2-アミノ-4-クロロフェノール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：　０４８３

APPENDICES

APPENDICES

APPENDICES (CONTINUED)

APPENDICES (CONTINUED)

APPENDIX A 1

IDENTITY AND IMPURITY OF 2-AMINO-4-CHLOROPHENOL IN THE 2-WEEK FEED STUDY

IDENTITY AND IMPURITY OF 2-AMINO-4-CHLOROPHENOL IN THE 2-WEEK FEED STUDY

Test Substance : 2-Amino-4-chlorophenol (Tokyo Kasei Kogyo Co., Ltd.)

Lot No. : FHM01

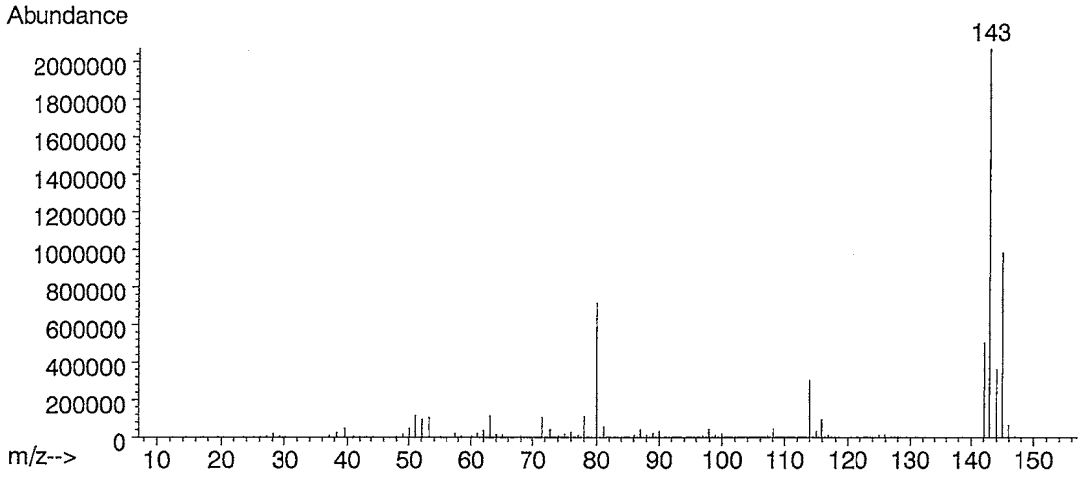
1. Spectral data

Mass Spectrometry

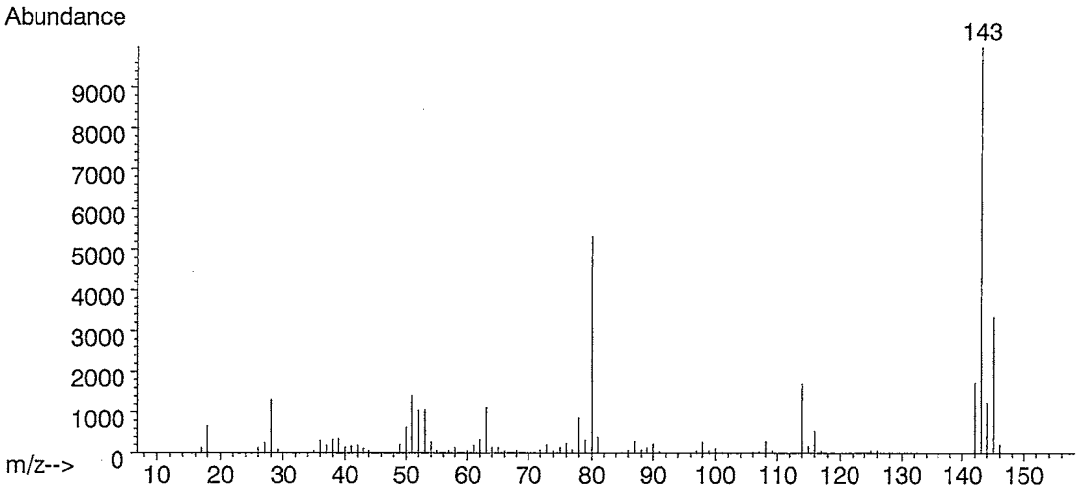
Instrument : Hewlett Packard 5989B Mass Spectrometer

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.

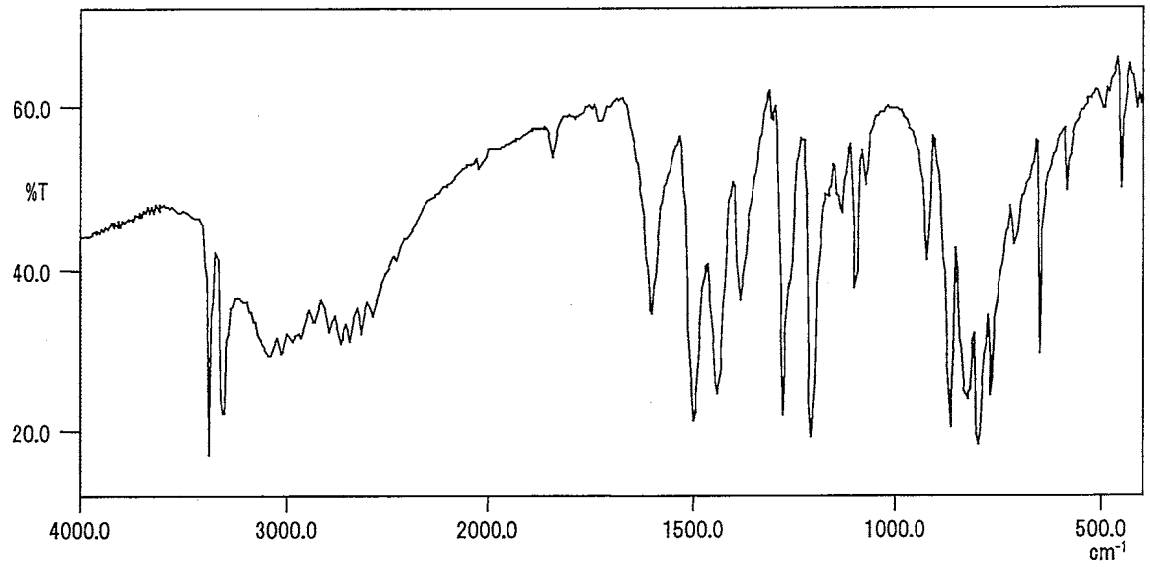
(*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed. New York, NY : John Wiley and Sons.)

