ジフェニルアミンのラットを用いた
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：0651

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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

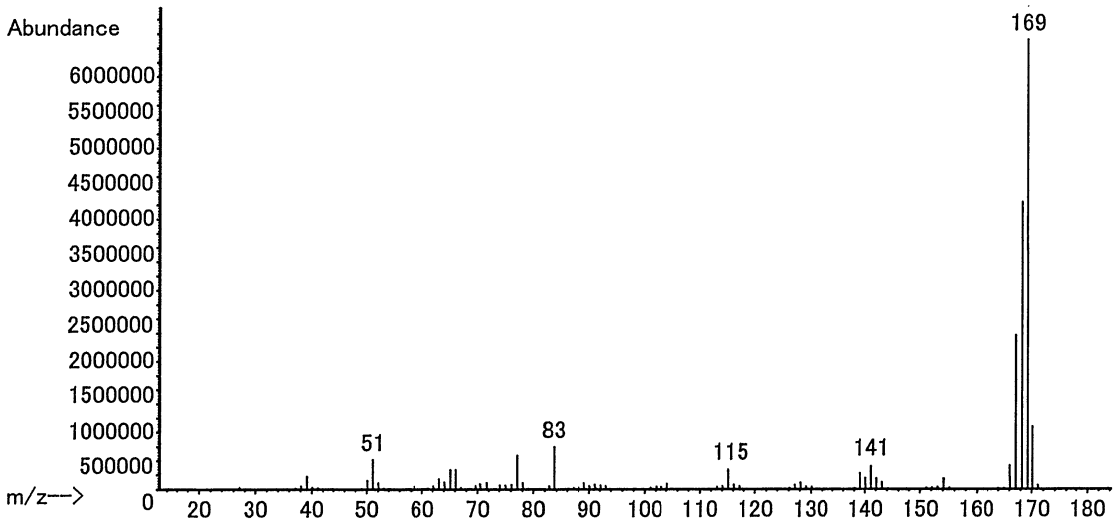
1. Spectral Data

Mass Spectrometry

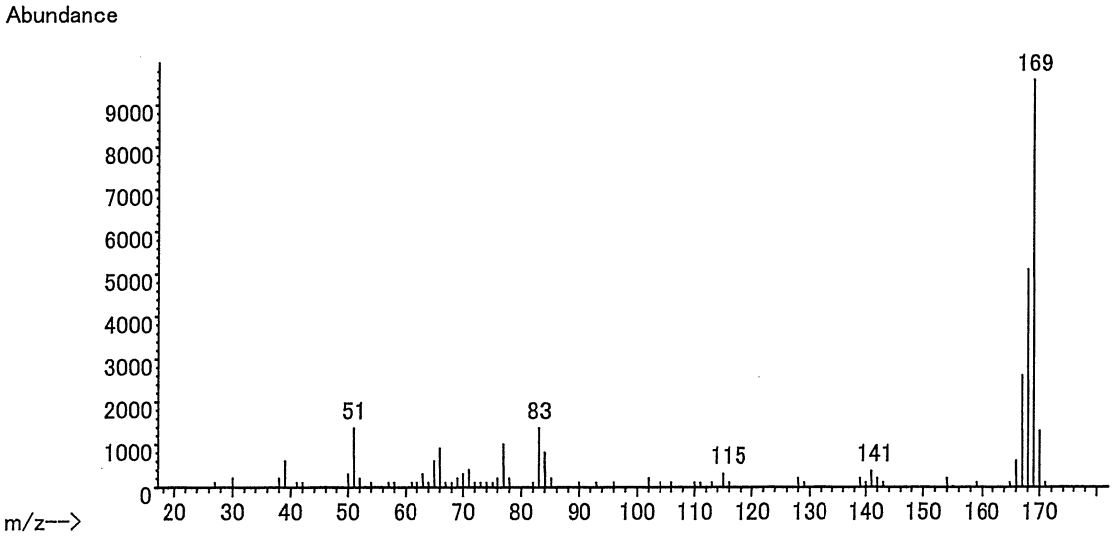
Instrument : Agilent Technologies 5973N Mass Spectrometer

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.

