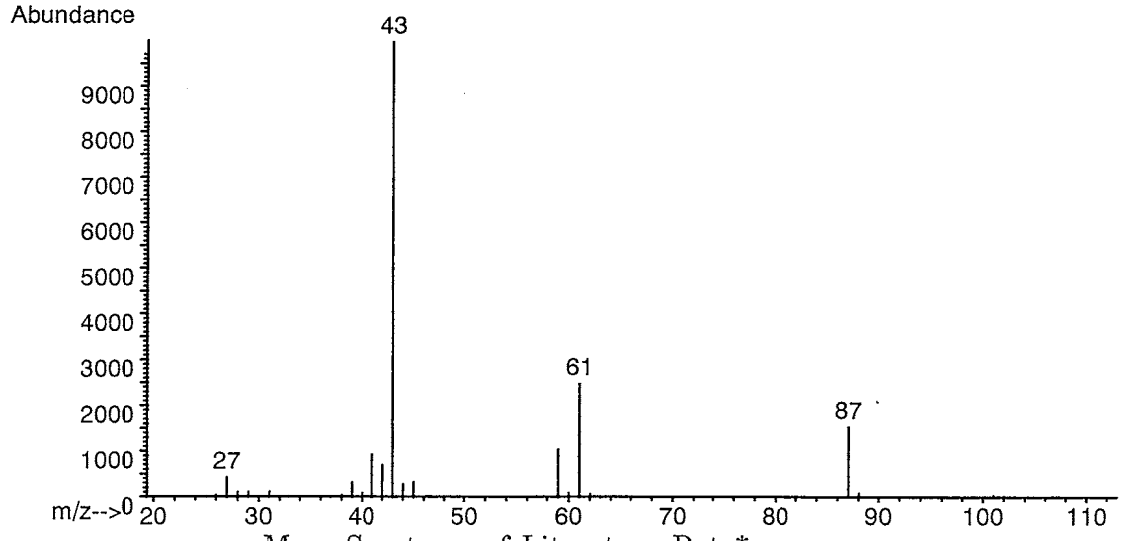
Instrument : Hitachi M-80B Mass Spectrometer

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.

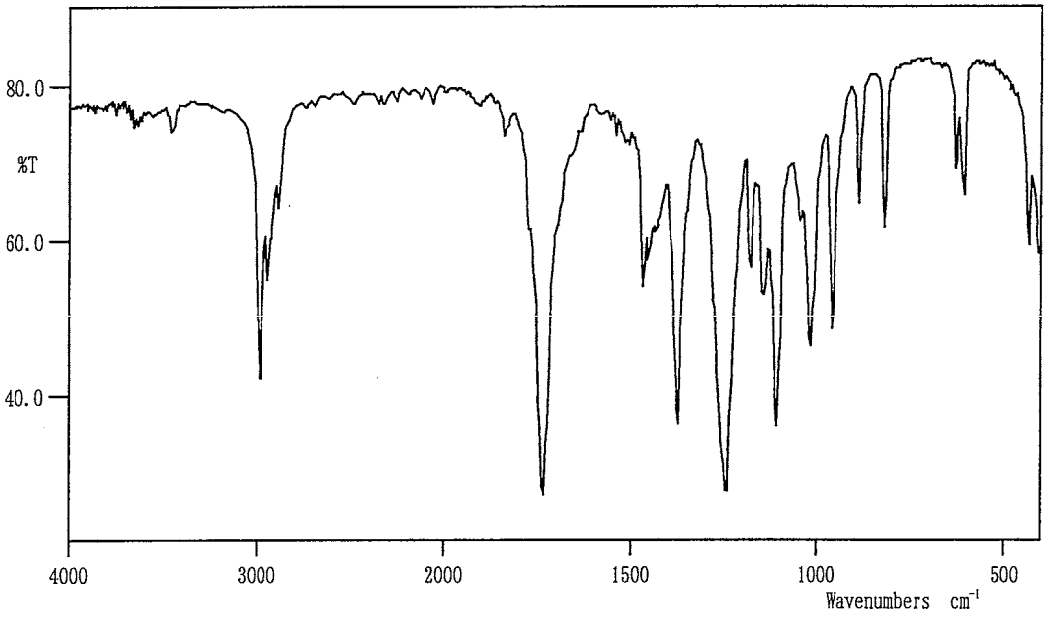
(*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed. New York, NY:John Wiley and Sons.)