Infrared Spectrometry

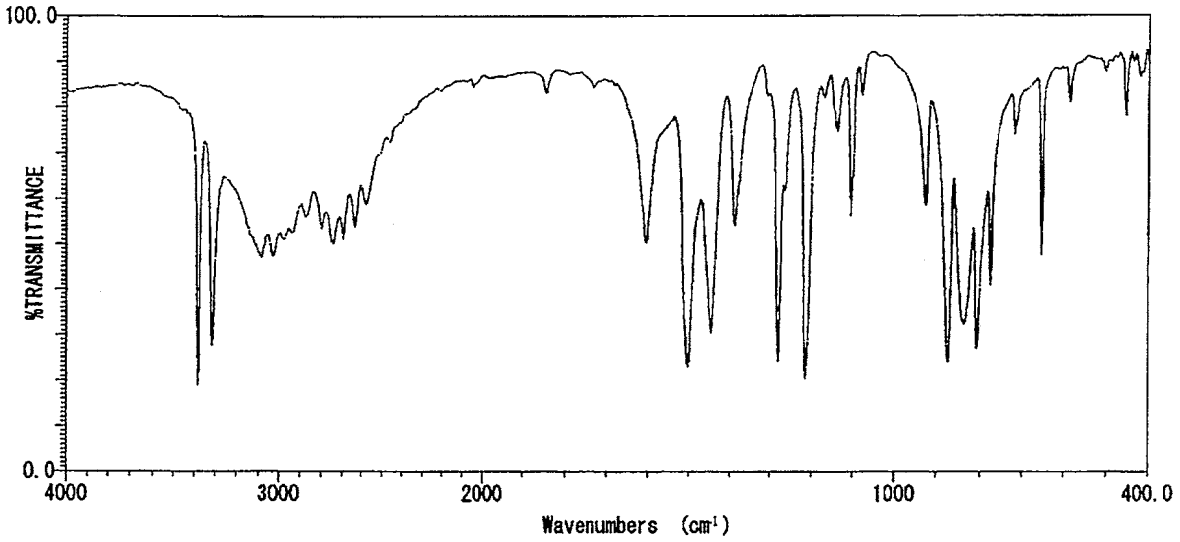
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 2.0 cm^{-1}



Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data*

Result: The infrared spectrum was consistent with literature spectrum.
(*Performed by Tokyo Kasei Kogyo Co., Ltd.)

2. Impurity

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : DB-1 (0.25 mmϕ × 60 m)

Column Temperature : 100 °C → (10 °C/min) → 250 °C (5 min)

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μL

Sample Name	Peak No.	Area (%)	Peak Name
Test Substance	1	0.90	2-Aminophenol
	2	99.10	2-Amino-4-chlorophenol

Result: Gas chromatography indicated one major peak (peak No.2) and one impurity. It was identified by comparing GC-MS with that of 2-aminophenol (peak No.1) in the 2-amino-4-chlorophenol. The amount in the test substance was 0.90% (The quantity value by the standard sample was 0.82%.) with a gas chromatograph.

3. Conclusion: The test substance was identified as 2-amino-4-chlorophenol by mass spectrum and infrared spectrum. Gas chromatography indicated one major peak (2-amino-4-chlorophenol) and one impurity. The impurity was 2-aminophenol in the test substance.

APPENDIX A 2

STABILITY OF 2-AMINO-4-CHLOROPHENOL IN THE 2-WEEK FEED STUDY

STABILITY OF 2-AMINO-4-CHLOROPHENOL IN THE 2-WEEK FEED STUDY

Test Substance : 2-Amino-4-chlorophenol (Tokyo Kasei Kogyo Co., Ltd.)

Lot No. : FHM01

1. Sample : This lot was used from 2003.5.15 to 2003.5.30. Test substance was stored in cold storage in a dark place.

2. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : DB-1 (0.25 mmϕ × 60 m)

Column Temperature : 100 °C → (10 °C/min) → 250 °C (5 min)

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μL

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
2003.04.24	1	9.030	0.90
	2	12.582	99.10
2003.06.19	1	9.149	0.85
	2	12.564	99.15

Result: Gas chromatography indicated one major peak (peak No.2) and one impurity (peak No.1 < 1% of total area) analyzed on 2003.4.24 and one major peak (peak No.2) and one impurity (peak No.1 < 1% of total area) analyzed on 2003.4.24. No new trace impurity peak in the test substance analyzed on 2003.6.19 was detected.

3. Conclusion: The test substance was stable for about 8 weeks in cold storage in a dark place.

APPENDIX A 3

CONCENTRATION OF 2-AMINO-4-CHLOROPHENOL IN FORMULATED DIETS IN THE 2-WEEK FEED STUDY

CONCENTRATION OF 2-AMINO-4-CHLOROPHENOL IN FORMULATED DIETS IN THE 2-WEEK FEED STUDY

	Target Concentration				
Date Analyzed	1280[a]	3200	8000	20000	50000
2003.05.15	1240 (96.9)[b]	3140 (98.1)	7820 (97.8)	19500 (97.5)	49400 (98.8)

[a] ppm
[b] %

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 ℃
Flow Rate : 0.8 mL/min
Mobile Phase : Methanol : Distilled Water (Phosphate Buffer Powder pH7.2) = 3 : 7
Detector : UV (284 nm)
Injection Volume : 10 μL

APPENDIX A 4

HOMOGENITY OF 2-AMINO-4-CHLOROPHENOL IN FORMULATED DIETS IN THE 2-WEEK FEED STUDY

HOMOGENEITY OF 2-AMINO-4-CHLOROPHENOL IN FORMULATED DIETS IN THE 2-WEEK FEED STUDY

	Target Concentration				
	1280[a]	3200	8000	20000	50000
Coefficient Variation	3.82[b]	3.66	3.09	3.45	1.14