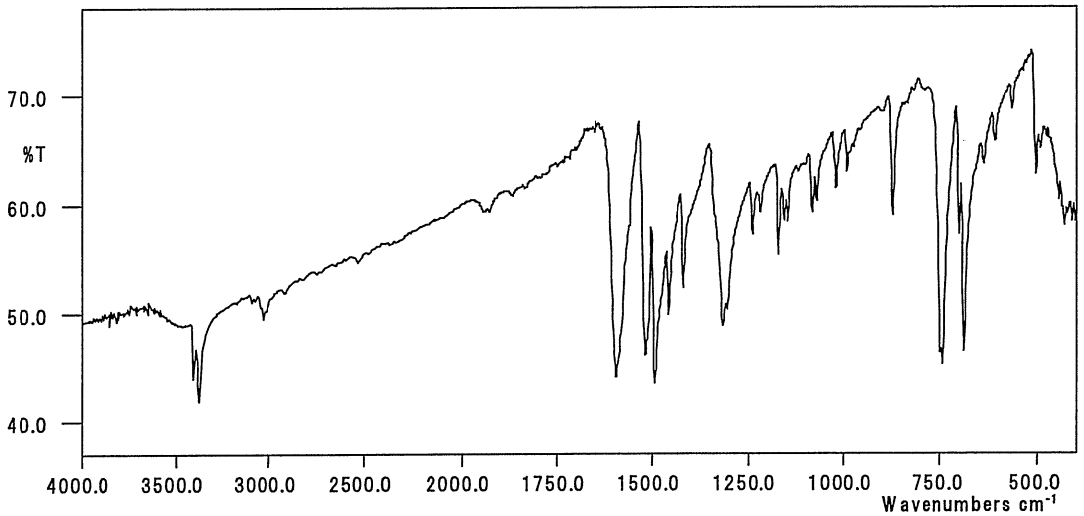
(*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed. New York, NY:John Wiley and Sons.)

Infrared Spectrometry

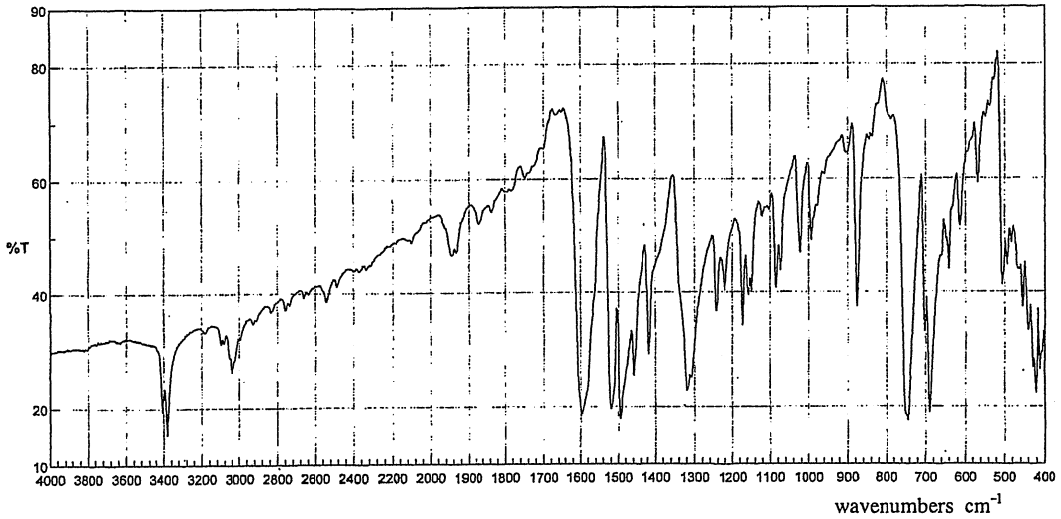
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

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
2006.08.16	1650[b] (103)[c]	4000 (100)	6950 (99.3)	9870 (98.7)	25000 (100)

[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	2.03[b]	3.39	2.78	3.19	1.60

[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]	1580 (101)	25800 (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. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	1	1	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	1	0	0	0
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	1	0	0	0
PILOERECTION	Control	0	0	0	0
	1600ppm	0	0	0	0
	4000ppm	0	0	0	0
	7000ppm	0	0	0	0
	10000ppm	4	0	0	0
	25000ppm	5	4	4	4
SMALL 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	3	3	3	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	4	4	4

STUDY NO. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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
	1600ppm	5	5	5	5
	4000ppm	5	5	5	5
	7000ppm	5	5	5	5
	10000ppm	1	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
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	2	2	2
PILOERECTION	Control	0	0	0	0
	1600ppm	0	0	0	0
	4000ppm	0	0	0	0
	7000ppm	0	0	0	0
	10000ppm	1	0	0	0
	25000ppm	5	3	3	3
SOILED PERI-GENITALIA	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	1	1
SMALL 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	3	3	3
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	3	3	3
NON REMARKABLE	Control	5	5	5	5
	1600ppm	5	5	5	5
	4000ppm	5	5	5	5
	7000ppm	5	5	5	5
	10000ppm	4	5	5	5
	25000ppm	0	0	0	0

