酢酸イソプロピルのラットを用いた
吸入による13週間毒性試験報告書

試験番号：0558

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. : KLE3931

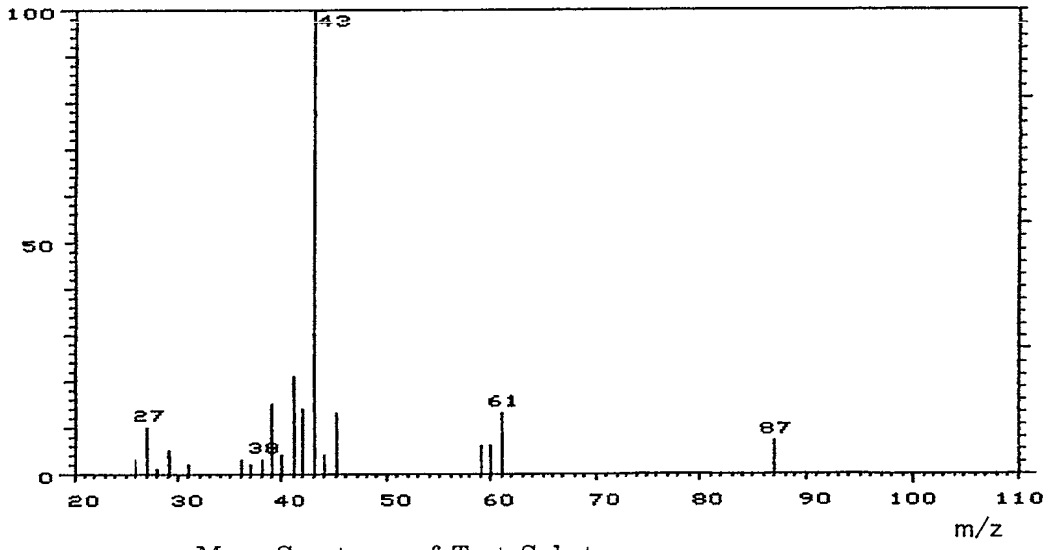
1. Spectral Data

Mass Spectrometry

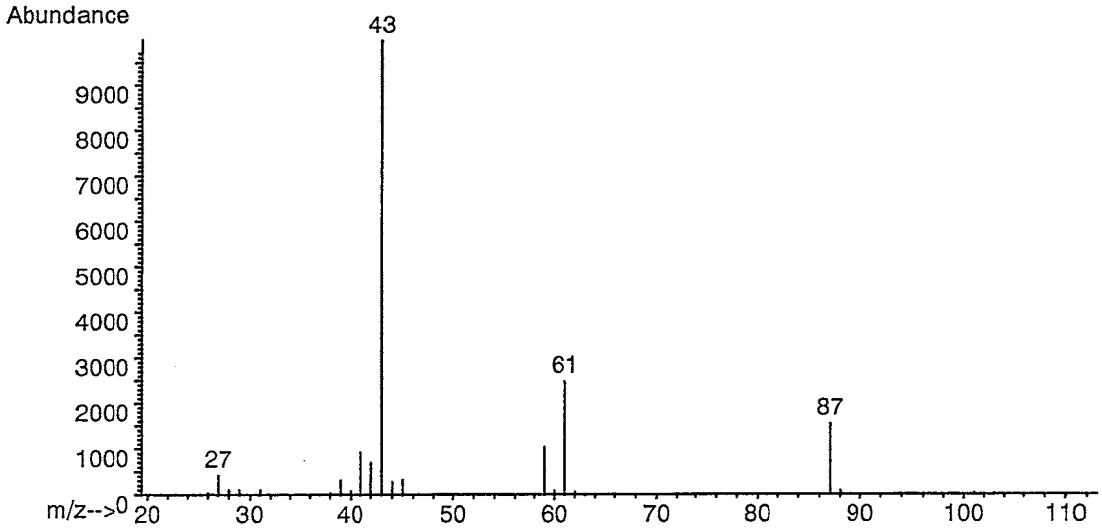
Instrument : Hitachi M-80B Mass Spectrometer

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.

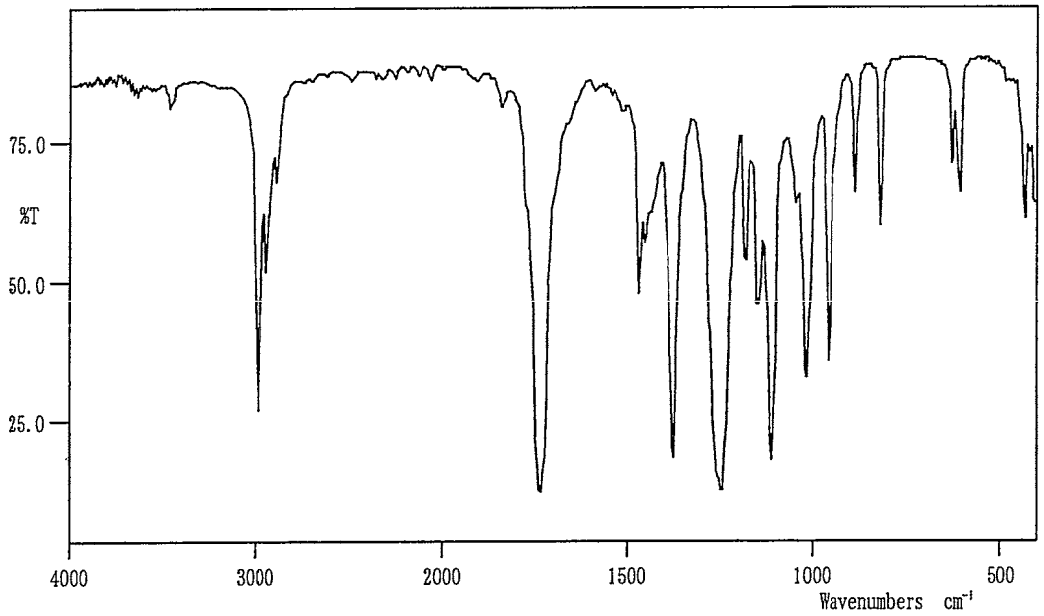
(*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed. New York, NY:John Wiley and Sons.)