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

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 ℃
Flow Rate : 0.8 mL/min
Mobile Phase : Methanol : Distilled Water (Phosphate Buffer Powder pH7.2) = 3 : 7
Detector : UV (284 nm)
Injection Volume : 10 μL

APPENDIX A 5

STABILITY OF 2-AMINO-4-CHLOROPHENOL IN FORMULATED DIETS IN THE 2-WEEK FEED STUDY

STABILITY OF 2-AMINO-4-CHLOROPHENOL IN FORMULATED DIETS IN THE 2-WEEK FEED STUDY

		Target Concentration	
Date Prepared	Date Analyzed	1280[a]	50000
2003.04.23	2003.04.23	1230 (100)[b]	48500 (100)
	2003.05.02[c]	1050 (85.4)	43800 (90.3)
	2003.05.02[d]	1170 (95.1)	47600 (98.1)

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

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 ℃
Flow Rate : 0.8 mL/min
Mobile Phase : Methanol : Distilled Water (Phosphate Buffer Powder pH7.2) = 3 : 7
Detector : UV (284 nm)
Injection Volume : 10 μL

APPENDIX B 1

CLINICAL OBSERVATION

SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0483
ANIMAL : MOUSE 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
	1280 ppm	0	0	0	0
	3200 ppm	0	0	0	0
	8000 ppm	0	0	0	0
	20000 ppm	0	0	0	0
	50000 ppm	0	2	4	4
MORIBUND SACRIFICE	Control	0	0	0	0
	1280 ppm	0	0	0	0
	3200 ppm	0	0	0	0
	8000 ppm	0	0	0	0
	20000 ppm	0	0	0	0
	50000 ppm	0	1	1	1
HUNCHBACK POSITION	Control	0	0	0	0
	1280 ppm	0	0	0	0
	3200 ppm	0	0	0	0
	8000 ppm	0	0	0	0
	20000 ppm	0	0	0	0
	50000 ppm	2	1	0	-
PILOERECTION	Control	0	0	0	0
	1280 ppm	0	0	0	0
	3200 ppm	0	0	0	0
	8000 ppm	0	0	0	0
	20000 ppm	0	0	0	0
	50000 ppm	2	2	0	-
YELLOW URINE	Control	0	0	0	0
	1280 ppm	0	0	0	0
	3200 ppm	0	0	0	0
	8000 ppm	0	0	0	0
	20000 ppm	0	5	5	5
	50000 ppm	0	2	0	-
OLIGO-STOOL	Control	0	0	0	0
	1280 ppm	0	0	0	0
	3200 ppm	0	0	0	0
	8000 ppm	0	0	0	0
	20000 ppm	0	0	0	0
	50000 ppm	5	2	0	-

STUDY NO. : 0483
ANIMAL : MOUSE 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
NON REMARKABLE	Control	5	5	5	5
	1280 ppm	5	5	5	5
	3200 ppm	5	5	5	5
	8000 ppm	5	5	5	5
	20000 ppm	5	0	0	0
	50000 ppm	0	0	0	-

APPENDIX B 2

CLINICAL OBSERVATION

SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

Clinical sign	Group Name	Administration Week-day 1-4	1-7	2-4	2-7
DEATH	Control	0	0	0	0
	1280 ppm	0	0	0	0
	3200 ppm	0	0	0	0
	8000 ppm	0	0	0	0
	20000 ppm	0	0	0	0
	50000 ppm	0	0	5	5
HUNCHBACK POSITION	Control	0	0	0	0
	1280 ppm	0	0	0	0
	3200 ppm	0	0	0	0
	8000 ppm	0	0	0	0
	20000 ppm	0	0	0	0
	50000 ppm	1	3	0	-
PILOERECTION	Control	0	0	0	0
	1280 ppm	0	0	0	0
	3200 ppm	0	0	0	0
	8000 ppm	0	0	0	0
	20000 ppm	0	0	0	0
	50000 ppm	1	4	0	-
YELLOW URINE	Control	0	0	0	0
	1280 ppm	0	0	0	0
	3200 ppm	0	0	0	0
	8000 ppm	0	0	0	0
	20000 ppm	0	5	5	5
	50000 ppm	0	5	0	-
OLIGO-STOOL	Control	0	0	0	0
	1280 ppm	0	0	0	0
	3200 ppm	0	0	0	0
	8000 ppm	0	0	0	0
	20000 ppm	0	0	0	0
	50000 ppm	5	5	0	-
NON REMARKABLE	Control	5	5	5	5
	1280 ppm	5	5	5	5
	3200 ppm	5	5	5	5
	8000 ppm	5	5	5	5
	20000 ppm	5	0	0	0
	50000 ppm	0	0	0	-

APPENDIX C 1

BODY WEIGHT CHANGES

SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0483
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-4	1-7	2-4	2-7
Control	24.2± 0.7	23.5± 0.9	24.4± 2.0	25.9± 0.9	26.6± 1.0
1280 ppm	24.3± 0.6	24.3± 0.7	25.0± 0.8	26.1± 1.0	26.5± 1.2
3200 ppm	24.2± 0.8	24.2± 1.2	25.1± 0.9	26.1± 1.2	26.8± 1.0
8000 ppm	24.2± 0.7	23.3± 0.6	24.1± 1.5	25.4± 1.4	26.0± 1.0
20000 ppm	24.2± 0.7	22.5± 0.6	23.6± 0.6	23.9± 1.3	24.6± 1.0*
50000 ppm	24.2± 0.7	16.7± 0.6**	16.0± 0.4 ?	-	-

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

? : Significant test is not applied, because No. of data in this group is less than 3.

