o－クロロニトロベンゼンのラットを用いた
経口投与による2週間毒性試験（混餌試験）報告書

試験番号：　０４３３

APPENDIXES

APPENDIXES

APPENDIXES (CONTINUED)

APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 1-3	1-7	2-3	2-7
HUNCHBACK POSITION	Control	0	0	0	0
	625 ppm	0	0	0	0
	1250 ppm	0	0	0	0
	2500 ppm	0	0	0	0
	5000 ppm	0	0	0	0
	10000 ppm	0	0	0	1
YELLOW URINE	Control	0	0	0	0
	625 ppm	0	0	0	0
	1250 ppm	0	0	0	0
	2500 ppm	0	5	5	5
	5000 ppm	0	5	5	5
	10000 ppm	0	5	5	5

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

Clinical sign	Group Name	Administration Week-day 1-3	1-7	2-3	2-7
COLORED	Control	0	0	0	0
	625 ppm	0	0	0	0
	1250 ppm	0	0	0	1
	2500 ppm	0	1	1	2
	5000 ppm	0	5	5	5
	10000 ppm	5	5	5	5
SOILED PERI GENITALIA	Control	0	0	0	0
	625 ppm	0	0	0	0
	1250 ppm	0	0	0	0
	2500 ppm	0	0	0	0
	5000 ppm	1	0	0	0
	10000 ppm	1	0	0	0
YELLOW URINE	Control	0	0	0	0
	625 ppm	0	0	0	0
	1250 ppm	0	0	0	0
	2500 ppm	0	5	5	5
	5000 ppm	0	5	5	5
	10000 ppm	0	5	5	5

APPENDIX B 1

BODY WEIGHT CHANGES : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-3	1-7	2-3	2-7
Control	125± 4	138± 4	158± 5	171± 6	186± 5
625 ppm	125± 4	138± 4	156± 6	169± 5	183± 5
1250 ppm	125± 5	136± 7	153± 8	166± 9	181± 9
2500 ppm	125± 4	129± 5*	142± 7**	154± 5**	168± 5**
5000 ppm	124± 5	117± 3**	127± 4**	134± 4**	143± 6**
10000 ppm	125± 4	103± 4**	107± 5**	107± 4**	106± 8**

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

APPENDIX B 2

BODY WEIGHT CHANGES : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0		1-3		1-7		2-3		2-7	
Control	97±	3	103±	3	111±	3	119±	5	123±	5
625 ppm	97±	2	103±	3	111±	3	119±	4	124±	5
1250 ppm	97±	2	103±	3	110±	4	118±	4	124±	4
2500 ppm	97±	2	94±	2**	102±	3**	109±	3**	116±	4
5000 ppm	97±	3	89±	4**	96±	5**	99±	4**	105±	4**
10000 ppm	97±	2	80±	3**	85±	3**	86±	3**	87±	3**

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

APPENDIX C 1

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-3 (3)	1-7 (4)	2-3 (3)	2-7 (4)
Control	12.7 ± 0.4	13.2 ± 0.5	13.4 ± 0.6	13.9 ± 0.5
625 ppm	12.3 ± 1.1	13.7 ± 0.9	14.3 ± 0.7	14.4 ± 0.6
1250 ppm	11.7 ± 0.7	13.3 ± 0.8	13.7 ± 0.7	13.9 ± 0.6
2500 ppm	9.0 ± 0.8 **	11.8 ± 0.9 *	12.4 ± 0.7 *	13.1 ± 0.4
5000 ppm	5.6 ± 0.3 **	10.1 ± 0.4 **	10.6 ± 0.5 **	11.0 ± 0.6 **
10000 ppm	3.3 ± 0.5 **	7.1 ± 0.2 **	7.1 ± 0.3 **	7.0 ± 0.7 **

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

APPENDIX C 2

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-3 (3)	1-7 (4)	2-3 (3)	2-7 (4)
Control	9.5 ± 0.4	10.1 ± 0.4	10.0 ± 0.6	10.3 ± 1.1
625 ppm	8.9 ± 0.5	9.8 ± 0.5	10.1 ± 0.6	10.2 ± 0.8
1250 ppm	8.0 ± 0.2 **	9.7 ± 0.5	10.3 ± 0.9	10.0 ± 1.0
2500 ppm	5.4 ± 0.3 **	8.7 ± 0.6 **	9.2 ± 0.5	9.5 ± 0.5
5000 ppm	3.8 ± 0.5 **	7.2 ± 0.9 **	7.8 ± 0.6 **	8.0 ± 0.4 **
10000 ppm	2.5 ± 0.5 **	5.8 ± 0.2 **	6.2 ± 0.4 **	6.5 ± 0.4 **

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

APPENDIX D 1

CHEMICAL INTAKE CHANGES : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
UNIT : g/kg/day
REPORT TYPE : A1 2
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 1-3	1-7	2-3	2-7
Control	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000
625 ppm	0.055 ± 0.003	0.055 ± 0.002	0.053 ± 0.002	0.049 ± 0.003
1250 ppm	0.108 ± 0.003	0.109 ± 0.002	0.103 ± 0.002	0.099 ± 0.008
2500 ppm	0.175 ± 0.009	0.208 ± 0.008	0.202 ± 0.006	0.195 ± 0.003
5000 ppm	0.238 ± 0.017	0.397 ± 0.011	0.396 ± 0.018	0.385 ± 0.006
10000 ppm	0.317 ± 0.051	0.664 ± 0.031	0.663 ± 0.043	0.660 ± 0.037

APPENDIX D 2

CHEMICAL INTAKE CHANGES : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
UNIT : g/kg/day
REPORT TYPE : A1 2
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 1-3	1-7	2-3	2-7
Control	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000
625 ppm	0.054 ± 0.004	0.055 ± 0.002	0.053 ± 0.002	0.051 ± 0.002
1250 ppm	0.097 ± 0.004	0.111 ± 0.004	0.110 ± 0.008	0.101 ± 0.010
2500 ppm	0.143 ± 0.008	0.212 ± 0.014	0.211 ± 0.011	0.204 ± 0.006
5000 ppm	0.216 ± 0.025	0.376 ± 0.035	0.395 ± 0.034	0.381 ± 0.013
10000 ppm	0.306 ± 0.055	0.684 ± 0.030	0.725 ± 0.049	0.756 ± 0.048

