

p-ニトロアニソールのマウス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：0361

APPENDIX

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APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0361
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

PAGE : 1

Clinical sign	Group Name	Administration Week-day				
		1-1	1-3	1-7	2-3	2-7
		1	1	1	1	1
DEATH	Control	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	0	0
	20000 ppm	0	0	0	0	0
	40000 ppm	0	0	0	4	-
	50000 ppm	0	0	4	-	-
HUNCHBACK POSITION	Control	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	0	0
	20000 ppm	0	0	0	0	0
	40000 ppm	0	0	5	1	-
	50000 ppm	0	0	1	-	-
PILOERECTION	Control	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	0	0
	20000 ppm	0	0	0	0	0
	40000 ppm	0	0	5	1	-
	50000 ppm	0	0	1	-	-
YELLOW URINE	Control	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	5	5	5	5
	20000 ppm	0	5	5	5	5
	40000 ppm	0	5	5	1	-
	50000 ppm	0	5	1	-	-
SMALL STOOL	Control	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	0	0
	20000 ppm	0	0	0	0	0
	40000 ppm	0	0	5	1	-
	50000 ppm	0	0	1	-	-
OLIGO-STOOL	Control	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	0	0
	20000 ppm	0	0	0	0	0
	40000 ppm	0	5	5	1	-
	50000 ppm	0	5	1	-	-

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, MOUSE : FEMALE
(2-WEEK STUDY)

STUDY NO. : 0361
 ANIMAL : MOUSE Crj:BDF1
 REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : FEMALE

PAGE : 2

Clinical sign	Group Name	Administration Week-day				
		1-1	1-3	1-7	2-3	2-7
		1	1	1	1	1
DEATH	Control	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	0	0
	20000 ppm	0	0	0	0	0
	40000 ppm	0	0	4	-	-
	50000 ppm	0	1	-	-	-
HUNCHBACK POSITION	Control	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	0	0
	20000 ppm	0	0	0	0	0
	40000 ppm	0	2	1	-	-
	50000 ppm	0	0	-	-	-
PILOERECTION	Control	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	0	0
	20000 ppm	0	0	0	0	0
	40000 ppm	0	0	1	-	-
	50000 ppm	0	0	-	-	-
YELLOW URINE	Control	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	5	5	5	5
	20000 ppm	0	5	5	5	5
	40000 ppm	0	5	1	-	-
	50000 ppm	0	4	-	-	-
SMALL STOOL	Control	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	0	0
	20000 ppm	0	0	0	0	0
	40000 ppm	0	5	1	-	-
	50000 ppm	0	4	-	-	-
OLIGO-STOOL	Control	0	0	0	0	0
	5000 ppm	0	0	0	0	0
	10000 ppm	0	0	0	0	0
	20000 ppm	0	5	5	0	0
	40000 ppm	0	5	1	-	-
	50000 ppm	0	4	-	-	-

APPENDIX B 1

BODY WEIGHT CHANGES : SUMMARY, MOUSE : MALE
(2-WEEK STUDY)

STUDY NO. : 0361
 ANIMAL : MOUSE Crj:BDF1
 UNIT : g
 REPORT TYPE : A1 2
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 1

Group Name	Administration week-day					
	0-0	1-1	1-3	1-7	2-3	2-7
Control	23.7± 0.5	23.9± 0.5	24.1± 0.6	24.6± 0.6	25.3± 0.5	26.2± 0.7
5000 ppm	23.6± 0.8	23.3± 0.4	23.7± 0.6	24.0± 0.8	24.4± 0.5	25.5± 0.8
10000 ppm	23.7± 0.7	22.7± 0.6*	23.6± 0.7	24.3± 1.0	24.7± 0.7	26.0± 0.8
20000 ppm	23.6± 0.6	21.5± 0.5**	21.3± 0.5**	22.1± 0.4**	22.3± 1.4**	24.1± 0.9**
40000 ppm	23.6± 0.6	21.1± 0.7**	19.0± 0.5**	15.3± 0.6**	14.7± 0.4 ?	-
50000 ppm	23.6± 0.8	20.4± 0.9**	17.8± 1.3**	15.4± 0.0 ?	-	-

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

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

APPENDIX B 2

BODY WEIGHT CHANGES : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0361
 ANIMAL : MOUSE Crj:BDF1
 UNIT : g
 REPORT TYPE : A1 2
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 2

Group Name	Administration week-day					
	0-0	1-1	1-3	1-7	2-3	2-7
Control	17.8± 0.7	17.7± 1.2	17.6± 0.9	18.4± 1.2	18.7± 0.5	19.0± 0.9
5000 ppm	17.8± 0.7	17.0± 0.6	17.9± 0.5	18.0± 0.4	18.8± 0.7	19.7± 0.4
10000 ppm	17.8± 0.7	16.6± 0.8	17.9± 0.5	18.3± 0.8	18.8± 0.7	20.1± 0.7
20000 ppm	17.8± 0.7	15.9± 0.7**	15.8± 0.7**	16.8± 0.5*	17.8± 0.9	20.1± 1.0
40000 ppm	17.8± 0.6	15.3± 0.8**	12.7± 1.0**	10.9± 0.0 ?	-	-
50000 ppm	17.8± 0.7	15.1± 0.9**	12.3± 0.7**	-	-	-

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

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

APPENDIX C 1

FOOD CONSUMPTION CHANGES : SUMMARY, MOUSE : MALE (2-WEEK STUDY)

STUDY NO. : 0361
 ANIMAL : MOUSE Crj:BDF1
 UNIT : g
 REPORT TYPE : A1 2
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 1

Group Name	Administration week-day(effective)			
	1-3(3)	1-7(4)	2-3(3)	2-7(4)
Control	4.1± 0.5	4.0± 0.3	4.1± 0.3	4.1± 0.3
5000 ppm	3.2± 0.3	3.7± 0.1	3.7± 0.4	3.8± 0.2
10000 ppm	3.5± 0.3	4.1± 0.3	4.1± 0.3	4.1± 0.3
20000 ppm	2.3± 0.6*	3.7± 0.8	3.6± 0.8	3.9± 0.3
40000 ppm	2.0± 1.7**	3.4± 1.5	1.2± 0.0 ?	-
50000 ppm	2.2± 0.8*	1.4± 0.0 ?	-	-

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

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

APPENDIX C 2

FOOD CONSUMPTION CHANGES : SUMMARY, MOUSE : FEMALE (2-WEEK STUDY)

STUDY NO. : 0361
 ANIMAL : MOUSE Grj:BDF1
 UNIT : g
 REPORT TYPE : A1 2
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 2

Group Name	Administration week-day(effective)			
	1-3(3)	1-7(4)	2-3(3)	2-7(4)
Control	3.5± 0.3	3.6± 0.2	3.4± 0.4	3.3± 0.4
5000 ppm	3.8± 1.1	3.9± 1.2	3.8± 1.0	4.0± 0.9
10000 ppm	3.7± 0.8	3.8± 0.6	4.0± 0.7	4.0± 1.0
20000 ppm	3.2± 1.8	4.8± 1.5	5.2± 2.0	3.6± 0.6
40000 ppm	1.2± 0.6*	0.7± 0.0 ?	-	-
50000 ppm	0.9± 0.3*	-	-	-