Infrared Spectrometry

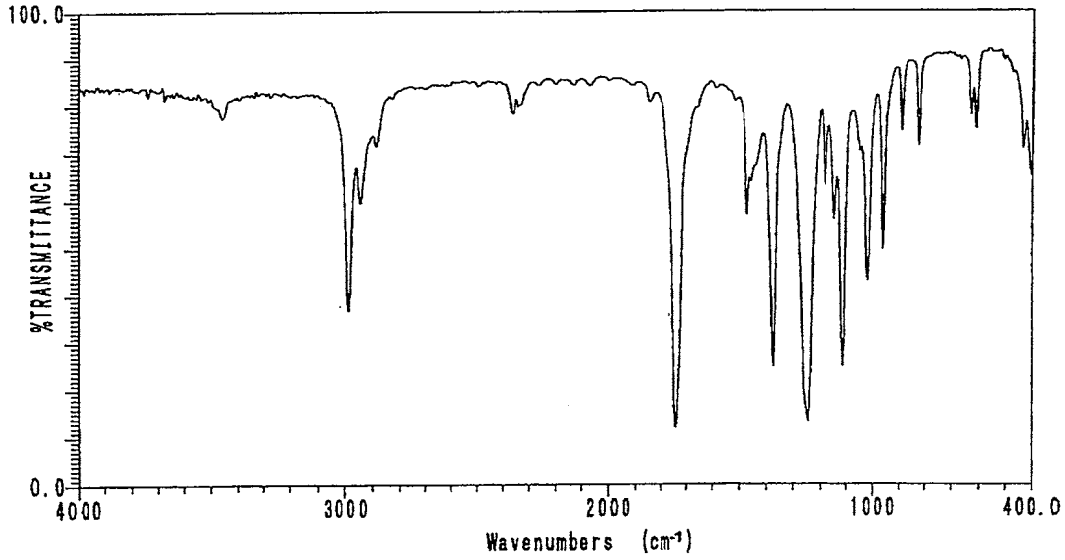
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

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	0.032	2-Propanol
Test Substance	2	99.968	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 0.032% (The quantity value by the standard sample was 0.027%.) 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. : KLE3931

1. Sample : This lot was used from 2005.1.12 to 2005.4.12. 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 (%)
2005.01.07	1	1.983	0.032
	2	4.018	99.968
2005.04.19	1	1.983	0.032
	2	4.020	99.968

Result: Gas chromatography indicated one major peak (peak No.2) and one impurity (peak No. 1 < 0.1% of total area) analyzed on 2005.1.7 and one major peak (peak No.2) and one impurity (peak No. 1 < 0.1% of total area) analyzed on 2005.4.19. No new trace impurity peak in the test substance analyzed on 2005.4.19 was detected.

3. Conclusion: The test substance was stable for about 14 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.*1	Ventilation Rate (L/min) Mean ± S.D.*2	Air Change (time/h) Mean*1	Air Change (time/h) Mean*2
Control	22.5 ± 0.4	56.7 ± 0.8	107.1 ± 0.5	212.3 ± 0.8	6.1	12.0
500 ppm	22.5 ± 0.4	56.7 ± 0.9	106.8 ± 0.4	212.4 ± 0.8	6.0	12.0
1000 ppm	22.5 ± 0.3	56.6 ± 1.3	106.3 ± 0.2	212.7 ± 0.9	6.0	12.0
2000 ppm	22.5 ± 0.4	55.8 ± 1.5	106.5 ± 0.3	212.8 ± 0.8	6.0	12.0
4000 ppm	22.4 ± 0.4	53.1 ± 2.1	106.8 ± 0.3	212.7 ± 0.9	6.0	12.0
8000 ppm	22.5 ± 0.3	52.3 ± 2.8	106.4 ± 0.3	212.9 ± 0.7	6.0	12.1

＊1：Exposure period　＊2：After exposure period

APPENDIX C 1

CLINICAL OBSERVATION : MALE

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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
REDDENING	Control	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
	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	1	0	0	0	0	0	0	0	0	0
	8000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
ABNORMAL TESTIS	Control	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
	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
	8000ppm	0	0	0	0	0	0	0	0	1	1	1	1	1

APPENDIX C 2

CLINICAL OBSERVATION : FEMALE

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

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
EXOPHTHALMOS	Control	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
	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	1	1	1	1	1	1	1
	8000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0

APPENDIX D 1

BODY WEIGHT CHANGES : MALE

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	126± 4	154± 7	188± 9	213± 8	235± 8	252± 8	264± 9
500ppm	125± 5	154± 7	187± 8	214± 7	236± 8	251± 9	264± 8
1000ppm	126± 4	157± 7	188± 9	214± 9	235± 10	252± 10	265± 11
2000ppm	125± 4	157± 5	192± 5	218± 6	238± 6	256± 7	268± 9
4000ppm	125± 4	149± 6	182± 7	209± 8	233± 9	253± 11	265± 13
8000ppm	126± 4	125± 5**	147± 6**	163± 7**	178± 8**	192± 8**	201± 9**

