p-ニトロアニソールのラットを用いた経口投与による
2 週 間 毒 性 試 験（混 餌 試 験）報 告 書

試験番号：０３６０

APPENDIX

APPENDIXES

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0360
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 1-1 1	1-3 1	1-7 1	2-3 1	2-7 1
COLORED	Control	0	0	0	0	0
	1250 ppm	0	0	0	0	0
	2500 ppm	0	0	0	0	0
	5000 ppm	0	0	0	5	5
	10000 ppm	0	0	0	5	5
	20000 ppm	0	0	0	0	0
PILOERECTION	Control	0	0	0	0	0
	1250 ppm	0	0	0	0	0
	2500 ppm	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	0	0
	20000 ppm	0	0	5	5	5
SOILED PERI GENITALIA	Control	0	0	0	0	0
	1250 ppm	0	0	0	0	0
	2500 ppm	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	0	0
	20000 ppm	0	0	3	3	3
YELLOW URINE	Control	0	0	0	0	0
	1250 ppm	0	0	0	0	0
	2500 ppm	0	0	0	0	5
	5000 ppm	0	0	0	5	5
	10000 ppm	0	0	0	5	5
	20000 ppm	0	5	5	5	5
OLIGO-STOOL	Control	0	0	0	0	0
	1250 ppm	0	0	0	0	0
	2500 ppm	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	5	5	5	0	0
	20000 ppm	5	5	5	5	5

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

Clinical sign	Group Name	Administration Week-day 1-1 1	1-3 1	1-7 1	2-3 1	2-7 1
DEATH	Control	0	0	0	0	0
	1250 ppm	0	0	0	0	0
	2500 ppm	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	0	0
	20000 ppm	0	0	0	1	5
HUNCHBACK POSITION	Control	0	0	0	0	0
	1250 ppm	0	0	0	0	0
	2500 ppm	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	0	0
	20000 ppm	0	0	1	1	0
WASTING	Control	0	0	0	0	0
	1250 ppm	0	0	0	0	0
	2500 ppm	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	0	0
	20000 ppm	0	0	0	4	0
COLORED	Control	0	0	0	0	0
	1250 ppm	0	0	0	0	4
	2500 ppm	0	0	0	2	5
	5000 ppm	0	0	0	5	5
	10000 ppm	0	5	5	5	5
	20000 ppm	0	5	5	4	0
PILOERECTION	Control	0	0	0	0	0
	1250 ppm	0	0	0	0	0
	2500 ppm	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	0	0
	20000 ppm	0	0	5	4	0
SOILED PERI GENITALIA	Control	0	0	0	0	0
	1250 ppm	0	0	0	0	0
	2500 ppm	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	0	0
	20000 ppm	0	0	5	4	0

Clinical sign	Group Name	Administration Week-day 1-1 1	1-3 1	1-7 1	2-3 1	2-7 1
YELLOW URINE	Control	0	0	0	0	0
	1250 ppm	0	0	0	4	5
	2500 ppm	0	0	0	5	5
	5000 ppm	0	0	0	5	5
	10000 ppm	0	0	1	5	5
	20000 ppm	0	5	5	4	0
OLIGO-STOOL	Control	0	0	0	0	0
	1250 ppm	0	0	0	0	0
	2500 ppm	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	5	5	5	0	0
	20000 ppm	5	5	5	4	0

APPENDIX B 1

BODY WEIGHT CHANGES : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0360
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	1-1	1-3	1-7	2-3	2-7
Control	130± 4	136± 3	144± 4	161± 4	178± 5	192± 4
1250 ppm	129± 4	133± 5	142± 6	160± 5	176± 6	190± 5
2500 ppm	130± 4	131± 3	141± 4	159± 4	174± 6	190± 6
5000 ppm	129± 5	125± 3**	134± 3**	153± 4	168± 5	184± 5
10000 ppm	129± 4	120± 4**	120± 4**	135± 5**	145± 4**	157± 3**
20000 ppm	129± 4	116± 3**	108± 3**	102± 6**	99± 9**	87± 10**

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. : 0360
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	1-1	1-3	1-7	2-3	2-7
Control	98± 3	99± 4	103± 6	111± 5	119± 5	126± 6
1250 ppm	98± 3	100± 5	103± 4	111± 4	118± 5	123± 7
2500 ppm	98± 3	97± 4	102± 4	109± 5	112± 7	120± 8
5000 ppm	98± 3	93± 3*	97± 4	105± 5	112± 5	118± 5
10000 ppm	98± 2	90± 2**	88± 2**	95± 2**	98± 4**	107± 6**
20000 ppm	98± 4	88± 5**	79± 5**	69± 5**	61± 6**	-

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. : 0360
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	13.8± 0.2	14.0± 0.6	14.7± 0.4	13.9± 0.2
1250 ppm	12.9± 0.5	13.4± 0.7	14.2± 0.8	14.1± 0.7
2500 ppm	11.8± 0.6**	13.0± 0.5*	14.1± 0.8	14.2± 0.6
5000 ppm	8.8± 0.6**	12.0± 0.4**	13.6± 0.4	14.1± 0.9
10000 ppm	6.3± 0.6**	9.7± 0.6**	10.5± 0.5**	11.5± 0.6
20000 ppm	5.5± 1.3**	6.3± 0.8**	6.9± 1.4**	7.8± 1.9*

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. : 0360
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	9.7± 0.6	10.2± 0.5	10.7± 0.4	10.1± 0.4
1250 ppm	9.2± 0.4	9.6± 0.5	9.7± 0.6	9.7± 0.6
2500 ppm	8.5± 0.4	9.1± 0.7	8.9± 1.0	9.4± 0.9
5000 ppm	7.2± 0.8*	8.7± 0.7	9.2± 0.7	9.2± 0.6
10000 ppm	8.5± 8.7*	6.7± 0.4**	6.8± 0.4**	7.8± 0.4**
20000 ppm	8.5± 7.1	6.2± 1.8**	9.6± 1.8	-

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. : 0360
ANIMAL : RAT F344/DuCrj
UNIT : mg/kg/day
REPORT TYPE : A1 2
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2
Control	0.000± 0.000	0.000± 0.000
1250 ppm	104.619± 3.495	92.523± 3.307
2500 ppm	204.014± 6.034	186.475± 5.544
5000 ppm	393.469± 7.635	383.459± 17.661
10000 ppm	714.559± 19.160	729.282± 42.825
20000 ppm	1245.493±211.429	1838.292±634.463

APPENDIX D 2

CHEMICAL INTAKE CHANGES : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0360
ANIMAL : RAT F344/DuCrj
UNIT : mg/kg/day
REPORT TYPE : A1 2
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2
Control	0.000± 0.000	0.000± 0.000
1250 ppm	108.059± 2.452	98.423± 2.684
2500 ppm	209.425± 7.183	196.728± 9.246
5000 ppm	415.143± 18.409	391.529± 16.011
10000 ppm	708.988± 58.196	730.714± 27.128
20000 ppm	1781.984±416.691	-

APPENDIX E 1

HEMATOLOGY : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0360
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	7.82± 0.14	14.4± 0.2	43.6± 0.9	55.8± 0.4	18.4± 0.2	33.0± 0.2	875± 32
1250 ppm	5	7.88± 0.28	14.3± 0.4	43.5± 1.6	55.2± 0.2	18.1± 0.2	32.8± 0.5	866± 73
2500 ppm	5	7.45± 0.28	13.6± 0.5	41.7± 1.5	56.0± 0.3	18.3± 0.2	32.6± 0.3	986± 25**
5000 ppm	5	6.32± 0.25**	12.1± 0.4**	38.2± 1.2**	60.5± 1.0	19.2± 0.4**	31.6± 0.8**	1098± 43**
10000 ppm	4	5.79± 0.26**	11.6± 0.5**	36.3± 1.0**	62.8± 1.3*	20.0± 0.5**	31.9± 0.4*	1056± 55**
20000 ppm	5	5.66± 0.33**	11.3± 0.7**	31.8± 2.7**	56.0± 1.5	20.0± 0.3**	35.8± 0.8**	619± 33**