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

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

APPENDIX D 1

CHEMICAL INTAKE CHANGES : SUMMARY, MOUSE : MALE
(2-WEEK STUDY)

STUDY NO. : 0361
ANIMAL : MOUSE Crj:BDF1
UNIT : g/kg/day
REPORT TYPE : A1 2
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

PAGE : 1

Group Name	Administration (weeks)	
	1	2
Control	0.000± 0.000	0.000± 0.000
5000 ppm	0.772± 0.019	0.749± 0.025
10000 ppm	1.668± 0.098	1.571± 0.098
20000 ppm	3.379± 0.679	3.265± 0.223
40000 ppm	8.903± 3.787	-
50000 ppm	4.545± 0.000	-

APPENDIX D 2

CHEMICAL INTAKE CHANGES : SUMMARY, MOUSE : FEMALE
(2-WEEK STUDY)

STUDY NO. : 0361
ANIMAL : MOUSE Crj:BDF1
UNIT : g/kg/day
REPORT TYPE : A1 2
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

PAGE : 2

Group Name	Administration (weeks)	
	1	2
Control	0.000± 0.000	0.000± 0.000
5000 ppm	1.087± 0.300	1.023± 0.224
10000 ppm	2.090± 0.290	1.991± 0.491
20000 ppm	5.643± 1.733	3.676± 0.361
40000 ppm	2.569± 0.000	-
50000 ppm	-	-

(HAN300)

BAIS3

APPENDIX E 1

HEMATOLOGY : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0361
 ANIMAL : MOUSE Crj:BDF1
 MEASURE. TIME : 1
 SEX : MALE

HEMATOLOGY (SUMMARY)
 ALL ANIMALS (2W)

REPORT TYPE : A1

PAGE : 1

Group Name	NO. of Animals	RED BLOOD CELL 10 ⁶ /μl		HEMOGLOBIN g/dl		HEMATOCRIT %		MCV fl		MCH pg		MCHC g/dl		PLATELET 10 ³ /μl	
Control	3	10.32±	0.63	15.9±	1.0	51.3±	2.7	49.8±	0.7	15.4±	0.1	30.9±	0.6	1237±	136
5000 ppm	5	10.52±	0.17	15.8±	0.4	52.1±	1.2	49.5±	0.6	15.0±	0.3*	30.3±	0.2	1210±	91
10000 ppm	5	10.01±	0.30	15.1±	0.6	49.2±	1.9	49.2±	0.5	15.0±	0.2*	30.6±	0.2	1243±	62
20000 ppm	5	10.40±	0.88	15.5±	0.6	50.3±	1.8	48.3±	0.3**	14.9±	0.2*	30.9±	0.3	1271±	112
40000 ppm	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-
50000 ppm	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS3

STUDY NO. : 0361
 ANIMAL : MOUSE Crj:BDF1
 MEASURE. TIME : 1
 SEX : MALE

REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
 ALL ANIMALS (2W)

PAGE : 2

Group Name	NO. of Animals	WBC 10 ³ /μl		Differential N-BAND		WBC (%) N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHER	
Control	3	3.06±	0.98	1±	2	13±	1	2±	2	0±	0	2±	1	82±	1	0±	0
5000 ppm	5	2.52±	1.38	1±	1	12±	5	1±	0	0±	0	2±	1	83±	5	0±	0
10000 ppm	5	2.37±	0.87	2±	1	12±	2	2±	1	0±	0	4±	3	80±	4	0±	0
20000 ppm	5	2.14±	1.22	2±	2	19±	4	2±	1	0±	0	5±	3	73±	7	0±	0
40000 ppm	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
50000 ppm	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Significant difference : * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 3

APPENDIX E 2

HEMATOLOGY : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0361
 ANIMAL : MOUSE Crj:BDF1
 MEASURE. TIME : 1
 SEX : FEMALE

HEMATOLOGY (SUMMARY)
 ALL ANIMALS (2W)

REPORT TYPE : A1

PAGE : 3

Group Name	NO. of Animals	RED BLOOD CELL 10 ⁶ /μl		HEMOGLOBIN g/dl		HEMATOCRIT %		MCV fl		MCH pg		MCHC g/dl		PLATELET 10 ³ /μl	
Control	5	10.44±	0.41	15.8±	0.8	51.3±	2.8	49.1±	0.8	15.1±	0.2	30.8±	0.4	1137±	341
5000 ppm	5	9.92±	0.44	15.1±	0.6	49.1±	2.4	49.5±	0.6	15.3±	0.3	30.9±	0.7	1052±	74
10000 ppm	5	9.79±	0.54	14.9±	0.7	48.4±	2.1	49.5±	0.8	15.2±	0.4	30.8±	0.5	1110±	92
20000 ppm	4	9.54±	0.44	14.5±	0.8	47.5±	2.5	49.7±	0.7	15.2±	0.2	30.6±	0.2	1080±	134
40000 ppm	0	-		-		-		-		-		-		-	
50000 ppm	0	-		-		-		-		-		-		-	

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

STUDY NO. : 0361
 ANIMAL : MOUSE Crj:BDF1
 MEASURE. TIME : 1
 SEX : FEMALE

HEMATOLOGY (SUMMARY)
 ALL ANIMALS (2W)

REPORT TYPE : A1

PAGE : 4

Group Name	NO. of Animals	WBC 10 ³ /μl		Differential N-BAND		WBC (%) N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHER	
Control	5	3.27±	1.77	1±	1	14±	3	2±	1	0±	0	5±	2	78±	2	0±	0
5000 ppm	5	3.00±	1.09	1±	1	9±	3	2±	1	0±	0	3±	2	85±	4	0±	0
10000 ppm	5	2.63±	1.11	1±	1	12±	3	2±	1	0±	0	5±	3	80±	5	1±	1
20000 ppm	4	1.96±	0.59	2±	1	14±	4	1±	1	0±	0	3±	2	80±	4	0±	1
40000 ppm	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
50000 ppm	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 3

APPENDIX F 1

BIOCHEMISTRY : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0361
 ANIMAL : MOUSE Crj:BDF1
 MEASURE. TIME : 1
 SEX : MALE

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (2W)

REPORT TYPE : A1

PAGE : 1

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	3	4.8±	0.3	2.7±	0.2	1.3±	0.0	0.14±	0.02	278±	18	87±	13	186±	19
5000 ppm	5	5.0±	0.1	2.9±	0.1	1.3±	0.0	0.15±	0.01	298±	10	86±	5	180±	4
10000 ppm	5	5.0±	0.2	2.8±	0.1	1.3±	0.0	0.14±	0.01	311±	14	100±	12	195±	17
20000 ppm	5	5.8±	0.2**	3.4±	0.1**	1.4±	0.0	0.17±	0.02*	287±	29	225±	21**	373±	25
40000 ppm	0	-		-		-		-		-		-		-	
50000 ppm	0	-		-		-		-		-		-		-	

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 3

STUDY NO. : 0361
 ANIMAL : MOUSE Crj:BDF1
 MEASURE. TIME : 1
 SEX : MALE

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (2W)