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

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	276± 9	287± 9	296± 9	304± 10	311± 12	316± 15	320± 16
500ppm	277± 10	289± 10	296± 11	302± 12	306± 14	313± 14	316± 15
1000ppm	279± 12	288± 13	298± 14	305± 16	309± 15	315± 15	320± 16
2000ppm	283± 9	295± 9	304± 11	307± 13	313± 13	319± 13	325± 15
4000ppm	281± 16	293± 16	302± 17	310± 19	314± 17	320± 17	324± 18
8000ppm	211± 9**	217± 9**	226± 10**	239± 11**	237± 11**	244± 10**	249± 10**

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

APPENDIX D 2

BODY WEIGHT CHANGES : FEMALE

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	99±	3	115±	3	128±	5	139±	5	147±	4	155±	5	160±	6
500ppm	99±	3	115±	4	128±	4	139±	6	146±	8	153±	8	158±	9
1000ppm	99±	3	114±	4	128±	5	138±	6	148±	6	154±	7	158±	8
2000ppm	99±	3	115±	4	128±	4	136±	5	147±	4	152±	5	158±	3
4000ppm	99±	3	110±	4*	126±	4	135±	5	144±	5	151±	5	158±	6
8000ppm	99±	3	97±	3**	110±	4**	119±	3**	128±	3**	135±	4**	139±	5**

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

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	165± 6	170± 7	174± 10	179± 10	180± 8	183± 8	184± 9
500ppm	163± 10	167± 10	171± 10	174± 11	177± 9	181± 8	182± 8
1000ppm	164± 9	167± 9	174± 10	178± 11	180± 10	183± 11	182± 10
2000ppm	165± 3	169± 3	173± 2	175± 4	179± 3	179± 5	180± 4
4000ppm	165± 5	167± 5	171± 5	176± 6	177± 7	179± 7	179± 6
8000ppm	145± 5**	147± 6**	151± 6**	157± 5**	156± 6**	160± 6**	164± 7**

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

APPENDIX E 1

FOOD CONSUMPTION CHANGES : MALE

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	13.8± 0.9	15.6± 1.1	16.6± 0.9	17.1± 0.9	16.5± 0.6	16.0± 0.6	16.6± 0.8
500ppm	13.9± 0.7	15.6± 0.7	16.9± 1.0	17.2± 1.0	16.9± 0.8	16.5± 0.7	17.0± 0.7
1000ppm	14.3± 0.9	15.7± 0.8	16.9± 0.9	16.5± 0.7	16.7± 0.7	16.4± 0.8	17.1± 0.7
2000ppm	14.3± 0.6	16.1± 0.6	17.2± 0.6	17.0± 0.8	17.2± 0.6	16.6± 0.8	17.5± 0.9
4000ppm	12.7± 0.8**	14.7± 0.7	15.7± 0.8	16.3± 1.0	16.8± 1.0	16.4± 1.1	17.5± 1.1
8000ppm	8.2± 0.5**	12.0± 0.7**	12.9± 0.7**	13.6± 1.2**	14.6± 0.9**	14.1± 0.9**	15.3± 0.9**

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

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	16.6± 0.9	16.9± 0.8	16.3± 0.6	16.1± 0.9	16.0± 1.1	15.4± 0.8
500ppm	17.1± 1.0	17.0± 1.0	16.6± 0.8	15.5± 1.2	15.7± 1.2	15.4± 1.1
1000ppm	17.4± 0.9	17.0± 1.1	16.2± 1.0	15.9± 1.2	15.6± 1.2	15.8± 1.2
2000ppm	17.7± 0.6*	17.4± 0.9	16.5± 1.1	16.2± 0.7	15.9± 1.0	15.6± 1.0
4000ppm	17.3± 1.2	16.9± 1.3	17.3± 1.4	15.6± 1.2	16.2± 1.3	15.8± 1.2
8000ppm	15.0± 0.7**	15.2± 0.7**	16.0± 0.8	13.9± 0.8**	15.2± 0.8	15.5± 0.7

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

APPENDIX E 2

FOOD CONSUMPTION CHANGES : FEMALE

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	10.5± 0.6	11.0± 0.6	11.3± 0.7	11.5± 0.6	11.4± 0.8	11.0± 0.8	11.2± 1.0
500ppm	10.5± 0.7	10.9± 0.5	11.2± 0.8	11.1± 1.2	11.1± 1.1	10.4± 0.9	10.8± 0.9
1000ppm	10.8± 0.5	11.1± 0.7	11.3± 0.8	11.4± 0.6	11.3± 0.6	10.9± 0.9	11.3± 1.2
2000ppm	10.3± 0.6	11.0± 0.8	10.7± 0.5	10.7± 0.5	10.9± 0.5	10.8± 0.5	11.1± 0.5
4000ppm	9.8± 0.5*	10.3± 0.4	10.6± 0.6	10.4± 0.4**	10.7± 0.5	10.9± 0.5	10.8± 0.4
8000ppm	7.0± 0.5**	9.2± 0.6**	9.9± 0.4**	10.2± 0.5**	10.4± 0.5**	10.2± 0.5	10.8± 0.7

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

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	11.1± 1.1	11.6± 1.1	11.0± 1.3	10.8± 0.7	10.8± 0.6	10.8± 1.0
500ppm	10.7± 0.7	10.9± 0.9	10.7± 0.7	10.5± 0.6	10.6± 0.5	10.3± 0.5
1000ppm	11.2± 0.8	11.5± 1.1	11.1± 0.8	11.1± 0.6	10.9± 0.5	10.6± 0.6
2000ppm	11.2± 0.8	11.0± 0.5	10.9± 0.4	10.9± 0.7	10.3± 0.6	10.3± 0.4
4000ppm	11.0± 0.4	10.8± 0.6	10.9± 0.6	10.7± 0.4	10.1± 0.5*	10.0± 0.5*
8000ppm	11.0± 0.6	10.9± 0.5	11.7± 0.6*	10.3± 0.8	10.8± 0.8	10.9± 0.6