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

STUDY NO. : 0360
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	26± 6	0.3± 0.1	14.0± 0.2	18.4± 2.8
1250 ppm	5	31± 6	0.3± 0.1	14.1± 0.2	15.9± 2.9
2500 ppm	5	38± 5	0.4± 0.1	14.1± 0.5	16.8± 2.4
5000 ppm	5	107± 12	0.5± 0.5	13.5± 0.2	14.3± 2.7
10000 ppm	4	194± 25**	0.7± 0.5	14.1± 0.3	11.9± 1.1*
20000 ppm	5	238± 92**	1.4± 1.0	16.0± 0.5**	21.9± 5.8

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

STUDY NO. : 0360
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	3.01± 0.52	0± 0	10± 4	1± 1	0± 0	1± 0	87± 4	0± 0
1250 ppm	5	3.47± 1.31	0± 1	13± 1	0± 1	0± 0	1± 1	85± 1	0± 0
2500 ppm	5	4.47± 0.97	0± 0	11± 3	1± 1	0± 0	2± 3	87± 4	0± 0
5000 ppm	5	4.23± 0.38	1± 1	16± 4	1± 1	0± 0	2± 1	81± 3	0± 0
10000 ppm	4	5.96± 1.90*	0± 1	21± 7	0± 0	0± 0	4± 4	75± 9	0± 0
20000 ppm	5	2.92± 0.59	1± 1	40± 18**	0± 0	0± 0	1± 1	57± 18**	0± 0

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

APPENDIX E 2

HEMATOLOGY : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0360
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±	0.26	15.2±	0.5	44.4±	1.2	54.1±	0.4	18.5±	0.2	34.2±	0.3	871±	49
1250 ppm	5	8.02±	0.11	14.8±	0.3	43.3±	0.4	53.9±	0.3	18.5±	0.2	34.3±	0.4	815±	75
2500 ppm	5	7.52±	0.29**	13.6±	0.7**	40.6±	1.6	53.9±	0.4	18.1±	0.2	33.6±	0.4	852±	63
5000 ppm	5	6.15±	0.23**	11.5±	0.5**	36.0±	1.4**	58.6±	0.4	18.8±	0.2	32.0±	0.6**	894±	48
10000 ppm	5	5.75±	0.28**	11.1±	0.7**	34.9±	2.6**	60.6±	1.6*	19.3±	0.3**	31.8±	0.6**	971±	56*
20000 ppm	0	-		-		-		-		-		-		-	

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

STUDY NO. : 0360
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	22±	9	0.2±	0.1	15.1±	0.2	20.7±	5.5
1250 ppm	5	22±	7	0.2±	0.1	14.7±	0.1	15.4±	2.9
2500 ppm	5	32±	13	0.3±	0.1	14.7±	0.4	16.6±	4.1
5000 ppm	5	111±	18*	0.7±	0.4	14.4±	0.5*	16.8±	2.9
10000 ppm	5	199±	41**	0.8±	0.4	15.2±	0.2	29.0±	8.7
20000 ppm	0	-		-		-		-	

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

STUDY NO. : 0360
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	4.08± 0.86	0± 0	14± 2	0± 1	0± 0	2± 2	83± 3	0± 1
1250 ppm	5	3.68± 0.93	0± 0	9± 5	2± 1	0± 0	2± 0	87± 6	0± 0
2500 ppm	5	5.07± 3.14	0± 1	15± 5	1± 1	0± 0	1± 1	83± 6	0± 0
5000 ppm	5	4.57± 1.20	1± 1	15± 4	1± 1	0± 0	1± 0	81± 3	0± 1
10000 ppm	5	4.05± 1.00	1± 1	13± 2	0± 1	0± 0	1± 1	84± 3	0± 1
20000 ppm	0	-	-	-	-	-	-	-	-

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

APPENDIX F 1

BIOCHEMISTRY : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0360
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	5.6±	0.1	3.6±	0.1	1.9±	0.0	0.12±	0.01	178±	11	64±	3	123±	5
1250 ppm	5	5.6±	0.2	3.7±	0.1	1.9±	0.1	0.12±	0.02	202±	16	63±	4	120±	6
2500 ppm	5	5.9±	0.1	3.8±	0.1	1.8±	0.1	0.13±	0.01	183±	12	74±	3	142±	5
5000 ppm	5	6.3±	0.3**	4.0±	0.2*	1.8±	0.0	0.15±	0.02*	179±	10	98±	8	180±	14
10000 ppm	4	6.6±	0.4**	4.2±	0.3*	1.8±	0.1	0.22±	0.02**	152±	2	141±	13**	255±	24**
20000 ppm	5	6.8±	0.2**	4.6±	0.2**	2.1±	0.1**	0.24±	0.02**	97±	22*	143±	23**	249±	43**

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

STUDY NO. : 0360
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	55±	2	29±	1	207±	77	2±	1	176±	59	14.8±	1.7	0.4±	0.0
1250 ppm	5	57±	3	28±	2	185±	70	2±	1	190±	87	16.5±	1.9	0.4±	0.1
2500 ppm	5	52±	3	29±	2	175±	66	2±	1	160±	41	15.6±	2.4	0.4±	0.1
5000 ppm	5	51±	1	29±	2	153±	33	2±	0	128±	14	16.5±	2.2	0.4±	0.0
10000 ppm	4	43±	3*	28±	5	168±	40	7±	1	123±	11	17.9±	1.0	0.4±	0.0
20000 ppm	5	90±	56	104±	79*	304±	137	53±	28	112±	55*	37.2±	9.2**	0.4±	0.0

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

STUDY NO. : 0360
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	140±	1	4.1±	0.3	105±	1	10.9±	0.1	7.7±	1.2
1250 ppm	5	140±	1	4.0±	0.2	104±	1	10.9±	0.2	7.8±	1.2
2500 ppm	5	139±	1	4.3±	0.3	104±	0	11.0±	0.1	8.6±	1.2
5000 ppm	5	140±	1	4.5±	0.2	102±	1*	11.3±	0.1*	9.7±	1.6*
10000 ppm	4	138±	2	5.3±	0.3**	101±	1**	11.4±	0.2**	9.5±	0.8
20000 ppm	5	143±	1**	4.8±	0.7*	105±	2	10.8±	0.3	6.8±	0.5

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

APPENDIX F 2

BIOCHEMISTRY : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0360
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	5.4± 0.1	3.6± 0.1	1.9± 0.1	0.12± 0.00	173± 12	69± 2	125± 6
1250 ppm	5	5.4± 0.2	3.5± 0.1	1.9± 0.1	0.13± 0.01	177± 14	68± 4	124± 10
2500 ppm	5	5.4± 0.1	3.5± 0.1	1.9± 0.1	0.14± 0.01	174± 12	73± 6	133± 11
5000 ppm	5	5.8± 0.2**	3.8± 0.2	1.9± 0.1	0.18± 0.02**	160± 13	105± 7**	177± 8**
10000 ppm	5	6.4± 0.1**	4.2± 0.1**	1.9± 0.1	0.22± 0.04**	145± 4**	141± 2**	235± 6**
20000 ppm	0	-	-	-	-	-	-	-

