2-メチル-1-プロパノールのラットを用いた
経口投与による2週間毒性試験（混水試験）報告書

試験番号：0555

APPENDICES

APPENDICES

APPENDICES (CONTINUED)

APPENDIX A 1

IDENTITY AND IMPURITY OF 2-METHYL-1-PROPANOLIN THE 2-WEEK DRINKING WATER STUDY

IDENTITY AND IMPURITY OF 2-METHYL-1-PROPANOL IN THE 2-WEEK DRINKING WATER STUDY

Test Substance : 2-Methyl-1-propanol (Wako Pure Chemical Industries, Ltd.)

Lot No. : KLN7146

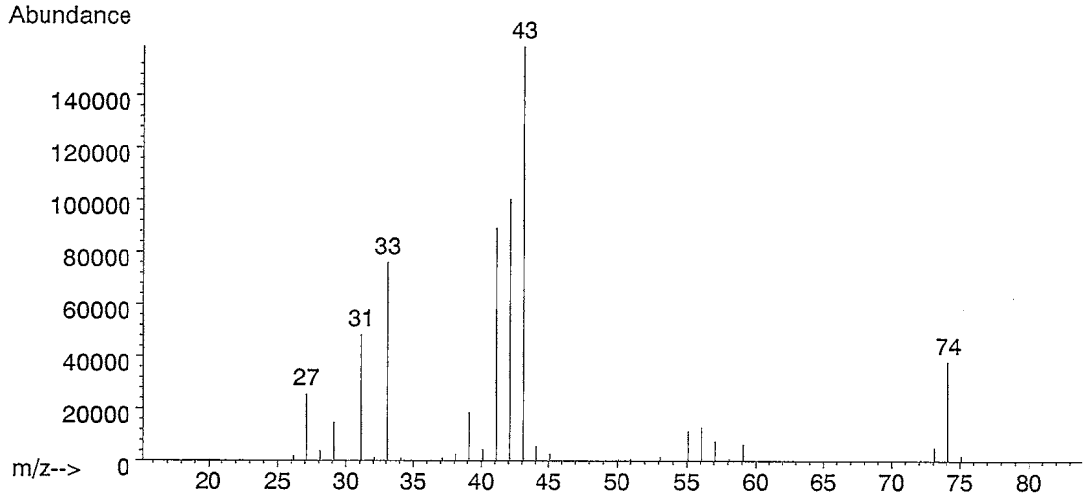
1. Spectral Data

Mass Spectrometry

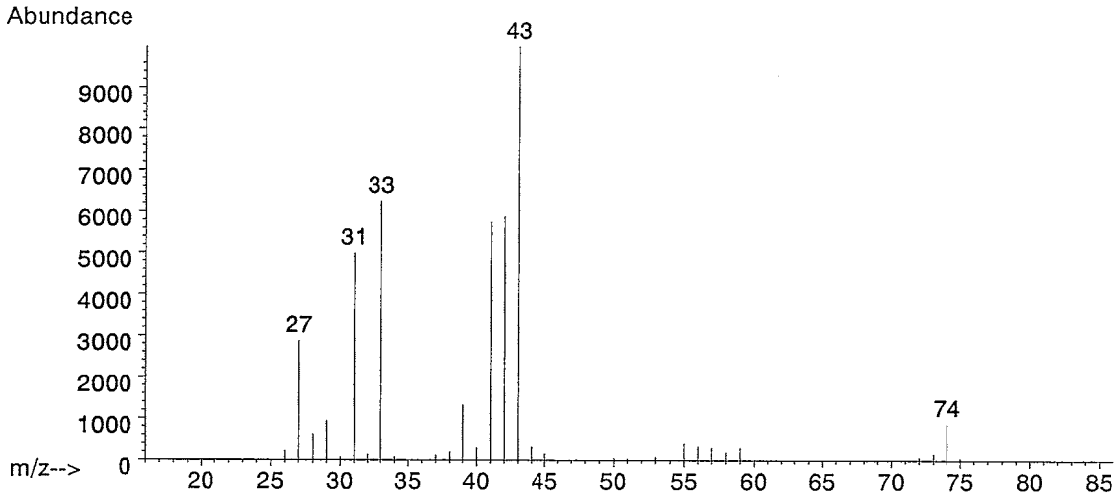
Instrument : Hewlett Packard 5989B Mass Spectrometer

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.

