2,4-ペンタンジオンのラットを用いた
吸入による 13 週間毒性試験報告書

試験番号：0600

APPENDICES

APPENDICES

APPENDICES (CONTINUED)

APPENDIX A 1

IDENTITY OF 2,4-PENTANEDIONE

IN THE 13-WEEK INHALATION STUDY

IDENTITY OF 2,4-PENTANEDIONE IN THE 13-WEEK INHALATION STUDY

Test Substance : 2,4-Pentanedione (Wako Pure Chemical Industries, Ltd.)

Lot No. : SDJ5794

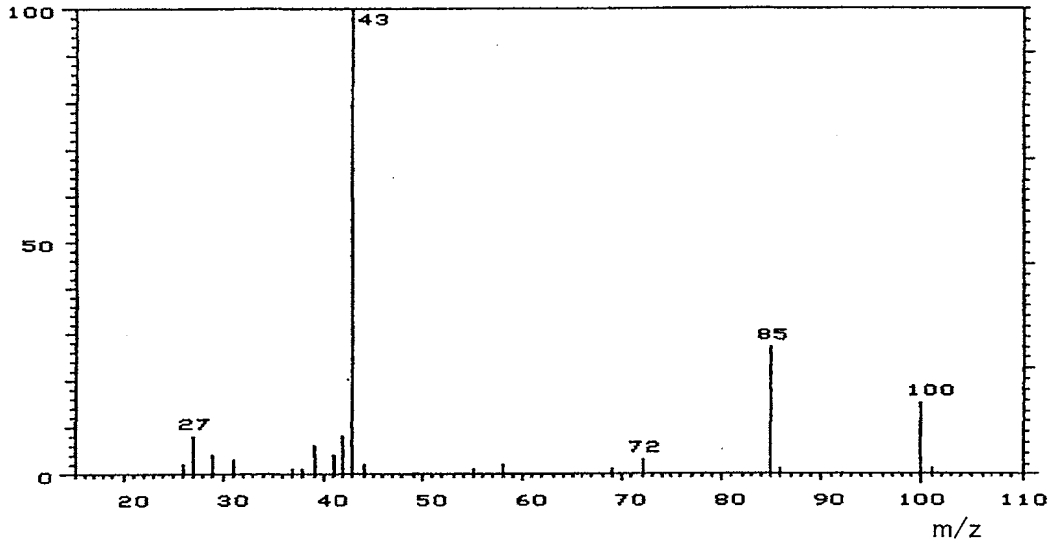
1. Spectral Data

Mass Spectrometry

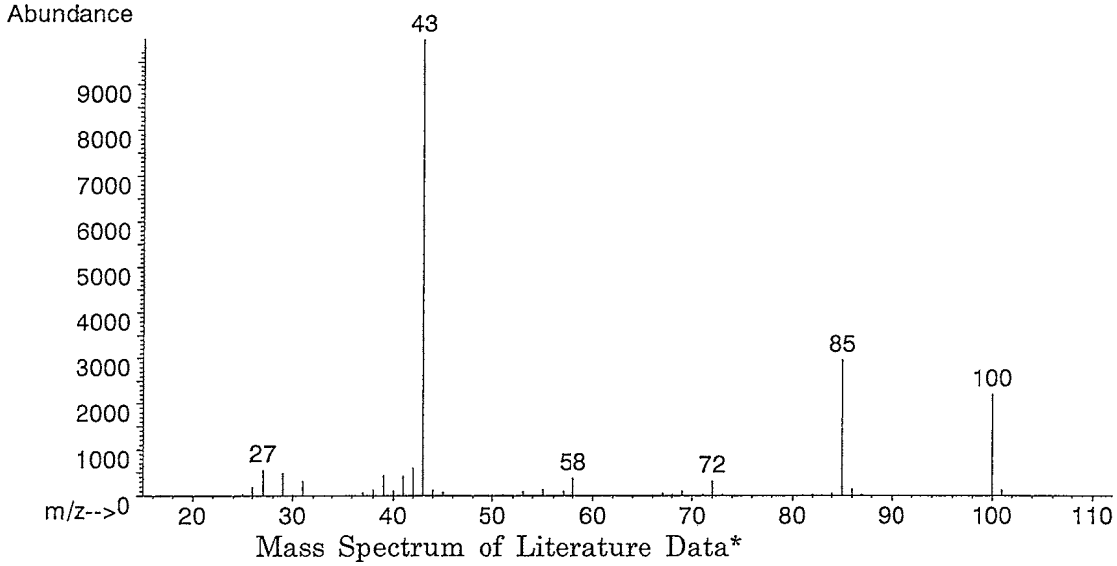
Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance



Mass Spectrum of Literature Data*

Result: The mass spectrum was consistent with literature spectrum.

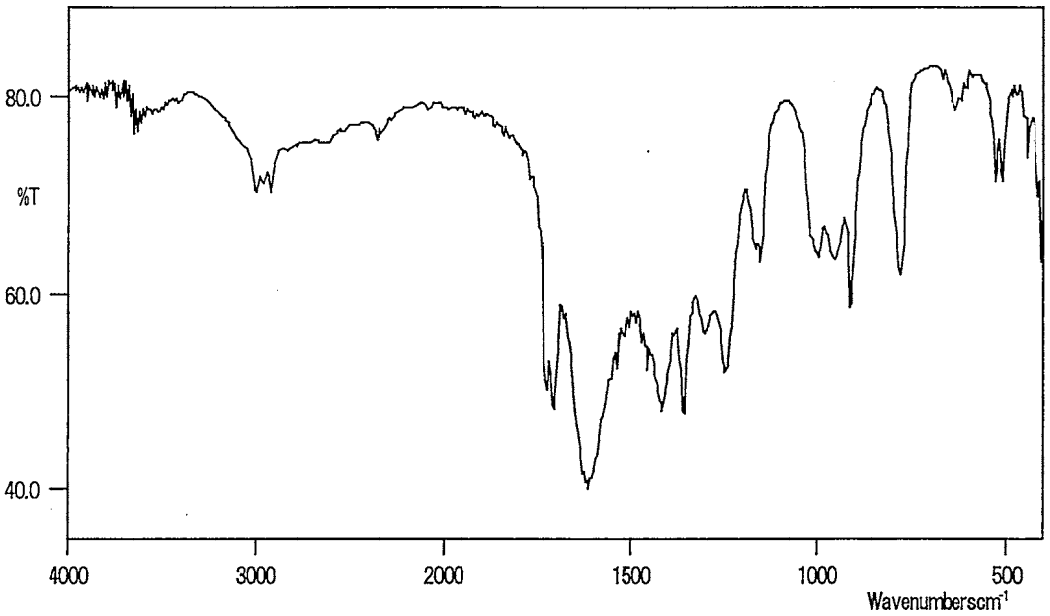
(*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed. New York, NY:John Wiley and Sons.)