APPENDIX E 1

HEMATOLOGY : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$		HEMOGLOBIN g/dℓ		HEMATOCRIT %		MCV fℓ		MCH pg		MCHC g/dℓ		PLATELET $10^3/\mu\ell$	
Control	5	7.80±	0.23	14.7±	0.5	42.7±	1.0	54.7±	0.5	18.8±	0.2	34.3±	0.6	977±	41
625 ppm	5	7.67±	0.17	14.0±	0.2	41.8±	0.5	54.5±	1.0	18.2±	0.2	33.4±	0.4	917±	70
1250 ppm	5	6.93±	0.04	12.8±	0.0	39.1±	0.3*	56.4±	0.4	18.5±	0.2	32.7±	0.2	934±	17
2500 ppm	5	6.03±	0.11	12.7±	0.5*	39.8±	1.5*	66.0±	2.4	21.1±	0.7	32.1±	0.4*	788±	30**
5000 ppm	5	5.00±	0.33**	12.2±	0.7**	39.4±	1.2**	78.9±	3.7*	24.3±	0.3	30.9±	1.1**	613±	51**
10000 ppm	5	4.45±	0.26**	11.3±	0.5**	40.4±	2.5	90.8±	4.0**	25.3±	0.5*	27.9±	0.8**	589±	55**

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

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	RETICULOCYTE %	METHEMOGLOBIN %	PROTHROMBIN TIME sec	APTT sec
Control	5	3.5± 0.3	0.3± 0.1	14.1± 0.4	19.0± 2.8
625 ppm	5	4.0± 0.6	0.5± 0.2	14.4± 0.5	18.4± 3.6
1250 ppm	5	8.2± 0.6	1.0± 0.4	14.3± 0.5	15.6± 2.8
2500 ppm	5	14.7± 0.6**	1.7± 0.5*	15.4± 0.9	15.8± 0.9
5000 ppm	5	23.5± 5.3**	2.6± 1.5**	17.0± 0.5*	15.2± 1.7
10000 ppm	5	13.3± 0.0 ?	2.8± 0.6**	18.1± 1.7**	19.9± 2.6

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

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

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHER
Control	5	3.55± 1.19	2± 1	14± 2	1± 0	0± 0	3± 1	81± 2	0± 0
625 ppm	5	3.92± 1.22	2± 2	12± 3	0± 0	0± 0	2± 1	84± 5	0± 0
1250 ppm	5	4.12± 1.11	2± 1	14± 4	1± 0	0± 0	2± 1	82± 5	0± 0
2500 ppm	5	4.28± 0.75	2± 1	13± 2	1± 1	0± 0	2± 1	83± 3	0± 0
5000 ppm	5	4.69± 1.02	1± 1	18± 4	1± 1	0± 0	2± 0	78± 6	0± 0
10000 ppm	5	3.80± 0.61	3± 2	21± 3**	1± 1	0± 0	2± 1	73± 5*	0± 0

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

(HCL070)

APPENDIX E 2

HEMATOLOGY : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV fℓ	MCH pg	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	5	8.21± 0.29	15.5± 0.5	43.7± 1.7	53.3± 0.4	18.9± 0.2	35.5± 0.2	798± 64
625 ppm	5	7.74± 0.28*	14.3± 0.5**	41.3± 1.3*	53.4± 0.6	18.5± 0.2	34.6± 0.5**	813± 66
1250 ppm	5	6.84± 0.25**	12.7± 0.3**	38.1± 0.9**	55.7± 1.2	18.6± 0.4	33.4± 0.3**	867± 64
2500 ppm	5	6.12± 0.25**	12.6± 0.5**	39.0± 1.6**	63.6± 1.4	20.6± 0.4**	32.4± 0.3**	720± 57
5000 ppm	5	5.91± 0.14**	13.4± 0.3**	41.2± 1.2*	69.7± 1.9**	22.6± 0.6**	32.4± 0.5**	546± 27**
10000 ppm	5	4.60± 0.12**	11.4± 0.3**	41.4± 1.4	90.0± 2.5**	24.8± 0.5**	27.5± 0.5**	595± 107**

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

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	RETICULOCYTE %		METHEMOGLOBIN %		PROTHROMBIN TIME sec		APTT sec	
Control	5	1.7±	0.1	0.4±	0.2	15.5±	0.6	18.2±	1.1
625 ppm	5	3.8±	0.8	0.6±	0.2	15.2±	0.2	15.1±	1.7
1250 ppm	5	8.1±	1.8	1.1±	0.3*	15.3±	0.8	15.4±	1.8
2500 ppm	5	14.8±	2.2**	1.2±	0.3*	16.7±	0.7	14.5±	4.2
5000 ppm	5	14.6±	1.8**	1.1±	0.4*	19.5±	0.8**	16.2±	1.6
10000 ppm	5	11.5±	8.2 ?	2.5±	0.7**	19.0±	1.0**	16.9±	1.1

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

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

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$		Differential WBC (%) N-BAND		N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHER	
Control	5	3.15±	0.95	1±	1	18±	6	1±	0	0±	0	2±	1	77±	6	0±	0
625 ppm	5	3.78±	0.64	2±	1	12±	3	1±	0	0±	0	2±	1	83±	3	0±	0
1250 ppm	5	4.52±	1.17	2±	2	17±	8	1±	1	0±	0	2±	0	78±	9	0±	0
2500 ppm	5	3.73±	0.66	2±	1	13±	5	1±	1	0±	0	2±	0	83±	6	0±	0
5000 ppm	5	3.70±	0.30	2±	2	16±	4	1±	0	0±	0	2±	1	78±	2	0±	0
10000 ppm	5	4.62±	1.06	1±	1	18±	5	0±	1	0±	0	2±	0	78±	6	0±	0

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

APPENDIX F 1

BIOCHEMISTRY : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	TOTAL PROTEIN g/dl		ALBUMIN g/dl		A/G RATIO		T-BILIRUBIN mg/dl		GLUCOSE mg/dl		T-CHOLESTEROL mg/dl		PHOSPHOLIPID mg/dl	
Control	5	5.7±	0.0	3.5±	0.1	1.6±	0.1	0.13±	0.02	182±	9	68±	3	137±	3
625 ppm	5	6.4±	0.2**	4.0±	0.1**	1.6±	0.1	0.16±	0.02	173±	6	119±	9	229±	11
1250 ppm	5	6.5±	0.1**	4.1±	0.1**	1.7±	0.1	0.22±	0.02	164±	6**	148±	11	283±	24
2500 ppm	5	6.4±	0.1**	4.0±	0.1**	1.7±	0.1	0.33±	0.03*	155±	8**	181±	22**	347±	36**
5000 ppm	5	6.4±	0.2**	4.0±	0.1**	1.7±	0.1*	0.76±	0.12**	135±	5**	186±	27**	394±	55**
10000 ppm	5	5.8±	0.2	3.8±	0.1*	1.9±	0.1**	0.65±	0.08**	118±	3**	142±	20	329±	45*

