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 13 週間毒性試験(混水試験)報告書

試験番号:0351

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APPENDIX A 1

CLINICAL OBSERVATION: SUMMARY, RAT: MALE

(13-WEEK STUDY)

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

Clinical sign	Group Name	Admini	stration We	eek-day											
		1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7	
OILED PERI GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	
~ va	250 ppm	Ŏ	Ŏ	ō .	Ö	0	Ō	Ō	0	0	0	Ō	0	Ō	
	500 ppm	0	0	0	Ō	Ô	Ō	Ō	0	0	0	0	0	Ō	
	1000 ppm	Ö	Ö	1	1	1	1	1	1	1	1	1	1	1	
	2000 ppm	Ö	Ö	Ō	0	0	ō	Õ	ō	Õ	ō	ō	ō	ō	
	3000 ppm	0	Ö	7	3	4	5	3	4	1	2	2	2	2	
KOPHTHALMOS	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	
	250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	500 ppm	0	1	1	1	1	1	1	1	1	1	1	1	1	
	1000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
YE OPACITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	
	250 ppm	0	0	0	0	0	0	0	. 0	0	0	0	0	0	
	500 ppm	0	1	0	0	0	0	0	0	0	0	0	0	0	
	1000 ppm	0	0	0	0 .	0	0	0	0	0	0	0	0	0	
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
ORNEAL OPACITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	
	250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	500 ppm	0	1	0	0	0	0	0	0	0	0	0	0	0	
	1000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
OSE HEMORRHAGIC DISCHA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	
	250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	1000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	3000 ppm	1	1	0	0	0	0	0	0	0	0	0	0	0	
ED URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	
	250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	1000 ppm	0	0	0	0	1	1	1	1	0	0	0	0	0	
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	3000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	

APPENDIX A 2

CLINICAL OBSERVATION: SUMMARY, RAT: FEMALE

(13-WEEK STUDY)

CLINICAL OBSERVATION (SUMMARY) STUDY NO. : 0351 ANIMAL : RAT F344/DuCrj ALL ANIMALS

REPORT TYPE : A1 13

SEX : FEMALE

Clinical sign	Group Name	Admini	stration W	eek-day											
		1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7	
EATH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	
	250 ppm	0	Ö	Ō	ō	ō	0	0	0	0	0	Ö	0	0	
	500 ppm	Ö	Ö	Õ	Õ	Ô	0	0	0	0	0	0	0	0	
	1000 ppm	0	0	Õ	Õ	0	Ö	0	0	0	0	0	0	0	
	2000 ppm	0	Ö	Ö	Ö	0	0	Ö	0	0	0	0	0	0	
	3000 ppm	1	2	2	2	2	2	2	2	2	2	2	2	2	
NCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	
	250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	1000 ppm	0	0	0	0	0	0	0	0	0	.0	0	0	0	
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	3000 ppm	0	0	0	0	0	0	1	1	1	1	1	0	0	
DILED PERI GENITALIA	Control	0	0	0	0	0	0	0	0	. 0	0	0	0	0	
	250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	1000 ppm	0	0	0	0	0	0	0	1	0	0	1	1	1	
	2000 ppm	0	0	4	4	4	6	4	6	6	6	6	6	7	
	3000 ppm	9	8	8	8	8	8	8	8	8	8	8	8	8	
SE HEMORRHAGIC DISCHA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	
	250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	1000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	3000 ppm	9	8	0	0	0	0	0	0	0	0	0	0	0	
MALL STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	
	250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	1000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	3000 ppm	0	0	0	0	0	0	0	0	2	2	1	0	0	

APPENDIX B 1

BODY WEIGHT CHANGES :SUMMARY, RAT : MALE (13-WEEK STUDY)

ANIMAL : RAT F344/DuCrj

UNIT : g

REPORT TYPE : A1 13

SEX : MALE

BODY WEIGHT CHANGES ALL ANIMALS

(SUMMARY)

roup Name	Admini	stration	week								, .,			
	0		1		2		3		4		5		6	
Control	122±	3	151±	5	182±	7	207±	10	226±	11	244±	11	257±	12
250 ppm	122±	3	152±	5	185±	7	211±	8	232±	10	247±	10	260±	11
500 ppm	122±	3	151±	5	182±	7	205±	6	226±	7	241±	8	254±	8
1000 ppm	122±	3	146±	5	174±	7	198±	8	217±	10	232±	10*	242±	11*
2000 ppm	122±	4	138±	2**	167±	4**	189±	6**	206±	7**	219±	7 **	230±	8 * *
3000 ppm	122±	3	124±	9**	147±	13**	166±	13**	182±	13**	196±	15**	205±	15**
Significant difference	ce; *:P≤0	. 05	** : P ≤ 0.0)1			Test of Du	innett						

(HAN260)

