o-フェニレンジアミン二塩酸塩のマウスを用いた 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:0337

APPENDIXES

APPENDIXES

APPENDIX A 1	CLINICAL OBSERVATION: SUMMARY, MOUSE : MALE (2-WEEK STUDY)
APPENDIX A 2	CLINICAL OBSERVATION: SUMMARY, MOUSE : FEMALE (2-WEEK STUDY)
APPENDIX B 1	BODY WEIGHT CHANGES: SUMMARY, MOUSE: MALE (2-WEEK STUDY)
APPENDIX B 2	BODY WEIGHT CHANGES: SUMMARY, MOUSE: FEMALE (2-WEEK STUDY)
APPENDIX C 1	WATER CONSUMPTION CHANGES: SUMMARY, MOUSE: MALE (2-WEEK STUDY)
APPENDIX C 2	WATER CONSUMPTION CHANGES: SUMMARY, MOUSE: FEMALE (2-WEEK STUDY)
APPENDIX D 1	FOOD CONSUMPTION CHANGES: SUMMARY, MOUSE: MALE (2-WEEK STUDY)
APPENDIX D 2	FOOD CONSUMPTION CHANGES: SUMMARY, MOUSE: FEMALE (2-WEEK STUDY)
APPENDIX E 1	CHEMICAL INTAKE CHANGES: SUMMARY, MOUSE: MALE (2-WEEK STUDY)
APPENDIX E 2	CHEMICAL INTAKE CHANGES: SUMMARY, MOUSE: FEMALE (2-WEEK STUDY)
APPENDIX F 1	HEMATOLOGY: SUMMARY, MOUSE: MALE (2-WEEK STUDY)
APPENDIX F 2	HEMATOLOGY: SUMMARY, MOUSE: FEMALE (2-WEEK STUDY)
APPENDIX G 1	BIOCHEMISTRY: SUMMARY, MOUSE: MALE (2-WEEK STUDY)
APPENDIX G 2	BIOCHEMISTRY: SUMMARY, MOUSE: FEMALE (2-WEEK STUDY)

APPENDIXES (CONTINUED)

APPENDIX H 1	GROSS FINDINGS: SUMMARY, MOUSE: MALE: ALL ANIMALS (2-WEEK STUDY)
APPENDIX H 2	GROSS FINDINGS: SUMMARY, MOUSE: FEMALE: ALL ANIMALS (2-WEEK STUDY)
APPENDIX H 3	GROSS FINDINGS: SUMMARY, MOUSE: FEMALE: SACRIFICED ANIMALS (2-WEEK STUDY)
APPENDIX H 4	GROSS FINDINGS: SUMMARY, MOUSE: FEMALE: DEAD AND MORIBUND ANIMALS (2-WEEK STUDY)
APPENDIX I 1	ORGAN WEIGHT: ABSOLUTE: SUMMARY, MOUSE: MALE (2-WEEK STUDY)
APPENDIX I 2	ORGAN WEIGHT: ABSOLUTE: SUMMARY, MOUSE: FEMALE (2-WEEK STUDY)
APPENDIX J 1	ORGAN WEIGHT: RELATIVE: SUMMARY, MOUSE: MALE (2-WEEK STUDY)
APPENDIX J 2	ORGAN WEIGHT: RELATIVE: SUMMARY, MOUSE: FEMALE (2-WEEK STUDY)
APPENDIX K 1	HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY, MOUSE: MALE: ALL ANIMALS (2-WEEK STUDY)
APPENDIX K 2	HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY, MOUSE: FEMALE: ALL ANIMALS (2-WEEK STUDY)
APPENDIX K 3	HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY, MOUSE: FEMALE: SACRIFICED ANIMALS (2-WEEK STUDY)
APPENDIX K 4	HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY, MOUSE: FEMALE: DEAD AND MORIBUND ANIMALS (2-WEEK STUDY)

APPENDIXES (CONTINUED)

APPENDIX L 1	IDENTITY OF o -PHENYLENEDIAMINE DIHYDROCHLORIDE IN THE 2-WEEK DRINKING WATER STUDY
APPENDIX L 2	STABILITY OF ϕ -PHENYLENEDIAMINE DIHYDROCHLORIDE IN THE 2-WEEK DRINKING WATER STUDY
APPENDIX L 3	CONCENTMOUSEION OF ϕ -PHENYLENEDIAMINE DIHYDROCHLORIDE IN FORMULATED WATER IN THE 2-WEEK DRINKING WATER STUDY
APPENDIX L 4	STABILITY OF ϕ -PHENYLENEDIAMINE DIHYDROCHLORIDE IN FORMULATED WATER IN THE 2-WEEK DRINKING WATER STUDY
APPENDIX M 1	METHODS FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK DRINKING WATER STUDY OF o -PHENYLENEDIAMINE DIHYDROCHLORIDE
APPENDIX N1	UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK DRINKING WATER STUDY OF σ -PHENYLENEDIAMINE DIHYDROCHLORIDE

APPENDIX A 1

CLINICAL OBSERVATION: SUMMARY, MOUSE: MALE

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 2

SEX : MALE

PAGE: 1

Clinical sign	Group Name	Admini	stration W	eek-day			
	•	1-1	1-3	1-7	2-3	2-7	
PILOERECTION	0 ppm	0	0	0	0	0	
	500 ppm	0	0	0	0	0	
	1000 ppm	0	0	1	0	0	
	2000 ppm	0	0	0	0	0	
	4000 ppm	0	0	0	0	0	
	6000 ppm	0	0	0	0 .	0	
OILED PERI GENITALIA	0 ppm	0	0	0	0	0	
	500 ppm	0	0	0	0	0	
	1000 ppm	0	0	Ö	0	0	
	2000 ppm	0	0	Ö	Ō	0	
	4000 ppm	Ō	0	0	0 -	0	
	6000 ppm	0	0	0	2	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 4	
	6000 ppm	0	0	0	4	4	
LIGO-STOOL	0 ppm	0	0	0	0	0	
	500 ppm	0	1	1	1	1	
	1000 ppm	0	0	1	0	0	
	2000 ppm	0	0	1	1	1	
	4000 ppm	0	0	0	0		
	6000 ppm	0	0	0	Ō	0	•

(HAN190)

BAIS 3

APPENDIX A 2

CLINICAL OBSERVATION: SUMMARY, MOUSE: FEMALE

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 2

SEX : FEMALE PAGE: 2

Clinical sign	Group Name	Admini	stration W	eek-day		
3	•	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	1	1
PILOERECTION	O 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	1	1
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	1	1
	••					

(HAN190) BAIS 3

APPENDIX B 1

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

ANIMAL : MOUSE Crj:BDF1

UNIT : g

REPORT TYPE : A1 2

SEX : MALE

BODY WEIGHT CHANGES ALL ANIMALS (SUMMARY)

PAGE: 1

oup Name	Administratio	n week-day					
	0-0	1-1	1-3	1-7	2-3	2-7	
0 ppm	22.8± 0.6	22.4± 0.8	23.2± 1.1	23.5± 1.3	23.5± 1.5	24.1± 1.0	
500 ppm	22.8± 0.6	21.4± 1.3	22.0± 2.0	22.5± 2.2	22.7± 2.9	23.0 ± 3.1	
1000 ppm	22.8± 1.0	22.0± 0.9	22.1± 1.5	22.1± 3.1	22.8± 1.9	23.6± 2.2	
2000 ppm	22.9± 0.4	21.0± 0.6	20.9± 2.0	21.4± 3.3	21.6± 2.3	23.3± 1.9	
4000 ppm	22.8± 0.8	19.9± 0.6**	18.4± 0.6**	19.4± 1.5*	19.8± 0.9*	21.5± 0.9	
6000 ppm	22.8± 0.7	20.0± 0.6**	17.9± 0.6**	15.5± 1.2**	15.4± 2.4**	15.7± 3.4**	
Significant difference	*; *: P ≤ 0.05	** : P ≤ 0.01		Test of Dunnett			

(HAN260)

BAIS 3

APPENDIX B 2

BODY WEIGHT CHANGES: SUMMARY, MOUSE: FEMALE

ANIMAL : MOUSE Crj:BDF1
UNIT : g

REPORT TYPE : A1 2

SEX : FEMALE

BODY WEIGHT CHANGES ALL ANIMALS

(SUMMARY)

PAGE: 2

oup Name	Administration	week-day					
	0-0	1-1	1-3	1-7	2-3	2-7	
O ppm	19.3± 0.7	18.6± 1.2	19.4± 0.4	20.1± 0.8	20.9± 0.9	20.7± 0.6	
500 ppm	19.3± 0.7	19.1± 0.2	19.8± 0.6	20.3± 0.4	20.8± 1.2	21.2± 0.3	
1000 ppm	19.3± 0.6	18.5± 0.5	19.3± 0.9	19.7± 0.5	19.8± 0.8	20.1± 0.7	
2000 ppm	19.3± 0.6	17.8± 0.5	18.6± 0.9	19.3± 0.5	20.5± 0.7	20.4± 0.7	
4000 ppm	19.3± 0.6	16.8± 0.5**	15.4± 0.4**	16.5± 1.9*	17.7± 2.2**	19.4± 1.3	
6000 ppm	19.3± 0.6	16.3± 0.7**	14.7± 1.0**	13.1± 1.5**	13.6± 2.2**	14.8± 3.1*	
Significant difference	* : P ≤ 0.05	** : P ≤ 0.01		Test of Dunnett			
N260)							