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

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	GOT IU/ℓ		GPT IU/ℓ		LDH IU/ℓ		G-GTP IU/ℓ		CPK IU/ℓ		UREA NITROGEN mg/dℓ		CREATININE mg/dℓ	
Control	5	56±	9	33±	8	237±	27	2±	1	193±	18	14.4±	1.5	0.4±	0.0
625 ppm	5	51±	3	37±	4	224±	44	1±	1	177±	21	16.4±	2.4	0.4±	0.1
1250 ppm	5	60±	4	58±	8	196±	42	4±	1	142±	6	15.8±	2.0	0.4±	0.0
2500 ppm	5	88±	8*	138±	33**	274±	92	30±	11	152±	40	16.9±	2.1	0.4±	0.0
5000 ppm	5	100±	23**	169±	83**	445±	145	131±	33**	160±	49	18.4±	0.6*	0.4±	0.0
10000 ppm	5	77±	12	90±	22*	413±	165	85±	7**	163±	46	24.3±	2.2**	0.4±	0.0

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

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	SODIUM mEq／ℓ		POTASSIUM mEq／ℓ		CHLORIDE mEq／ℓ		CALCIUM mg／dℓ		INORGANIC PHOSPHORUS mg／dℓ	
Control	5	138±	1	4.4±	0.2	103±	1	11.0±	0.2	8.2±	1.0
625 ppm	5	139±	1	4.4±	0.3	102±	1	11.2±	0.2	7.7±	1.0
1250 ppm	5	138±	1	4.2±	0.3	102±	2	11.3±	0.2	7.9±	1.2
2500 ppm	5	138±	1	4.6±	0.1	102±	1	11.1±	0.2	8.0±	0.9
5000 ppm	5	137±	0*	4.9±	0.4*	102±	2	11.2±	0.2	7.0±	0.7
10000 ppm	5	138±	1	5.6±	0.3**	105±	1	10.7±	0.2	7.3±	0.6

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

APPENDIX F 2

BIOCHEMISTRY : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	TOTAL PROTEIN g/dl		ALBUMIN g/dl		A/G RATIO		T-BILIRUBIN mg/dl		GLUCOSE mg/dl		T-CHOLESTEROL mg/dl		PHOSPHOLIPID mg/dl	
Control	5	5.7±	0.2	3.6±	0.1	1.7±	0.0	0.14±	0.01	180±	7	75±	5	148±	9
625 ppm	5	6.2±	0.1**	4.0±	0.1	1.8±	0.1	0.18±	0.01	172±	8	103±	6**	197±	13**
1250 ppm	5	6.3±	0.2**	4.0±	0.2	1.8±	0.1	0.21±	0.02	163±	3*	115±	9**	226±	20**
2500 ppm	5	6.6±	0.2**	4.2±	0.1**	1.8±	0.1	0.30±	0.02*	159±	9**	158±	14**	314±	30**
5000 ppm	5	6.5±	0.1**	4.2±	0.0**	1.8±	0.1	0.58±	0.08**	140±	12**	180±	7**	392±	13**
10000 ppm	5	6.0±	0.2	3.8±	0.3	1.8±	0.3	0.80±	0.05**	118±	12**	178±	16**	434±	36**

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

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	GOT IU/ℓ		GPT IU/ℓ		LDH IU/ℓ		G-GTP IU/ℓ		CPK IU/ℓ		UREA NITROGEN mg/dℓ		CREATININE mg/dℓ	
Control	5	57±	5	28±	3	376±	202	2±	1	257±	146	16.6±	2.4	0.4±	0.0
625 ppm	5	49±	5	26±	2	350±	196	2±	1	206±	89	17.4±	1.9	0.4±	0.0
1250 ppm	5	48±	7	28±	3	289±	111	6±	2	177±	64	16.7±	2.4	0.4±	0.0
2500 ppm	5	77±	11	60±	16	418±	171	44±	13	182±	49	18.7±	1.2	0.4±	0.0
5000 ppm	5	114±	3*	144±	18**	548±	147	156±	23**	185±	68	21.2±	1.2**	0.4±	0.0
10000 ppm	5	93±	31	120±	29*	621±	154	117±	8**	178±	45	27.4±	2.1**	0.4±	0.0

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

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	SODIUM mEq/ℓ		POTASSIUM mEq/ℓ		CHLORIDE mEq/ℓ		CALCIUM mg/dℓ		INORGANIC PHOSPHORUS mg/dℓ	
Control	5	137±	1	4.1±	0.4	105±	1	10.5±	0.1	6.8±	0.9
625 ppm	5	138±	1	4.0±	0.2	104±	1	10.9±	0.1*	7.2±	0.8
1250 ppm	5	137±	1	4.2±	0.2	104±	2	10.9±	0.2**	6.9±	1.2
2500 ppm	5	138±	2	4.5±	0.2	104±	1	11.1±	0.2**	7.1±	0.6
5000 ppm	5	136±	2	5.0±	0.3**	103±	2	11.0±	0.2**	7.0±	0.8
10000 ppm	5	136±	2	6.0±	0.6**	105±	2	10.8±	0.4	7.6±	0.5

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

APPENDIX G 1

GROSS FINDINGS : SUMMARY, RAT : MALE : ALL ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name / NO. of Animals	Control 5 (%)	625 ppm 5 (%)	1250 ppm 5 (%)	2500 ppm 5 (%)
spleen	enlarged		0 (0)	0 (0)	5 (100)	5 (100)
	dark		0 (0)	0 (0)	5 (100)	5 (100)
liver	dark		0 (0)	0 (0)	0 (0)	0 (0)
	herniation		0 (0)	0 (0)	0 (0)	0 (0)

Organ	Findings	Group Name NO. of Animals	5000 ppm 5 (%)	10000 ppm 5 (%)
spleen	enlarged		5 (100)	5 (100)
	dark		5 (100)	5 (100)
liver	dark		5 (100)	5 (100)
	herniation		1 (20)	0 (0)

