

o-フェニレンジアミン二塩酸塩のラットを用いた
経口投与による 2 週間毒性試験(混水試験)報告書

試験番号：0336

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APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0336
 ANIMAL : RAT F344/DuCrj
 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
DEATH	0 ppm	0	0	0	0	0
	500 ppm	0	0	0	0	0
	1000 ppm	0	0	0	0	0
	2000 ppm	0	0	0	0	0
	4000 ppm	0	0	0	0	0
	6000 ppm	0	0	0	0	2
PILORECTION	0 ppm	0	0	0	0	0
	500 ppm	0	0	0	0	0
	1000 ppm	0	0	0	0	0
	2000 ppm	0	0	0	0	0
	4000 ppm	0	0	1	4	4
	6000 ppm	0	0	5	5	3
SOILED PERI GENITALIA	0 ppm	0	0	0	0	0
	500 ppm	0	0	0	0	0
	1000 ppm	0	0	0	0	0
	2000 ppm	0	0	0	0	0
	4000 ppm	0	0	0	0	0
	6000 ppm	0	0	1	1	2
NOSE HEMORRHAGIC DISCHA	0 ppm	0	0	0	0	0
	500 ppm	0	0	0	0	0
	1000 ppm	0	0	0	0	0
	2000 ppm	0	0	0	0	0
	4000 ppm	0	0	0	0	0
	6000 ppm	0	0	1	5	3
SMALL STOOL	0 ppm	0	0	0	0	0
	500 ppm	0	0	0	0	0
	1000 ppm	0	0	0	0	0
	2000 ppm	0	0	0	0	0
	4000 ppm	0	0	0	0	0
	6000 ppm	0	0	0	5	3
OLIGO-STOOL	0 ppm	0	0	0	0	0
	500 ppm	0	0	0	0	0
	1000 ppm	0	0	0	0	0
	2000 ppm	0	0	0	0	0
	4000 ppm	0	0	0	0	0
	6000 ppm	0	0	5	5	3

APPENDIX A 2

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

STUDY NO. : 0336
 ANIMAL : RAT F344/DuCrj
 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
DEATH	0 ppm	0	0	0	0	0
	500 ppm	0	0	0	0	0
	1000 ppm	0	0	0	0	0
	2000 ppm	0	0	0	0	0
	4000 ppm	0	0	0	0	1
	6000 ppm	0	0	0	3	5
PILOERECTION	0 ppm	0	0	0	0	0
	500 ppm	0	0	0	0	0
	1000 ppm	0	0	0	0	0
	2000 ppm	0	0	0	0	0
	4000 ppm	0	0	5	5	4
	6000 ppm	0	0	5	2	0
SOILED PERI GENITALIA	0 ppm	0	0	0	0	0
	500 ppm	0	0	0	0	0
	1000 ppm	0	0	0	0	0
	2000 ppm	0	0	0	0	0
	4000 ppm	0	0	2	2	4
	6000 ppm	0	2	5	2	0
NOSE HEMORRHAGIC DISCHA	0 ppm	0	0	0	0	0
	500 ppm	0	0	0	0	0
	1000 ppm	0	0	0	0	0
	2000 ppm	0	0	0	0	0
	4000 ppm	0	0	0	2	1
	6000 ppm	0	0	2	2	0
SMALL STOOL	0 ppm	0	0	0	0	0
	500 ppm	0	0	0	0	0
	1000 ppm	0	0	0	0	0
	2000 ppm	0	0	0	0	0
	4000 ppm	0	0	0	4	3
	6000 ppm	0	0	0	2	0
OLIGO-STOOL	0 ppm	0	0	0	0	0
	500 ppm	0	0	0	0	0
	1000 ppm	0	0	0	0	0
	2000 ppm	0	0	0	0	0
	4000 ppm	0	0	0	2	1
	6000 ppm	0	0	5	2	0

APPENDIX B 1

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

STUDY NO. : 0336
 ANIMAL : RAT F344/DuCrj
 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	
0 ppm	123±	5	128±	5	137±	6	154±	7	168±	8	185±	8
500 ppm	123±	5	125±	5	134±	5	151±	7	163±	8	180±	9
1000 ppm	123±	5	122±	5	132±	5	148±	6	161±	8	178±	10
2000 ppm	123±	4	118±	5**	123±	6**	138±	8**	149±	9*	163±	11*
4000 ppm	123±	5	115±	4**	109±	6**	106±	10**	110±	13**	120±	12**
6000 ppm	123±	5	112±	4**	101±	4**	86±	5**	77±	6**	73±	14**

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

Test of Dunnett

(HAN260)

BAIS 3

APPENDIX B 2

BODY WEIGHT CHANGES : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0336
 ANIMAL : RAT F344/DuCrj
 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	
0 ppm	99±	4	102±	5	104±	5	110±	3	116±	4	119±	3
500 ppm	99±	4	100±	4	105±	5	112±	5	115±	5	120±	4
1000 ppm	99±	4	98±	4	104±	4	111±	5	115±	6	119±	6
2000 ppm	99±	4	95±	4	93±	6**	103±	6	107±	6	112±	5
4000 ppm	99±	4	91±	3**	84±	4**	77±	7**	76±	12**	81±	10**
6000 ppm	99±	5	90±	5**	81±	5**	67±	7**	60±	9 ?	-	

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

WATER CONSUMPTION CHANGES : SUMMARY, RAT : MALE
(2-WEEK STUDY)

STUDY NO. : 0336
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 2
 SEX : MALE

WATER 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)
0 ppm	17.6± 1.3	16.7± 1.3	17.7± 0.9	18.0± 1.1
500 ppm	14.8± 0.3**	14.9± 0.4	15.5± 0.6	16.3± 1.2
1000 ppm	12.9± 1.0**	13.1± 1.2**	13.8± 1.1	14.5± 1.3**
2000 ppm	9.2± 1.1**	11.9± 0.7**	12.0± 0.8*	12.5± 1.2**
4000 ppm	3.9± 1.0**	5.3± 1.8**	10.2± 5.0*	8.8± 1.1**
6000 ppm	2.2± 0.7**	2.1± 0.9**	2.6± 1.2**	2.8± 1.8**

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

Test of Dunnett

APPENDIX C 2

WATER CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0336
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 2
 SEX : FEMALE

WATER 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)
0 ppm	15.5± 1.5	16.3± 2.9	16.7± 3.0	16.7± 3.0
500 ppm	13.0± 0.6	12.5± 1.4	12.7± 1.9*	13.9± 3.8
1000 ppm	10.6± 0.6	9.8± 0.6	9.8± 1.0**	9.8± 0.8
2000 ppm	6.4± 1.6*	9.1± 1.0	8.8± 1.0**	9.2± 0.6*
4000 ppm	2.8± 0.5**	3.7± 1.2**	4.9± 1.9**	5.6± 1.3**
6000 ppm	2.6± 0.4**	2.4± 0.2**	2.4± 0.2 ?	-

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

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

STUDY NO. : 0336
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

PAGE : 1

Group Name	Administration week-day(effective)	
	1-7(7)	2-7(7)
0 ppm	13.9± 1.0	15.1± 0.9
500 ppm	13.2± 0.6	14.9± 0.8
1000 ppm	12.3± 0.4*	13.7± 0.9
2000 ppm	11.0± 0.6**	12.6± 1.0**
4000 ppm	7.0± 1.2**	9.0± 1.2**
6000 ppm	4.5± 1.0**	4.9± 0.8**

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

Test of Dunnett

(HAN260)

BAIS 3

APPENDIX D 2

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

STUDY NO. : 0336
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

PAGE : 2

Group Name	Administration week-day(effective)	
	1-7(7)	2-7(7)
0 ppm	10.1± 0.6	10.1± 0.5
500 ppm	9.7± 0.7	10.1± 0.6
1000 ppm	9.2± 0.5	9.2± 0.8
2000 ppm	7.8± 0.6**	9.1± 0.5
4000 ppm	4.2± 0.6**	6.4± 0.9**
6000 ppm	2.9± 0.7**	-

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

Test of Dunnett

(HAN260)

BAIS 3

APPENDIX E 1

CHEMICAL INTAKE CHANGES : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0336
ANIMAL : RAT F344/DuCrj
UNIT : g/kgBW/day
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