Infrared Spectrometry

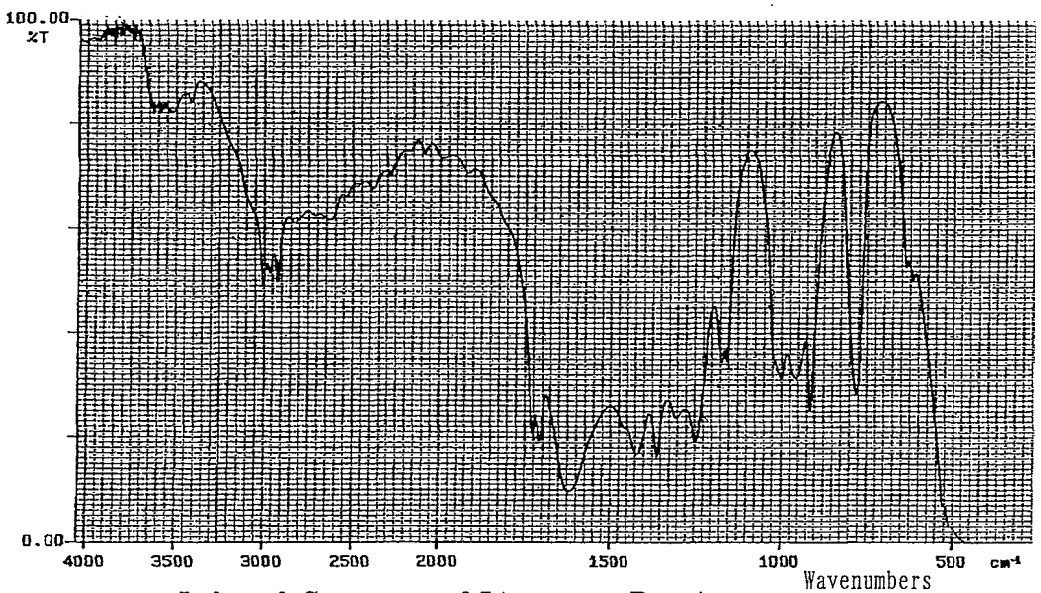
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 4 cm^{-1}



Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data*

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

2. Conclusion: The test substance was identified as 2,4-pentanedione by mass spectrum and infrared spectrum.

APPENDIX A 2

STABILITY OF 2,4-PENTANEDIONE

IN THE 13-WEEK INHALATION STUDY

STABILITY OF 2,4-PENTANEDIONE IN THE 13-WEEK INHALATION STUDY

Test Substance : 2,4-Pentanedione (Wako Pure Chemical Industries, Ltd.)

Lot No. : SDJ5794

1. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : INNOWAX (0.53 mmϕ × 60 m)

Column Temperature: 150° C

Flow Rate : 3 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μL

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
2005.09.20	1	5.678	100
2006.01.11	1	5.674	100

Result: Gas chromatography indicated one major peak (peak No.1) analyzed on 2005.9.20 and one major peak (peak No.1) analyzed on 2006.1.11. No new trace impurity peak in the test substance analyzed on 2006.1.11 was detected.

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

APPENDIX B

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 13-WEEK INHALATION STUDY OF 2,4-PENTANEDIONE

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 13-WEEK INHALATION STUDY OF 2,4-PENTANEDIONE

Group Name	Temperature (℃) Mean ± S.D.	Humidity (%) Mean ± S.D.	Ventilation Rate (L/min) Mean ± S.D.	Air Change (time/h) Mean
Control	22.5 ± 0.3	58.1 ± 1.1	212.2 ± 0.8	12.0
25 ppm	22.6 ± 0.3	57.4 ± 1.8	212.3 ± 0.9	12.0
50 ppm	22.6 ± 0.3	56.3 ± 2.5	212.5 ± 0.8	12.0
100 ppm	22.5 ± 0.3	56.7 ± 1.8	212.1 ± 0.9	12.0
200 ppm	22.6 ± 0.3	55.6 ± 1.9	211.7 ± 0.8	12.0
400 ppm	22.6 ± 0.3	56.3 ± 2.6	212.1 ± 0.8	12.0

APPENDIX C 1

CLINICAL OBSERVATION : MALE

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7
		1	1	1	1	1	1	1	1	1	1	1	1	1
NON REMARKABLE	Control	10	10	10	10	10	10	10	10	10	10	10	10	10
	25ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	50ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	100ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	200ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	400ppm	10	10	10	10	10	10	10	10	10	10	10	10	10

APPENDIX C 2

CLINICAL OBSERVATION : FEMALE

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day 1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7
		1	1	1	1	1	1	1	1	1	1	1	1	1
EXOPHTHALMOS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	25ppm	0	0	0	0	0	0	0	0	0	0	0	1	1
	50ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	100ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	200ppm	0	0	0	0	1	1	1	1	1	1	1	1	1
	400ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
CATARACT	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	25ppm	0	0	0	0	0	0	0	0	0	0	0	1	1
	50ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	100ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	200ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	400ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
CORNEAL OPACITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	25ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	50ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	100ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	200ppm	0	0	1	1	1	1	1	1	1	1	1	1	1
	400ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
NON REMARKABLE	Control	10	10	10	10	10	10	10	10	10	10	10	10	10
	25ppm	10	10	10	10	10	10	10	10	10	10	10	9	9
	50ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	100ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	200ppm	10	10	9	9	9	9	9	9	9	9	9	9	9
	400ppm	10	10	10	10	10	10	10	10	10	10	10	10	10