APPENDIX C 1

BODY WEIGHT CHANGES : MALE

STUDY NO. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	127± 4	143± 7	157± 7	176± 8	186± 9
1600ppm	127± 4	144± 3	155± 6	175± 7	185± 7
4000ppm	127± 3	140± 6	153± 6	167± 6	177± 9
7000ppm	127± 4	134± 6	143± 7**	160± 7**	173± 6*
10000ppm	127± 4	123± 4**	137± 5**	154± 5**	164± 5**
25000ppm	127± 4	92± 8**	103± 2**	108± 2**	113± 5**

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

APPENDIX C 2

BODY WEIGHT CHANGES : FEMALE

STUDY NO. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	100± 4	108± 6	115± 5	124± 6	126± 6
1600ppm	100± 3	109± 5	114± 4	122± 5	124± 4
4000ppm	100± 4	105± 4	109± 3	117± 4	120± 4
7000ppm	99± 4	102± 4	107± 5	114± 7	118± 6
10000ppm	100± 4	99± 3*	104± 5*	113± 6*	118± 7
25000ppm	100± 4	74± 7**	80± 9**	85± 9**	87± 8**

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

APPENDIX D 1

FOOD CONSUMPTION CHANGES : MALE

STUDY NO. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	13.0± 1.1	13.7± 0.8	14.0± 0.7	14.2± 0.7
1600ppm	12.6± 0.4	13.3± 0.6	13.8± 0.8	14.1± 0.5
4000ppm	11.5± 0.8*	13.3± 0.4	13.3± 0.8	13.9± 0.8
7000ppm	9.7± 0.5**	12.6± 1.0	13.4± 0.7	13.5± 0.7
10000ppm	8.0± 0.4**	12.8± 0.2	13.0± 0.6	13.2± 0.7
25000ppm	4.4± 1.0**	8.8± 1.0**	8.4± 0.5**	10.2± 1.2**

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

APPENDIX D 2

FOOD CONSUMPTION CHANGES : FEMALE

STUDY NO. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	9.9± 0.9	10.2± 0.8	10.4± 0.8	10.2± 0.7
1600ppm	9.7± 0.4	10.0± 0.4	10.0± 0.4	9.8± 0.4
4000ppm	8.3± 0.5**	9.6± 0.4	9.7± 0.6	9.5± 0.3
7000ppm	7.6± 0.3**	9.4± 0.8	9.3± 1.2	9.1± 0.9
10000ppm	6.5± 1.1**	9.6± 1.3	8.9± 0.6	9.2± 0.5
25000ppm	3.0± 2.1**	8.6± 0.7	9.2± 2.2	9.8± 2.0

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

APPENDIX E 1

CHEMICAL INTAKE CHANGES : MALE

STUDY NO. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : mg／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±	0	0±	0	0±	0	0±	0
1600ppm	140±	2	137±	4	126±	3	122±	2
4000ppm	327±	14	349±	8	318±	10	313±	8
7000ppm	509±	18	614±	22	586±	7	547±	16
10000ppm	649±	24	936±	24	842±	19	803±	32
25000ppm	1184±	189	2134±	237	1960±	113	2256±	249

APPENDIX E 2

CHEMICAL INTAKE CHANGES : FEMALE

STUDY NO. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : mg/kg/day
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	142±	4	141±	4	131±	7	126±	6
4000ppm	316±	14	353±	11	332±	16	318±	5
7000ppm	525±	26	619±	43	572±	50	543±	47
10000ppm	662±	100	922±	90	789±	19	785±	22
25000ppm	1039±	768	2716±	529	2752±	862	2874±	853

APPENDIX F 1

HEMATOLOGY : MALE

STUDY NO. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	7.90± 0.13	15.4± 0.2	41.0± 0.7	51.8± 0.2	19.5± 0.2	37.5± 0.4	858± 56
1600ppm	5	7.61± 0.09**	14.8± 0.1**	39.5± 0.4**	51.9± 0.6	19.4± 0.1	37.4± 0.3	943± 44**
4000ppm	5	6.47± 0.13**	13.8± 0.1**	38.1± 0.3**	58.9± 1.3**	21.3± 0.3**	36.2± 0.3**	944± 14**
7000ppm	5	5.92± 0.09**	14.0± 0.3**	40.0± 0.9*	67.6± 1.5**	23.6± 0.4**	35.0± 0.7**	890± 17
10000ppm	5	5.86± 0.13**	14.3± 0.1**	41.4± 0.3	70.8± 1.4**	24.4± 0.4**	34.6± 0.4**	875± 43
25000ppm	4	5.06± 0.13**	12.9± 0.2**	38.1± 0.4**	75.4± 1.3**	25.5± 0.5**	33.8± 0.5**	874± 19