REPORT TYPE : A1

PAGE : 2

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		SODIUM mEq/ℓ	
Control	3	37±	7	23±	6	216±	58	1±	1	62±	24	24.4±	3.6	149±	1
5000 ppm	5	38±	2	24±	2	207±	40	1±	1	76±	32	25.4±	2.2	149±	1
10000 ppm	5	38±	5	23±	5	254±	100	1±	1	99±	69	25.4±	3.1	149±	1
20000 ppm	5	56±	10**	53±	12*	285±	66	1±	1	116±	68	25.7±	2.3	148±	0
40000 ppm	0	-		-		-		-		-		-		-	
50000 ppm	0	-		-		-		-		-		-		-	

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 3

STUDY NO. : 0361
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE

REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

PAGE : 3

Group Name	NO. of Animals	POTASSIUM mEq/ℓ		CHLORIDE mEq/ℓ		CALCIUM mg/dℓ		INORGANIC PHOSPHORUS mg/dℓ	
Control	3	5.1±	0.6	117±	3	9.3±	0.1	7.9±	2.4
5000 ppm	5	5.0±	0.7	118±	3	9.6±	0.3	8.2±	1.9
10000 ppm	5	4.2±	0.6	116±	2	9.4±	0.2	6.9±	1.4
20000 ppm	5	5.0±	0.8	114±	2	9.9±	0.3**	8.7±	0.6
40000 ppm	0	-		-		-		-	
50000 ppm	0	-		-		-		-	

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 3

APPENDIX F 2

BIOCHEMISTRY : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0361
 ANIMAL : MOUSE Crj:BDF1
 MEASURE. TIME : 1
 SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (2W)

REPORT TYPE : A1

PAGE : 4

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	4.9±	0.2	3.0±	0.1	1.6±	0.2	0.16±	0.03	231±	25	75±	12	148±	14
5000 ppm	5	4.7±	0.1	2.9±	0.1	1.6±	0.1	0.17±	0.03	252±	18	76±	5	151±	7
10000 ppm	5	4.8±	0.3	2.9±	0.1	1.5±	0.1	0.14±	0.01	269±	22	78±	41	173±	14
20000 ppm	5	5.6±	0.2**	3.3±	0.1**	1.5±	0.1	0.15±	0.03	241±	23	202±	29**	325±	40**
40000 ppm	0	-		-		-		-		-		-		-	
50000 ppm	0	-		-		-		-		-		-		-	

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

STUDY NO. : 0361
 ANIMAL : MOUSE Crj:BDF1
 MEASURE. TIME : 1
 SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (2W)

REPORT TYPE : A1

PAGE : 5

Group Name	NO. of Animals	GOT I U / ℓ		GPT I U / ℓ		LDH I U / ℓ		G-GTP I U / ℓ		CPK I U / ℓ		UREA NITROGEN mg / dl		SODIUM mEq / ℓ	
Control	5	52±	6	27±	5	257±	51	1±	1	120±	63	23.9±	3.6	149±	1
5000 ppm	5	45±	2	24±	4	243±	43	1±	1	70±	21	23.9±	2.8	149±	1
10000 ppm	5	53±	9	35±	6*	246±	63	1±	0	114±	60	22.1±	4.5	148±	3
20000 ppm	5	47±	11	41±	5**	259±	37	1±	1	112±	28	26.3±	3.9	147±	2
40000 ppm	0	-		-		-		-		-		-		-	
50000 ppm	0	-		-		-		-		-		-		-	

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS3

STUDY NO. : 0361
ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : FEMALE

REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

PAGE : 6

Group Name	NO. of Animals	POTASSIUM mEq/ℓ		CHLORIDE mEq/ℓ		CALCIUM mg/dℓ		INORGANIC PHOSPHORUS mg/dℓ	
Control	5	5.7±	0.7	120±	2	9.4±	0.3	7.3±	1.8
5000 ppm	5	5.0±	0.4	121±	1	9.2±	0.1	7.5±	0.9
10000 ppm	5	5.3±	0.6	119±	2	9.1±	0.3	7.9±	0.3
20000 ppm	5	5.1±	0.6	117±	3	9.8±	0.7	9.4±	1.7
40000 ppm	0	-		-		-		-	
50000 ppm	0	-		-		-		-	

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS3

APPENDIX G 1

GROSS FINDINGS : SUMMARY, MOUSE : MALE ALL ANIMALS
(2-WEEK STUDY)

STUDY NO. : 0361
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

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

PAGE : 1

Organ	Findings	Group Name NO. of Animals	Control	5000 ppm	10000 ppm	20000 ppm
			5 (%)	5 (%)	5 (%)	5 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
spleen	black zone		0 (0)	0 (0)	0 (0)	1 (20)

(HPT080)

BAIS3

STUDY NO. : 0361
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

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

PAGE : 2

Organ_____	Findings_____	Group Name	40000 ppm	50000 ppm
		NO. of Animals	5 (%)	5 (%)
thymus	atrophic		4 (80)	3 (60)
spleen	black zone		0 (0)	0 (0)

(HPT080)

BAIS3

APPENDIX G 2

GROSS FINDINGS : SUMMARY, MOUSE : FEMALE ALL ANIMALS
(2-WEEK STUDY)

STUDY NO. : 0361
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 3

Organ	Findings	Group Name	Control	5000 ppm	10000 ppm	20000 ppm
		NO. of Animals	5 (%)	5 (%)	5 (%)	5 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
kidney	hydronephrosis		1 (20)	0 (0)	0 (0)	0 (0)

(HPT080)

BAIS3

STUDY NO. : 0361
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 4

Organ_____	Findings_____	Group Name	40000 ppm	50000 ppm
		NO. of Animals	5 (%)	5 (%)
thymus	atrophic		3 (60)	0 (0)
kidney	hydronephrosis		0 (0)	0 (0)

(HPT080)

BAIS3

APPENDIX G 3

GROSS FINDINGS : SUMMARY, MOUSE : MALE : DEAD AND MORIBUND ANIMALS
(2-WEEK STUDY)

STUDY NO. : 0361
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

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

PAGE : 1

Organ	Findings	Group Name	Control	5000 ppm	10000 ppm	20000 ppm
		NO. of Animals	0 (%)	0 (%)	0 (%)	0 (%)
thymus	atrophic		- (-)	- (-)	- (-)	- (-)

(HPT080)

BAIS3

STUDY NO. : 0361
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

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

PAGE : 2

Organ_____	Findings_____	Group Name NO. of Animals	40000 ppm 5 (%)	50000 ppm 5 (%)
<hr/>				
thymus	atrophic		4 (80)	3 (60)

(HPT080)

BAIS3

APPENDIX G 4

GROSS FINDINGS : SUMMARY, MOUSE : FEMALE : DEAD AND MORIBUND ANIMALS
(2-WEEK STUDY)

STUDY NO. : 0361
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 3

Organ	Findings	Group Name	Control	5000 ppm	10000 ppm	20000 ppm
		NO. of Animals	0 (%)	0 (%)	0 (%)	0 (%)
thymus	atrophic		- (-)	- (-)	- (-)	- (-)

(HPT080)

BAIS3

STUDY NO. : 0361
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 4

Organ_____	Findings_____	Group Name	40000 ppm	50000 ppm
		NO. of Animals	5 (%)	5 (%)

thymus	atrophic		3 (60)	0 (0)
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(HPT080)

BAIS3

APPENDIX G 5

GROSS FINDINGS : SUMMARY, MOUSE : MALE : SACRIFICED ANIMALS
(2-WEEK STUDY)