APPENDIX D 1

BODY WEIGHT CHANGES : MALE

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	122± 4	150± 7	177± 6	202± 7	223± 7	237± 8	252± 9
25ppm	122± 4	150± 7	178± 8	202± 8	223± 8	239± 10	253± 11
50ppm	122± 4	150± 6	178± 7	202± 8	222± 8	239± 11	253± 11
100ppm	122± 4	150± 6	180± 6	205± 7	228± 9	243± 11	257± 11
200ppm	122± 4	150± 4	179± 5	206± 6	230± 7	244± 7	259± 8
400ppm	122± 4	143± 5*	168± 4**	194± 6*	210± 8**	224± 7**	237± 7**

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

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-7
Control	262± 8	272± 10	283± 11	290± 12	294± 11	302± 12	306± 13
25ppm	263± 15	274± 14	282± 15	288± 14	293± 15	299± 15	303± 17
50ppm	264± 12	273± 11	285± 13	288± 11	292± 10	300± 11	304± 11
100ppm	269± 11	279± 11	289± 11	295± 10	299± 10	303± 12	308± 13
200ppm	270± 9	280± 10	289± 11	293± 10	299± 11	305± 10	308± 12
400ppm	250± 8*	259± 8*	268± 8*	275± 8*	280± 8*	285± 7**	287± 8**

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

APPENDIX D 2

BODY WEIGHT CHANGES : FEMALE

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	95± 2	109± 3	123± 4	133± 4	142± 6	148± 7	154± 7
25ppm	95± 2	108± 2	121± 4	131± 4	140± 4	147± 4	152± 5
50ppm	95± 2	109± 3	122± 4	131± 5	140± 5	147± 6	153± 7
100ppm	95± 2	109± 3	122± 3	133± 4	140± 4	147± 5	154± 5
200ppm	95± 3	107± 3	120± 4	132± 4	141± 5	146± 5	154± 7
400ppm	95± 2	104± 3**	115± 3**	126± 4**	134± 4**	141± 4*	149± 5

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

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-7
Control	160± 8	163± 7	167± 8	172± 8	174± 8	175± 7	177± 7
25ppm	157± 5	162± 7	166± 7	169± 7	172± 7	175± 7	178± 6
50ppm	156± 9	159± 9	163± 10	166± 12	169± 11	171± 13	174± 10
100ppm	158± 5	163± 8	167± 8	170± 9	173± 11	175± 12	177± 12
200ppm	159± 7	163± 8	167± 9	169± 9	172± 9	175± 8	175± 8
400ppm	155± 5	158± 5	163± 3	166± 5	168± 5	171± 4	172± 4

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

APPENDIX E 1

FOOD CONSUMPTION CHANGES : MALE

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(7)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	14.5± 0.5	15.4± 0.9	16.5± 0.9	16.9± 0.8	16.9± 0.8	16.2± 0.8	16.2± 0.7
25ppm	14.6± 0.6	15.5± 0.5	16.1± 0.9	16.8± 0.6	16.5± 0.8	16.0± 0.7	16.3± 1.0
50ppm	14.1± 0.8	15.2± 0.9	16.3± 0.9	16.7± 0.7	16.4± 0.9	16.2± 0.7	16.6± 0.7
100ppm	13.9± 0.8	15.5± 0.8	16.6± 0.7	16.6± 0.9	17.0± 1.0	16.6± 0.8	16.7± 0.9
200ppm	14.2± 0.6	15.0± 0.5	17.0± 0.7	17.1± 0.6	17.0± 0.4	16.5± 0.5	16.7± 0.5
400ppm	13.2± 0.6**	13.3± 0.6**	15.4± 0.7*	15.0± 0.6**	15.5± 0.7**	15.5± 0.6	15.9± 0.8

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

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)
Control	16.5± 0.8	16.7± 1.0	16.5± 0.8	16.2± 0.8	16.2± 0.9	15.8± 0.7
25ppm	16.0± 0.8	16.0± 1.2	16.1± 0.9	16.3± 1.0	16.1± 0.8	15.8± 1.0
50ppm	16.4± 0.5	16.5± 0.7	16.1± 0.7	15.7± 0.8	15.6± 0.8	15.8± 0.9
100ppm	16.1± 0.8	16.6± 0.4	16.5± 0.4	16.0± 0.7	16.0± 0.8	16.0± 0.9
200ppm	16.6± 0.9	16.6± 0.8	16.4± 0.8	16.2± 0.6	16.2± 0.6	15.7± 0.8
400ppm	15.8± 0.9	15.6± 0.8	16.0± 0.7	15.0± 0.7**	14.8± 0.5**	14.8± 0.6*

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

APPENDIX E 2

FOOD CONSUMPTION CHANGES : FEMALE

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(7)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	10.6± 0.6	10.5± 0.5	10.9± 0.6	11.0± 0.8	11.0± 0.9	11.0± 0.7	11.0± 0.6
25ppm	10.8± 0.6	10.8± 0.7	11.1± 0.7	11.1± 0.5	11.0± 0.3	10.4± 0.4	10.7± 0.8
50ppm	10.6± 0.4	10.6± 0.3	10.8± 0.5	10.8± 0.6	10.7± 0.7	10.3± 0.8	10.5± 0.7
100ppm	10.5± 0.5	11.1± 0.5	11.2± 0.5	11.1± 0.6	11.3± 0.5	10.9± 0.6	11.1± 0.6
200ppm	10.4± 0.5	10.4± 0.9	11.1± 0.7	10.7± 1.2	11.2± 0.8	10.9± 0.6	11.4± 0.7
400ppm	9.8± 0.5**	9.7± 0.4*	10.2± 0.6*	10.2± 0.4**	10.4± 0.3	10.6± 0.4	11.0± 0.6