APPENDIX G 2

GROSS FINDINGS : SUMMARY, RAT : FEMALE : ALL ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name NO. of Animals	Control 5 (%)	625 ppm 5 (%)	1250 ppm 5 (%)	2500 ppm 5 (%)
spleen	enlarged		0 (0)	0 (0)	5 (100)	5 (100)
	dark		0 (0)	0 (0)	5 (100)	5 (100)
liver	dark		0 (0)	0 (0)	0 (0)	0 (0)
	herniation		0 (0)	0 (0)	0 (0)	0 (0)

Organ	Findings	Group Name / NO. of Animals	5000 ppm 5 (%)	10000 ppm 5 (%)
spleen	enlarged		5 (100)	5 (100)
	dark		5 (100)	5 (100)
liver	dark		0 (0)	5 (100)
	herniation		0 (0)	1 (20)

APPENDIX H 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	5	186± 7	0.357± 0.024	0.045± 0.006	2.369± 0.120	0.664± 0.025	0.839± 0.060
625 ppm	5	181± 5	0.332± 0.018	0.043± 0.005	2.427± 0.155	0.665± 0.022	0.813± 0.017
1250 ppm	5	180± 8	0.347± 0.045	0.043± 0.004	2.395± 0.066	0.664± 0.038	0.797± 0.032
2500 ppm	5	167± 5**	0.338± 0.021	0.039± 0.003	2.157± 0.250	0.621± 0.033	0.734± 0.028**
5000 ppm	5	142± 6**	0.264± 0.007*	0.041± 0.005	1.320± 0.261	0.567± 0.010**	0.679± 0.044**
10000 ppm	5	105± 8**	0.129± 0.014**	0.038± 0.004	0.717± 0.067**	0.446± 0.022**	0.599± 0.015**

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

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	1.431± 0.077	0.466± 0.029	7.187± 0.432	1.690± 0.036
625 ppm	5	1.515± 0.070	0.479± 0.022	10.446± 0.263**	1.690± 0.033
1250 ppm	5	1.493± 0.082	0.683± 0.065	11.221± 0.356**	1.688± 0.032
2500 ppm	5	1.452± 0.066	0.871± 0.082*	11.762± 0.587**	1.635± 0.042
5000 ppm	5	1.423± 0.047	1.114± 0.122**	10.994± 0.847**	1.609± 0.048*
10000 ppm	5	1.289± 0.057*	0.895± 0.057*	8.069± 0.268*	1.583± 0.049**

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

APPENDIX H 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	Body Weight		THYMUS		ADRENALS		OVARIES		HEART		LUNGS	
Control	5	122±	5	0.280±	0.021	0.048±	0.003	0.077±	0.009	0.472±	0.015	0.644±	0.023
625 ppm	5	123±	4	0.276±	0.012	0.047±	0.003	0.089±	0.015	0.496±	0.045	0.622±	0.017
1250 ppm	5	122±	3	0.268±	0.020	0.044±	0.006	0.083±	0.009	0.490±	0.036	0.640±	0.016
2500 ppm	5	115±	4*	0.271±	0.012	0.037±	0.004**	0.063±	0.017	0.459±	0.016	0.585±	0.020**
5000 ppm	5	104±	4**	0.225±	0.018**	0.041±	0.005	0.052±	0.008**	0.429±	0.016	0.563±	0.026**
10000 ppm	5	86±	3**	0.131±	0.023**	0.036±	0.004**	0.041±	0.004**	0.374±	0.019**	0.529±	0.017**

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

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.993± 0.057	0.312± 0.009	4.408± 0.387	1.592± 0.037
625 ppm	5	1.074± 0.037	0.352± 0.024	6.388± 0.578**	1.565± 0.036
1250 ppm	5	1.048± 0.057	0.500± 0.057	7.173± 0.373**	1.597± 0.032
2500 ppm	5	1.071± 0.034	0.613± 0.051*	7.943± 0.310**	1.576± 0.040
5000 ppm	5	1.058± 0.055	0.656± 0.046**	7.890± 0.232**	1.531± 0.035*
10000 ppm	5	1.088± 0.030	0.720± 0.073**	7.349± 0.197**	1.520± 0.022*

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

APPENDIX I 1

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	5	186± 7	0.192± 0.016	0.024± 0.004	1.272± 0.030	0.357± 0.008	0.450± 0.015
625 ppm	5	181± 5	0.183± 0.010	0.024± 0.003	1.339± 0.097	0.367± 0.011	0.449± 0.017
1250 ppm	5	180± 8	0.194± 0.028	0.024± 0.002	1.336± 0.063	0.370± 0.034	0.444± 0.019
2500 ppm	5	167± 5**	0.203± 0.014	0.023± 0.002	1.290± 0.126	0.372± 0.019	0.440± 0.019
5000 ppm	5	142± 6**	0.186± 0.011	0.029± 0.004	0.931± 0.190*	0.400± 0.019**	0.479± 0.030
10000 ppm	5	105± 8**	0.122± 0.007**	0.036± 0.003**	0.680± 0.028**	0.425± 0.038**	0.570± 0.042**

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

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.768± 0.029	0.250± 0.015	3.858± 0.123	0.908± 0.018
625 ppm	5	0.835± 0.026*	0.264± 0.006	5.762± 0.208**	0.933± 0.034
1250 ppm	5	0.831± 0.027*	0.381± 0.042**	6.252± 0.142**	0.941± 0.027
2500 ppm	5	0.870± 0.030**	0.521± 0.038**	7.042± 0.271**	0.980± 0.037
5000 ppm	5	1.003± 0.036**	0.784± 0.071**	7.735± 0.326**	1.134± 0.034**
10000 ppm	5	1.225± 0.044**	0.850± 0.029**	7.673± 0.318**	1.506± 0.080**

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

APPENDIX I 2

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	5	122± 5	0.229± 0.026	0.039± 0.001	0.063± 0.006	0.385± 0.011	0.527± 0.034
625 ppm	5	123± 4	0.225± 0.005	0.038± 0.003	0.072± 0.011	0.404± 0.031	0.507± 0.025
1250 ppm	5	122± 3	0.220± 0.020	0.036± 0.005	0.068± 0.007	0.400± 0.023	0.524± 0.012
2500 ppm	5	115± 4*	0.237± 0.009	0.033± 0.004	0.055± 0.015	0.400± 0.015	0.510± 0.009
5000 ppm	5	104± 4**	0.217± 0.013	0.040± 0.005	0.051± 0.006	0.414± 0.018	0.544± 0.026
10000 ppm	5	86± 3**	0.152± 0.024**	0.042± 0.005	0.048± 0.004	0.437± 0.031**	0.619± 0.023**