Infrared Spectrometry

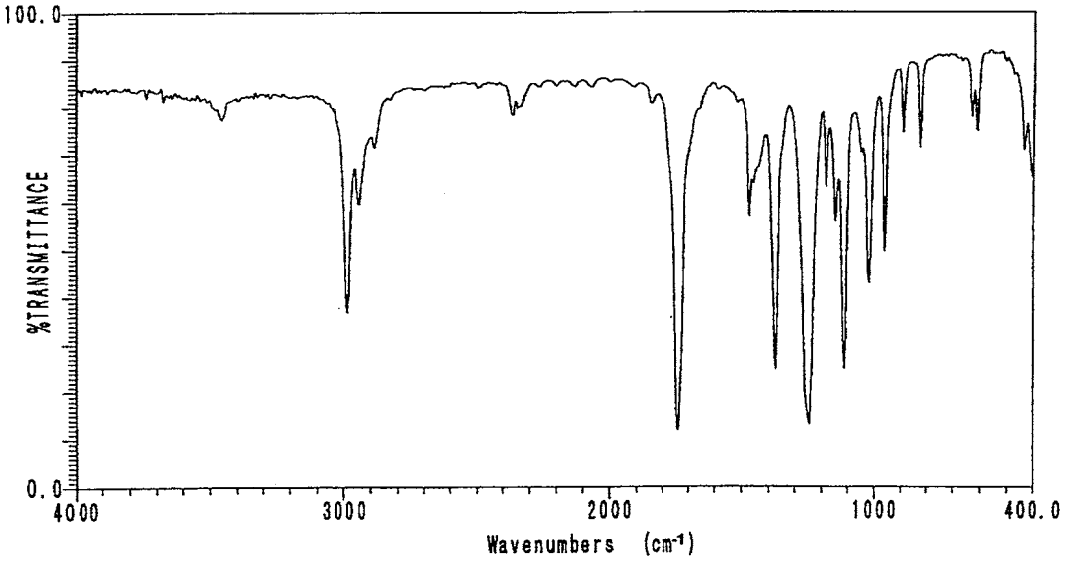
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

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. Impurity

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : Methyl Silicone (0.53 mmϕ × 60 m)

Column Temperature: 80° C

Flow Rate : 15 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μL

Sample Name	Peak No.	Area (%)	Peak Name
	1	0.038	2-Propanol
Test Substance	2	99.962	Isopropyl acetate

Result: Gas chromatography indicated one major peak (peak No. 2) and one impurity. The impurity (peak No. 1) was identified as 2-propanol by comparing GC-MS with that of standard sample. The amount of 2-propanol in the test substance was 0.038% (The quantity value by the standard sample was 0.043%.) with a gas chromatograph.

3. Conclusion: The test substance was identified as isopropyl acetate by mass spectrum and infrared spectrum. Gas chromatography indicated one major peak (isopropyl acetate) and one impurity. The impurity was 2-propanol in the test substance.

APPENDIX A 2

STABILITY OF ISOPROPYL ACETATE IN THE 13-WEEK INHALATION STUDY

STABILITY OF ISOPROPYL ACETATE IN THE 13-WEEK INHALATION STUDY

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

Lot No. : KLL5209

1. Sample : This lot was used from 2004.9.15 to 2004.12.14. 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 : 15 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μL

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
2004.09.14	1	1.947	0.038
	2	4.099	99.962
2004.12.17	1	1.977	0.039
	2	4.031	99.961

Result: Gas chromatography indicated one major peak (peak No.2) and one impurity (peak No. 1 < 0.1% of total area) analyzed on 2004.9.14 and one major peak (peak No.2) and one impurity (peak No. 1 < 0.1% of total area) analyzed on 2004.12.17. No new trace impurity peak in the test substance analyzed on 2004.12.17 was detected.

3. Conclusion: The test substance was stable for about 13 weeks in a dark place at room temperature.

APPENDIX B

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 13-WEEK INHALATION STUDY OF ISOPROPYL ACETATE

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 13-WEEK INHALATION STUDY OF ISOPROPYL ACETATE

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 ± 0.3	59.7 ± 1.5	104.6 ± 0.2	12.1
250 ppm	22.3 ± 0.3	57.5 ± 1.2	104.5 ± 0.6	12.1
500 ppm	22.3 ± 0.3	57.8 ± 1.5	104.7 ± 0.5	12.1
1000 ppm	22.4 ± 0.3	57.0 ± 1.8	104.9 ± 0.4	12.1
2000 ppm	22.4 ± 0.3	52.9 ± 2.0	104.5 ± 0.4	12.1
4000 ppm	22.5 ± 0.2	51.5 ± 3.0	104.5 ± 0.5	12.1

APPENDIX C

CLINICAL OBSERVATION : MALE

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[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
DEATH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	250ppm	0	0	0	1	1	1	1	1	1	1	1	1	1
	500ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
INTERNAL MASS	Control	0	1	1	3	3	3	3	3	3	2	2	2	2
	250ppm	0	2	2	1	1	2	2	2	2	1	1	1	1
	500ppm	1	1	1	1	1	1	1	0	1	1	0	0	0
	1000ppm	0	1	1	1	1	1	0	1	1	1	0	0	0
	2000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000ppm	0	1	1	1	1	1	1	1	1	1	1	1	1

APPENDIX D 1

BODY WEIGHT CHANGES : MALE

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[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	23.5± 0.9	24.2± 1.1	25.1± 1.8	25.7± 1.5	26.6± 1.6	27.7± 1.5	28.3± 1.6
250ppm	23.5± 0.9	23.8± 1.4	24.3± 1.9	24.6± 2.2	26.2± 0.8	26.9± 0.9	27.4± 1.1
500ppm	23.5± 0.9	24.7± 1.0	26.1± 0.9	26.7± 1.2	27.6± 1.1	28.2± 1.2	28.6± 1.2
1000ppm	23.5± 0.9	24.4± 1.9	25.1± 1.4	25.6± 1.3	26.6± 1.3	27.1± 1.4	27.9± 1.8
2000ppm	23.5± 0.9	25.0± 0.9	25.7± 1.3	26.2± 1.3	26.9± 1.3	27.1± 1.8	27.9± 1.6
4000ppm	23.5± 0.9	24.9± 0.9	25.0± 2.2	25.9± 1.6	27.0± 1.5	27.4± 1.3	28.1± 1.2