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

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)
Control	10.9± 0.9	10.8± 0.5	11.2± 0.8	11.1± 0.7	10.6± 0.6	10.6± 0.8
25ppm	10.7± 0.9	10.8± 0.7	10.8± 0.7	10.7± 0.7	11.1± 0.5	10.9± 0.7
50ppm	10.0± 0.8	10.4± 0.7	10.4± 0.8	10.6± 0.9	10.7± 0.6	10.5± 0.6
100ppm	10.9± 0.8	11.0± 0.9	11.0± 0.8	10.9± 1.1	11.1± 0.9	10.5± 0.8
200ppm	10.9± 0.6	10.8± 0.6	11.0± 0.5	10.9± 0.5	10.8± 0.6	10.2± 0.6
400ppm	10.7± 0.6	10.8± 0.7	10.7± 0.5	10.7± 0.6	10.4± 0.5	9.9± 0.8

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

APPENDIX F 1

HEMATOLOGY : MALE

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	10	9.40± 0.14	16.2± 0.3	44.4± 0.7	47.2± 0.5	17.2± 0.2	36.5± 0.4	701± 31
25ppm	10	9.32± 0.16	16.1± 0.2	44.1± 0.5	47.4± 0.5	17.3± 0.2	36.6± 0.3	720± 35
50ppm	10	9.40± 0.10	16.3± 0.1	44.3± 0.4	47.1± 0.4	17.3± 0.2	36.7± 0.4	705± 44
100ppm	10	9.35± 0.19	16.2± 0.3	44.1± 0.8	47.2± 0.5	17.3± 0.1	36.7± 0.3	751± 40*
200ppm	10	9.32± 0.11	16.1± 0.3	43.8± 0.7	47.0± 0.4	17.3± 0.2	36.8± 0.4	744± 39*
400ppm	10	9.20± 0.11*	16.2± 0.2	43.6± 0.8	47.4± 0.3	17.6± 0.1**	37.1± 0.2**	765± 25**

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

Group Name	NO. of Animals	RETICULOCYTE %	PROTHROMBIN TIME sec	APTT sec
Control	10	1.6± 0.1	13.6± 1.9	24.2± 2.5
25ppm	10	1.6± 0.3	12.4± 0.6	22.4± 1.8
50ppm	10	1.6± 0.2	12.9± 1.0	23.4± 1.3
100ppm	10	1.7± 0.2	12.5± 1.1	23.1± 1.5
200ppm	10	1.6± 0.2	13.8± 1.5	25.6± 1.6
400ppm	10	2.0± 0.2**	13.1± 1.9	23.7± 2.0

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

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHER
Control	10	7.16± 1.72	0± 1	21± 3	1± 1	0± 0	3± 1	75± 3	0± 0
25ppm	10	6.75± 1.64	0± 0	21± 4	1± 0	0± 0	3± 2	75± 5	0± 0
50ppm	10	7.58± 1.54	1± 1	22± 5	1± 1	0± 0	3± 2	74± 5	0± 0
100ppm	10	7.35± 0.87	1± 1	23± 2	2± 1	0± 0	3± 1	72± 2	0± 0
200ppm	10	7.31± 1.25	1± 1	20± 4	1± 1	0± 0	3± 1	75± 3	0± 1
400ppm	10	7.94± 1.43	1± 1	23± 5	1± 1	0± 0	2± 1	73± 6	0± 0

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

APPENDIX F 2

HEMATOLOGY : FEMALE

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	10	8.68± 0.15	16.2± 0.2	43.0± 0.6	49.6± 0.4	18.7± 0.1	37.7± 0.3	745± 51
25ppm	10	8.64± 0.16	16.1± 0.3	43.1± 0.8	49.9± 0.4	18.7± 0.1	37.4± 0.3	745± 43
50ppm	10	8.72± 0.22	16.4± 0.4	43.4± 1.0	49.8± 0.4	18.7± 0.3	37.6± 0.3	780± 21
100ppm	10	8.70± 0.13	16.3± 0.2	43.4± 0.7	49.9± 0.7	18.8± 0.3	37.6± 0.4	770± 35
200ppm	10	8.57± 0.14	16.2± 0.3	42.8± 0.7	49.9± 0.4	18.9± 0.3	37.9± 0.4	772± 48
400ppm	10	8.38± 0.13**	15.9± 0.3	42.2± 0.7	50.3± 0.5**	19.0± 0.2*	37.8± 0.4	818± 54**

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

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RETICULOCYTE %	PROTHROMBIN TIME sec	APTT sec
Control	10	1.6± 0.2	11.6± 0.3	19.0± 1.0
25ppm	10	1.6± 0.1	11.5± 0.7	18.9± 0.7
50ppm	10	1.7± 0.2	11.6± 0.3	19.0± 1.0
100ppm	10	1.7± 0.2	11.5± 0.4	18.6± 0.8
200ppm	10	1.7± 0.2	11.6± 0.3	18.9± 0.9
400ppm	10	2.4± 0.5**	11.8± 0.4	19.2± 0.6

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

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$		Differential WBC (%) N-BAND		N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHER	
Control	10	4.74±	1.79	1±	1	19±	5	1±	1	0±	0	3±	1	76±	5	0±	0
25ppm	10	4.95±	1.40	0±	1	22±	3	2±	1	0±	0	3±	1	73±	2	0±	0
50ppm	10	4.31±	1.40	1±	1	21±	3	1±	1	0±	0	4±	1	74±	5	0±	0
100ppm	10	4.44±	0.87	1±	1	20±	6	1±	1	0±	0	3±	1	74±	6	0±	0
200ppm	10	4.16±	1.20	0±	1	20±	3	1±	1	0±	0	3±	2	75±	4	0±	0
400ppm	10	4.71±	1.16	0±	0	19±	4	1±	1	0±	0	3±	1	77±	5	0±	0