APPENDIX C 2

BODY WEIGHT CHANGES

SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0483
ANIMAL : MOUSE Crj:BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-4	1-7	2-4	2-7
Control	19.0± 0.9	19.1± 0.8	19.8± 0.7	20.7± 0.8	19.9± 0.9
1280 ppm	19.0± 0.8	18.9± 1.0	19.9± 0.7	20.7± 0.5	20.8± 0.6
3200 ppm	19.0± 1.0	19.0± 1.1	19.0± 0.9	19.7± 1.4	20.1± 0.7
8000 ppm	19.0± 0.9	18.4± 0.7	19.1± 0.6	19.7± 0.8	19.4± 0.9
20000 ppm	19.0± 0.8	18.2± 0.6	19.1± 0.5	20.1± 0.9	20.1± 0.8
50000 ppm	19.1± 0.8	13.3± 0.7**	12.4± 0.7**	-	-

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

APPENDIX D 1

FOOD CONSUMPTION CHANGES

SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0483
ANIMAL : MOUSE 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	3.4± 0.3	4.3± 0.8	3.9± 0.9	3.8± 0.4
1280 ppm	4.0± 0.2**	4.3± 0.1	4.0± 0.3	4.0± 0.1
3200 ppm	3.9± 0.5*	4.2± 0.2	3.8± 0.2	4.0± 0.2
8000 ppm	3.3± 0.3	4.1± 0.5	4.1± 0.3	3.9± 0.4
20000 ppm	2.8± 0.1**	4.3± 0.3	3.7± 0.7	4.0± 0.3
50000 ppm	1.2± 0.2**	1.8± 0.4 ?	-	-

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

? : Significant test is not applied, because No. of data in this group is less than 3.

APPENDIX D 2

FOOD CONSUMPTION CHANGES

SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0483
ANIMAL : MOUSE 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	3.6± 0.2	3.7± 0.3	3.4± 0.2	3.3± 0.3
1280 ppm	3.4± 0.4	4.0± 0.3	3.3± 0.2	3.5± 0.1
3200 ppm	3.6± 0.2	3.6± 0.2	3.4± 0.3	3.8± 0.4*
8000 ppm	3.2± 0.1	3.7± 0.4	3.2± 0.3	3.2± 0.3
20000 ppm	3.0± 0.7	3.7± 0.3	3.4± 0.2	3.3± 0.1
50000 ppm	1.5± 0.6**	1.7± 0.3**	-	-

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

APPENDIX E 1

CHEMICAL INTAKE CHANGES

SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0483
ANIMAL : MOUSE Crj:BDF1
UNIT : g／kg／d a y
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	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
1280 ppm	0.212± 0.010	0.221± 0.007	0.195± 0.012	0.194± 0.006
3200 ppm	0.519± 0.041	0.539± 0.031	0.463± 0.017	0.473± 0.029
8000 ppm	1.128± 0.101	1.372± 0.088	1.287± 0.076	1.215± 0.151
20000 ppm	2.456± 0.087	3.640± 0.249	3.064± 0.473	3.259± 0.381
50000 ppm	3.490± 0.560	5.610± 1.177	-	-

APPENDIX E 2

CHEMICAL INTAKE CHANGES

SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0483
ANIMAL : MOUSE Crj:BDF1
UNIT : g／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	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
1280 ppm	0.231± 0.018	0.257± 0.018	0.206± 0.008	0.215± 0.009
3200 ppm	0.613± 0.028	0.614± 0.021	0.549± 0.028	0.601± 0.065
8000 ppm	1.398± 0.057	1.556± 0.103	1.299± 0.073	1.316± 0.116
20000 ppm	3.327± 0.744	3.891± 0.253	3.422± 0.233	3.334± 0.249
50000 ppm	5.472± 2.064	6.757± 1.113	-	-

APPENDIX F 1

HEMATOLOGY

SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0483
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	5	10.70± 0.31	15.7± 0.5	47.8± 1.8	44.7± 0.7	14.7± 0.1	32.9± 0.5	1125± 96
1280 ppm	5	10.70± 0.17	15.6± 0.4	47.4± 0.8	44.3± 0.4	14.6± 0.2	32.9± 0.4	1110± 58
3200 ppm	5	10.84± 0.38	15.7± 0.6	47.8± 1.5	44.1± 0.5	14.5± 0.2	32.8± 0.3	1093± 95
8000 ppm	4	9.86± 0.62*	14.8± 0.6	43.2± 2.5**	43.8± 0.9	15.1± 0.5	34.4± 0.7**	1222± 198
20000 ppm	4	8.35± 0.39**	14.4± 0.8*	40.0± 1.9**	47.8± 0.9**	17.2± 0.3	36.1± 1.0**	1186± 46
50000 ppm	0	-	-	-	-	-	-	-

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

(HCL070)

STUDY NO. : 0483
ANIMAL : MOUSE 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 (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHER
Control	5	1.68± 0.58	1± 1	11± 1	1± 1	0± 0	2± 1	85± 3	0± 0
1280 ppm	5	3.58± 1.64	1± 1	13± 5	3± 1	0± 0	2± 1	82± 5	0± 0
3200 ppm	5	2.66± 1.59	0± 1	10± 3	1± 1	0± 0	1± 1	87± 3	0± 0
8000 ppm	4	3.03± 1.52	2± 1	13± 2	2± 1	0± 0	2± 1	83± 3	0± 0
20000 ppm	4	5.33± 0.73**	1± 1	17± 3	2± 1	0± 0	1± 1	80± 4	0± 0
50000 ppm	0	-	-	-	-	-	-	-	-

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

(HCL070)

APPENDIX F 2

HEMATOLOGY

SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0483
ANIMAL : MOUSE 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	10.61± 0.44	15.5± 0.5	46.9± 1.7	44.2± 0.4	14.6± 0.1	33.0± 0.3	1000± 44
1280 ppm	5	10.58± 0.35	15.3± 0.5	46.2± 1.3	43.6± 0.6	14.5± 0.2	33.2± 0.3	970± 52
3200 ppm	4	10.39± 0.13	15.3± 0.2	45.7± 0.4	44.0± 0.3	14.7± 0.1	33.4± 0.2	966± 36
8000 ppm	4	9.63± 0.39**	14.7± 0.7	43.0+ 1.9**	44.6± 0.5	15.2± 0.1**	34.1± 0.5*	1041± 28
20000 ppm	5	8.77± 0.14**	14.7± 0.4*	42.6± 0.7**	48.5± 0.5**	16.7± 0.2**	34.5± 0.7**	1104± 82*
50000 ppm	0	-	-	-	-	-	-	-