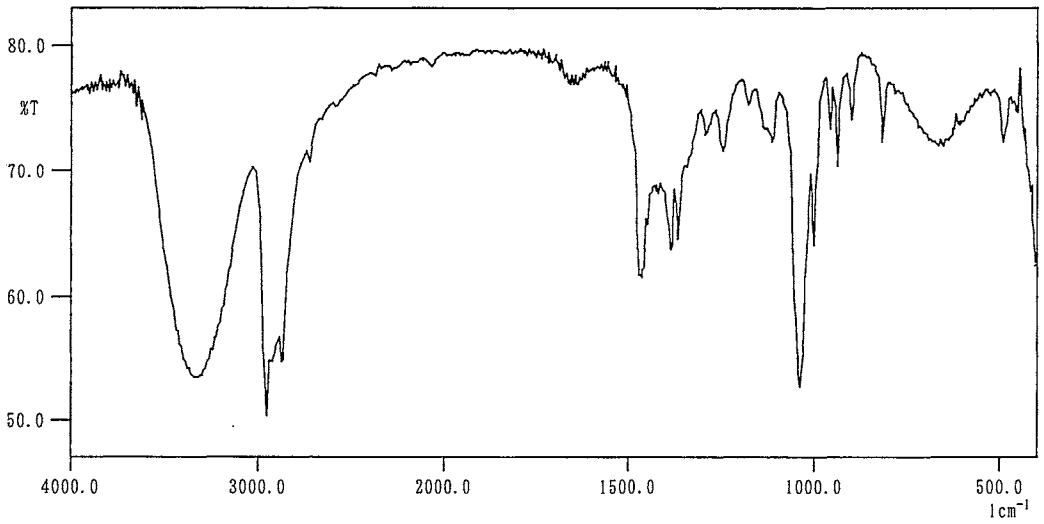
(*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed. New York, NY : John Wiley and Sons.)

Infrared Spectrometry

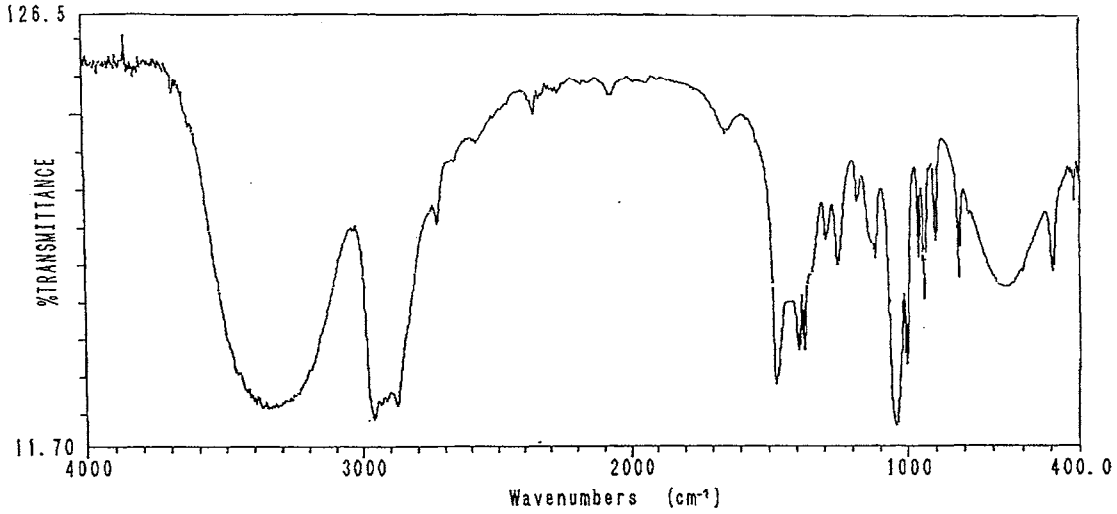
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 2 cm^{-1}



Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data*

Result: The infrared spectrum was consistent with literature spectrum.
(*Performed by Wako Pure Chemical Industries, Ltd.)

2. Impurity

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : INNOWAX (0.2 mmϕ × 50 m)

Column Temperature : 80 °C (1 min) → (10 °C/min) → 200 °C

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μL

Sample Name	Peak No.	Area (%)	Peak Name
	1	0.071	Diisobutyl ether
Test Substance	2	99.886	2-Methyl-1-propanol
	3	0.043	1-Butanol

Result: Gas chromatography indicated one major peak (peak No.2) and two impurities. Those impurities (peak No.1 and peak No.3) were identified as diisobutyl ether and 1-butanol by comparing GC-MS with the standard samples. The amount in the test substance was 0.071% (The quantity value by the standard sample was 0.069%.) for diisobutyl ether and 0.043% (The quantity value by the standard sample was 0.043%.) for 1-butanol with a gas chromatograph.

3. Conclusion: The test substance was identified as 2-methyl-1-propanol by mass spectrum and infrared spectrum. Gas chromatography indicated one major peak (2-methyl-1-propanol) and two impurities. Those impurities were diisobutyl ether and 1-butanol in the test substance.