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

APPENDIX G 1

BIOCHEMISTRY : MALE

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	TOTAL PROTEIN g／dℓ	ALBUMIN g／dℓ	A/G RATIO	T-BILIRUBIN mg／dℓ	GLUCOSE mg／dℓ	T-CHOLESTEROL mg／dℓ	TRIGLYCERIDE mg／dℓ
Control	10	6.6± 0.2	3.7± 0.1	1.3± 0.1	0.11± 0.01	193± 8	62± 6	58± 18
25ppm	10	6.5± 0.1	3.7± 0.1	1.3± 0.1	0.11± 0.00	186± 11	60± 6	48± 14
50ppm	10	6.6± 0.1	3.7± 0.1	1.2± 0.1	0.11± 0.01	186± 14	65± 5	54± 13
100ppm	10	6.6± 0.1	3.7± 0.1	1.2± 0.0	0.12± 0.01	180± 10	64± 5	56± 15
200ppm	10	6.6± 0.2	3.7± 0.1	1.3± 0.1	0.11± 0.01	179± 14	63± 6	54± 10
400ppm	10	6.6± 0.1	3.7± 0.1	1.3± 0.1	0.12± 0.01	181± 13	62± 5	52± 10

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

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dℓ	AST IU/ℓ	ALT IU/ℓ	LDH IU/ℓ	ALP IU/ℓ	G-GTP IU/ℓ	CK IU/ℓ
Control	10	113± 6	98± 21	54± 6	181± 46	273± 18	1± 0	118± 11
25ppm	10	108± 7	84± 15	45± 5*	169± 52	261± 19	1± 1	122± 19
50ppm	10	116± 7	95± 29	49± 13	191± 44	260± 25	1± 0	122± 21
100ppm	10	113± 6	88± 22	47± 10*	183± 31	259± 17	1± 1	125± 18
200ppm	10	113± 9	91± 25	48± 10	178± 50	244± 24*	1± 1	112± 17
400ppm	10	112± 8	75± 13	41± 5**	154± 26	238± 27**	1± 0	107± 14

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

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	UREA NITOROGEN mg/dℓ	CREATININE mg/dℓ	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dℓ	INORGANIC PHOSPHORUS mg/dℓ
Control	10	18.8± 1.2	0.6± 0.1	142± 1	3.2± 0.2	104± 1	10.3± 0.3	5.5± 0.7
25ppm	10	18.2± 1.5	0.5± 0.1	141± 1	3.2± 0.2	104± 2	10.2± 0.2	5.3± 1.0
50ppm	10	18.6± 0.8	0.6± 0.1	141± 1	3.2± 0.1	104± 1	10.2± 0.2	5.3± 0.9
100ppm	10	19.2± 1.4	0.5± 0.0	142± 1	3.3± 0.2	104± 1	10.1± 0.2	5.3± 0.9
200ppm	10	19.0± 1.2	0.6± 0.1	142± 2	3.3± 0.1	104± 2	10.2± 0.2	5.4± 0.8
400ppm	10	19.4± 1.6	0.6± 0.1	142± 1	3.3± 0.2	104± 2	9.9± 0.3**	5.5± 0.9

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

APPENDIX G 2

BIOCHEMISTRY : FEMALE

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	TOTAL PROTEIN g/dℓ		ALBUMIN g/dℓ		A/G RATIO		T-BILIRUBIN mg/dℓ		GLUCOSE mg/dℓ		T-CHOLESTEROL mg/dℓ		TRIGLYCERIDE mg/dℓ	
Control	10	6.4±	0.3	3.6±	0.1	1.3±	0.1	0.12±	0.01	153±	11	73±	7	14±	2
25ppm	10	6.3±	0.2	3.5±	0.1	1.3±	0.1	0.12±	0.01	148±	12	72±	6	12±	2
50ppm	10	6.3±	0.2	3.6±	0.1	1.3±	0.1	0.12±	0.01	147±	9	75±	7	14±	5
100ppm	10	6.4±	0.2	3.6±	0.1	1.3±	0.1	0.13±	0.01	157±	16	74±	6	13±	2
200ppm	10	6.4±	0.2	3.6±	0.1	1.3±	0.1	0.12±	0.01	152±	10	74±	8	13±	3
400ppm	10	6.2±	0.2	3.5±	0.1	1.3±	0.1	0.13±	0.01	154±	8	72±	7	13±	1

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

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dℓ	AST IU/ℓ	ALT IU/ℓ	LDH IU/ℓ	ALP IU/ℓ	G-GTP IU/ℓ	CK IU/ℓ
Control	10	136± 10	73± 9	37± 7	181± 43	203± 18	2± 1	121± 24
25ppm	10	134± 9	78± 13	41± 9	192± 67	223± 17*	2± 0	119± 24
50ppm	10	138± 13	74± 8	37± 4	188± 60	215± 19	2± 0	115± 18
100ppm	10	139± 10	77± 7	41± 5	176± 50	213± 21	2± 1	115± 25
200ppm	10	138± 14	69± 6	35± 3	147± 57	204± 17	2± 0	99± 22
400ppm	10	135± 13	63± 5*	33± 5	131± 57	189± 13	2± 0	94± 20*

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

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	UREA NITOROGEN mg/dℓ	CREATININE mg/dℓ	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dℓ	INORGANIC PHOSPHORUS mg/dℓ
Control	10	20.2± 1.6	0.6± 0.1	142± 1	3.2± 0.2	106± 1	10.1± 0.2	4.9± 1.2
25ppm	10	19.3± 1.2	0.6± 0.1	141± 1	3.2± 0.2	106± 1	9.9± 0.2	4.8± 1.1
50ppm	10	20.2± 1.7	0.6± 0.1	141± 1	3.2± 0.2	106± 2	9.9± 0.2	4.8± 1.0
100ppm	10	19.6± 1.9	0.6± 0.0	141± 1	3.2± 0.3	106± 1	9.9± 0.2	4.3± 1.1
200ppm	10	19.7± 1.9	0.6± 0.0	142± 1	3.1± 0.1	106± 0	9.8± 0.2*	4.7± 0.9
400ppm	10	19.0± 1.4	0.6± 0.1	142± 1	3.4± 0.2	106± 1	9.5± 0.3**	5.0± 0.8