BAIS 3

ANIMAL : RAT F344/DuCrj

UNIT : g

REPORT TYPE : A1 13

SEX : MALE

BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS

		week											
7		8		9		10		11		12		13	
269±	13	281±	14	290±	14	299±	15	306±	13	313±	14	316±	14
272±	11	284±	12	293±	12	301±	13	308±	14	313±	15	317±	17
266±	8	277±	9	287±	10	294±	10	301±	9	307±	10	310±	10
253±	12*	263±	12**	271±	13*	277±	13**	282±	13**	287±	14**	291±	14**
237±	10**	246±	11**	254±	13**	260±	12**	265±	13**	268±	14**	271±	15**
214±	16**	222±	17**	229±	18**	236±	18**	239±	19**	243±	18**	246±	18**
	272± 266± 253± 237±	272± 11 266± 8 253± 12* 237± 10**	269 ± 13 $281\pm$ 272 ± 11 $284\pm$ 266 ± 8 $277\pm$ $253\pm 12*$ $263\pm$ $237\pm 10**$ $246\pm$	269 ± 13 281 ± 14 272 ± 11 284 ± 12 266 ± 8 277 ± 9 $253 \pm 12*$ $263 \pm 12**$ $246 \pm 11**$	269 ± 13 281 ± 14 $290 \pm 272 \pm 11$ 284 ± 12 $293 \pm 266 \pm 8$ 277 ± 9 $287 \pm 253 \pm 12*$ $263 \pm 12**$ $271 \pm 237 \pm 10**$ $246 \pm 11**$ $254 \pm 254 \pm 271 \pm 271$	269 ± 13 281 ± 14 290 ± 14 272 ± 11 284 ± 12 293 ± 12 266 ± 8 277 ± 9 287 ± 10 $253\pm 12*$ $263\pm 12**$ $271\pm 13*$ $237\pm 10**$ $246\pm 11**$ $254\pm 13**$	$269\pm$ 13 $281\pm$ 14 $290\pm$ 14 $299\pm$ 272± 11 $284\pm$ 12 $293\pm$ 12 $301\pm$ 266± 8 $277\pm$ 9 $287\pm$ 10 $294\pm$ 253± 12* $263\pm$ 12** $271\pm$ 13* $277\pm$ 237± 10** $246\pm$ 11** $254\pm$ 13** $260\pm$	269 ± 13 281 ± 14 290 ± 14 299 ± 15 272 ± 11 284 ± 12 293 ± 12 301 ± 13 266 ± 8 277 ± 9 287 ± 10 294 ± 10 $253\pm 12*$ $263\pm 12**$ $271\pm 13*$ $277\pm 13**$ $237\pm 10**$ $246\pm 11**$ $254\pm 13**$ $260\pm 12**$	$ 269 \pm 13 \qquad 281 \pm 14 \qquad 290 \pm 14 \qquad 299 \pm 15 \qquad 306 \pm \\ 272 \pm 11 \qquad 284 \pm 12 \qquad 293 \pm 12 \qquad 301 \pm 13 \qquad 308 \pm \\ 266 \pm 8 \qquad 277 \pm 9 \qquad 287 \pm 10 \qquad 294 \pm 10 \qquad 301 \pm \\ 253 \pm 12 * \qquad 263 \pm 12 * \qquad 271 \pm 13 * \qquad 277 \pm 13 * * \qquad 282 \pm \\ 237 \pm 10 * * \qquad 246 \pm 11 * * \qquad 254 \pm 13 * * \qquad 260 \pm 12 * * \qquad 265 \pm \\ $	269 ± 13 281 ± 14 290 ± 14 299 ± 15 306 ± 13 272 ± 11 284 ± 12 293 ± 12 301 ± 13 308 ± 14 266 ± 8 277 ± 9 287 ± 10 294 ± 10 301 ± 9 $253\pm 12*$ $263\pm 12**$ $271\pm 13*$ $277\pm 13**$ $282\pm 13**$ $237\pm 10**$ $246\pm 11**$ $254\pm 13**$ $260\pm 12**$ $265\pm 13**$	269 ± 13	$ 269 \pm 13 \qquad 281 \pm 14 \qquad 290 \pm 14 \qquad 299 \pm 15 \qquad 306 \pm 13 \qquad 313 \pm 14 $ $ 272 \pm 11 \qquad 284 \pm 12 \qquad 293 \pm 12 \qquad 301 \pm 13 \qquad 308 \pm 14 \qquad 313 \pm 15 $ $ 266 \pm 8 \qquad 277 \pm 9 \qquad 287 \pm 10 \qquad 294 \pm 10 \qquad 301 \pm 9 \qquad 307 \pm 10 $ $ 253 \pm 12 * \qquad 263 \pm 12 * * \qquad 271 \pm 13 * \qquad 277 \pm 13 * * \qquad 282 \pm 13 * * \qquad 287 \pm 14 * * $ $ 237 \pm 10 * * \qquad 246 \pm 11 * * \qquad 254 \pm 13 * * \qquad 260 \pm 12 * * \qquad 265 \pm 13 * * \qquad 268 \pm 14 * * $	269± 13