APPENDIX A 2

STABILITY OF 2-METHYL-1-PROPANOL

IN THE 2-WEEK DRINKING WATER STUDY

STABILITY OF 2-METHYL-1-PROPANOL IN THE 2-WEEK DRINKING WATER STUDY

Test Substance : 2-Methyl-1-propanol (Wako Pure Chemical Industries, Ltd.)

Lot No. : KLN7146

1. Sample : This lot was used from 2004.9.30 to 2004.10.14. Test substance was stored in a dark place at room temperature.

2. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : INNOWAX (0.2 mmϕ × 50 m)

Column Temperature : 80 °C (1 min) → (10 °C/min) → 200 °C

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μL

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
2004.09.21	1	3.751	0.071
	2	5.266	99.886
	3	5.580	0.043
2004.10.19	1	3.744	0.070
	2	5.252	99.884
	3	5.569	0.046

Result: Gas chromatography indicated one major peak (peak No.2) and two impurities (peak No.1 and No.3 < 0.2% of total area) analyzed on 2004.9.21 and one major peak (peak No.2) and two impurities (peak No.1 and No.3 < 0.2% of total area) analyzed on 2004.10.19. No new trace impurity peak in the test substance analyzed on 2004.10.19 was detected.

3. Conclusion: The test substance was stable for about 4 weeks in a dark place at room temperature.

APPENDIX A 3

CONCENTRATION OF 2-METHYL-1-PROPANOL IN FORMULATED WATER IN THE 2-WEEK DRINKING WATER STUDY

CONCENTRATION OF 2-METHYL-1-PROPANOL IN FORMULATED WATER IN THE 2-WEEK DRINKING WATER STUDY

	Target Concentration				
Date Analyzed	2500[a]	5000	10000	20000	40000
2004.09.30	2380 (95.2)[b]	5070 (101)	10100 (101)	20800 (104)	41500 (104)

[a] ppm
[b] %

Analytical method : The samples were analyzed by gas chromatography.

Instrument : Hewlett Packard 5890A Gas Chromatograph
Column : INNOWAX (0.2 mmϕ × 50 m)
Column Temperature : 80 °C (1 min) → (10 °C/min) → 200 °C
Flow Rate : 1 mL/min
Detector : FID (Flame Ionization Detector)
Injection Volume : 1 μL

APPENDIX A 4

STABILITY OF 2-METHYL-1-PROPANOL IN FORMULATED WATER IN THE 2-WEEK DRINKING WATER STUDY

STABILITY OF 2-METHYL-1-PROPANOL IN FORMULATED WATER IN THE 2-WEEK DRINKING WATER STUDY

		Target Concentration	
Date Prepared	Date Analyzed	2500[a]	40000
2004.08.12	2004.08.12	2450 (100)[b]	40800 (100)
	2004.08.16[c]	2250 (91.8)	38300 (93.9)

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

Analytical method : The samples were analyzed by gas chromatography.

Instrument : Hewlett Packard 5890A Gas Chromatograph
Column : INNOWAX (0.2 mmϕ × 50 m)
Column Temperature : 80 °C (1 min) → (10 °C/min) → 200 °C
Flow Rate : 1 mL/min
Detector : FID (Flame Ionization Detector)
Injection Volume : 1 μL

APPENDIX B 1

CLINICAL OBSERVATION : MALE

STUDY NO. : 0555
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
	2500 ppm	5	5	5	5
	5000 ppm	5	5	5	5
	10000 ppm	5	5	5	5
	20000 ppm	5	5	5	5
	40000 ppm	5	5	5	5

APPENDIX B 2

CLINICAL OBSERVATION : FEMALE

STUDY NO. : 0555
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day 1-4	1-7	2-4	2-7
SOILED PERI-GENITALIA	Control	0	0	0	0
	2500 ppm	0	0	0	0
	5000 ppm	0	0	0	0
	10000 ppm	0	1	1	0
	20000 ppm	0	1	1	0
	40000 ppm	0	0	0	0
NON REMARKABLE	Control	5	5	5	5
	2500 ppm	5	5	5	5
	5000 ppm	5	5	5	5
	10000 ppm	5	4	4	5
	20000 ppm	5	4	4	5
	40000 ppm	5	5	5	5

APPENDIX C 1

BODY WEIGHT CHANGES : MALE

STUDY NO. : 0555
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	123± 4	140± 5	151± 7	173± 8	184± 10
2500 ppm	123± 5	140± 6	153± 7	178± 9	190± 8
5000 ppm	123± 5	140± 5	153± 4	175± 5	186± 4
10000 ppm	123± 4	140± 4	153± 5	176± 5	189± 7
20000 ppm	123± 5	136± 9	148± 11	170± 11	181± 14
40000 ppm	123± 5	132± 7	146± 8	168± 9	179± 9