PAGE: 1

Group Name	Administration week-day			
	1-3	1-7	2-3	2-7
Control	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000
500ppm	0.055 ± 0.002	0.049 ± 0.001	0.047 ± 0.001	0.045 ± 0.003
1000ppm	0.098 ± 0.005	0.088 ± 0.005	0.086 ± 0.004	0.082 ± 0.003
2000ppm	0.150 ± 0.011	0.173 ± 0.005	0.161 ± 0.006	0.153 ± 0.005
4000ppm	0.144 ± 0.031	0.197 ± 0.049	0.373 ± 0.188	0.293 ± 0.017
6000ppm	0.128 ± 0.037	0.144 ± 0.056	0.197 ± 0.085	0.219 ± 0.105

APPENDIX E 2

CHEMICAL INTAKE CHANGES : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0336

ANIMAL : RAT F344/DuCrj

UNIT : g/kgBW/day

SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)

ALL ANIMALS

PAGE: 1

Group Name	Administration week-day			
	1-3	1-7	2-3	2-7
Control	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000
500ppm	0.061 ± 0.001	0.056 ± 0.006	0.055 ± 0.008	0.058 ± 0.015
1000ppm	0.101 ± 0.004	0.088 ± 0.003	0.085 ± 0.005	0.082 ± 0.004
2000ppm	0.136 ± 0.028	0.177 ± 0.013	0.165 ± 0.012	0.165 ± 0.007
4000ppm	0.132 ± 0.024	0.194 ± 0.059	0.254 ± 0.080	0.257 ± 0.034
6000ppm	0.191 ± 0.037	0.219 ± 0.033	0.238 ± 0.015	

APPENDIX F 1

HEMATOLOGY : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0336
 ANIMAL : RAT F344/DuCrj
 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	
0 ppm	5	7.79±	0.19	14.5±	0.4	44.5±	1.1	57.1±	0.5	18.5±	0.3	32.5±	0.3	936±	45
500 ppm	5	7.82±	0.30	14.6±	0.5	44.6±	1.6	57.0±	0.5	18.7±	0.1	32.8±	0.2	923±	50
1000 ppm	5	7.69±	0.45	14.4±	0.7	43.7±	2.6	56.8±	0.5	18.7±	0.2	33.0±	0.5	840±	155
2000 ppm	5	7.83±	0.27	14.7±	0.4	44.6±	1.2	57.0±	0.6	18.8±	0.1	33.0±	0.2	865±	83
4000 ppm	5	8.50±	0.40*	16.0±	0.7*	47.7±	2.1	56.1±	0.3	18.8±	0.1	33.5±	0.2**	610±	78**
6000 ppm	3	9.81±	1.32*	20.4±	1.9*	57.1±	9.8*	58.0±	2.6	20.9±	2.1	36.1±	4.2	154±	84**

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

Test of Dunnett

(HCL070)

BAIS 3

STUDY NO. : 0336
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : MALE

HEMATOLOGY (SUMMARY)
 ALL ANIMALS (2W)

REPORT TYPE : A1

PAGE : 2

Group Name	NO. of Animals	RETICULOCYTE ‰		METHEMOGLOBIN %		PROTHROMBIN TIME s e c		APTT s e c	
0 ppm	5	52±	11	0.3±	0.1	10.7±	0.7	16.1±	2.5
500 ppm	5	55±	9	0.3±	0.2	11.1±	0.5	16.6±	4.0
1000 ppm	5	47±	10	0.3±	0.0	11.1±	0.2	15.6±	3.5
2000 ppm	5	36±	7	0.3±	0.1	11.1±	0.7	17.1±	2.8
4000 ppm	5	19±	15**	0.3±	0.1	11.5±	0.9	15.6±	3.9
6000 ppm	3	3±	1**	0.5±	0.3	13.5±	0.1 ?	20.6±	1.3 ?

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.

STUDY NO. : 0336
 ANIMAL : RAT F344/DuCrJ
 MEASURE. TIME : 1
 SEX : MALE

REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
 ALL ANIMALS (2W)

PAGE : 3

Group Name	NO. of Animals	WBC 10 ³ /μl		Differential N-BAND		WBC (%) N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHERS	
0 ppm	5	5.32±	0.62	0±	0	18±	3	0±	0	0±	0	3±	1	78±	3	1±	1
500 ppm	5	4.45±	0.44	0±	0	16±	4	1±	1	0±	0	4±	2	78±	4	0±	1
1000 ppm	5	4.36±	2.15	0±	0	17±	6	1±	1	0±	0	4±	1	78±	7	1±	1
2000 ppm	5	4.36±	1.15	0±	0	13±	2	1±	1	0±	0	3±	1	83±	3	1±	1
4000 ppm	5	4.76±	1.04	0±	0	15±	3	1±	1	0±	0	4±	2	80±	3	1±	1
6000 ppm	3	2.82±	1.58	0±	0	31±	21	0±	1	0±	0	5±	3	64±	19	0±	0

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 3

APPENDIX F 2

HEMATOLOGY : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0336
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

REPORT TYPE : A1

PAGE : 4

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	
0 ppm	5	8.27±	0.35	15.8±	0.3	45.7±	1.8	55.2±	0.3	19.1±	0.7	34.6±	1.0	813±	35
500 ppm	5	8.26±	0.23	15.5±	0.5	45.9±	1.5	55.6±	0.5	18.8±	0.1	33.8±	0.1	784±	55
1000 ppm	5	8.26±	0.20	15.6±	0.4	45.8±	1.2	55.4±	0.2	18.8±	0.2	34.0±	0.3	777±	34
2000 ppm	5	8.36±	0.29	15.7±	0.4	46.6±	1.4	55.7±	0.4	18.8±	0.2	33.7±	0.3	703±	55*
4000 ppm	4	9.52±	0.63**	17.7±	1.1**	51.9±	3.3**	54.6±	0.3*	18.6±	0.3	34.1±	0.4	521±	104**
6000 ppm	0	-		-		-		-		-		-		-	

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

Test of Dunnett

STUDY NO. : 0336
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE

REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

PAGE : 5

Group Name	NO. of Animals	RETICULOCYTE ‰		METHEMOGLOBIN %		PROTHROMBIN TIME s e c		APTT s e c	
0 ppm	5	27±	8	0.3±	0.2	10.7±	0.3	14.0±	2.2
500 ppm	5	24±	10	0.3±	0.1	10.9±	0.4	17.4±	2.2
1000 ppm	5	25±	8	0.2±	0.2	11.3±	0.5	15.9±	3.6
2000 ppm	5	21±	8	0.2±	0.1	11.4±	0.6	16.4±	2.6
4000 ppm	4	6±	3**	0.3±	0.1	11.8±	0.2**	15.4±	0.6
6000 ppm	0	-		-		-		-	

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

Test of Dunnett

(HCL070)

BAIS 3

STUDY NO. : 0336
 ANIMAL : RAT F344/DuCrj
 MEASURE, TIME : 1
 SEX : FEMALE

HEMATOLOGY (SUMMARY)
 ALL ANIMALS (2W)

REPORT TYPE : A1

PAGE : 6

Group Name	NO. of Animals	WBC 10 ³ /μl		Differential N-BAND		WBC (%) N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHERS	
0 ppm	5	5.12±	1.55	0±	0	19±	3	1±	1	0±	0	4±	1	76±	4	0±	0
500 ppm	5	4.58±	1.27	0±	0	22±	7	1±	1	0±	0	4±	2	72±	7	0±	1
1000 ppm	5	5.27±	2.79	0±	0	14±	4	1±	1	0±	0	4±	2	80±	4	0±	0
2000 ppm	5	4.94±	0.33	0±	0	14±	4	1±	1	0±	0	4±	2	81±	4	0±	1
4000 ppm	4	4.86±	1.49	0±	0	18±	5	1±	1	0±	0	3±	1	78±	4	0±	0
6000 ppm	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 3