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

APPENDIX F 1

HEMATOLOGY : MALE

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	10	9.59± 0.12	16.1± 0.3	47.0± 0.6	49.0± 0.3	16.8± 0.2	34.2± 0.3	782± 63
500ppm	10	9.64± 0.09	16.1± 0.2	47.1± 0.7	48.9± 0.5	16.7± 0.2	34.1± 0.3	752± 69
1000ppm	10	9.69± 0.12	16.1± 0.2	47.3± 0.6	48.8± 0.3	16.6± 0.2	34.0± 0.2	749± 44
2000ppm	10	9.53± 0.19	16.0± 0.3	46.8± 0.9	49.1± 0.4	16.8± 0.1	34.1± 0.3	741± 51
4000ppm	10	9.42± 0.21	16.1± 0.4	46.7± 1.1	49.6± 0.6**	17.1± 0.5	34.5± 0.8	776± 61
8000ppm	10	9.47± 0.19	16.4± 0.3*	47.9± 0.9	50.5± 0.3**	17.3± 0.3**	34.3± 0.4	740± 119

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

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RETICULOCYTE %		PROTHROMBIN TIME sec		APTT sec	
Control	10	2.2±	0.1	13.3±	1.3	23.0±	1.6
500ppm	10	2.0±	0.2	12.8±	0.7	22.7±	1.0
1000ppm	10	1.9±	0.2**	12.7±	0.8	22.8±	1.3
2000ppm	10	1.9±	0.1**	12.8±	1.2	21.9±	1.7
4000ppm	10	1.9±	0.1**	12.5±	0.6	21.4±	1.6*
8000ppm	10	1.5±	0.2**	12.2±	0.5	18.5±	0.8**

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

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$		Differential WBC (%) N-BAND		N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHER	
Control	10	7.02±	1.21	0±	0	21±	3	1±	1	0±	0	3±	1	74±	4	0±	0
500ppm	10	7.67±	1.77	0±	0	22±	3	1±	1	0±	0	3±	1	74±	4	0±	0
1000ppm	10	7.55±	1.65	0±	0	22±	6	1±	1	0±	0	3±	1	74±	5	0±	0
2000ppm	10	7.36±	1.47	0±	0	21±	4	1±	1	0±	0	3±	2	74±	5	0±	0
4000ppm	10	7.37±	1.41	0±	0	23±	4	1±	1	0±	0	3±	1	73±	3	0±	0
8000ppm	10	5.77±	0.73	0±	0	35±	3**	1±	1	0±	0	4±	1	60±	5**	0±	0

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

APPENDIX F 2

HEMATOLOGY : FEMALE

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	8.66± 0.19	15.8± 0.3	44.8± 0.9	51.7± 0.5	18.2± 0.2	35.2± 0.2	800± 50
500ppm	10	8.79± 0.17	16.0± 0.3	45.5± 0.9	51.7± 0.2	18.3± 0.2	35.3± 0.3	811± 40
1000ppm	10	8.86± 0.12	16.1± 0.3	45.7± 0.6	51.6± 0.3	18.2± 0.1	35.3± 0.2	809± 43
2000ppm	10	8.95± 0.18**	16.3± 0.4**	46.3± 1.0**	51.7± 0.4	18.2± 0.2	35.3± 0.4	796± 40
4000ppm	10	8.83± 0.16	16.0± 0.3	45.5± 0.9	51.5± 0.3	18.2± 0.2	35.2± 0.3	761± 65
8000ppm	10	9.41± 0.24**	16.5± 0.5**	47.7± 1.4**	50.7± 0.5**	17.6± 0.3**	34.7± 0.3**	722± 119

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

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RETICULOCYTE %	PROTHROMBIN TIME sec	APTT sec
Control	10	2.2± 0.3	11.7± 0.3	18.1± 1.1
500ppm	10	2.1± 0.1	11.9± 0.3	18.5± 0.9
1000ppm	10	1.8± 0.2	11.8± 0.3	18.2± 1.0
2000ppm	10	1.8± 0.2	11.7± 0.4	17.8± 1.0
4000ppm	10	1.6± 0.2**	11.7± 0.3	18.0± 1.1
8000ppm	10	1.3± 0.4**	12.1± 0.3	17.5± 0.7

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

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHER
Control	10	4.41± 1.58	0± 0	21± 5	2± 1	0± 0	3± 1	74± 5	0± 0
500ppm	10	4.60± 1.52	0± 0	22± 4	1± 1	0± 0	3± 1	74± 3	0± 0
1000ppm	10	4.31± 0.90	0± 0	21± 4	2± 1	0± 0	3± 1	75± 4	0± 0
2000ppm	10	4.24± 1.01	0± 0	20± 3	1± 1	0± 0	4± 1	75± 3	0± 0
4000ppm	10	4.32± 0.88	0± 0	24± 6	1± 1	0± 0	3± 1	72± 4	0± 0
8000ppm	10	4.17± 0.64	0± 0	34± 4**	1± 1	0± 0	4± 1	61± 3**	0± 0