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

APPENDIX C 2

BODY WEIGHT CHANGES : FEMALE

STUDY NO. : 0555
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	98± 3	106± 4	112± 6	121± 6	126± 6
2500 ppm	98± 2	107± 4	111± 3	122± 3	127± 4
5000 ppm	98± 2	105± 2	109± 3	121± 4	124± 7
10000 ppm	99± 2	105± 1	110± 2	121± 2	125± 2
20000 ppm	98± 3	105± 3	109± 3	120± 3	124± 3
40000 ppm	99± 2	103± 3	110± 2	120± 2	125± 2

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

APPENDIX D 1

FOOD CONSUMPTION CHANGES : MALE

STUDY NO. : 0555
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	13.8± 0.5	15.1± 0.8	16.3± 0.4	15.8± 0.9
2500 ppm	13.7± 0.7	15.4± 0.7	16.5± 1.1	15.9± 1.0
5000 ppm	13.3± 0.6	15.1± 0.7	15.8± 0.4	16.1± 0.7
10000 ppm	13.0± 0.8	14.4± 1.1	15.5± 0.8	15.1± 0.8
20000 ppm	11.4± 1.2**	12.9± 1.2*	14.1± 1.5**	13.9± 1.4*
40000 ppm	10.4± 1.0**	12.1± 1.4**	13.2± 1.0**	13.4± 0.7**

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

APPENDIX D 2

FOOD CONSUMPTION CHANGES : FEMALE

STUDY NO. : 0555
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	10.5± 1.0	11.0± 1.1	11.3± 0.8	11.0± 0.9
2500 ppm	10.3± 0.3	10.8± 0.2	11.2± 0.3	10.8± 0.2
5000 ppm	9.9± 0.3	10.3± 0.6	10.7± 0.9	10.4± 1.3
10000 ppm	9.6± 0.3	10.6± 0.5	10.7± 0.7	10.4± 0.6
20000 ppm	9.4± 0.1	10.2± 0.4	10.3± 0.3	9.8± 0.3
40000 ppm	8.1± 0.8**	9.5± 0.8**	9.2± 0.5**	9.6± 0.9

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

APPENDIX E 1

WATER CONSUMPTION CHANGES : MALE

STUDY NO. : 0555
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-4(4)	1-7(3)	2-4(4)	2-7(3)
Control	16.1± 0.4	17.4± 1.2	20.2± 0.6	19.6± 1.0
2500 ppm	15.8± 0.7	17.2± 0.9	20.4± 1.3	19.4± 1.5
5000 ppm	15.6± 0.7	17.3± 0.9	19.9± 1.1	18.6± 1.4
10000 ppm	15.6± 1.7	17.0± 1.8	18.8± 1.5	17.5± 1.0
20000 ppm	13.3± 1.6*	14.9± 1.9*	16.6± 1.8**	15.2± 2.0**
40000 ppm	12.9± 2.0*	14.2± 1.0**	15.5± 1.5**	13.9± 0.4**

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

APPENDIX E 2

WATER CONSUMPTION CHANGES : FEMALE

STUDY NO. : 0555
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-4(4)	1-7(3)	2-4(4)	2-7(3)
Control	12.7± 1.0	14.0± 1.6	18.8± 4.7	15.7± 1.2
2500 ppm	13.3± 0.5	14.4± 0.7	18.8± 2.6	17.7± 3.2
5000 ppm	12.3± 0.7	13.8± 2.4	16.5± 3.9	14.7± 4.3
10000 ppm	12.4± 2.4	12.9± 2.0	14.2± 1.7	13.6± 4.6
20000 ppm	11.1± 0.3	11.9± 1.1	13.7± 1.9*	11.3± 0.7
40000 ppm	9.4± 0.8**	11.1± 0.7*	12.0± 1.0**	10.8± 0.9

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

APPENDIX F 1

CHEMICAL INTAKE CHANGES : MALE

STUDY NO. : 0555
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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
2500 ppm	0.282± 0.007	0.281± 0.011	0.287± 0.008	0.255± 0.013
5000 ppm	0.558± 0.022	0.565± 0.028	0.568± 0.040	0.501± 0.044
10000 ppm	1.114± 0.101	1.108± 0.093	1.070± 0.061	0.924± 0.023
20000 ppm	1.962± 0.133	2.009± 0.147	1.956± 0.148	1.676± 0.149
40000 ppm	3.907± 0.570	3.889± 0.150	3.676± 0.188	3.111± 0.067

