1，2 - ジクロロプロパンのラットを用いた
吸 入 に よ る 1 3 週 間 毒 性 試 験 報 告 書

試験番号：0435

APPENDICES

APPENDICES

APPENDICES (CONTINUED)

APPENDICES (CONTINUED)

APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0435
ANIMAL : RAT 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
DEATH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	125ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	250ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	500ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000ppm	0	0	0	0	0	0	0	0	0	0	0	1	1
EXOPHTHALMOS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	125ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	250ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	500ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000ppm	0	0	0	0	0	0	0	1	1	1	1	1	1
	2000ppm	0	0	0	0	0	0	0	0	0	0	0	0	0

APPENDIX B 1

BODY WEIGHT CHANGES : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0435
ANIMAL : RAT 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	149± 6	181± 10	203± 10	222± 12	238± 11	251± 14
125ppm	123± 4	141± 5*	167± 6**	188± 7**	206± 7**	221± 9*	234± 7*
250ppm	123± 4	143± 6	170± 9*	192± 10*	213± 11	228± 12	240± 12
500ppm	123± 4	139± 7**	165± 8**	186± 9**	203± 10**	219± 11**	231± 11**
1000ppm	123± 4	138± 5**	164± 7**	182± 8**	197± 11**	209± 13**	218± 16**
2000ppm	123± 4	128± 7**	138± 5**	151± 13**	166± 12**	177± 13**	190± 17**

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

STUDY NO. : 0435
ANIMAL : RAT 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± 15	271± 18	280± 17	289± 17	296± 16	304± 18	307± 16
125ppm	244± 9*	255± 11	264± 11	272± 9	277± 10*	282± 10*	286± 10*
250ppm	252± 14	263± 14	271± 14	277± 13	283± 14	289± 14	292± 14
500ppm	242± 10*	253± 10*	261± 10*	268± 11*	274± 12*	279± 12**	281± 12**
1000ppm	227± 17**	233± 18**	242± 20**	248± 19**	252± 20**	256± 20**	257± 19**
2000ppm	187± 15**	202± 17**	206± 17**	210± 19**	212± 18**	218± 20**	223± 21**

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

APPENDIX B 2

BODY WEIGHT CHANGES : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0435
ANIMAL : RAT 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± 3	108± 4	120± 5	129± 6	137± 8	143± 7	148± 7
125ppm	95± 3	103± 3*	115± 3	124± 4	131± 4	138± 5	143± 5
250ppm	95± 3	102± 5**	113± 5	124± 5	132± 5	140± 4	145± 5
500ppm	95± 3	101± 3**	113± 3	123± 4*	130± 4	138± 4	142± 5
1000ppm	95± 2	102± 3**	113± 3*	124± 3	129± 3	134± 3**	139± 4*
2000ppm	95± 2	98± 4**	103± 8**	111± 6**	115± 12**	124± 8**	128± 11**

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

STUDY NO. : 0435
ANIMAL : RAT 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	152± 7	156± 7	161± 7	164± 8	167± 9	170± 9	173± 9
125ppm	147± 5	152± 5	157± 6	162± 6	165± 8	166± 7	167± 7
250ppm	149± 6	152± 7	157± 8	160± 8	163± 8	166± 9	166± 9
500ppm	146± 5	151± 4	154± 5	157± 4	161± 5	163± 4	164± 4
1000ppm	142± 3**	145± 5**	149± 4**	152± 4*	155± 4*	156± 4**	157± 3**
2000ppm	130± 13**	134± 10**	136± 11**	138± 11**	139± 11**	140± 12**	142± 12**

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

APPENDIX C 1

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0435
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(6)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	14.0± 0.9	15.0± 1.1	16.1± 0.8	16.0± 0.7	15.8± 0.9	15.5± 1.3	15.5± 1.4
125ppm	11.9± 0.5**	13.4± 0.8**	14.9± 0.9	15.6± 0.7	15.3± 0.8	15.2± 0.8	14.9± 0.9
250ppm	12.0± 0.5**	13.8± 0.8*	14.7± 0.9*	15.7± 0.9	15.5± 1.3	15.7± 1.0	15.2± 1.1
500ppm	11.6± 0.9**	14.2± 1.0	14.9± 0.9	15.5± 0.8	15.5± 1.0	15.5± 1.0	15.4± 0.8
1000ppm	11.0± 0.5**	14.3± 0.8	15.0± 1.3	16.6± 1.9	15.6± 0.9	16.2± 1.5	15.6± 0.8
2000ppm	8.8± 1.1**	9.7± 1.1**	12.2± 2.9**	13.9± 2.3	13.0± 2.1**	15.3± 2.4	11.6± 2.4*

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

STUDY NO. : 0435
ANIMAL : RAT 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	16.2± 1.4	15.7± 1.0	15.7± 0.9	15.9± 0.8	16.0± 1.0	15.8± 0.8
125ppm	15.6± 0.9	15.5± 1.0	15.5± 0.7	15.5± 0.8	14.9± 1.0	14.7± 1.0
250ppm	15.7± 1.1	16.0± 1.1	15.3± 0.8	15.3± 1.0	15.3± 1.0	14.7± 1.0
500ppm	16.2± 1.1	16.0± 0.8	15.7± 1.0	15.2± 1.0	15.3± 1.1	14.6± 0.9
1000ppm	16.5± 1.5	16.2± 1.0	15.4± 0.9	15.4± 0.8	15.5± 0.8	14.4± 0.6*
2000ppm	14.9± 2.2	13.5± 1.9**	13.8± 2.4	13.3± 1.6**	14.7± 2.0	14.1± 2.1*

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

APPENDIX C 2

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0435
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(6)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	10.1± 0.4	10.4± 0.4	10.7± 0.4	10.7± 0.7	10.7± 0.5	10.4± 0.7	9.8± 0.6
125ppm	9.0± 0.3**	9.9± 0.5	10.1± 0.7	10.3± 0.7	10.3± 0.8	10.2± 0.6	10.1± 0.5
250ppm	8.7± 0.6**	9.7± 0.7	10.3± 0.5	10.3± 0.6	10.4± 0.6	10.4± 0.6	10.0± 0.7
500ppm	8.5± 0.5**	10.2± 0.4	10.1± 0.5	10.7± 0.5	10.6± 0.4	10.2± 0.5	10.2± 0.4
1000ppm	8.7± 0.4**	10.3± 0.6	10.5± 0.6	11.2± 0.6	10.5± 0.5	10.8± 0.6	10.5± 0.7
2000ppm	7.1± 0.7**	7.6± 1.6**	9.1± 1.1**	9.3± 2.4	9.9± 0.6**	9.9± 1.9	9.3± 1.9

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

STUDY NO. : 0435
ANIMAL : RAT 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	10.1± 0.6	10.4± 0.3	10.1± 0.5	10.4± 0.7	10.5± 0.5	10.4± 0.6
125ppm	10.5± 0.7	10.5± 0.6	10.9± 0.8	10.7± 0.6	10.4± 0.4	10.0± 0.6
250ppm	10.1± 0.8	10.5± 0.8	10.3± 0.5	10.1± 1.2	10.1± 1.0	10.0± 0.7
500ppm	10.5± 0.4	10.7± 0.7	10.5± 0.7	10.3± 0.7	10.4± 0.5	9.8± 0.6
1000ppm	10.8± 0.4	10.7± 0.7	10.8± 0.4	10.4± 0.3	10.5± 0.5	10.3± 0.6
2000ppm	10.1± 1.7	9.3± 2.0	9.9± 1.7	9.4± 1.7	10.0± 1.6	9.0± 1.7

