ジフェニルアミンのマウスを用いた
経口投与による2週間毒性試験（混餌試験）報告書

試験番号：0652

APPENDICES

APPENDICES

APPENDICES (CONTINUED)

APPENDIX A 1

IDENTITY OF DIPHENYLAMINE

IN THE 2-WEEK FEED STUDY

IDENTITY OF DIPHENYLAMINE IN THE 2-WEEK FEED STUDY

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

Lot No. : SDH5697

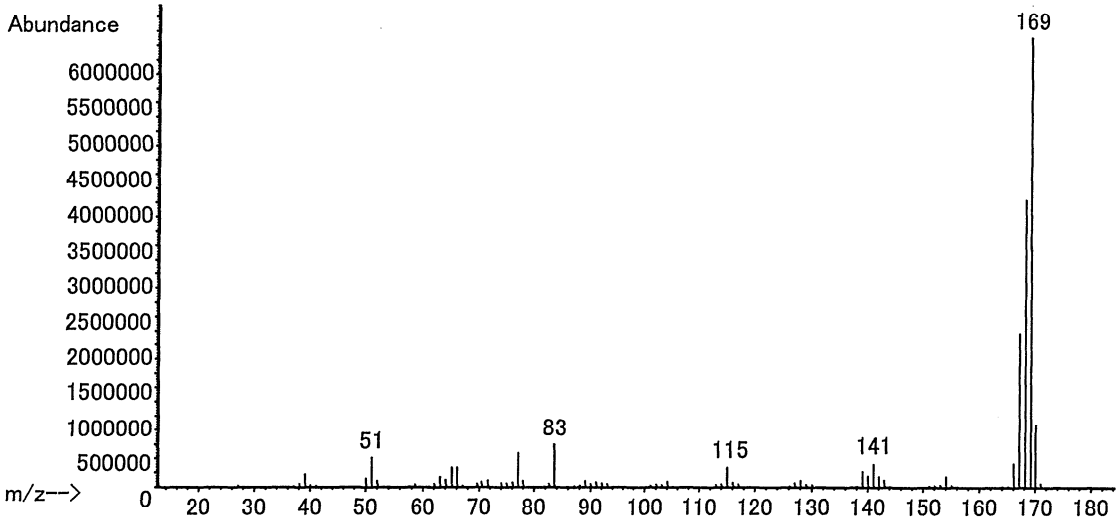
1. Spectral Data

Mass Spectrometry

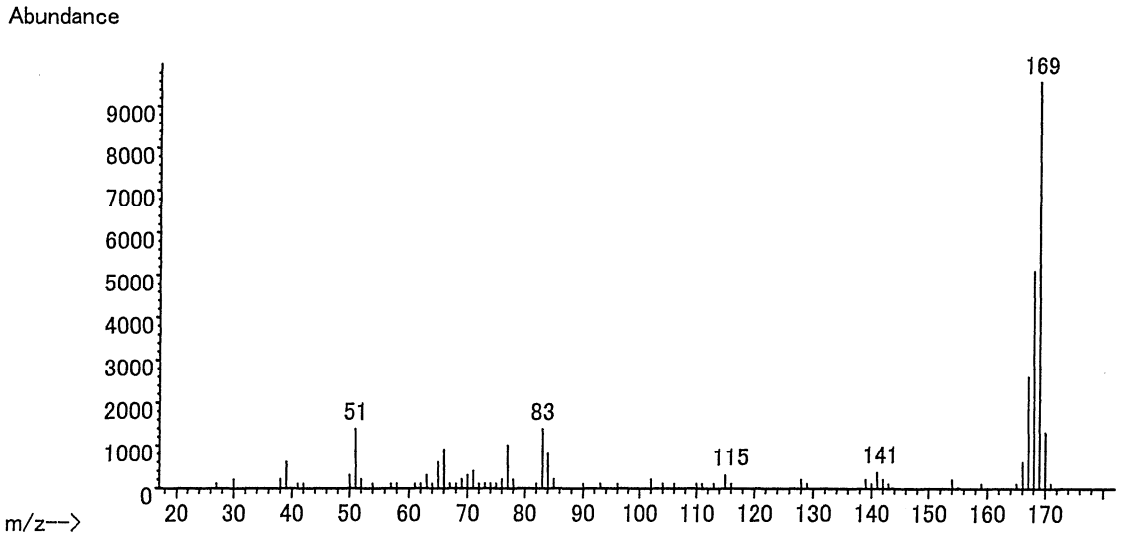
Instrument : Agilent Technologies 5973N Mass Spectrometer

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.

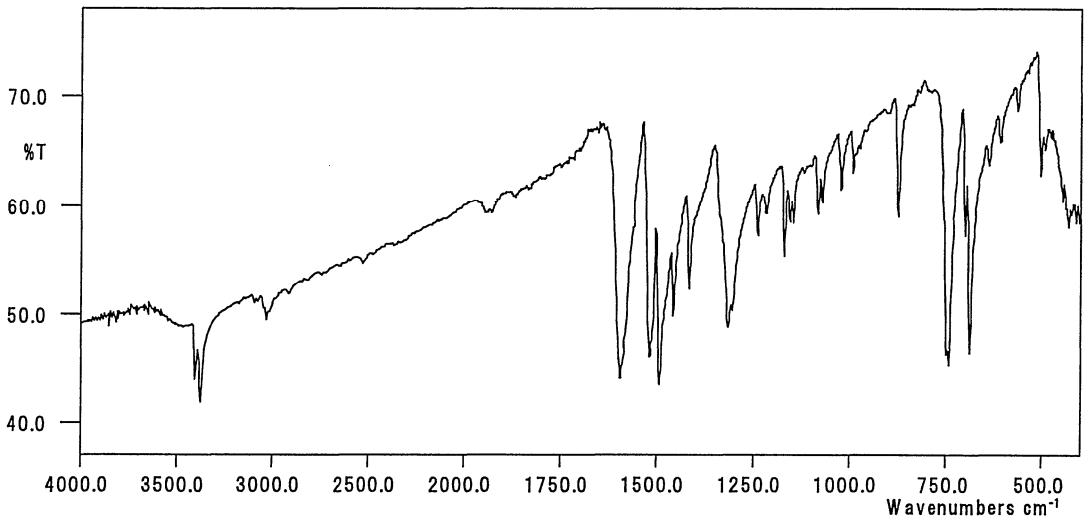
(*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed. New York, NY:John Wiley and Sons.)