APPENDIX C 1

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

ANIMAL : MOUSE Crj:BDF1

UNIT : g

REPORT TYPE : A1 2

WATER CONSUMPTION CHANGES (SUMMARY)

ALL ANIMALS

p Name	Administration	week-day(effective)			
	1-3 (3)	1-7 (4)	2-3 (3)	2-7 (4)	
O ppm	4.2± 0.1	4.0± 0.3	3.8 ± 0.3	4.0± 0,8	
500 ppm	3.2± 1.1	3.8± 0.6	3.7± 1.0	3.5± 0.7	
1000 ppm	3.2± 0.8	3.1± 1.4	3.1± 0.8	3.1± 0.9	
2000 ppm	1.8± 0.7*	2.1± 0.5	1.8± 0.6**	2.2± 0.2**	
4000 ppm	0.9± 0.2**	1.6± 0.3*	1.7± 0.5**	1.9± 0.3**	
6000 ppm	0.6± 0.1**	0.6± 0.2**	0.9± 0.6**	1.2± 0.5**	
Significant difference;	*: P ≤ 0.05	**: P ≤ 0.01		Test of Dunnett	

APPENDIX C 2

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

ANIMAL : MOUSE Crj:BDF1

UNIT : g

REPORT TYPE : A1 2

SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)

ALL ANIMALS

Administration week-day(effective)_ Group Name 1-3(3) 1-7(4)2-3(3)2-7(4)0 ppm 4.8± 0.8 4.8± 0.5 4.3± 0.4 4.3± 1.8 500 ppm 4.2± 0.3 4.0± 0.2 4.0± 0.4* 4.2± 0.4 1000 ppm 3.2 ± 0.5 2.9± 0.5** 3.1 ± 0.5 3.0± 0.6** 2.2± 0.2** 2000 ppm 2.2 ± 0.3 2.1± 0.1** 2.2 ± 0.2 4000 ppm 1.0± 0.2** 1.5± 0.4** 1.9± 0.5** 1.9± 0.2* 6000 ppm 0.7± 0.1** 0.7± 0.3** 1.0± 0.3** 1.6± 0.4**

Significant difference; $*: P \leq 0.05$

** : P ≤ 0.01

Test of Dunnett

(HAN260)

BAIS 3

PAGE: 2

APPENDIX D 1

FOOD CONSUMPTION CHANGES: SUMMARY, MOUSE: MALE

FOOD CONSUMPTION CHANGES (SUMMARY)

ANIMAL : MOUSE Crj:BDF1 ALL ANIMALS

UNIT : g

REPORT TYPE : A1 2

SEX : MALE

PAGE: 1

O ppm				
→ Phm	3.8± 0.4	3.9± 0.2		
500 ppm	3.6± 0.6	3.9± 0.5		
1000 ppm	3.5± 0.6	4.0± 0.1		
2000 ppm	3.4± 0.9	4.4± 0.4		
4000 ppm	2.8± 0.2*	3.9± 0.2		
6000 ppm	2.2± 0.3**	2.9± 0.6		

(HAN260)

BAIS 3

APPENDIX D 2

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

ANIMAL : MOUSE Crj:BDF1

UNIT : g

REPORT TYPE : A1 2

FOOD CONSUMPTION CHANGES (SUMMARY)

ALL ANIMALS

up Name	Administration 1-7(7)	week-day(effective) 2-7(7)		
	1-(()	2-1(1)		
0 ppm	3.4± 0.2	3.5± 0.3		
500 ppm	3.5± 0.1	3.6± 0.1		
1000 ppm	3.4± 0.3	3.6± 0.3		
2000 ppm	3.3± 0.2	3.6± 0.2		
4000 ppm	2.4± 0.2**	3.8± 0.2		
6000 ppm	1.8± 0.4**	2.6± 0.6		
Significant differen	nce; *:P≦0.05 *	* : P ≤ 0.01	Test of Dunnett	

(HAN260)

BAIS 3

APPENDIX E 1

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

CHEMICAL INTAKE CHANGES (SUMMARY)

PAGE: 1

ANIMAL

: MOUSE Crj:BDF1

ALL ANIMALS

UNIT

: g/kgBW/day

SEX

: MALE

coup Name	Administration weel	k-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	0.071 ± 0.020	0.084 ± 0.010	0.080 ± 0.014	0.076 ± 0.009
1000ppm	0.143 ± 0.037	$0.135~\pm~0.056$	0.138 ± 0.035	0.133 ± 0.036
2000ppm	0.164 ± 0.055	0.190 ± 0.024	0.169 ± 0.062	0.191 ± 0.016
4000ppm	0.187 ± 0.034	0.336 ± 0.043	0.346 ± 0.095	0.361 ± 0.060
6000ppm	0.201 ± 0.038	0.230 ± 0.056	0.351 ± 0.153	0.438 ± 0.246

APPENDIX E 2

CHEMICAL INTAKE CHANGES: SUMMARY, MOUSE: FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)

PAGE: 1

ANIMAL

: MOUSE Crj:BDF1

ALL ANIMALS

UNIT

: g/kgBW/day

SEX

: FEMALE

Group Name	Administration weel	x-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	0.106 ± 0.009	0.099 ± 0.010	0.102 ± 0.012	0.094 ± 0.004
1000ppm	0.169 ± 0.029	0.154 ± 0.032	0.145 ± 0.028	0.152 ± 0.029
2000ppm	0.232 ± 0.024	0.228 ± 0.018	0.207 ± 0.005	0.211 ± 0.019
4000ppm	0.270 ± 0.043	0.353 ± 0.056	0.423 ± 0.105	0.389 ± 0.057
6000ppm	0.268 ± 0.032	0.323 ± 0.103	0.445 ± 0.082	0.635 ± 0.043

APPENDIX F 1

HEMATOLOGY: SUMMARY, MOUSE: MALE

HEMATOLOGY (SUMMARY) ALL ANIMALS (2W)

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : A1

PAGE: 1

roup Name	NO. of Animals	RED BLOOD 1 O ^s /µl		HEMOGLO g/dl	BIN	HEMATOC %	RIT	MCV f l	,	MCH pg		MCHC g/dl		PLATELE 1 0³/µ	
0 ppm	3	9.98± 0	0.68	16.1±	0.8	50.2±	3, 5	50.4±	2. 4	16.2±	2.0	32.2±	3. 3	1069±	532
500 ppm	5	9.81± 0	0. 47	15.2±	0.9	48.3±	3. 1	49.1±	1. 3	15.5±	0.9	31.4±	1.8	1269土	333
1000 ppm	5	9.90± 0	0, 39	15.4±	0.3	50.2±	1.9	50.7±	1. 3	15.6±	0.8	30.7±	1. 4	1243±	358
2000 ppm	5	10.02± 0	0.64	15.3±	0.8	49.9±	3, 3	49.7±	0.3	15.3±	0.9	30.8±	1.7	1148±	175
4000 ppm	4	10.19± 0	0. 46	15.2±	0.4	50.4±	2. 1	49.5±	0.8	15.0±	0.3	30.2±	0.4	1324±	239
6000 ppm	4	10.81± (0.50	16.7±	0.8	53.6±	2.4	49.6±	0.4	15.4 \pm	0.2	31.1±	0.6	1284±	338

(IICLO70) BAIS 3

HEMATOLOGY (SUMMARY) ALL ANIMALS (2W)

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME : 1 SEX : MALE

REPORT TYPE : A1

PAGE: 2

Group Name	NO. of Animals	WBC 1 0 ³ /		Dif N-BAND	ferentia	1 WBC (% N-SEG	6)	EOSINO		BAS0		MONO		LYMPHO		OTHERS	·
0 ppm	3	1.96±	0, 48	0±	0	23±	14	2±	3	0±	0	1±	0	74±	17	0±	0
500 ppm	5	1.62±	0.67	0±	0	22土	18	1±	1	0±	0	2±	1	76±	17	0±	0
1000 ppm	5	2.07±	1. 27	0±	0	20±	10	1±	1	0±	0	2±	2	77±	12	0±	0
2000 ppm	5	1.78±	0.45	0±	1	21±	12	1±	1	0±	0	2±	1	75±	12	0±	0
4000 ppm	4	1.88±	0.34	1±	1	16±	3	2±	1	0±	0	2±	2	79±	2	0±	0
6000 ppm	4	0.60±	0.54	2±	2	43±	19	1±	1	0±	0	3±	2	53±	21	0±	0

(HCL070) BAIS 3

APPENDIX F 2

HEMATOLOGY: SUMMARY, MOUSE: FEMALE

HEMATOLOGY (SUMMARY) ALL ANIMALS (2W)