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

APPENDIX D 1

URINALYSIS : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0435 URINALYSIS
ANIMAL : RAT 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	6	3	1		0	6	3	1	0	0		10	0	0	0	0	0		7	2	1	0	0	0		10	0	0	0	
125ppm	10	0	0	0	1	3	6	0		0	6	4	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
250ppm	10	0	0	0	1	1	8	0	*	0	5	4	1	0	0		10	0	0	0	0	0		7	2	1	0	0	0		10	0	0	0	
500ppm	10	0	0	0	0	3	6	1		0	5	4	1	0	0		10	0	0	0	0	0		9	0	1	0	0	0		10	0	0	0	
1000ppm	10	0	0	0	1	5	4	0		1	4	5	0	0	0		10	0	0	0	0	0		5	4	1	0	0	0		10	0	0	0	
2000ppm	10	0	0	0	0	4	6	0		0	6	4	0	0	0		10	0	0	0	0	0		1	6	2	1	0	0	*	10	0	0	0	

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

STUDY NO. : 0435 URINALYSIS
ANIMAL : RAT 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	
125ppm	10	10	0	0	0	0		10	0	0	0	0	
250ppm	10	10	0	0	0	0		10	0	0	0	0	
500ppm	10	10	0	0	0	0		10	0	0	0	0	
1000ppm	10	10	0	0	0	0		10	0	0	0	0	
2000ppm	10	10	0	0	0	0		10	0	0	0	0	

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

APPENDIX D 2

URINALYSIS : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0435 URINALYSIS
ANIMAL : RAT 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	1	5	4		7	2	1	0	0	0		10	0	0	0	0	0		9	1	0	0	0	0		10	0	0	0	
125ppm	10	0	0	0	0	1	5	4		7	3	0	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
250ppm	10	0	0	0	0	0	7	3		9	1	0	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
500ppm	10	0	0	0	0	1	7	2		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
1000ppm	10	0	0	0	0	1	6	3		7	3	0	0	0	0		10	0	0	0	0	0		7	3	0	0	0	0		10	0	0	0	
2000ppm	9	0	0	0	2	1	5	1		5	4	0	0	0	0		9	0	0	0	0	0		3	4	1	1	0	0		8	1	0	0	

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

STUDY NO. : 0435 URINALYSIS
ANIMAL : RAT 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	
125ppm	10	10	0	0	0	0		10	0	0	0	0	
250ppm	10	10	0	0	0	0		10	0	0	0	0	
500ppm	10	10	0	0	0	0		10	0	0	0	0	
1000ppm	10	10	0	0	0	0		10	0	0	0	0	
2000ppm	9	9	0	0	0	0		9	0	0	0	0	

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

APPENDIX E 1

HEMATOLOGY : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0435
ANIMAL : RAT 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 fℓ		MCH pg		MCHC g/dℓ		PLATELET $10^3/\mu\ell$	
Control	10	9.31±	0.21	15.9±	0.4	45.6±	1.2	49.0±	0.6	17.1±	0.3	34.9±	0.7	780±	57
125ppm	10	9.36±	0.19	16.0±	0.4	46.1±	1.1	49.2±	0.7	17.1±	0.2	34.8±	0.6	804±	39
250ppm	10	9.33±	0.16	15.8±	0.4	46.0±	0.7	49.3±	0.5	17.0±	0.2	34.4±	0.4	809±	53
500ppm	10	8.95±	0.17**	15.4±	0.3*	45.2±	0.8	50.5±	0.8*	17.2±	0.2	34.0±	0.5**	816±	67
1000ppm	9	8.00±	0.22**	14.7±	0.2**	43.4±	0.8**	54.3±	1.6**	18.3±	0.6**	33.8±	0.3**	925±	59**
2000ppm	10	7.58±	0.36**	14.6±	0.5**	43.7±	1.2**	57.8±	1.8**	19.3±	0.5**	33.3±	0.5**	959±	64**

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

STUDY NO. : 0435
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RETICULOCYTE %		PROTHROMBIN TIME sec		APTT sec	
Control	10	1.9±	0.1	17.0±	2.0	26.3±	2.7
125ppm	10	1.8±	0.2	17.5±	3.2	25.8±	3.4
250ppm	10	1.9±	0.2	17.3±	3.3	27.9±	5.1
500ppm	10	2.3±	0.2	18.9±	3.7	27.2±	3.8
1000ppm	9	5.5±	0.6**	16.7±	2.5	25.4±	4.1
2000ppm	10	10.5±	3.0**	17.3±	3.1	21.0±	3.8*

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

STUDY NO. : 0435
ANIMAL : RAT 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	5.17± 1.19	1± 1	18± 4	1± 1	0± 0	4± 2	76± 5	0± 0
125ppm	10	5.08± 1.27	2± 1	20± 3	1± 1	0± 0	3± 1	74± 2	0± 0
250ppm	10	5.03± 1.59	2± 1	23± 6	2± 1	0± 0	3± 2	70± 7	0± 0
500ppm	10	4.62± 1.66	2± 1	24± 6*	1± 1	0± 0	3± 1	70± 6*	0± 0
1000ppm	9	3.91± 0.93	2± 2	22± 3	1± 1	0± 0	2± 2	73± 4	0± 0
2000ppm	10	4.82± 2.12	2± 1	22± 3	1± 1	0± 0	4± 2	70± 4	0± 0

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

APPENDIX E 2

HEMATOLOGY : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0435
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

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	9	8.60±	0.21	15.9±	0.5	44.3±	0.9	51.5±	0.3	18.5±	0.2	36.0±	0.5	817±	64
125ppm	10	8.59±	0.20	15.8±	0.4	44.4±	1.0	51.7±	0.4	18.4±	0.2	35.6±	0.4	783±	56
250ppm	10	8.44±	0.24	15.7±	0.4	44.2±	1.0	52.4±	0.5	18.6±	0.1	35.4±	0.4	825±	58
500ppm	10	8.13±	0.27**	15.4±	0.6	43.7±	1.2	53.7±	0.6**	18.9±	0.2	35.3±	0.5	863±	78
1000ppm	10	7.77±	0.24**	15.1±	0.4**	43.7±	1.1	56.2±	1.2**	19.4±	0.2**	34.6±	0.6**	874±	54
2000ppm	9	7.18±	0.39**	14.3±	0.8**	42.5±	1.4**	59.3±	2.5**	19.9±	0.5**	33.6±	1.0**	932±	114**

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

STUDY NO. : 0435
ANIMAL : RAT 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	9	1.9±	0.2	15.2±	0.7	17.3±	1.8
125ppm	10	1.9±	0.3	15.1±	1.0	17.8±	3.5
250ppm	10	2.5±	0.3	15.4±	0.8	17.3±	1.9
500ppm	10	3.5±	0.4*	15.5±	1.3	17.3±	2.3
1000ppm	10	6.4±	2.7**	16.7±	1.6	16.6±	1.9
2000ppm	9	11.5±	4.5**	18.3±	2.9*	18.9±	3.9