(HAN260)

BAIS 3

APPENDIX B 2

BODY WEIGHT CHANGES: SUMMARY, RAT: FEMALE

(13-WEEK STUDY)

ANIMAL : RAT F344/DuCrj

UNIT : g

REPORT TYPE : A1 13

SEX : FEMALE

BODY WEIGHT CHANGES

(SUMMARY)

ALL ANIMALS

up Name	Admini	stration	week											
	0		1		2		3		4		5		6	
Control	99±	3	115±	6	129±	4	137±	5	146±	5	153±	6	158±	7
250 ppm	99±	2	115±	3	126±	3	135±	3	143±	4	149±	4	154±	5
500 ppm	99±	3	112±	2	123±	2	133±	4	140±	4*	145±	6*	150±	7
1000 ppm	99±	3	108±	3*	120±	4**	128±	5**	136±	6**	141±	7**	145±	7**
2000 ppm	99±	3	103±	3**	113±	4**	121±	4**	125±	4**	130±	5**	131±	6**
3000 ppm	99±	3	76±	8**	87±	8**	100±	5**	106±	5**	108±	8**	108±	8**

(HAN260)

BAIS 3

ANIMAL : RAT F344/DuCrj

UNIT : g

REPORT TYPE : A1 13

SEX : FEMALE

BODY WEIGHT CHANGES ALL ANIMALS (SUMMARY)

oup Name	Admini	istration	week											
	7		8		9		10		11		12		13	
Control	163±	7	168±	8	172±	8	178±	8	179±	8	182±	8	183±	8
250 ppm	157±	5	161±	5	164土	5	168±	5	171±	4	172±	7*	175±	6
500 ppm	156±	8	158±	8	162±	9*	166±	10*	168±	10*	170±	9**	170±	9**
1000 ppm	149±	7**	151±	8**	156±	7**	158±	8**	160±	7**	163±	8**	163±	7**
2000 ppm	135±	6**	135±	9**	139±	8**	142±	8**	145±	7 * *	146±	8**	148±	8**
3000 ppm	109±	11**	112±	11**	113±	10**	114±	14**	120±	11**	121±	8**	122±	8 * *

(HAN260)

BAIS 3

APPENDIX C 1

WATER CONSUMPTION CHANGES : SUMMARY, RAT : MALE (13-WEEK STUDY)

ANIMAL : RAT F344/DuCrj

UNIT : g

REPORT TYPE : A1 13

SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)

ALL ANIMALS

PAGE: 1 Administration week_ Group Name 2 3 4 5 6 7 1 Control 17.2 ± 0.9 19.2± 1.4 19.7 ± 1.5 20.0 ± 1.3 19.0± 1.4 19.2± 1.6 18.0 ± 1.4 19.8± 1.5 250 ppm 17.0± 1.2 19.7± 1.7 19.0 ± 1.5 19.2± 2.0 19.2 ± 1.9 17.8± 1.4 500 ppm 14.9± 0.9 16.1 \pm 0.9 16.6 ± 0.7 17.4± 0.6** 17.1± 0.9 17.1 ± 0.9 16.5 ± 0.9 15.5± 4.3* 1000 ppm 14.4± 3.3* 15.7± 3.7* 16.1± 4.0** 15.9± 0.7** 16.4± 3.7* 16.1± 3.9* 14.3± 0.8** 2000 ppm 12.4± 0.6** 13.4± 0.8** 14.9± 1.0** 13.7± 1.1** 13.8± 1.0** 13.5± 1.3** 3000 ppm 9.8± 2.0** 11.6± 1.0** 12.4± 1.2** 13.2± 1.2** 12.8± 1.4** 12.6± 1.3** 12.3± 1.2** Significant difference; $*: P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett

(HAN260)

ANIMAL : RAT F344/DuCrj

UNIT : g

REPORT TYPE : A1 13

WATER CONSUMPTION CHANGES (SUMMARY)

ALL ANIMALS

oup Name	Administration	week					
	8	9	10	11	12	13	
Control	18.4± 1.6	18.2± 1.0	18.4± 1.7	17.7± 1.1	17.5± 1.2	17.2± 1.4	
250 ppm	18.1± 1.8	17.9± 1.5	17.7± 1.5	17.7± 1.5	17.1± 1.5	17.6± 1.2	
500 ppm	16.0± 1.0	16.0± 0.8	15.8± 0.8	15.4± 0.7	15.6± 0.8	15.4± 0.9	
1000 ppm	15.7± 3.9*	15.6± 4.2*	15.4± 4.6*	14.6± 4.1*	14.3± 4.1**	15.0± 4.1*	
2000 ppm	12.9± 1.2**	12.8± 1.0**	12.7± 1.0**	12.2± 0.9**	12.2± 1.1**	12.6± 0.6**	
3000 ppm	11.8± 1.4**	13.3± 3.8**	14.5± 5.0**	11.5± 1.5**	11.6± 1.3**	11.8± 1.1**	
Significant difference	; *: P ≤ 0.05	** : P ≤ 0.01		Test of Dunnett			