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1 SEX : FEMALE

REPORT TYPE : A1 PAGE: 3

NO. of Animals			HEMOGLO g/dl	BIN	HEMATOC %	RIT	MCV f &		MCH pg		MCHC g/dl		PLATELE 1 0³/µ	
5	9.49±	1.11	15.2±	0.6	47.0±	5, 6	49.5±	0.4	16.1±	1.6	32.6±	3, 5	1013±	139
5	9.83±	0.47	14.6±	0.7	49.0±	2. 9	49.8±	1.0	14.8±	0.2	29.9±	0.8	1116±	110
4	9.93±	0.31	15.1±	0.2	49.3±	1.8	49.6±	1.5	15.2±	0.3	30.7±	0.8	1104±	60
5	9.98±	0.32	15.0±	0.5	48.8±	1. 4	49.0±	0.9	15.0±	0.2	30.6±	0.6	1118±	79
5	10.26±	0.33	15.4±	0.6	50.8±	1.8	49.5±	0.4	15.0±	0.2	30.3±	0.7	1174±	131
4	10.14±	0.16	15.5±	0.3	49.2±	1.3	48.6±	0.6	15.2±	0.1	31.3±	0.3	1369±	92**
	Animals 5 4 5 5	Animals 1 0 ⁶ /μ 5 9.49± 5 9.83± 4 9.93± 5 9.98± 5 10.26±	1 0 ⁶ /μl 5 9.49± 1.11 5 9.83± 0.47 4 9.93± 0.31 5 9.98± 0.32 5 10.26± 0.33	Animals $10^6 / \mu \ell$ g/d ℓ 8 g/d ℓ 5 9.49 \pm 1.11 15.2 \pm 5 9.83 \pm 0.47 14.6 \pm 4 9.93 \pm 0.31 15.1 \pm 5 9.98 \pm 0.32 15.0 \pm 5 10.26 \pm 0.33 15.4 \pm	Animals 10 ⁶ /µl g/dl 5 9.49± 1.11 15.2± 0.6 5 9.83± 0.47 14.6± 0.7 4 9.93± 0.31 15.1± 0.2 5 9.98± 0.32 15.0± 0.5 5 10.26± 0.33 15.4± 0.6	Animals 1 0 ⁶ /μl g/dl % 5 9.49± 1.11 15.2± 0.6 47.0± 5 9.83± 0.47 14.6± 0.7 49.0± 4 9.93± 0.31 15.1± 0.2 49.3± 5 9.98± 0.32 15.0± 0.5 48.8± 5 10.26± 0.33 15.4± 0.6 50.8±	Animals 1 0 ⁶ /μl g/dl % 5 9.49± 1.11 15.2± 0.6 47.0± 5.6 5 9.83± 0.47 14.6± 0.7 49.0± 2.9 4 9.93± 0.31 15.1± 0.2 49.3± 1.8 5 9.98± 0.32 15.0± 0.5 48.8± 1.4 5 10.26± 0.33 15.4± 0.6 50.8± 1.8	Animals 1 0 ⁶ /μl g/dl % f l 5 9.49± 1.11 15.2± 0.6 47.0± 5.6 49.5± 5 9.83± 0.47 14.6± 0.7 49.0± 2.9 49.8± 4 9.93± 0.31 15.1± 0.2 49.3± 1.8 49.6± 5 9.98± 0.32 15.0± 0.5 48.8± 1.4 49.0± 5 10.26± 0.33 15.4± 0.6 50.8± 1.8 49.5±	Animals 10 ⁶ /μℓ g/dℓ % fℓ 5 9.49± 1.11 15.2± 0.6 47.0± 5.6 49.5± 0.4 5 9.83± 0.47 14.6± 0.7 49.0± 2.9 49.8± 1.0 4 9.93± 0.31 15.1± 0.2 49.3± 1.8 49.6± 1.5 5 9.98± 0.32 15.0± 0.5 48.8± 1.4 49.0± 0.9 5 10.26± 0.33 15.4± 0.6 50.8± 1.8 49.5± 0.4	Animals 10 ⁶ /µl g/dl % f l pg 5 9.49± 1.11 15.2± 0.6 47.0± 5.6 49.5± 0.4 16.1± 5 9.83± 0.47 14.6± 0.7 49.0± 2.9 49.8± 1.0 14.8± 4 9.93± 0.31 15.1± 0.2 49.3± 1.8 49.6± 1.5 15.2± 5 9.98± 0.32 15.0± 0.5 48.8± 1.4 49.0± 0.9 15.0± 5 10.26± 0.33 15.4± 0.6 50.8± 1.8 49.5± 0.4 15.0±	Animals 106/µl g/dl % f l pg 5 9.49± 1.11 15.2± 0.6 47.0± 5.6 49.5± 0.4 16.1± 1.6 5 9.83± 0.47 14.6± 0.7 49.0± 2.9 49.8± 1.0 14.8± 0.2 4 9.93± 0.31 15.1± 0.2 49.3± 1.8 49.6± 1.5 15.2± 0.3 5 9.98± 0.32 15.0± 0.5 48.8± 1.4 49.0± 0.9 15.0± 0.2 5 10.26± 0.33 15.4± 0.6 50.8± 1.8 49.5± 0.4 15.0± 0.2	Animals $1.0^6 / \mu \ell$ g/d ℓ % f ℓ pg g/d ℓ % $1.0^6 / \mu \ell$ 1.11 15.2 ± 0.6 15.2 ± 0.6 16.1 ± 1.6	Animals 10%/µl g/dl % f l pg g/dl 5 9.49± 1.11 15.2± 0.6 47.0± 5.6 49.5± 0.4 16.1± 1.6 32.6± 3.5 5 9.83± 0.47 14.6± 0.7 49.0± 2.9 49.8± 1.0 14.8± 0.2 29.9± 0.8 4 9.93± 0.31 15.1± 0.2 49.3± 1.8 49.6± 1.5 15.2± 0.3 30.7± 0.8 5 9.98± 0.32 15.0± 0.5 48.8± 1.4 49.0± 0.9 15.0± 0.2 30.6± 0.6 5 10.26± 0.33 15.4± 0.6 50.8± 1.8 49.5± 0.4 15.0± 0.2 30.3± 0.7	Animals 10%/µl g/dl % f l pg g/dl 10%/µl 5 9.49± 1.11 15.2± 0.6 47.0± 5.6 49.5± 0.4 16.1± 1.6 32.6± 3.5 1013± 5 9.83± 0.47 14.6± 0.7 49.0± 2.9 49.8± 1.0 14.8± 0.2 29.9± 0.8 1116± 4 9.93± 0.31 15.1± 0.2 49.3± 1.8 49.6± 1.5 15.2± 0.3 30.7± 0.8 1104± 5 9.98± 0.32 15.0± 0.5 48.8± 1.4 49.0± 0.9 15.0± 0.2 30.6± 0.6 1118± 5 10.26± 0.33 15.4± 0.6 50.8± 1.8 49.5± 0.4 15.0± 0.2 30.3± 0.7 1174±

(HCL070) BAIS 3

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1

HEMATOLOGY (SUMMARY) ALL ANIMALS (2W)