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

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.812± 0.034	0.255± 0.008	3.600± 0.258	1.302± 0.050
625 ppm	5	0.875± 0.018	0.286± 0.014**	5.196± 0.330**	1.275± 0.038
1250 ppm	5	0.858± 0.036	0.409± 0.038**	5.871± 0.281**	1.308± 0.038
2500 ppm	5	0.934± 0.030**	0.534± 0.030**	6.919± 0.192**	1.374± 0.051
5000 ppm	5	1.022± 0.053**	0.632± 0.026**	7.619± 0.103**	1.479± 0.055**
10000 ppm	5	1.272± 0.060**	0.841± 0.072**	8.594± 0.343**	1.778± 0.076**

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

APPENDIX J 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : ALL ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0433
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0- 2W)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 5				625 ppm 5				1250 ppm 5				2500 ppm 5			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Respiratory system}																		
nasal cavit			< 5>				< 5>				< 5>				< 5>			
	respiratory metaplasia:gland		1 (20)	0 (0)	0 (0)	0 (0)	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			< 5>				< 5>				< 5>				< 5>			
	erythropoiesis:increased		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (80)	0 (0)	0 (0)	0 (0)	5 (100)	0 (0)	0 (0)	0 (0)
thymus			< 5>				< 5>				< 5>				< 5>			
	atrophy		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
spleen			< 5>				< 5>				< 5>				< 5>			
	deposit of hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	5 (100)	0 (0)	0 (0)	0 (0)	5 (100)	0 (0)	0 (0)	0 (0)
	extramedullary hematopoiesis		0 (0)	0 (0)	0 (0)	0 (0)	5 (100)	0 (0)	0 (0)	0 (0)	0 (0)	5 (100)	0 (0)	0 (0)	0 (0)	5 (100)	0 (0)	0 (0)
	engorgement of erythrocyte		0 (0)	0 (0)	0 (0)	0 (0)	5 (100)	0 (0)	0 (0)	0 (0)	1 (20)	4 (80)	0 (0)	0 (0)	0 (0)	5 (100)	0 (0)	0 (0)

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

Organ	Findings	Group Name	5000 ppm				10000 ppm			
		No. of Animals on Study	5				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			< 5>				< 5>			
	respiratory metaplasia:gland		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}										
bone marrow			< 5>				< 5>			
	erythropoiesis:increased		5	0	0	0	5	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
thymus			< 5>				< 5>			
	atrophy		0	0	0	0	5	0	0	0
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
spleen			< 5>				< 5>			
	deposit of hemosiderin		0	5	0	0	0	5	0	0
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
	extramedullary hematopoiesis		0	5	0	0	0	5	0	0
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
	engorgement of erythrocyte		0	5	0	0	0	5	0	0
			(0)	(100)	(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 / No. of Animals on Study / Grade	Control 5				625 ppm 5				1250 ppm 5				2500 ppm 5			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Digestive system}																		
liver			< 5>				< 5>				< 5>				< 5>			
	herniation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)
	increase in mitosis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	4 (80)	0 (0)	0 (0)	0 (0)
	necrosis:single cell		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (60)	0 (0)	0 (0)	0 (0)
	deposit of hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	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)
	hepatocellular hypertrophy:central		0 (0)	0 (0)	0 (0)	0 (0)	5 (100)	0 (0)	0 (0)	0 (0)	5 (100)	0 (0)	0 (0)	0 (0)	1 (20)	4 (80)	0 (0)	0 (0)
{Urinary system}																		
kidney			< 5>				< 5>				< 5>				< 5>			
	deposit of hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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

Organ	Findings	Group Name	5000 ppm				10000 ppm			
		No. of Animals on Study	5				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
liver			< 5>				< 5>			
	herniation		1	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	increase in mitosis		3	0	0	0	0	0	0	0
			(60)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:single cell		4	0	0	0	3	0	0	0
			(80)	(0)	(0)	(0)	(60)	(0)	(0)	(0)
	deposit of hemosiderin		5	0	0	0	5	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	extramedullary hematopoiesis		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	hepatocellular hypertrophy:central		0	5	0	0	0	0	5	0
			(0)	(100)	(0)	(0)	(0)	(0)	(100)	(0)
{Urinary system}										
kidney			< 5>				< 5>			
	deposit of hemosiderin		5	0	0	0	5	0	0	0
			(100)	(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 5				625 ppm 5				1250 ppm 5				2500 ppm 5			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Urinary system}																		
kidney			< 5>				< 5>				< 5>				< 5>			
	eosinophilic body		5 (100)	0 (0)	0 (0)	0 (0)	5 (100)	0 (0)	0 (0)	0 (0)	4 (80)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	mineralization:papilla		0 (0)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
{Reproductive system}																		
testis			< 5>				< 5>				< 5>				< 5>			
	germ cell necrosis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)
epididymis			< 5>				< 5>				< 5>				< 5>			
	decreased:sperma		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	debris of spermatic elements		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)
prostate			< 5>				< 5>				< 5>				< 5>			
	lymphocytic infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)

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

Organ	Findings	Group Name	5000 ppm				10000 ppm			
		No. of Animals on Study	5				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}										
kidney			< 5>				< 5>			
	eosinophilic body		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:papilla		1	0	0	0	1	0	0	0
			(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
{Reproductive system}										
testis			< 5>				< 5>			
	germ cell necrosis		0	5	0	0	0	5	0	0
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
epididymis			< 5>				< 5>			
	decreased:sperma		0	5	0	0	0	0	5	0
			(0)	(100)	(0)	(0)	(0)	(0)	(100)	(0)
	debris of spermatic elements		0	0	5	0	0	0	0	0
			(0)	(0)	(100)	(0)	(0)	(0)	(0)	(0)
prostate			< 5>				< 5>			
	lymphocytic infiltration		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				625 ppm				1250 ppm				2500 ppm			
		No. of Animals on Study	5				5				5				5			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Nervous system}																		
brain			< 5>				< 5>				< 5>				< 5>			
	hemorrhage		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	5000 ppm				10000 ppm			
		No. of Animals on Study	5				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Nervous system)										
brain			< 5>				< 5>			
	hemorrhage		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(40)	(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 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : ALL ANIMALS