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

APPENDIX G 1

BIOCHEMISTRY : MALE

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	6.5± 0.2	3.6± 0.1	1.2± 0.1	0.11± 0.01	197± 12	66± 6	61± 16
500ppm	10	6.6± 0.2	3.6± 0.1	1.3± 0.1	0.10± 0.01	194± 8	64± 6	57± 9
1000ppm	10	6.5± 0.1	3.6± 0.1	1.2± 0.1	0.11± 0.01	195± 12	66± 5	65± 24
2000ppm	10	6.5± 0.2	3.6± 0.1	1.2± 0.1	0.11± 0.01	188± 15	68± 4	52± 22
4000ppm	10	6.6± 0.1	3.6± 0.1	1.2± 0.0	0.11± 0.01	183± 9	80± 6**	43± 11
8000ppm	10	6.7± 0.1	3.6± 0.1	1.2± 0.1	0.12± 0.01	165± 17**	91± 5**	28± 9**

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

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	10	114± 10	93± 25	52± 10	166± 61	250± 18	1± 0	92± 11
500ppm	10	112± 9	103± 30	55± 9	175± 69	241± 19	1± 0	91± 8
1000ppm	10	116± 8	93± 22	52± 9	167± 84	248± 15	1± 0	95± 18
2000ppm	10	114± 8	89± 19	51± 7	143± 41	247± 19	1± 0	84± 6
4000ppm	10	124± 9	85± 17	45± 6	144± 38	234± 17	1± 0	84± 5
8000ppm	10	138± 7**	71± 10	48± 6	145± 61	265± 33	1± 0	113± 47

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

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	UREA NITOROGEN mg/dℓ	CREATININE mg/dℓ	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dℓ	INORGANIC PHOSPHORUS mg/dℓ
Control	10	18.8± 0.5	0.5± 0.1	141± 1	3.4± 0.2	104± 1	10.2± 0.2	5.5± 0.6
500ppm	10	19.2± 1.0	0.5± 0.1	141± 1	3.3± 0.3	103± 2	10.3± 0.2	5.5± 0.6
1000ppm	10	19.9± 1.2	0.6± 0.1	141± 1	3.5± 0.2	104± 1	10.2± 0.2	5.5± 0.5
2000ppm	10	21.2± 1.6**	0.6± 0.1	141± 1	3.4± 0.3	104± 1	10.2± 0.2	5.7± 0.6
4000ppm	10	20.2± 1.4*	0.6± 0.1	141± 1	3.4± 0.3	103± 1	10.2± 0.1	5.7± 0.4
8000ppm	10	18.5± 1.6	0.5± 0.1	140± 1	3.9± 0.4**	103± 2	10.4± 0.3	6.3± 0.5**

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

APPENDIX G 2

BIOCHEMISTRY : FEMALE

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	6.3±	0.3	3.6±	0.2	1.3±	0.1	0.12±	0.01	148±	16	78±	9	14±	5
500ppm	10	6.3±	0.2	3.5±	0.1	1.3±	0.0	0.12±	0.01	144±	11	78±	5	14±	4
1000ppm	10	6.3±	0.1	3.5±	0.1	1.3±	0.1	0.12±	0.01	149±	18	80±	4	15±	7
2000ppm	10	6.3±	0.1	3.5±	0.1	1.3±	0.1	0.12±	0.01	155±	14	83±	7	15±	3
4000ppm	10	6.3±	0.2	3.5±	0.1	1.2±	0.1**	0.13±	0.02	146±	15	85±	7	15±	2
8000ppm	10	6.4±	0.2	3.4±	0.1	1.2±	0.1**	0.13±	0.01	160±	20	96±	7**	17±	4

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

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	140± 16	72± 14	38± 14	198± 134	195± 24	1± 1	103± 38
500ppm	10	139± 7	72± 8	36± 5	179± 87	197± 19	1± 0	95± 22
1000ppm	10	143± 8	71± 8	37± 6	202± 104	188± 22	1± 0	107± 31
2000ppm	10	146± 10	78± 12	40± 10	198± 74	191± 19	2± 1	101± 20
4000ppm	10	146± 13	69± 6	37± 10	207± 102	188± 25	2± 0	97± 24
8000ppm	10	149± 10	71± 5	51± 6**	243± 87	267± 42**	2± 1	110± 18

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

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	UREA NITROGEN mg/dl		CREATININE mg/dl		SODIUM mEq/l		POTASSIUM mEq/l		CHLORIDE mEq/l		CALCIUM mg/dl		INORGANIC PHOSPHORUS mg/dl	
Control	10	19.9±	1.7	0.5±	0.1	140±	2	3.5±	0.4	105±	1	9.9±	0.2	5.0±	0.9
500ppm	10	18.7±	1.3	0.5±	0.1	141±	1	3.3±	0.3	106±	1	9.8±	0.2	5.1±	1.0
1000ppm	10	19.6±	1.4	0.5±	0.1	141±	1	3.5±	0.2	105±	2	9.9±	0.2	5.2±	0.9
2000ppm	10	20.3±	1.1	0.5±	0.1	140±	1	3.4±	0.3	105±	2	9.8±	0.1	5.1±	1.0
4000ppm	10	19.5±	1.5	0.5±	0.1	140±	1	3.6±	0.3	105±	2	9.8±	0.2	5.3±	0.8
8000ppm	10	17.7±	1.4**	0.5±	0.0	140±	2	3.8±	0.2*	104±	2	10.1±	0.2	5.7±	0.4