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

STUDY NO. : 0483
ANIMAL : MOUSE 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 (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHER
Control	5	4.24± 1.23	0± 0	8± 2	2± 1	0± 0	2± 1	87± 2	0± 0
1280 ppm	5	2.39± 1.05	0± 0	13± 5	1± 1	0± 0	3± 1	84± 6	0± 0
3200 ppm	4	3.42± 1.05	0± 0	11± 2	3± 1	0± 0	3± 2	84± 2	0± 0
8000 ppm	4	4.22± 2.06	1± 1	12± 4	3± 1	0± 0	2± 1	83± 5	0± 0
20000 ppm	5	5.39± 1.25	1± 1	11± 2	2± 1	0± 0	3± 1	83± 2	0± 0
50000 ppm	0	-	-	-	-	-	-	-	-

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

(HCL070)

APPENDIX G 1

BIOCHEMISTRY

SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0483
ANIMAL : MOUSE 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	4.9± 0.2	2.9± 0.2	1.4± 0.1	0.15± 0.04	299± 22	88± 1	190± 6
1280 ppm	5	4.8± 0.1	2.8± 0.2	1.4± 0.1	0.11± 0.01	309± 25	93± 12	203± 20
3200 ppm	5	4.8± 0.1	2.8± 0.1	1.4± 0.1	0.13± 0.03	308± 24	102± 5	213± 11
8000 ppm	4	4.8± 0.1	2.9± 0.3	1.5± 0.4	0.17± 0.04	311± 7	98± 20	201± 23
20000 ppm	5	5.0± 0.2	3.1± 0.2	1.6± 0.2	0.24± 0.03**	268± 17	104± 11	214± 22
50000 ppm	0	-	-	-	-	-	-	-

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

STUDY NO. : 0483
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	GOT IU/ℓ		GPT IU/ℓ		LDH IU/ℓ		G-GTP IU/ℓ		CPK IU/ℓ		UREA NITROGEN mg/dℓ		SODIUM mEq/ℓ	
Control	5	35±	5	24±	6	229±	134	1±	0	234±	338	21.2±	1.5	149±	1
1280 ppm	5	33±	5	21±	3	180±	49	1±	1	77±	25	21.1±	4.8	148±	2
3200 ppm	5	30±	2	19±	5	175±	60	1±	1	74±	37	21.5±	2.6	148±	2
8000 ppm	4	32±	3	19±	2	179±	29	1±	1	116±	64	22.2±	1.7	149±	1
20000 ppm	5	41±	6	29±	4	282±	93	0±	1	111±	51	19.3±	2.3	150±	2
50000 ppm	0	-		-		-		-		-		-		-	

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

STUDY NO. : 0483
ANIMAL : MOUSE 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	4.7± 0.3	117± 1	9.1± 0.2	8.4± 0.7
1280 ppm	5	4.8± 0.5	116± 1	9.1± 0.2	7.5± 1.4
3200 ppm	5	4.8± 0.3	116± 1	8.9± 0.1	7.6± 1.6
8000 ppm	4	4.6± 0.3	116± 1	9.0± 0.4	8.4+ 0.9
20000 ppm	5	5.0± 0.3	115± 1	9.3± 0.4	7.9± 0.6
50000 ppm	0	-	-	-	-

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

APPENDIX G 2

BIOCHEMISTRY

SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0483
ANIMAL : MOUSE 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	4.8± 0.1	3.2± 0.1	2.0± 0.3	0.14± 0.02	262± 12	72± 4	154± 7
1280 ppm	5	4.8± 0.3	3.2± 0.2	1.9± 0.2	0.14± 0.01	283± 16	83± 9	168± 14
3200 ppm	5	4.7± 0.2	3.1± 0.1	2.0± 0.3	0.14± 0.02	278± 25	78± 6	162± 13
8000 ppm	5	4.8± 0.2	3.1± 0.2	1.9± 0.2	0.19± 0.02**	262± 28	80± 2	166± 7
20000 ppm	5	4.9± 0.1	3.3± 0.1	2.1± 0.3	0.20± 0.03**	270± 19	95± 10**	192± 19**
50000 ppm	0	-	-	-	-	-	-	-

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

(HCL074)

STUDY NO. : 0483
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	GOT IU/ℓ	GPT IU/ℓ	LDH IU/ℓ	G-GTP IU/ℓ	CPK IU/ℓ	UREA NITROGEN mg/dℓ	SODIUM mEq/ℓ
Control	5	41± 4	23± 3	195± 43	1± 1	69± 18	20.2± 1.9	147± 1
1280 ppm	5	42± 8	23± 4	213± 90	1± 1	122± 130	22.6± 3.7	147± 0
3200 ppm	5	39± 4	20± 3	180± 33	1± 1	81± 37	22.0± 2.5	147± 0
8000 ppm	5	40± 5	21± 2	247± 67	1± 1	109± 53	19.5± 1.5	147± 1
20000 ppm	5	38± 5	26± 5	225± 34	1± 1	84± 43	20.0± 2.3	147± 1
50000 ppm	0	-	-	-	-	-	-	-

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

(HCL074)

STUDY NO. : 0483
ANIMAL : MOUSE 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	4.7± 0.3	117± 0	8.7± 0.2	7.8± 1.2
1280 ppm	5	4.4± 0.3	116± 1	8.8± 0.5	7.6± 0.4
3200 ppm	5	4.5± 0.2	116± 1	8.6± 0.4	7.9± 0.9
8000 ppm	5	4.8± 0.4	117+ 2	8.8± 0.4	8.7± 1.5
20000 ppm	5	4.9± 0.2	116± 1	8.8± 0.3	7.7± 1.6
50000 ppm	0	-	-	-	-