APPENDIX G 1

BIOCHEMISTRY : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0336
 ANIMAL : RAT F344/DuCrj
 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	
0 ppm	5	5.6±	0.2	3.6±	0.1	1.7±	0.1	0.14±	0.00	190±	9	69±	5	135±	8
500 ppm	5	5.5±	0.1	3.5±	0.1	1.8±	0.1	0.15±	0.01	199±	14	70±	6	136±	8
1000 ppm	5	5.5±	0.2	3.5±	0.1	1.7±	0.1	0.15±	0.01	197±	17	73±	9	146±	19
2000 ppm	5	5.5±	0.1	3.4±	0.1	1.7±	0.1	0.15±	0.01	185±	5	79±	1	156±	7*
4000 ppm	5	5.6±	0.0	3.5±	0.1	1.7±	0.1	0.17±	0.01*	186±	11	82±	7*	163±	13**
6000 ppm	3	5.5±	0.1	3.3±	0.2**	1.5±	0.3	0.36±	0.20**	123±	44	76±	10	123±	11

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

Test of Dunnett

STUDY NO. : 0336
 ANIMAL : RAT F344/DuCrj
 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		CREATININE mg/dℓ	
0 ppm	5	56±	5	33±	3	225±	62	2±	1	179±	26	14.4±	2.5	0.4±	0.0
500 ppm	5	55±	1	32±	2	213±	28	1±	1	208±	27	15.7±	1.5	0.4±	0.0
1000 ppm	5	53±	2	31±	1	199±	51	2±	1	187±	28	15.8±	1.7	0.4±	0.0
2000 ppm	5	54±	3	31±	2	199±	64	3±	1	168±	36	17.5±	2.3	0.4±	0.0
4000 ppm	5	61±	4	36±	7	249±	64	2±	1	165±	35	21.1±	1.2**	0.4±	0.0
6000 ppm	3	336±	205	192±	85	766±	594	4±	1	233±	94	45.5±	15.8**	0.4±	0.1

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

Test of Dunnett

(HCL074)

BAIS 3

STUDY NO. : 0336
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : MALE

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (2W)

REPORT TYPE : A1

PAGE : 3

Group Name	NO. of Animals	SODIUM mEq/ℓ		POTASSIUM mEq/ℓ		CHLORIDE mEq/ℓ		CALCIUM mg/dℓ		INORGANIC PHOSPHORUS mg/dℓ	
0 ppm	5	140±	0	3.9±	0.2	103±	2	11.0±	0.1	8.2±	1.0
500 ppm	5	139±	1	3.9±	0.4	103±	1	10.9±	0.3	8.0±	1.1
1000 ppm	5	139±	1	3.9±	0.2	103±	3	10.8±	0.3	8.1±	1.4
2000 ppm	5	139±	1	4.1±	0.4	103±	2	10.7±	0.4	8.2±	0.9
4000 ppm	5	141±	1	3.8±	0.3	106±	1	10.5±	0.2*	6.3±	1.0
6000 ppm	3	163±	16	4.0±	0.8	133±	17*	9.9±	0.3**	7.7±	1.6

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

Test of Dunnett

(HCL074)

BAIS 3

APPENDIX G 2

BIOCHEMISTRY : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0336
 ANIMAL : RAT F344/DuCrj
 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	
0 ppm	5	5.6±	0.1	3.6±	0.1	1.8±	0.1	0.16±	0.01	192±	9	71±	3	132±	7
500 ppm	5	5.6±	0.2	3.5±	0.2	1.6±	0.1	0.20±	0.02*	191±	8	76±	4	143±	11
1000 ppm	5	5.5±	0.1	3.5±	0.1	1.8±	0.1	0.17±	0.01	188±	8	73±	7	133±	9
2000 ppm	5	5.3±	0.2	3.4±	0.1	1.8±	0.0	0.18±	0.01	182±	4	77±	3	143±	5
4000 ppm	4	5.4±	0.2	3.3±	0.1**	1.6±	0.1**	0.23±	0.04**	166±	9**	78±	7	150±	11*
6000 ppm	0	-		-		-		-		-		-		-	

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 3

STUDY NO. : 0336
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (2W)

REPORT TYPE : A1

PAGE : 5

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	
0 ppm	5	62±	6	32±	4	304±	64	3±	1	190±	29	17.1±	0.8	0.5±	0.2
500 ppm	5	59±	4	29±	2	411±	171	2±	1	322±	159	18.8±	1.9	0.4±	0.0
1000 ppm	5	62±	3	34±	3	360±	155	3±	0	355±	205	18.8±	1.4	0.4±	0.1
2000 ppm	5	61±	5	33±	3	364±	115	2±	2	193±	61	21.3±	4.2	0.4±	0.1
4000 ppm	4	80±	15*	47±	8**	460±	113	5±	2	207±	77	25.5±	3.8**	0.4±	0.0
6000 ppm	0	-		-		-		-		-		-		-	

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

Test of Dunnett

(HCL074)

BAIS 3

STUDY NO. : 0336
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (2W)

REPORT TYPE : A1

PAGE : 6

Group Name	NO. of Animals	SODIUM mEq/ℓ		POTASSIUM mEq/ℓ		CHLORIDE mEq/ℓ		CALCIUM mg/dℓ		INORGANIC PHOSPHORUS mg/dℓ	
0 ppm	5	138±	1	3.9±	0.3	105±	1	10.5±	0.2	7.2±	0.7
500 ppm	5	137±	1	4.0±	0.3	105±	1	10.5±	0.2	7.6±	0.7
1000 ppm	5	138±	1	3.8±	0.2	105±	1	10.6±	0.1	7.1±	0.7
2000 ppm	5	139±	1	3.9±	0.2	106±	0	10.4±	0.2	7.0±	0.6
4000 ppm	4	141±	3	3.9±	0.1	111±	4*	10.1±	0.2**	6.1±	0.4
6000 ppm	0	-		-		-		-		-	

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 3

APPENDIX H 1

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

STUDY NO. : 0336
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 1

Organ	Findings	Group Name NO. of Animals	0 ppm		500 ppm		1000 ppm		2000 ppm	
			5	(%)	5	(%)	5	(%)	5	(%)
thymus	atrophic		0	(0)	0	(0)	0	(0)	0	(0)
	red zone		0	(0)	1	(20)	0	(0)	0	(0)
liver	herniation		0	(0)	1	(20)	0	(0)	1	(20)

(HPT080)

BAIS 3

STUDY NO. : 0336
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 2

Organ	Findings	Group Name	4000 ppm	6000 ppm
		NO. of Animals	5 (%)	5 (%)
thymus	atrophic		0 (0)	4 (80)
	red zone		0 (0)	0 (0)
liver	herniation		0 (0)	0 (0)

(HPT080)

BAIS 3

APPENDIX H 2

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

STUDY NO. : 0336
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 3

Organ	Findings	Group Name NO. of Animals	0 ppm		500 ppm		1000 ppm		2000 ppm	
			5	(%)	5	(%)	5	(%)	5	(%)
subcutis	dry		0	(0)	0	(0)	0	(0)	0	(0)
thymus	atrophic		0	(0)	0	(0)	0	(0)	0	(0)
liver	herniation		0	(0)	1	(20)	1	(20)	0	(0)

(HPT080)

BAIS 3

STUDY NO. : 0336
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 4

Organ	Findings	Group Name NO. of Animals	4000 ppm	6000 ppm
			5 (%)	5 (%)
subcutis	dry		0 (0)	1 (20)
thymus	atrophic		1 (20)	1 (20)
liver	herniation		0 (0)	0 (0)

(HPT080)

BAIS 3

APPENDIX H 3

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

STUDY NO. : 0336
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

PAGE : 1

Organ	Findings	Group Name NO. of Animals	0 ppm		500 ppm		1000 ppm		2000 ppm	
			5	(%)	5	(%)	5	(%)	5	(%)
thymus	atrophic		0	(0)	0	(0)	0	(0)	0	(0)
	red zone		0	(0)	1	(20)	0	(0)	0	(0)
liver	herniation		0	(0)	1	(20)	0	(0)	1	(20)

(HPT080)

BAIS 3

STUDY NO. : 0336
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

PAGE : 2

Organ	Findings	Group Name	4000 ppm	6000 ppm
		NO. of Animals	5 (%)	3 (%)
thymus	atrophic		0 (0)	3 (100)
	red zone		0 (0)	0 (0)
liver	herniation		0 (0)	0 (0)

(HPT080)

BAIS 3

APPENDIX H 4

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

STUDY NO. : 0336
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

PAGE : 3

Organ_____	Findings_____	Group Name	0 ppm		500 ppm		1000 ppm		2000 ppm	
		NO. of Animals	5	(%)	5	(%)	5	(%)	5	(%)
liver	herniation		0	(0)	1	(20)	1	(20)	0	(0)