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

APPENDIX H 1

URINALYSIS : MALE

STUDY NO. : 0558 URINALYSIS
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	Bilirubin −	+	2+	3+	CHI
Control	10	0	0	0	0	1	8	1		0	3	3	4	0	0		10	0	0	0	0	0		6	4	0	0	0	0		10	0	0	0	
500ppm	10	0	0	0	1	1	8	0		0	3	4	3	0	0		10	0	0	0	0	0		6	4	0	0	0	0		10	0	0	0	
1000ppm	10	0	0	0	0	0	9	1		0	3	6	1	0	0		10	0	0	0	0	0		8	2	0	0	0	0		10	0	0	0	
2000ppm	10	0	0	0	0	2	8	0		0	4	3	2	1	0		10	0	0	0	0	0		6	3	1	0	0	0		10	0	0	0	
4000ppm	10	0	0	0	0	1	8	1		0	1	7	2	0	0		10	0	0	0	0	0		7	3	0	0	0	0		10	0	0	0	
8000ppm	10	0	0	0	0	0	10	0		0	0	9	1	0	0	*	10	0	0	0	0	0		8	2	0	0	0	0		10	0	0	0	

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

(HCL101)

STUDY NO. : 0558 URINALYSIS
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

Group Name	NO. of Animals	Occult blood −	±	+	2+	3+	CHI	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0		10	0	0	0	0	
500ppm	10	10	0	0	0	0		10	0	0	0	0	
1000ppm	10	10	0	0	0	0		10	0	0	0	0	
2000ppm	10	10	0	0	0	0		10	0	0	0	0	
4000ppm	10	10	0	0	0	0		10	0	0	0	0	
8000ppm	10	10	0	0	0	0		10	0	0	0	0	

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

APPENDIX H 2

URINALYSIS : FEMALE

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE 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	Bilirubin −	+	2+	3+	CHI
Control	10	0	0	0	0	1	7	2		3	7	0	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
500ppm	10	0	0	0	1	0	8	1		5	5	0	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
1000ppm	10	0	0	0	1	2	7	0		6	4	0	0	0	0		10	0	0	0	0	0		9	1	0	0	0	0		10	0	0	0	
2000ppm	10	0	0	0	0	2	8	0		3	6	1	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
4000ppm	10	0	0	0	0	1	8	1		4	5	1	0	0	0		10	0	0	0	0	0		8	2	0	0	0	0		10	0	0	0	
8000ppm	10	0	0	0	0	1	9	0		4	4	2	0	0	0		10	0	0	0	0	0		6	4	0	0	0	0	*	10	0	0	0	

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

STUDY NO. : 0558 URINALYSIS
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

Group Name	NO. of Animals	Occult blood −	±	+	2+	3+	CHI	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0		10	0	0	0	0	
500ppm	10	10	0	0	0	0		10	0	0	0	0	
1000ppm	10	10	0	0	0	0		10	0	0	0	0	
2000ppm	10	10	0	0	0	0		10	0	0	0	0	
4000ppm	10	10	0	0	0	0		10	0	0	0	0	
8000ppm	10	10	0	0	0	0		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. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	500ppm 10 (%)	1000ppm 10 (%)	2000ppm 10 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
liver	herniation		2 (20)	2 (20)	2 (20)	1 (10)
testis	small		0 (0)	0 (0)	0 (0)	0 (0)

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name / NO. of Animals	4000ppm 10	(%)	8000ppm 10	(%)
thymus	atrophic		0	(0)	1	(10)
liver	herniation		5	(50)	0	(0)
testis	small		0	(0)	1	(10)

APPENDIX I 2

GROSS FINDINGS : FEMALE

Organ	Findings	Group Name / NO. of Animals	Control 10	(%)	500ppm 10	(%)	1000ppm 10	(%)	2000ppm 10	(%)
liver	herniation		0	(0)	0	(0)	2	(20)	1	(10)
uterus	small		0	(0)	0	(0)	0	(0)	0	(0)

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name	4000ppm		8000ppm	
		NO. of Animals	10	(%)	10	(%)
liver	herniation		0	(0)	2	(20)
uterus	small		0	(0)	10	(100)

APPENDIX J 1

ORGAN WEIGHT, ABSOLUTE : MALE

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	301± 15	0.249± 0.051	0.049± 0.004	3.274± 0.318	0.915± 0.054	0.971± 0.069
500ppm	10	295± 14	0.238± 0.023	0.049± 0.003	3.167± 0.102	0.907± 0.047	0.960± 0.062
1000ppm	10	297± 16	0.244± 0.033	0.051± 0.005	3.191± 0.090	0.907± 0.039	0.970± 0.039
2000ppm	10	302± 14	0.241± 0.022	0.051± 0.003	3.204± 0.091	0.918± 0.036	0.984± 0.050
4000ppm	10	303± 18	0.226± 0.025	0.052± 0.005	3.255± 0.099	0.928± 0.048	0.999± 0.040
8000ppm	10	230± 11**	0.144± 0.020**	0.060± 0.004**	2.607± 0.483**	0.849± 0.051*	0.904± 0.040*

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

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	1.798± 0.075	0.562± 0.042	7.495± 0.468	1.921± 0.028
500ppm	10	1.810± 0.117	0.557± 0.027	7.395± 0.431	1.907± 0.034
1000ppm	10	1.820± 0.067	0.565± 0.039	7.578± 0.489	1.930± 0.028
2000ppm	10	1.844± 0.050	0.581± 0.033	7.597± 0.416	1.934± 0.026
4000ppm	10	1.897± 0.096	0.572± 0.038	8.059± 0.644	1.890± 0.033
8000ppm	10	1.737± 0.113	0.390± 0.036**	7.513± 0.591	1.753± 0.034**