Infrared Spectrometry

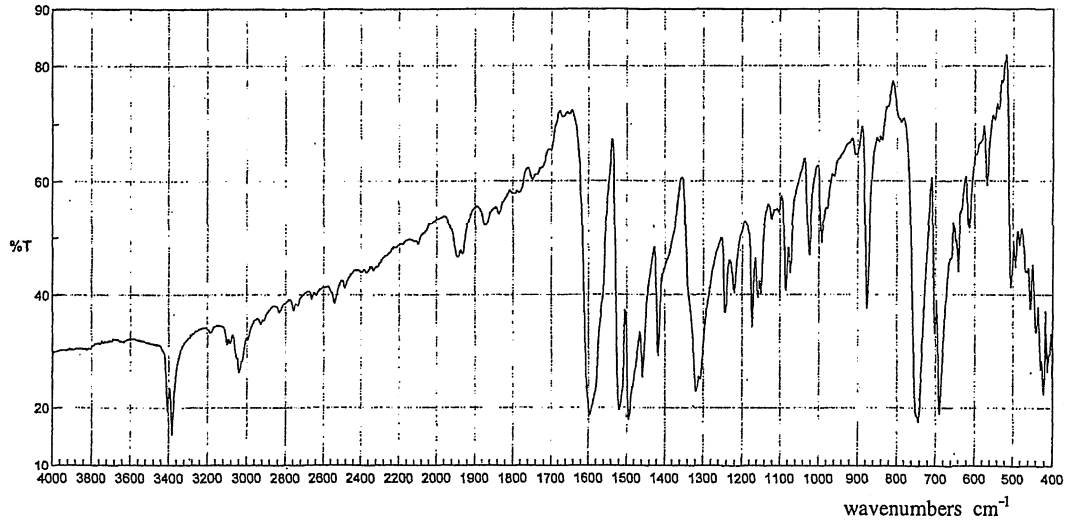
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr

Resolution : 2 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 diphenylamine by mass spectrum and infrared spectrum.

APPENDIX A 2

STABILITY OF DIPHENYLAMINE IN THE 2-WEEK FEED STUDY

STABILITY OF DIPHENYLAMINE IN THE 2-WEEK FEED STUDY

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

Lot No. : SDH5697

1. High Performance Liquid Chromatography

Instrument : Shimadzu LC-10 High Performance Liquid Chromatograph

Column : TSK-GEL ODS-80TM (4.6 mmϕ × 15 cm)

Column Temperature: 40 °C

Flow Rate : 1 mL/min

Mobile Phase : Acetonitrile : Distilled Water = 70 : 30

Detector : UV (285 nm)

Injection Volume : 10 μL

Date analyzed	Peak No.	Retention Time (min)	Area (%)
2006.08.14	1	4.323	100
2006.09.08	1	4.325	100

Result: High performance liquid chromatography indicated one major peak (peak No.1) analyzed on 2006.8.14 and one major peak (peak No.1) analyzed on 2006.9.8. No new trace impurity peak in the test substance analyzed on 2006.9.8 was detected.

2. Conclusion: The test substance was stable for the period that the test substance had been used for the study.

APPENDIX A 3

CONCENTRATION OF DIPHENYLAMINE IN FORMULATED DIETS IN THE 2-WEEK FEED STUDY

CONCENTRATION OF DIPHENYLAMINE IN FORMULATED DIETS IN THE 2-WEEK FEED STUDY

Analytical Method : The samples were analyzed by high performance liquid chromatography.

Instrument : Shimadzu LC-10 High Performance Liquid Chromatograph

Column : TSK-GEL ODS-80TM (4.6 mmϕ × 15 cm)

Column Temperature: 40 °C

Flow Rate : 1 mL/min

Mobile Phase : Acetonitrile : Distilled Water = 70 : 30

Detector : UV (285 nm)

Injection Volume : 10 μL

	Target Concentration				
Date Analyzed	1600[a]	4000	7000	10000	25000
2006.08.23	1640[b] (103)[c]	4080 (102)	6990 (99.9)	10000 (100)	25400 (102)

[a] ppm
[b] ppm (Mean measured concentration.)
[c] % (Mean measured concentration/target concentration × 100.)

APPENDIX A 4

HOMOGENEITY OF DIPHENYLAMINE IN FORMULATED DIETS IN THE 2-WEEK FEED STUDY

HOMOGENEITY OF DIPHENYLAMINE IN FORMULATED DIETS IN THE 2-WEEK FEED STUDY

Analytical Method : The samples were analyzed by high performance liquid chromatography.

Instrument : Shimadzu LC-10 High Performance Liquid Chromatograph

Column : TSK-GEL ODS-80TM (4.6 mmϕ × 15 cm)

Column Temperature: 40 °C

Flow Rate : 1 mL/min

Mobile Phase : Acetonitrile : Distilled Water = 70 : 30

Detector : UV (285 nm)

Injection Volume : 10 μL

	Target Concentration				
	1600[a]	4000	7000	10000	25000
Coefficient Variation	1.85[b]	1.55	2.89	2.33	2.12

[a] ppm
[b] % (n=7)

APPENDIX A 5

STABILITY OF DIPHENYLAMINE

IN FORMULATED DIETS IN THE 2-WEEK FEED STUDY

STABILITY OF DIPHENYLAMINE IN FORMULATED DIETS IN THE 2-WEEK FEED STUDY

Analytical Method : The samples were analyzed by high performance liquid chromatography.