NO. of Animals			Dif N-BAND	ferentia	1 WBC (% N-SEG	6)	EOSINO		BASO		MONO		LYMPHO		OTHERS	
5	2.32±	0.71	0±	0	16±	7	2±	1	0±	0	2±	1	79±	6	1±	;
5	2.67±	1.30	1±	1	11±	3	2±	1	0±	0	2±	1	84±	2	0±	:
4	2.38±	0.72	0±	0	13生	1	2±	1	0±	0	3±	1	83±	3	0±	(
5	2.58±	0.72	1±	1	12±	4	2±	1	0±	0	1±	0	84±	4	0±	;
5	2.52±	1.09	0±	1	17±	4	2±	1	0±	0	2±	0	78±	3	0±	
4	1.31±	1.11	0±	1	40±	14	1±	1	0±	0	2±	1	58±	14	0±	ı
	Animals 5 4 5	Animals 103/ 5 2.32± 5 2.67± 4 2.38± 5 2.58± 5 2.52±	Animals $10^{3} / \mu \ell$ 5 2.32 ± 0.71 5 2.67 ± 1.30 4 2.38 ± 0.72 5 2.58 ± 0.72 5 2.52 ± 1.09	Animals $10^{3} / \mu \ell$ N-BAND 5 2.32 ± 0.71 $0 \pm$ 5 2.67 ± 1.30 $1 \pm$ 4 2.38 ± 0.72 $0 \pm$ 5 2.58 ± 0.72 $1 \pm$ 5 2.52 ± 1.09 $0 \pm$	Animals $1 \ 0^3 / \mu \ell$ N-BAND 5 2.32 ± 0.71 0 ± 0 5 2.67 ± 1.30 1 ± 1 4 2.38 ± 0.72 0 ± 0 5 2.58 ± 0.72 1 ± 1 5 2.58 ± 1.09 0 ± 1	Animals $10^{3} / \mu \ell$ N-BAND N-SEG 5 2.32 ± 0.71 0 ± 0 $16\pm$ 5 2.67 ± 1.30 1 ± 1 $11\pm$ 4 2.38 ± 0.72 0 ± 0 $13\pm$ 5 2.58 ± 0.72 1 ± 1 $12\pm$ 5 2.58 ± 1.09 0 ± 1 $17\pm$	Animals $1 \ 0^3 / \mu \ell$ N-BAND N-SEG 5 2.32 ± 0.71 0 ± 0 16 ± 7 5 2.67 ± 1.30 1 ± 1 11 ± 3 4 2.38 ± 0.72 0 ± 0 13 ± 1 5 2.58 ± 0.72 1 ± 1 12 ± 4 5 2.52 ± 1.09 0 ± 1 17 ± 4	Animals $1 \ 0^3 / \mu \ell$ N-BAND N-SEG EOSINO 5 2.32 \pm 0.71 0 \pm 0 16 \pm 7 2 \pm 5 2.67 \pm 1.30 1 \pm 1 11 \pm 3 2 \pm 4 2.38 \pm 0.72 0 \pm 0 13 \pm 1 2 \pm 5 2.58 \pm 0.72 1 \pm 1 12 \pm 4 2 \pm 5 2.52 \pm 1.09 0 \pm 1 17 \pm 4 2 \pm	Animals $1 \ 0^3 / \mu \ell$ N-BAND N-SEG EOSINO 5 2.32 \pm 0.71 0 \pm 0 16 \pm 7 2 \pm 1 5 2.67 \pm 1.30 1 \pm 1 11 \pm 3 2 \pm 1 4 2.38 \pm 0.72 0 \pm 0 13 \pm 1 2 \pm 1 5 2.58 \pm 0.72 1 \pm 1 12 \pm 4 2 \pm 1 5 2.52 \pm 1.09 0 \pm 1 17 \pm 4 2 \pm 1	Animals 1 0³ / μℓ N-BAND N-SEG EOSINO BASO 5 2.32± 0.71 0± 0 16± 7 2± 1 0± 5 2.67± 1.30 1± 1 11± 3 2± 1 0± 4 2.38± 0.72 0± 0 13± 1 2± 1 0± 5 2.58± 0.72 1± 1 12± 4 2± 1 0± 5 2.52± 1.09 0± 1 17± 4 2± 1 0±	Animals $1 \ 0^3 / \mu \ell$ N-BAND N-SEG EOSINO BASO 5 2.32± 0.71 0± 0 16± 7 2± 1 0± 0 5 2.67± 1.30 1± 1 11± 3 2± 1 0± 0 4 2.38± 0.72 0± 0 13± 1 2± 1 0± 0 5 2.58± 0.72 1± 1 12± 4 2± 1 0± 0 5 2.52± 1.09 0± 1 17± 4 2± 1 0± 0	Animals 1 0 ³ /μℓ N-BAND N-SEG EOSINO BASO MONO 5 2.32± 0.71 0± 0 16± 7 2± 1 0± 0 2± 5 2.67± 1.30 1± 1 11± 3 2± 1 0± 0 2± 4 2.38± 0.72 0± 0 13± 1 2± 1 0± 0 3± 5 2.58± 0.72 1± 1 12± 4 2± 1 0± 0 1± 5 2.52± 1.09 0± 1 17± 4 2± 1 0± 0 2±	Animals 1 0 ⁹ /μl N-BAND N-SEG EOSINO BASO MONO 5 2.32± 0.71 0± 0 16± 7 2± 1 0± 0 2± 1 5 2.67± 1.30 1± 1 11± 3 2± 1 0± 0 2± 1 4 2.38± 0.72 0± 0 13± 1 2± 1 0± 0 3± 1 5 2.58± 0.72 1± 1 12± 4 2± 1 0± 0 1± 0 5 2.52± 1.09 0± 1 17± 4 2± 1 0± 0 2± 0	Animals $1.0^{9} / \mu \ell$ N-BAND N-SEG EOSINO BASO MONO LYMPHO 5 2.32 ± 0.71 0 ± 0 16 ± 7 2 ± 1 0 ± 0 2 ± 1 79 ± 5 2.67 ± 1.30 1 ± 1 11 ± 3 2 ± 1 0 ± 0 2 ± 1 84 ± 4 2.38 ± 0.72 0 ± 0 13 ± 1 2 ± 1 0 ± 0 3 ± 1 83 ± 5 2.58 ± 0.72 1 ± 1 12 ± 4 2 ± 1 0 ± 0 1 ± 0 84 ± 5 2.52 ± 1.09 0 ± 1 17 ± 4 2 ± 1 0 ± 0 2 ± 0 78 ±	Animals 1 0 ³ /μℓ N-BAND N-SEG EOSINO BASO MONO LYMPHO 5 2.32± 0.71 0± 0 16± 7 2± 1 0± 0 2± 1 79± 6 5 2.67± 1.30 1± 1 11± 3 2± 1 0± 0 2± 1 84± 2 4 2.38± 0.72 0± 0 13± 1 2± 1 0± 0 3± 1 83± 3 5 2.58± 0.72 1± 1 12± 4 2± 1 0± 0 1± 0 84± 4 5 2.52± 1.09 0± 1 17± 4 2± 1 0± 0 2± 0 78± 3	Animals 10°/µl N-BAND N-SEG EOSINO BASO MONO LYMPHO OTHERS 5 2.32± 0.71 0± 0 16± 7 2± 1 0± 0 2± 1 79± 6 1± 5 2.67± 1.30 1± 1 11± 3 2± 1 0± 0 2± 1 84± 2 0± 4 2.38± 0.72 0± 0 13± 1 2± 1 0± 0 3± 1 83± 3 0± 5 2.58± 0.72 1± 1 12± 4 2± 1 0± 0 1± 0 84± 4 0± 5 2.52± 1.09 0± 1 17± 4 2± 1 0± 0 2± 0 78± 3 0±

BAIS 3 (HCL070)

APPENDIX G 1

BIOCHEMISTRY: SUMMARY, MOUSE: MALE

BIOCHEMISTRY (SUMMARY)

ANIMAL : MOUSE Crj:BDF1

ALL ANIMALS (2W)

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : A1

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	3	5.4± 0.2	2.9± 0.2	1.2± 0.1	0.23± 0.04	178± 144	99± 8	201± 15
500 ppm	5	5.0± 0.4	2.8± 0.1	1.3± 0.1	0.18± 0.01	280± 82	97± 28	193± 12
1000 ppm	5	5.0± 0.3	2.7± 0.1	1.2± 0.1	0.24± 0.08	294± 56	93± 21	194± 25
2000 ppm	5	4.8± 0.4	2.7± 0.3	1.3± 0.2	0.21± 0.02	300± 51	92± 20	193± 32
4000 ppm	4	4.9± 0.1	2.8± 0.1	1.4± 0.1	0.22± 0.03	310± 37	87± 6	183± 15
6000 ppm	4	5.6± 0.3	3.2± 0.3	1.4± 0.1	0.36± 0.11	141± 112	92± 28	162± 76

(HCL074)

BAIS 3

PAGE: 1

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (2W)

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : A1

PAGE: 2

Group Name	NO. of Animals	GOT I U/	e	GPT IU/l		LDH IU/1		G-GTP I U/l		CPK IU/	l	UREA N mg/dl	ITROGEN	SODIUM m Eq / l	
0 ppm	3	43±	9	43±	9	517±	273	3±	1	297±	207	29. 2±	7.3	152±	0
500 ppm	5	38±	9	26±	1	264±	132	2±	1	204±	119	38.4±	24. 1	151±	6
1000 ppm	5	38±	6	29±	4	321±	138	2±	2	204±	83	28.6±	4. 6	150±	2
2000 ppm	5	34±	4	25±	8	272±	108	2±	1	194±	82	31.0±	6. 5	149土	2
4000 ppm	4	36±	3	25±	6	208±	55	2±	1	126±	51	29.2±	4. 7	149±	1
6000 ppm	4	148±	124	43±	12	607±	577	5±	2	741±	1101	61.3±	26. 0	168±	15

(HCL074) BAIS 3

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (2W)

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1

SEX : MALE PAGE: 3 REPORT TYPE : A1

Group Name	NO. of Animals	POTASSIUM m Eq / l		ORIDE 1/L	CALCI mg/d		INORGAN mg/dl	GANIC PHOSPHORUS dl	
0 ppm	3	5.2± 0.9	114:	± 2	9,5±	0.3	10.3±	= 2.9	
500 ppm	5	5.8± 1.2	123:	± 5	9,5±	0.6	9.4±	2.5	
1000 ppm	5	5.2± 1.0	121:	± 3	9.3±	0.3	9.9±	2.0	
2000 ppm	5	5.3± 0.3	121:	± 2	8.9±	0.6	9.1±	2 0.8	
4000 ppm	4	4.7± 0.6	119:	± 1	9.2±	0.3	9.0±	= 1.4	
6000 ppm	4	5.6± 1.0	137:	± 14	8.9±	1.1	10.8±	2.5	

(HCL074) BAIS 3

APPENDIX G 2

BIOCHEMISTRY: SUMMARY, MOUSE: FEMALE

BIOCHEMISTRY (SUMMARY)

ANIMAL : MOUSE Crj:BDF1

ALL ANIMALS (2W)

MEASURE. TIME: 1 SEX: FEMALE

REPORT TYPE : A1

PAGE: 4

oup Name	NO. of Animals	TOTAL P	ROTEIN	ALBUMIN g/dl		A/G RAT	.10	T-BILI mg/dl		GLUCOSE mg/dl		T-CHOLES mg/dl	STEROL	PHOSPHO mg/dl	LIPID
0 ppm	5	4,9±	0.3	3.0±	0.1	1.5±	0.1	0.19±	0,02	252±	40	79±	15	164±	31
500 ppm	5	4,8±	0.3	2.9±	0.2	1.5±	0.2	0.22±	0.08	270±	14	78±	9	167±	20
1000 ppm	4	4.9±	0.2	2.9±	0.2	1.4±	0.2	0.20±	0.02	265±	41	76±	11	156±	22
2000 ppm	5	4.8±	0.2	$2.9\pm$	0.1	1.6±	0.1	0.21±	0.05	296±	30	76±	5	167±	14
4000 ppm	5	4.9±	0.3	3.0±	0.2	1.5±	0.1	0.20±	0.02	290±	34	89±	12	181±	24
6000 ppm	4	5.5±	0.4	3.4±	0.2**	1.7±	0.1	0.23±	0.04	170±	96	105±	8**	186±	26