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

APPENDIX J 2

ORGAN WEIGHT, ABSOLUTE : FEMALE

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	170± 9	0.194± 0.026	0.057± 0.005	0.099± 0.015	0.604± 0.033	0.722± 0.045
500ppm	10	167± 8	0.191± 0.018	0.053± 0.003	0.089± 0.009	0.604± 0.026	0.727± 0.026
1000ppm	10	169± 9	0.199± 0.025	0.058± 0.005	0.099± 0.004	0.628± 0.029	0.745± 0.039
2000ppm	10	167± 4	0.179± 0.016	0.053± 0.004	0.086± 0.008	0.600± 0.020	0.720± 0.018
4000ppm	10	165± 6	0.172± 0.017	0.056± 0.005	0.094± 0.007	0.623± 0.041	0.732± 0.025
8000ppm	10	150± 8**	0.136± 0.021**	0.066± 0.005**	0.074± 0.014**	0.615± 0.040	0.703± 0.035

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

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	1.138± 0.047	0.384± 0.027	4.059± 0.222	1.801± 0.028
500ppm	10	1.149± 0.046	0.378± 0.030	4.014± 0.250	1.793± 0.024
1000ppm	10	1.153± 0.061	0.376± 0.022	4.084± 0.201	1.797± 0.020
2000ppm	10	1.134± 0.029	0.364± 0.015	4.003± 0.154	1.784± 0.028
4000ppm	10	1.174± 0.031	0.358± 0.017	4.171± 0.133	1.771± 0.020
8000ppm	10	1.230± 0.046**	0.272± 0.023**	4.944± 0.396**	1.635± 0.034**

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

APPENDIX K 1

ORGAN WEIGHT, RELATIVE : MALE

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	301± 15	0.083± 0.015	0.016± 0.002	1.088± 0.073	0.304± 0.015	0.323± 0.011
500ppm	10	295± 14	0.081± 0.009	0.017± 0.001	1.074± 0.046	0.307± 0.007	0.325± 0.014
1000ppm	10	297± 16	0.082± 0.008	0.017± 0.002	1.076± 0.057	0.305± 0.011	0.327± 0.007
2000ppm	10	302± 14	0.080± 0.007	0.017± 0.001	1.062± 0.045	0.304± 0.013	0.326± 0.011
4000ppm	10	303± 18	0.074± 0.007	0.017± 0.001	1.078± 0.068	0.307± 0.014	0.330± 0.018
8000ppm	10	230± 11**	0.063± 0.007**	0.026± 0.002**	1.138± 0.217	0.369± 0.019**	0.394± 0.011**

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

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.599± 0.023	0.187± 0.010	2.493± 0.072	0.640± 0.034
500ppm	10	0.613± 0.023	0.189± 0.008	2.503± 0.074	0.647± 0.028
1000ppm	10	0.613± 0.015	0.190± 0.005	2.548± 0.046	0.650± 0.030
2000ppm	10	0.611± 0.016	0.192± 0.009	2.515± 0.068	0.641± 0.029
4000ppm	10	0.626± 0.021*	0.189± 0.010	2.658± 0.097**	0.625± 0.029
8000ppm	10	0.755± 0.030**	0.170± 0.014**	3.267± 0.189**	0.764± 0.030**

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

APPENDIX K 2

ORGAN WEIGHT, RELATIVE : FEMALE

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	170± 9	0.114± 0.015	0.034± 0.002	0.058± 0.011	0.355± 0.015	0.425± 0.022
500ppm	10	167± 8	0.114± 0.009	0.032± 0.002	0.053± 0.004	0.361± 0.014	0.435± 0.020
1000ppm	10	169± 9	0.118± 0.013	0.035± 0.004	0.059± 0.005	0.372± 0.015	0.442± 0.036
2000ppm	10	167± 4	0.107± 0.009	0.032± 0.002	0.052± 0.004	0.359± 0.014	0.431± 0.016
4000ppm	10	165± 6	0.104± 0.011	0.034± 0.004	0.057± 0.004	0.377± 0.017*	0.444± 0.021
8000ppm	10	150± 8**	0.090± 0.012**	0.044± 0.004**	0.049± 0.008	0.411± 0.029**	0.469± 0.012**

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

STUDY NO. : 0558
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.669± 0.024	0.226± 0.015	2.388± 0.088	1.061± 0.052
500ppm	10	0.687± 0.020	0.226± 0.016	2.399± 0.074	1.073± 0.047
1000ppm	10	0.683± 0.029	0.222± 0.011	2.417± 0.090	1.066± 0.058
2000ppm	10	0.678± 0.012	0.218± 0.008	2.394± 0.083	1.068± 0.033
4000ppm	10	0.712± 0.021*	0.217± 0.010	2.528± 0.084*	1.074± 0.045
8000ppm	10	0.823± 0.038**	0.182± 0.017**	3.301± 0.205**	1.094± 0.042