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

STUDY NO. : 0435
ANIMAL : RAT 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	9	3.12±	1.01	2±	1	20±	6	1±	1	0±	0	2±	1	74±	6	0±	0
125ppm	10	3.54±	1.35	1±	1	21±	4	1±	1	0±	0	4±	2	73±	4	0±	0
250ppm	10	3.13±	1.28	2±	1	23±	6	1±	1	0±	0	3±	2	71±	6	0±	0
500ppm	10	4.50±	1.81	2±	1	22±	6	2±	1	0±	0	3±	2	72±	7	0±	0
1000ppm	10	3.93±	2.02	2±	1	19±	5	1±	0	0±	0	3±	1	74±	5	0±	0
2000ppm	9	4.36±	2.21	3±	1	22±	7	1±	1	0±	0	3±	2	71±	7	0±	0

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

APPENDIX F 1

BIOCHEMISTRY : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0435
ANIMAL : RAT 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±	0.1	3.9±	0.1	1.5±	0.1	0.13±	0.02	182±	23	66±	4	53±	14
125ppm	10	6.6±	0.1	3.9±	0.1	1.4±	0.1	0.13±	0.01	174±	18	63±	4	36±	8**
250ppm	10	6.6±	0.1	3.9±	0.1	1.4±	0.1	0.13±	0.01	182±	13	62±	4	39±	11*
500ppm	10	6.7±	0.1	4.0±	0.1	1.4±	0.1	0.13±	0.01	179±	17	64±	4	43±	12
1000ppm	9	6.8±	0.2**	4.1±	0.1**	1.5±	0.1*	0.14±	0.01	167±	8	53±	6**	26±	9**
2000ppm	10	6.6±	0.1	4.0±	0.1**	1.5±	0.1*	0.18±	0.02**	161±	10*	60±	4*	34±	10**

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

STUDY NO. : 0435
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dl	GOT IU/l	GPT IU/l	LDH IU/l	ALP IU/l	G-GTP IU/l	CPK IU/l
Control	10	122± 8	62± 16	43± 5	183± 63	243± 13	2± 1	105± 12
125ppm	10	116± 7	65± 12	43± 8	191± 41	250± 33	4± 5	116± 23
250ppm	10	116± 8	70± 18	41± 8	193± 58	238± 31	3± 1	110± 19
500ppm	10	119± 8	61± 16	36± 8	180± 37	212± 23	2± 1	103± 15
1000ppm	9	101± 10**	46± 3	20± 5**	159± 43	200± 18**	2± 1	101± 17
2000ppm	10	119± 8	40± 5**	19± 8**	238± 93	262± 40	6± 10*	116± 26

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

STUDY NO. : 0435
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	UREA NITROGEN mg/dℓ	CREATININE mg/dℓ	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dℓ	INORGANIC PHOSPHORUS mg/dℓ
Control	10	18.7± 1.5	0.5± 0.1	141± 1	3.6± 0.2	105± 1	10.1± 0.1	5.6± 0.6
125ppm	10	18.6± 2.2	0.6± 0.1	142± 1	3.8± 0.3	106± 1	10.0± 0.2	5.8± 0.7
250ppm	10	19.5± 1.6	0.5± 0.0	142± 2	3.7± 0.3	106± 1	10.1± 0.2	5.4± 0.9
500ppm	10	18.2± 1.4	0.5± 0.0	142± 1	4.0± 0.3*	106± 2	10.1± 0.2	5.5± 0.7
1000ppm	9	17.7± 2.3	0.5± 0.0	142± 2	4.1± 0.3**	106± 2	10.1± 0.2	5.7± 0.8
2000ppm	10	19.0± 2.1	0.6± 0.2	140± 1	4.8± 0.4**	106± 2	9.9± 0.2	6.2± 1.2

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

APPENDIX F 2

BIOCHEMISTRY : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0435
ANIMAL : RAT 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	9	6.3±	0.1	3.6±	0.1	1.3±	0.1	0.16±	0.02	129±	12	68±	5	13±	4
125ppm	10	6.2±	0.2	3.6±	0.1	1.4±	0.1	0.16±	0.03	139±	12	65±	6	12±	5
250ppm	10	6.2±	0.2	3.6±	0.1	1.4±	0.0	0.15±	0.03	143±	15*	63±	8	13±	2
500ppm	10	6.3±	0.1	3.7±	0.1	1.4±	0.1	0.16±	0.02	144±	12*	71±	10	16±	3
1000ppm	10	6.3±	0.2	3.8±	0.1**	1.5±	0.1**	0.20±	0.03*	147±	10**	63±	11	20±	7*
2000ppm	9	6.3±	0.2	3.8±	0.2**	1.5±	0.1**	0.25±	0.06**	151±	7**	64±	20	25±	8**

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

(HCL074)

STUDY NO. : 0435
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dl	GOT IU/l	GPT IU/l	LDH IU/l	ALP IU/l	G-GTP IU/l	CPK IU/l
Control	9	132± 10	67± 10	36± 14	254± 153	201± 18	3± 1	124± 37
125ppm	10	126± 8	66± 10	33± 9	264± 126	202± 18	2± 1	119± 34
250ppm	10	124± 10	65± 15	31± 13	268± 118	199± 22	3± 1	123± 39
500ppm	10	139± 15	53± 3**	21± 4**	254± 100	182± 19	3± 1	105± 24
1000ppm	10	128± 18	52± 6**	19± 2**	298± 130	208± 28	5± 2**	114± 31
2000ppm	9	135± 32	206± 269	62± 77	542± 477	267± 62	10± 2**	109± 31

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

STUDY NO. : 0435
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	UREA NITROGEN mg/dℓ	CREATININE mg/dℓ	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dℓ	INORGANIC PHOSPHORUS mg/dℓ
Control	9	19.9± 2.2	0.5± 0.1	140± 2	3.6± 0.3	107± 2	9.7± 0.2	5.1± 1.1
125ppm	10	20.2± 2.7	0.5± 0.0	140± 1	3.7± 0.2	107± 1	9.5± 0.3	5.0± 0.7
250ppm	10	18.1± 2.6	0.5± 0.0	140± 2	3.9± 0.2	108± 2	9.6± 0.3	5.2± 1.2
500ppm	10	19.3± 2.6	0.5± 0.0	140± 1	3.9± 0.3	107± 2	9.6± 0.2	5.1± 1.2
1000ppm	10	19.3± 2.0	0.6± 0.1	139± 2	4.2± 0.5**	106± 3	9.5± 0.3	5.5± 1.0
2000ppm	9	20.3± 3.5	0.6± 0.1	138± 2	4.7± 0.2**	105± 2	9.5± 0.2	5.8± 1.1

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

APPENDIX G 1

GROSS FINDINGS : SUMMARY, RAT : MALE : SACRIFICED ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0435
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name	Control	125ppm	250ppm	500ppm
		NO. of Animals	10 (%)	10 (%)	10 (%)	10 (%)
liver	herniation		0 (0)	1 (10)	0 (0)	1 (10)

STUDY NO. : 0435
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name	1000ppm		2000ppm	
		NO. of Animals	10	(%)	10	(%)
liver	herniation		0	(0)	1	(10)

APPENDIX G 2

GROSS FINDINGS : SUMMARY, RAT : FEMALE : DEAD AND MORIBUND ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0435
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 14W)