Instrument : Shimadzu LC-10 High Performance Liquid Chromatograph

Column : TSK-GEL ODS-80TM (4.6 mmϕ × 15 cm)

Column Temperature: 40 °C

Flow Rate : 1 mL/min

Mobile Phase : Acetonitrile : Distilled Water = 70 : 30

Detector : UV (285 nm)

Injection Volume : 10 μL

	Target Concentration	
Date Analyzed	1600[a]	25000
2006.07.20	1570 (100)[b]	24600 (100)
2006.07.28[c]	1600 (102)	25700 (105)
2006.07.28[d]	1660 (106)	26300 (107)

[a] ppm
[b] % (Percentage was based on the concentration at the date of preparation.)
[c] Animal room samples
[d] Cold storage samples

APPENDIX B 1

CLINICAL OBSERVATION : MALE

STUDY NO. : 0652
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 1-4	1-7	2-4	2-7
DEATH	Control	0	0	0	0
	1600ppm	0	0	0	0
	4000ppm	0	0	0	0
	7000ppm	0	0	0	0
	10000ppm	0	0	0	0
	25000ppm	0	0	0	1
LOCOMOTOR MOVEMENT DECR	Control	0	0	0	0
	1600ppm	0	0	0	0
	4000ppm	0	0	0	0
	7000ppm	0	0	0	0
	10000ppm	0	0	0	0
	25000ppm	0	0	5	4
HUNCHBACK POSITION	Control	0	0	0	0
	1600ppm	0	0	0	0
	4000ppm	0	0	0	0
	7000ppm	0	0	0	0
	10000ppm	0	0	0	0
	25000ppm	0	0	5	4
PILOERECTION	Control	0	0	0	0
	1600ppm	0	0	0	0
	4000ppm	0	0	0	0
	7000ppm	0	0	0	0
	10000ppm	0	0	0	0
	25000ppm	0	1	5	4
OLIGO-STOOL	Control	0	0	0	0
	1600ppm	0	0	0	0
	4000ppm	0	0	0	0
	7000ppm	0	0	0	0
	10000ppm	0	0	0	0
	25000ppm	5	5	5	4
NON REMARKABLE	Control	5	5	5	5
	1600ppm	5	5	5	5
	4000ppm	5	5	5	5
	7000ppm	5	5	5	5
	10000ppm	5	5	5	5
	25000ppm	0	0	0	0

APPENDIX B 2

CLINICAL OBSERVATION : FEMALE

Clinical sign	Group Name	Administration Week-day 1-4	1-7	2-4	2-7
LOCOMOTOR MOVEMENT DECR	Control	0	0	0	0
	1600ppm	0	0	0	0
	4000ppm	0	0	0	0
	7000ppm	0	0	0	0
	10000ppm	0	0	0	0
	25000ppm	0	0	5	5
HUNCHBACK POSITION	Control	0	0	0	0
	1600ppm	0	0	0	0
	4000ppm	0	0	0	0
	7000ppm	0	0	0	0
	10000ppm	0	0	0	0
	25000ppm	0	0	5	5
PILOERECTION	Control	0	0	0	0
	1600ppm	0	0	0	0
	4000ppm	0	0	0	0
	7000ppm	0	0	0	0
	10000ppm	0	0	0	0
	25000ppm	0	0	5	5
OLIGO-STOOL	Control	0	0	0	0
	1600ppm	0	0	0	0
	4000ppm	0	0	0	0
	7000ppm	0	0	0	0
	10000ppm	0	0	0	0
	25000ppm	5	5	5	5
NON REMARKABLE	Control	5	5	5	5
	1600ppm	5	5	5	5
	4000ppm	5	5	5	5
	7000ppm	5	5	5	5
	10000ppm	5	5	5	5
	25000ppm	0	0	0	0

APPENDIX C 1

BODY WEIGHT CHANGES : MALE

STUDY NO. : 0652
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-4	1-7	2-4	2-7
Control	23.0± 0.5	23.4± 0.8	24.3± 1.0	25.3± 1.0	25.5± 0.9
1600ppm	22.9± 0.6	23.3± 0.9	24.0± 0.9	24.9± 0.9	25.5± 0.8
4000ppm	22.9± 0.6	22.8± 0.4	23.0± 0.7	24.4± 0.6	25.1± 0.6
7000ppm	23.0± 0.5	21.9± 1.0*	22.1± 0.7**	24.1± 1.0	24.8± 0.8
10000ppm	22.7± 1.0	19.3± 1.1**	20.0± 1.5**	22.2± 1.1**	22.8± 1.3**
25000ppm	22.9± 0.6	16.1± 0.5**	15.0± 0.4**	14.4± 0.5**	14.3± 1.1**

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

APPENDIX C 2

BODY WEIGHT CHANGES : FEMALE

STUDY NO. : 0652
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-4	1-7	2-4	2-7
Control	19.0± 0.6	19.8± 0.3	19.7± 0.7	20.3± 0.8	20.6± 0.4
1600ppm	19.1± 0.5	19.2± 0.5	19.4± 0.4	20.3± 0.7	20.9± 0.9
4000ppm	19.0± 0.6	18.5± 0.3**	19.5± 0.8	20.3± 0.9	20.5± 0.3
7000ppm	19.0± 0.7	17.7± 0.5**	18.4± 0.5*	20.3± 1.0	20.4± 0.8
10000ppm	19.0± 1.1	16.5± 1.4**	16.9± 1.7**	18.8± 1.3*	19.5± 1.3
25000ppm	19.0± 0.7	13.7± 0.2**	12.6± 0.4**	12.0± 0.4**	11.4± 1.0**

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

APPENDIX D 1

FOOD CONSUMPTION CHANGES : MALE

STUDY NO. : 0652
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-4(4)	1-7(3)	2-4(4)	2-7(3)
Control	3.9± 0.4	4.5± 0.5	4.0± 0.4	3.9± 0.2
1600ppm	3.7± 0.4	4.2± 0.4	3.7± 0.2	4.0± 0.6
4000ppm	3.7± 0.2	3.7± 0.7*	4.0± 0.2	4.1± 0.2
7000ppm	3.3± 0.3*	3.9± 0.5	4.4± 0.6	4.8± 0.7*
10000ppm	2.1± 0.4**	3.5± 0.5*	3.8± 0.3	4.2± 0.3
25000ppm	0.7± 0.1**	1.6± 0.2**	1.5± 0.3**	1.2± 0.3**

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

APPENDIX D 2

FOOD CONSUMPTION CHANGES : FEMALE

STUDY NO. : 0652
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-4(4)	1-7(3)	2-4(4)	2-7(3)
Control	3.5± 0.2	3.5± 0.3	3.5± 0.2	3.7± 0.3
1600ppm	3.3± 0.3	3.3± 0.2	3.3± 0.3	3.8± 0.5
4000ppm	3.5± 0.3	3.6± 0.7	3.5± 0.4	3.8± 0.4
7000ppm	2.7± 0.2**	3.4± 0.4	3.8± 0.4	3.4± 0.1
10000ppm	1.9± 0.3**	2.8± 0.4	3.2± 0.2	4.4± 0.9
25000ppm	0.8± 0.1**	1.5± 0.2**	1.5± 0.1**	1.2± 0.6**