APPENDIX F 2

CHEMICAL INTAKE CHANGES : FEMALE

STUDY NO. : 0555
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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
2500 ppm	0.312± 0.021	0.325± 0.024	0.385± 0.050	0.348± 0.059
5000 ppm	0.582± 0.037	0.634± 0.117	0.685± 0.154	0.592± 0.156
10000 ppm	1.181± 0.231	1.174± 0.160	1.175± 0.136	1.083± 0.348
20000 ppm	2.116± 0.096	2.182± 0.168	2.287± 0.322	1.811± 0.107
40000 ppm	3.656± 0.248	4.036± 0.245	3.998± 0.273	3.454± 0.240

APPENDIX G 1

HEMATOLOGY : MALE

STUDY NO. : 0555
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 $10^5/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	5	7.64± 0.24	14.8± 0.4	40.8± 1.0	53.5± 0.6	19.4± 0.2	36.2± 0.5	897± 42
2500 ppm	5	7.60± 0.24	14.8± 0.4	40.6± 1.0	53.5± 0.6	19.4± 0.3	36.4± 0.6	904± 10
5000 ppm	5	7.69± 0.20	15.0± 0.4	41.1± 0.8	53.5± 0.4	19.4± 0.2	36.3± 0.4	908± 22
10000 ppm	5	7.67± 0.17	14.9± 0.3	41.0± 0.6	53.5± 0.6	19.5± 0.2	36.4± 0.3	875± 54
20000 ppm	5	7.78± 0.11	15.2± 0.2	41.6± 0.5	53.4± 0.3	19.5± 0.2	36.5± 0.2	859± 32
40000 ppm	5	7.80± 0.19	15.0± 0.3	41.7± 0.9	53.5± 0.5	19.3± 0.2	36.0± 0.5	775± 31**

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

STUDY NO. : 0555
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 %	PROTHROMBIN TIME sec	APTT sec
Control	5	3.1± 0.5	12.4± 0.2	18.9± 0.6
2500 ppm	5	3.5± 0.4	12.3± 0.1	18.0± 1.3
5000 ppm	5	3.4± 0.4	12.4± 0.1	18.7± 0.4
10000 ppm	5	3.2± 0.4	12.4± 0.3	18.7± 0.9
20000 ppm	5	2.9± 0.2	12.5± 0.1	19.0± 0.9
40000 ppm	5	3.0± 0.1	12.6± 0.3	19.1± 0.8

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

STUDY NO. : 0555
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	6.02± 0.86	
2500 ppm	5	5.68± 0.21	
5000 ppm	5	5.48± 1.01	
10000 ppm	5	5.22± 0.47	
20000 ppm	5	5.52± 0.87	
40000 ppm	5	5.87± 0.74	

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

APPENDIX G 2

HEMATOLOGY : FEMALE

STUDY NO. : 0555
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 $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	5	8.04± 0.20	15.7± 0.4	42.3± 0.7	52.6± 0.6	19.6± 0.2	37.2± 0.5	726± 21
2500 ppm	5	8.12± 0.20	16.0± 0.3	42.8± 0.9	52.7± 0.4	19.7± 0.2	37.4± 0.4	771± 15
5000 ppm	5	8.20± 0.26	16.0± 0.4	43.1± 1.0	52.5± 0.5	19.5± 0.1	37.2± 0.3	748± 65
10000 ppm	5	8.16± 0.14	16.0± 0.2	43.0± 0.3	52.7± 0.7	19.6± 0.2	37.1± 0.5	729± 29
20000 ppm	5	8.13± 0.22	15.9± 0.4	43.0± 1.0	52.8± 0.6	19.5± 0.1	36.9± 0.4	724± 49
40000 ppm	5	8.03± 0.18	15.8± 0.5	42.7± 0.5	53.1± 0.9	19.7± 0.3	37.0± 0.9	691± 33

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

STUDY NO. : 0555
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 %	PROTHROMBIN TIME sec	APTT sec
Control	5	1.6± 0.2	12.6± 0.3	18.8± 0.5
2500 ppm	5	1.6± 0.1	12.5± 0.2	18.5± 1.2
5000 ppm	5	1.7± 0.2	12.6± 0.5	18.6± 0.7
10000 ppm	5	1.6± 0.2	12.9± 0.4	19.0± 0.7
20000 ppm	5	1.5± 0.2	12.7± 0.2	19.0± 0.8
40000 ppm	5	1.8± 0.3	12.8± 0.1	19.1± 0.9

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

STUDY NO. : 0555
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
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	6.30± 0.88	
2500 ppm	5	4.97± 0.72	
5000 ppm	5	4.70± 0.97*	
10000 ppm	5	4.79± 0.35*	
20000 ppm	5	4.56± 0.80*	
40000 ppm	5	4.47± 1.19*	