(2-WEEK STUDY)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 5				625 ppm 5				1250 ppm 5				2500 ppm 5			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Respiratory system}																		
nasal cavit		< 5>																
	respiratory metaplasia:gland		1 (20)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
lung		< 5>																
	hemorrhage		0 (0)	0 (0)	0 (0)	0 (0)	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		< 5>																
	granulation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	erythropoiesis:increased		0 (0)	0 (0)	0 (0)	0 (0)	3 (60)	0 (0)	0 (0)	0 (0)	5 (100)	0 (0)	0 (0)	0 (0)	5 (100)	0 (0)	0 (0)	0 (0)
thymus		< 5>																
	atrophy		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
spleen		< 5>																
	deposit of hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	5 (100)	0 (0)	0 (0)	0 (0)	4 (80)	1 (20)	0 (0)	0 (0)

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

Organ	Findings	Group Name	5000 ppm				10000 ppm			
		No. of Animals on Study	5				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			< 5>				< 5>			
	respiratory metaplasia:gland		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lung			< 5>				< 5>			
	hemorrhage		1	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}										
bone marrow			< 5>				< 5>			
	granulation		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	erythropoiesis:increased		5	0	0	0	5	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
thymus			< 5>				< 4>			
	atrophy		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(25)	(0)	(0)	(0)
spleen			< 5>				< 5>			
	deposit of hemosiderin		0	5	0	0	0	5	0	0
			(0)	(100)	(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 / No. of Animals on Study / Grade	Control 5 1 (%)	Control 5 2 (%)	Control 5 3 (%)	Control 5 4 (%)	625 ppm 5 1 (%)	625 ppm 5 2 (%)	625 ppm 5 3 (%)	625 ppm 5 4 (%)	1250 ppm 5 1 (%)	1250 ppm 5 2 (%)	1250 ppm 5 3 (%)	1250 ppm 5 4 (%)	2500 ppm 5 1 (%)	2500 ppm 5 2 (%)	2500 ppm 5 3 (%)	2500 ppm 5 4 (%)
{Hematopoietic system}																		
spleen		< 5>	0	0	0	0	5	0	0	0	0	5	0	0	0	5	0	0
	extramedullary hematopoiesis		(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
	engorgement of erythrocyte		0 (0)	0 (0)	0 (0)	0 (0)	5 (100)	0 (0)	0 (0)	0 (0)	0 (0)	5 (100)	0 (0)	0 (0)	0 (0)	5 (100)	0 (0)	0 (0)
{Digestive system}																		
liver		< 5>	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	herniation		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	increase in mitosis		0 (0)	0 (0)	0 (0)	0 (0)	2 (40)	0 (0)	0 (0)	0 (0)	2 (40)	0 (0)	0 (0)	0 (0)	4 (80)	0 (0)	0 (0)	0 (0)
	necrosis:single cell		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (40)	0 (0)	0 (0)	0 (0)	4 (80)	0 (0)	0 (0)	0 (0)
	deposit of hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hepatocellular hypertrophy:central		0 (0)	0 (0)	0 (0)	0 (0)	5 (100)	0 (0)	0 (0)	0 (0)	5 (100)	0 (0)	0 (0)	0 (0)	0 (0)	5 (100)	0 (0)	0 (0)

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

Organ	Findings	Group Name	5000 ppm				10000 ppm			
		No. of Animals on Study	5				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
spleen			< 5>				< 5>			
	extramedullary hematopoiesis		0	5	0	0	0	5	0	0
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
	engorgement of erythrocyte		0	5	0	0	0	5	0	0
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
{Digestive system}										
liver			< 5>				< 5>			
	herniation		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	increase in mitosis		5	0	0	0	0	0	0	0
			(100)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:single cell		5	0	0	0	5	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	deposit of hemosiderin		5	0	0	0	5	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	hepatocellular hypertrophy:central		0	5	0	0	0	0	5	0
			(0)	(100)	(0)	(0)	(0)	(0)	(100)	(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				625 ppm				1250 ppm				2500 ppm			
		No. of Animals on Study	5				5				5				5			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}																		
kidney			< 5>				< 5>				< 5>				< 5>			
	basophilic 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)
	deposit of hemosiderin		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:cortico-medullary junction		0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Nervous system}																		
brain			< 5>				< 5>				< 5>				< 5>			
	hemorrhage		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	5000 ppm				10000 ppm			
		No. of Animals on Study	5				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}										
kidney			< 5>				< 5>			
	basophilic change		1	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	deposit of hemosiderin		5	0	0	0	5	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	mineralization:cortico-medullary junction		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Nervous system}										
brain			< 5>				< 5>			
	hemorrhage		0	0	0	0	1	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

APPENDIX K 1

IDENTITY OF *o*-CHLORONITROBENZENE IN THE 2-WEEK FEED STUDY

IDENTITY OF o-CHLORONITROBENZENE IN THE 2-WEEK FEED STUDY

Test Substance : o-Chloronitrobenzene (Wako Pure Chemical Industries, Ltd.)