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

APPENDIX E 1

CHEMICAL INTAKE CHANGES : MALE

STUDY NO. : 0652
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : mg/kg/day
REPORT TYPE : A1 2
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (Week-Day) 1-4		1-7		2-4		2-7	
Control	0±	0	0±	0	0±	0	0±	0
1600ppm	254±	18	278±	24	235±	16	252±	32
4000ppm	651±	48	635±	100	658±	28	657±	35
7000ppm	1047±	69	1230±	154	1288±	125	1346±	179
10000ppm	1085±	189	1752±	186	1725±	125	1835±	176
25000ppm	1145±	166	2668±	269	2605±	502	2006±	463

APPENDIX E 2

CHEMICAL INTAKE CHANGES : FEMALE

STUDY NO. : 0652
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
UNIT : mg/kg/d a y
REPORT TYPE : A1 2
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (Week-Day) 1-4		1-7		2-4		2-7	
Control	0±	0	0±	0	0±	0	0±	0
1600ppm	274±	20	276±	12	263±	20	292±	24
4000ppm	753±	63	745±	130	685±	58	733±	68
7000ppm	1063±	80	1280±	143	1320±	81	1154±	59
10000ppm	1172±	193	1685±	234	1716±	100	2279±	534
25000ppm	1385±	193	2938±	394	3044±	171	2485±	1117

APPENDIX F 1

HEMATOLOGY : MALE

STUDY NO. : 0652
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	RED BLOOD CELL 10^6/μℓ	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV fℓ	MCH pg	MCHC g/dℓ	PLATELET 10^3/μℓ
Control	5	10.31± 0.27	15.9± 0.4	47.5± 1.7	46.0± 0.7	15.4± 0.1	33.5± 0.4	1042± 84
1600ppm	5	8.19± 0.40**	16.0± 1.0	40.6± 2.8**	49.5± 1.3**	19.5± 0.3**	39.4± 0.8**	1087± 65
4000ppm	5	6.73± 0.10**	13.4± 0.4**	37.9± 1.3**	56.3± 1.5**	19.8± 0.4**	35.2± 0.4	942± 80
7000ppm	5	5.97± 0.22**	10.7± 0.3**	39.6± 1.9**	66.4± 1.5**	18.0± 0.3**	27.1± 0.6**	835± 47**
10000ppm	5	5.76± 0.21**	10.0± 0.5**	39.9± 1.3**	69.4± 1.8**	17.4± 0.3**	25.1± 0.9**	741± 41**
25000ppm	4	2.49± 0.54**	3.8± 0.8**	14.8± 3.5**	59.2± 2.3**	15.3± 0.9	25.8± 2.2**	1018± 146

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

Group Name	NO. of Animals	RETICULOCYTE %	METHEMOGLOBIN %
Control	5	1.8± 0.2	0.5± 0.1
1600ppm	5	-	3.1± 0.8
4000ppm	5	-	9.9± 0.5**
7000ppm	5	-	15.7± 3.6**
10000ppm	5	-	17.6± 1.8**
25000ppm	4	-	15.9± 1.9**

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

STUDY NO. : 0652
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%)
Control	5	3.71± 1.34	
1600ppm	5	5.04± 2.64	
4000ppm	5	5.89± 1.42	
7000ppm	5	4.90± 1.04	
10000ppm	5	5.08± 1.70	
25000ppm	4	12.23± 5.51**	

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

APPENDIX F 2

HEMATOLOGY : FEMALE

STUDY NO. : 0652
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV fℓ	MCH pg	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	5	9.74± 0.48	15.0± 0.6	44.7± 1.6	45.8± 1.0	15.4± 0.2	33.6± 0.3	945± 46
1600ppm	4	8.18± 0.33**	15.3± 0.6	40.9± 2.4	49.9± 0.9*	18.7± 0.1**	37.5± 0.6**	930± 58
4000ppm	5	7.54± 0.44**	16.0± 0.9	39.2± 2.2**	52.0± 1.4**	21.2± 0.2**	40.8± 1.5**	898± 37
7000ppm	5	6.46± 0.29**	11.9± 0.5**	39.8± 2.3*	61.5± 2.9**	18.5± 0.5**	30.1± 1.4**	843± 91
10000ppm	5	5.71± 0.34**	10.2± 0.6**	39.0± 2.8**	67.9± 1.4**	17.8± 0.3**	26.2± 0.8**	710± 72**
25000ppm	3	1.69± 0.25**	2.7± 0.5**	9.1± 1.5**	54.0± 2.6**	15.9± 0.8	29.6± 2.6**	817± 201

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

STUDY NO. : 0652
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	RETICULOCYTE %	METHEMOGLOBIN %
Control	5	2.3± 0.3	0.5± 0.1
1600ppm	4	-	4.0± 2.1
4000ppm	5	-	8.6± 2.4**
7000ppm	5	-	9.6± 3.0**
10000ppm	5	-	11.5± 2.0**
25000ppm	3	-	13.2± 1.8**

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

STUDY NO. : 0652
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%)
Control	5	3.30± 0.69	
1600ppm	4	5.78± 2.77	
4000ppm	5	5.67± 1.47	
7000ppm	5	4.66± 1.97	
10000ppm	5	2.63± 0.74	
25000ppm	3	11.07± 2.47**	

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

APPENDIX G 1

BIOCHEMISTRY : MALE

STUDY NO. : 0652
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

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	PHOSPHOLIPID mg／dℓ
Control	5	4.7± 0.1	2.6± 0.1	1.2± 0.1	0.12± 0.01	315± 10	92± 17	198± 29
1600ppm	5	5.1± 0.2**	2.9± 0.1**	1.4± 0.1*	0.24± 0.02*	296± 16	109± 13	225± 5
4000ppm	5	5.1± 0.1**	3.0± 0.1**	1.4± 0.1**	0.34± 0.03**	269± 19*	100± 8	214± 16
7000ppm	5	5.3± 0.1**	3.2± 0.0**	1.6± 0.1**	0.48± 0.08**	280± 32	99± 6	202± 12
10000ppm	5	5.6± 0.1**	3.5± 0.1**	1.7± 0.1**	0.58± 0.08**	248± 24**	91± 11	181± 20
25000ppm	4	4.7± 0.1	2.9± 0.1**	1.7± 0.1**	0.69± 0.12**	60± 45**	95± 18	143± 29**