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

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[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	28.9± 1.5	29.6± 1.8	30.6± 2.0	31.5± 2.1	31.8± 2.1	32.4± 2.0	32.9± 2.2
250ppm	27.9± 1.2	28.6± 1.0	28.9± 1.3	29.7± 1.5	30.2± 1.7	30.5± 1.6	31.0± 1.8
500ppm	29.4± 1.4	29.7± 1.4	30.3± 1.8	30.9± 1.8	31.0± 1.8	31.5± 2.1	32.6± 2.0
1000ppm	28.2± 1.9	28.9± 2.1	29.6± 2.1	30.3± 2.4	30.7± 2.5	31.2± 2.7	31.8± 2.7
2000ppm	28.0± 1.9	29.0± 1.9	29.9± 2.0	30.4± 2.1	30.9± 2.5	31.3± 2.6	31.6± 2.7
4000ppm	28.6± 1.2	28.7± 1.5	29.7± 1.8	29.9± 2.0	30.5± 2.3	30.7± 2.2	31.1± 2.4

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

APPENDIX D 2

BODY WEIGHT CHANGES : FEMALE

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[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	19.1± 0.7	20.6± 0.8	21.3± 1.0	21.8± 1.1	22.6± 1.3	23.3± 1.0	23.8± 1.0
250ppm	19.1± 0.7	20.2± 0.8	20.6± 0.6	21.0± 0.9	22.0± 0.7	22.6± 0.8	23.0± 0.7
500ppm	19.1± 0.7	20.4± 0.8	21.2± 0.7	21.7± 0.5	22.6± 0.7	22.9± 0.7	23.8± 1.3
1000ppm	19.1± 0.7	20.6± 0.8	21.5± 1.0	22.1± 0.7	23.0± 1.4	23.4± 1.2	24.1± 1.0
2000ppm	19.1± 0.8	20.0± 0.7	20.7± 0.7	21.3± 0.6	22.2± 0.6	22.4± 0.6	22.8± 0.7
4000ppm	19.1± 0.7	20.3± 0.9	20.8± 0.7	21.6± 0.8	22.9± 1.1	22.6± 0.6	23.7± 0.8

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

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[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	24.1± 0.7	24.5± 1.0	24.9± 1.2	25.1± 1.2	25.5± 0.9	25.5± 1.1	25.4± 1.3
250ppm	23.5± 0.4	24.1± 1.3	24.1± 1.0	24.7± 0.8	24.7± 0.9	24.5± 0.9	24.8± 1.2
500ppm	24.1± 0.5	24.9± 0.8	24.7± 0.8	26.0± 1.1	25.8± 1.1	26.3± 1.3	26.4± 1.5
1000ppm	24.4± 0.9	25.2± 1.5	25.3± 1.5	25.6± 1.3	25.5± 1.4	25.9± 1.8	26.0± 1.6
2000ppm	23.5± 0.9	23.9± 0.7	24.1± 1.1	24.7± 0.9	25.3± 1.4	25.6± 1.0	24.9± 1.1
4000ppm	23.8± 1.4	24.7± 1.1	24.9± 0.9	24.8± 0.9	25.4± 1.2	25.5± 1.0	25.8± 1.0

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

APPENDIX E 1

FOOD CONSUMPTION CHANGES : MALE

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[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	3.8± 0.3	3.8± 0.4	4.2± 0.6	4.3± 0.4	4.3± 0.4	4.4± 0.5	4.4± 0.4
250ppm	3.8± 0.6	4.0± 0.5	4.1± 0.3	4.4± 0.6	4.4± 0.3	4.3± 0.3	4.3± 0.3
500ppm	4.2± 0.4	4.3± 0.3*	4.3± 0.4	4.7± 0.4	4.7± 0.4	4.7± 0.4	4.6± 0.4
1000ppm	4.0± 0.6	4.0± 0.3	4.1± 0.3	4.4± 0.4	4.3± 0.3	4.4± 0.4	4.3± 0.3
2000ppm	4.1± 0.2	3.8± 0.3	4.0± 0.3	4.2± 0.3	4.1± 0.2	4.2± 0.2	4.1± 0.3
4000ppm	4.0± 0.3	3.6± 0.5	3.9± 0.2	4.1± 0.3	4.0± 0.2	4.1± 0.2	4.0± 0.2*

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

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[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	4.5± 0.4	4.5± 0.4	4.6± 0.4	4.5± 0.4	4.5± 0.4	4.4± 0.2
250ppm	4.5± 0.3	4.4± 0.3	4.5± 0.4	4.5± 0.4	4.5± 0.3	4.4± 0.3
500ppm	4.8± 0.3	4.6± 0.4	4.7± 0.4	4.6± 0.3	4.7± 0.3	4.6± 0.3
1000ppm	4.4± 0.3	4.4± 0.4	4.5± 0.4	4.4± 0.3	4.5± 0.3	4.5± 0.3
2000ppm	4.3± 0.3	4.2± 0.2	4.3± 0.3	4.3± 0.1	4.3± 0.2	4.2± 0.1
4000ppm	4.1± 0.2**	4.1± 0.2	4.1± 0.3*	4.2± 0.3	4.2± 0.2	4.1± 0.2*