Organ	Findings	Group Name / NO. of Animals	Control 0 (%)	125ppm 0 (%)	250ppm 0 (%)	500ppm 0 (%)
lung	red zone		- (-)	- (-)	- (-)	- (-)
thymus	red zone		- (-)	- (-)	- (-)	- (-)
liver	accentuation of lobular structure		- (-)	- (-)	- (-)	- (-)

Organ	Findings	Group Name	1000ppm		2000ppm	
		NO. of Animals	0	(%)	1	(%)
lung	red zone		-	(-)	1	(100)
thymus	red zone		-	(-)	1	(100)
liver	accentuation of lobular structure		-	(-)	1	(100)

APPENDIX G 3

GROSS FINDINGS : SUMMARY, RAT : FEMALE : SACRIFICED ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0435
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	125ppm 10 (%)	250ppm 10 (%)	500ppm 10 (%)
liver	herniation		2 (20)	0 (0)	1 (10)	0 (0)
ovary	cyst		0 (0)	1 (10)	0 (0)	0 (0)

Organ	Findings	Group Name	1000ppm		2000ppm	
		NO. of Animals	10	(%)	9	(%)
liver	herniation		2	(20)	2	(22)
ovary	cyst		0	(0)	0	(0)

APPENDIX H 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0435
ANIMAL : RAT 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	287± 16	0.248± 0.043	0.051± 0.004	2.906± 0.212	0.878± 0.059	0.989± 0.049
125ppm	10	264± 10**	0.218± 0.029	0.049± 0.004	2.953± 0.089	0.846± 0.033	0.944± 0.047
250ppm	10	268± 12*	0.223± 0.016	0.048± 0.005	2.952± 0.128	0.862± 0.040	0.940± 0.045
500ppm	10	259± 12**	0.209± 0.018	0.047± 0.005	2.979± 0.103	0.834± 0.048	0.898± 0.046**
1000ppm	10	237± 18**	0.204± 0.032	0.044± 0.004**	3.015± 0.201	0.800± 0.033**	0.874± 0.067**
2000ppm	10	203± 21**	0.175± 0.034**	0.048± 0.005	2.902± 0.148	0.765± 0.055**	0.836± 0.060**

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

STUDY NO. : 0435
ANIMAL : RAT 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	1.764± 0.113	0.526± 0.035	7.215± 0.524	1.872± 0.037
125ppm	10	1.663± 0.066	0.485± 0.027	6.681± 0.405	1.848± 0.021
250ppm	10	1.726± 0.086	0.488± 0.031	6.939± 0.460	1.854± 0.053
500ppm	10	1.704± 0.074	0.501± 0.032	6.976± 0.440	1.836± 0.032
1000ppm	10	1.727± 0.115	0.652± 0.054**	6.815± 0.599	1.795± 0.038**
2000ppm	10	1.613± 0.149**	0.731± 0.041**	6.315± 0.651**	1.708± 0.045**

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

APPENDIX H 2

ORGAN WEIGHT, ABSOLUTE: SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0435
ANIMAL : RAT 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	158± 8	0.190± 0.021	0.051± 0.007	0.090± 0.010	0.569± 0.037	0.706± 0.035
125ppm	10	153± 7	0.185± 0.016	0.054± 0.002	0.112± 0.085	0.554± 0.016	0.713± 0.039
250ppm	10	152± 7	0.180± 0.012	0.053± 0.004	0.086± 0.012	0.566± 0.030	0.694± 0.034
500ppm	10	149± 3	0.173± 0.012	0.054± 0.005	0.084± 0.011	0.539± 0.023	0.677± 0.025
1000ppm	10	142± 4**	0.169± 0.013*	0.053± 0.005	0.079± 0.008	0.530± 0.025*	0.670± 0.027
2000ppm	9	129± 11**	0.146± 0.024**	0.055± 0.012	0.066± 0.015**	0.541± 0.049	0.636± 0.049**

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

STUDY NO. : 0435
ANIMAL : RAT 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	1.062± 0.046	0.355± 0.022	3.777± 0.253	1.754± 0.029
125ppm	10	1.058± 0.041	0.341± 0.010	3.744± 0.194	1.721± 0.030
250ppm	10	1.074± 0.064	0.333± 0.022	3.814± 0.194	1.720± 0.043
500ppm	10	1.078± 0.060	0.380± 0.025	4.014± 0.119	1.671± 0.045**
1000ppm	10	1.112± 0.061	0.451± 0.053**	4.406± 0.319**	1.680± 0.032**
2000ppm	9	1.153± 0.103*	0.509± 0.070**	4.655± 0.678**	1.571± 0.049**

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

APPENDIX I 1

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0435
ANIMAL : RAT 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	287± 16	0.086± 0.012	0.018± 0.002	1.015± 0.072	0.307± 0.014	0.345± 0.009
125ppm	10	264± 10**	0.082± 0.009	0.019± 0.001	1.119± 0.051*	0.320± 0.011	0.357± 0.011
250ppm	10	268± 12*	0.083± 0.005	0.018± 0.002	1.102± 0.055	0.321± 0.013	0.351± 0.010
500ppm	10	259± 12**	0.081± 0.006	0.018± 0.002	1.154± 0.061**	0.323± 0.011	0.348± 0.018
1000ppm	10	237± 18**	0.086± 0.008	0.019± 0.002	1.279± 0.122**	0.339± 0.017**	0.369± 0.016**
2000ppm	10	203± 21**	0.086± 0.011	0.024± 0.003**	1.437± 0.089**	0.378± 0.019**	0.413± 0.021**

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

STUDY NO. : 0435
ANIMAL : RAT 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	0.616± 0.020	0.184± 0.009	2.516± 0.063	0.655± 0.027
125ppm	10	0.630± 0.012	0.184± 0.006	2.527± 0.067	0.700± 0.030
250ppm	10	0.644± 0.021	0.182± 0.007	2.585± 0.098	0.692± 0.033
500ppm	10	0.659± 0.010*	0.194± 0.009	2.697± 0.084*	0.711± 0.026*
1000ppm	10	0.731± 0.044**	0.275± 0.018**	2.878± 0.165**	0.761± 0.059**
2000ppm	10	0.795± 0.027**	0.363± 0.039**	3.112± 0.146**	0.847± 0.066**

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

APPENDIX I 2

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0435
ANIMAL : RAT 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	158± 8	0.120± 0.012	0.033± 0.004	0.057± 0.006	0.361± 0.021	0.448± 0.017
125ppm	10	153± 7	0.121± 0.009	0.035± 0.001	0.074± 0.059	0.364± 0.015	0.468± 0.022
250ppm	10	152± 7	0.119± 0.009	0.035± 0.002	0.057± 0.006	0.373± 0.014	0.458± 0.022
500ppm	10	149± 3	0.117± 0.009	0.036± 0.003*	0.057± 0.007	0.362± 0.015	0.455± 0.011
1000ppm	10	142± 4**	0.119± 0.009	0.037± 0.004*	0.056± 0.006	0.372± 0.018	0.470± 0.011*
2000ppm	9	129± 11**	0.113± 0.014	0.042± 0.009**	0.051± 0.011	0.419± 0.028**	0.493± 0.026**