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

STUDY NO. : 0652
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	AST IU/ℓ		ALT IU/ℓ		LDH IU/ℓ		G-GTP IU/ℓ		CK IU/ℓ		UREA NITOROGEN mg/dℓ		SODIUM mEq/ℓ	
Control	5	31±	2	18±	1	150±	27	1±	1	53±	13	21.7±	4.5	151±	1
1600ppm	5	32±	2	18±	1	282±	50**	1±	1	39±	5	22.5±	5.3	151±	1
4000ppm	5	35±	2**	19±	0	319±	67**	0±	1	44±	8	26.0±	7.9	151±	2
7000ppm	5	44±	4**	22±	3**	464±	100**	0±	1	66±	22	23.9±	7.1	150±	1
10000ppm	5	52±	7**	27±	6**	550±	96**	1±	1	44±	12	22.1±	4.4	152±	2
25000ppm	4	501±	53**	398±	23**	6840±	1222**	2±	1	474±	368*	37.5±	19.9	160±	4**

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

STUDY NO. : 0652
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	POTASSIUM mEq/ℓ		CHLORIDE mEq/ℓ		CALCIUM mg/dℓ		INORGANIC PHOSPHORUS mg/dℓ	
Control	5	4.5±	0.2	118±	1	9.2±	0.3	6.0±	2.1
1600ppm	5	4.5±	0.2	117±	1	9.4±	0.1	6.4±	2.0
4000ppm	5	5.4±	0.5	117±	2	9.4±	0.1	6.7±	1.8
7000ppm	5	4.9±	0.9	118±	2	9.5±	0.4	6.1±	1.3
10000ppm	5	4.9±	1.4	117±	2	9.8±	0.4	6.5±	1.0
25000ppm	4	4.7±	0.7	124±	6	9.5±	0.4	7.1±	2.1

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

APPENDIX G 2

BIOCHEMISTRY : FEMALE

STUDY NO. : 0652
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

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		PHOSPHOLIPID mg／dℓ	
Control	5	4.7±	0.2	2.9±	0.1	1.5±	0.1	0.15±	0.05	287±	17	73±	10	155±	17
1600ppm	4	4.8±	0.2	3.0±	0.1	1.7±	0.1	0.19±	0.02	271±	24	88±	6	183±	9
4000ppm	5	5.1±	0.2	3.2±	0.1**	1.7±	0.1	0.26±	0.04**	253±	31	130±	59**	227±	49**
7000ppm	5	5.5±	0.2**	3.4±	0.2**	1.7±	0.2	0.43±	0.03**	241±	22	125±	6**	237±	9**
10000ppm	5	5.9±	0.2**	3.7±	0.1**	1.8±	0.2	0.54±	0.07**	252±	22	125±	26**	235±	38**
25000ppm	3	5.0±	0.6	3.2±	0.5	1.7±	0.2	0.78±	0.18**	48±	64**	65±	9	107±	29

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

STUDY NO. : 0652
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	AST IU/ℓ	ALT IU/ℓ	LDH IU/ℓ	G-GTP IU/ℓ	CK IU/ℓ	UREA NITOROGEN mg/dℓ	SODIUM mEq/ℓ
Control	5	40± 4	19± 3	238± 105	1± 1	92± 61	20.7± 2.7	149± 2
1600ppm	4	35± 2	19± 3	228± 65	1± 1	58± 15	22.9± 4.7	150± 1
4000ppm	5	45± 7	20± 5	282± 66	0± 1	56± 15	20.8± 4.1	150± 1
7000ppm	5	46± 5	19± 2	351± 53	0± 1	50± 15	21.4± 3.1	149± 1
10000ppm	5	49± 3**	26± 3*	464± 67**	1± 1	51± 12	25.1± 3.1	152± 1*
25000ppm	3	578± 72**	321± 27**	7697± 465**	1± 0	745± 513	77.3± 47.0	166± 4**

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

STUDY NO. : 0652
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	POTASSIUM mEq/ℓ		CHLORIDE mEq/ℓ		CALCIUM mg/dℓ		INORGANIC PHOSPHORUS mg/dℓ	
Control	5	4.2±	0.4	120±	1	9.2±	0.5	7.4±	1.9
1600ppm	4	4.1±	0.5	118±	2	9.2±	0.2	7.4±	1.5
4000ppm	5	5.0±	0.6	118±	2*	9.3±	0.2	7.3±	1.3
7000ppm	5	4.9±	0.4	118±	1*	9.3±	0.3	6.2±	0.7
10000ppm	5	4.3±	0.4	118±	1	10.1±	0.4**	6.0±	0.6
25000ppm	3	3.8±	0.8	131±	6	10.2±	0.3**	5.3±	1.0

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

APPENDIX H 1

URINALYSIS : MALE

STUDY NO. : 0652 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	5	0	0	0	0	0	4	1		0	0	1	4	0	0		5	0	0	0	0	0		0	3	2	0	0	0		5	0	0	0	0	
1600ppm	5	0	0	0	0	0	4	1		0	0	1	4	0	0		5	0	0	0	0	0		0	4	1	0	0	0		5	0	0	0	0	
4000ppm	5	0	0	0	0	0	5	0		0	0	4	1	0	0		5	0	0	0	0	0		1	4	0	0	0	0		4	1	0	0	0	
7000ppm	5	0	0	0	0	1	3	1		0	0	5	0	0	0		5	0	0	0	0	0									5	0	0	0	0	
10000ppm	5	0	0	0	0	0	5	0		0	2	3	0	0	0		5	0	0	0	0	0									5	0	0	0	0	
25000ppm	4	0	2	2	0	0	0	0		1	2	1	0	0	0		4	0	0	0	0	0									4	0	0	0	0	

STUDY NO. : 0652 URINALYSIS
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

Group Name	NO. of Animals	Urobilinogen ±	+	2+	3+	4+	CHI
Control	5	5	0	0	0	0	
1600ppm	5	5	0	0	0	0	
4000ppm	5	5	0	0	0	0	
7000ppm	5	5	0	0	0	0	
10000ppm	5	5	0	0	0	0	
25000ppm	4	4	0	0	0	0	