STUDY NO. : 0361
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

PAGE : 1

Organ	Findings	Group Name	Control	5000 ppm	10000 ppm	20000 ppm
		NO. of Animals	5 (%)	5 (%)	5 (%)	5 (%)
spleen	black zone		0 (0)	0 (0)	0 (0)	1 (20)

(HPT080)

BAIS3

STUDY NO. : 0361
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

PAGE : 2

Organ_____	Findings_____	Group Name	40000 ppm	50000 ppm
		NO. of Animals	0 (%)	0 (%)
spleen	black zone		- (-)	- (-)

(HPT080)

BAIS3

APPENDIX G 6

GROSS FINDINGS : SUMMARY, MOUSE : FEMALE : SACRIFICED ANIMALS
(2-WEEK STUDY)

STUDY NO. : 0361
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

PAGE : 3

Organ	Findings	Group Name	Control	5000 ppm	10000 ppm	20000 ppm
		NO. of Animals	5 (%)	5 (%)	5 (%)	5 (%)
kidney	hydronephrosis		1 (20)	0 (0)	0 (0)	0 (0)

(HPT080)

BAIS3

STUDY NO. : 0361
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

PAGE : 4

Organ_____	Findings_____	Group Name	40000 ppm	50000 ppm
		NO. of Animals	0 (%)	0 (%)

kidney	hydronephrosis		- (-)	- (-)
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(HPT080)

BAIS3

APPENDIX H 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0381
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

PAGE : 1

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	5	26.2± 0.7	0.056± 0.003	0.010± 0.001	0.198± 0.023	0.144± 0.007	0.162± 0.009
5000 ppm	5	25.5± 0.8	0.060± 0.002	0.012± 0.002	0.192± 0.017	0.138± 0.003	0.158± 0.006
10000 ppm	5	26.0± 0.8	0.059± 0.008	0.012± 0.002	0.203± 0.016	0.137± 0.007	0.159± 0.010
20000 ppm	5	24.1± 0.9**	0.040± 0.018	0.012± 0.001	0.184± 0.026	0.123± 0.002**	0.146± 0.009*
40000 ppm	0	-	-	-	-	-	-
50000 ppm	0	-	-	-	-	-	-

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HCL040)

BAIS3

STUDY NO. : 0361
 ANIMAL : MOUSE Crj:BDF1
 REPORT TYPE : A1
 SEX : MALE
 UNIT: g

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

PAGE : 2

Group Name	NO. of Animals	KIDNEYS		SPLEEN		LIVER		BRAIN	
Control	5	0.403±	0.025	0.058±	0.005	1.410±	0.077	0.441±	0.020
5000 ppm	5	0.374±	0.008	0.059±	0.003	1.369±	0.116	0.431±	0.014
10000 ppm	5	0.368±	0.034	0.065±	0.004	1.607±	0.076**	0.439±	0.024
20000 ppm	5	0.351±	0.013**	0.058±	0.013	2.037±	0.029**	0.433±	0.016
40000 ppm	0	-		-		-		-	
50000 ppm	0	-		-		-		-	

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HCL040)

BAIS3

APPENDIX H 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0361
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

PAGE : 3

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	5	19.0± 0.9	0.068± 0.014	0.011± 0.002	0.027± 0.005	0.106± 0.007	0.136± 0.008
5000 ppm	5	19.7± 0.4	0.077± 0.009	0.011± 0.002	0.028± 0.006	0.108± 0.004	0.149± 0.008*
10000 ppm	5	20.1± 0.7	0.074± 0.009	0.012± 0.002	0.027± 0.007	0.106± 0.005	0.149± 0.004*
20000 ppm	5	20.1± 1.0	0.066± 0.007	0.014± 0.003	0.027± 0.004	0.106± 0.004	0.140± 0.004
40000 ppm	0	-	-	-	-	-	-
50000 ppm	0	-	-	-	-	-	-

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HCL040)

BAIS3

STUDY NO. : 0361
 ANIMAL : MOUSE Crj:BDF1
 REPORT TYPE : A1
 SEX : FEMALE
 UNIT: g

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

PAGE : 4

Group Name	NO. of Animals	KIDNEYS		SPLEEN		LIVER		BRAIN	
Control	5	0.268±	0.047	0.061±	0.014	0.879±	0.063	0.432±	0.019
5000 ppm	5	0.245±	0.012	0.068±	0.005	1.064±	0.135*	0.424±	0.021
10000 ppm	5	0.242±	0.007	0.083±	0.012	1.157±	0.104**	0.440±	0.016
20000 ppm	5	0.258±	0.017	0.101±	0.025**	1.694±	0.103**	0.422±	0.019
40000 ppm	0	-		-		-		-	
50000 ppm	0	-		-		-		-	

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HCL040)

BAIS3

APPENDIX I 1

ORGAN WEIGHT, RELATIVE : SUMMARY, MOUSE : MALE

(2-WEEK STUDY)

STUDY NO. : 0361
 ANIMAL : MOUSE Crj:BDF1
 REPORT TYPE : A1
 SEX : MALE
 UNIT: %

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

PAGE : 1

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	5	26.2± 0.7	0.214± 0.012	0.040± 0.005	0.758± 0.096	0.550± 0.019	0.618± 0.025
5000 ppm	5	25.5± 0.8	0.236± 0.011	0.046± 0.008	0.753± 0.077	0.541± 0.025	0.619± 0.025
10000 ppm	5	26.0± 0.8	0.225± 0.024	0.046± 0.010	0.781± 0.080	0.527± 0.033	0.612± 0.039
20000 ppm	5	24.1± 0.9**	0.162± 0.069	0.052± 0.004	0.764± 0.130	0.511± 0.021	0.604± 0.035
40000 ppm	0	-	-	-	-	-	-
50000 ppm	0	-	-	-	-	-	-

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HCL042)

BAIS3

STUDY NO. : 0361
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

PAGE : 2

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	1.537± 0.067	0.223± 0.021	5.387± 0.382	1.685± 0.083
5000 ppm	5	1.467± 0.063	0.232± 0.011	5.371± 0.475	1.682± 0.063
10000 ppm	5	1.419± 0.148	0.249± 0.012	6.190± 0.351*	1.691± 0.136
20000 ppm	5	1.455± 0.054	0.239± 0.048	8.454± 0.272**	1.797± 0.127
40000 ppm	0	-	-	-	-
50000 ppm	0	-	-	-	-

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HCL042)

BAIS3

APPENDIX I 2

ORGAN WEIGHT, RELATIVE : SUMMARY, MOUSE : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0361
 ANIMAL : MOUSE Crj:BDF1
 REPORT TYPE : A1
 SEX : FEMALE
 UNIT: %

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

PAGE : 3

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	5	19.0± 0.9	0.354± 0.062	0.057± 0.007	0.141± 0.022	0.557± 0.048	0.714± 0.023
5000 ppm	5	19.7± 0.4	0.392± 0.045	0.057± 0.009	0.140± 0.030	0.548± 0.016	0.758± 0.032*
10000 ppm	5	20.1± 0.7	0.369± 0.044	0.059± 0.011	0.136± 0.031	0.530± 0.031	0.740± 0.022
20000 ppm	5	20.1± 1.0	0.326± 0.022	0.068± 0.014	0.133± 0.018	0.527± 0.013	0.696± 0.019
40000 ppm	0	-	-	-	-	-	-
50000 ppm	0	-	-	-	-	-	-