(HAN260)

APPENDIX C 2

WATER CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE (13-WEEK STUDY)

ANIMAL : RAT F344/DuCrj

UNIT : g

REPORT TYPE : A1 13

SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)

ALL ANIMALS

SCA · FEMALE

Group Name	Administration	week					
•	1	2	3	4	5	6	7
Control	14.9± 1.7	16.0± 1.5	16.2± 2.0	15.7± 1.6	17.8± 4.8	17.0± 3.5	17.1± 4.0
250 ppm	15.2± 0.8	15.3± 1.1	15.8± 1.7	16.1± 4.3	16.6± 4.5	15.1± 1.9	16.9± 5.5
500 ppm	14.2± 3.5	13.4± 1.0**	13.4± 1.0	14.1± 2.5	16.4± 10.4	13.7± 2.5	13.3± 1.8
1000 ppm	11.0± 0.8*	11.3± 0.9**	11.2± 1.3**	11.4± 1.1**	11.1± 0.9**	10.7± 0.8**	10.6± 0.6**
0000	0.01.05.	0.51	0.51.0.4	0.51.0.5	0.773 0.411	0.4 1 0.5 1	0.01.05
2000 ppm	9.8± 0.5**	9.7± 0.6**	9.7± 0.4**	9.7± 0.7**	9.5± 0.4**	9.1± 0.7**	9.0± 0.5**
3000 ppm	3.8± 1.7**	8.0± 1.4**	7.8± 0.7**	7.9± 0.9**	6.9± 0.7**	7.0± 0.4**	6.5± 0.6**
Significant differen	uce; *:P≦0.05	**: P ≤ 0.01		Test of Dunnett			

(HAN260)

BAIS 3

ANIMAL : RAT F344/DuCrj

UNIT : g

REPORT TYPE : A1 13

SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

PAGE: 4

oup Name	Administration	week				
	8	9	10	11	12	13
Control	19.1± 7.8	18.7± 7.1	23.3± 13.4	16.9± 5.1	19.9± 9.1	18.7± 8.3
250 ppm	18.3± 9.2	16.8± 4.7	17.5± 6.0	18.9± 8.8	15.4± 3.4	16.1± 4.2
500 ppm	12.4± 1.4	12.1± 0.8	12.7± 0.8	12.4± 0.6	12.4± 1.2	12.0± 0.5
1000 ppm	9.8± 0.8**	10.1± 0.8**	10.1± 1.0**	9.9± 1.0**	10.2± 1.0**	10.3± 1.1**
2000 ppm	8.2± 0.4**	9.8± 3.4**	8.9± 0.8**	8.4± 0.7**	8.6± 0.6**	8.7± 0.9**
3000 ppm	6.2± 0.5**	6.3± 1.1**	6.3± 1.0**	7.1± 0.6**	6.8± 0.8**	6.8± 0.5**
Significant difference	ce; *: P ≤ 0.05 →	* : P ≤ 0.01		Test of Dunnett		

(HAN260)

APPENDIX D 1

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : MALE (13-WEEK STUDY)

ANIMAL : RAT F344/DuCrj

UNIT : g

REPORT TYPE : A1 13

SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)

ALL ANIMALS

Control 13.8± 0.4 15.7± 0.9 15.5 ± 1.0 16.3 ± 0.9 16.0 ± 0.6 15.6 ± 0.8 15.7± 1.0 250 ppm 13.4± 0.5 15.4± 0.6 15.4± 0.9 16.4± 0.9 15.7生 0.6 15.7± 1.0 15.7± 1.2 500 ppm 13.0 ± 0.5 14.9± 0.4 14.7生 0.7* 15.6± 0.6 15.4± 0.6 15.2 ± 0.5 15.6± 0.8 1000 ppm 12.4± 0.8* 14.1± 0.6** 14.8± 1.0 15.6 ± 1.2 15.2 ± 0.9 14.8± 0.9 15.0± 1.1 2000 ppm 11.0± 0.3** 13.3± 0.5** 14.2± 0.6** 14.7± 0.9** 14.6± 0.8** 14.4± 0.8* 14.3± 1.1* 3000 ppm 9.1± 1.1** 11.7± 1.1** 12.8± 0.8** 13.6± 0.9** 14.0± 1.2** 13.9± 1.2** 14.2± 1.2*

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

(HAN260)

BAIS 3

ANIMAL : RAT F344/DuCrj

UNIT : g

REPORT TYPE : A1 13

SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)