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

APPENDIX E 2

FOOD CONSUMPTION CHANGES : FEMALE

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[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	3.6± 0.2	3.7± 0.2	4.0± 0.3	4.3± 0.2	4.5± 0.2	4.5± 0.2	4.6± 0.2
250ppm	3.5± 0.2	3.5± 0.3	3.7± 0.2	4.0± 0.2*	4.1± 0.3**	4.2± 0.2**	4.2± 0.3**
500ppm	3.6± 0.3	3.7± 0.3	3.8± 0.2	4.2± 0.3	4.1± 0.2**	4.4± 0.3	4.4± 0.2
1000ppm	3.6± 0.2	3.7± 0.2	3.9± 0.1	4.1± 0.2	4.1± 0.2**	4.3± 0.2	4.3± 0.2*
2000ppm	3.4± 0.2	3.5± 0.2	3.6± 0.3**	3.8± 0.3**	3.7± 0.3**	3.9± 0.2**	3.8± 0.4**
4000ppm	3.2± 0.5*	3.4± 0.3*	3.5± 0.2**	3.8± 0.3**	3.6± 0.2**	3.9± 0.2**	3.8± 0.3**

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

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[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	4.6± 0.2	4.7± 0.2	4.6± 0.2	4.7± 0.3	4.5± 0.2	4.5± 0.3
250ppm	4.5± 0.4	4.2± 0.2**	4.3± 0.2*	4.3± 0.3*	4.3± 0.3	4.4± 0.3
500ppm	4.6± 0.3	4.4± 0.3	4.6± 0.2	4.4± 0.2	4.7± 0.2	4.5± 0.3
1000ppm	4.4± 0.2	4.3± 0.2**	4.4± 0.2*	4.2± 0.3**	4.4± 0.2	4.4± 0.3
2000ppm	4.0± 0.2**	3.9± 0.3**	4.1± 0.2**	3.9± 0.4**	4.0± 0.3**	3.8± 0.3**
4000ppm	3.9± 0.2**	3.9± 0.2**	4.0± 0.3**	4.0± 0.3**	4.0± 0.2**	4.0± 0.3**

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

APPENDIX F 1

HEMATOLOGY : MALE

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[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 f ℓ		MCH p g		MCHC g/dℓ		PLATELET $10^3/\mu\ell$	
Control	9	10.91±	0.44	16.1±	0.7	51.6±	1.2	47.3±	1.0	14.7±	0.3	31.2±	0.6	1356±	89
250ppm	8	10.88±	0.15	15.9±	0.5	51.0±	1.3	46.8±	1.2	14.6±	0.5	31.1±	0.7	1324±	93
500ppm	9	10.71±	0.22	16.0±	0.2	51.1±	1.2	47.7±	0.8	14.9±	0.2	31.3±	0.5	1278±	39
1000ppm	9	10.91±	0.26	16.1±	0.3	51.9±	0.9	47.6±	0.6	14.8±	0.2	31.1±	0.4	1305±	61
2000ppm	10	11.08±	0.23	16.6±	0.4	52.8±	1.3	47.6±	0.5	15.0±	0.1	31.5±	0.5	1358±	66
4000ppm	9	11.14±	0.33	16.9±	0.5*	54.3±	2.0**	48.7±	1.0**	15.2±	0.1**	31.3±	0.6	1369±	93

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

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RETICULOCYTE %
Control	9	2.2± 0.3
250ppm	8	2.3± 0.3
500ppm	9	2.4± 0.3
1000ppm	9	2.2± 0.2
2000ppm	10	2.2± 0.3
4000ppm	9	2.1± 0.2

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

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[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	2.00± 0.72	1± 1	13± 3	2± 2	0± 0	3± 2	81± 4	0± 0
250ppm	8	2.14± 0.75	0± 0	15± 3	1± 1	0± 0	2± 1	81± 3	0± 0
500ppm	9	2.01± 0.64	0± 1	13± 3	1± 1	0± 0	3± 1	83± 3	0± 0
1000ppm	9	1.94± 0.58	0± 1	12± 3	2± 1	0± 0	2± 1	84± 3	0± 0
2000ppm	10	2.16± 0.79	0± 0	14± 3	2± 1	0± 0	2± 1	82± 3	0± 0
4000ppm	9	1.80± 0.70	1± 1	13± 6	2± 1	0± 0	3± 1	82± 6	0± 0

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

APPENDIX F 2

HEMATOLOGY : FEMALE

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[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	10	10.70± 0.23	16.1± 0.4	50.8± 1.8	47.5± 1.0	15.1± 0.2	31.8± 1.0	1233± 91
250ppm	10	10.55± 0.31	15.7± 0.6	50.1± 1.5	47.5± 0.5	14.9± 0.1	31.4± 0.5	1196± 72
500ppm	9	10.84± 0.33	16.5± 0.6	51.5± 1.5	47.5± 0.7	15.2± 0.2	32.1± 0.6	1231± 120
1000ppm	10	10.97± 0.19	16.6± 0.4	52.2± 1.0	47.6± 0.7	15.1± 0.1	31.8± 0.5	1206± 54
2000ppm	10	10.89± 0.15	16.7± 0.3	52.5± 0.9	48.2± 0.5	15.3± 0.2*	31.8± 0.4	1217± 80
4000ppm	9	10.78± 0.46	16.8± 0.8	53.2± 2.0**	49.3± 0.5**	15.6± 0.2**	31.5± 0.6	1213± 108