(HPT080)

BAIS 3

STUDY NO. : 0336
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

PAGE : 4

Organ	Findings	Group Name NO. of Animals	4000 ppm 4 (%)	6000 ppm 0 (%)
liver	herniation		0 (0)	- (-)

(HPT080)

BAIS 3

APPENDIX H 5

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

STUDY NO. : 0336
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 1

Organ	Findings	Group Name NO. of Animals	0 ppm 0 (%)	500 ppm 0 (%)	1000 ppm 0 (%)	2000 ppm 0 (%)
thymus	atrophic		- (-)	- (-)	- (-)	- (-)

(HPT080)

BAIS 3

STUDY NO. : 0336
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 2

Organ	Findings	Group Name NO. of Animals	4000 ppm 0 (%)	6000 ppm 2 (%)
thymus	atrophic		- (-)	1 (50)

(HPT080)

BAIS 3

APPENDIX H 6

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

STUDY NO. : 0336
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 3

Organ	Findings	Group Name	0 ppm		500 ppm		1000 ppm		2000 ppm	
		NO. of Animals	0	(%)	0	(%)	0	(%)	0	(%)
subcutis	dry		-	(-)	-	(-)	-	(-)	-	(-)
thymus	atrophic		-	(-)	-	(-)	-	(-)	-	(-)

(HPT080)

BAIS 3

STUDY NO. : 0336
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 4

Organ	Findings	Group Name	4000 ppm	6000 ppm
		NO. of Animals	1 (%)	5 (%)
subcutis	dry		0 (0)	1 (20)
thymus	atrophic		1 (100)	1 (20)

(HPT080)

BAIS 3

APPENDIX I 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0336
ANIMAL : RAT F344/DuCrj
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	
0 ppm	5	185±	8	0.373±	0.041	0.034±	0.003	2.413±	0.203	0.630±	0.070	0.821±	0.044
500 ppm	5	180±	9	0.361±	0.031	0.035±	0.002	2.451±	0.066	0.639±	0.043	0.798±	0.046
1000 ppm	5	178±	10	0.335±	0.027	0.036±	0.004	2.372±	0.159	0.632±	0.061	0.786±	0.040
2000 ppm	5	163±	11*	0.314±	0.024*	0.036±	0.002	2.278±	0.196	0.605±	0.058	0.742±	0.034*
4000 ppm	5	120±	12**	0.157±	0.046**	0.032±	0.003	2.171±	0.153	0.428±	0.035**	0.621±	0.029**
6000 ppm	3	73±	14**	0.036±	0.028**	0.030±	0.003	1.053±	0.418**	0.329±	0.045**	0.525±	0.027**

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

Test of Dunnett

(HCL040)

BAIS 3

STUDY NO. : 0336
ANIMAL : RAT F344/DuCrj
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	
0 ppm	5	1.445±	0.095	0.468±	0.024	7.398±	0.541	1.774±	0.035
500 ppm	5	1.421±	0.079	0.449±	0.025	7.318±	0.655	1.726±	0.029
1000 ppm	5	1.437±	0.083	0.430±	0.014	7.571±	0.484	1.710±	0.045*
2000 ppm	5	1.369±	0.096	0.401±	0.028*	6.867±	0.773	1.718±	0.042
4000 ppm	5	1.144±	0.109**	0.277±	0.044**	5.120±	0.646**	1.668±	0.025**
6000 ppm	3	0.860±	0.089**	0.129±	0.056**	2.402±	0.769**	1.593±	0.042**

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

Test of Dunnett

(HCL040)

BAIS 3

APPENDIX I 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0336
ANIMAL : RAT F344/DuCrj
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	
0 ppm	5	119±	3	0.271±	0.014	0.044±	0.002	0.086±	0.007	0.462±	0.021	0.613±	0.022
500 ppm	5	120±	4	0.272±	0.015	0.043±	0.001	0.091±	0.018	0.480±	0.031	0.622±	0.014
1000 ppm	5	119±	6	0.282±	0.029	0.040±	0.004*	0.078±	0.012	0.448±	0.020	0.625±	0.042
2000 ppm	5	112±	5	0.247±	0.027	0.040±	0.003*	0.075±	0.014	0.465±	0.043	0.585±	0.033
4000 ppm	4	81±	10**	0.109±	0.036**	0.032±	0.003**	0.052±	0.009**	0.334±	0.023**	0.502±	0.020**
6000 ppm	0	-		-		-		-		-		-	

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

Test of Dunnett

(HCL040)

BAIS 3

STUDY NO. : 0336
ANIMAL : RAT F344/DuCrj
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	
0 ppm	5	0.938±	0.030	0.318±	0.016	4.384±	0.197	1.612±	0.038
500 ppm	5	0.965±	0.040	0.311±	0.013	4.677±	0.191	1.610±	0.028
1000 ppm	5	0.992±	0.050	0.304±	0.022	4.386±	0.426	1.614±	0.018
2000 ppm	5	1.021±	0.037*	0.279±	0.005**	4.249±	0.327	1.607±	0.030
4000 ppm	4	0.833±	0.059**	0.192±	0.026**	3.047±	0.578**	1.559±	0.012*
6000 ppm	0	-		-		-		-	

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

Test of Dunnett

(HCL040)

BAIS 3

APPENDIX J 1

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0336
ANIMAL : RAT F344/DuCrJ
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
0 ppm	5	185± 8	0.202± 0.025	0.018± 0.001	1.302± 0.067	0.340± 0.029	0.443± 0.016
500 ppm	5	180± 9	0.201± 0.009	0.019± 0.002	1.367± 0.058	0.355± 0.008	0.445± 0.022
1000 ppm	5	178± 10	0.189± 0.006	0.020± 0.003	1.338± 0.097	0.355± 0.014	0.443± 0.015
2000 ppm	5	163± 11*	0.192± 0.009	0.022± 0.003**	1.394± 0.081	0.370± 0.021	0.455± 0.022
4000 ppm	5	120± 12**	0.129± 0.028**	0.027± 0.004**	1.825± 0.166**	0.358± 0.012	0.522± 0.036**
6000 ppm	3	73± 14**	0.046± 0.028**	0.042± 0.009**	1.412± 0.306	0.456± 0.054**	0.734± 0.093**

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

Test of Dunnett

(HCL042)

BAIS 3

STUDY NO. : 0336
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

PAGE : 2

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
0 ppm	5	0.780± 0.022	0.253± 0.010	3.994± 0.234	0.959± 0.029
500 ppm	5	0.791± 0.019	0.250± 0.009	4.071± 0.229	0.963± 0.048
1000 ppm	5	0.810± 0.038	0.243± 0.008	4.263± 0.121	0.965± 0.051
2000 ppm	5	0.838± 0.013**	0.245± 0.008	4.195± 0.232	1.054± 0.055**
4000 ppm	5	0.957± 0.031**	0.231± 0.014*	4.273± 0.145	1.405± 0.134**
6000 ppm	3	1.196± 0.110**	0.172± 0.042**	3.254± 0.423**	2.234± 0.336**

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

Test of Dunnett

APPENDIX J 2

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0336
ANIMAL : RAT F344/DuCrj
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
0 ppm	5	119±	3	0.228± 0.012	0.037± 0.001	0.073± 0.007	0.389± 0.012	0.515± 0.014
500 ppm	5	120±	4	0.226± 0.013	0.036± 0.001	0.076± 0.014	0.399± 0.016	0.518± 0.012
1000 ppm	5	119±	6	0.220± 0.023	0.033± 0.003*	0.065± 0.007	0.375± 0.014	0.523± 0.013
2000 ppm	5	112±	5	0.220± 0.021	0.035± 0.001	0.067± 0.011	0.415± 0.027	0.522± 0.015
4000 ppm	4	81±	10**	0.132± 0.032**	0.040± 0.002	0.064± 0.009	0.415± 0.032	0.626± 0.063**
6000 ppm	0	-		-	-	-	-	-

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

Test of Dunnett

(HCL042)