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

STUDY NO. : 0435
ANIMAL : RAT 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	0.673± 0.028	0.225± 0.009	2.391± 0.119	1.113± 0.057
125ppm	10	0.694± 0.028	0.224± 0.010	2.453± 0.059	1.129± 0.047
250ppm	10	0.709± 0.025	0.220± 0.010	2.518± 0.115	1.137± 0.064
500ppm	10	0.725± 0.039**	0.256± 0.017	2.700± 0.080**	1.124± 0.028
1000ppm	10	0.781± 0.034**	0.317± 0.038**	3.095± 0.218**	1.180± 0.021*
2000ppm	9	0.893± 0.048**	0.394± 0.041**	3.588± 0.288**	1.224± 0.114**

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

APPENDIX J 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY, RAT : MALE : SACRIFICED ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0435
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name	Control				125ppm				250ppm				500ppm			
		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>			
	goblet cell hyperplasia		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)
	inflammation:respiratory epithelium		0	0	0	0	0	0	0	0	2	0	0	0	4	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(40)	(0)	(0)	(0)
	disarrangement:olfactory epithelium		0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		0	0	0	0	0	0	0	0	2	0	0	0	5	0	0	0 *
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
	atrophy:olfactory epithelium		0	0	0	0	10	0	0	0 **	8	2	0	0 **	5	5	0	0 **
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(80)	(20)	(0)	(0)	(50)	(50)	(0)	(0)
	necrosis:olfactory epithelium		0	0	0	0	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)
	hyperplasia:respiratory epithelium		0	0	0	0	10	0	0	0 **	7	3	0	0 **	7	3	0	0 **
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(70)	(30)	(0)	(0)	(70)	(30)	(0)	(0)
{Hematopoietic system}																		
bone marrow			<10>				<10>				<10>				<10>			
	increased hematopoiesis		0	0	0	0	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)

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	1000ppm				2000ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			<10>				<10>			
	goblet cell hyperplasia		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	inflammation:respiratory epithelium		6	2	0	0 **	4	4	0	0 **
			(60)	(20)	(0)	(0)	(40)	(40)	(0)	(0)
	disarrangement:olfactory epithelium		3	0	0	0	0	0	0	0
			(30)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		10	0	0	0 **	10	0	0	0 **
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	atrophy:olfactory epithelium		0	8	2	0 **	0	3	7	0 **
			(0)	(80)	(20)	(0)	(0)	(30)	(70)	(0)
	necrosis:olfactory epithelium		1	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	hyperplasia:respiratory epithelium		1	8	1	0 **	0	10	0	0 **
			(10)	(80)	(10)	(0)	(0)	(100)	(0)	(0)
{Hematopoietic system}										
bone marrow			<10>				<10>			
	increased hematopoiesis		9	1	0	0 **	5	5	0	0 **
			(90)	(10)	(0)	(0)	(50)	(50)	(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	Grade	Control				125ppm				250ppm				500ppm			
		No. of Animals on Study	10				10				10				10			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Hematopoietic system}																		
spleen			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		0	0	0	0	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)
	increased extramedullary hematopoiesis		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		0	0	0	0	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)
	necrosis:central		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	deposit of ceroid		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)
	swelling:central		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	basophilic change		2	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(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	1000ppm				2000ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
spleen			<10>				<10>			
	deposit of hemosiderin		0	10	0	0 **	0	10	0	0 **
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
	increased extramedullary hematopoiesis		9	1	0	0 **	5	5	0	0 **
			(90)	(10)	(0)	(0)	(50)	(50)	(0)	(0)
{Digestive system}										
liver			<10>				<10>			
	herniation		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	necrosis:central		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	deposit of ceroid		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	swelling:central		0	0	0	0	9	0	0	0 **
			(0)	(0)	(0)	(0)	(90)	(0)	(0)	(0)
{Urinary system}										
kidney			<10>				<10>			
	basophilic change		1	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	Control				125ppm				250ppm				500ppm			
		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>			
	eosinophilic body		8	0	0	0	10	0	0	0	9	0	0	0	10	0	0	0
			(80)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(90)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	retention cyst		0	0	0	0	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)
	mineralization:papilla		2	0	0	0	1	0	0	0	3	0	0	0	2	0	0	0
			(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
{Endocrine system}																		
pituitary			<10>				<10>				<10>				<10>			
	Rathke pouch		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)
thyroid			<10>				<10>				<10>				<10>			
	ultimibranchial body remanet		0	0	0	0	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)
adrenal			<10>				<10>				<10>				<10>			
	fatty change		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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	1000ppm				2000ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}										
kidney			<10>				<10>			
	eosinophilic body		10	0	0	0	0	0	0	0 **
			(100)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	retention cyst		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:papilla		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
{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	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
adrenal			<10>				<10>			
	fatty change		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				125ppm				250ppm				500ppm			
		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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Reproductive system}																		
testis			<10>				<10>				<10>				<10>			
	hypoplasia		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)
epididymis			<10>				<10>				<10>				<10>			
	spermatogenic granuloma		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)
{Special sense organs/appendage}																		
Harder gl			<10>				<10>				<10>				<10>			
	lymphocytic infiltration		0	0	0	0	0	0	0	0	1	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(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	1000ppm				2000ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Reproductive system}										
testis			<10>				<10>			
	hypoplasia		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
epididymis			<10>				<10>			
	spermatogenic granuloma		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Special sense organs/appendage}										
Harder gl			<10>				<10>			
	lymphocytic infiltration		0	0	0	0	3	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

APPENDIX J 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY, RAT : FEMALE : DEAD AND MORIBUND ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0435
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 14W)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 0				125ppm 0				250ppm 0				500ppm 0			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Respiratory system}																		
nasal cavit			< 0>				< 0>				< 0>				< 0>			
	inflammation:respiratory epithelium		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
	respiratory metaplasia:olfactory epithelium		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
	atrophy:olfactory epithelium		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
	hyperplasia:respiratory epithelium		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
lung			< 0>				< 0>				< 0>				< 0>			
	congestion		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
{Hematopoietic system}																		
bone marrow			< 0>				< 0>				< 0>				< 0>			
	increased hematopoiesis		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)

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	1000ppm				2000ppm			
		No. of Animals on Study	0				1			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			< 0>				< 1>			
	inflammation:respiratory epithelium		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
	atrophy:olfactory epithelium		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
	hyperplasia:respiratory epithelium		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
lung			< 0>				< 1>			
	congestion		-	-	-	-	0	0	1	0
			(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)
{Hematopoietic system}										
bone marrow			< 0>				< 1>			
	increased hematopoiesis		-	-	-	-	1	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 / No. of Animals on Study / Grade	Control				125ppm				250ppm				500ppm			
			0				0				0				0			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Hematopoietic system}																		
thymus		< a >	< 0>				< 0>				< 0>				< 0>			
	hemorrhage	b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
spleen		< a >	< 0>				< 0>				< 0>				< 0>			
	deposit of hemosiderin	b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{Digestive system}																		
liver		< a >	< 0>				< 0>				< 0>				< 0>			
	necrosis:central	b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	fatty change:central	b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{Endocrine system}																		
adrenal		< a >	< 0>				< 0>				< 0>				< 0>			
	fatty change	b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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	1000ppm				2000ppm			
		No. of Animals on Study	0				1			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
thymus			< 0>				< 1>			
	hemorrhage		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
spleen			< 0>				< 1>			
	deposit of hemosiderin		-	-	-	-	0	0	1	0
			(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)
{Digestive system}										
liver			< 0>				< 1>			
	necrosis:central		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
	fatty change:central		-	-	-	-	0	0	1	0
			(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)
{Endocrine system}										
adrenal			< 0>				< 1>			
	fatty change		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)