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

APPENDIX H 1

URINALYSIS

SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0483
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Occult blood −	±	+	2+	3+	CHI
Control	5	0	0	5	0	0	0		5	0	0	0	0	0		5	0	0	0	0	
1280 ppm	5	0	1	4	0	0	0		5	0	0	0	0	0		5	0	0	0	0	
3200 ppm	5	0	2	3	0	0	0		5	0	0	0	0	0		5	0	0	0	0	
8000 ppm	4	0	1	3	0	0	0		4	0	0	0	0	0		4	0	0	0	0	
20000 ppm	5	0	2	3	0	0	0		5	0	0	0	0	0		5	0	0	0	0	
50000 ppm	0	-	-	-	-	-	-		-	-	-	-	-	-		-	-	-	-	-	

APPENDIX H 2

URINALYSIS

SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0483
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Occult blood −	±	+	2+	3+	CHI
Control	5	0	3	2	0	0	0		5	0	0	0	0	0		5	0	0	0	0	
1280 ppm	5	0	4	1	0	0	0		5	0	0	0	0	0		5	0	0	0	0	
3200 ppm	5	0	4	1	0	0	0		5	0	0	0	0	0		5	0	0	0	0	
8000 ppm	5	1	3	1	0	0	0		5	0	0	0	0	0		5	0	0	0	0	
20000 ppm	4	2	2	0	0	0	0		4	0	0	0	0	0		4	0	0	0	0	
50000 ppm	0	-	-	-	-	-	-		-	-	-	-	-	-		-	-	-	-	-	

APPENDIX I 1

GROSS FINDINGS

SUMMARY, MOUSE : MALE :

DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0483
ANIMAL : MOUSE 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	(%)	1280 ppm 0	(%)	3200 ppm 0	(%)	8000 ppm 0	(%)
thymus	atrophic		-	(-)	-	(-)	-	(-)	-	(-)
urin bladd	urine:marked retention		-	(-)	-	(-)	-	(-)	-	(-)
brain	brown zone		-	(-)	-	(-)	-	(-)	-	(-)
	fluid:transparent		-	(-)	-	(-)	-	(-)	-	(-)

Organ	Findings	Group Name NO. of Animals	20000 ppm 0 (%)	50000 ppm 5 (%)
thymus	atrophic		- (-)	5 (100)
urin bladd	urine:marked retention		- (-)	1 (20)
brain	brown zone		- (-)	1 (20)
	fluid:transparent		- (-)	1 (20)

APPENDIX I 2

GROSS FINDINGS

SUMMARY, MOUSE : MALE :

SACRIFICED ANIMALS ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0483
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name / NO. of Animals	Control 5 (%)	1280 ppm 5 (%)	3200 ppm 5 (%)	8000 ppm 5 (%)
spleen	enlarged		0 (0)	0 (0)	0 (0)	0 (0)
	dark		0 (0)	0 (0)	0 (0)	0 (0)
forestomach	thick		0 (0)	0 (0)	0 (0)	0 (0)

STUDY NO. : 0483
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name NO. of Animals	20000 ppm 5 (%)	50000 ppm 0 (%)
spleen	enlarged		5 (100)	- (-)
	dark		5 (100)	- (-)
forestomach	thick		4 (80)	- (-)

APPENDIX I 3

GROSS FINDINGS

SUMMARY, MOUSE : FEMALE :

DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0483
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name	Control	1280 ppm	3200 ppm	8000 ppm
		NO. of Animals	0 (%)	0 (%)	0 (%)	0 (%)
thymus	atrophic		- (-)	- (-)	- (-)	- (-)

Organ	Findings	Group Name	20000 ppm		50000 ppm	
		NO. of Animals	0	(%)	5	(%)
thymus	atrophic		-	(-)	5	(100)

APPENDIX I 4

GROSS FINDINGS

SUMMARY, MOUSE : FEMALE :

SACRIFICED ANIMALS ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0483
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name / NO. of Animals	Control 5 (%)	1280 ppm 5 (%)	3200 ppm 5 (%)	8000 ppm 5 (%)
spleen	enlarged		0 (0)	0 (0)	0 (0)	0 (0)
	dark		0 (0)	0 (0)	0 (0)	1 (20)
	black zone		0 (0)	1 (20)	1 (20)	0 (0)
forestomach	thick		0 (0)	0 (0)	0 (0)	1 (20)
kidney	hydronephrosis		0 (0)	1 (20)	0 (0)	0 (0)

Organ	Findings	Group Name NO. of Animals	20000 ppm 5 (%)	50000 ppm 0 (%)
spleen	enlarged		5 (100)	- (-)
	dark		5 (100)	- (-)
	black zone		0 (0)	- (-)
forestomach	thick		4 (80)	- (-)
kidney	hydronephrosis		0 (0)	- (-)

APPENDIX J 1

ORGAN WEIGHT, ABSOLUTE

SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0483
ANIMAL : MOUSE 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	26.6± 1.0	0.051± 0.009	0.009± 0.002	0.185± 0.016	0.129± 0.010	0.147± 0.009
1280 ppm	5	26.5± 1.2	0.053± 0.006	0.011± 0.005	0.188± 0.022	0.134± 0.007	0.149± 0.009
3200 ppm	5	26.8± 1.0	0.051± 0.004	0.009± 0.002	0.200± 0.018	0.131± 0.009	0.150± 0.007
8000 ppm	5	26.0± 1.0	0.057± 0.005	0.009± 0.001	0.183± 0.017	0.136± 0.007	0.147± 0.008
20000 ppm	5	24.6± 1.0*	0.041± 0.011	0.011± 0.002	0.182± 0.013	0.122± 0.007	0.147± 0.008
50000 ppm	0	-	-	-	-	-	-

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

STUDY NO. : 0483
ANIMAL : MOUSE 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	0.351± 0.024	0.044± 0.005	1.202± 0.076	0.428± 0.011
1280 ppm	5	0.373± 0.023	0.054± 0.003	1.335± 0.153	0.436± 0.011
3200 ppm	5	0.364± 0.023	0.054± 0.007	1.299± 0.091	0.427± 0.013
8000 ppm	5	0.356± 0.030	0.086± 0.014**	1.277± 0.058	0.426± 0.012
20000 ppm	5	0.369± 0.014	0.197± 0.024**	1.384± 0.093	0.428± 0.010
50000 ppm	0	-	-	-	-