BAIS 3

STUDY NO. : 0336
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

PAGE : 4

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
0 ppm	5	0.789± 0.030	0.267± 0.010	3.684± 0.152	1.355± 0.036
500 ppm	5	0.802± 0.008	0.259± 0.007	3.892± 0.124	1.341± 0.044
1000 ppm	5	0.831± 0.016**	0.254± 0.009	3.667± 0.183	1.355± 0.075
2000 ppm	5	0.912± 0.011**	0.250± 0.012*	3.790± 0.152	1.437± 0.068
4000 ppm	4	1.035± 0.071**	0.237± 0.004**	3.736± 0.264	1.952± 0.285**
6000 ppm	0	-	-	-	-

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

Test of Dunnett

(HCL042)

BAIS 3

APPENDIX K 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : ALL ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0336
 ANIMAL : RAT F344/DuCrj
 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				0 ppm				500 ppm				1000 ppm				2000 ppm			
		Grade				5				5				5				5			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
{Respiratory system}																					
nasal cavit		< 5>				< 5>				< 5>				< 5>							
	atrophy:olfactory epithelium	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:olfactory epithelium	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lung		< 5>				< 5>				< 5>				< 5>							
	hemorrhage	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(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)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	decreased hematopoiesis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(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)	(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. : 0336
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 2

		Group Name				4000 ppm				6000 ppm				
		No. of Animals on Study				5				5				
Organ	Findings	Grade	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}														
nasal cavit			< 5>				< 5>							
	atrophy:olfactory epithelium		2	0	0	0	0	0	0	0	0	0	0	0
			(40)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:olfactory epithelium		1	2	0	0	2	2	0	0	(40)	(40)	(0)	(0)
			(20)	(40)	(0)	(0)	(40)	(40)	(0)	(0)				
lung			< 5>				< 5>							
	hemorrhage		0	0	0	0	4	0	0	0	(0)	(0)	(0)	(0)
			(0)	(0)	(0)	(0)	(80)	(0)	(0)	(0)				
{Hematopoietic system}														
bone marrow			< 5>				< 5>							
	congestion		0	0	0	0	0	4	0	0	(0)	(80)	(0)	(0)
			(0)	(0)	(0)	(0)	(0)	(80)	(0)	(0)				
	decreased hematopoiesis		4	0	0	0	0	0	5	0	(0)	(0)	(100)	(0)
			(80)	(0)	(0)	(0)	(0)	(0)	(0)	(0)				
thymus			< 5>				< 5>							
	atrophy		3	0	0	0	1	0	4	0	(60)	(0)	(0)	(80)
			(60)	(0)	(0)	(0)	(20)	(0)	(80)	(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. : 0336
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 3

Organ	Findings	Group Name No. of Animals on Study Grade	0 ppm				500 ppm				1000 ppm				2000 ppm			
			5				5				5				5			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Hematopoietic system)																		
thymus	congestion		< 5>				< 5>				< 5>				< 5>			
			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)
(Digestive system)																		
liver	herniation		< 5>				< 5>				< 5>				< 5>			
			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)
	necrosis: single cell		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
(Urinary system)																		
kidney	papillary 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)
(Reproductive system)																		
testis	germ cell 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 : Number of animals with lesion
(c) c : b / a * 100

STUDY NO. : 0336
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 4

		Group Name		4000 ppm				6000 ppm			
		No. of Animals on Study		5				5			
Organ_____	Findings_____	Grade		1	2	3	4	1	2	3	4
				(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
<hr/>											
{Hematopoietic system}											
thymus		< 5>				< 5>					
	congestion	0	0	0	0	0	0	0	0	0	0
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(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)	(0)	(0)	(0)	(0)
	necrosis: single cell	0	0	0	0	4	0	0	0	0	0
		(0)	(0)	(0)	(0)	(80)	(0)	(0)	(0)	(0)	(0)
 {Urinary system}											
kidney		< 5>				< 5>					
	papillary necrosis	3	0	0	0	2	0	0	0	0	0
		(60)	(0)	(0)	(0)	(40)	(0)	(0)	(0)	(0)	(0)
 {Reproductive system}											
testis		< 5>				< 5>					
	germ cell necrosis	0	0	0	0	4	0	0	0	0	0
		(0)	(0)	(0)	(0)	(80)	(0)	(0)	(0)	(0)	(0)

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

STUDY NO. : 0336
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 5

Organ	Findings	Group Name				0 ppm				500 ppm				1000 ppm				2000 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	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

{Reproductive system}

epididymis	debris of spermatic elements	< 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

(HPT150)

BAIS3

STUDY NO. : 0336
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 6

Organ	Findings	Group Name		4000 ppm				6000 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	5	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 : Number of animals with lesion
(c) c : b / a * 100

(HPT150)

BAIS3

APPENDIX K 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE: ALL ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0336
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 7

		Group Name	0 ppm				500 ppm				1000 ppm				2000 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		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}																		
nasal cavit			< 5>				< 5>				< 5>				< 5>			
	necrosis:olfactory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}																		
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)
			< 5>				< 5>				< 5>				< 5>			
	decreased hematopoiesis		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
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)
{Digestive system}																		
liver			< 5>				< 5>				< 5>				< 5>			
	herniation		0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
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. : 0336
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 8

		4000 ppm				6000 ppm				
		No. of Animals on Study				5				
Organ	Findings	Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
<hr/>										
{Respiratory system}										
nasal cavit			< 5>				< 5>			
	necrosis:olfactory epithelium		1	1	0	0	1	1	1	0
			(20)	(20)	(0)	(0)	(20)	(20)	(20)	(0)
{Hematopoietic system}										
bone marrow			< 5>				< 5>			
	congestion		0	1	0	0	0	5	0	0
			(0)	(20)	(0)	(0)	(0)	(100)	(0)	(0)
	decreased hematopoiesis		0	2	3	0	0	3	2	0
			(0)	(40)	(60)	(0)	(0)	(60)	(40)	(0)
thymus			< 5>				< 1>			
	atrophy		1	0	1	0	0	0	1	0
			(20)	(0)	(20)	(0)	(0)	(0)	(100)	(0)
{Digestive system}										
liver			< 5>				< 5>			
	herniation		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. : 0336
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 9

Organ	Findings	Group Name	0 ppm				500 ppm				1000 ppm				2000 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
liver			< 5>				< 5>				< 5>				< 5>			
	necrosis: single cell		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Urinary system}																		
kidney			< 5>				< 5>				< 5>				< 5>			
	papillary necrosis		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)	(20)	(0)	(0)	(0)	(0)
{Special sense organs/appendage}																		
Harder gl			< 5>				< 5>				< 5>				< 5>			
	inflammation		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)	(20)	(0)	(0)	(0)	(0)

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

(HPT150)

BAIS3

STUDY NO. : 0336
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 10

		4000 ppm				6000 ppm			
		5				5			
		Grade				Grade			
Organ	Findings	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

{Digestive system}

liver	necrosis:single cell	< 5>				< 5>			
		1	0	0	0	4	0	0	0
		(20)	(0)	(0)	(0)	(80)	(0)	(0)	(0)

{Urinary system}

kidney	papillary necrosis	< 5>				< 5>			
		4	0	0	0	0	0	0	0
		(80)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

{Special sense organs/appendage}

Harder gl	inflammation	< 5>				< 5>			
		1	2	0	0	0	0	0	0
		(20)	(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 : Number of animals with lesion
 (c) c : b / a * 100

(HPT150)

BAIS3

APPENDIX K 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0336
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 1

Organ	Findings	Group Name	0 ppm				500 ppm				1000 ppm				2000 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>			
	atrophy:olfactory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
			< 5>				< 5>				< 5>				< 5>			
	necrosis:olfactory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lung			< 5>				< 5>				< 5>				< 5>			
	hemorrhage		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{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)
			< 5>				< 5>				< 5>				< 5>			
	decreased hematopoiesis		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
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)
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. : 0336
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 2

		Group Name	4000 ppm				6000 ppm			
		No. of Animals on Study	5				3			
Organ	Findings	Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			< 5>				< 3>			
	atrophy:olfactory epithelium		2	0	0	0	0	0	0	0
			(40)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:olfactory epithelium		1	2	0	0	2	1	0	0
			(20)	(40)	(0)	(0)	(67)	(33)	(0)	(0)
lung			< 5>				< 3>			
	hemorrhage		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(67)	(0)	(0)	(0)
{Hematopoietic system}										
bone marrow			< 5>				< 3>			
	congestion		0	0	0	0	0	2	0	0
			(0)	(0)	(0)	(0)	(0)	(67)	(0)	(0)
	decreased hematopoiesis		4	0	0	0	0	0	3	0
			(80)	(0)	(0)	(0)	(0)	(0)	(100)	(0)
thymus			< 5>				< 3>			
	atrophy		3	0	0	0	1	0	2	0
			(60)	(0)	(0)	(0)	(33)	(0)	(67)	(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. : 0336
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 3