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

STUDY NO. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	RETICULOCYTE %	METHEMOGLOBIN %
Control	5	3.9± 0.3	0.5± 0.1
1600ppm	5	5.3± 0.6**	1.2± 0.6
4000ppm	5	12.6± 1.1**	3.3± 0.8**
7000ppm	5	16.1± 0.8**	2.2± 0.4**
10000ppm	5	17.2± 1.4**	2.8± 0.9**
25000ppm	4	28.2± 3.6**	7.2± 3.7**

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

STUDY NO. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	5.48± 0.44	
1600ppm	5	7.03± 0.78	
4000ppm	5	7.56± 0.57*	
7000ppm	5	7.47± 0.89*	
10000ppm	5	7.39± 1.65*	
25000ppm	4	7.24± 1.08	

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

APPENDIX F 2

HEMATOLOGY : FEMALE

STUDY NO. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	RED BLOOD CELL $10^5/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV fℓ	MCH pg	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	5	8.33± 0.24	16.2± 0.5	42.0± 1.1	50.4± 0.3	19.4± 0.1	38.6± 0.3	774± 28
1600ppm	5	7.44± 0.19**	14.5± 0.3**	38.1± 0.9**	51.3± 0.3**	19.6± 0.1*	38.2± 0.2	855± 54
4000ppm	5	6.37± 0.10**	13.7± 0.2**	37.0± 0.9**	58.1± 1.5**	21.4± 0.3**	36.9± 0.4**	860± 68
7000ppm	5	6.03± 0.27**	13.8± 0.5**	38.9± 1.3**	64.6± 1.3**	22.9± 0.5**	35.5± 0.1**	800± 50
10000ppm	5	5.76± 0.23**	13.7± 0.4**	39.2± 1.1**	68.1± 0.9**	23.9± 0.4**	35.1± 0.2**	785± 45
25000ppm	3	4.79± 0.36**	12.5± 0.7**	37.1± 1.5**	77.6± 2.8**	26.1± 0.7**	33.6± 0.6**	851± 65

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

STUDY NO. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	RETICULOCYTE %	METHEMOGLOBIN %
Control	5	2.0± 0.2	0.4± 0.2
1600ppm	5	5.0± 0.3**	1.4± 0.4
4000ppm	5	12.8± 0.9**	2.4± 0.3**
7000ppm	5	16.3± 1.1**	2.0± 0.5**
10000ppm	5	16.3± 1.5**	2.5± 1.1**
25000ppm	3	23.7± 4.8**	6.4± 1.0**

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

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%)
Control	5	5.62± 1.68	
1600ppm	5	6.63± 0.54	
4000ppm	5	8.11± 1.42*	
7000ppm	5	7.49± 1.72	
10000ppm	5	8.27± 1.26*	
25000ppm	3	8.08± 0.86	

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

APPENDIX G 1

BIOCHEMISTRY : MALE

STUDY NO. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	5.7± 0.1	3.3± 0.1	1.4± 0.0	0.10± 0.01	193± 4	66± 2	136± 8
1600ppm	5	6.0± 0.1*	3.6± 0.2**	1.6± 0.2	0.13± 0.01	195± 10	61± 5	130± 5
4000ppm	5	6.3± 0.1**	4.0± 0.1**	1.8± 0.2**	0.20± 0.02**	190± 5	71± 5	145± 8
7000ppm	5	6.3± 0.1**	4.0± 0.1**	1.8± 0.1**	0.22± 0.02**	175± 13**	84± 3**	159± 5**
10000ppm	5	6.3± 0.2**	4.1± 0.2**	1.8± 0.1**	0.26± 0.03**	166± 5**	92± 6**	170± 9**
25000ppm	4	7.0± 0.2**	4.7± 0.1**	2.0± 0.1**	0.38± 0.02**	129± 4**	106± 9**	196± 18**

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

STUDY NO. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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		CREATININE mg/dℓ	
Control	5	67±	12	35±	9	203±	6	1±	0	203±	9	16.0±	1.2	0.5±	0.0
1600ppm	5	63±	7	33±	4	212±	12	1±	0	186±	14	18.4±	2.7	0.5±	0.0
4000ppm	5	68±	19	37±	9	251±	64	1±	0	181±	19	19.1±	2.0*	0.5±	0.0
7000ppm	5	59±	6	33±	3	225±	28	1±	1	191±	28	19.1±	1.1*	0.5±	0.1
10000ppm	5	60±	5	35±	3	262±	33*	1±	0	173±	12	19.2±	0.7**	0.5±	0.1
25000ppm	4	77±	5	73±	9**	373±	67**	3±	1	190±	28	23.9±	3.6**	0.5±	0.1