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

APPENDIX H 1

BIOCHEMISTRY : MALE

STUDY NO. : 0555
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	3.2± 0.0	1.3± 0.0	0.12± 0.01	180± 11	66± 4	134± 8
2500 ppm	5	5.7± 0.1	3.2± 0.1	1.3± 0.1	0.12± 0.01	182± 9	68± 4	135± 10
5000 ppm	5	5.7± 0.1	3.2± 0.1	1.3± 0.1	0.11± 0.01	182± 6	66± 3	136± 6
10000 ppm	5	5.5± 0.1*	3.1± 0.1	1.3± 0.0	0.11± 0.01	183± 5	66± 3	132± 8
20000 ppm	5	5.5± 0.1**	3.1± 0.1	1.3± 0.0	0.12± 0.01	187± 8	65± 1	137± 8
40000 ppm	5	5.4± 0.1**	3.1± 0.1	1.4± 0.1	0.12± 0.02	183± 3	63± 3	135± 8

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

STUDY NO. : 0555
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	56±	2	32±	2	115±	12	1±	1	163±	12	16.2±	2.4	0.4±	0.0
2500 ppm	5	57±	2	32±	3	126±	20	1±	0	169±	22	15.6±	2.1	0.4±	0.0
5000 ppm	5	58±	2	33±	1	149±	54	1±	1	215±	75	16.2±	1.6	0.4±	0.0
10000 ppm	5	55±	1	31±	2	140±	51	1±	0	164±	20	15.3±	1.6	0.4±	0.1
20000 ppm	5	52±	2	29±	2	159±	67	1±	1	160±	28	16.1±	1.1	0.4±	0.0
40000 ppm	5	54±	4	29±	2	134±	37	1±	0	166±	26	16.5±	1.5	0.4±	0.0

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

STUDY NO. : 0555
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	140± 1	4.3± 0.2	101± 1	11.0± 0.2	8.1± 0.7
2500 ppm	5	140± 1	4.2± 0.2	101± 1	11.1± 0.1	8.1± 0.9
5000 ppm	5	140± 1	4.2± 0.4	101± 1	10.8± 0.1	8.1± 1.0
10000 ppm	5	140± 2	4.1± 0.1	101± 2	10.9± 0.3	7.8± 1.0
20000 ppm	5	139± 2	4.1± 0.3	101± 2	10.7± 0.2	7.3± 1.0
40000 ppm	5	139± 1	4.2± 0.1	101± 1	10.6± 0.2*	7.5± 1.3

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

APPENDIX H 2

BIOCHEMISTRY : FEMALE

STUDY NO. : 0555
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	5.5± 0.1	3.2± 0.1	1.3± 0.1	0.12± 0.02	186± 3	71± 6	133± 8
2500 ppm	5	5.6± 0.1	3.3± 0.1	1.4± 0.0	0.13± 0.01	184± 4	75± 1	138± 7
5000 ppm	5	5.6± 0.1	3.3± 0.1	1.4± 0.1	0.13± 0.01	188± 14	72± 4	132± 7
10000 ppm	5	5.5± 0.1	3.2± 0.1	1.4± 0.1	0.12± 0.01	184± 8	71± 5	137± 13
20000 ppm	5	5.4± 0.2	3.1± 0.1	1.4± 0.0	0.13± 0.01	183± 16	71± 3	138± 8
40000 ppm	5	5.4± 0.1	3.2± 0.1	1.4± 0.1	0.14± 0.01	185± 8	67± 3	133± 5

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

STUDY NO. : 0555
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	58±	3	27±	3	214±	75	2±	1	179±	19	17.7±	2.3	0.5±	0.1
2500 ppm	5	62±	4	31±	2	228±	123	2±	1	174±	52	17.4±	1.8	0.4±	0.0
5000 ppm	5	66±	10	31±	5	269±	91	1±	1	191±	64	18.9±	3.1	0.4±	0.1
10000 ppm	5	63±	7	30±	4	249±	80	1±	0	178±	16	19.3±	2.5	0.4±	0.0
20000 ppm	5	58±	7	28±	3	218±	77	1±	0	163±	23	18.4±	2.4	0.5±	0.1
40000 ppm	5	55±	3	25±	2	219±	81	1±	0	189±	69	17.9±	3.3	0.4±	0.0

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

STUDY NO. : 0555
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE 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	138± 1	3.9± 0.2	102± 2	10.4± 0.2	7.0± 0.7
2500 ppm	5	139± 2	3.8± 0.1	102± 1	10.4± 0.2	7.2± 0.8
5000 ppm	5	140± 2	3.8± 0.3	103± 1	10.3± 0.1	6.9± 0.6
10000 ppm	5	139± 2	4.0± 0.3	103± 2	10.3± 0.3	6.8± 1.0
20000 ppm	5	138± 1	4.0± 0.4	102± 2	10.1± 0.2	5.7± 1.5
40000 ppm	5	138± 2	4.1± 0.1	102± 1	10.1± 0.2	5.9± 1.8