Organ	Findings	Group Name No. of Animals on Study Grade	0 ppm 5				500 ppm 5				1000 ppm 5				2000 ppm 5			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Hematopoietic system)																		
thymus			< 5>				< 5>				< 5>				< 5>			
	congestion		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)
(Digestive system)																		
liver			< 5>				< 5>				< 5>				< 5>			
	herniation		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)
	necrosis: single cell		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
(Urinary system)																		
kidney			< 5>				< 5>				< 5>				< 5>			
	papillary 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)
(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)

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

STUDY NO. : 0336
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 4

		4000 ppm				6000 ppm			
		No. of Animals on Study				3			
		Grade							
Organ_____	Findings_____	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
<hr/>									
{Hematopoietic system}									
thymus		< 5>				< 3>			
	congestion	0	0	0	0	0	0	0	0
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}									
liver		< 5>				< 3>			
	herniation	0	0	0	0	0	0	0	0
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis: single cell	0	0	0	0	2	0	0	0
		(0)	(0)	(0)	(0)	(67)	(0)	(0)	(0)
{Urinary system}									
kidney		< 5>				< 3>			
	papillary necrosis	3	0	0	0	1	0	0	0
		(60)	(0)	(0)	(0)	(33)	(0)	(0)	(0)
{Reproductive system}									
testis		< 5>				< 3>			
	germ cell necrosis	0	0	0	0	2	0	0	0
		(0)	(0)	(0)	(0)	(67)	(0)	(0)	(0)

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

STUDY NO. : 0336
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 5

Organ	Findings	Group Name				0 ppm				500 ppm				1000 ppm				2000 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	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. : 0336
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 6

Organ	Findings	4000 ppm				6000 ppm			
		No. of Animals on Study				3			
		Grade				3			
		1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

{Reproductive system}

epididymis		< 5>				< 3>			
debris of spermatic elements		0	0	0	0	3	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

APPENDIX K 4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0336
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 7

Organ	Findings	Group Name No. of Animals on Study Grade	0 ppm				500 ppm				1000 ppm				2000 ppm			
			5				5				5				5			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}																		
nasal cavit	necrosis:olfactory epithelium		< 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)
{Hematopoietic system}																		
bone marrow	decreased hematopoiesis		< 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)
{Digestive system}																		
liver	herniation		< 5>				< 5>				< 5>				< 5>			
			0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Urinary system}																		
kidney	papillary necrosis		< 5>				< 5>				< 5>				< 5>			
			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 : Number of animals with lesion
 (c) c : b / a * 100

STUDY NO. : 0336
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 8

		4000 ppm				6000 ppm			
		No. of Animals on Study				0			
		Grade							
Organ	Findings	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}									
nasal cavit	necrosis:olfactory epithelium	< 4>				< 0>			
		1	0	0	0	-	-	-	-
		(25)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
{Hematopoietic system}									
bone marrow	decreased hematopoiesis	< 4>				< 0>			
		0	2	2	0	-	-	-	-
		(0)	(50)	(50)	(0)	(-)	(-)	(-)	(-)
thymus	atrophy	< 4>				< 0>			
		1	0	0	0	-	-	-	-
		(25)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
{Digestive system}									
liver	herniation	< 4>				< 0>			
		0	0	0	0	-	-	-	-
		(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
{Urinary system}									
kidney	papillary necrosis	< 4>				< 0>			
		4	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

STUDY NO. : 0336
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 9

Organ	Findings	Group Name				0 ppm				500 ppm				1000 ppm				2000 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	inflammation	< 5>				< 5>				< 5>				< 5>			
		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 : Number of animals with lesion
 (c) c : b / a * 100

(HPT150)

BAIS3

STUDY NO. : 0336
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 10

		Group Name				4000 ppm				6000 ppm											
		No. of Animals on Study				4				0											
		Grade				1				2											
		3				4				1				2							
		4				1				2				3				4			
Organ	Findings	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)			

{Special sense organs/appendage}

Harder gl	inflammation	< 4>				< 0>			
		1	2	0	0	-	-	-	-
		(25)	(50)	(0)	(0)	(-)	(-)	(-)	(-)

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

(HPT150)

BAIS3

APPENDIX K 5

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0336
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 1

		Group Name	0 ppm				500 ppm				1000 ppm				2000 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
Organ	Findings		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}																		
nasal cavit			< 0>				< 0>				< 0>				< 0>			
	necrosis:olfactory epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
lung			< 0>				< 0>				< 0>				< 0>			
	hemorrhage		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{Hematopoietic system}																		
bone marrow			< 0>				< 0>				< 0>				< 0>			
	congestion		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	decreased hematopoiesis		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
thymus			< 0>				< 0>				< 0>				< 0>			
	atrophy		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{Digestive system}																		
liver			< 0>				< 0>				< 0>				< 0>			
	necrosis:single cell		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
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. : 0336
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 2

		Group Name	4000 ppm				6000 ppm			
		No. of Animals on Study	0				2			
Organ	Findings	Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit	necrosis:olfactory epithelium		< 0>				< 2>			
		-	-	-	-	0	1	0	0	
			(-)	(-)	(-)	(-)	(0)	(50)	(0)	(0)
lung	hemorrhage		< 0>				< 2>			
		-	-	-	-	2	0	0	0	
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
{Hematopoietic system}										
bone marrow	congestion		< 0>				< 2>			
		-	-	-	-	0	2	0	0	
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
	decreased hematopoiesis		< 0>				< 2>			
		-	-	-	-	0	0	2	0	
			(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)
thymus	atrophy		< 0>				< 2>			
		-	-	-	-	0	0	2	0	
			(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)
{Digestive system}										
liver	necrosis:single cell		< 0>				< 2>			
		-	-	-	-	2	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									

STUDY NO. : 0336
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 3

Organ	Findings	Group Name No. of Animals on Study				0 ppm				500 ppm				1000 ppm				2000 ppm			
		Grade				0				0				0				0			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}																					
kidney		< 0>				< 0>				< 0>				< 0>				< 0>			
	papillary necrosis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{Reproductive system}																					
testis		< 0>				< 0>				< 0>				< 0>				< 0>			
	germ cell necrosis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
epididymis		< 0>				< 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. : 0336
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 4

		4000 ppm				6000 ppm			
		No. of Animals on Study				2			
		Grade							
Organ	Findings	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Urinary system)									
kidney		< 0>				< 2>			
	papillary necrosis	-	-	-	-	1	0	0	0
		(-)	(-)	(-)	(-)	(50)	(0)	(0)	(0)
(Reproductive system)									
testis		< 0>				< 2>			
	germ cell necrosis	-	-	-	-	2	0	0	0
		(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
epididymis		< 0>				< 2>			
	debris of spermatic elements	-	-	-	-	2	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

APPENDIX K 6

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0396
 ANIMAL : RAT F344/DuCrj
 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				0 ppm 0				500 ppm 0				1000 ppm 0				2000 ppm 0			
		Grade				1				1				1				1			
		1 2 3 4				1 2 3 4				1 2 3 4				1 2 3 4				1 2 3 4			
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}																					
nasal cavit		< 0>				< 0>				< 0>				< 0>				< 0>			
	necrosis:olfactory epithelium	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{Hematopoietic system}																					
bone marrow		< 0>				< 0>				< 0>				< 0>				< 0>			
	congestion	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	decreased hematopoiesis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
thymus		< 0>				< 0>				< 0>				< 0>				< 0>			
	atrophy	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{Digestive system}																					
liver		< 0>				< 0>				< 0>				< 0>				< 0>			
	necrosis:single cell	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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

STUDY NO. : 0336
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 6

Organ	Findings	Group Name		4000 ppm				6000 ppm			
		No. of Animals on Study		1				5			
		Grade		1	2	3	4	1	2	3	4
				(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}											
nasal cavit	necrosis:olfactory epithelium			< 1>				< 5>			
				0	1	0	0	1	1	1	0
				(0)	(100)	(0)	(0)	(20)	(20)	(20)	(0)
{Hematopoietic system}											
bone marrow	congestion			< 1>				< 5>			
				0	1	0	0	0	5	0	0
				(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
	decreased hematopoiesis			0	0	1	0	0	3	2	0
				(0)	(0)	(100)	(0)	(0)	(60)	(40)	(0)
thymus	atrophy			< 1>				< 1>			
				0	0	1	0	0	0	1	0
				(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)
{Digestive system}											
liver	necrosis:single cell			< 1>				< 5>			
				1	0	0	0	4	0	0	0
				(100)	(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 : Number of animals with lesion
 (c) c : b / a * 100

APPENDIX L 1

IDENTITY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE
IN THE 2-WEEK DRINKING WATER STUDY

IDENTITY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE IN THE 2-WEEK DRINKING WATER STUDYTest Substance : *o*-Phenylenediamine Dihydrochloride (Wako Pure Chemical Industries, Ltd.)