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

Organ	Findings	Group Name	Control				125ppm				250ppm				500ppm			
		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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Special sense organs/appendage}																		
Harder gl			< 0>				< 0>				< 0>				< 0>			
	lymphocytic infiltration		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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	1000ppm				2000ppm			
		No. of Animals on Study	0				1			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Special sense organs/appendage}										
Harder gl			< 0>				< 1>			
	lymphocytic infiltration		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)

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

APPENDIX J 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY, RAT : FEMALE : SACRIFICED ANIMALS

(13-WEEK STUDY)

Organ	Findings	Group Name	Control				125ppm				250ppm				500ppm			
		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>			
	inflammation: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)
	disarrangement:olfactory epithelium		0	0	0	0	0	0	0	0	2	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		0	0	0	0	0	0	0	0	1	0	0	0	7	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(70)	(0)	(0)	(0)
	atrophy:olfactory epithelium		0	0	0	0	10	0	0	0 **	10	0	0	0 **	9	1	0	0 **
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(90)	(10)	(0)	(0)
	necrosis:olfactory epithelium		0	0	0	0	0	0	0	0	1	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(30)	(0)	(0)	(0)
	hyperplasia:respiratory epithelium		0	0	0	0	7	0	0	0 **	10	0	0	0 **	9	0	0	0 **
			(0)	(0)	(0)	(0)	(70)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(90)	(0)	(0)	(0)
{Hematopoietic system}																		
bone marrow			<10>				<10>				<10>				<10>			
	increased hematopoiesis		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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	1000ppm				2000ppm			
		No. of Animals on Study	10				9			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			<10>				< 9>			
	inflammation:respiratory epithelium		0	3	0	0	3	1	0	0
			(0)	(30)	(0)	(0)	(33)	(11)	(0)	(0)
	disarrangement:olfactory epithelium		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		9	0	0	0 **	7	0	0	0 **
			(90)	(0)	(0)	(0)	(78)	(0)	(0)	(0)
	atrophy:olfactory epitholium		10	0	0	0 **	2	4	3	0 **
			(100)	(0)	(0)	(0)	(22)	(44)	(33)	(0)
	necrosis:olfactory epithelium		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia:respiratory epithelium		8	2	0	0 **	8	1	0	0 **
			(80)	(20)	(0)	(0)	(89)	(11)	(0)	(0)
{Hematopoietic system}										
bone marrow			<10>				< 9>			
	increased hematopoiesis		10	0	0	0 **	6	2	1	0 **
			(100)	(0)	(0)	(0)	(67)	(22)	(11)	(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				125ppm				250ppm				500ppm			
		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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}																		
spleen			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		0	0	0	0	0	0	0	0	4	0	0	0	8	2	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(40)	(0)	(0)	(0)	(80)	(20)	(0)	(0)
	increased extramedullary hematopoiesis		0	0	0	0	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)
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	herniation		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)
	necrosis:central		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	fatty change: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)
	deposit of ceroid		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)
	extramedullary hematopoiesis		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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	1000ppm				2000ppm			
		No. of Animals on Study	10				9			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
spleen			<10>				< 9>			
	deposit of hemosiderin		3	7	0	0 **	1	8	0	0 **
			(30)	(70)	(0)	(0)	(11)	(89)	(0)	(0)
	increased extramedullary hematopoiesis		6	2	0	0 **	4	5	0	0 **
			(60)	(20)	(0)	(0)	(44)	(56)	(0)	(0)
{Digestive system}										
liver			<10>				< 9>			
	herniation		2	0	0	0	2	0	0	0
			(20)	(0)	(0)	(0)	(22)	(0)	(0)	(0)
	necrosis:central		0	0	0	0	1	2	0	0
			(0)	(0)	(0)	(0)	(11)	(22)	(0)	(0)
	fatty change:central		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)
	deposit of ceroid		0	0	0	0	6	0	0	0 **
			(0)	(0)	(0)	(0)	(67)	(0)	(0)	(0)
	extramedullary hematopoiesis		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(11)	(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				125ppm				250ppm				500ppm			
		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>			
	swelling:central		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	mineralization:papilla		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)
{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		2	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
adrenal			<10>				<10>				<10>				<10>			
	fatty change		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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	1000ppm				2000ppm			
		No. of Animals on Study	10				9			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
liver			<10>				< 9>			
	swelling:central		1	0	0	0	1	5	0	0 **
			(10)	(0)	(0)	(0)	(11)	(56)	(0)	(0)
{Urinary system}										
kidney			<10>				< 9>			
	mineralization:papilla		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)
{Endocrine system}										
pituitary			<10>				< 9>			
	Rathke pouch		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(11)	(0)	(0)	(0)
thyroid			<10>				< 9>			
	ultimibranchial body remanet		1	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(11)	(0)	(0)	(0)
adrenal			<10>				< 9>			
	fatty change		1	1	0	0	3	6	0	0 **
			(10)	(10)	(0)	(0)	(33)	(67)	(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				125ppm				250ppm				500ppm			
		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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Reproductive system}																		
ovary			<10>				<10>				<10>				<10>			
	cyst		0	0	0	0	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)
{Special sense organs/appendage}																		
Harder gl			<10>				<10>				<10>				<10>			
	lymphocytic infiltration		4	0	0	0	3	0	0	0	0	0	0	0	2	0	0	0
			(40)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(0)	(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	1000ppm				2000ppm			
		No. of Animals on Study	10				9			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Reproductive system}										
ovary			<10>				< 9>			
	cyst		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Special sense organs/appendage}										
Harder gl			<10>				< 9>			
	lymphocytic infiltration		3	0	0	0	4	0	0	0
			(30)	(0)	(0)	(0)	(44)	(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 K 1