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

STUDY NO. : 0360
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	59± 4	28± 1	246± 54	2± 1	153± 29	16.9± 3.4	0.4± 0.1
1250 ppm	5	63± 5	30± 3	358± 198	3± 1	183± 66	17.4± 2.8	0.4± 0.1
2500 ppm	5	64± 6	29± 3	346± 94	3± 1	183± 45	18.8± 3.5	0.4± 0.1
5000 ppm	5	58± 4	28± 3	333± 141	3± 1	161± 43	20.4± 1.5	0.4± 0.0
10000 ppm	5	59± 4	31± 5	498± 230	13± 1**	192± 52	20.4± 2.7	0.4± 0.0
20000 ppm	0	-	-	-	-	-	-	-

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

STUDY NO. : 0360
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	139±	1	4.1±	0.4	106±	1	10.5±	0.1	7.0±	1.1
1250 ppm	5	139±	1	4.3±	0.6	106±	2	10.5±	0.1	7.1±	1.5
2500 ppm	5	139±	1	4.0±	0.4	107±	3	10.4±	0.1	6.3±	1.6
5000 ppm	5	138±	1	4.7±	0.4	105±	2	10.8±	0.2*	7.9±	1.9
10000 ppm	5	139±	1	5.1±	0.7*	105±	2	11.0±	0.1**	7.9±	0.9
20000 ppm	0	-		-		-		-		-	

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. : 0360
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 (%)	1250 ppm 5 (%)	2500 ppm 5 (%)	5000 ppm 5 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
spleen	dark		0 (0)	0 (0)	0 (0)	5 (100)
liver	dark		0 (0)	0 (0)	0 (0)	0 (0)
	herniation		0 (0)	1 (20)	0 (0)	0 (0)

Organ	Findings	Group Name NO. of Animals	10000 ppm 5 (%)	20000 ppm 5 (%)
thymus	atrophic		0 (0)	5 (100)
spleen	dark		4 (80)	5 (100)
liver	dark		0 (0)	5 (100)
	herniation		0 (0)	0 (0)

APPENDIX G 2

GROSS FINDINGS : SUMMARY, RAT : FEMALE ALL ANIMALS

(2-WEEK STUDY)

Organ	Findings	Group Name / NO. of Animals	Control 5 (%)	1250 ppm 5 (%)	2500 ppm 5 (%)	5000 ppm 5 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
spleen	dark		0 (0)	0 (0)	0 (0)	5 (100)
liver	herniation		0 (0)	2 (40)	0 (0)	0 (0)

Organ	Findings	Group Name NO. of Animals	10000 ppm 5 (%)	20000 ppm 5 (%)
thymus	atrophic		0 (0)	5 (100)
spleen	dark		4 (80)	0 (0)
liver	herniation		0 (0)	0 (0)

APPENDIX G 3

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

(2-WEEK STUDY)

STUDY NO. : 0360
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name / NO. of Animals	Control 0 (%)	1250 ppm 0 (%)	2500 ppm 0 (%)	5000 ppm 0 (%)
thymus	atrophic		- (-)	- (-)	- (-)	- (-)

STUDY NO. : 0360
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name NO. of Animals	10000 ppm 0 (%)	20000 ppm 5 (%)
thymus	atrophic		- (-)	5 (100)

APPENDIX G 4

GROSS FINDINGS : SUMMARY, RAT : MALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0360
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name / NO. of Animals	Control 5 (%)	1250 ppm 5 (%)	2500 ppm 5 (%)	5000 ppm 5 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
spleen	dark		0 (0)	0 (0)	0 (0)	5 (100)
liver	dark		0 (0)	0 (0)	0 (0)	0 (0)
	herniation		0 (0)	1 (20)	0 (0)	0 (0)

STUDY NO. : 0360
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name NO. of Animals	10000 ppm 5 (%)	20000 ppm 5 (%)
thymus	atrophic		0 (0)	5 (100)
spleen	dark		4 (80)	5 (100)
liver	dark		0 (0)	5 (100)
	herniation		0 (0)	0 (0)

APPENDIX G 5

GROSS FINDINGS : SUMMARY, RAT : FEMALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0360
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name NO. of Animals	Control 5 (%)	1250 ppm 5 (%)	2500 ppm 5 (%)	5000 ppm 5 (%)
spleen	dark		0 (0)	0 (0)	0 (0)	5 (100)
liver	herniation		0 (0)	2 (40)	0 (0)	0 (0)

STUDY NO. : 0360
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name NO. of Animals	10000 ppm 5 (%)	20000 ppm 0 (%)
spleen	dark		4 (80)	- (-)
liver	herniation		0 (0)	- (-)

APPENDIX H 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0360
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	192± 4	0.361± 0.019	0.045± 0.003	2.469± 0.110	0.662± 0.046	0.839± 0.020
1250 ppm	5	190± 5	0.354± 0.031	0.044± 0.004	2.465± 0.078	0.692± 0.028	0.818± 0.046
2500 ppm	5	190± 6	0.360± 0.030	0.043± 0.004	2.482± 0.124	0.697± 0.042	0.825± 0.033
5000 ppm	5	184± 5	0.349± 0.032	0.046± 0.004	2.567± 0.134	0.691± 0.062	0.819± 0.023
10000 ppm	5	157± 3**	0.282± 0.018**	0.046± 0.004	2.472± 0.111	0.562± 0.020**	0.767± 0.098
20000 ppm	5	87± 10**	0.039± 0.016**	0.043± 0.003	1.545± 0.387	0.369± 0.049**	0.540± 0.031**

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

STUDY NO. : 0360
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	1.473± 0.059	0.483± 0.028	7.582± 0.408	1.716± 0.042
1250 ppm	5	1.459± 0.025	0.472± 0.018	7.648± 0.380	1.726± 0.029
2500 ppm	5	1.575± 0.102	0.539± 0.040	8.612± 0.378	1.759± 0.062
5000 ppm	5	1.725± 0.079**	0.820± 0.065**	9.830± 0.353*	1.752± 0.061
10000 ppm	5	1.577± 0.105	0.858± 0.078**	10.952± 1.061**	1.678± 0.054
20000 ppm	5	1.204± 0.106**	0.381± 0.041*	6.960± 1.232	1.616± 0.022*

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. : 0360
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	126± 6	0.286± 0.020	0.050± 0.005	0.105± 0.015	0.499± 0.020	0.646± 0.046
1250 ppm	5	123± 7	0.293± 0.014	0.052± 0.008	0.098± 0.007	0.484± 0.030	0.647± 0.036
2500 ppm	5	120± 8	0.280± 0.026	0.049± 0.006	0.097± 0.015	0.480± 0.046	0.615± 0.031
5000 ppm	5	118± 5	0.271± 0.022	0.044± 0.006	0.095± 0.020	0.491± 0.027	0.628± 0.043
10000 ppm	5	107± 6**	0.248± 0.021*	0.042± 0.004	0.064± 0.009**	0.424± 0.026**	0.573± 0.022*
20000 ppm	0	-	-	-	-	-	-

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

STUDY NO. : 0360
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	1.006± 0.040	0.330± 0.026	4.462± 0.381	1.611± 0.039
1250 ppm	5	1.021± 0.079	0.340± 0.024	4.485± 0.233	1.619± 0.024
2500 ppm	5	1.026± 0.059	0.354± 0.027	4.767± 0.496	1.637± 0.024
5000 ppm	5	1.076± 0.089	0.606± 0.054**	6.022± 0.363**	1.618± 0.070
10000 ppm	5	1.045± 0.066	0.580± 0.028**	7.019± 0.509**	1.606± 0.025
20000 ppm	0	-	-	-	-