Lot No. : WTM0491

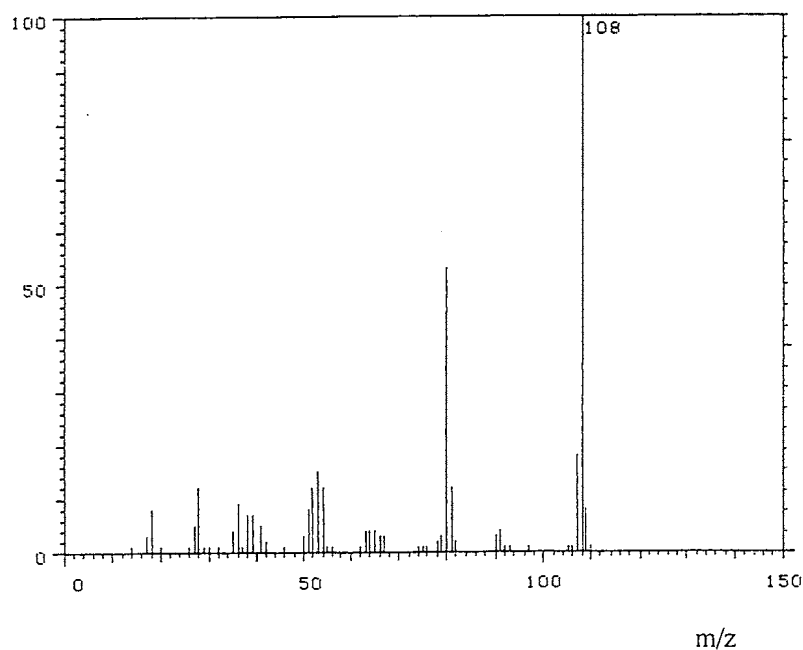
1. Spectral Data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Determined Value

Fragment Peak (m/z)

108

Calculated Value

Fragment Peak (m/z)

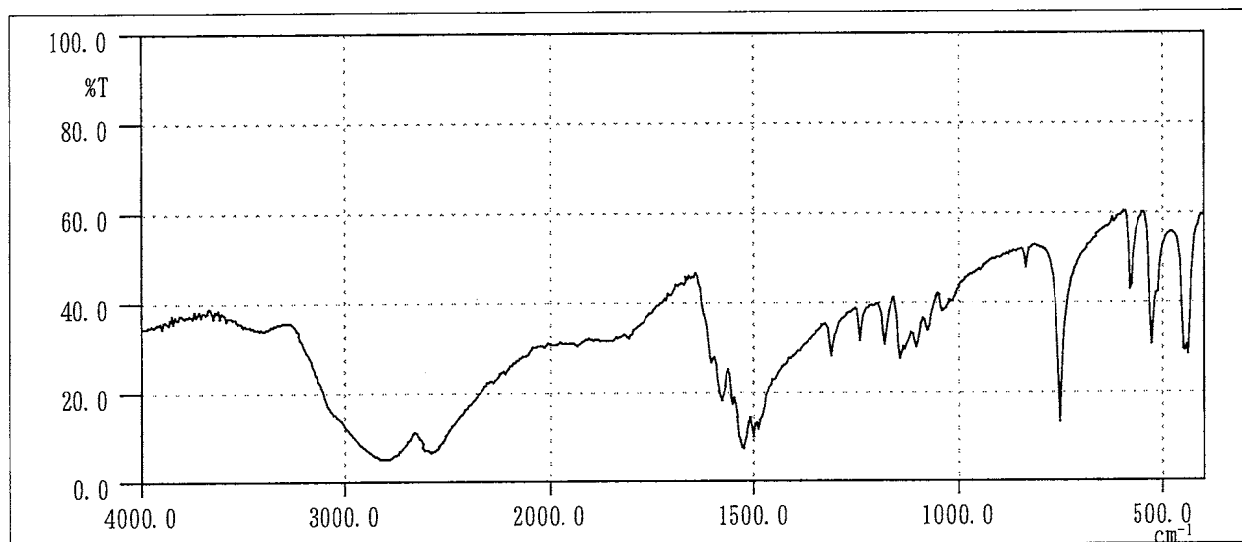
108 ($\text{NH}_2\text{C}_6\text{H}_4\text{NH}_2 \cdot 2\text{HCl}$) - (2HCl)

Results: The mass spectrum was consistent with calculated spectrum.

Infrared Spectrometry

Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr

Resolution : 2 cm^{-1} 

Infrared Spectrum of Test Substance

<u>Determined Values</u>	<u>Literature Values</u> *
Wave Number (cm^{-1})	Wave Number (cm^{-1})
410~480	410~480
480~550	480~550
550~600	550~600
680~800	680~800
820~850	820~850
1010~1050	1010~1050
1050~1160	1050~1160
1160~1200	1160~1200
1250~1280	1250~1280
1280~1330	1280~1330
1330~1640	1330~1640
2100~3200	2100~3200

Results: The infrared spectrum was consistent with literature spectrum.

(*Performed by Wako Pure Chemical Industries, Ltd.)

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

APPENDIX L 2

STABILITY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE IN THE 2-WEEK DRINKING WATER STUDY

STABILITY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE IN THE 2-WEEK DRINKING WATER STUDY

Test Substance : *o*-Phenylenediamine Dihydrochloride (Wako Pure Chemical Industries, Ltd.)

Lot No. : WTM0491

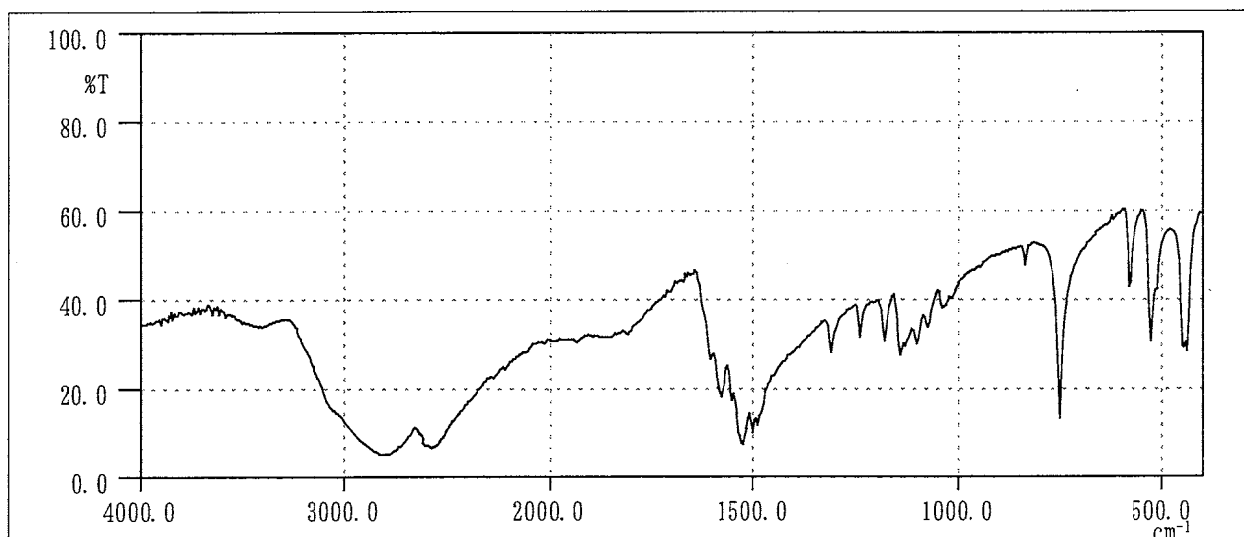
1. Sample : This lot was used from 1997.9.12 to 1997.9.26. Test substance was stored in cold storage in a dark place.