IDENTITY OF 1,2-DICHLOROPROPANE IN THE 13-WEEK INHALATION STUDY

IDENTITY OF 1,2-DICHLOROPROPANE IN THE 13-WEEK INHALATION STUDY

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

Lot No. : LDL5937

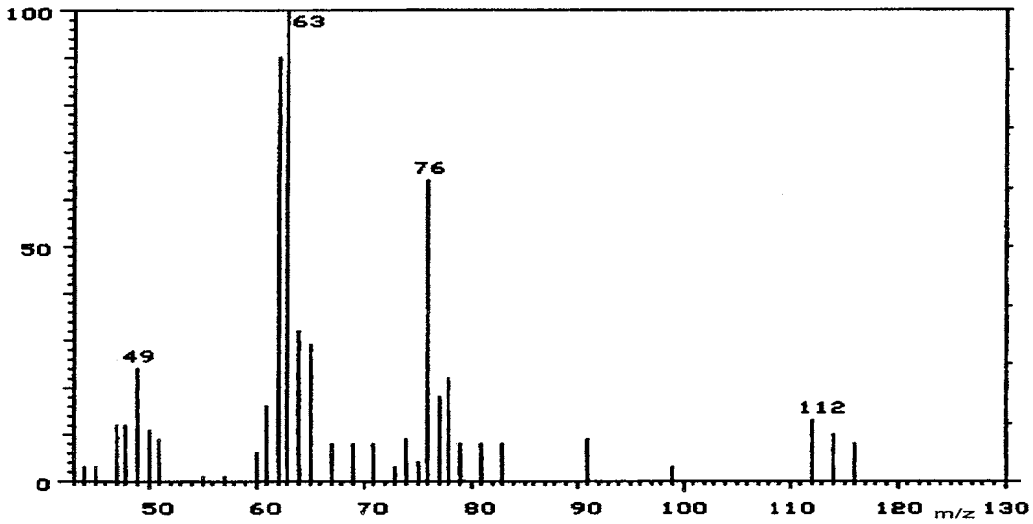
1. Spectral Data

Mass Spectrometry

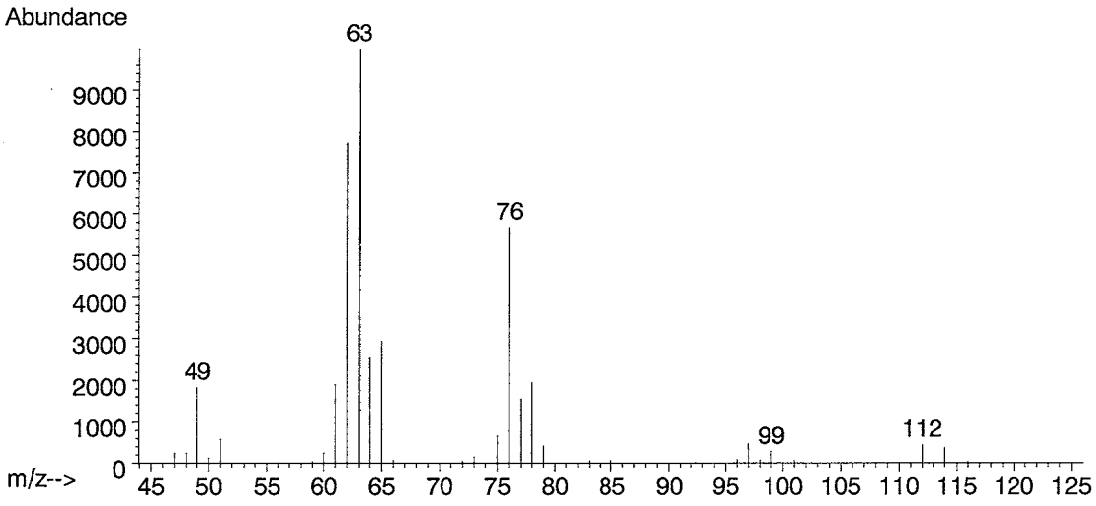
Instrument : Hitachi M-80B Mass Spectrometer

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.

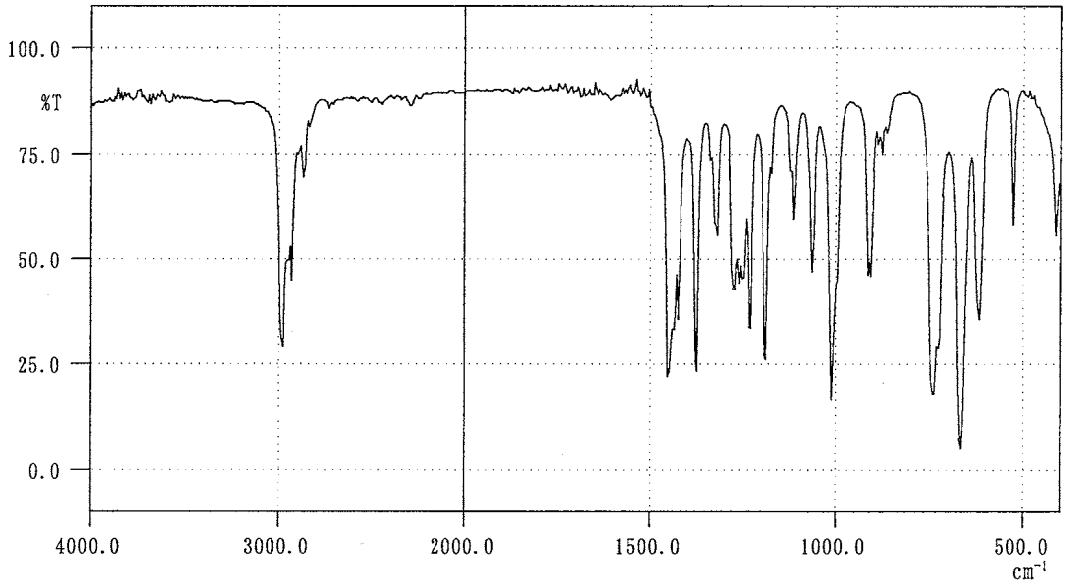
(*McLafferty F. W. (1994)
Wiley Registry of Mass Spectral Data, (6th edition), Entry Number 10229.
John Wiley and Sons, New York, NY)

Infrared Spectrometry

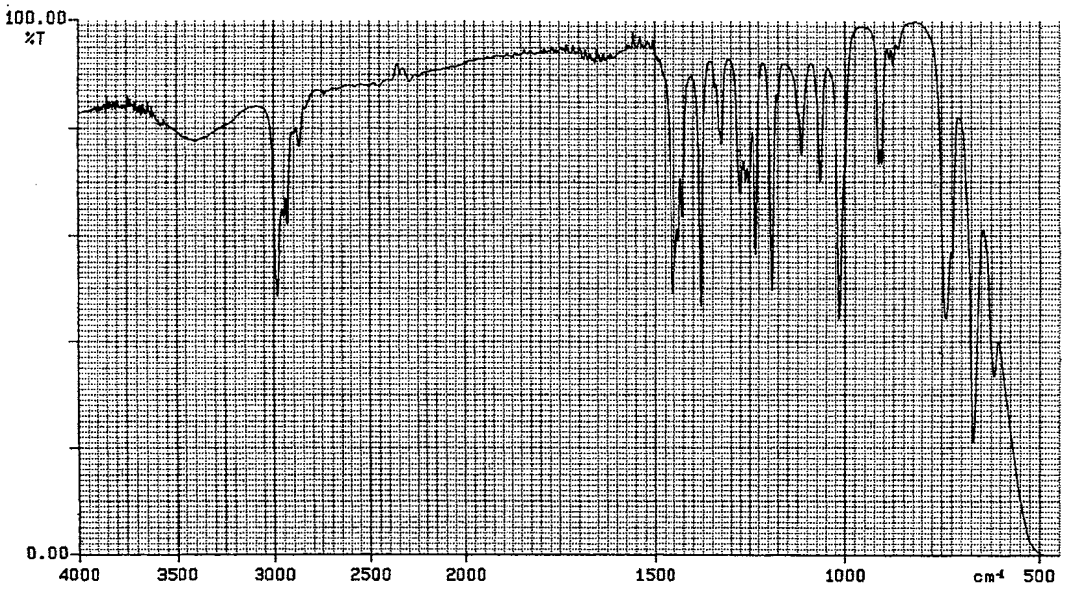
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

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 the Wako Pure Chemical Industries, Ltd.)