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. : 0360
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	192± 4	0.188± 0.007	0.023± 0.002	1.287± 0.032	0.345± 0.019	0.438± 0.015
1250 ppm	5	190± 5	0.186± 0.011	0.023± 0.001	1.296± 0.029	0.364± 0.007	0.430± 0.016
2500 ppm	5	190± 6	0.189± 0.015	0.023± 0.003	1.304± 0.054	0.366± 0.016	0.433± 0.007
5000 ppm	5	184± 5	0.190± 0.017	0.025± 0.002	1.396± 0.059	0.376± 0.025	0.446± 0.009
10000 ppm	5	157± 3**	0.179± 0.014	0.029± 0.002	1.572± 0.051*	0.358± 0.019	0.487± 0.055
20000 ppm	5	87± 10**	0.043± 0.013**	0.050± 0.008**	1.755± 0.298*	0.422± 0.024**	0.624± 0.059*

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

STUDY NO. : 0360
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	0.769± 0.034	0.252± 0.015	3.954± 0.207	0.895± 0.029
1250 ppm	5	0.767± 0.017	0.248± 0.011	4.021± 0.158	0.908± 0.024
2500 ppm	5	0.827± 0.035	0.283± 0.015	4.524± 0.171	0.924± 0.025
5000 ppm	5	0.938± 0.030**	0.446± 0.029**	5.350± 0.210	0.953± 0.033
10000 ppm	5	1.003± 0.052**	0.545± 0.040**	6.963± 0.607**	1.067± 0.024*
20000 ppm	5	1.385± 0.057**	0.438± 0.040**	7.943± 0.613**	1.869± 0.186**

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. : 0360
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	126± 6	0.226± 0.013	0.040± 0.004	0.083± 0.014	0.396± 0.021	0.512± 0.019
1250 ppm	5	123± 7	0.238± 0.019	0.042± 0.005	0.079± 0.007	0.393± 0.025	0.525± 0.017
2500 ppm	5	120± 8	0.234± 0.015	0.041± 0.004	0.081± 0.008	0.400± 0.017	0.514± 0.024
5000 ppm	5	118± 5	0.230± 0.011	0.037± 0.005	0.080± 0.014	0.416± 0.017	0.532± 0.021
10000 ppm	5	107± 6**	0.232± 0.011	0.040± 0.004	0.060± 0.006**	0.398± 0.022	0.538± 0.020
20000 ppm	0	-	-	-	-	-	-

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

STUDY NO. : 0360
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	0.798± 0.030	0.262± 0.016	3.532± 0.177	1.278± 0.051
1250 ppm	5	0.828± 0.031	0.276± 0.010	3.644± 0.160	1.317± 0.057
2500 ppm	5	0.857± 0.025*	0.296± 0.020	3.973± 0.194**	1.372± 0.097
5000 ppm	5	0.911± 0.047**	0.514± 0.046**	5.103± 0.189**	1.372± 0.046
10000 ppm	5	0.979± 0.032**	0.543± 0.026**	6.568± 0.190**	1.506± 0.058**
20000 ppm	0	-	-	-	-

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. : 0360
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control				1250 ppm				2500 ppm				5000 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
[Respiratory system]																		
nasal cavit			< 5>				< 5>				< 5>				< 5>			
	respiratory metaplasia:gland		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	engorgement of erythrocyte		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Hematopoietic system]																		
bone marrow			< 5>				< 5>				< 5>				< 5>			
	congestion		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(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
			(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	4	0	0	0	5	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(80)	(0)	(0)	(0)	(100)	(0)	(0)	(0)

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

Organ	Findings	Group Name	10000 ppm				20000 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		1	0	0	0	1	0	0	0
			(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	engorgement of erythrocyte		0	1	0	0	0	0	0	0
			(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)
[Hematopoietic system]										
bone marrow			< 5>				< 5>			
	congestion		0	0	0	0	2	1	0	0
			(0)	(0)	(0)	(0)	(40)	(20)	(0)	(0)
thymus			< 5>				< 5>			
	atrophy		0	0	0	0	0	0	5	0
			(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)
spleen			< 5>				< 5>			
	deposit of hemosiderin		2	0	0	0	5	0	0	0
			(40)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	extramedullary hematopoiesis		5	0	0	0	0	0	0	0
			(100)	(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				1250 ppm				2500 ppm				5000 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
[Hematopoietic system]																		
spleen			< 5>				< 5>				< 5>				< 5>			
	engorgement of erythrocyte		0	0	0	0	0	0	0	0	4	0	0	0	5	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(80)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
[Digestive system]																		
liver			< 5>				< 5>				< 5>				< 5>			
	herniation		0	0	0	0	1	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)
	necrosis:focal		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hepatocellular hypertrophy:central		0	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(60)	(0)	(0)	(0)
[Urinary system]																		
kidney			< 5>				< 5>				< 5>				< 5>			
	basophilic change		1	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)	(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	10000 ppm				20000 ppm			
		No. of Animals on Study	5				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
spleen			< 5>				< 5>			
	engorgement of erythrocyte		5	0	0	0	5	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
[Digestive system]										
liver			< 5>				< 5>			
	herniation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:focal		0	0	0	0	0	3	0	0
			(0)	(0)	(0)	(0)	(0)	(60)	(0)	(0)
	hepatocellular hypertrophy:central		5	0	0	0	0	0	0	0
			(100)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Urinary system]										
kidney			< 5>				< 5>			
	basophilic change		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				1250 ppm				2500 ppm				5000 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>			
	eosinophilic body		4	0	0	0	5	0	0	0	0	5	0	0	0	2	3	0
			(80)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(40)	(60)	(0)
	mineralization:cortico-medullary junction		1	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)	(0)	(0)	(0)	(0)
[Endocrine system]																		
pituitary			< 5>				< 5>				< 5>				< 5>			
	Rathke pouch		2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(40)	(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)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
epididymis			< 5>				< 5>				< 5>				< 5>			
	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)	(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	10000 ppm				20000 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	2	3	0	3	0	0	0
			(0)	(40)	(60)	(0)	(60)	(0)	(0)	(0)
	mineralization:cortico-medullary junction		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Endocrine system]										
pituitary			< 5>				< 5>			
	Rathke pouch		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Reproductive system]										
testis			< 5>				< 5>			
	germ cell necrosis		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(40)	(0)	(0)	(0)
epididymis			< 5>				< 5>			
	debris of spermatic elements		0	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(60)	(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				1250 ppm				2500 ppm				5000 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
[Special sense organs/appendage]																		
Harder gl			< 5>				< 5>				< 5>				< 5>			
	degeneration		0	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	lymphocytic infiltration		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)	(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

Organ	Findings	Group Name	10000 ppm				20000 ppm			
		No. of Animals on Study	5				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Special sense organs/appendage]										
Harder gl			< 5>				< 5>			
	degeneration		4	1	0	0	0	5	0	0
			(80)	(20)	(0)	(0)	(0)	(100)	(0)	(0)
	lymphocytic infiltration		1	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