2. Infrared Spectrometry

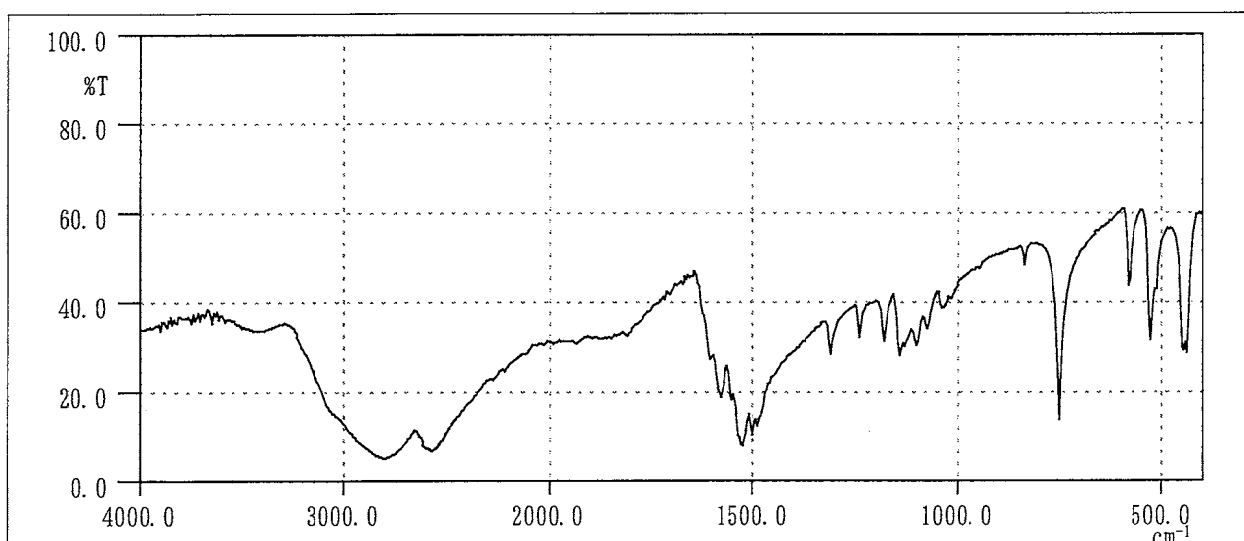
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr

Resolution : 2 cm^{-1}



Infrared Spectrum of Test Substance (date analyzed : 1997.09.09)



Infrared Spectrum of Test Substance (date analyzed : 1997.09.30)

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

3. High Performance Liquid Chromatography

Instrument : Hewlett Packard 1090 High Performance Liquid Chromatograph
Column : TSK GEL ODS-80TM (4.6 m ϕ \times 15 cm)
Column Temperature : Room Temperature
Flow Rate : 1 mL/min
Mobile Phase : Distilled Water (10mM Potassium Dihydrogenphosphate, 5mM
1-Hexanesulfonic Acid Sodium Salt) : Acetonitrile = 80 : 20
Detector : UV (290 nm)
Injection Volume : 20 μ L

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
1997.09.09	1	3.267	100
1997.09.30	1	3.229	100

Results: High performance liquid chromatography indicated one major peak (peak No.1) analyzed on 1997.9.09 and one major peak (peak No.1) analyzed on 1997.9.30. No new trace impurity peak in the test substance analyzed on 1997.9.30 was detected.

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

APPENDIX L 3

CONCENTRATION OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE
IN FORMULATED WATER IN THE 2-WEEK DRINKING WATER STUDY

CONCENTRATION OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE IN FORMULATED WATER IN THE 2-WEEK DRINKING WATER STUDY

Date Analyzed	Target Concentration				
	500 ^a	1000	2000	4000	6000
1997.09.12	490 (98.0) ^b	977 (97.7)	1930 (96.5)	3810 (95.3)	5770 (96.2)

^a ppm

^b %

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

Instrument : Hewlett Packard 1090 High Performance Liquid Chromatograph

Column : TSK GEL ODS-80TM (4.6 mm ϕ \times 15 cm)

Column Temperature : Room Temperature

Flow Rate : 1 mL/min

Mobile Phase : Distilled Water (10mM Potassium Dihydrogenphosphate, 5mM 1-Hexanesulfonic Acid Sodium Salt) :
Acetonitrile = 80 : 20

Detector : UV (290 nm)

Injection Volume : 20 μ L

APPENDIX L 4

STABILITY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE IN FORMULATED WATER
IN THE 2-WEEK DRINKING WATER STUDY

STABILITY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE IN FORMULATED WATER IN
THE 2-WEEK DRINKING WATER STUDY

Date Prepared	Date Analyzed	Target Concentration	
		500 ^a	6000
1997.09.01	1997.09.01	477 (100) ^b	5790 (100)
	1997.09.05 ^c	477 (100)	5840 (101)

^a ppm

^b % (Percentage was based on the concentration on date of preparation.)

^c Animal room samples

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

Instrument : Hewlett Packard 1090 High Performance Liquid Chromatograph

Column : TSK GEL ODS-80TM (4.6 mm ϕ \times 15 cm)

Column Temperature : Room Temperature

Flow Rate : 1 mL/min

Mobile Phase : Distilled Water (10mM Potassium Dihydrogenphosphate, 5mM 1-Hexanesulfonic Acid Sodium Salt) : Acetonitrile = 80 : 20

Detector : UV (290 nm)

Injection Volume : 20 μ L

APPENDIX M 1

METHODS FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK
DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

METHODS FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK DRINKING
WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

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 $RBC \times MCV / 10$ 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⁾
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⁾ (May-Grunwald-Giemsa 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	Enzymatic method (GLK · G-6-PDH) ⁴⁾
T-cholesterol	Enzymatic method (CE · COD · POD) ⁴⁾
Phospholipid	Enzymatic method (PLD · COD · POD) ⁴⁾
Glutamic oxaloacetic transaminase (GOT)	IFCC method ⁴⁾
Glutamic pyruvic transaminase (GPT)	IFCC method ⁴⁾
Lactate dehydrogenase (LDH)	Wroblewski-LaDue method ⁴⁾
γ -Glutamyl transpeptidase (γ -GTP)	L- γ -Glutamyl-p-nitroanilide method ⁴⁾
Creatine phosphokinase (CPK)	GSCC method ⁴⁾
Urea nitrogen	Enzymatic method (Urease · GLDH) 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	Enzymatic method (PNP · XOD · POD) ⁴⁾

1) Automatic blood cell analyzer (Technicon H·1 : Technicon Instruments Corporation)

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

3) Automatic blood cell differential analyzer (Hitachi 8200 : Hitachi,Ltd.)

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

5) CO-oximeter (CIBA · CORNING 270 : Ciba Corning Diagnostics Corp)

APPENDIX N 1

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK
DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK
DRINKING WATER STUDY OF *o*-PHENYLENEDIAMINE DIHYDROCHLORIDE

Item	Unit	Decimal Place
Hematology		
Red blood cell (RBC)	$\times 10^6 / \mu\text{L}$	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	$\times 10^3 / \mu\text{L}$	0
Reticulocyte	‰	0
Prothrombin time	sec	1
Activated partial thromboplastin time (APTT)	sec	1
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 transaminase (GOT)	IU/L	0
Glutamic pyruvic transaminase (GPT)	IU/L	0
Lactate dehydrogenase (LDH)	IU/L	0
γ -Glutamyl transpeptidase (γ -GTP)	IU/L	0
Creatine phosphokinase (CPK)	IU/L	0
Urea nitrogen	mg/dL	1
Creatinine	mg/dL	1
Sodium	mEq/L	0
Potassium	mEq/L	1
Chloride	mEq/L	0
Calcium	mg/dL	1
Inorganic phosphorus	mg/dL	1