ALL ANIMALS

roup Name	Administration week										
-	8	9	10	11	12	13					
Control	15.8± 1.3	15.9± 1.2	15.9± 1.0	15.8± 1.0	15.5± 0.8	15.4± 1.0					
250 ppm	16.0± 1.0	15.7± 1.2	15.6± 1.4	15.7± 1.1	15.0± 1.1	15.0± 1.1					
mqq 003	15.6± 0.6	15.5± 0.7	15.2± 0.7	15.3± 0.6	15.0± 0.5	14.7± 0.5					
1000 ppm	15.0± 0.9	15.2± 0.9	15.1± 1.1	14.8± 1.0	14.4± 1.1	14.6± 1.1					
2000 ppm	14.7± 1.3	14.4± 1.3*	14.3± 1.0**	14.3± 1.3**	14.2± 1.2*	14.1± 1.1					
3000 ppm	14.2± 1.1**	14.3± 1.4**	14.6± 1.1*	14.1± 1.0**	14.3± 1.1*	14.5± 1.0					

(HAN260)

BAIS 3

APPENDIX D 2

FOOD CONSUMPTION CHANGES: SUMMARY, RAT: FEMALE

(13-WEEK STUDY)

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

ANIMAL : RAT F344/DuCrj

UNIT : g

REPORT TYPE : A1 13

SEX : FEMALE

PAGE: 3

oup Name	Admin	istration	week											
	1		2		3		4		5		6		7	
Control	11.2±	0.7	11.6±	0.6	10.8±	0.6	11.2±	0.5	11.1±	0.6	10.9±	0. 6	11.1±	0.6
250 ppm	11.2±	0.5	11.0±	0.4	11.1±	0.3	11.0±	0.3	10.6±	0.4	10.3±	0.6	10.5±	0.4
500 ppm	10.5±	0.3	10.8±	0.4	10.8±	0.7	10.8±	0.6	10.5±	0.8	10.5±	0.6	10.3±	0.8*
1000 ppm	9.8±	0.5*	10.3±	0. 7*	10.4±	1.0	10.2±	1.0**	10.2±	1.0*	9.8±	0.8**	9.9±	0. 7**
2000 ppm	8.3±	0.7**	9.3±	0.5**	9.6±	0.5*	9.3±	0.5**	9.5±	0.5**	8.8±	0.6**	9,1±	0.5**
3000 ppm	4.5±	1.2**	7.1±	1.0**	8.5±	0.4**	8.4±	0.7**	7.7±	1.0**	7.5±	0. 7**	7.8±	0.9**
Significant differe	ence; *:P≦	0. 05	**: P ≤ 0.0)1			Test of I	unnett						

(HAN260)

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

ANIMAL : RAT F344/DuCrj

UNIT : g

REPORT TYPE : A1 13

SEX : FEMALE

PAGE: 4

oup Name	Administration	week					
	8	9	10	11	12	13	
Control	11.0 \pm 0.7	11.1± 0.6	11.4± 0.7	11.0± 0.6	11.0± 0.5	10.9± 0.7	
250 ppm	10.4± 0.6	10.5± 0.6	10.5± 0.5*	10.6± 0.5	10.2± 0.5*	10.4± 0.5	
500 ppm	10.4± 0.7	10.4± 0.8	10.4± 0.7**	10.3± 0.5*	10.1± 0.4**	9.9± 0.3**	
1000 ppm	9.9± 0.6**	10.0± 0.6**	9.8± 0.8**	9.8± 0.7**	9.7± 0.6**	9.7± 0.6**	
2000 ppm	8.9± 0.6**	9.4± 0.4**	9.3± 0.4**	9.4± 0.4**	9.4± 0.5**	9.6± 0.4**	
3000 ppm	8.2± 0.8**	8.4± 0.5**	8.1± 1.1**	8.9± 0.6**	8.7± 0.9**	8.6± 0.4**	
Significant differe	ence; *: P ≤ 0.05	** : P ≤ 0.01		Test of Dunnett			

(HAN260)

APPENDIX E 1

CHEMICAL INTAKE CHANGES: SUMMARY, RAT: MALE

(13-WEEK STUDY)

CHEMICAL INTAKE CHANGES (SUMMARY)

ANIMAL : RAT F344/DuCrj

ALL ANIMALS

UNIT : g/kg/day
REPORT TYPE : A1 13
SEX : MALE

PAGE: 1

Froup Name	Administration	(weeks)					
	1	2	3	4	5	6	7
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000 ± 0.000	0.000± 0.000	0.000± 0.000
250 ppm	0.028± 0.001	0.027± 0.002	0.022± 0.001	0.021± 0.001	0.019± 0.001	0.018± 0.001	0.016± 0.001
500 ppm	0.049± 0.003	0.045± 0.003	0.041± 0.002	0.039± 0.002	0.035± 0.002	0.034± 0.002	0.031± 0.002
1000 ppm	0.098± 0.024	0.090± 0.023	0.082± 0.021	0.073± 0.003	0.071± 0.018	0.067± 0.018	0.061± 0.018
2000 ppm	0.180± 0.007	0.161± 0.008	0.152± 0.008	0.145± 0.011	0.126± 0.009	0.120± 0.007	0.113± 0.008
3000 ppm	0.235± 0.038	0.238± 0.011	0.224± 0.013	0.218± 0.014	0.196± 0.010	0.184± 0.011	0.173± 0.008