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HCL042)

BAIS3

STUDY NO. : 0361
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

PAGE : 4

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	1.413± 0.270	0.323± 0.079	4.628± 0.254	2.274± 0.104
5000 ppm	5	1.244± 0.044	0.344± 0.023	5.393± 0.616	2.153± 0.137
10000 ppm	5	1.209± 0.057	0.414± 0.062	5.770± 0.564**	2.194± 0.064
20000 ppm	5	1.281± 0.056	0.499± 0.105**	8.424± 0.410**	2.099± 0.129
40000 ppm	0	-	-	-	-
50000 ppm	0	-	-	-	-

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

(HCL042)

BAIS3

APPENDIX J 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : MALE : ALL ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0361
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

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

PAGE : 1

Organ	Findings	Group Name No. of Animals on Study Grade	Control 5				5000 ppm 5				10000 ppm 5				20000 ppm 5			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
bone marrow	congestion		< 5>				< 5>				< 5>				< 5>			
		0 (0)	0 (0)	0 (0)	0 (0)	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	atrophy		< 5>				< 5>				< 5>				< 5>			
		0 (0)	0 (0)	0 (0)	0 (0)	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	atrophy		< 5>				< 5>				< 5>				< 5>			
		0 (0)	0 (0)	0 (0)	0 (0)	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)	2 (40)	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	hepatocellular hypertrophy:central		< 5>				< 5>				< 5>				< 5>			
		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	5 (100)	0 (0)	0 (0)	0 (0)	
[Urinary system]																		
kidney	tubular necrosis		< 5>				< 5>				< 5>				< 5>			
		0 (0)	0 (0)	0 (0)	0 (0)	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																	

STUDY NO. : 0361
 ANIMAL : MOUSE Crj:BDF1
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 2

		40000 ppm				50000 ppm			
		5				5			
Organ	Findings	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]									
bone marrow		< 5>				< 5>			
	congestion	2 (40)	0 (0)	0 (0)	0 (0)	3 (60)	0 (0)	0 (0)	0 (0)
thymus		< 5>				< 5>			
	atrophy	0 (0)	0 (0)	5 (100)	0 (0)	0 (0)	0 (0)	5 (100)	0 (0)
spleen		< 5>				< 5>			
	atrophy	0 (0)	1 (20)	4 (80)	0 (0)	1 (20)	0 (0)	4 (80)	0 (0)
	extramedullary hematopoiesis	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Digestive system]									
liver		< 5>				< 5>			
	hepatocellular hypertrophy:central	2 (40)	2 (40)	0 (0)	0 (0)	3 (60)	2 (40)	0 (0)	0 (0)
[Urinary system]									
kidney		< 5>				< 5>			
	tubular necrosis	1 (20)	0 (0)	0 (0)	0 (0)	0 (0)	2 (40)	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

STUDY NO. : 0361
 ANIMAL : MOUSE Crj:BDF1
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 3

		Group Name	Control				5000 ppm				10000 ppm				20000 ppm			
		No. of Animals on Study	5				5				5				5			
Organ_____	Findings_____	Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Reproductive system]																		
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																	
(HPT150)																		

BAIS3

STUDY NO. : 0361
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

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

PAGE : 4

Organ	Findings	Group Name		40000 ppm				50000 ppm			
		No. of Animals on Study		5				5			
		Grade		1	2	3	4	1	2	3	4
				(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

[Reproductive system]

epididymis		< 5>				< 5>			
debris of spermatic elements		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

(HPT150)

BAIS3

APPENDIX J 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : FEMALE : ALL ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0361
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 5

		Group Name	Control				5000 ppm				10000 ppm				20000 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
Organ_____	Findings_____		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
<hr/>																		
[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>			
	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)
	extramedullary hematopoiesis		0	0	0	0	1	0	0	0	5	0	0	0	1	4	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(20)	(80)	(0)	(0)
[Digestive system]																		
liver			< 5>				< 5>				< 5>				< 5>			
	granulation		1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hepatocellular hypertrophy:central		0	0	0	0	0	0	0	1	0	0	0	4	0	0	0	
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(80)	(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

STUDY NO. : 0361
 ANIMAL : MOUSE Crj:BDF1
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 6

Organ	Findings	Group Name No. of Animals on Study Grade	40000 ppm				50000 ppm			
			1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
bone marrow	congestion		< 5>				< 5>			
			5	0	0	0	3	0	0	0
			(100)	(0)	(0)	(0)	(60)	(0)	(0)	(0)
thymus	atrophy		< 5>				< 5>			
			0	0	5	0	0	0	5	0
			(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)
spleen	atrophy		< 5>				< 5>			
			0	0	5	0	0	0	5	0
			(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)
	extramedullary hematopoiesis		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]										
liver	granulation		< 5>				< 5>			
			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)

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

STUDY NO. : 0361
 ANIMAL : MOUSE Crj:BDF1
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 7

		Group Name	Control				5000 ppm				10000 ppm				20000 ppm			
		No. of Animals on Study	5				5				5				5			
Organ_____	Findings_____	Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]																		
kidney			< 5>				< 5>				< 5>				< 5>			
	hydronephrosis		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)	(0)	(0)	(0)
	mineralization:papilla		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)
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																	

(HPT150)

BAIS3

STUDY NO. : 0361
 ANIMAL : MOUSE Crj:BDF1
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 8

		Group Name	40000 ppm				50000 ppm			
		No. of Animals on Study	5				5			
Organ_____	Findings_____	Grade	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>	<u>1</u>	<u>2</u>	<u>3</u>	<u>4</u>
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Urinary system]										
kidney			< 5>				< 5>			
	hydronephrosis		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)
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									

(HPT150)

BAIS3

APPENDIX J 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : MALE : DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0361
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

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

PAGE : 1

Organ_____	Findings_____	Group Name	Control				5000 ppm				10000 ppm				20000 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
bone marrow	congestion		< 0>				< 0>				< 0>				< 0>			
			-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
thymus	atrophy		< 0>				< 0>				< 0>				< 0>			
			-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
spleen	atrophy		< 0>				< 0>				< 0>				< 0>			
			-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Digestive system]																		
liver	hepatocellular hypertrophy:central		< 0>				< 0>				< 0>				< 0>			
			-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Urinary system]																		
kidney	tubular necrosis		< 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																	

STUDY NO. : 0361
 ANIMAL : MOUSE Crj:BDF1
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 2

Organ	Findings	40000 ppm				50000 ppm			
		5				5			
		1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]									
bone marrow	congestion	< 5>				< 5>			
		2	0	0	0	3	0	0	0
		(40)	(0)	(0)	(0)	(60)	(0)	(0)	(0)
thymus	atrophy	< 5>				< 5>			
		0	0	5	0	0	0	5	0
		(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)
spleen	atrophy	< 5>				< 5>			
		0	1	4	0	1	0	4	0
		(0)	(20)	(80)	(0)	(20)	(0)	(80)	(0)
[Digestive system]									
liver	hepatocellular hypertrophy:central	< 5>				< 5>			
		2	2	0	0	3	2	0	0
		(40)	(40)	(0)	(0)	(60)	(40)	(0)	(0)
[Urinary system]									
kidney	tubular necrosis	< 5>				< 5>			
		1	0	0	0	0	2	0	0
		(20)	(0)	(0)	(0)	(0)	(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