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

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RETICULOCYTE %
Control	10	2.0± 0.3
250ppm	10	2.3± 0.5
500ppm	9	2.2± 0.5
1000ppm	10	2.3± 0.3
2000ppm	10	2.0± 0.3
4000ppm	9	2.1± 0.6

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

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	WBC $10^3/\mu l$		Differential WBC (%) N-BAND		N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHER	
Control	10	1.25±	0.73	0±	0	17±	6	1±	1	0±	0	2±	2	80±	6	0±	0
250ppm	10	0.98±	0.65	0±	0	17±	5	1±	1	0±	0	1±	1	81±	4	0±	0
500ppm	9	1.62±	0.91	1±	1	13±	3	2±	2	0±	0	1±	1	83±	4	0±	0
1000ppm	10	1.64±	0.90	0±	0	16±	4	1±	1	0±	0	2±	3	81±	4	0±	0
2000ppm	10	1.71±	0.93	0±	1	12±	4	1±	1	0±	0	2±	1	85±	5	0±	0
4000ppm	9	1.91±	0.74	0±	0	14±	4	2±	1	0±	0	1±	0	83±	4	0±	0

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

APPENDIX G 1

BIOCHEMISTRY : MALE

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[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	9	5.3± 0.2	2.9± 0.1	1.2± 0.1	0.18± 0.07	235± 43	86± 10	22± 7
250ppm	8	5.2± 0.2	2.8± 0.2	1.2± 0.2	0.15± 0.02	207± 24	81± 16	15± 5
500ppm	9	5.1± 0.2	2.8± 0.2	1.3± 0.1	0.15± 0.01	184± 29	76± 13	18± 6
1000ppm	10	5.1± 0.1	2.8± 0.1	1.3± 0.1	0.17± 0.04	206± 29	75± 8	21± 11
2000ppm	10	5.2± 0.2	2.9± 0.1	1.3± 0.1	0.15± 0.02	226± 56	81± 15	22± 9
4000ppm	9	5.4± 0.2	3.0± 0.1	1.3± 0.1	0.17± 0.03	210± 47	80± 12	15± 7

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

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dl	AST IU/l	ALT IU/l	LDH IU/l	ALP IU/l	G-GTP IU/l	CK IU/l
Control	9	175± 20	49± 11	21± 9	256± 125	152± 14	1± 0	100± 101
250ppm	8	161± 29	57± 14	19± 4	263± 69	141± 21	1± 0	123± 57
500ppm	9	156± 22	56± 15	19± 3	235± 56	146± 9	1± 1	98± 53
1000ppm	10	155± 15	47± 5	17± 2	262± 97	148± 12	1± 1	80± 33
2000ppm	10	161± 20	55± 23	20± 5	238± 69	141± 6	1± 0	111± 69
4000ppm	9	157± 17	48± 14	18± 5	231± 54	145± 9	0± 1	89± 37

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

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[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	9	25.5± 4.2	151± 1	4.6± 0.3	121± 2	8.7± 0.2	6.7± 0.8
250ppm	8	25.6± 3.7	152± 1	4.7± 0.3	122± 2	8.7± 0.4	6.7± 0.8
500ppm	9	26.8± 3.3	152± 1	4.6± 0.3	122± 1	8.5± 0.3	5.9± 0.7
1000ppm	10	27.9± 3.2	152± 2	4.7± 0.3	123± 1	8.7± 0.2	6.5± 0.9
2000ppm	10	24.7± 1.5	152± 1	4.6± 0.3	122± 1	8.6± 0.2	6.1± 0.8
4000ppm	9	25.2± 3.9	151± 1	4.7± 0.5	122± 2	8.7± 0.2	6.0± 0.8

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

APPENDIX G 2

BIOCHEMISTRY : FEMALE

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[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	5.5± 0.3	3.3± 0.1	1.5± 0.1	0.19± 0.09	190± 20	72± 11	14± 5
250ppm	10	5.3± 0.2	3.2± 0.1	1.6± 0.1	0.16± 0.02	175± 31	74± 10	16± 7
500ppm	9	5.4± 0.1	3.2± 0.1	1.5± 0.1	0.16± 0.03	187± 20	81± 12	17± 9
1000ppm	10	5.5± 0.2	3.3± 0.1	1.5± 0.1	0.17± 0.04	188± 24	86± 13*	21± 7
2000ppm	10	5.4± 0.2	3.3± 0.1	1.5± 0.1	0.19± 0.05	192± 23	76± 9	15± 3
4000ppm	9	5.4± 0.1	3.2± 0.1	1.5± 0.1	0.18± 0.05	207± 27	88± 9**	15± 5

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

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dℓ	AST IU/ℓ	ALT IU/ℓ	LDH IU/ℓ	ALP IU/ℓ	G-GTP IU/ℓ	CK IU/ℓ
Control	10	145± 13	84± 32	29± 10	340± 150	260± 31	1± 1	130± 104
250ppm	10	140± 24	80± 29	28± 8	348± 138	252± 40	0± 1	175± 142
500ppm	9	154± 15	66± 24	24± 4	272± 68	228± 31	1± 1	137± 111
1000ppm	10	167± 25*	73± 29	24± 8	326± 130	243± 37	1± 0	169± 111
2000ppm	10	149± 15	60± 15	22± 4	319± 107	223± 18*	1± 1	193± 142
4000ppm	9	163± 12	57± 14	22± 4	274± 62	193± 20**	1± 0	165± 81