Lot No. : PAK9795

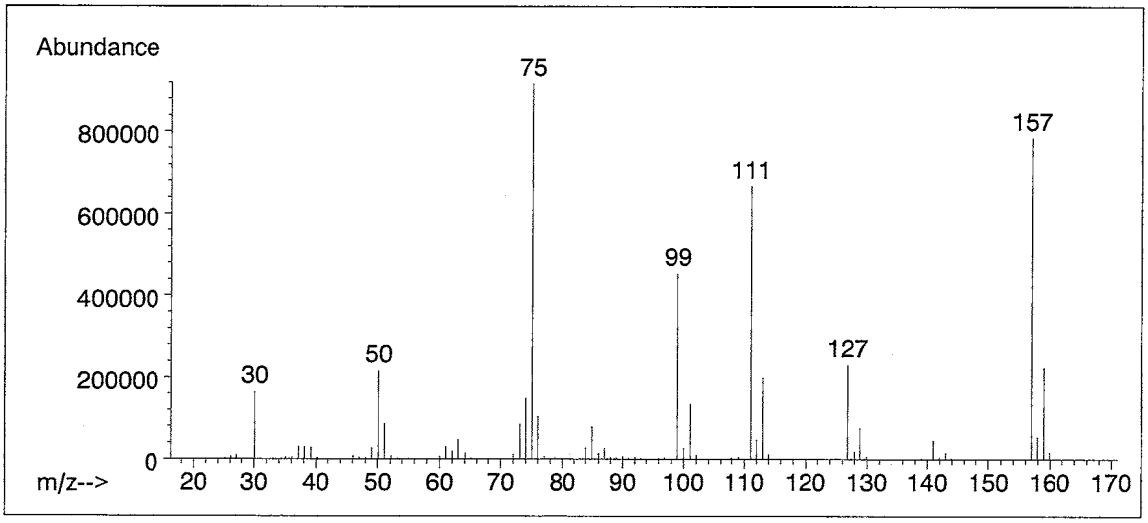
1. Spectral Data

Mass Spectrometry

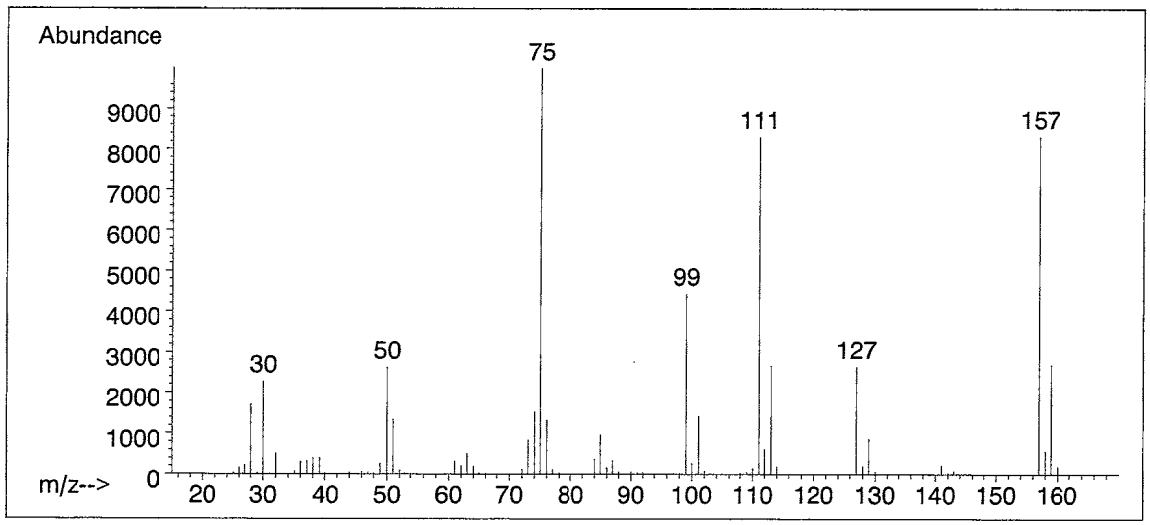
Instrument : Hewlett Packard 5989B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance



Mass Spectrum of Literature Data*

Results: The mass spectrum was consistent with literature spectrum.

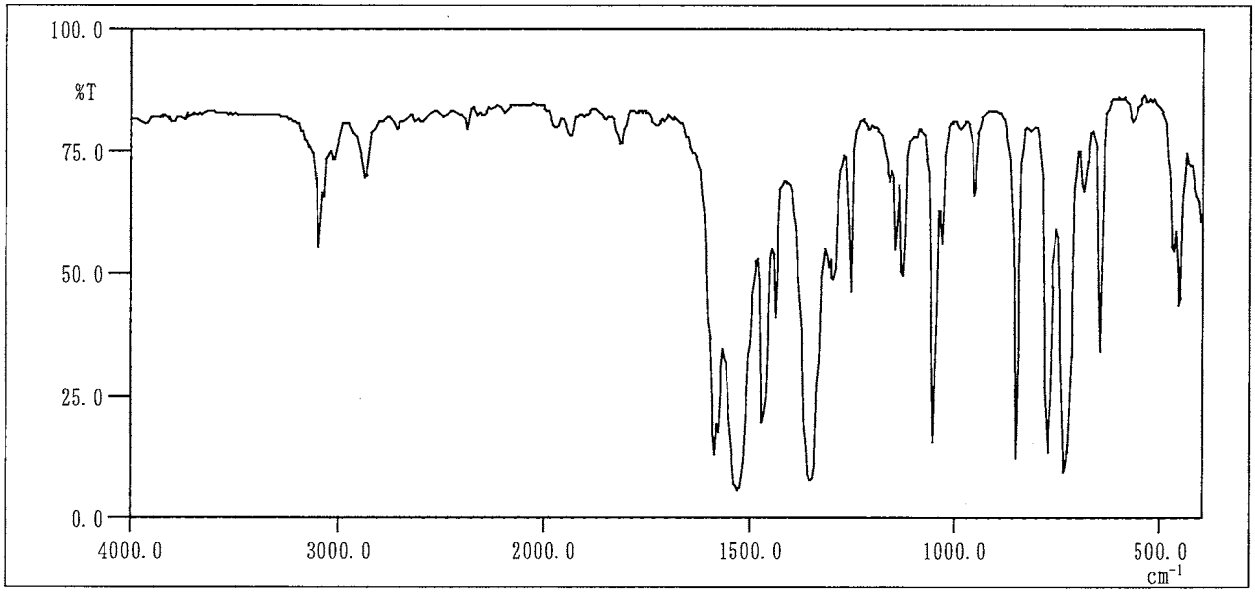
(*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition. John Wiley and Sons, Inc. (U.S.), Entry Number 42503)

Infrared Spectrometry

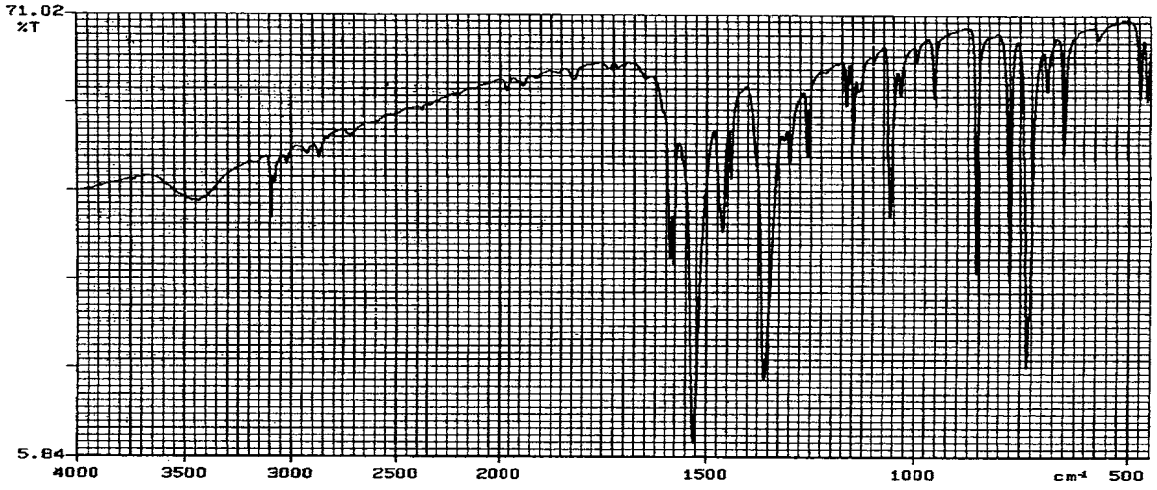
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr

Resolution : 2 cm^{-1}



Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data*

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

2. Conclusions: The test substance was identified as o-chloronitrobenzene by the mass spectrum and the infrared spectrum.