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

APPENDIX H 1

URINALYSIS : MALE

STUDY NO. : 0600 URINALYSIS
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Bilirubin −	+	2+	3+	CHI
Control	10	0	0	0	0	3	4	3		0	6	4	0	0	0		10	0	0	0	0	0		7	3	0	0	0	0		10	0	0	0	
25ppm	10	0	0	0	0	2	6	2		1	8	1	0	0	0		10	0	0	0	0	0		9	1	0	0	0	0		10	0	0	0	
50ppm	10	0	0	0	0	2	4	4		1	8	1	0	0	0		10	0	0	0	0	0		9	1	0	0	0	0		10	0	0	0	
100ppm	10	0	0	0	0	2	4	4		0	7	3	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
200ppm	10	0	0	0	0	1	5	4		1	7	2	0	0	0		10	0	0	0	0	0		9	1	0	0	0	0		10	0	0	0	
400ppm	10	0	0	0	0	2	5	3		1	5	4	0	0	0		10	0	0	0	0	0		8	2	0	0	0	0		10	0	0	0	

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

STUDY NO. : 0600 URINALYSIS
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

Group Name	NO. of Animals	Occult blood −	±	+	2+	3+	CHI	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0		10	0	0	0	0	
25ppm	10	10	0	0	0	0		10	0	0	0	0	
50ppm	10	10	0	0	0	0		10	0	0	0	0	
100ppm	10	10	0	0	0	0		10	0	0	0	0	
200ppm	10	10	0	0	0	0		10	0	0	0	0	
400ppm	10	10	0	0	0	0		10	0	0	0	0	

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

APPENDIX H 2

URINALYSIS : FEMALE

STUDY NO. : 0600 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	10	0	0	0	0	0	3	7		5	4	1	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
25ppm	10	0	0	0	0	0	4	6		4	5	1	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
50ppm	10	0	0	0	0	1	6	3		7	2	1	0	0	0		10	0	0	0	0	0		9	1	0	0	0	0		10	0	0	0	
100ppm	10	0	0	0	0	0	5	5		6	3	1	0	0	0		10	0	0	0	0	0		9	1	0	0	0	0		10	0	0	0	
200ppm	10	0	0	0	0	0	6	4		6	4	0	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
400ppm	10	0	0	0	0	0	2	8		4	6	0	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	

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

STUDY NO. : 0600 URINALYSIS
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

Group Name	NO. of Animals	Occult blood −	±	+	2+	3+	CHI	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0		10	0	0	0	0	
25ppm	10	10	0	0	0	0		10	0	0	0	0	
50ppm	10	10	0	0	0	0		10	0	0	0	0	
100ppm	10	10	0	0	0	0		10	0	0	0	0	
200ppm	10	10	0	0	0	0		10	0	0	0	0	
400ppm	10	10	0	0	0	0		10	0	0	0	0	

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

APPENDIX I 1

GROSS FINDINGS : MALE

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control	25ppm	50ppm	100ppm
		NO. of Animals	10 (%)	10 (%)	10 (%)	10 (%)
liver	herniation		3 (30)	0 (0)	1 (10)	0 (0)

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	200ppm		400ppm	
		NO. of Animals	10	(%)	10	(%)
liver	herniation		1	(10)	2	(20)

APPENDIX I 2

GROSS FINDINGS : FEMALE

Organ	Findings	Group Name / NO. of Animals	Control 10	(%)	25ppm 10	(%)	50ppm 10	(%)	100ppm 10	(%)
liver	herniation		2	(20)	1	(10)	0	(0)	3	(30)
eye	white		0	(0)	1	(10)	0	(0)	0	(0)

Organ	Findings	Group Name	200ppm		400ppm	
		NO. of Animals	10	(%)	10	(%)
liver	herniation		2	(20)	2	(20)
eye	white		0	(0)	0	(0)

APPENDIX J 1

ORGAN WEIGHT, ABSOLUTE : MALE

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	284± 11	0.225± 0.019	0.053± 0.009	3.162± 0.097	0.896± 0.047	0.916± 0.051
25ppm	10	280± 15	0.222± 0.026	0.056± 0.007	3.166± 0.110	0.901± 0.063	0.922± 0.042
50ppm	10	281± 11	0.211± 0.025	0.055± 0.006	3.116± 0.201	0.891± 0.030	0.904± 0.028
100ppm	10	285± 10	0.218± 0.029	0.054± 0.008	3.209± 0.129	0.930± 0.026	0.937± 0.048
200ppm	10	285± 10	0.218± 0.032	0.054± 0.005	3.210± 0.092	0.919± 0.034	0.940± 0.040
400ppm	10	265± 7**	0.199± 0.013	0.051± 0.006	3.208± 0.096	0.896± 0.034	0.914± 0.050

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

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.739± 0.106	0.515± 0.026	7.122± 0.404	1.891± 0.051
25ppm	10	1.724± 0.111	0.506± 0.026	6.965± 0.478	1.922± 0.030
50ppm	10	1.754± 0.100	0.516± 0.028	7.043± 0.419	1.900± 0.053
100ppm	10	1.817± 0.058	0.531± 0.023	7.190± 0.253	1.898± 0.038
200ppm	10	1.850± 0.073*	0.539± 0.029	7.253± 0.340	1.915± 0.027
400ppm	10	1.792± 0.047	0.531± 0.020	6.986± 0.288	1.880± 0.053