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

APPENDIX J 2

ORGAN WEIGHT, ABSOLUTE

SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0483
ANIMAL : MOUSE 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	19.9± 0.9	0.074± 0.007	0.012± 0.002	0.019± 0.003	0.114± 0.006	0.138± 0.006
1280 ppm	5	20.8± 0.6	0.072± 0.009	0.010± 0.002	0.019± 0.003	0.119± 0.010	0.139± 0.007
3200 ppm	5	20.1± 0.7	0.068± 0.007	0.010± 0.002	0.019± 0.004	0.114± 0.008	0.138± 0.007
8000 ppm	5	19.4± 0.9	0.069± 0.006	0.010± 0.003	0.022± 0.007	0.109± 0.008	0.135± 0.005
20000 ppm	5	20.1± 0.8	0.065± 0.009	0.011± 0.002	0.017± 0.001	0.110± 0.005	0.137± 0.005
50000 ppm	0	-	-	-	-	-	-

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

STUDY NO. : 0483
ANIMAL : MOUSE 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	0.255± 0.021	0.059± 0.008	0.873± 0.072	0.440± 0.010
1280 ppm	5	0.331± 0.170	0.067± 0.018	0.949± 0.017	0.433± 0.011
3200 ppm	5	0.254± 0.014	0.069± 0.006	0.929± 0.086	0.426± 0.004
8000 ppm	5	0.258± 0.022	0.096± 0.010**	0.915± 0.077	0.434± 0.020
20000 ppm	5	0.269± 0.012	0.160± 0.019**	1.167± 0.058**	0.421± 0.006
50000 ppm	0	-	-	-	-

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

APPENDIX K 1

ORGAN WEIGHT, RELATIVE

SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0483
ANIMAL : MOUSE 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	26.6± 1.0	0.192± 0.030	0.033± 0.007	0.696± 0.036	0.484± 0.026	0.554± 0.023
1280 ppm	5	26.5± 1.2	0.199± 0.017	0.042± 0.015	0.707± 0.052	0.504± 0.010	0.560± 0.015
3200 ppm	5	26.8± 1.0	0.189± 0.015	0.035± 0.007	0.744± 0.051	0.488± 0.026	0.558± 0.020
8000 ppm	5	26.0± 1.0	0.221± 0.020	0.036± 0.006	0.704± 0.063	0.524± 0.023	0.567± 0.039
20000 ppm	5	24.6± 1.0*	0.167± 0.038	0.043± 0.009	0.741± 0.039	0.498± 0.026	0.600± 0.017*
50000 ppm	0	-	-	-	-	-	-

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

STUDY NO. : 0483
ANIMAL : MOUSE 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	1.320± 0.079	0.166± 0.018	4.520± 0.194	1.614± 0.077
1280 ppm	5	1.404± 0.059	0.202± 0.016	5.016± 0.349*	1.646± 0.057
3200 ppm	5	1.357± 0.078	0.203± 0.022	4.842± 0.261	1.593± 0.039
8000 ppm	5	1.367± 0.062	0.333± 0.051**	4.915± 0.118	1.641± 0.040
20000 ppm	5	1.502± 0.017**	0.802± 0.094**	5.636± 0.289**	1.744± 0.089*
50000 ppm	0	-	-	-	-

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

APPENDIX K 2

ORGAN WEIGHT, RELATIVE

SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0483
ANIMAL : MOUSE 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	19.9± 0.9	0.370± 0.032	0.062± 0.012	0.098± 0.015	0.570± 0.034	0.691± 0.032
1280 ppm	5	20.8± 0.6	0.345± 0.037	0.049± 0.007	0.093± 0.014	0.576± 0.056	0.668± 0.035
3200 ppm	5	20.1± 0.7	0.335± 0.029	0.051± 0.009	0.096± 0.016	0.566± 0.022	0.685± 0.026
8000 ppm	5	19.4± 0.9	0.357± 0.033	0.052± 0.013	0.113± 0.030	0.562± 0.038	0.700± 0.023
20000 ppm	5	20.1± 0.8	0.324± 0.037	0.055± 0.008	0.086± 0.007	0.546± 0.014	0.683± 0.042
50000 ppm	0	-	-	-	-	-	-

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

STUDY NO. : 0483
ANIMAL : MOUSE 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	1.280± 0.080	0.294± 0.034	4.376± 0.296	2.210± 0.071
1280 ppm	5	1.600± 0.847	0.322± 0.090	4.575± 0.147	2.087± 0.061*
3200 ppm	5	1.260± 0.066	0.341± 0.029	4.609± 0.314	2.118± 0.083
8000 ppm	5	1.331± 0.093	0.497± 0.058**	4.730± 0.409	2.241± 0.058
20000 ppm	5	1.341± 0.071	0.794± 0.082**	5.811± 0.213**	2.096± 0.052*
50000 ppm	0	-	-	-	-

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

APPENDIX L 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

SUMMARY, MOUSE : MALE :

DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0483
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 0				1280 ppm 0				3200 ppm 0				8000 ppm 0			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Hematopoietic system}																		
thymus		< 0>																
	atrophy		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
spleen		< 0>																
	engorgement of erythrocyte		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
{Urinary system}																		
urin bladd		< 0>																
	dilatation		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
{Reproductive system}																		
testis		< 0>																
	germ cell necrosis		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
epididymis		< 0>																
	debris of spermatic elements		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)

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	20000 ppm				50000 ppm			
		No. of Animals on Study	0				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
thymus			< 0>				< 5>			
	atrophy		-	-	-	-	0	0	5	0
			(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)
spleen			< 0>				< 5>			
	engorgement of erythrocyte		-	-	-	-	1	2	0	0
			(-)	(-)	(-)	(-)	(20)	(40)	(0)	(0)
{Urinary system}										
urin bladd			< 0>				< 5>			
	dilatation		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(20)	(0)	(0)	(0)
{Reproductive system}										
testis			< 0>				< 5>			
	germ cell necrosis		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(20)	(0)	(0)	(0)
epididymis			< 0>				< 5>			
	debris of spermatic elements		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(20)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