(HCL074)

BAIS 3

ANIMAL : MOUSE Crj:BDF1

MEASURE, TIME: 1 SEX: FEMALE

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (2W)

NO. of Animals	GOT IU/£	!	GPT IU/l	!	LDH IU/£		G-GTP I U/l		CPK IU/.	2			SODIUM m Eq / l	
5	44±	5	29±	3	284±	87	2±	1	192±	65 ·	23.1±	3.0	149±	2
5	39±	5	35±	13	249±	87	2±	1	183±	85	22.3±	5. 1	148±	4
4	41±	7	30±	7	228±	52	2±	1	194±	99	21.5±	4.6	147±	3
5	37±	2	29±	8	226±	53	3±	1	130±	62	28.9±	5. 7	146±	2
5	46±	14	30±	11	267±	51	2±	1	249±	93	30.0±	5.7	147±	1
4	75±	53	38±	13	322±	54	$2\pm$	1	259±	118	46.0±	17.4*	158±	9
	Animals 5 5 4 5 5	5 44± 5 39± 4 41± 5 37± 5 46±	Animals I U ∕ ℓ 5 44± 5 5 39± 5 4 41± 7 5 37± 2 5 46± 14	Animals I U/l I U/l 5 44± 5 29± 5 39± 5 35± 4 41± 7 30± 5 37± 2 29± 5 46± 14 30±	Animals I U/l 5 44± 5 29± 3 5 39± 5 35± 13 4 41± 7 30± 7 5 37± 2 29± 8 5 46± 14 30± 11	Animals I U/l I U/l I U/l 5 44± 5 29± 3 284± 5 39± 5 35± 13 249± 4 41± 7 30± 7 228± 5 37± 2 29± 8 226± 5 46± 14 30± 11 267±	Animals I U/l I U/l 5 44± 5 29± 3 284± 87 5 39± 5 35± 13 249± 87 4 41± 7 30± 7 228± 52 5 37± 2 29± 8 226± 53 5 46± 14 30± 11 267± 51	Animals I U/l I U/l I U/l I U/l 5 44± 5 29± 3 284± 87 2± 5 39± 5 35± 13 249± 87 2± 4 41± 7 30± 7 228± 52 2± 5 37± 2 29± 8 226± 53 3± 5 46± 14 30± 11 267± 51 2±	Animals I U/l I U/l I U/l I U/l 5 44± 5 29± 3 284± 87 2± 1 5 39± 5 35± 13 249± 87 2± 1 4 41± 7 30± 7 228± 52 2± 1 5 37± 2 29± 8 226± 53 3± 1 5 46± 14 30± 11 267± 51 2± 1	Animals I U/l I U/l I U/l I U/l I U/l I U/l 5 44± 5 29± 3 284± 87 2± 1 192± 5 39± 5 35± 13 249± 87 2± 1 183± 4 41± 7 30± 7 228± 52 2± 1 194± 5 37± 2 29± 8 226± 53 3± 1 130± 5 46± 14 30± 11 267± 51 2± 1 249±	Animals I U/l	Animals I U/L I U/L I U/L I U/L I U/L mg/dL $\frac{1}{5}$ $\frac{1}{44\pm}$ 5 $\frac{1}{5}$ $\frac{29\pm}{3}$ $\frac{3}{284\pm}$ 87 $\frac{2\pm}{1}$ $\frac{1}{192\pm}$ 65 $\frac{23.1\pm}{5}$ $\frac{1}{5}$ $\frac{39\pm}{5}$ $\frac{1}{35\pm}$ 13 $\frac{249\pm}{52}$ 87 $\frac{2\pm}{1}$ $\frac{1}{183\pm}$ 85 $\frac{22.3\pm}{12}$ $\frac{1}{194\pm}$ 99 $\frac{1}{194\pm}$ 10 $\frac{1}{194\pm}$ 11 $\frac{1}{194\pm}$ 12 $\frac{1}{194\pm}$ 12 $\frac{1}{194\pm}$ 13 $\frac{1}{194\pm}$ 13 $\frac{1}{194\pm}$ 14 $\frac{1}{194\pm}$ 15 $\frac{1}{194\pm}$ 15 $\frac{1}{194\pm}$ 16 $\frac{1}{194\pm}$ 17 $\frac{1}{194\pm}$ 18 $\frac{1}{194\pm}$ 19 $\frac{1}{194\pm$	Animals I U/L mg/dL 5 44± 5 29± 3 284± 87 2± 1 192± 65 23.1± 3.0 5 39± 5 35± 13 249± 87 2± 1 183± 85 22.3± 5.1 4 41± 7 30± 7 228± 52 2± 1 194± 99 21.5± 4.6 5 37± 2 29± 8 226± 53 3± 1 130± 62 28.9± 5.7 5 46± 14 30± 11 267± 51 2± 1 249± 93 30.0± 5.7	Animals IU/L IU/L IU/L IU/L IU/L mg/dL mEq/L 5 44± 5 29± 3 284± 87 2± 1 192± 65 23.1± 3.0 149± 5 39± 5 35± 13 249± 87 2± 1 183± 85 22.3± 5.1 148± 4 41± 7 30± 7 228± 52 2± 1 194± 99 21.5± 4.6 147± 5 37± 2 29± 8 226± 53 3± 1 130± 62 28.9± 5.7 146± 5 46± 14 30± 11 267± 51 2± 1 249± 93 30.0± 5.7 147±

BAIS 3 (HCL074)

ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (2W)

SEX : FEMALE

REPORT TYPE : A1

PAGE: 6

up Name	NO. of Animals	POTASS1 m Eq /		CHLORIDE m Eq / l		CALCIUM mg/dl	·	INORGAN mg/dl	C PHOSPHORUS	
0 ppm	5	5.0±	0.8	121±	3	9.4±	0, 9	8.8±	0.8	
500 ppm	5	5.7±	0.4	120±	4	9.2±	0.7	9.2±	1.1	
1000 ppm	4	5.7±	0.4	121±	3	8.8±	0.7	9.7±	2. 7	
2000 ppm	5	5.2±	0.5	119±	5	9.0±	0.2	8.3±	1. 1	
4000 ppm	5	5.3±	0.5	119±	1	9.0±	0.7	9.0±	2. 1	
6000 ppm	4	5.7±	0.5	128±	8	9.3±	0.7	8.3±	1.6	
Significant	difference;	*: P ≤ (). 05	** : P ≤ 0.01				Test of Dun	ıett	

(HCL074)

APPENDIX H 1

GROSS FINDINGS: SUMMARY, MOUSE: MALE ALL ANIMALS

ANIMAL : MOUSE Crj:BDF1

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

REPORT TYPE : A1

SEX : MALE

PAGE: 1

Organ	Findings	Group Name NO. of Animals	5	0 ppm (%)	5	500 ppm (%)	5	1000 ppm (%)	5	2000 ppm (%)
pleen	black zone		0	(0)	1	(20)	0	(0)	0	(0)
dney	hydronephrosis		1	(20)	1	(20)	1	(20)	1	(20)

ANIMAL : MOUSE Crj:BDF1

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

REPORT TYPE : A1

SEX : MALE

PAGE: 2

Organ	Findings	Group Name NO. of Animals	4000 ppm 5 (%)	6000 ppm 5 (%)	
spleen	black zone		0 (0)	0 (0)	
kidney	hydronephrosis		0 (0)	0 (0)	
(HPT080)					BAIS 3

APPENDIX H 2

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

ANIMAL : MOUSE Crj:BDF1

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

REPORT TYPE : A1

SEX : FEMALE

Organ	Findings	Group Name 0 ppm NO. of Animals 5 (%)	500 ppm 5 (%)	1000 ppm 5 (%)	2000 ppm 5 (%)
spleen	black zone	0 (0)	0 (0)	1 (20)	1 (20)
idney	hydronephrosis	1 (20)	0 (0)	0 (0)	0 (0)

PAGE : 3

ANIMAL : MOUSE Crj:BDF1

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

REPORT TYPE : A1

SEX : FEMALE

Organ	Findings	Group Name NO. of Animals	4000 ppm 5 (%)	6000 ppm 5 (%)	
spleen	black zone		0 (0)	0 (0)	
kidney	hydronephrosis		0 (0)	0 (0)	
(HPT080)				<u> </u>	BAIS 3

PAGE: 4

APPENDIX H 3

GROSS FINDINGS: SUMMARY, MOUSE: FEMALE: SACRIFICED ANIMALS

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (2W)

SEX : FEMALE PAGE: 3

Organ	Findings	Group Name 0 p NO. of Animals 5 (%)	pm 500 ppm 5 (%)	1000 ppm 5 (%)	2000 ppm 5 (%)
spleen	black zone	0 (0)	0 (0)	1 (20)	1 (20)
idney	hydronephrosis	1 (20)	0 (0)	0 (0)	0 (0)