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

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	UREA NITOROGEN mg/dℓ	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dℓ	INORGANIC PHOSPHORUS mg/dℓ
Control	10	23.4± 2.7	151± 1	4.5± 0.2	121± 2	8.7± 0.3	6.1± 1.0
250ppm	10	24.1± 5.5	152± 2	4.4± 0.4	123± 2	8.5± 0.3	6.5± 0.9
500ppm	9	20.9± 1.3	151± 2	4.6± 0.4	121± 1	8.7± 0.2	5.9± 0.5
1000ppm	10	22.3± 4.2	152± 1	4.5± 0.3	122± 1	8.8± 0.2	5.6± 0.5
2000ppm	10	20.7± 2.8	151± 2	4.6± 0.2	121± 1	8.8± 0.2	6.0± 0.8
4000ppm	9	20.7± 2.2	150± 2	4.7± 0.3	121± 3	8.9± 0.4	6.0± 0.4

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

APPENDIX H 1

URINALYSIS : MALE

STUDY NO. : 0559 URINALYSIS
ANIMAL : MOUSE B6D2F1/Crlj[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	3	1	1	2	3	0		0	4	6	0	0	0		10	0	0	0	0	0		5	3	2	0	0	0		9	0	0	0	1	
250ppm	9	0	1	1	1	1	4	1		0	4	4	1	0	0		9	0	0	0	0	0		2	4	3	0	0	0		9	0	0	0	0	
500ppm	9	0	0	3	0	4	1	1		0	3	5	1	0	0		9	0	0	0	0	0		2	2	4	1	0	0		9	0	0	0	0	
1000ppm	10	0	0	1	0	3	5	1		0	1	8	1	0	0		10	0	0	0	0	0		4	3	3	0	0	0		10	0	0	0	0	
2000ppm	9	0	0	1	3	2	2	1		0	3	5	1	0	0		9	0	0	0	0	0		5	1	3	0	0	0		9	0	0	0	0	
4000ppm	10	0	0	0	3	3	3	1		0	4	6	0	0	0		10	0	0	0	0	0		3	3	3	1	0	0		10	0	0	0	0	

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

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0	
250ppm	9	9	0	0	0	0	
500ppm	9	9	0	0	0	0	
1000ppm	10	10	0	0	0	0	
2000ppm	9	9	0	0	0	0	
4000ppm	10	10	0	0	0	0	

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

APPENDIX H 2

URINALYSIS : FEMALE

STUDY NO. : 0559 URINALYSIS
ANIMAL : MOUSE B6D2F1/Crlj[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	2	6	1		0	2	7	1	0	0		10	0	0	0	0	0		1	8	1	0	0	0		10	0	0	0	0	
250ppm	10	0	0	0	1	0	9	0		0	3	6	1	0	0		10	0	0	0	0	0		3	5	1	1	0	0		10	0	0	0	0	
500ppm	10	0	0	0	0	2	8	0		0	4	6	0	0	0		10	0	0	0	0	0		6	4	0	0	0	0		10	0	0	0	0	
1000ppm	10	0	0	0	0	2	8	0		0	3	7	0	0	0		10	0	0	0	0	0		4	5	1	0	0	0		10	0	0	0	0	
2000ppm	10	0	0	3	0	1	5	1		0	4	6	0	0	0		10	0	0	0	0	0		4	6	0	0	0	0		10	0	0	0	0	
4000ppm	10	0	0	0	2	2	5	1		0	5	5	0	0	0		10	0	0	0	0	0		4	6	0	0	0	0		10	0	0	0	0	

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

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[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	
250ppm	10	10	0	0	0	0	
500ppm	10	10	0	0	0	0	
1000ppm	10	10	0	0	0	0	
2000ppm	10	10	0	0	0	0	
4000ppm	10	10	0	0	0	0	

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

APPENDIX I 1

GROSS FINDINGS : MALE

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name / NO. of Animals	Control 10	(%)	250ppm 10	(%)	500ppm 10	(%)	1000ppm 10	(%)
thymus	atrophic		0	(0)	1	(10)	0	(0)	0	(0)
spleen	black zone		2	(20)	0	(0)	0	(0)	0	(0)
kidney	white zone		0	(0)	1	(10)	0	(0)	0	(0)
	hydronephrosis		4	(40)	3	(30)	1	(10)	1	(10)

Organ	Findings	Group Name	2000ppm		4000ppm	
		NO. of Animals	10	(%)	10	(%)
thymus	atrophic		0	(0)	0	(0)
spleen	black zone		0	(0)	0	(0)
kidney	white zone		0	(0)	0	(0)
	hydronephrosis		0	(0)	1	(10)

APPENDIX I 2

GROSS FINDINGS : FEMALE

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name / NO. of Animals	Control 10	(%)	250ppm 10	(%)	500ppm 10	(%)	1000ppm 10	(%)
spleen	black zone		0	(0)	2	(20)	1	(10)	0	(0)
ovary	cyst		0	(0)	1	(10)	0	(0)	0	(0)

Organ	Findings	Group Name	2000ppm		4000ppm	
		NO. of Animals	10	(%)	10	(%)
spleen	black zone		1	(10)	0	(0)
ovary	cyst		1	(10)	0	(0)