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				1250 ppm 5				2500 ppm 5				5000 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		0 (0)	0 (0)	0 (0)	0 (0)	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>																
	congestion		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	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>																
	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)
	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)	1 (20)	0 (0)	0 (0)	0 (0)	5 (100)	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	10000 ppm				20000 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	1	0	0	0	0	0	0
			(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)
[Hematopoietic system]										
bone marrow			< 5>				< 5>			
	congestion		0	0	0	0	0	5	0	0
			(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
thymus			< 5>				< 5>			
	atrophy		0	0	0	0	0	0	5	0
			(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)
spleen			< 5>				< 5>			
	atrophy		0	0	0	0	0	5	0	0
			(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
	deposit of hemosiderin		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(40)	(0)	(0)	(0)
	extramedullary hematopoiesis		5	0	0	0	0	0	0	0
			(100)	(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				1250 ppm				2500 ppm				5000 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
[Hematopoietic system]																		
spleen			< 5>				< 5>				< 5>				< 5>			
	engorgement of erythrocyte		0	0	0	0	0	0	0	0	5	0	0	0	5	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
[Digestive system]																		
liver			< 5>				< 5>				< 5>				< 5>			
	herniation		0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(40)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hepatocellular hypertrophy:central		0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(40)	(0)	(0)	(0)
[Urinary system]																		
kidney			< 5>				< 5>				< 5>				< 5>			
	basophilic change		0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	tubular necrosis		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

Organ	Findings	Group Name	10000 ppm				20000 ppm			
		No. of Animals on Study	5				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
spleen			< 5>				< 5>			
	engorgement of erythrocyte		5	0	0	0	3	0	0	0
			(100)	(0)	(0)	(0)	(60)	(0)	(0)	(0)
[Digestive system]										
liver			< 5>				< 5>			
	herniation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hepatocellular hypertrophy:central		4	0	0	0	0	0	0	0
			(80)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Urinary system]										
kidney			< 5>				< 5>			
	basophilic change		1	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	tubular necrosis		0	0	0	0	0	2	2	0
			(0)	(0)	(0)	(0)	(0)	(40)	(40)	(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				1250 ppm 5				2500 ppm 5				5000 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>			
	mineralization:cortico-medullary junction		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)
	mineralization:papilla		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	mineralization:cortex		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)
[Endocrine system]																		
pituitary			< 5>				< 5>				< 5>				< 5>			
	Rathke pouch		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)
thyroid			< 5>				< 5>				< 5>				< 5>			
	ultimibranchial body remanet		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Special sense organs/appendage]																		
Harder gl			< 5>				< 5>				< 5>				< 5>			
	degeneration		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)

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	10000 ppm				20000 ppm			
		No. of Animals on Study	5				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]										
kidney			< 5>				< 5>			
	mineralization:cortico-medullary junction		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:papilla		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:cortex		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Endocrine system]										
pituitary			< 5>				< 5>			
	Rathke pouch		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thyroid			< 5>				< 5>			
	ultimibranchial body remanet		1	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Special sense organs/appendage]										
Harder gl			< 5>				< 5>			
	degeneration		2	0	0	0	0	3	0	0
			(40)	(0)	(0)	(0)	(0)	(60)	(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				1250 ppm				2500 ppm				5000 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Special sense organs/appendage]																		
Harder gl			< 5>				< 5>				< 5>				< 5>			
	lymphocytic infiltration		0	0	0	0	0	0	0	0	0	0	0	0	2	2	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(40)	(40)	(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	10000 ppm				20000 ppm			
		No. of Animals on Study	5				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Special sense organs/appendage]										
Harder gl			< 5>				< 5>			
	lymphocytic infiltration		5	0	0	0	0	0	0	0
			(100)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

APPENDIX J 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0360
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 0 1 (%)	Control 0 2 (%)	Control 0 3 (%)	Control 0 4 (%)	1250 ppm 0 1 (%)	1250 ppm 0 2 (%)	1250 ppm 0 3 (%)	1250 ppm 0 4 (%)	2500 ppm 0 1 (%)	2500 ppm 0 2 (%)	2500 ppm 0 3 (%)	2500 ppm 0 4 (%)	5000 ppm 0 1 (%)	5000 ppm 0 2 (%)	5000 ppm 0 3 (%)	5000 ppm 0 4 (%)
[Hematopoietic system]																		
bone marrow		< a >	< 0>				< 0>				< 0>				< 0>			
	congestion	b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
thymus		< a >	< 0>				< 0>				< 0>				< 0>			
	atrophy	b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
spleen		< a >	< 0>				< 0>				< 0>				< 0>			
	atrophy	b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	deposit of hemosiderin	b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	engorgement of erythrocyte	b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Urinary system]																		
kidney		< a >	< 0>				< 0>				< 0>				< 0>			
	tubular necrosis	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	10000 ppm				20000 ppm			
		No. of Animals on Study	0				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
bone marrow			< 0>				< 5>			
	congestion		-	-	-	-	0	5	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
thymus			< 0>				< 5>			
	atrophy		-	-	-	-	0	0	5	0
			(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)
spleen			< 0>				< 5>			
	atrophy		-	-	-	-	0	5	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
	deposit of hemosiderin		-	-	-	-	2	0	0	0
			(-)	(-)	(-)	(-)	(40)	(0)	(0)	(0)
	engorgement of erythrocyte		-	-	-	-	3	0	0	0
			(-)	(-)	(-)	(-)	(60)	(0)	(0)	(0)
[Urinary system]										
kidney			< 0>				< 5>			
	tubular necrosis		-	-	-	-	0	2	2	0
			(-)	(-)	(-)	(-)	(0)	(40)	(40)	(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				1250 ppm				2500 ppm				5000 ppm			
		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>			
	degeneration		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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	10000 ppm				20000 ppm			
		No. of Animals on Study	0				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Special sense organs/appendage]										
Harder gl			< 0>				< 5>			
	degeneration		-	-	-	-	0	3	0	0
			(-)	(-)	(-)	(-)	(0)	(60)	(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 4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0360
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control				1250 ppm				2500 ppm				5000 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
[Respiratory system]																		
nasal cavit			< 5>				< 5>				< 5>				< 5>			
	respiratory metaplasia:gland		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	engorgement of erythrocyte		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Hematopoietic system]																		
bone marrow			< 5>				< 5>				< 5>				< 5>			
	congestion		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(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
			(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	4	0	0	0	5	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(80)	(0)	(0)	(0)	(100)	(0)	(0)	(0)

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

Organ	Findings	Group Name	10000 ppm				20000 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		1	0	0	0	1	0	0	0
			(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	engorgement of erythrocyte		0	1	0	0	0	0	0	0
			(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)
[Hematopoietic system]										
bone marrow			< 5>				< 5>			
	congestion		0	0	0	0	2	1	0	0
			(0)	(0)	(0)	(0)	(40)	(20)	(0)	(0)
thymus			< 5>				< 5>			
	atrophy		0	0	0	0	0	0	5	0
			(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)
spleen			< 5>				< 5>			
	deposit of hemosiderin		2	0	0	0	5	0	0	0
			(40)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	extramedullary hematopoiesis		5	0	0	0	0	0	0	0
			(100)	(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 / No. of Animals on Study / Grade	Control 5				1250 ppm 5				2500 ppm 5				5000 ppm 5			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]																		
spleen		< 5>																
	engorgement of erythrocyte		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)
[Digestive system]																		
liver		< 5>																
	herniation		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)
	necrosis:focal		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hepatocellular hypertrophy:central		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (60)	0 (0)	0 (0)	0 (0)
[Urinary system]																		
kidney		< 5>																
	basophilic change		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)