(HPT080) BAIS 3

ANIMAL : MOUSE Crj:BDF1

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (2W)

REPORT TYPE : A1

SEX : FEMALE

PAGE: 4

Organ	Findings	Group Name NO. of Animals	4000 ppm 5 (%)	6000 ppm 4 (%)	
spleen	black zone		0 (0)	0 (0)	
kidney	hydronephrosis		0 (0)	0 (0)	
(IIDTOOA)					DATE O

(HPT080) BAIS 3

APPENDIX H 4

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

GROSS FINDINGS (SUMMARY)

ANIMAL

: MOUSE Crj:BDF1

DEAD AND MORIBUND ANIMALS (2W)

PAGE: 1

REPORT TYPE: A1

SEX

: FEMALE

		Group Name	$0~{ m ppm}$	500 ppm	1000 ppm	2000 ppm	
Organ	Findings	_ No. of Animals	0 (%)	0 (%)	0 (%)	0 (%)	
					· · · · · · · · · · · · · · · · · · ·		
			- (-)	- (-)	- (-)	-(-)	
			()	()	()	()	

GROSS FINDINGS (SUMMARY)

ANIMAL

: MOUSE Crj:BDF1

DEAD AND MORIBUND ANIMALS (2W)

PAGE: 2

REPORT TYPE: A1

SEX

: FEMALE

	Group Name	4000 ppm	6000 ppm	
Organ Findings	No. of Animals	0 (%)	1 (%)	

-(-) Non remarkable

APPENDIX I 1

ORGAN WEIGHT, ABSOLUTE: SUMMARY, MOUSE: MALE

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : MALE UNIT: g ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (2W)

7

PAGE: 1

oup Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
0 ppm	5	24.1± 1.0	0.046± 0.010	0.009± 0.001	0.182± 0.031	0.128± 0.006	0.134± 0.008
500 ppm	5	23.0± 3.1	0.043± 0.017	0.008± 0.002	0.179± 0.014	0.121± 0.012	0.136± 0.005
1000 ppm	5	23.6± 2.2	0.046± 0.016	0.010± 0.003	0.161± 0.033	0.127± 0.013	0.145± 0.010
2000 ppm	5	23.3± 1.9	0.043± 0.016	0.009± 0.002	0.173± 0.040	0.121± 0.014	0.150± 0.012
4000 ppm	5	21.5± 0.9	0.032± 0.008	0.010± 0.003	0.161± 0.022	0.112± 0.007	0.140± 0.011
mqq 0006	5	15.7± 3.4**	0.011± 0.008**	0.007± 0.002	0.156± 0.017	0.088± 0.010**	0.132± 0.015
Significant	difference;	*: P ≤ 0.05 **:	P ≤ 0.01	Test	of Dunnett		
7 (140)							

(HCL040) BAIS 3

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : MALE ORGAN WEIGHT: ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2W)

SEX: MALE
UNIT: g

roup Name	NO. of Animals	KIDN	EYS	SPLI	EEN	LIV	ER	BRA	IN	
0 ppm	5	0.376±	0. 032	0.060±	0.023	1.218±	0. 085	0. 434±	0. 005	
500 ppm	5	0.428±	0. 143	0.049±	0.004	1.212±	0. 272	0.425±	0.013	
1000 ppm	5	0.417±	0. 103	0.054±	0.007	1.365±	0. 178	0.427±	0.004	
2000 ppm	5	0.386±	0.017	0.045±	0.004	1.307±	0.119	0.431±	0.015	
4000 ppm	5	0.358±	0.010	0.039±	0.004*	1.279±	0. 104	0.417±	0.007*	
6000 ppm	5	0.275±	0.054*	0.017±	0.010**	0.760±	0. 283**	0.400±	0.021**	
Significant	difference;	*: P ≤ 0.0)5 **	: P ≤ 0.01			Tes	st of Dunnet	t	

(HCL040)

BAIS 3

PAGE: 2

APPENDIX I 2

ORGAN WEIGHT, ABSOLUTE: SUMMARY, MOUSE: FEMALE

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : FEMALE UNIT: g

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

PAGE: 3

roup Name	NO. of Animals	Body	Weight	ТНҮМ	JS	ADRE	NALS	OVAR.	IES	HEAR'	Γ	LUNG	S
0 ppm	5	20.7±	0.6	0.068±	0.007	0.011±	0.002	0.030±	0.008	0.118±	0.006	0.146±	0.006
500 ppm	5	21.2±	0.3	0.077±	0.008	0.012±	0.003	0.026±	0.006	0.118±	0.008	0.152±	0.010
1000 ppm	5	20.1±	0.7	0.075±	0.007	0.012±	0. 001	0.027±	0.003	0.112±	0.007	0.149±	0.010
2000 ppm	5	20.4±	0.7	0.075±	0.009	0.010±	0.003	0.029±	0.005	0.112±	0.008	0.149±	0.008
4000 ppm	5	19.4±	1. 3	0.060±	0.020	0.012±	0.001	0.023±	0.005	0.101±	0.009*	0.142±	0.006
6000 ppm	4	14.8±	3.1*	0.016±	0.011**	0.010±	0.002	0.017±	0.006**	0.085±	0.019**	0.136±	0.018
Significant	difference ;	*: P ≤ 0.	05 *	* : P ≤ 0.01			Test	t of Dunnett					

(HCL040)

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : FEMALE UNIT: g

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

PAGE: 4

oup Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	
0 ppm	5	0.327± 0.160	0.060± 0.009	1.010± 0.030	0.446± 0.008	
500 ppm	5	0.259± 0.006	0.057± 0.006	1.118± 0.033	0.450± 0.014	
1000 ppm	5	0.275± 0.010	0.057± 0.006	1.091± 0.093	0.444± 0.017	
2000 ppm	5	0.290± 0.009	0.056± 0.003	1.155± 0.101	0.439± 0.003	
4000 ppm	5	0.286± 0.019	0.050± 0.009	1.215± 0.093*	0.429± 0.010	
6000 ppm	4	0.260± 0.037	0.025± 0.011**	0.836± 0.283	0.410± 0.023*	

(HCL040) BAIS 3

APPENDIX J 1

ORGAN WEIGHT, RELATIVE: SUMMARY, MOUSE: MALE

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1

SEX : MALE UNIT: %

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

PAGE: 1

oup Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS	
0 ppm	Б	24.1± 1.0	0.189± 0.039	0.037± 0.006	0.752± 0.105	0.532± 0.034	0.559± 0.036	
500 ppm	5	23.0± 3.1	0.182± 0.058	0.037± 0.010	0.786± 0.096	0.533± 0.063	0.602± 0.079	
1000 ppm	5	23.6± 2.2	0.192± 0.056	0.042± 0.013	0.679± 0.096	0.540± 0.024	0.617± 0.059	
2000 ppm	5	23.3± 1.9	0.182± 0.059	0.037± 0.009	0.743± 0.155	0.521± 0.054	0.649± 0.061	
4000 ppm	5	21.5± 0.9	0.150± 0.036	0.047± 0.012	0.746± 0.089	0.519± 0.033	0.647± 0.027	
6000 ppm	5	15.7± 3.4**	0.069± 0.033**	0.047± 0.012	1.025± 0.225*	0.568± 0.059	0.851± 0.086**	

(HCL042) BAIS 3

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : MALE UNIT: % ORGAN WEIGHT: RELATIVE (SUMMARY) SURVIVAL ANIMALS (2W)

PAGE: 2

roup Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	
0 ppm	5	1.567± 0.186	0.254± 0.111	5.074± 0.477	1.807± 0.077	
500 ppm	5	1.972± 1.062	0.219± 0.039	5. 218± 0. 622	1.876± 0.246	
1000 ppm	5	1.809± 0.638	0.230± 0.045	5.772± 0.312	1.824± 0.169	
2000 ppm	5	1.673± 0.216	0.193± 0.020	5.620± 0.250	1.862± 0.121	
4000 ppm	5	1.664± 0.058	0.182± 0.021	5.941± 0.482	1.937± 0.074	
6000 ppm	5	1.769± 0.305	0.101± 0.033**	4.722± 0.782	2.609± 0.406**	
Significant	difference;	*: P ≤ 0.05 **:	P ≤ 0.01	Tes	t of Dunnett	
1101 0 40)						р

(HCL042) BAIS 3

APPENDIX J 2

ORGAN WEIGHT, RELATIVE : SUMMARY, MOUSE : FEMALE

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : FEMALE UNIT: %

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

PAGE: 3

oup Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
0 ppm	5	20.7± 0.6	0.328± 0.028	0.055± 0.010	0.144± 0.036	0.572± 0.037	0.707± 0.032
500 ppm	5	21.2± 0.3	0.363± 0.038	0.056± 0.013	0.124± 0.029	0.555± 0.042	0.717± 0.039
1000 ppm	5	20.1± 0.7	0.371± 0.026	0.061± 0.005	0.134± 0.016	0.557± 0.031	0.743± 0.066
2000 ppm	5	20.4± 0.7	0.364± 0.032	0.050± 0.013	0.142± 0.023	0.548± 0.041	0.731± 0.050
4000 ppm	5	19.4± 1.3	0.303± 0.092	0.061± 0.009	0.121± 0.024	0.520± 0.035	0.731± 0.049
6000 ppm	4	14.8± 3.1**	0.102± 0.053**	0.065± 0.011	0.109± 0.021	0.575± 0.039	0.926± 0.090**