APPENDIX J 1

ORGAN WEIGHT, ABSOLUTE : MALE

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[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	29.1± 2.1	0.032± 0.006	0.013± 0.002	0.239± 0.039	0.155± 0.015	0.159± 0.012
250ppm	9	27.3± 1.9	0.029± 0.003	0.014± 0.003	0.227± 0.019	0.150± 0.014	0.151± 0.011
500ppm	10	28.7± 2.0	0.032± 0.006	0.013± 0.002	0.238± 0.013	0.160± 0.010	0.158± 0.007
1000ppm	10	28.0± 2.8	0.031± 0.006	0.013± 0.002	0.231± 0.031	0.152± 0.013	0.152± 0.006
2000ppm	10	28.1± 2.5	0.031± 0.005	0.013± 0.002	0.243± 0.015	0.149± 0.008	0.155± 0.009
4000ppm	10	27.5± 2.2	0.031± 0.005	0.014± 0.003	0.229± 0.036	0.147± 0.016	0.156± 0.011

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

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[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	0.666± 0.464	0.061± 0.016	1.131± 0.070	0.442± 0.013
250ppm	9	0.598± 0.364	0.057± 0.015	1.121± 0.070	0.444± 0.015
500ppm	10	0.485± 0.103	0.054± 0.007	1.148± 0.080	0.441± 0.018
1000ppm	10	0.500± 0.177	0.052± 0.003	1.093± 0.091	0.435± 0.010
2000ppm	10	0.443± 0.018	0.050± 0.006	1.116± 0.075	0.437± 0.011
4000ppm	10	0.461± 0.091	0.049± 0.007	1.137± 0.105	0.434± 0.013

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

APPENDIX J 2

ORGAN WEIGHT, ABSOLUTE : FEMALE

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[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	21.1± 1.2	0.036± 0.008	0.015± 0.001	0.030± 0.004	0.127± 0.006	0.147± 0.012
250ppm	10	20.9± 1.1	0.035± 0.005	0.015± 0.001	0.031± 0.007	0.124± 0.007	0.144± 0.010
500ppm	10	22.0± 1.0	0.037± 0.008	0.016± 0.002	0.030± 0.004	0.130± 0.009	0.148± 0.013
1000ppm	10	21.9± 1.6	0.041± 0.006	0.016± 0.001	0.028± 0.004	0.128± 0.008	0.149± 0.010
2000ppm	10	21.6± 1.0	0.039± 0.006	0.016± 0.002	0.030± 0.008	0.121± 0.003	0.144± 0.011
4000ppm	10	22.3± 1.0	0.042± 0.005	0.016± 0.002	0.029± 0.003	0.123± 0.010	0.148± 0.010

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

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[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	0.302± 0.019	0.057± 0.008	0.907± 0.041	0.457± 0.016
250ppm	10	0.305± 0.009	0.057± 0.010	0.882± 0.093	0.451± 0.008
500ppm	10	0.312± 0.019	0.063± 0.007	0.975± 0.051	0.453± 0.008
1000ppm	10	0.309± 0.020	0.062± 0.010	0.945± 0.102	0.453± 0.014
2000ppm	10	0.296± 0.011	0.058± 0.007	0.918± 0.049	0.449± 0.011
4000ppm	10	0.305± 0.016	0.060± 0.007	0.998± 0.063*	0.435± 0.011**

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

APPENDIX K 1

ORGAN WEIGHT, RELATIVE : MALE

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[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	29.1± 2.1	0.110± 0.017	0.045± 0.006	0.824± 0.148	0.535± 0.063	0.548± 0.031
250ppm	9	27.3± 1.9	0.107± 0.015	0.051± 0.010	0.836± 0.085	0.550± 0.039	0.554± 0.050
500ppm	10	28.7± 2.0	0.113± 0.014	0.046± 0.008	0.834± 0.068	0.560± 0.047	0.551± 0.026
1000ppm	10	28.0± 2.8	0.109± 0.013	0.046± 0.008	0.831± 0.126	0.546± 0.048	0.549± 0.054
2000ppm	10	28.1± 2.5	0.110± 0.014	0.046± 0.008	0.875± 0.105	0.534± 0.035	0.554± 0.058
4000ppm	10	27.5± 2.2	0.113± 0.017	0.050± 0.010	0.840± 0.150	0.536± 0.049	0.570± 0.034

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

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[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	2.374± 1.924	0.213± 0.067	3.885± 0.123	1.525± 0.136
250ppm	9	2.199± 1.314	0.211± 0.066	4.116± 0.174*	1.633± 0.124
500ppm	10	1.698± 0.376	0.188± 0.022	4.008± 0.211	1.544± 0.085
1000ppm	10	1.802± 0.677	0.189± 0.022	3.916± 0.180	1.567± 0.144
2000ppm	10	1.588± 0.124	0.180± 0.031	3.990± 0.224	1.569± 0.161
4000ppm	10	1.687± 0.374	0.179± 0.026	4.139± 0.179*	1.587± 0.119

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

APPENDIX K 2

ORGAN WEIGHT, RELATIVE : FEMALE

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[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	21.1± 1.2	0.171± 0.030	0.073± 0.007	0.141± 0.019	0.604± 0.029	0.695± 0.040
250ppm	10	20.9± 1.1	0.165± 0.022	0.073± 0.008	0.150± 0.032	0.593± 0.042	0.689± 0.038
500ppm	10	22.0± 1.0	0.169± 0.035	0.071± 0.007	0.137± 0.013	0.593± 0.048	0.674± 0.058
1000ppm	10	21.9± 1.6	0.186± 0.019	0.074± 0.009	0.129± 0.024	0.587± 0.036	0.682± 0.039
2000ppm	10	21.6± 1.0	0.178± 0.021	0.074± 0.007	0.139± 0.037	0.560± 0.027*	0.666± 0.046
4000ppm	10	22.3± 1.0	0.189± 0.023	0.072± 0.010	0.129± 0.014	0.553± 0.039*	0.663± 0.047