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	10000 ppm				20000 ppm			
		No. of Animals on Study	5				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
spleen			< 5>				< 5>			
	engorgement of erythrocyte		5	0	0	0	5	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
[Digestive system]										
liver			< 5>				< 5>			
	herniation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:focal		0	0	0	0	0	3	0	0
			(0)	(0)	(0)	(0)	(0)	(60)	(0)	(0)
	hepatocellular hypertrophy:central		5	0	0	0	0	0	0	0
			(100)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Urinary system]										
kidney			< 5>				< 5>			
	basophilic change		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				1250 ppm				2500 ppm				5000 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>			
	eosinophilic body		4	0	0	0	5	0	0	0	0	5	0	0	0	2	3	0
			(80)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(40)	(60)	(0)
	mineralization:cortico-medullary junction		1	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)	(0)	(0)	(0)	(0)
[Endocrine system]																		
pituitary			< 5>				< 5>				< 5>				< 5>			
	Rathke pouch		2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(40)	(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)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
epididymis			< 5>				< 5>				< 5>				< 5>			
	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)	(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	10000 ppm				20000 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	2	3	0	3	0	0	0
			(0)	(40)	(60)	(0)	(60)	(0)	(0)	(0)
	mineralization:cortico-medullary junction		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Endocrine system]										
pituitary			< 5>				< 5>			
	Rathke pouch		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Reproductive system]										
testis			< 5>				< 5>			
	germ cell necrosis		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(40)	(0)	(0)	(0)
epididymis			< 5>				< 5>			
	debris of spermatic elements		0	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(60)	(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				1250 ppm				2500 ppm				5000 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Special sense organs/appendage]																		
Harder gl			< 5>				< 5>				< 5>				< 5>			
	degeneration		0	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	lymphocytic infiltration		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)	(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

Organ	Findings	Group Name	10000 ppm				20000 ppm			
		No. of Animals on Study	5				5			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Special sense organs/appendage]										
Harder gl			< 5>				< 5>			
	degeneration		4	1	0	0	0	5	0	0
			(80)	(20)	(0)	(0)	(0)	(100)	(0)	(0)
	lymphocytic infiltration		1	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

APPENDIX J 5

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 5				1250 ppm 5				2500 ppm 5				5000 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		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Hematopoietic system]																		
spleen		< 5>																
	extramedullary hematopoiesis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)	5 (100)	0 (0)	0 (0)	0 (0)
	engorgement of erythrocyte		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)
[Digestive system]																		
liver		< 5>																
	herniation		0 (0)	0 (0)	0 (0)	0 (0)	2 (40)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hepatocellular hypertrophy:central		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (40)	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	10000 ppm				20000 ppm			
		No. of Animals on Study	5				0			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
nasal cavit			< 5>				< 0>			
	respiratory metaplasia:gland		0	1	0	0	-	-	-	-
			(0)	(20)	(0)	(0)	(-)	(-)	(-)	(-)
[Hematopoietic system]										
spleen			< 5>				< 0>			
	extramedullary hematopoiesis		5	0	0	0	-	-	-	-
			(100)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
	engorgement of erythrocyte		5	0	0	0	-	-	-	-
			(100)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
[Digestive system]										
liver			< 5>				< 0>			
	herniation		0	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
	hepatocellular hypertrophy:central		4	0	0	0	-	-	-	-
			(80)	(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				1250 ppm 5				2500 ppm 5				5000 ppm 5			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Urinary system]																		
kidney		< 5>																
	basophilic change		0 (0)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)
	mineralization:cortico-medullary junction		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)
	mineralization:papilla		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	mineralization:cortex		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)
[Endocrine system]																		
pituitary		< 5>																
	Rathke pouch		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)
thyroid		< 5>																
	ultimibranchial body remanet		0 (0)	0 (0)	0 (0)	0 (0)	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	10000 ppm				20000 ppm			
		No. of Animals on Study	5				0			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]										
kidney			< 5>				< 0>			
	basophilic change		1	0	0	0	-	-	-	-
			(20)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
	mineralization:cortico-medullary junction		0	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
	mineralization:papilla		0	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
	mineralization:cortex		0	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
[Endocrine system]										
pituitary			< 5>				< 0>			
	Rathke pouch		0	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
thyroid			< 5>				< 0>			
	ultimibranchial body remanet		1	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

Organ	Findings	Group Name	Control				1250 ppm				2500 ppm				5000 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Special sense organs/appendage]																		
Harder gl			< 5>				< 5>				< 5>				< 5>			
	degeneration		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)	(20)	(0)	(0)	(0)
	lymphocytic infiltration		0	0	0	0	0	0	0	0	0	0	0	0	2	2	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(40)	(40)	(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	10000 ppm				20000 ppm			
		No. of Animals on Study	5				0			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Special sense organs/appendage]										
Harder gl			< 5>				< 0>			
	degeneration		2	0	0	0	-	-	-	-
			(40)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
	lymphocytic infiltration		5	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 K 1

IDENTITY AND IMPURITY OF p-NITROANISOLE

IN THE 2-WEEK FEED STUDY

IDENTITY AND IMPURITY OF p-NITROANISOLE IN THE 2-WEEK FEED STUDY

Test Substance : p-Nitroanisole (Kanto Chemical Co., Inc.)

Lot No. : 704S4061

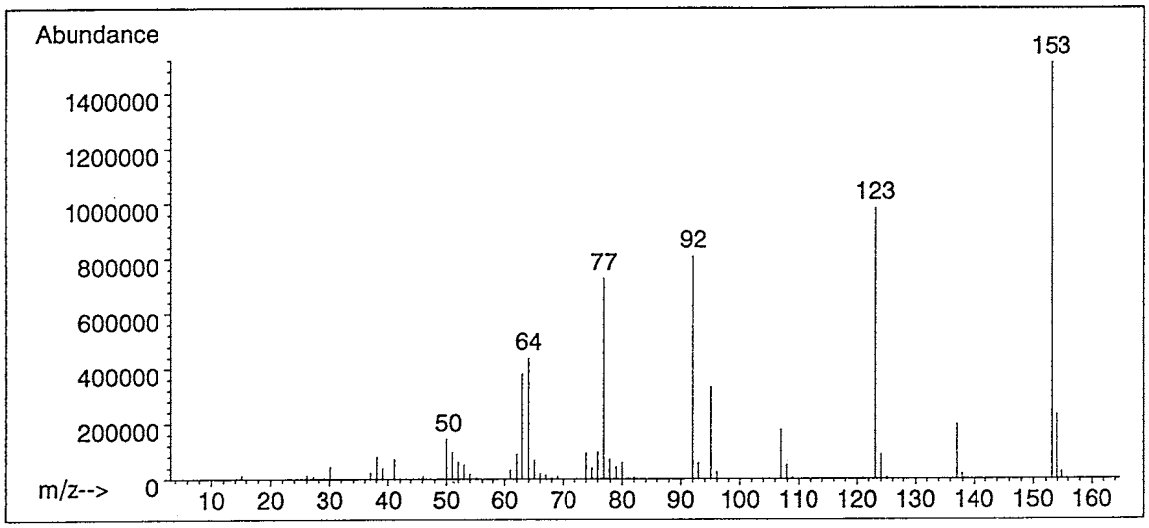
1. Spectral data

Mass Spectrometry

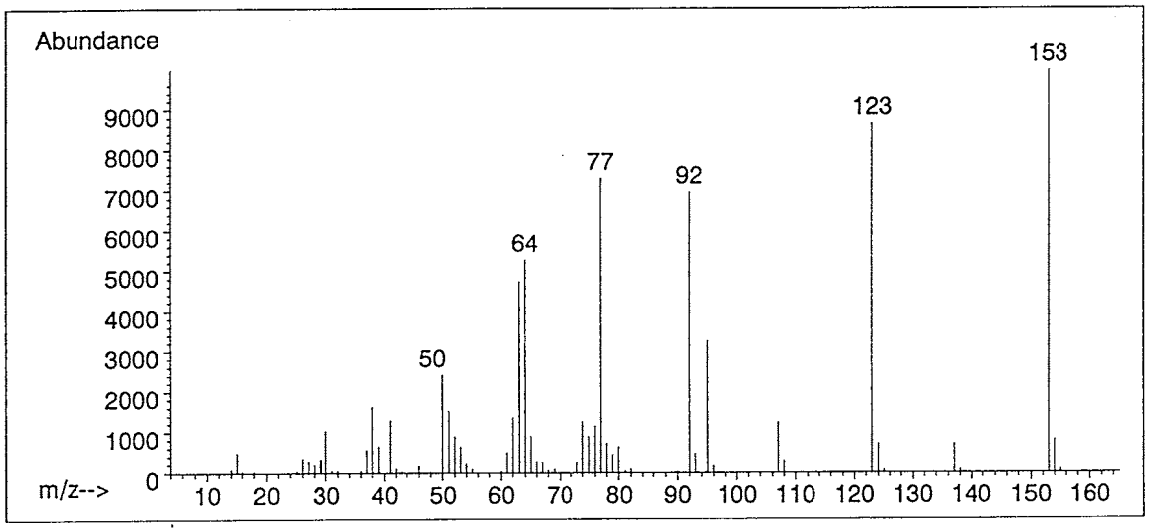
Instrument : Hewlett Packard 5989B Mass Spectrometer

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.