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

APPENDIX J 2

ORGAN WEIGHT, ABSOLUTE : FEMALE

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	162± 7	0.193± 0.022	0.060± 0.006	0.099± 0.015	0.629± 0.055	0.700± 0.043
25ppm	10	162± 6	0.184± 0.014	0.058± 0.006	0.095± 0.008	0.616± 0.023	0.703± 0.026
50ppm	10	158± 10	0.177± 0.027	0.059± 0.009	0.092± 0.011	0.605± 0.051	0.683± 0.038
100ppm	10	161± 10	0.175± 0.016	0.060± 0.008	0.094± 0.010	0.610± 0.040	0.695± 0.043
200ppm	10	161± 7	0.169± 0.021	0.058± 0.007	0.095± 0.019	0.603± 0.042	0.700± 0.040
400ppm	10	155± 4	0.172± 0.014	0.057± 0.007	0.097± 0.008	0.609± 0.017	0.690± 0.040

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

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.098± 0.027	0.352± 0.026	3.918± 0.269	1.756± 0.026
25ppm	10	1.099± 0.046	0.349± 0.018	3.874± 0.203	1.747± 0.036
50ppm	10	1.088± 0.066	0.343± 0.023	3.778± 0.330	1.761± 0.029
100ppm	10	1.096± 0.038	0.336± 0.028	3.849± 0.278	1.764± 0.028
200ppm	10	1.110± 0.058	0.362± 0.022	3.926± 0.271	1.743± 0.066
400ppm	10	1.114± 0.042	0.383± 0.008**	3.987± 0.108	1.736± 0.024

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

APPENDIX K 1

ORGAN WEIGHT, RELATIVE : MALE

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	284± 11	0.079± 0.007	0.018± 0.003	1.113± 0.043	0.315± 0.009	0.322± 0.018
25ppm	10	280± 15	0.079± 0.009	0.020± 0.002	1.134± 0.055	0.322± 0.012	0.330± 0.016
50ppm	10	281± 11	0.075± 0.008	0.020± 0.003	1.111± 0.061	0.318± 0.009	0.322± 0.007
100ppm	10	285± 10	0.077± 0.011	0.019± 0.003	1.127± 0.056	0.327± 0.014	0.329± 0.016
200ppm	10	285± 10	0.077± 0.012	0.019± 0.001	1.130± 0.065	0.323± 0.010	0.331± 0.014
400ppm	10	265± 7**	0.075± 0.004	0.019± 0.003	1.211± 0.042**	0.339± 0.017**	0.345± 0.023*

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

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.611± 0.025	0.181± 0.009	2.504± 0.068	0.666± 0.029
25ppm	10	0.616± 0.025	0.181± 0.007	2.488± 0.057	0.688± 0.030
50ppm	10	0.625± 0.021	0.184± 0.010	2.509± 0.083	0.678± 0.024
100ppm	10	0.638± 0.018	0.186± 0.006	2.522± 0.031	0.666± 0.016
200ppm	10	0.651± 0.026**	0.189± 0.006	2.549± 0.060	0.674± 0.022
400ppm	10	0.677± 0.022**	0.200± 0.005**	2.636± 0.054**	0.710± 0.030**

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

APPENDIX K 2

ORGAN WEIGHT, RELATIVE : FEMALE

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	162± 7	0.119± 0.014	0.037± 0.003	0.061± 0.008	0.388± 0.024	0.433± 0.022
25ppm	10	162± 6	0.114± 0.010	0.036± 0.005	0.058± 0.005	0.381± 0.019	0.434± 0.023
50ppm	10	158± 10	0.111± 0.012	0.037± 0.005	0.058± 0.005	0.383± 0.014	0.432± 0.018
100ppm	10	161± 10	0.108± 0.006	0.037± 0.004	0.059± 0.006	0.378± 0.018	0.431± 0.025
200ppm	10	161± 7	0.105± 0.011	0.036± 0.004	0.059± 0.012	0.376± 0.018	0.437± 0.025
400ppm	10	155± 4	0.111± 0.009	0.037± 0.004	0.062± 0.005	0.392± 0.016	0.444± 0.024

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

STUDY NO. : 0600
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.679± 0.025	0.218± 0.014	2.420± 0.084	1.087± 0.048
25ppm	10	0.678± 0.016	0.216± 0.010	2.391± 0.068	1.080± 0.046
50ppm	10	0.688± 0.014	0.217± 0.008	2.388± 0.093	1.117± 0.059
100ppm	10	0.681± 0.030	0.208± 0.013	2.385± 0.098	1.097± 0.071
200ppm	10	0.692± 0.029	0.226± 0.009	2.445± 0.095	1.088± 0.054
400ppm	10	0.717± 0.017**	0.247± 0.005**	2.566± 0.061**	1.118± 0.033

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

APPENDIX L 1

HISTOPATHOLOGICAL FINDINGS :

NON-NEOPLASTIC LESIONS : MALE

Organ	Findings	Group Name	Control				25ppm				50ppm				100ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}																		
nasal cavit			<10>				<10>				<10>				<10>			
	respiratory metaplasia:gland		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)
	squamous cell metaplasia:respiratory epithelium		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)
	transitional cell like change:ciliated respiratory epithelium		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)
{Hematopoietic system}																		
spleen			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		10	0	0	0	10	0	0	0	10	0	0	0	10	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(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)
{Circulatory system}																		
heart			<10>				<10>				<10>				<10>			
	inflammatory cell nest		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	200ppm				400ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			<10>				<10>			
	respiratory metaplasia:gland		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	squamous cell metaplasia:respiratory epithelium		0	0	0	0	3	2	0	0 *
			(0)	(0)	(0)	(0)	(30)	(20)	(0)	(0)
	transitional cell like change:ciliated respiratory epith		0	0	0	0	7	2	0	0 **
			(0)	(0)	(0)	(0)	(70)	(20)	(0)	(0)
{Hematopoietic system}										
spleen			<10>				<10>			
	deposit of hemosiderin		7	3	0	0	1	9	0	0 **
			(70)	(30)	(0)	(0)	(10)	(90)	(0)	(0)
	engorgement of erythrocyte		0	0	0	0	8	0	0	0 **
			(0)	(0)	(0)	(0)	(80)	(0)	(0)	(0)
{Circulatory system}										
heart			<10>				<10>			
	inflammatory cell nest		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				25ppm				50ppm				100ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	herniation		3	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(30)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
pancreas			<10>				<10>				<10>				<10>			
	atrophy		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	eosinophilic body		0	10	0	0	1	9	0	0	0	10	0	0	0	10	0	0
			(0)	(100)	(0)	(0)	(10)	(90)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
	mineralization:papilla		1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	regeneration:proximal tubule		0	0	0	0	2	0	0	0	0	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(30)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	200ppm				400ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
liver			<10>				<10>			
	herniation		1	0	0	0	2	0	0	0
			(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	granulation		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
pancreas			<10>				<10>			
	atrophy		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Urinary system}										
kidney			<10>				<10>			
	eosinophilic body		0	10	0	0	0	10	0	0
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
	mineralization:papilla		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	regeneration:proximal tubule		3	0	0	0	1	0	0	0
			(30)	(0)	(0)	(0)	(10)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				25ppm				50ppm				100ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Endocrine system}																		
pituitary			<10>				<10>				<10>				<10>			
	Rathke pouch		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thyroid			<10>				<10>				<10>				<10>			
	ultimibranchial body remanet		3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(30)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	200ppm				400ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Endocrine system}										
pituitary			<10>				<10>			
	Rathke pouch		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thyroid			<10>				<10>			
	ultimibranchial body remanet		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