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

STUDY NO. : 0559
ANIMAL : MOUSE B6D2F1/Crlj[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	1.432± 0.074	0.271± 0.023	4.303± 0.175	2.168± 0.089
250ppm	10	1.462± 0.082	0.273± 0.034	4.217± 0.353	2.167± 0.125
500ppm	10	1.422± 0.081	0.286± 0.028	4.438± 0.162	2.066± 0.117
1000ppm	10	1.415± 0.085	0.279± 0.031	4.303± 0.223	2.076± 0.149
2000ppm	10	1.371± 0.043	0.268± 0.029	4.249± 0.186	2.078± 0.065
4000ppm	10	1.369± 0.061	0.267± 0.034	4.477± 0.287	1.955± 0.100**

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

APPENDIX L 1

HISTOPATHOLOGICAL FINDINGS :

NON-NEOPLASTIC LESIONS : MALE

Organ	Findings	Group Name	Control				250ppm				500ppm				1000ppm			
		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>			
	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)
	atrophy: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)
{Hematopoietic system}																		
thymus			<10>				<10>				<10>				<10>			
	atrophy		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)	(0)	(0)	(0)
spleen			<10>				<10>				<10>				<10>			
	deposit of melanin		2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}																		
tongue			<10>				<10>				<10>				<10>			
	inflammatory infiltration		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	2000ppm				4000ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			<10>				<10>			
	respiratory metaplasia:olfactory epithelium		0	0	0	0	10	0	0	0 **
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	atrophy:olfactory epithelium		10	0	0	0 **	10	0	0	0 **
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Hematopoietic system}										
thymus			<10>				<10>			
	atrophy		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			<10>				<10>			
	deposit of melanin		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}										
tongue			<10>				<10>			
	inflammatory infiltration		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				250ppm 10				500ppm 10				1000ppm 10			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	granulation		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
	hepatocellular hypertrophy: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)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	inflammatory polyp		0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hydronephrosis		0 (0)	0 (0)	4 (40)	0 (0)	0 (0)	1 (10)	2 (20)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)
{Endocrine system}																		
thyroid			<10>				< 9>				<10>				<10>			
	arteritis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (11)	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	2000ppm				4000ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
liver			<10>				<10>			
	granulation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hepatocellular hypertrophy:central		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(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)
	hydronephrosis		0	0	0	0	0	0	1	0
			(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)
{Endocrine system}										
thyroid			<10>				<10>			
	arteritis		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				250ppm				500ppm				1000ppm			
		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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Endocrine system}																		
adrenal			<10>				<10>				<10>				<10>			
	spindle-cell hyperplasia		2	0	0	0	0	0	0	0	2	0	0	0	1	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(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	2000ppm				4000ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Endocrine system}										
adrenal			<10>				<10>			
	spindle-cell hyperplasia		1	0	0	0	1	0	0	0
			(10)	(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

APPENDIX L 2

HISTOPATHOLOGICAL FINDINGS :

NON-NEOPLASTIC LESIONS : FEMALE

Organ	Findings	Group Name	Control				250ppm				500ppm				1000ppm			
		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	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	eosinophilic change:respiratory 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)
	atrophy: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)
{Hematopoietic system}																		
spleen			<10>				<10>				<10>				<10>			
	deposit of melanin		0	0	0	0	2	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	granulation		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	2000ppm				4000ppm			
		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		1	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	eosinophilic change:respiratory epithelium		8	0	0	0 **	5	2	0	0 **
			(80)	(0)	(0)	(0)	(50)	(20)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		1	0	0	0	10	0	0	0 **
			(10)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	atrophy:olfactory epithelium		9	0	0	0 **	10	0	0	0 **
			(90)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Hematopoietic system}										
spleen			<10>				<10>			
	deposit of melanin		1	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Digestive system}										
liver			<10>				<10>			
	granulation		0	0	0	0	1	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	Control				250ppm				500ppm				1000ppm			
		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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Endocrine system}																		
adrenal			<10>				<10>				<10>				<10>			
	spindle-cell hyperplasia		10	0	0	0	9	0	0	0	10	0	0	0	8	0	0	0
			(100)	(0)	(0)	(0)	(90)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(80)	(0)	(0)	(0)
{Reproductive system}																		
ovary			<10>				<10>				<10>				<10>			
	cyst		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	2000ppm				4000ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Endocrine system}										
adrenal			<10>				<10>			
	spindle-cell hyperplasia		10	0	0	0	8	0	0	0
			(100)	(0)	(0)	(0)	(80)	(0)	(0)	(0)
{Reproductive system}										
ovary			<10>				<10>			
	cyst		1	0	0	0	0	0	0	0
			(10)	(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 ISOPROPYL ACETATE

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

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
Aspartate aminotransferase (AST)	JSCC method [3]	IU/L	0
Alanine aminotransferase (ALT)	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 kinase (CK)	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 7080 : Hitachi,Ltd.)