APPENDIX H 2

URINALYSIS : FEMALE

STUDY NO. : 0652 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	5	0	0	0	0	0	5	0		0	0	3	2	0	0		5	0	0	0	0	0		3	2	0	0	0	0		5	0	0	0	0	
1600ppm	5	0	0	0	0	0	5	0		0	0	4	1	0	0		5	0	0	0	0	0		2	3	0	0	0	0		5	0	0	0	0	
4000ppm	5	0	0	0	1	0	4	0		0	0	5	0	0	0		5	0	0	0	0	0		1	1	0	0	0	0		5	0	0	0	0	
7000ppm	5	0	0	0	0	0	5	0		0	3	2	0	0	0		5	0	0	0	0	0									5	0	0	0	0	
10000ppm	5	0	0	0	0	0	5	0		0	4	1	0	0	0		5	0	0	0	0	0									5	0	0	0	0	
25000ppm	5	0	2	3	0	0	0	0		1	3	1	0	0	0		5	0	0	0	0	0									4	0	0	0	1	

STUDY NO. : 0652
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	5	5	0	0	0	0	
1600ppm	5	5	0	0	0	0	
4000ppm	5	5	0	0	0	0	
7000ppm	5	5	0	0	0	0	
10000ppm	5	5	0	0	0	0	
25000ppm	5	5	0	0	0	0	

APPENDIX I 1

GROSS FINDINGS : MALE :

DEAD AND MORIBUND ANIMALS

STUDY NO. : 0652
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name / NO. of Animals	Control 0	(%)	1600ppm 0	(%)	4000ppm 0	(%)	7000ppm 0	(%)
thymus	atrophic		-	(-)	-	(-)	-	(-)	-	(-)
spleen	dark		-	(-)	-	(-)	-	(-)	-	(-)
urin bladd	urine:brown		-	(-)	-	(-)	-	(-)	-	(-)

Organ	Findings	Group Name	10000ppm		25000ppm	
		NO. of Animals	0	(%)	1	(%)
thymus	atrophic		-	(-)	1	(100)
spleen	dark		-	(-)	1	(100)
urin bladd	urine:brown		-	(-)	1	(100)

APPENDIX I 2

GROSS FINDINGS : MALE :

SACRIFICED ANIMALS

STUDY NO. : 0652
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name / NO. of Animals	Control 5 (%)	1600ppm 5 (%)	4000ppm 5 (%)	7000ppm 5 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
spleen	dark		0 (0)	5 (100)	5 (100)	5 (100)
kidney	cyst		0 (0)	0 (0)	1 (20)	0 (0)

Organ	Findings	Group Name	10000ppm	25000ppm
		NO. of Animals	5 (%)	4 (%)
thymus	atrophic		0 (0)	4 (100)
spleen	dark		5 (100)	4 (100)
kidney	cyst		0 (0)	0 (0)

APPENDIX I 3

GROSS FINDINGS : FEMALE :

ALL ANIMALS

Organ	Findings	Group Name / NO. of Animals	Control 5 (%)	1600ppm 5 (%)	4000ppm 5 (%)	7000ppm 5 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
spleen	dark		0 (0)	5 (100)	5 (100)	5 (100)

Organ	Findings	Group Name	10000ppm	25000ppm
		NO. of Animals	5 (%)	5 (%)
thymus	atrophic		0 (0)	5 (100)
spleen	dark		5 (100)	5 (100)

APPENDIX J 1

ORGAN WEIGHT, ABSOLUTE : MALE

STUDY NO. : 0652
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	5	25.5± 0.9	0.051± 0.006	0.007± 0.001	0.174± 0.023	0.134± 0.005	0.135± 0.005
1600ppm	5	25.5± 0.8	0.056± 0.006	0.006± 0.001	0.169± 0.022	0.131± 0.015	0.130± 0.006
4000ppm	5	25.1± 0.6	0.045± 0.007	0.007± 0.002	0.159± 0.020	0.131± 0.004	0.132± 0.004
7000ppm	5	24.8± 0.8	0.039± 0.006*	0.007± 0.001	0.176± 0.022	0.134± 0.005	0.142± 0.011
10000ppm	5	22.8± 1.3**	0.025± 0.005**	0.008± 0.002	0.174± 0.038	0.127± 0.006	0.132± 0.009
25000ppm	4	14.3± 1.1**	0.007± 0.003**	0.008± 0.002	0.126± 0.018	0.105± 0.010**	0.123± 0.012

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

STUDY NO. : 0652
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.367± 0.006	0.053± 0.003	1.270± 0.095	0.428± 0.008
1600ppm	5	0.372± 0.012	0.161± 0.009	1.386± 0.104	0.435± 0.016
4000ppm	5	0.420± 0.073**	0.245± 0.021**	1.491± 0.074*	0.433± 0.004
7000ppm	5	0.382± 0.013	0.298± 0.028**	1.573± 0.150**	0.430± 0.012
10000ppm	5	0.332± 0.013*	0.327± 0.027**	1.623± 0.121**	0.419± 0.011
25000ppm	4	0.248± 0.025**	0.238± 0.086**	0.828± 0.160**	0.406± 0.008*

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

APPENDIX J 2

ORGAN WEIGHT, ABSOLUTE : FEMALE

STUDY NO. : 0652
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	5	20.6± 0.4	0.076± 0.008	0.011± 0.002	0.016± 0.005	0.119± 0.008	0.124± 0.011
1600ppm	5	20.9± 0.9	0.075± 0.004	0.010± 0.001	0.015± 0.004	0.115± 0.012	0.126± 0.005
4000ppm	5	20.5± 0.3	0.067± 0.002**	0.010± 0.001	0.013± 0.003	0.110± 0.013	0.123± 0.007
7000ppm	5	20.4± 0.8	0.059± 0.004**	0.009± 0.001	0.014± 0.002	0.113± 0.007	0.121± 0.009
10000ppm	5	19.5± 1.3	0.037± 0.009**	0.009± 0.001	0.012± 0.003	0.107± 0.011	0.121± 0.014
25000ppm	5	11.4± 1.0**	0.006± 0.002**	0.008± 0.002	0.008± 0.001**	0.097± 0.008**	0.108± 0.004

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

STUDY NO. : 0652
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.267± 0.011	0.064± 0.008	1.009± 0.081	0.441± 0.015
1600ppm	5	0.266± 0.011	0.153± 0.011	1.084± 0.111	0.440± 0.009
4000ppm	5	0.266± 0.019	0.211± 0.042**	1.144± 0.056	0.435± 0.019
7000ppm	5	0.263± 0.010	0.262± 0.040**	1.234± 0.066**	0.438± 0.008
10000ppm	5	0.245± 0.017	0.250± 0.023**	1.322± 0.061**	0.416± 0.010*
25000ppm	5	0.211± 0.014**	0.157± 0.068*	0.649± 0.187**	0.404± 0.004**