APPENDIX L 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

SUMMARY, MOUSE : MALE :

SACRIFICED ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0483
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

HISTOPATHOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 5				1280 ppm 5				3200 ppm 5				8000 ppm 5			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}																		
spleen		< 5>																
	extramedullary hematopoiesis		0	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)
	engorgement of erythrocyte		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)
{Digestive system}																		
stomach		< 5>																
	ulcer: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	1	0	0	0	1	1	0	0	2	2	1	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(20)	(20)	(0)	(0)	(40)	(40)	(20)	(0)
liver		< 5>																
	swelling: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}																		
urin bladd		< 5>																
	dilatation		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)

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	20000 ppm				50000 ppm			
		No. of Animals on Study	5				0			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
spleen			< 5>				< 0>			
	extramedullary hematopoiesis		0	5	0	0	-	-	-	-
			(0)	(100)	(0)	(0)	(-)	(-)	(-)	(-)
	engorgement of erythrocyte		5	0	0	0	-	-	-	-
			(100)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
{Digestive system}										
stomach			< 5>				< 0>			
	ulcer:forestomach		4	0	0	0	-	-	-	-
			(80)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
	hyperplasia:forestomach		0	3	2	0	-	-	-	-
			(0)	(60)	(40)	(0)	(-)	(-)	(-)	(-)
liver			< 5>				< 0>			
	swelling:central		4	0	0	0	-	-	-	-
			(80)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
{Urinary system}										
urin bladd			< 5>				< 0>			
	dilatation		0	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	Control				1280 ppm				3200 ppm				8000 ppm			
		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
{Urinary system}																		
urin bladd			< 5>				< 5>				< 5>				< 5>			
	degeneration		0	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(60)	(0)	(0)	(0)
{Reproductive system}																		
epididymis			< 5>				< 5>				< 5>				< 5>			
	spermatogenic granuloma		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	20000 ppm				50000 ppm			
		No. of Animals on Study	5				0			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}										
urin bladd			< 5>				< 0>			
	degeneration		4	0	0	0	-	-	-	-
			(80)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
{Reproductive system}										
epididymis			< 5>				< 0>			
	spermatogenic granuloma		0	1	0	0	-	-	-	-
			(0)	(20)	(0)	(0)	(-)	(-)	(-)	(-)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

APPENDIX L 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

SUMMARY, MOUSE : FEMALE :

DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

Organ	Findings	Group Name	Control				1280 ppm				3200 ppm				8000 ppm			
		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}																		
thymus			< 0>				< 0>				< 0>				< 0>			
	atrophy		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
spleen			< 0>				< 0>				< 0>				< 0>			
	engorgement of erythrocyte		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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	20000 ppm				50000 ppm			
		No. of Animals on Study	0				5			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Hematopoietic system}										
thymus			< 0>				< 5>			
	atrophy		-	-	-	-	0	0	5	0
			(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)
spleen			< 0>				< 5>			
	engorgement of erythrocyte		-	-	-	-	1	4	0	0
			(-)	(-)	(-)	(-)	(20)	(80)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

APPENDIX L 4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

SUMMARY, MOUSE : FEMALE :

SACRIFICED ANIMALS

(2-WEEK STUDY)

Organ	Findings	Group Name	Control				1280 ppm				3200 ppm				8000 ppm			
		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 melanin		0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	extramedullary hematopoiesis		0	0	0	0	0	0	0	0	2	0	0	0	0	5	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(40)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
	engorgement of erythrocyte		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)
{Digestive system}																		
stomach			< 5>				< 5>				< 5>				< 5>			
	ulcer: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	2	0	0	2	2	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(40)	(0)	(0)	(40)	(40)	(0)	(0)
liver			< 5>				< 5>				< 5>				< 5>			
	swelling: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)

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	20000 ppm				50000 ppm			
		No. of Animals on Study	5				0			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
spleen			< 5>				< 0>			
	deposit of melanin		0	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
	extramedullary hematopoiesis		1	4	0	0	-	-	-	-
			(20)	(80)	(0)	(0)	(-)	(-)	(-)	(-)
	engorgement of erythrocyte		5	0	0	0	-	-	-	-
			(100)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
{Digestive system}										
stomach			< 5>				< 0>			
	ulcer:forestomach		0	0	2	0	-	-	-	-
			(0)	(0)	(40)	(0)	(-)	(-)	(-)	(-)
	hyperplasia:forestomach		2	1	2	0	-	-	-	-
			(40)	(20)	(40)	(0)	(-)	(-)	(-)	(-)
liver			< 5>				< 0>			
	swelling:central		5	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

Organ	Findings	Group Name / Grade	Control 1 (%)	Control 2 (%)	Control 3 (%)	Control 4 (%)	1280 ppm 1 (%)	1280 ppm 2 (%)	1280 ppm 3 (%)	1280 ppm 4 (%)	3200 ppm 1 (%)	3200 ppm 2 (%)	3200 ppm 3 (%)	3200 ppm 4 (%)	8000 ppm 1 (%)	8000 ppm 2 (%)	8000 ppm 3 (%)	8000 ppm 4 (%)
		No. of Animals on Study	5				5				5				5			
{Urinary system}																		
kidney		< 5>																
	hydronephrosis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
urin bladd		< 5>																
	degeneration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	5 (100)	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	20000 ppm				50000 ppm			
		No. of Animals on Study	5				0			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}										
kidney			< 5>				< 0>			
	hydronephrosis		0	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
urin bladd			< 5>				< 0>			
	degeneration		5	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 M

METHODS, UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

METHODS, UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

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

1) Automatic blood cell analyzer (ADVIA120 : Bayer Corporation)
2) Automatic blood cell differential analyzer (MICROX HEG-120NA : OMRON Corporation)
3) Automatic analyzer (Hitachi 7070 : Hitachi,Ltd.)