(HCL042)

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : FEMALE UNIT: % ORGAN WEIGHT: RELATIVE (SUMMARY) SURVIVAL ANIMALS (2W)

PAGE: 4

oup Name	NO, of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	
O ppm	5	1.586± 0.794	0.290± 0.042	4.881± 0.086	2.156± 0.056	
500 ppm	Б	1.220± 0.041	0.269± 0.026	5.263± 0.170	2.120± 0.070	
1000 ppm	5	1.370± 0.066	0.284± 0.027	5.422± 0.350*	2.212± 0.079	
2000 ppm	5	1.422± 0.077	0.276± 0.010	5.646± 0.410**	2.151± 0.086	
4000 ppm	5	1.472± 0.055*	0.254± 0.031	6.252± 0.219**	2.215± 0.126	
6000 ppm	4	1.774± 0.119**	0.159± 0.046**	5.519± 0.790*	2.832± 0.438*	

(HCL042)

APPENDIX K 1

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY

MOUSE: MALE: ALL ANIMALS

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0- 2W)

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1

SEX : MALE PAGE : 1

		oup Name 0 ppm	500 ppm 5	1000 ppm	2000 ppm 5
Organ		ade 1 2 3 4 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)	5 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)
{Hematopoiet	cic system)				
thymus	atrophy	<pre></pre>	<pre></pre>	(5) 0 0 0 0 (0) (0) (0) (0)	<pre></pre>
spleen	atrophy	(0) (0) (0) (0)	< 5> 0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	<pre></pre>
	deposit of melanin	0 0 0 0 0 (0)	1 0 0 0 (20) (0) (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0
{Urinary sys	stem)				
kidney	inflammatory polyp	<pre></pre>	<pre></pre>	<pre></pre>	(5> 0 1 0 0 (0) (20) (0) (0)
	hydronephrosis	0 1 0 0 (0) (0)	0 0 1 0 (0) (20) (0)	0 1 0 0 (0) (20) (0) (0)	0 1 0 0 (0) (0) (0)
{Musculoskel	Letal system)				
muscle	necrosis	<pre></pre>	< 5> 0 0 0 0 (0) (0) (0) (0)	< 5> 0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)
Grade <a> b (c) Significant	1: Slight 2: Moderate 3: a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 difference: *: P \leq 0.05 **: P \leq 0				

(HPT150)

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 2\(\mathbf{W}\))

ANIMAL : MOUSE Crj:BDF1 REPORT TYPE : A1

SEX : MALE PAGE: 2

Organ	Findings	Group Name No. of Animals on Grade	4000 ppm 1 Study 5 1 2 3 4 1 (%) (%) (%) (%)	6000 ppm 5 1 2 3 4 (%) (%) (%) (%)	
{Hematopoie	etic system}				
thymus	atrophy		<pre></pre>	<pre></pre>	
spleen	atrophy		<pre></pre>	<pre></pre>	
	deposit of melanin		0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0) (0)	
(Urinary sy	ystem}				
kidney	inflammatory polyp		< 5> 0 0 0 0 0 0 0 0 0 0 0 0 0 0	< 5> 0 0 0 0 (0) (0) (0) (0)	
	hydronephrosis		0 0 0 0 0 (0) (0) (0)	0 1 0 0 (0) (20) (0) (0)	
{Musculoske	eletal system}				
muscle	necrosis		0 0 0 0 (0) (0) (0) (0)	2 1 0 0 (40) (20) (0) (0)	
Grade <a> b (c) Significant	1: Slight 2: Moderate a: Number of animals examined b: Number of animals with lesi c: b/a * 100 t difference; *: P ≤ 0.05	at the site on	4 : Severe Chi Square		

(HPT150)

APPENDIX K 2

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY

MOUSE: FEMALE: ALL ANIMALS

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0- 2W)

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1

SEX : FEMALE

		Group Name 0 ppm No. of Animals on Study 5 Grade 1 2 3 4	500 ppm 5 _1 2 3 4_	1000 ppm 5 1 2 3 4	2000 ppm 5 1 2 3 4
Organ	Findings	(%) (%) (%) (%)	(%) (%) (%) (%)	(%) (%) (%) (%)	(%) (%) (%) (%)
{Hematopoietic	c system)				
bone marrow	.congestion	< 5> 0 0 0 0 (0) (0) (0) (0)	<pre></pre>	0 0 0 0 (0) (0) (0) (0)	<pre></pre>
thymus	atrophy	<pre></pre>	< 5> 0 0 0 0 (0) (0) (0) (0)	< 5> 0 0 0 0 (0) (0) (0) (0)	< 5> 0 0 0 0 (0) (0) (0) (0)
spleen	atrophy	<pre></pre>	<pre></pre>	< 5> 0 0 0 0 (0) (0) (0) (0)	<pre></pre>
	deposit of melanin	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (20) (0) (0)	1 0 0 0 (20) (0) (0) (0)
{Circulatory	system}				
heart	inflammatory infiltration	(20) (0) (0)	<pre></pre>	<pre></pre>	(5> 0 0 0 0 (0) (0) (0) (0)
{Urinary syst	em)				
kidney	hydronephrosis	< 5> 0 1 0 0 (0) (20) (0) (0)	<pre></pre>	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)
Grade <a>> b (c) Significant d	1: Slight 2: Moderate a: Number of animals examined at t b: Number of animals with lesion c: b / a * 100 ifference; *: P ≤ 0.05 **:	3 : Marked 4 : Severe			

PAGE: 3

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

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1

SEX : FEMALE

PAGE: 4

Organ		Group Name 4000 ppm No. of Animals on Study 5 Grade 1 2 3 4 (%) (%) (%) (%)	6000 ppm 5 1 2 3 4 (%) (%) (%) (%)	
{Hematopoietic	c system)			
bone marrow	congestion	< 5> 0 0 0 0 (0) (0) (0) (0)	<pre></pre>	
thymus	atrophy	<pre></pre>	<pre></pre>	
spleen	atrophy	<pre></pre>	< 5> 0 1 0 0 (0) (20) (0) (0)	
	deposit of melanin	0 0 0 0 0 (0) (0)	1 0 0 0 0 (20) (0) (0)	
{Circulatory	system)			
heart	inflammatory infiltration	(5) 0 0 0 0 (0) (0) (0) (0)	<pre></pre>	
{Urinary syst	em)			
kidney	lydronephrosis	0 0 0 0 (0) (0) (0) (0)	<pre></pre>	
Grade < a > b (c) Significant d	 a: Number of animals examined at the si b: Number of animals with lesion c: b / a * 100 			

(HPT150)

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0- 2W)

Organ	Findings	Group Name No. of Animals on Grade	Study 	5 2	3 4 %) (%)	<u>1</u> (%)	500 5 2 (%)	3 4 (%) (%)	1 (%)	1000 p 5 2 3 (%) (9	3 4	(%)	200 2 (%)	00 ppm 5 3 (%)	(%)
{Musculosk	eletal system}														
muscle	necrosis		0 (0) (< 5> 0 0) (0 0	0 (0)	0 (0) (0 (0) (< 5> 0 (0) (0 0	0 (0) (< E 0 (0) (0	0
Grade <a> b (c)	1: Slight 2: Moderate a: Number of animals examined b: Number of animals with les c: b / a * 100 t difference; *: P ≤ 0.05	d at the site sion	: Severe												

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0- 2W)

SEX	: FEMALE		PAGE: 6
Organ	Findings	Group Name 4000 ppm 6000 ppm No. of Animals on Study 5 5 Grade 1 2 3 4 (%) (%) (%) (%) (%) (%) (%) (%) (%) (%)	
{Musculos	keletal system}		
muscle	necrosis	<pre></pre>	
Grade <a> b (c) Signification	1: Slight 2: Modera a: Number of animals examine b: Number of animals with 1 c: b / a * 100 nt difference; *: P ≤ 0.05	d at the site sion	
(HPT150)			BAIS3

APPENDIX K 3

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY

MOUSE: FEMALE: SACRIFICED ANIMALS

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

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1

SEX : FEMALE

PAGE: 3

Organ		Froup Name 0 ppm	500 ppm	1000 ppm	2000 ppm
		fo. of Animals on Study 5 frade 1 2 3 4 (%) (%) (%) (%)	5 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)
{Hematopoie	tic system)				
thymus	atrophy	< 5> 0 0 0 0 (0) (0) (0) (0)	< 5> 0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	<pre></pre>
spleen	deposit of melanin	< 5> 0 0 0 0 (0) (0) (0) (0)	< 5> 0 0 0 0 (0) (0) (0) (0)	(5) 1 0 0 0 (20) (0) (0) (0)	<pre></pre>
{Circulator	y system}				
heart	inflammatory infiltration	<pre></pre>	< 5> 0 0 0 0 (0) (0) (0) (0)	(5> 0 0 0 0 (0) (0) (0) (0)	<pre></pre>
{Urinary sy	stem)				
kidney	hydronephrosis	<pre></pre>	<pre></pre>	< 5> 0 0 0 0 (0) (0) (0) (0)	<pre></pre>
{Musculoske	detal system)				
muscle	necrosis	< 5> 0 0 0 0 (0) (0) (0) (0)	< 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)
Grade <a>> b (c) Significant	1: Slight 2: Moderate 3: a: Number of animals examined at the sit b: Number of animals with lesion c: b / a * 100 difference; *: P ≤ 0.05 **: P ≤				