APPENDIX L 2

HISTOPATHOLOGICAL FINDINGS :

NON-NEOPLASTIC LESIONS : FEMALE

Organ	Findings	Group Name / Grade	Control 1 (%)	Control 2 (%)	Control 3 (%)	Control 4 (%)	25ppm 1 (%)	25ppm 2 (%)	25ppm 3 (%)	25ppm 4 (%)	50ppm 1 (%)	50ppm 2 (%)	50ppm 3 (%)	50ppm 4 (%)	100ppm 1 (%)	100ppm 2 (%)	100ppm 3 (%)	100ppm 4 (%)
		No. of Animals on Study	10				10				10				10			
{Respiratory system}																		
nasal cavit			<10>				<10>				<10>				<10>			
	respiratory metaplasia:gland		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)
{Hematopoietic system}																		
bone marrow			<10>				<10>				<10>				<10>			
	granulation		0	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(10)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		10	0	0	0	10	0	0	0	10	0	0	0	9	1	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(90)	(10)	(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}																		
liver			<10>				<10>				<10>				<10>			
	herniation		2	0	0	0	1	0	0	0	0	0	0	0	3	0	0	0
			(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(30)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	200ppm				400ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			<10>				<10>			
	respiratory metaplasia:gland		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
{Hematopoietic system}										
bone marrow			<10>				<10>			
	granulation		0	0	0	0	2	1	0	0
			(0)	(0)	(0)	(0)	(20)	(10)	(0)	(0)
spleen			<10>				<10>			
	deposit of hemosiderin		9	1	0	0	3	7	0	0 **
			(90)	(10)	(0)	(0)	(30)	(70)	(0)	(0)
	engorgement of erythrocyte		0	0	0	0	10	0	0	0 **
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Digestive system}										
liver			<10>				<10>			
	herniation		2	0	0	0	2	0	0	0
			(20)	(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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				25ppm				50ppm				100ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	mineralization:papilla		0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Endocrine system}																		
pituitary			<10>				<10>				<10>				<10>			
	Rathke pouch		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thyroid			<10>				<10>				<10>				<10>			
	ultimibranchial body remanet		1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Special sense organs/appendage}																		
eye			<10>				<10>				<10>				<10>			
	cataract		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	retinal atrophy		0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	200ppm				400ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}										
kidney			<10>				<10>			
	mineralization:papilla		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Endocrine system}										
pituitary			<10>				<10>			
	Rathke pouch		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
thyroid			<10>				<10>			
	ultimibranchial body remanet		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Special sense organs/appendage}										
eye			<10>				<10>			
	cataract		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	retinal atrophy		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				25ppm				50ppm				100ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Special sense organs/appendage}																		
Harder gl			<10>				<10>				<10>				<10>			
	lymphocytic infiltration		2	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	200ppm				400ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Special sense organs/appendage}										
Harder gl			<10>				<10>			
	lymphocytic infiltration		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

APPENDIX M

METHODS, UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK INHALATION STUDY OF 2,4-PENTANEDIONE

METHODS, UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK INHALATION STUDY OF 2,4-PENTANEDIONE

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 activated method [2]	sec	1
White blood cell(WBC)	Light scattering method [1]	$\times 10^3/\mu L$	2
Differential WBC	Pattern recognition method [3] (Wright staining)	%	0
Biochemistry			
Total protein(TP)	Biuret method [4]	g/dL	1
Albumin (Alb)	BCG method [4]	g/dL	1
A/G ratio	Calculated as Alb/(TP−Alb) [4]	−	1
T-bilirubin	Alkaline azobilirubin method [4]	mg/dL	2
Glucose	GlcK·G-6-PDH method [4]	mg/dL	0
T-cholesterol	CE·COD·POD method [4]	mg/dL	0
Triglyceride	LPL·GK·GPO·POD method [4]	mg/dL	0
Phospholipid	PLD·ChOD·POD method [4]	mg/dL	0
Aspartate aminotransferase (AST)	JSCC method [4]	IU/L	0
Alanine aminotransferase (ALT)	JSCC method [4]	IU/L	0
Lactate dehydrogenase (LDH)	SFBC method [4]	IU/L	0
Alkaline phosphatase (ALP)	GSCC method [4]	IU/L	0
γ-Glutamyl transpeptidase (γ-GTP)	JSCC method [4]	IU/L	0
Creatine kinase (CK)	JSCC method [4]	IU/L	0
Urea nitrogen	Urease·GLDH method [4]	mg/dL	1
Creatinine	Jaffé method [4]	mg/dL	1
Sodium	Ion selective electrode method [4]	mEq/L	0
Potassium	Ion selective electrode method [4]	mEq/L	1
Chloride	Ion selective electrode method [4]	mEq/L	0
Calcium	OCPC method [4]	mg/dL	1
Inorganic phosphorus	PNP·XOD·POD method [4]	mg/dL	1

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