APPENDIX K 2

STABILITY OF *o*-CHLORONITROBENZENE IN THE 2-WEEK FEED STUDY

STABILITY OF o-CHLORONITROBENZENE IN THE 2-WEEK FEED STUDY

Test Substance : o-Chloronitrobenzene (Wako Pure Chemical Industries, Ltd.)

Lot No. : PAK9795

1. Sample : This lot was used from 2001.7.17 to 2001.7.31. Test substance was stored in cold storage in a dark place.

2. High Performance Liquid Chromatography

Instrument : Hewlett Packard 1090 High Performance Liquid Chromatograph

Column : TSK GEL ODS-80TM (4.6 mmϕ × 15 cm)

Column Temperature : Room Temperature

Mobile Phase : Acetonitrile : Distilled Water = 1 : 1

Flow Rate : 1 mL/min

Detector : UV (254 nm)

Injection Volume : 20 μL

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
2001.07.04	1	6.955	100
2001.08.10	1	6.923	100

Results: Gas chromatography indicated one major peak (peak No.1) analyzed on 2001.7.4 and one major peak (peak No.1) analyzed on 2001.8.10. No new trace impurity peak in the test substance analyzed on 2001.8.10 was detected.

3. Conclusions: The test substance was stable for about 1 month in cold storage in a dark place.

APPENDIX K 3

CONCENTRATION OF *o*-CHLORONITROBENZENE IN FORMULATED DIETS IN THE 2-WEEK FEED STUDY

CONCENTRATION OF o-CHLORONITROBENZENE IN FORMULATED DIETS IN THE 2-WEEK FEED STUDY

	Target Concentration				
Date Analyzed	625[a]	1250	2500	5000	10000
2001.07.16	609 (97.4)[b]	1170 (93.6)	2440 (97.6)	4730 (94.6)	9410 (94.1)

[a] ppm
[b] %

Analytical Method : The samples were analyzed by high performance liquid chromatography.

Instrument : Hewlett Packard 1090 High Performance Liquid Chromatograph
Column : TSK GEL ODS-80TM (4.6 mmϕ $\times$ 15 cm)
Column Temperature : Room Temperature
Mobile Phase : Acetonitrile : Distilled Water = 1 : 1
Flow Rate : 1 mL/min
Detector : UV (254 nm)
Injection Volume : 20 µL

APPENDIX K 4

HOMOGENITY OF *o*-CHLORONITROBENZENE IN FORMULATED DIETS IN THE 2-WEEK FEED STUDY

HOMOGENEITY OF o-CHLORONITROBENZENE IN FORMULATED DIETS IN THE 2-WEEK FEED STUDY

	Target Concentration				
	625[a]	1250	2500	5000	10000
Coefficient Variation	4.79[b]	2.54	5.70	3.08	3.36

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

Analytical Method : The samples were analyzed by high performance liquid chromatography.

Instrument : Hewlett Packard 1090 High Performance Liquid Chromatograph
Column : TSK GEL ODS-80TM (4.6 mmϕ $\times$ 15 cm)
Column Temperature : Room Temperature
Mobile Phase : Acetonitrile : Distilled Water = 1 : 1
Flow Rate : 1 mL/min
Detector : UV (254 nm)
Injection Volume : 20 µL

APPENDIX K 5

STABILITY OF *o*-CHLORONITROBENZENE IN FORMULATED DIETS IN THE 2-WEEK FEED STUDY

STABILITY OF o-CHLORONITROBENZENE IN FORMULATED DIETS IN THE 2-WEEK FEED STUDY

		Target Concentration	
Date Prepared	Date Analyzed	500[a]	10000
2001.06.07	2001.06.07	489 (100)[b]	9990 (100)
	2001.06.15[c]	377 (77.1)	7770 (77.8)
	2001.06.15[d]	486 (99.4)	9670 (96.8)
	2001.08.02[d]	515 (105)	9610 (96.2)

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

Analytical Method : The samples were analyzed by high performance liquid chromatography.

Instrument : Hewlett Packard 1090 High Performance Liquid Chromatograph
Column : TSK GEL ODS-80TM (4.6 mmϕ $\times$ 15 cm)
Column Temperature : Room Temperature
Mobile Phase : Acetonitrile : Distilled Water = 1 : 1
Flow Rate : 1 mL/min
Detector : UV (254 nm)
Injection Volume : 20 µL

APPENDIX L 1

METHODS FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

METHODS FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

Item	Method
Hematology	
Red blood cell (RBC)	Light scattering method [1]
Hemoglobin (Hgb)	Cyanmethemoglobin method [1]
Methemoglobin	Multiple-wavelength Spectrophotometric method [5]
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]
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]
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]

1) Automatic blood cell analyzer (ADVIA120 : Bayer Corporation)

2) Automatic coagulometer (Sysmex CA-5000 : Toa Medical Electronics Co.,Ltd.)

3) Automatic blood cell differential analyzer (MICROX HEG-120NA : OMRON Corporation)

4) Automatic analyzer (Hitachi 7070 : Hitachi,Ltd.)

5) CO-oximeter (CIBA·CORNING 270 : Bayer Corporation)

APPENDIX M 1

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

Item	Unit	Decimal Place
Hematology		
Red blood cell (RBC)	$\times 10^6/\mu L$	2
Hemoglobin	g/dL	1
Methemoglobin	%	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
Phospholipid	mg/dL	0
Glutamic oxaloacetic transaminase (GOT)	IU/L	0
Glutamic pyruvic transaminase (GPT)	IU/L	0
Lactate dehydrogenase (LDH)	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