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				500ppm				1000ppm				2000ppm			
		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
{Hematopoietic system}																		
thymus			<10>				<10>				<10>				<10>			
	atrophy		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Circulatory system}																		
heart			<10>				<10>				<10>				<10>			
	granulation		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)
{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>			
	herniation		2	0	0	0	2	0	0	0	2	0	0	0	1	0	0	0
			(20)	(0)	(0)	(0)	(20)	(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	4000ppm				8000ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
thymus			<10>				<10>			
	atrophy		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Circulatory system}										
heart			<10>				<10>			
	granulation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}										
stomach			<10>				<10>			
	erosion:forestomach		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	hyperplasia:forestomach		0	0	0	0	5	0	0	0 *
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
liver			<10>				<10>			
	herniation		5	0	0	0	0	0	0	0
			(50)	(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 (%)	500ppm 10 1 (%)	500ppm 10 2 (%)	500ppm 10 3 (%)	500ppm 10 4 (%)	1000ppm 10 1 (%)	1000ppm 10 2 (%)	1000ppm 10 3 (%)	1000ppm 10 4 (%)	2000ppm 10 1 (%)	2000ppm 10 2 (%)	2000ppm 10 3 (%)	2000ppm 10 4 (%)
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	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>			
	eosinophilic body		10 (100)	0 (0)	0 (0)	0 (0)	8 (80)	1 (10)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0)
{Endocrine system}																		
pituitary			<10>				<10>				<10>				<10>			
	cyst		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
{Reproductive system}																		
testis			<10>				<10>				<10>				<10>			
	germ cell necrosis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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	4000ppm				8000ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
liver			<10>				<10>			
	hepatocellular hypertrophy:central		0	0	0	0	10	0	0	0 **
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Urinary system}										
kidney			<10>				<10>			
	eosinophilic body		10	0	0	0	10	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Endocrine system}										
pituitary			<10>				<10>			
	cyst		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Reproductive system}										
testis			<10>				<10>			
	germ cell necrosis		0	0	0	0	8	2	0	0 **
			(0)	(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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				500ppm				1000ppm				2000ppm			
		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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Reproductive system}																		
epididymis			<10>				<10>				<10>				<10>			
	decreased:sperma		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Special sense organs/appendage}																		
Harder gl			<10>				<10>				<10>				<10>			
	lymphocytic infiltration		1	0	0	0	1	0	0	0	1	0	0	0	3	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(30)	(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	4000ppm				8000ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Reproductive system}										
epididymis			<10>				<10>			
	decreased:sperma		0	0	0	0	0	1	1	0
			(0)	(0)	(0)	(0)	(0)	(10)	(10)	(0)
{Special sense organs/appendage}										
Harder gl			<10>				<10>			
	lymphocytic infiltration		4	0	0	0	1	0	0	0
			(40)	(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				500ppm				1000ppm				2000ppm			
		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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}																		
bone marrow			<10>				<10>				<10>				<10>			
	granulation		0	1	0	0	1	0	0	0	3	0	0	0	1	1	0	0
			(0)	(10)	(0)	(0)	(10)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(10)	(10)	(0)	(0)
{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>			
	herniation		0	0	0	0	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)
	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>			
	pyelitis		0	0	0	0	0	0	0	0	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	4000ppm				8000ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
bone marrow			<10>				<10>			
	granulation		2	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}										
stomach			<10>				<10>			
	hyperplasia:forestomach		0	0	0	0	4	0	0	0
			(0)	(0)	(0)	(0)	(40)	(0)	(0)	(0)
liver			<10>				<10>			
	herniation		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	hepatocellular hypertrophy:central		0	0	0	0	6	0	0	0 *
			(0)	(0)	(0)	(0)	(60)	(0)	(0)	(0)
{Urinary system}										
kidney			<10>				<10>			
	pyelitis		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 / No. of Animals on Study / Grade	Control 10				500ppm 10				1000ppm 10				2000ppm 10			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Endocrine system}																		
pituitary			<10>				<10>				<10>				<10>			
	Rathke pouch		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
{Special sense organs/appendage}																		
Harder gl			<10>				<10>				<10>				<10>			
	lymphocytic infiltration		3 (30)	0 (0)	0 (0)	0 (0)	5 (50)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	5 (50)	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	4000ppm				8000ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Endocrine system}										
pituitary			<10>				<10>			
	Rathke pouch		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Special sense organs/appendage}										
Harder gl			<10>				<10>			
	lymphocytic infiltration		3	0	0	0	3	0	0	0
			(30)	(0)	(0)	(0)	(30)	(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
Prothrombin time	Quick one stage method [2]	sec	1
Activated partial thromboplastin time (APTT)	Ellagic acid activaterd method [2]	sec	1
White blood cell(WBC)	Light scattering method [1]	$\times 10^3/\mu L$	2
Differential WBC	Pattern recognition method [3] (Wright staining)	%	0
Biochemistry			
Total protein(TP)	Biuret method [4]	g/dL	1
Albumin (Alb)	BCG method [4]	g/dL	1
A/G ratio	Calculated as Alb/(TP−Alb) [4]	−	1
T-bilirubin	Alkaline azobilirubin method [4]	mg/dL	2
Glucose	GlcK·G-6-PDH method [4]	mg/dL	0
T-cholesterol	CE·COD·POD method [4]	mg/dL	0
Triglyceride	LPL·GK·GPO·POD method [4]	mg/dL	0
Phospholipid	PLD·ChOD·POD method [4]	mg/dL	0
Aspartate aminotransferase (AST)	JSCC method [4]	IU/L	0
Alanine aminotransferase (ALT)	JSCC method [4]	IU/L	0
Lactate dehydrogenase (LDH)	SFBC method [4]	IU/L	0
Alkaline phosphatase (ALP)	GSCC method [4]	IU/L	0
γ-Glutamyl transpeptidase (γ-GTP)	JSCC method [4]	IU/L	0
Creatine kinase (CK)	JSCC method [4]	IU/L	0
Urea nitrogen	Urease·GLDH method [4]	mg/dL	1
Creatinine	Jaffe method [4]	mg/dL	1
Sodium	Ion selective electrode method [4]	mEq/L	0
Potassium	Ion selective electrode method [4]	mEq/L	1
Chloride	Ion selective electrode method [4]	mEq/L	0
Calcium	OCPC method [4]	mg/dL	1
Inorganic phosphorus	PNP·XOD·POD method [4]	mg/dL	1

1) Automatic blood cell analyzer (ADVIA120 : Bayer Corporation)
2) Automatic coagulometer (Sysmex CA-5000 : Sysmex Corporation)
3) Automatic blood cell differential analyzer (MICROX HEG-120NA : OMRON Corporation)
4) Automatic analyzer (Hitachi 7080 : Hitachi,Ltd.)