(HPT150)

STUDY NO. : 0337

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (2W)

ANIMAL : MOUSE Cri:BDF1 REPORT TYPE : A1

SEX : FEMALE

> 6000 ppm Group Name 4000 ppm No. of Animals on Study 5 4

Findings_

{Hematopoietic system}

thymus

< 5> < 4> atrophy 0 0 0 1 2 0 0 (0)(0)(0)(0) (25) (50) (0) (0)

spleem

< 5> < 4> 0 0 0 0 1 0 0 0 deposit of melanin (0)(0)(0)(0) (25) (0) (0) (0)

4 : Severe

{Circulatory system}

heart

inflammatory infiltration

< 5> < 4> 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0)

{Urinary system}

kidney

hydronephrosis

< 5> 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0)

{Musculoskeletal system}

muscle

necrosis

< 5> 0 0 0 (0)(0)(0)(0)

< 4> 0 1 0 0 (0)(25)(0)(0)

< 4>

Grade < a >

2 : Moderate

a : Number of animals examined at the site

b b: Number of animals with lesion

c:b/a*100 (c)

Significant difference : * : $P \le 0.05$ ** : $P \le 0.01$ Test of Chi Square

(HPT150)

BAIS3

PAGE: 4

APPENDIX K 4

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY

MOUSE: FEMALE: DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0337

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1

SEX : FEMALE

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

PAGE: 1 500 ppm 1000 ppm Group Name 0 ppm 2000 ppm No. of Animals on Study 0 0 0 0 Findings_ (%) (%) (%) (%) (%) (%) (%) (%) (%) {Hematopoietic system} < 0> < 0> bone marrow < 0> < 0> congestion (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) thymus < 0> < 0> < 0> atrophy (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) spleen < 0> < 0> < 0> < 0> atrophy (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) 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. : 0337

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 2W)

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1

SEX : FEMALE

Organ		Name 4000 ppm f Animals on Study 0 1 2 3 4 (%) (%) (%) (%)	6000 ppm 1 1 2 3 4 (%) (%) (%) (%)	
{Hematopoiet	ic system}			
bone marrow	congestion	(-) (-) (-) (-)	<pre></pre>	
thymus	atrophy	< 0> (-) (-) (-) (-)	<pre></pre>	
spleen	atrophy	< 0> (-) (-) (-) (-)	<pre></pre>	
Grade < a > b (c)	1: Slight 2: Moderate 3: Man a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	ked 4: Severe		
(HPT150)				

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

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

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

Lot No. : WTM0491

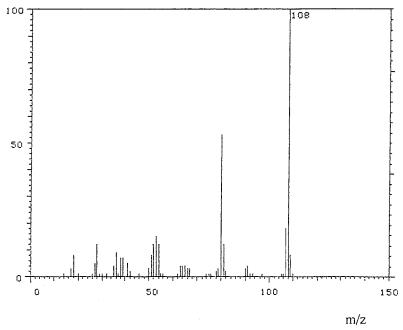
1. Spectral Data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

<u>Determined Value</u>
Fragment Peak (m/z)

Calculated Value
Fragment Peak (m/z)

108 $108 (NH_2C_6H_4NH_2 \cdot 2HCl) = (2HCl)$

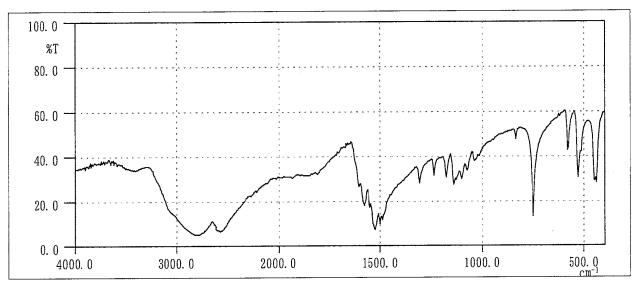
Results: The mass spectrum was consistent with calculated spectrum.

Infrared Spectrometry

Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr

Resolution : 2 cm⁻¹



Infrared Spectrum of Test Substance

70 4 1 17-1	* * *
Determined Values	<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	$1010 \sim 1050$
1050~1160	$1050\sim 1160$
1160~1200	$1160 \sim 1200$
$1250\sim 1280$	$1250\sim 1280$
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.

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 1997.9.15 to 1997.9.29. Test substance was stored

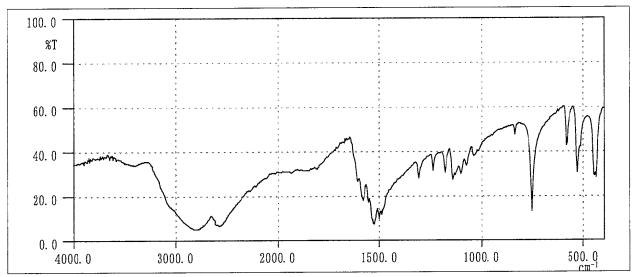
in cold storage in a dark place.

2. Infrared Spectrometry

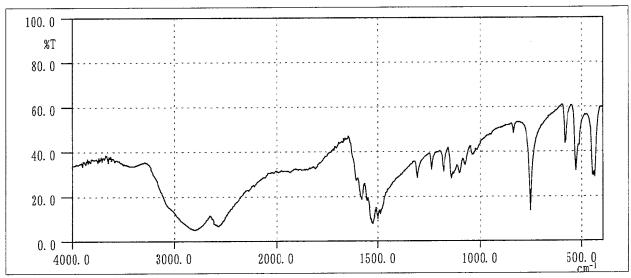
Instrument: Shimadzu FTIR-8200PC Infrared Spectrometer

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 imes 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 µL

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.

CONCENTMOUSEION 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

Target Concentration					
Date Analyzed	500ª	1000	2000	4000	6000
1997.09.15	497 (99.4) ^b	988 (98.8)	2050 (103)	3960 (99.0)	5840 (97.3)

^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 × 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 µL

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

	_	Target Concentration		
Date Prepared	Date Analyzed	500 ^a	6000	
1997.09.01	1997.09.01	477 (100) ^b	5790 (100)	
	1997.09.05°	474 (99.4)	5920 (102)	

a ppm

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 × 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 µL

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

^c Animal room samples

APPENDIX N 1

UNITS AND DECIMAL PLACE 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)
Hematocrit (Hct)	Calculated as RBC×MCV/10 1)
Mean corpuscular volume (MCV)	Light scattering method 1)
Mean corpuscular hemoglobin (MCH)	Calculated as Hgb/RBC×10 1)
Mean corpuscular hemoglobin concentration (MCHC)	Calculated as Hgb/Hct×100 1)
Platelet	Light scattering method 1)
White blood cell (WBC)	Light scattering method 1)
Differential WBC	Pattern recognition method 2 (May-Grunwald-Giemsa 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	Enzymatic method (GLK·G-6-PDH) 3)
T-cholesterol	Enzymatic method (CE·COD·POD) 3)
Phospholipid	Enzymatic method (PLD·COD·POD) 3)
Glutamic oxaloacetic transaminase (GOT)	IFCC method 3)
Glutamic pyruvic transaminase (GPT)	IFCC method 3)
Lactate dehydrogenase (LDH)	Wroblewski-LaDue method 3)
γ -Glutamyl transpeptidase (γ -GTP)	L- γ -Glutamyl-p-nitroanilide method 3)
Creatine phosphokinase (CPK)	GSCC method 3)
Urea nitrogen	Enzymatic method (Urease · GLDH) 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	Enzymatic method (PNP·XOD·POD) 3)

- 1) Automatic blood cell analyzer (Technicon H·1: Technicon Instruments Corporation)
- 2) Automatic blood cell differential analyzer (Hitachi 8200 : Hitachi,Ltd.)
- 3) Automatic analyzer (Hitachi 7070 : Hitachi, Ltd.)

APPENDIX M 1

METHODS 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)	$\times 10^6/\mu$ L	2
Hemoglobin	g/dL	1
Hematocrit	%	1
Mean corpuscular volume (MCV)	fL	1
Mean corpuscular hemoglobin (MCH)	pg	1
Mean corpuscular hemoglobin concentration (MCHC)	g/dL	1
Platelet	$\times 10^3/\mu L$	0
White blood cell (WBC)	$\times 10^3/\mu L$	2
Differential WBC	%	0
Biochemistry		
Total protein	g/dL	1
Albumin	g/dL	1
A/G ratio	_	1
T-bilirubin	mg/dL	2
Glucose	mg/dL	0
T-cholesterol	mg/dL	0
Phospholipid	mg/dL	0
Glutamic oxaloacetic transaminase (GOT)	IU/L	0
Glutamic pyruvic transaminase (GPT)	IU/L	0
Lactate dehydrogenase (LDH)	IU/L	0
γ -Glutamyl transpeptidase (γ -GTP)	IU/L	0
Creatine phosphokinase (CPK)	IU/L	0
Urea nitrogen	mg/dL	1
Sodium	mEq/L	0
Potassium	mEq/L	1
Chloride	mEq/L	0
Calcium	mg/dL	1
Inorganic phosphorus	mg/dL	1