(HAN300)

CHEMICAL INTAKE CHANGES (SUMMARY)

ANIMAL : RAT F344/DuCrj

ALL ANIMALS

UNIT : g/kg/day REPORT TYPE : A1 13

SEX : MALE

PAGE: 2

Group Name	Administration	(weeks)					
	8	9	10	11	12	13	
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	
250 ppm	0.016± 0.001	0.015± 0.001	0.015± 0.001	0.014± 0.001	0.014± 0.001	0.014± 0.001	
500 ppm	0.029± 0.002	0.028± 0.001	0.027± 0.002	0.026± 0.002	0.026± 0.001	0.025± 0.001	
1000 ppm	0.060± 0.016	0.058± 0.017	0.056± 0.017	0.052± 0.015	0.050± 0.015	0.052± 0.015	
2000 ppm	0.104± 0.006	0.101± 0.004	0.098± 0.005	0.092± 0.004	0.091± 0.005	0.093± 0.004	
3000 ppm	0.160± 0.010	0.174± 0.048	0.186± 0.068	0.144± 0.013	0.143± 0.009	0.144± 0.008	

(HAN300) BAIS 3

APPENDIX E 2

CHEMICAL INTAKE CHANGES : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

CHEMICAL INTAKE CHANGES (SUMMARY)

ANIMAL : RAT F344/DuCrj

ALL ANIMALS

UNIT : g/kg/day REPORT TYPE : A1 13

SEX : FEMALE

PAGE: 3

0.000± 0.000	2	3	4	5	6	7
0.000± 0.000						
	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
0.033± 0.002	0.031± 0.002	0.029± 0.003	0.029± 0.008	0.028± 0.008	0.025± 0.003	0.027± 0.009
0.064± 0.015	0.054± 0.004	0.051± 0.003	0.050± 0.008	0.056± 0.034	0.046± 0.007	0.043± 0.005
0.102± 0.008	0.094± 0.006	0.087± 0.007	0.084± 0.006	0.079± 0.004	0.074± 0.005	0.071 ± 0.003
0.191± 0.011	0.172± 0.009	0.161± 0.004	0.155± 0.013	0.147± 0.010	0.139± 0.011	0.134± 0.010
0.145± 0.057	0.278± 0.059	0.235± 0.020	0.221± 0.019	0.191± 0.013	0.196± 0.018	0.179± 0.011
	0.064± 0.015 0.102± 0.008 0.191± 0.011	0.064± 0.015 0.054± 0.004 0.102± 0.008 0.094± 0.006 0.191± 0.011 0.172± 0.009	0.064± 0.015	0.064 ± 0.015 0.054 ± 0.004 0.051 ± 0.003 0.050 ± 0.008 0.102 ± 0.008 0.094 ± 0.006 0.087 ± 0.007 0.084 ± 0.006 0.191 ± 0.011 0.172 ± 0.009 0.161 ± 0.004 0.155 ± 0.013	0.064± 0.015	$0.064\pm \ 0.015$ $0.054\pm \ 0.004$ $0.051\pm \ 0.003$ $0.050\pm \ 0.008$ $0.056\pm \ 0.034$ $0.046\pm \ 0.007$ $0.102\pm \ 0.008$ $0.094\pm \ 0.006$ $0.087\pm \ 0.007$ $0.084\pm \ 0.006$ $0.079\pm \ 0.004$ $0.074\pm \ 0.005$ $0.191\pm \ 0.011$ $0.172\pm \ 0.009$ $0.161\pm \ 0.004$ $0.155\pm \ 0.013$ $0.147\pm \ 0.010$ $0.139\pm \ 0.011$

(HAN300)

ANIMAL : RAT F344/DuCrj UNIT : g/kg/day

REPORT TYPE : A1 13

CHEMICAL INTAKE CHANGES (SUMMARY)

SEX : FEMALE

ALL ANIMALS

Group Name	Administration	(weeks)					
	8	9	10	11	12	13	
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	
250 ppm	0.029± 0.015	0.025± 0.007	0.026± 0.009	0.027± 0.013	0.022± 0.005	0.023± 0.006	
500 ppm	0.039± 0.004	0.038± 0.002	0.038± 0.003	0.037± 0.002	0.037± 0.004	0.035± 0.001	
1000 ppm	0.065± 0.004	0.065± 0.005	0.064± 0.005	0.062± 0.005	0.062± 0.005	0.063± 0.006	
2000 ppm	0.122± 0.007	0.141± 0.046	0.126± 0.019	0.117± 0.010	0.118± 0.010	0.118± 0.010	
3000 ppm	0.166± 0.013	0.169± 0.039	0.167± 0.016	0.179± 0.026	0.169± 0.029	0.168± 0.017	
				٤			