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

STUDY NO. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dℓ	INORGANIC PHOSPHORUS mg/dℓ
Control	5	141± 1	3.9± 0.3	102± 1	11.0± 0.2	7.8± 1.3
1600ppm	5	142± 1	3.6± 0.1	101± 2	11.1± 0.1	8.3± 1.2
4000ppm	5	142± 2	3.6± 0.3	102± 2	11.1± 0.2	8.4± 1.1
7000ppm	5	142± 1	3.7± 0.2	101± 1	11.1± 0.1	7.9± 1.1
10000ppm	5	143± 2	3.9± 0.2	103± 2	10.9± 0.3	7.6± 1.0
25000ppm	4	142± 1	4.8± 0.5**	103± 1	11.5± 0.1**	6.6± 0.3

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

APPENDIX G 2

BIOCHEMISTRY : FEMALE

STUDY NO. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	5.6± 0.2	3.4± 0.1	1.5± 0.1	0.10± 0.01	186± 11	74± 5	144± 6
1600ppm	5	5.9± 0.1*	3.8± 0.1**	1.8± 0.1**	0.15± 0.01*	179± 7	64± 3*	124± 5**
4000ppm	5	6.1± 0.2**	4.0± 0.1**	1.8± 0.1**	0.18± 0.01**	173± 10	74± 5	140± 8
7000ppm	5	6.2± 0.1**	4.1± 0.1**	1.9± 0.1**	0.20± 0.02**	165± 10	84± 6*	154± 8
10000ppm	5	6.2± 0.0**	4.1± 0.0**	2.0± 0.0**	0.23± 0.04**	165± 10	95± 7**	175± 11**
25000ppm	3	6.8± 0.2**	4.6± 0.1**	2.1± 0.1**	0.48± 0.13**	117± 27**	106± 5**	207± 11**

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

STUDY NO. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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		CREATININE mg/dℓ	
Control	5	62±	3	28±	3	306±	32	1±	0	209±	39	17.7±	2.4	0.5±	0.0
1600ppm	5	66±	7	30±	5	308±	62	1±	0	191±	40	20.0±	2.1	0.5±	0.0
4000ppm	5	66±	3	29±	3	352±	113	1±	0	194±	41	20.1±	2.2	0.5±	0.0
7000ppm	5	63±	3	32±	4	345±	99	1±	0	178±	16	20.7±	1.2	0.5±	0.0
10000ppm	5	63±	7	34±	7	307±	43	1±	0	192±	42	22.0±	2.7*	0.5±	0.0
25000ppm	3	107±	30	94±	35**	544±	138**	4±	2	202±	19	27.5±	2.9**	0.5±	0.0

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

Group Name	NO. of Animals	SODIUM mEq／ℓ	POTASSIUM mEq／ℓ	CHLORIDE mEq／ℓ	CALCIUM mg／dℓ	INORGANIC PHOSPHORUS mg／dℓ
Control	5	139± 1	3.9± 0.2	104± 1	10.7± 0.2	6.1± 1.5
1600ppm	5	140± 1	3.6± 0.2	103± 1	10.7± 0.2	6.6± 0.9
4000ppm	5	141± 1	3.7± 0.3	104± 2	10.8± 0.2	7.3± 1.4
7000ppm	5	140± 1	3.8± 0.2	104± 2	10.8± 0.1	6.8± 1.1
10000ppm	5	141± 1	3.8± 0.3	104± 2	10.7± 0.1	7.0± 0.8
25000ppm	3	141± 3	4.6± 0.2**	102± 2	11.6± 0.3**	7.3± 0.2

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

APPENDIX H 1

URINALYSIS : MALE

STUDY NO. : 0651 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	5	0	0	0	0	0	2	3		0	0	2	3	0	0		5	0	0	0	0	0		5	0	0	0	0	0		5	0	0	0	
1600ppm	5	0	0	0	0	0	2	3		0	0	2	3	0	0		5	0	0	0	0	0		5	0	0	0	0	0		5	0	0	0	
4000ppm	5	0	0	0	0	0	3	2		0	0	4	1	0	0		5	0	0	0	0	0												
7000ppm	5	0	0	0	0	0	3	2		0	1	2	2	0	0		5	0	0	0	0	0												
10000ppm	5	0	0	0	0	1	3	1		0	2	2	1	0	0		5	0	0	0	0	0												
25000ppm	4	0	0	0	1	2	1	0		1	2	1	0	0	0		4	0	0	0	0	0												

STUDY NO. : 0651 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	5	5	0	0	0	0		5	0	0	0	0	
1600ppm	5	5	0	0	0	0		5	0	0	0	0	
4000ppm	5	5	0	0	0	0		5	0	0	0	0	
7000ppm	5	5	0	0	0	0		5	0	0	0	0	
10000ppm	5	5	0	0	0.	0		5	0	0	0	0	
25000ppm	4	4	0	0	0	0		4	0	0	0	0	