STUDY NO. : 0361
 ANIMAL : MOUSE Crj:BDF1
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 3

		Group Name	Control				5000 ppm				10000 ppm				20000 ppm			
		No. of Animals on Study	0				0				0				0			
Organ	Findings	Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Reproductive system]																		
epididymis			< 0>				< 0>				< 0>				< 0>			
	debris of spermatic elements		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
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																	

(HPT150)

BAIS3

STUDY NO. : 0361
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

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

PAGE : 4

Organ	Findings	40000 ppm				50000 ppm			
		5				5			
		1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

[Reproductive system]

epididymis		< 5>				< 5>			
debris of spermatic elements		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

(HPT150)

BAIS3

APPENDIX J 4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : FEMALE : DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0361
 ANIMAL : MOUSE Crj:BDF1
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 5

Organ_____	Findings_____	Group Name No. of Animals on Study Grade	Control 0				5000 ppm 0				10000 ppm 0				20000 ppm 0			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]																		
bone marrow	congestion		< 0>				< 0>				< 0>				< 0>			
		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	
thymus	atrophy		< 0>				< 0>				< 0>				< 0>			
		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	
spleen	atrophy		< 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																	

(HPT150)

BAIS3

STUDY NO. : 0361
 ANIMAL : MOUSE Crj:BDF1
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 6

Organ	Findings	Group Name No. of Animals on Study Grade				40000 ppm 5				50000 ppm 5			
		1				2				3			
		Grade				Grade				Grade			
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]													
bone marrow	congestion	< 5>				< 5>				< 5>			
		5	0	0	0	3	0	0	0	60	0	0	0
		(100)	(0)	(0)	(0)	(60)	(0)	(0)	(0)				
thymus	atrophy	< 5>				< 5>				< 5>			
		0	0	5	0	0	0	5	0	0	0	100	0
		(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)				
spleen	atrophy	< 5>				< 5>				< 5>			
		0	0	5	0	0	0	5	0	0	0	100	0
		(0)	(0)	(100)	(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

(HPT150)

BAIS3

APPENDIX J 5

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : MALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0361
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : MALE

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

PAGE : 1

Organ	Findings	Group Name	Control				5000 ppm				10000 ppm				20000 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>			
	extramedullary hematopoiesis		0	0	0	0	2	0	0	0	5	0	0	0	5	0	0	0
			(0)	(0)	(0)	(0)	(40)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
[Digestive system]																		
liver			< 5>				< 5>				< 5>				< 5>			
	hepatocellular hypertrophy:central		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)
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																	

(HPT150)

BAIS3

STUDY NO. : 0361
 ANIMAL : MOUSE Crj:BDF1
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 2

Organ	Findings	40000 ppm				50000 ppm			
		No. of Animals on Study				No. of Animals on Study			
		Grade				Grade			
		1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

[Hematopoietic system]

spleen	extramedullary hematopoiesis	< 0>				< 0>			
		(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

[Digestive system]

liver	hepatocellular hypertrophy:central	< 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

(HPT150)

BAIS3

APPENDIX J 6

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

MOUSE : FEMALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0361
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 3

		Group Name	Control				5000 ppm				10000 ppm				20000 ppm			
		No. of Animals on Study	5				5				5				5			
Organ	Findings	Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]																		
spleen			< 5>				< 5>				< 5>				< 5>			
	extramedullary hematopoiesis		0	0	0	0	1	0	0	0	5	0	0	0	1	4	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(20)	(80)	(0)	(0)
[Digestive system]																		
liver			< 5>				< 5>				< 5>				< 5>			
	granulation		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)	(0)	(0)	(0)	(0)
	hepatocellular hypertrophy:central		0	0	0	0	0	0	0	0	1	0	0	0	4	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(80)	(0)	(0)	(0)
[Urinary system]																		
kidney			< 5>				< 5>				< 5>				< 5>			
	hydronephrosis		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)	(0)	(0)	(0)
	mineralization:papilla		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)
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																	

STUDY NO. : 0361
 ANIMAL : MOUSE Crj:BDF1
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 4

Organ	Findings	Group Name No. of Animals on Study Grade	40000 ppm				50000 ppm			
			0				0			
			1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

[Hematopoietic system]

spleen	extramedullary hematopoiesis	< 0>				< 0>			
		-	-	-	-	-	-	-	-
		(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

[Digestive system]

liver	granulation	< 0>				< 0>			
		-	-	-	-	-	-	-	-
		(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	hepatocellular hypertrophy:central	< 0>				< 0>			
		-	-	-	-	-	-	-	-
		(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

[Urinary system]

kidney	hydronephrosis	< 0>				< 0>			
		-	-	-	-	-	-	-	-
		(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	mineralization:papilla	< 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

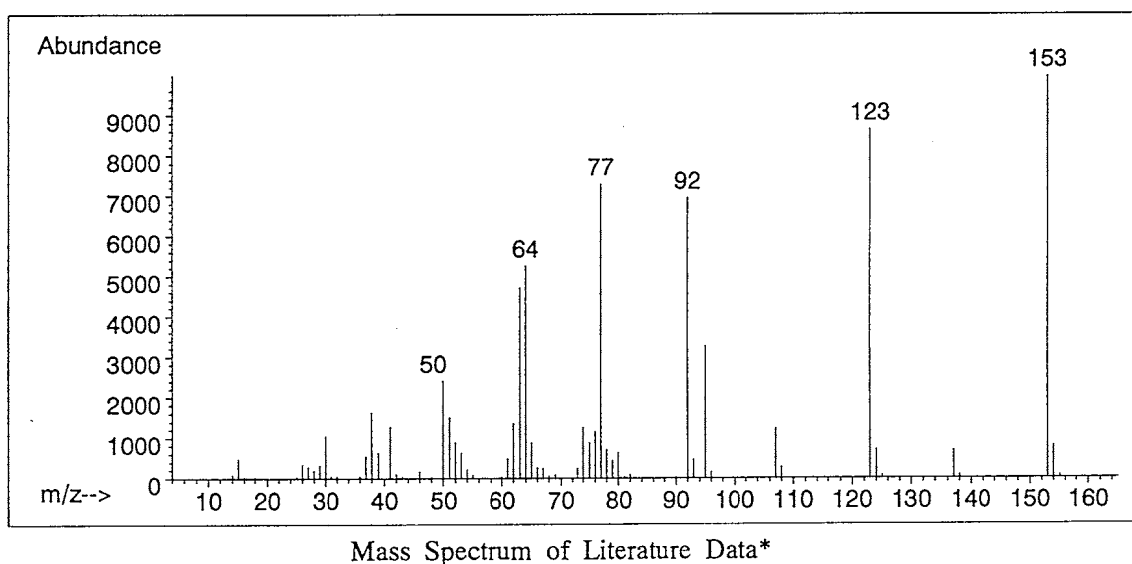
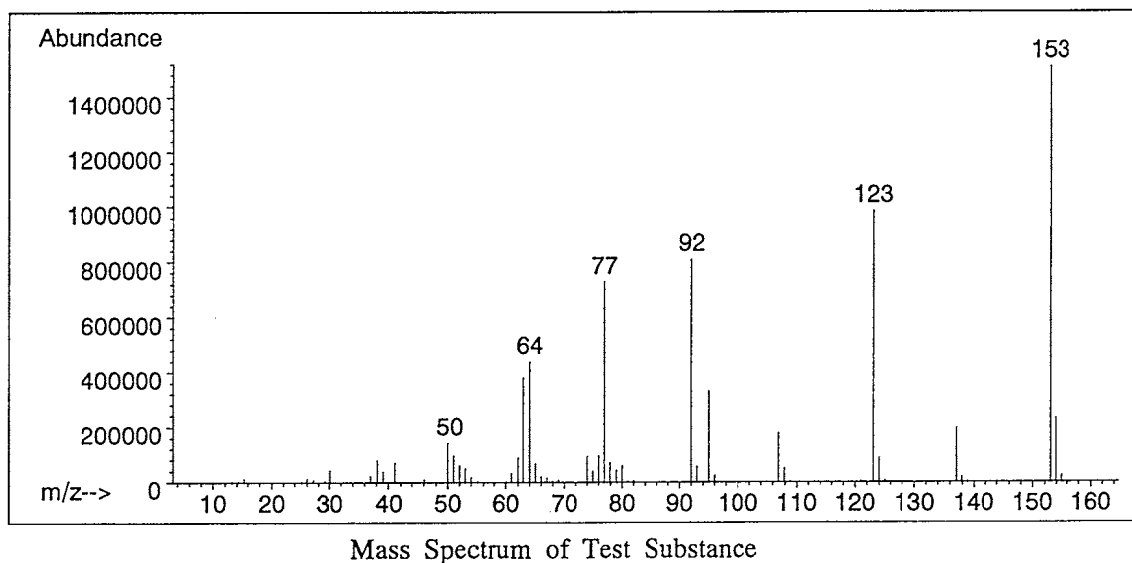
1. Spectral data