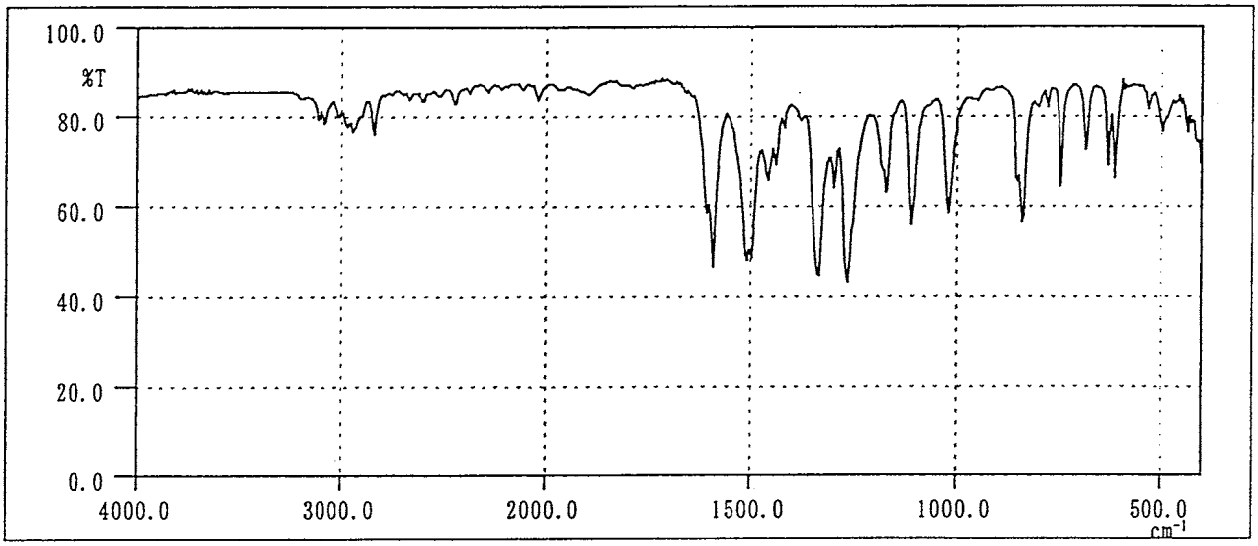
(*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition. John Wiley and Sons, Inc. (U.S.), Entry Number 38330)

Infrared Spectrometry

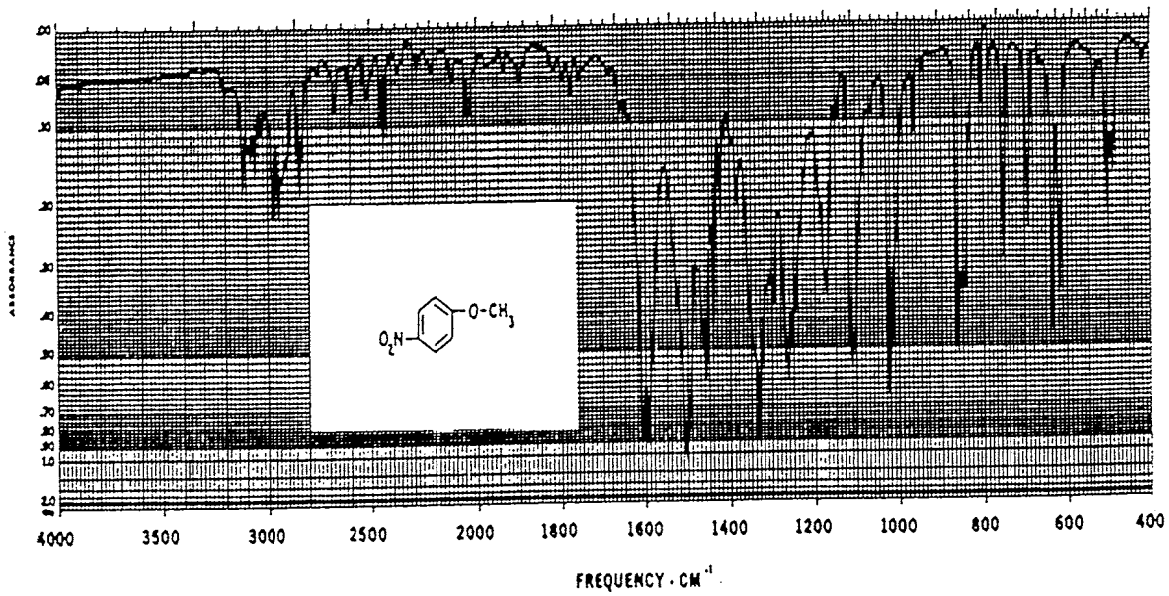
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 2.0 cm^{-1}



Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data*

Results: The infrared spectrum was consistent with literature spectrum.

(*William W. Simons (1978) The Sadtler Handbook of Infrared Spectra. Sadtler Research Laboratories, Inc. (U.K.), pp.443)

2. Impurity

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : INNOWAX (0.2 mmϕ × 50 m)

Column Temperature : 80 °C → (15 °C/min) → 280 °C (5 min)

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μL

Sample Name	Peak No.	Area (%)	Peak Name
Test Substance	1	0.14	m-Chloronitrobenzene
	2	0.11	p-Chloronitrobenzene
	3	0.01	o-Chloronitrobenzene
	4	99.74	p-Nitroanisole

Results: Gas chromatography indicated one major peak (peak No.4) and three impurities. It was identified only by comparing its gas chromatograph with that of m-chloronitrobenzene (peak No.1), p-chloronitrobenzene (peak No.2) and o-chloronitrobenzene (peak No.3) in the p-nitroanisole, the amount in the test substance were 0.14%, 0.11% and 0.01%.

3. Conclusions: The test substance was identified as p-nitroanisole, by the mass spectrum and the infrared spectrum. Gas chromatography indicated one major peak (peak No.4) and three impurities. It was identified only by comparing its gas chromatograph with that of m-chloronitrobenzene, p-chloronitrobenzene and o-chloronitrobenzene, the amount in the test substance were 0.14%, 0.11% and 0.01%.

APPENDIX K 2

STABILITY OF p-NITROANISOLE IN FEEDING OF RATS IN THE 2-WEEK FEED STUDY

STABILITY OF p-NITROANISOLE IN THE 2-WEEK FEED STUDY

Test Substance : p-Nitroanisole (Kanto Chemical Co., Inc.)