(HAN300)

BAIS 3

APPENDIX F 1

HEMATOLOGY: SUMMARY, RAT: MALE

(13-WEEK STUDY)

HEMATOLOGY (SUMMARY)

ANIMAL : RAT F344/DuCrj

ALL ANIMALS (14W)

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : A1

PAGE: 1

oup Name	NO. of Animals	RED BLO	OOD CELL	HEMOGLO g/dl	BIN	HEMATOC %	CRIT	MCV f l		MCH pg		MCHC g/dl		PLATELET 1 O³/w	
Control	10	9.42±	0. 29	15.8±	0.5	46.9±	1.4	49.8±	0.7	16.7±	0.2	33.6±	0,5	687±	41
250 ppm	10	9.34±	0. 25	15.7±	0.3	46.4±	0.9	49.6±	0.8	16.8±	0.1	33.8±	0.5	661±	38
500 ppm	10	9.16±	0.22	15.5±	0.4	45.7±	1. 2	49.9±	0.7	16.9±	0.3	33.9±	0.7	660±	39
1000 ppm	10	9.14±	0. 25	15.4±	0.6	45.7±	1.2	50.0±	0.9	16.9±	0.3	33.7±	0.6	650±	65
2000 ppm	10	8.83±	0.28**	15.2±	0.5	44.9±	1.4**	50.8±	0.8*	17.3±	0.4**	34.0±	0.4	647±	52
3000 ppm	10	8.75±	0. 28**	15.3±	0.4	45.1±	1.0**	51.6±	1.0**	17.5±	0.3**	33.9±	0.4	644±	64

(HCL070)

HEMATOLOGY (SUMMARY) ALL ANIMALS (14W)

ANIMAL : RAT F344/DuCrj

MEASURE. TIME: 1

SEX: MALE REPORT TYPE: A1

oup Name	NO. of Animals	RETICULO ‰	OCYTE	PROTHROM s e c	BIN TIME	APTT sec		
Control	10	28±	7	12.1±	0.8	23.5±	1,5	
250 ppm	10	28±	5	12.4±	0.9	23.5±	2.7	
500 ppm	10	27±	6	12.0±	0.6	22.6±	3. 1	
1000 ppm	10	29±	6	12.0±	0.8	23.1±	2.0	
2000 ppm	10	26±	7	12.0±	0.6	23.0±	2.4	
3000 ppm	10	27±	5	11.8±	0.7	22.5±	1.2	

(HCL070)

ANIMAL : RAT F344/DuCrj

MEASURE. TIME : 1 SEX : MALE

REPORT TYPE : A1

HEMATOLOGY (SUMMARY) ALL ANIMALS (14W)

Differential WBC (%) Group Name NO. of WBC $10^{3}/\mu l$ Animals MONO LYMPHO N-BAND N-SEG EOSINO BASO OTHERS Control 10 4.15± 2.25 0± 0 $33\pm$ 10 1± 0± $3\pm$ 62± 1± 1± 250 ppm 10 4.15± 2.39 $0\pm$ 0 $32\pm$ 10 0土 $4\pm$ 62± $1\pm$ 0± 500 ppm 3.28± 1.91 $0\pm$ 0 30± 9 1± 0 4± $1\pm$ 10 1 2 63± 1 $0\pm$ 12 $1\pm$ $0\pm$ $3\pm$ 1000 ppm 10 3.68 ± 2.52 0 $36\pm$ 1 0 1 $59 \pm$ 12 $1\pm$ 1 $0\pm$ 2000 ppm 10 4.39± 2.06 0± 0 $29\pm$ 7 $1\pm$ 1 0 $4\pm$ 1 64± 1± 1 29± 0± 3000 ppm 10 5.28 ± 3.26 0± 0 7 1± 1 0 $5\pm$ 64± $1\pm$ 1 1

PAGE: 3

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

(HCLO70) BAIS 3

APPENDIX F 2

HEMATOLOGY: SUMMARY, RAT: FEMALE

HEMATOLOGY (SUMMARY) ALL ANIMALS (14W)