APPENDIX H 2

URINALYSIS : FEMALE

STUDY NO. : 0651 URINALYSIS
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	Bilirubin −	+	2+	3+	CHI
Control	5	0	0	0	0	0	3	2		0	4	1	0	0	0		5	0	0	0	0	0		5	0	0	0	0	0		5	0	0	0	
1600ppm	5	0	0	0	0	0	2	3		0	4	1	0	0	0		5	0	0	0	0	0		5	0	0	0	0	0		5	0	0	0	
4000ppm	5	0	0	0	0	0	1	4		2	3	0	0	0	0		5	0	0	0	0	0												
7000ppm	5	0	0	0	0	0	4	1		0	2	2	1	0	0		5	0	0	0	0	0												
10000ppm	5	0	0	0	0	0	4	1		1	3	1	0	0	0		5	0	0	0	0	0												
25000ppm	3	0	0	0	0	3	0	0		1	2	0	0	0	0		3	0	0	0	0	0												

STUDY NO. : 0651 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	5	5	0	0	0	0		5	0	0	0	0	
1600ppm	5	5	0	0	0	0		5	0	0	0	0	
4000ppm	5	5	0	0	0	0		5	0	0	0	0	
7000ppm	5	5	0	0	0	0		5	0	0	0	0	
10000ppm	5	5	0	0	0	0		5	0	0	0	0	
25000ppm	3	3	0	0	0	0		3	0	0	0	0	

APPENDIX I 1

GROSS FINDINGS : MALE :

DEAD AND MORIBUND ANIMALS

STUDY NO. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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		-	(-)	-	(-)	-	(-)	-	(-)
urin bladd	urine:red		-	(-)	-	(-)	-	(-)	-	(-)

STUDY NO. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE

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

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

APPENDIX I 2

GROSS FINDINGS : MALE :

SACRIFICED ANIMALS

STUDY NO. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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 (%)
spleen	adhesion		0 (0)	0 (0)	0 (0)	0 (0)
liver	adhesion		0 (0)	0 (0)	0 (0)	0 (0)
	herniation		0 (0)	0 (0)	0 (0)	1 (20)

Organ	Findings	Group Name / NO. of Animals	10000ppm 5 (%)	25000ppm 4 (%)
spleen	adhesion		1 (20)	0 (0)
liver	adhesion		1 (20)	0 (0)
	herniation		0 (0)	0 (0)

APPENDIX I 3

GROSS FINDINGS : FEMALE :

DEAD AND MORIBUND ANIMALS

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

Organ	Findings	Group Name / NO. of Animals	10000ppm 0 (%)	25000ppm 2 (%)
thymus	atrophic		- (-)	2 (100)
urin bladd	urine:red		- (-)	2 (100)

APPENDIX I 4

GROSS FINDINGS : FEMALE :

SACRIFICED 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)
liver	herniation		3 (60)	0 (0)	0 (0)	0 (0)

Organ	Findings	Group Name	10000ppm	25000ppm
		NO. of Animals	5 (%)	3 (%)
thymus	atrophic		0 (0)	1 (33)
liver	herniation		0 (0)	0 (0)

APPENDIX J 1

ORGAN WEIGHT, ABSOLUTE : MALE

STUDY NO. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	186± 9	0.352± 0.021	0.034± 0.003	2.380± 0.153	0.661± 0.022	0.744± 0.030
1600ppm	5	185± 7	0.365± 0.029	0.034± 0.003	2.254± 0.053	0.659± 0.039	0.744± 0.042
4000ppm	5	177± 9	0.335± 0.012	0.033± 0.002	2.289± 0.165	0.654± 0.031	0.728± 0.035
7000ppm	5	173± 6*	0.335± 0.027	0.033± 0.003	2.301± 0.089	0.624± 0.016	0.716± 0.029
10000ppm	5	164± 5**	0.291± 0.007**	0.032± 0.003	2.219± 0.260	0.612± 0.024*	0.661± 0.032**
25000ppm	4	113± 5**	0.123± 0.026**	0.029± 0.003	1.294± 0.375**	0.451± 0.024**	0.535± 0.015**

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

STUDY NO. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	1.392± 0.085	0.458± 0.024	7.041± 0.594	1.748± 0.034
1600ppm	5	1.460± 0.046	0.531± 0.039*	8.572± 0.409**	1.756± 0.027
4000ppm	5	1.482± 0.067	0.844± 0.053**	9.199± 0.695**	1.744± 0.035
7000ppm	5	1.464± 0.060	0.921± 0.064**	9.216± 0.567**	1.724± 0.051
10000ppm	5	1.437± 0.075	0.837± 0.018**	8.917± 0.537**	1.723± 0.018
25000ppm	4	1.154± 0.020**	0.581± 0.037**	7.040± 0.384	1.630± 0.027**