2. Conclusion: The test substance was identified as 1,2-dichloropropane by the mass spectrum and the infrared spectrum.

APPENDIX K 2

STABILITY OF 1,2-DICHLOROPROPANE IN THE 13-WEEK INHALATION STUDY

STABILITY OF 1,2-DICHLOROPROPANE IN THE 13-WEEK INHALATION STUDY

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

Lot No. : LDL5937

1. Sample : This lot was used from 2001.8.28 to 2001.11.26. Test substance was stored in a dark place at room temperature.

2. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : Methyl Silicone (0.53 mmϕ × 60 m)

Column Temperature: 100° C

Flow Rate : 15 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μL

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
2001.08.21	1	3.348	99.72
	2	4.659	0.28
2001.12.17	1	3.347	99.71
	2	4.658	0.29

Result: Gas chromatography indicated one major peak (peak No.1) and one impurity (peak No.2 < 0.3% of total area) analyzed on 2001.8.21 and one major peak (peak No.1) and one impurity (peak No.2 < 0.3% of total area) analyzed on 2001.12.17. No new trace impurity peak in the test substance analyzed on 2001.12.17 was detected.

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

APPENDIX L 1

CONCENTRATION OF 1,2-DICHLOROPROPANE IN THE INHALATION CHAMBER OF THE 13-WEEK INHALATION STUDY

CONCENTRATION OF 1,2-DICHLOROPROPANE IN THE INHALATION CHAMBER
OF THE 13-WEEK INHALATION STUDY

Group Name	Concentration(ppm) Mean ± S.D.
Control	0.0 ± 0.0
125 ppm	125.3 ± 0.7
250 ppm	250.8 ± 1.0
500 ppm	500.5 ± 2.6
1000 ppm	1000.4 ± 3.4
2000 ppm	2001.3 ± 5.9

APPENDIX L 2

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 13-WEEK INHALATION STUDY OF 1,2-DICHLOROPROPANE

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 13-WEEK INHALATION STUDY OF 1,2-DICHLOROPROPANE

Group Name	Temperature(℃) Mean ± S.D.	Humidity(%) Mean ± S.D.	Ventilation Rate(L/min) Mean ± S.D.	Air Change(time/h) Mean
Control	22.0 ± 0.3	57.5 ± 0.9	212.2 ± 0.8	12.0
125ppm	21.9 ± 0.4	56.8 ± 1.3	211.9 ± 1.6	12.0
250ppm	22.2 ± 0.4	55.9 ± 1.1	212.0 ± 0.8	12.0
500ppm	22.2 ± 0.3	55.0 ± 1.1	211.8 ± 0.9	12.0
1000ppm	21.9 ± 0.3	55.6 ± 1.1	212.3 ± 0.8	12.0
2000ppm	22.6 ± 0.3	54.5 ± 1.2	212.3 ± 0.9	12.0

APPENDIX M 1

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS IN THE 13-WEEK INHALATION STUDY OF 1,2-DICHLOROPROPANE

METHODS FOR HEMATOLOGY,BIOCHEMISTRY AND URINALYSIS IN THE 13-WEEK INHALATION STUDY OF 1,2-DICHLOROPROPANE

Item	Method
Hematology	
Red blood cell (RBC)	Light scattering method [1]
Hemoglobin (Hgb)	Cyanmethemoglobin method [1]
Hematocrit (Hct)	Calculated as RBC×MCV/10 [1]
Mean corpuscular volume (MCV)	Light scattering method [1]
Mean corpuscular hemoglobin (MCH)	Calculated as Hgb/RBC×10 [1]
Mean corpuscular hemoglobin concentration (MCHC)	Calculated as Hgb/Hct×100 [1]
Platelet	Light scattering method [1]
Reticulocyte	Light scattering method [1]
Prothrombin time	Quick one stage method [2]
Activated partial thromboplastin time (APTT)	Ellagic acid activaterd method [2]
White blood cell (WBC)	Light scattering method [1]
Differential WBC	Pattern recognition method [3] (Wright staining)
Biochemistry	
Total protein (TP)	Biuret method [4]
Albumin (Alb)	BCG method [4]
A/G ratio	Calculated as Alb/(TP−Alb) [4]
T-bilirubin	Alkaline azobilirubin method [4]
Glucose	GlcK·G-6-PDH method [4]
T-cholesterol	CE·COD·POD method [4]
Triglyceride	LPL·GK·GPO·POD method [4]
Phospholipid	PLD·ChOD·POD method [4]
Glutamic oxaloacetic transaminase (GOT)	JSCC method [4]
Glutamic pyruvic transaminase (GPT)	JSCC method [4]
Lactate dehydrogenase (LDH)	SFBC method [4]
Alkaline phosphatase (ALP)	GSCC method [4]
γ-Glutamyl transpeptidase (γ-GTP)	L-γ-Glutamyl-p-nitroanilide method [4]
Creatine phosphokinase (CPK)	JSCC method [4]
Urea nitrogen	Urease·GLDH method [4]
Creatinine	Jaffe method [4]
Sodium	Ion selective electrode method [4]
Potassium	Ion selective electrode method [4]
Chloride	Ion selective electrode method [4]
Calcium	OCPC method [4]
Inorganic phosphorus	PNP·XOD·POD method [4]
Urinalysis	
pH,Protein,Glucose,Ketone body,Bilirubin,Occult blood,Urobilinogen	Urinalysis reagent paper method [5]

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 7070 : Hitachi,Ltd.)
5) Ames reagent strips for urinalysis (Multistix : Bayer Corporation)

APPENDIX M 2

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK INHALATION STUDY OF 1,2-DICHLOROPROPANE

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK INHALATION STUDY OF 1,2-DICHLOROPROPANE

Item	Unit	Decimal place
Hematology		
Red blood cell (RBC)	$\times 10^6/\mu L$	2
Hemoglobin	g/dL	1
Hematocrit	%	1
Mean corpuscular volume (MCV)	fL	1
Mean corpuscular hemoglobin (MCH)	pg	1
Mean corpuscular hemoglobin concentration (MCHC)	g/dL	1
Platelet	$\times 10^3/\mu L$	0
Reticulocyte	%	1
Prothrombin time	sec	1
Activated partial thromboplastin time (APTT)	sec	1
White blood cell (WBC)	$\times 10^3/\mu L$	2
Differential WBC	%	0
Biochemistry		
Total protein	g/dL	1
Albumin	g/dL	1
A/G ratio	–	1
T-bilirubin	mg/dL	2
Glucose	mg/dL	0
T-cholesterol	mg/dL	0
Triglyceride	mg/dL	0
Phospholipid	mg/dL	0
Glutamic oxaloacetic transaminase (GOT)	IU/L	0
Glutamic pyruvic transaminase (GPT)	IU/L	0
Lactate dehydrogenase (LDH)	IU/L	0
Alkaline phosphatase (ALP)	IU/L	0
γ-Glutamyl transpeptidase (γ-GTP)	IU/L	0
Creatine phosphokinase (CPK)	IU/L	0
Urea nitrogen	mg/dL	1
Creatinine	mg/dL	1
Sodium	mEq/L	0
Potassium	mEq/L	1
Chloride	mEq/L	0
Calcium	mg/dL	1
Inorganic phosphorus	mg/dL	1