Lot No. : 704S4061

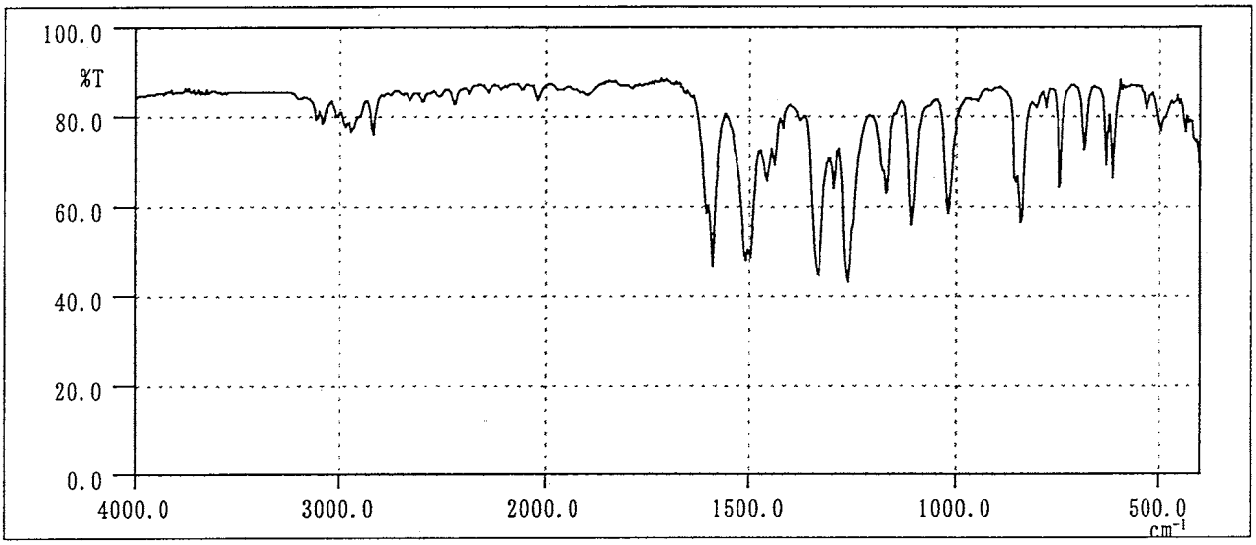
1. Sample : This lot was used from 1998.6.26 to 1998.7.10. Test substance was stored in a dark place at room temperature.

2. Infrared Spectrometry

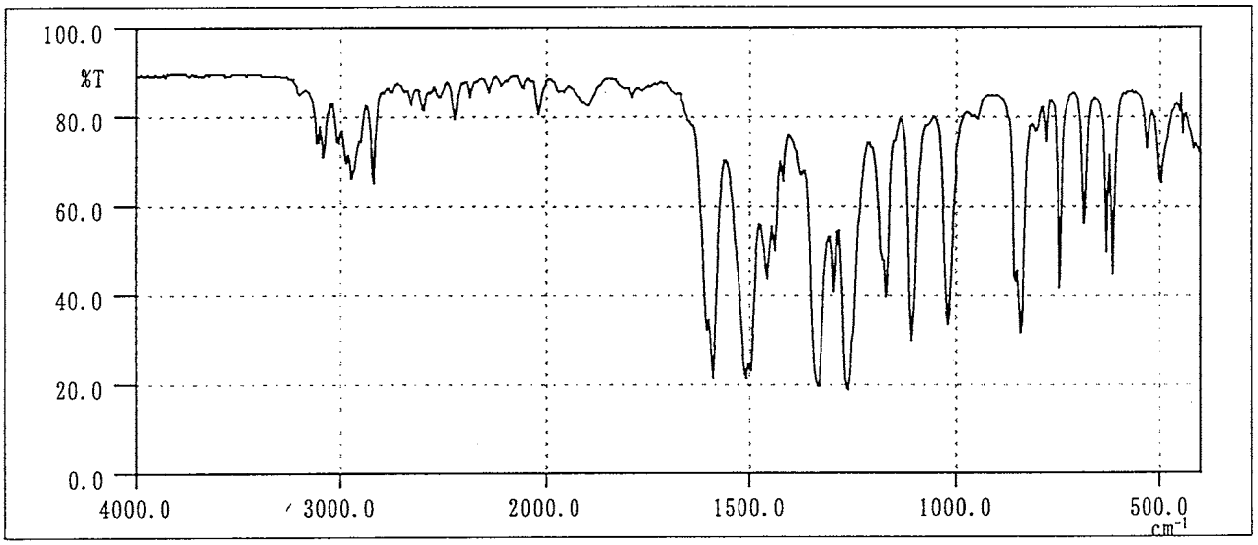
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 2.0 cm^{-1}



Infrared Spectrum of Test Substance (date analyzed : 1998.06.08)



Infrared Spectrum of Test Substance (date analyzed : 1998.07.27)

Results: The results of infrared spectrum did not change before and after the study.

3. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : INNOWAX (0.2 mmϕ × 50 m)

Column Temperature : 80 °C → (15 °C/min) → 280 °C (5 min)

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μL

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
1998.06.08	1	10.230	0.14
	2	10.518	0.11
	3	10.983	0.01
	4	13.106	99.74
1998.07.28	1	10.235	0.15
	2	10.521	0.12
	3	10.982	0.01
	4	13.127	99.72

Results: Gas chromatography indicated one major peak (peak No.4) and three impurities (peak No. 1, 2, 3 < 0.3% of total area) analyzed at 1998.6.8 and one major peak (peak No.4) and three impurities (peak No.1, 2, 3 < 0.3% of total area) analyzed at 1998.7.28. No new trace impurity peak in the test substance analyzed at 1998.7.28 was detected.

4. Conclusions: The test substance was stable for about 2 months in a dark place at room temperature.

APPENDIX K 3

CONCENTRATION OF p-NITROANISOLE IN FORMULATED DIETS IN THE 2-WEEK FEED STUDY

CONCENTRATION OF p-NITROANISOLE IN FORMULATED DIETS IN THE 2-WEEK FEED STUDY

	Target Concentration				
Date Analyzed	1250[a]	2500	5000	10000	20000
1998.06.25	1270 (102)[b]	2470 (98.8)	4930 (98.6)	9860 (98.6)	19500 (97.5)

[a] ppm
[b] %

Analytical method : The samples were analyzed by the 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
Flow Rate : 1 mL/min
Mobile Phase : Distilled Water : Acetonitrile = 1 : 1
Detector : UV (295 nm)
Injection Volume : 10 μL

APPENDIX K 4

STABILITY OF p-NITROANISOLE IN FORMULATED DIETS

IN THE 2-WEEK FEED STUDY

STABILITY OF p-NITROANISOLE IN FORMULATED DIETS IN THE 2-WEEK FEED STUDY

		Target Concentration	
Date Prepared	Date Analyzed	1250[a]	20000
1998.05.28	1998.05.28	1250 (100)[b]	19200 (100)
	1998.06.05[c]	1040 (83.2)	17900 (93.2)
	1998.06.05[d]	1260 (101)	19400 (101)

[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 the 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
Flow Rate : 1 mL/min
Mobile Phase : Distilled Water : Acetonitrile = 1 : 1
Detector : UV (295 nm)
Injection Volume : 10 μL

APPENDIX L 1

METHODS FOR HEMATOLOGY, BIOCHEMISTRY

IN THE 2-WEEK FEED STUDY OF p-NITROANISOLE

METHODS FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK FEED STUDY OF p-NITROANISOLE

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	Pattern recognition method [3] (New methyleneblue staining)
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 (Technicon H・1 : 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) 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 p-NITROANISOLE

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK FEED STUDY OF p-NITROANISOLE

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	‰	0
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 transminase (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