Mass Spectrometry

Instrument : Hewlett Packard 5989B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



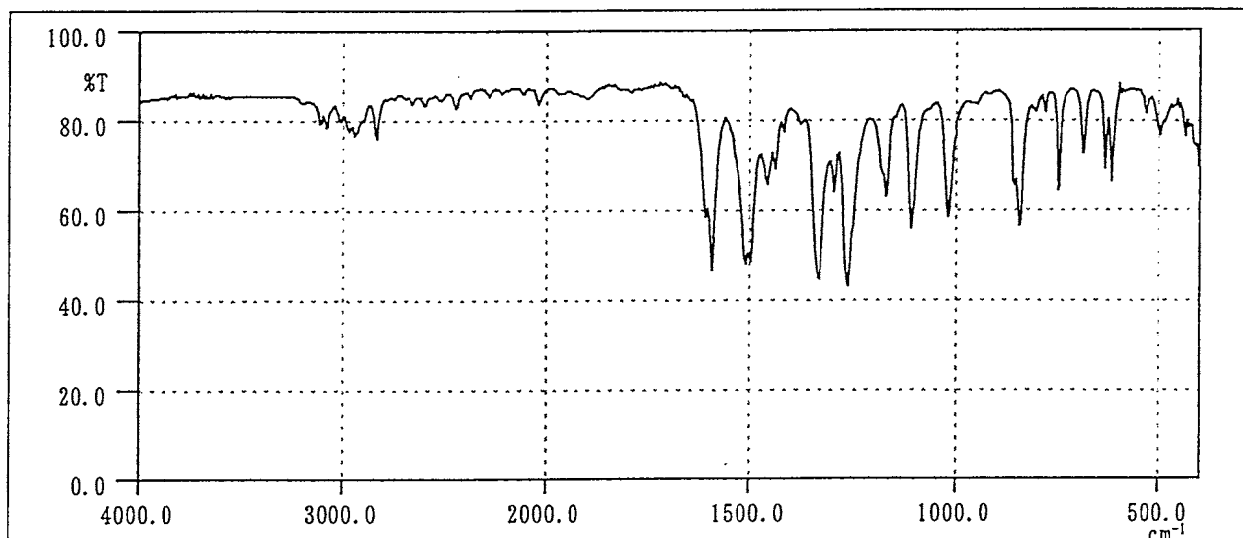
Results: The mass spectrum was consistent with literature spectrum.

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

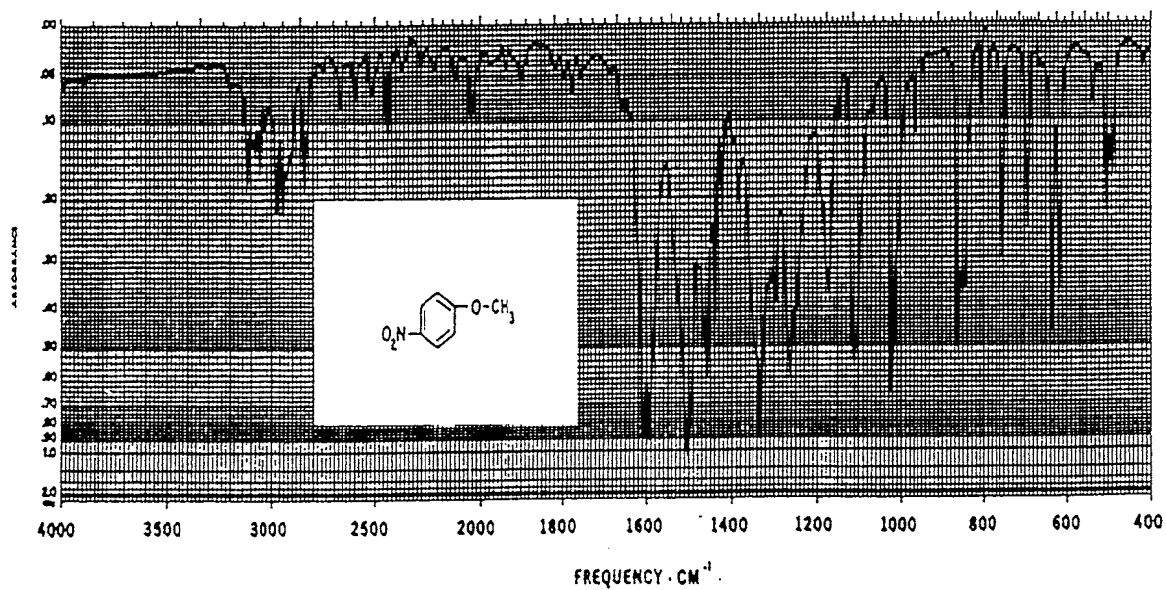
Infrared Spectrometry

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 mm ϕ \times 50 m)

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

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μ L

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 MICE IN THE 2-WEEK FEED STUDY