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

APPENDIX J 2

ORGAN WEIGHT, ABSOLUTE : FEMALE

STUDY NO. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	126± 6	0.274± 0.018	0.042± 0.002	0.053± 0.005	0.475± 0.022	0.592± 0.028
1600ppm	5	124± 4	0.280± 0.018	0.039± 0.002	0.048± 0.005	0.489± 0.025	0.585± 0.016
4000ppm	5	120± 4	0.277± 0.013	0.037± 0.005	0.047± 0.006	0.480± 0.017	0.570± 0.027
7000ppm	5	118± 6	0.260± 0.017	0.034± 0.001**	0.042± 0.005	0.453± 0.042	0.551± 0.025
10000ppm	5	118± 7	0.285± 0.015	0.031± 0.002**	0.037± 0.011**	0.449± 0.028	0.540± 0.030*
25000ppm	3	87± 8**	0.092± 0.033**	0.030± 0.003**	0.022± 0.003**	0.356± 0.039**	0.449± 0.017**

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

STUDY NO. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	0.971± 0.043	0.327± 0.020	4.483± 0.200	1.635± 0.019
1600ppm	5	0.997± 0.036	0.421± 0.027**	5.334± 0.177**	1.627± 0.019
4000ppm	5	0.996± 0.063	0.626± 0.028**	5.583± 0.162**	1.587± 0.043
7000ppm	5	1.017± 0.062	0.652± 0.060**	5.645± 0.432**	1.595± 0.040
10000ppm	5	1.001± 0.056	0.633± 0.040**	5.890± 0.192**	1.589± 0.033
25000ppm	3	0.871± 0.070	0.469± 0.053**	5.089± 0.228*	1.530± 0.022**

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

APPENDIX K 1

ORGAN WEIGHT, RELATIVE : MALE

STUDY NO. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	186± 9	0.189± 0.014	0.018± 0.001	1.279± 0.043	0.356± 0.011	0.400± 0.012
1600ppm	5	185± 7	0.197± 0.011	0.019± 0.001	1.220± 0.053	0.356± 0.011	0.402± 0.014
4000ppm	5	177± 9	0.189± 0.006	0.019± 0.001	1.289± 0.035	0.369± 0.002	0.410± 0.011
7000ppm	5	173± 6*	0.194± 0.015	0.019± 0.001	1.330± 0.062	0.361± 0.012	0.414± 0.015
10000ppm	5	164± 5**	0.178± 0.008	0.019± 0.002	1.350± 0.124	0.373± 0.005*	0.403± 0.009
25000ppm	4	113± 5**	0.108± 0.019**	0.026± 0.003**	1.141± 0.306	0.400± 0.022**	0.475± 0.024**

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

STUDY NO. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.748± 0.025	0.246± 0.005	3.781± 0.165	0.942± 0.048
1600ppm	5	0.789± 0.017	0.287± 0.017**	4.638± 0.260**	0.950± 0.021
4000ppm	5	0.835± 0.027**	0.476± 0.014**	5.180± 0.175**	0.984± 0.039
7000ppm	5	0.846± 0.023**	0.531± 0.018**	5.318± 0.153**	0.997± 0.042
10000ppm	5	0.875± 0.022**	0.511± 0.021**	5.434± 0.199**	1.051± 0.022**
25000ppm	4	1.025± 0.033**	0.515± 0.019**	6.243± 0.122**	1.448± 0.083**

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

APPENDIX K 2

ORGAN WEIGHT, RELATIVE : FEMALE

STUDY NO. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	126± 6	0.217± 0.017	0.033± 0.001	0.042± 0.004	0.376± 0.019	0.469± 0.023
1600ppm	5	124± 4	0.225± 0.009	0.032± 0.001	0.038± 0.004	0.393± 0.020	0.470± 0.010
4000ppm	5	120± 4	0.231± 0.008	0.031± 0.005	0.039± 0.004	0.401± 0.016	0.476± 0.015
7000ppm	5	118± 6	0.221± 0.020	0.029± 0.000*	0.035± 0.005	0.384± 0.021	0.468± 0.023
10000ppm	5	118± 7	0.242± 0.006**	0.026± 0.001**	0.031± 0.008*	0.382± 0.021	0.458± 0.011
25000ppm	3	87± 8**	0.104± 0.030	0.035± 0.006	0.026± 0.003**	0.410± 0.018	0.519± 0.028**