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

APPENDIX K 1

ORGAN WEIGHT, RELATIVE : MALE

STUDY NO. : 0652
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	5	25.5± 0.9	0.199± 0.030	0.028± 0.005	0.684± 0.090	0.527± 0.029	0.528± 0.010
1600ppm	5	25.5± 0.8	0.220± 0.018	0.025± 0.005	0.661± 0.074	0.515± 0.067	0.511± 0.034
4000ppm	5	25.1± 0.6	0.179± 0.025	0.029± 0.006	0.634± 0.075	0.523± 0.009	0.528± 0.017
7000ppm	5	24.8± 0.8	0.159± 0.025*	0.027± 0.006	0.707± 0.079	0.540± 0.027	0.573± 0.047
10000ppm	5	22.8± 1.3**	0.109± 0.018**	0.036± 0.007	0.765± 0.169	0.556± 0.031	0.578± 0.021
25000ppm	4	14.3± 1.1**	0.048± 0.020**	0.058± 0.011**	0.885± 0.106*	0.736± 0.029*	0.861± 0.038**

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

STUDY NO. : 0652
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	1.439± 0.051	0.207± 0.020	4.978± 0.259	1.682± 0.069
1600ppm	5	1.462± 0.060	0.632± 0.035	5.445± 0.467	1.710± 0.089
4000ppm	5	1.676± 0.326**	0.976± 0.074**	5.938± 0.241**	1.725± 0.048
7000ppm	5	1.540± 0.022**	1.201± 0.076**	6.333± 0.489**	1.734± 0.069
10000ppm	5	1.454± 0.040	1.430± 0.083**	7.104± 0.322**	1.837± 0.086
25000ppm	4	1.737± 0.079**	1.643± 0.507**	5.776± 0.742*	2.860± 0.215**

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

APPENDIX K 2

ORGAN WEIGHT, RELATIVE : FEMALE

STUDY NO. : 0652
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	5	20.6± 0.4	0.368± 0.038	0.052± 0.010	0.076± 0.024	0.581± 0.043	0.603± 0.051
1600ppm	5	20.9± 0.9	0.358± 0.011	0.048± 0.004	0.072± 0.020	0.553± 0.053	0.606± 0.038
4000ppm	5	20.5± 0.3	0.327± 0.006*	0.050± 0.005	0.065± 0.016	0.538± 0.060	0.599± 0.032
7000ppm	5	20.4± 0.8	0.291± 0.018**	0.046± 0.005	0.068± 0.011	0.556± 0.036	0.592± 0.050
10000ppm	5	19.5± 1.3	0.187± 0.037**	0.047± 0.005	0.061± 0.012	0.550± 0.054	0.621± 0.065
25000ppm	5	11.4± 1.0**	0.049± 0.013**	0.074± 0.008**	0.071± 0.016	0.854± 0.114**	0.955± 0.092**

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

STUDY NO. : 0652
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	1.298± 0.038	0.313± 0.041	4.905± 0.336	2.146± 0.051
1600ppm	5	1.278± 0.025	0.734± 0.027	5.184± 0.307	2.110± 0.056
4000ppm	5	1.299± 0.091	1.030± 0.196**	5.576± 0.192	2.121± 0.083
7000ppm	5	1.289± 0.077	1.284± 0.202**	6.049± 0.218**	2.148± 0.106
10000ppm	5	1.256± 0.045	1.285± 0.123**	6.796± 0.233**	2.142± 0.097
25000ppm	5	1.864± 0.142*	1.347± 0.467**	5.632± 1.159	3.570± 0.285*

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

APPENDIX L 1

HISTOPATHOLOGICAL FINDINGS :

NON-NEOPLASTIC LESIONS : MALE :

DEAD AND MORIBUND ANIMALS

STUDY NO. : 0652
ANIMAL : MOUSE B6D2F1/Crlj[Crj:BDF1]
REPORT TYPE : A1
SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name	Control				1600ppm				4000ppm				7000ppm			
		No. of Animals on Study	0				0				0				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
{Hematopoietic system}																		
spleen			< 0>				< 0>				< 0>				< 0>			
	deposit of hemosiderin		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	extramedullary hematopoiesis		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	engorgement of erythrocyte		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{Digestive system}																		
liver			< 0>				< 0>				< 0>				< 0>			
	necrosis:central		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	deposit of pigment		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	hepatocellular hypertrophy:central		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{Urinary system}																		
kidney			< 0>				< 0>				< 0>				< 0>			
	hyaline cast		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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	10000ppm				25000ppm			
		No. of Animals on Study	0				1			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
spleen			< 0>				< 1>			
	deposit of hemosiderin		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
	extramedullary hematopoiesis		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
	engorgement of erythrocyte		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
{Digestive system}										
liver			< 0>				< 1>			
	necrosis:central		-	-	-	-	0	0	1	0
			(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)
	deposit of pigment		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
	hepatocellular hypertrophy:central		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
{Urinary system}										
kidney			< 0>				< 1>			
	hyaline cast		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(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				1600ppm				4000ppm				7000ppm			
		No. of Animals on Study	0				0				0				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}																		
kidney			< 0>				< 0>				< 0>				< 0>			
	tubular necrosis		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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	10000ppm				25000ppm			
		No. of Animals on Study	0				1			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Urinary system}										
kidney			< 0>				< 1>			
	tubular necrosis		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(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 L 2

HISTOPATHOLOGICAL FINDINGS :

NON-NEOPLASTIC LESIONS : MALE :