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

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

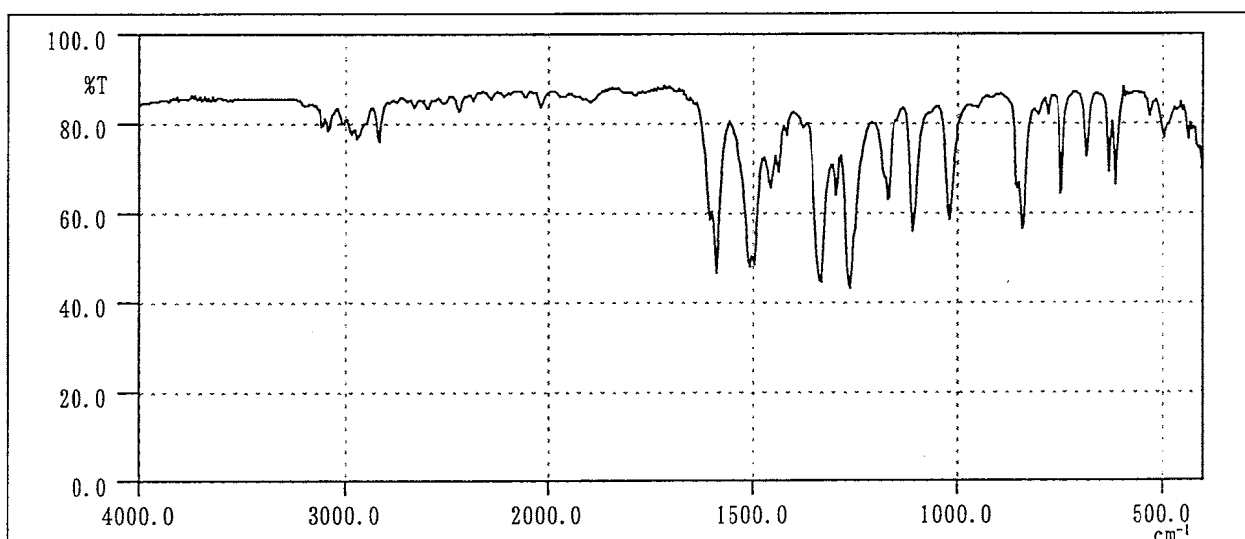
Lot No. : 704S4061

1. Sample : This lot was used from 1998.7.3 to 1998.7.17. Test substance was stored in a dark place at room temperature.

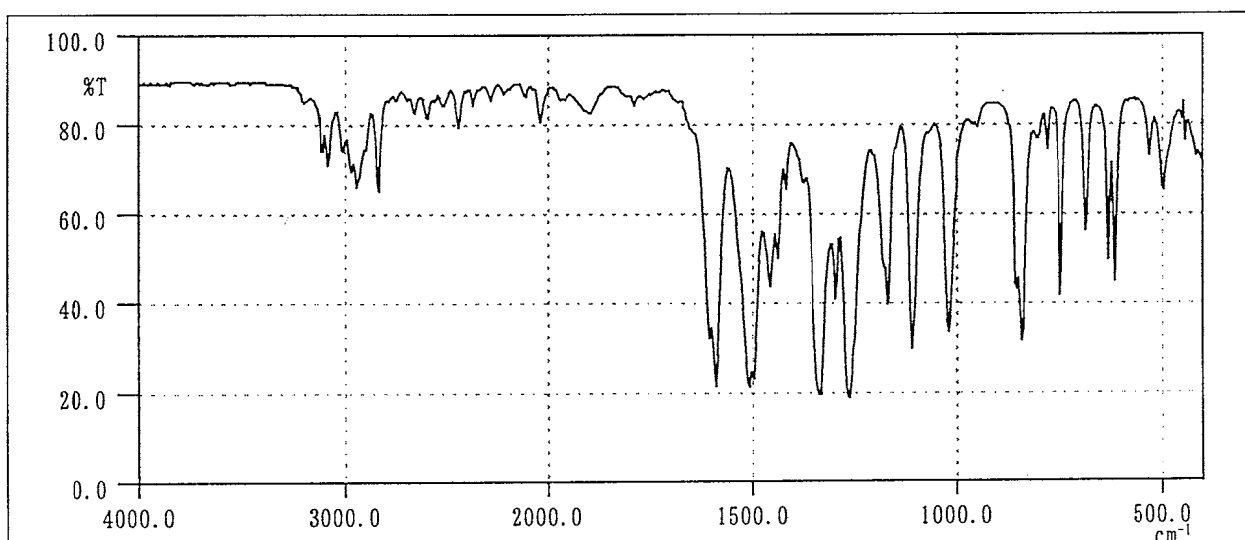
2. Infrared Spectrometry

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 mm ϕ \times 50 m)

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

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μ L

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

Date Analyzed	Target Concentration				
	5000 ^a	10000	20000	40000	50000
1998.07.02	4910 (98.2) ^b	9990 (99.9)	19700 (98.5)	40100 (100)	50800 (102)

^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 mm ϕ \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 μ L

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

Date Prepared	Date Analyzed	Target Concentration	
		5000 ^a	50000
1998.05.28	1998.05.28	4790 (100) ^b	47500 (100)
	1998.06.05 ^c	4260 (88.9)	46500 (97.9)
	1998.06.05 ^d	4860 (101)	47800 (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 mm ϕ \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 μ L

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⁾
Hematocrit (Hct)	Calculated as $RBC \times MCV / 10$ ¹⁾
Mean corpuscular volume (MCV)	Light scattering method ¹⁾
Mean corpuscular hemoglobin (MCH)	Calculated as $Hgb / RBC \times 10$ ¹⁾
Mean corpuscular hemoglobin concentration (MCHC)	Calculated as $Hgb / Hct \times 100$ ¹⁾
Platelet	Light scattering method ¹⁾
White blood cell (WBC)	Light scattering method ¹⁾
Differential WBC	Pattern recognition method ²⁾ (Wright staining)
Biochemistry	
Total protein (TP)	Biuret method ³⁾
Albumin (Alb)	BCG method ³⁾
A/G ratio	Calculated as $Alb / (TP - Alb)$ ³⁾
T-bilirubin	Alkaline azobilirubin method ³⁾
Glucose	GlcK • G-6-PDH method ³⁾
T-cholesterol	CE • COD • POD method ³⁾
Phospholipid	PLD • ChOD • POD method ³⁾
Glutamic oxaloacetic transaminase (GOT)	JSCC method ³⁾
Glutamic pyruvic transaminase (GPT)	JSCC method ³⁾
Lactate dehydrogenase (LDH)	SFBC method ³⁾
γ -Glutamyl transpeptidase (γ -GTP)	L- γ -Glutamyl-p-nitroanilide method ³⁾
Creatine phosphokinase (CPK)	JSCC method ³⁾
Urea nitrogen	Urease • GLDH method ³⁾
Sodium	Ion selective electrode method ³⁾
Potassium	Ion selective electrode method ³⁾
Chloride	Ion selective electrode method ³⁾
Calcium	OCPC method ³⁾
Inorganic phosphorus	PNP • XOD • POD method ³⁾

1) Automatic blood cell analyzer (Technicon H•1 : Bayer Corporation)

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

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

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)	$\times 10^6/\mu\text{L}$	2
Hemoglobin	g/dL	1
Hematocrit	%	1
Mean corpuscular volume (MCV)	fL	1
Mean corpuscular hemoglobin (MCH)	pg	1
Mean corpuscular hemoglobin concentration (MCHC)	g/dL	1
Platelet	$\times 10^3/\mu\text{L}$	0
White blood cell (WBC)	$\times 10^3/\mu\text{L}$	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
Sodium	mEq/L	0
Potassium	mEq/L	1
Chloride	mEq/L	0
Calcium	mg/dL	1
Inorganic phosphorus	mg/dL	1