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

APPENDIX I 1

GROSS FINDINGS : MALE

STUDY NO. : 0555
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
ALL ANIMALS (0- 2W)

Organ	Findings	Group Name / NO. of Animals	Control 5 (%)	2500 ppm 5 (%)	5000 ppm 5 (%)	10000 ppm 5 (%)
liver	herniation		0 (0)	0 (0)	0 (0)	0 (0)

Organ	Findings	Group Name	20000 ppm	40000 ppm
		NO. of Animals	5 (%)	5 (%)
liver	herniation		0 (0)	1 (20)

APPENDIX I 2

GROSS FINDINGS : FEMALE

STUDY NO. : 0555
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
ALL ANIMALS (0- 2W)

Organ	Findings	Group Name NO. of Animals	Control 5 (%)	2500 ppm 5 (%)	5000 ppm 5 (%)	10000 ppm 5 (%)
liver	herniation		1 (20)	0 (0)	0 (0)	2 (40)

STUDY NO. : 0555
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
ALL ANIMALS (0- 2W)

Organ	Findings	Group Name / NO. of Animals	20000 ppm 5 (%)	40000 ppm 5 (%)
liver	herniation		1 (20)	1 (20)

APPENDIX J 1

ORGAN WEIGHT, ABSOLUTE : MALE

STUDY NO. : 0555
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	184± 10	0.363± 0.044	0.038± 0.002	2.428± 0.055	0.672± 0.027	0.833± 0.035
2500 ppm	5	190± 8	0.392± 0.032	0.036± 0.001	2.455± 0.039	0.711± 0.036	0.830± 0.043
5000 ppm	5	186± 4	0.355± 0.032	0.037± 0.001	2.440± 0.052	0.693± 0.019	0.825± 0.025
10000 ppm	5	189± 7	0.361± 0.009	0.034± 0.006	2.472± 0.077	0.713± 0.024	0.820± 0.040
20000 ppm	5	181± 14	0.330± 0.018	0.036± 0.004	2.429± 0.083	0.666± 0.052	0.809± 0.033
40000 ppm	5	179± 9	0.298± 0.022**	0.035± 0.006	2.378± 0.150	0.680± 0.018	0.789± 0.038

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

STUDY NO. : 0555
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	1.488± 0.106	0.468± 0.037	7.133± 0.512	1.748± 0.052
2500 ppm	5	1.560± 0.098	0.481± 0.025	7.549± 0.649	1.764± 0.052
5000 ppm	5	1.515± 0.056	0.462± 0.014	7.426± 0.383	1.732± 0.007
10000 ppm	5	1.540± 0.090	0.479± 0.023	7.330± 0.609	1.771± 0.056
20000 ppm	5	1.483± 0.104	0.452± 0.037	7.274± 0.619	1.720± 0.089
40000 ppm	5	1.526± 0.111	0.439± 0.027	7.084± 0.542	1.689± 0.071

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

APPENDIX J 2

ORGAN WEIGHT, ABSOLUTE : FEMALE

STUDY NO. : 0555
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	0.310± 0.017	0.042± 0.002	0.098± 0.016	0.504± 0.047	0.641± 0.042
2500 ppm	5	127± 4	0.297± 0.018	0.044± 0.005	0.097± 0.005	0.510± 0.031	0.647± 0.043
5000 ppm	5	124± 7	0.289± 0.015	0.043± 0.003	0.095± 0.015	0.524± 0.032	0.627± 0.020
10000 ppm	5	125± 2	0.285± 0.018	0.042± 0.003	0.095± 0.016	0.514± 0.043	0.651± 0.036
20000 ppm	5	124± 3	0.312± 0.012	0.043± 0.005	0.094± 0.006	0.514± 0.040	0.650± 0.021
40000 ppm	5	125± 2	0.274± 0.008**	0.042± 0.002	0.095± 0.008	0.506± 0.009	0.646± 0.034

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

STUDY NO. : 0555
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	1.003± 0.058	0.340± 0.026	4.710± 0.463	1.607± 0.054
2500 ppm	5	1.021± 0.066	0.332± 0.007	4.604± 0.204	1.622± 0.046
5000 ppm	5	1.013± 0.030	0.323± 0.006	4.515± 0.301	1.633± 0.035
10000 ppm	5	1.074± 0.051	0.332± 0.014	4.595± 0.235	1.634± 0.026
20000 ppm	5	1.050± 0.047	0.333± 0.011	4.684± 0.073	1.605± 0.033
40000 ppm	5	1.072± 0.044	0.332± 0.022	4.721± 0.336	1.618± 0.024