SACRIFICED ANIMALS

Organ	Findings	Group Name	Control				1600ppm				4000ppm				7000ppm			
		No. of Animals on Study	5				5				5				5			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
{Hematopoietic system}																		
spleen			< 5>				< 5>				< 5>				< 5>			
	deposit of hemosiderin		0	0	0	0	5	0	0	0	1	4	0	0	0	5	0	0
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(20)	(80)	(0)	(0)	(0)	(100)	(0)	(0)
	extramedullary hematopoiesis		0	0	0	0	0	5	0	0	0	5	0	0	0	4	1	0
			(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(80)	(20)	(0)
	engorgement of erythrocyte		0	0	0	0	5	0	0	0	5	0	0	0	5	0	0	0
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Digestive system}																		
liver			< 5>				< 5>				< 5>				< 5>			
	necrosis:central		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:focal		1	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)
	deposit of pigment		0	0	0	0	0	0	0	0	4	0	0	0	5	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(80)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	extramedullary hematopoiesis		0	0	0	0	1	0	0	0	3	0	0	0	4	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(60)	(0)	(0)	(0)	(80)	(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	10000ppm				25000ppm			
		No. of Animals on Study	5				4			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
spleen			< 5>				< 4>			
	deposit of hemosiderin		0	5	0	0	0	4	0	0
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
	extramedullary hematopoiesis		0	5	0	0	0	0	4	0
			(0)	(100)	(0)	(0)	(0)	(0)	(100)	(0)
	engorgement of erythrocyte		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(25)	(0)	(0)	(0)
{Digestive system}										
liver			< 5>				< 4>			
	necrosis:central		0	0	0	0	2	2	0	0
			(0)	(0)	(0)	(0)	(50)	(50)	(0)	(0)
	necrosis:focal		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	deposit of pigment		5	0	0	0	0	4	0	0
			(100)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
	extramedullary hematopoiesis		5	0	0	0	0	0	0	0
			(100)	(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 / No. of Animals on Study / Grade	Control 5 1 (%)	Control 5 2 (%)	Control 5 3 (%)	Control 5 4 (%)	1600ppm 5 1 (%)	1600ppm 5 2 (%)	1600ppm 5 3 (%)	1600ppm 5 4 (%)	4000ppm 5 1 (%)	4000ppm 5 2 (%)	4000ppm 5 3 (%)	4000ppm 5 4 (%)	7000ppm 5 1 (%)	7000ppm 5 2 (%)	7000ppm 5 3 (%)	7000ppm 5 4 (%)
{Digestive system}																		
liver		< a >	< 5>				< 5>				< 5>				< 5>			
	hepatocellular hypertrophy:central	b	0	0	0	0	4	0	0	0	0	5	0	0	0	5	0	0
		(c)	(0)	(0)	(0)	(0)	(80)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
{Urinary system}																		
kidney		< a >	< 5>				< 5>				< 5>				< 5>			
	inflammatory polyp	b	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
		(c)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hydronephrosis	b	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
		(c)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)
	dilatation:tubular lumen	b	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(c)	(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	10000ppm				25000ppm			
		No. of Animals on Study	5				4			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
liver			< 5>				< 4>			
	hepatocellular hypertrophy:central		0	1	4	0	1	3	0	0
			(0)	(20)	(80)	(0)	(25)	(75)	(0)	(0)
{Urinary system}										
kidney			< 5>				< 4>			
	inflammatory polyp		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hydronephrosis		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	dilatation:tubular lumen		0	0	0	0	4	0	0	0
			(0)	(0)	(0)	(0)	(100)	(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 L 3

HISTOPATHOLOGICAL FINDINGS :

NON-NEOPLASTIC LESIONS : FEMALE :

ALL ANIMALS

Organ	Findings	Group Name	Control				1600ppm				4000ppm				7000ppm			
		No. of Animals on Study	5				5				5				5			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
{Hematopoietic system}																		
spleen			< 5>				< 5>				< 5>				< 5>			
	deposit of hemosiderin		0	0	0	0	5	0	0	0	5	0	0	0	4	1	0	0
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(80)	(20)	(0)	(0)
	extramedullary hematopoiesis		0	0	0	0	5	0	0	0	5	0	0	0	4	1	0	0
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(80)	(20)	(0)	(0)
	engorgement of erythrocyte		0	0	0	0	5	0	0	0	5	0	0	0	5	0	0	0
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Digestive system}																		
liver			< 5>				< 5>				< 5>				< 5>			
	necrosis:central		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:focal		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	deposit of pigment		0	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	extramedullary hematopoiesis		0	0	0	0	0	0	0	0	1	0	0	0	4	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(80)	(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	10000ppm				25000ppm			
		No. of Animals on Study	5				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
spleen			< 5>				< 5>			
	deposit of hemosiderin		0	5	0	0	1	4	0	0
			(0)	(100)	(0)	(0)	(20)	(80)	(0)	(0)
	extramedullary hematopoiesis		0	5	0	0	0	2	3	0
			(0)	(100)	(0)	(0)	(0)	(40)	(60)	(0)
	engorgement of erythrocyte		4	0	0	0	3	1	0	0
			(80)	(0)	(0)	(0)	(60)	(20)	(0)	(0)
{Digestive system}										
liver			< 5>				< 5>			
	necrosis:central		0	0	0	0	2	2	1	0
			(0)	(0)	(0)	(0)	(40)	(40)	(20)	(0)
	necrosis:focal		1	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	deposit of pigment		5	0	0	0	0	3	2	0
			(100)	(0)	(0)	(0)	(0)	(60)	(40)	(0)
	extramedullary hematopoiesis		3	0	0	0	0	0	0	0
			(60)	(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				1600ppm				4000ppm				7000ppm			
		No. of Animals on Study	5				5				5				5			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
liver			< 5>				< 5>				< 5>				< 5>			
	hepatocellular hypertrophy:central		0	0	0	0	2	0	0	0	5	0	0	0	2	3	0	0
			(0)	(0)	(0)	(0)	(40)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(40)	(60)	(0)	(0)
{Urinary system}																		
kidney			< 5>				< 5>				< 5>				< 5>			
	tubular 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)
	dilatation:tubular lumen		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

Organ	Findings	Group Name	10000ppm				25000ppm			
		No. of Animals on Study	5				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
liver			< 5>				< 5>			
	hepatocellular hypertrophy:central		0	5	0	0	0	0	0	0
			(0)	(100)	(0)	(0)	(0)	(0)	(0)	(0)
{Urinary system}										
kidney			< 5>				< 5>			
	tubular necrosis		0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)
	dilatation:tubular lumen		1	0	0	0	4	0	0	0
			(20)	(0)	(0)	(0)	(80)	(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 M

METHODS, UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK FEED STUDY OF DIPHENYLAMINE

METHODS, UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK FEED STUDY OF DIPHENYLAMINE

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
Methemoglobin	Van Assendelft method[2)]	%	1
White blood cell(WBC)	Light scattering method[1)]	$\times 10^3/\mu L$	2
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	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
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
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) Spectrophotometer (UV-240 : Shimadzu Corporation)
3) Automatic analyzer (Hitachi 7080 : Hitachi,Ltd.)