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

STUDY NO. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.768± 0.024	0.258± 0.013	3.549± 0.145	1.295± 0.055
1600ppm	5	0.801± 0.027	0.338± 0.017**	4.288± 0.132**	1.309± 0.032
4000ppm	5	0.832± 0.041*	0.523± 0.013**	4.662± 0.091**	1.325± 0.028
7000ppm	5	0.864± 0.042**	0.553± 0.031**	4.790± 0.237**	1.355± 0.032
10000ppm	5	0.851± 0.024**	0.538± 0.022**	5.008± 0.206**	1.351± 0.055
25000ppm	3	1.006± 0.059**	0.540± 0.023**	5.889± 0.311**	1.777± 0.189**

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. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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>			
	atrophy		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	engorgement of erythrocyte		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
spleen			< 0>				< 1>			
	atrophy		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
	engorgement of erythrocyte		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
{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

STUDY NO. : 0651
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE

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

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	0	0	0	0	0	0	0	0	4	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(80)	(0)	(0)	(0)
	extramedullary hematopoiesis		0	0	0	0	5	0	0	0	0	5	0	0	0	5	0	0
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
	engorgement of erythrocyte		0	0	0	0	5	0	0	0	0	5	0	0	0	5	0	0
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
{Digestive system}																		
liver			< 5>				< 5>				< 5>				< 5>			
	necrosis:single cell		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)
	hepatocellular hypertrophy:central		0	0	0	0	2	0	0	0	4	0	0	0	5	0	0	0
			(0)	(0)	(0)	(0)	(40)	(0)	(0)	(0)	(80)	(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	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		5	0	0	0	1	3	0	0
			(100)	(0)	(0)	(0)	(25)	(75)	(0)	(0)
	extramedullary hematopoiesis		0	5	0	0	0	4	0	0
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
	engorgement of erythrocyte		0	5	0	0	0	4	0	0
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
{Digestive system}										
liver			< 5>				< 4>			
	necrosis:single cell		0	0	0	0	1	1	0	0
			(0)	(0)	(0)	(0)	(25)	(25)	(0)	(0)
	hepatocellular hypertrophy:central		5	0	0	0	0	4	0	0
			(100)	(0)	(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 3

HISTOPATHOLOGICAL FINDINGS :

NON-NEOPLASTIC LESIONS : FEMALE :

DEAD AND MORIBUND ANIMALS

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>		
	atrophy		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{Digestive system}																		
liver				< 0>				< 0>				< 0>				< 0>		
	necrosis:central		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{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				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Hematopoietic system)										
spleen			< 0>				< 2>			
	atrophy		-	-	-	-	0	2	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
(Digestive system)										
liver			< 0>				< 2>			
	necrosis:central		-	-	-	-	2	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
(Urinary system)										
kidney			< 0>				< 2>			
	tubular necrosis		-	-	-	-	0	2	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 4

HISTOPATHOLOGICAL FINDINGS :

NON-NEOPLASTIC LESIONS : FEMALE :

SACRIFICED ANIMALS

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 5				1600ppm 5				4000ppm 5				7000ppm 5			
			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	0	0	0	0	5	0	0	0	5	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	extramedullary hematopoiesis		0	0	0	0	4	0	0	0	1	4	0	0	0	5	0	0
			(0)	(0)	(0)	(0)	(80)	(0)	(0)	(0)	(20)	(80)	(0)	(0)	(0)	(100)	(0)	(0)
	engorgement of erythrocyte		0	0	0	0	4	0	0	0	0	5	0	0	0	5	0	0
			(0)	(0)	(0)	(0)	(80)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
{Digestive system}																		
liver			< 5>				< 5>				< 5>				< 5>			
	herniation		3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(60)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:single cell		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)
	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			< 5>				< 5>				< 5>				< 5>			
	papillary 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

Organ	Findings	Group Name	10000ppm				25000ppm			
		No. of Animals on Study	5				3			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
spleen			< 5>				< 3>			
	deposit of hemosiderin		2	3	0	0	0	3	0	0
			(40)	(60)	(0)	(0)	(0)	(100)	(0)	(0)
	extramedullary hematopoiesis		0	5	0	0	0	3	0	0
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
	engorgement of erythrocyte		0	5	0	0	0	3	0	0
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
{Digestive system}										
liver			< 5>				< 3>			
	herniation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:single cell		0	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	hepatocellular hypertrophy:central		4	0	0	0	0	3	0	0
			(80)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
{Urinary system}										
kidney			< 5>				< 3>			
	papillary necrosis		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(33)	(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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Urinary system)																		
kidney			< 5>				< 5>				< 5>				< 5>			
	mineralization:cortico-medullary junction		1	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	10000ppm				25000ppm			
		No. of Animals on Study	5				3			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Urinary system)										
kidney			< 5>				< 3>			
	mineralization:cortico-medullary junction		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

APPENDIX 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
Creatinine	Jaffé 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.)