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

APPENDIX K 1

ORGAN WEIGHT, RELATIVE : MALE

STUDY NO. : 0555
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	184± 10	0.198± 0.024	0.021± 0.002	1.320± 0.050	0.365± 0.009	0.453± 0.020
2500 ppm	5	190± 8	0.206± 0.011	0.019± 0.001	1.294± 0.050	0.374± 0.016	0.437± 0.012
5000 ppm	5	186± 4	0.191± 0.020	0.020± 0.000	1.309± 0.037	0.372± 0.009	0.443± 0.020
10000 ppm	5	189± 7	0.191± 0.010	0.018± 0.004	1.305± 0.037	0.377± 0.017	0.433± 0.009
20000 ppm	5	181± 14	0.183± 0.009	0.020± 0.002	1.347± 0.063	0.368± 0.013	0.448± 0.017
40000 ppm	5	179± 9	0.166± 0.007*	0.020± 0.004	1.325± 0.034	0.379± 0.014	0.440± 0.006

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

STUDY NO. : 0555
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	0.807± 0.024	0.254± 0.007	3.872± 0.172	0.950± 0.028
2500 ppm	5	0.821± 0.019	0.253± 0.008	3.968± 0.200	0.929± 0.019
5000 ppm	5	0.813± 0.017	0.248± 0.009	3.983± 0.166	0.929± 0.019
10000 ppm	5	0.813± 0.019	0.252± 0.006	3.865± 0.192	0.936± 0.017
20000 ppm	5	0.821± 0.013	0.250± 0.014	4.022± 0.111	0.953± 0.031
40000 ppm	5	0.850± 0.020**	0.245± 0.010	3.945± 0.130	0.943± 0.051

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

APPENDIX K 2

ORGAN WEIGHT, RELATIVE : FEMALE

STUDY NO. : 0555
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	0.246± 0.018	0.033± 0.001	0.078± 0.009	0.399± 0.022	0.508± 0.027
2500 ppm	5	127± 4	0.234± 0.010	0.035± 0.003	0.076± 0.005	0.402± 0.017	0.509± 0.025
5000 ppm	5	124± 7	0.233± 0.010	0.035± 0.004	0.077± 0.011	0.424± 0.030	0.508± 0.028
10000 ppm	5	125± 2	0.227± 0.015	0.034± 0.002	0.076± 0.013	0.410± 0.031	0.520± 0.026
20000 ppm	5	124± 3	0.251± 0.013	0.035± 0.004	0.076± 0.006	0.413± 0.035	0.522± 0.011
40000 ppm	5	125± 2	0.219± 0.007**	0.034± 0.001	0.076± 0.007	0.404± 0.006	0.516± 0.023

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

STUDY NO. : 0555
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	0.795± 0.032	0.269± 0.011	3.726± 0.233	1.276± 0.078
2500 ppm	5	0.804± 0.033	0.261± 0.009	3.627± 0.149	1.277± 0.028
5000 ppm	5	0.820± 0.049	0.261± 0.012	3.648± 0.139	1.322± 0.073
10000 ppm	5	0.857± 0.040*	0.266± 0.011	3.672± 0.218	1.306± 0.031
20000 ppm	5	0.844± 0.027	0.268± 0.006	3.766± 0.080	1.290± 0.026
40000 ppm	5	0.856± 0.023*	0.265± 0.014	3.768± 0.207	1.292± 0.028

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

APPENDIX L

METHODS, UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK DRINKING WATER STUDY OF 2-METHYL-1-PROPANOL

METHODS, UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2- WEEK DRINKING WATER STUDY OF 2-METHYL-1-PROPANOL

Item	Method	Unit	Decimal place
Hematology			
Red blood cell (RBC)	Light scattering method[1)]	$\times 10^6/\mu L$	2
Hemoglobin(Hgb)	Cyanmethemoglobin method[1)]	g/dL	1
Hematocrit(Hct)	Calculated as RBC×MCV/10[1)]	%	1
Mean corpuscular volume(MCV)	Light scattering method[1)]	fL	1
Mean corpuscular hemoglobin(MCH)	Calculated as Hgb/RBC×10[1)]	pg	1
Mean corpuscular hemoglobin concentration (MCHC)	Calculated as Hgb/Hct×100[1)]	g/dL	1
Platelet	Light scattering method[1)]	$\times 10^3/\mu L$	0
Reticulocyte	Light scattering method[1)]	%	1
Prothrombin time	Quick one stage method[2)]	sec	1
Activated partial thromboplastin time(APTT)	Ellagic acid activaterd method[2)]	sec	1
White blood cell(WBC)	Light scattering method[1)]	$\times 10^3/\mu L$	2
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
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	Jaffe 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 coagulometer (Sysmex CA-5000 : Sysmex Corporation)
3) Automatic analyzer (Hitachi 7080 : Hitachi,Ltd.)