ANIMAL : RAT F344/DuCrj

MEASURE. TIME: 1

SEX : FEMALE

REPORT TYPE : A1

PAGE: 4

roup Name	NO. of Animals	RED BLOOD CE 1 O ^s /µl	LL HEMOG g/d		HEMATOC %	RIT	MCV f &		MCH pg		MCHC g∕dl		PLATELE 1 0 ³ /µ	
Control	10	8.52± 0.30	15.6±	0.5	44.8±	1, 4	52.6±	0.5	18.3±	0, 2	34.8±	0,6	716±	83
250 ppm	10	8.69± 0.20	15.7±	0.4	45.5±	1.3	52.3±	0.8	18.1±	0.2	34.5±	0.7	714±	54
500 ppm	10	8.56± 0.26	15.5±	0.5	44.6土	1.5	52.1±	0.5	18.1±	0.1	34.7±	0.6	711±	81
1000 ppm	10	8.42± 0.28	15.4±	0.5	44.3±	1.5	52.6±	0.6	18.3±	0.1	34.8±	0.4	682±	80
2000 ppm	10	8. 22± 0. 23	15.4±	0.5	44.4±	1.0	54.1±	0.9**	18.7±	0.2**	34.6±	0.6	630±	78*
3000 ppm	8	8.14± 0.37	* 15.4±	0.6	44.5±	1.7	54.7±	0.7**	18.9±	0.3**	34.6±	0.6	505±	62**

(HCL070)

BAIS 3

HEMATOLOGY (SUMMARY) ALL ANIMALS (14W)

ANIMAL : RAT F344/DuCrj

MEASURE. TIME : 1 SEX : FEMALE REPORT TYPE : A1 PAGE: 5

oup Name	NO. of Animals	RETICULO ‰	CYTE	PROTHRO s e c	MBIN TIME	APTT sec		
Control	10	21±	7	10.7±	0.2	18.3±	1.5	
250 ppm	10	24±	4	10.9±	0, 3	18.0±	1.0	
500 ppm	10	22±	5	10.8±	0.4	18.7±	1.1	
1000 ppm	10	24±	6	11.1±	0.4	19.6±	1.5	
2000 ppm	10	24±	6	11.4±	0. 4**	19.3±	1.4	
3000 ppm	8	19±	4	11.6±	0.3**	19.4±	1.6	

(HCL070) BAIS 3

ANIMAL : RAT F344/DuCrj

HEMATOLOGY (SUMMARY) ALL ANIMALS (14W)

MEASURE. TIME: 1

SEX : FEMALE

REPORT TYPE : A1

PAGE: 6

roup Name	NO. of Animals	WBC 1 O³∕µl		Dif N-BAND	ferentia	1 WBC (% N-SEG	6)	EOSINO		BASO		MONO		LYMPHO		OTHERS	
Control	10	2. 28±	1. 49	0±	0	33±	12	1±	1	0±	0	3±	2	63±	12	0±	0
250 ppm	10	1.91±	1. 25	0±	1	31±	11	2±	1	0±	0	3±	2	64±	11	1±	1
500 ppm	10	1.96±	1.02	0±	0	29±	9	1±	1	0±	0	5±	2	64土	12	1±	2
1000 ppm	10	2.56±	1.80	1±	1	27±	9	2±	1	0±	0	4±	2	66±	12	1±	1
2000 ppm	10	2.66±	1.84	0±	0	29±	9	2±	1	0±	0	4±	2	65±	11	1±	1
3000 ppm	8	2.07±	1. 34	1±	1	33±	9	1±	1	0±	0	4土	2	59±	10	$2\pm$	1*
Significant	difference ;	: *: P ≦	0. 05	**: P ≦	0.01			Test	of Dunn	ıett							BATS :

(HCLO70) BAIS 3

APPENDIX G 1

BIOCHEMISTRY: SUMMARY, RAT: MALE

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (14W)

ANIMAL : RAT F344/DuCrj

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : A1

TOTAL PROTEIN Group Name NO. of ALBUMIN A/G RATIO T-BILIRUBIN GLUCOSE T-CHOLESTEROL TRIGLYCERIDE Animals g/dl g/dl mg/dl mg/dl mg/dl mg/dl Control 10 $6.3 \pm$ 0.2 $3.9 \pm$ 0.1 1.6± 0.1 0.13± 0.01 170± 12 64± 5 $65\pm$ 32 250 ppm 10 $6.4 \pm$ 0.1 $3.9 \pm$ 0.1 1.6± 0.1 0.12± 0.01 171± 12 66± 5 $72\pm$ 33 500 ppm 10 $6.3 \pm$ 0.2 $3.8 \pm$ 0.1 1.6± 0.1 0.13± 0.01 174± 64± 3 $68 \pm$ 20 1000 ppm $6.2 \pm$ 0.1 10 $3.8 \pm$ 0.1 1.6± 0.1 0.13± 0.01 8 171± 68± 2 87± 33 2000 ppm 10 $6.2 \pm$ 0.2 $3.8 \pm$ 0.13± 0.01 0.1** $1.6 \pm$ 0.1 $165 \pm$ 7 $70 \pm$ 5* $82\pm$ 33 3000 ppm 10 $6.1\pm$ 0.3** 3.7± 0.1** 1.6 ± 0.1 0.13± 0.01 159± 11 69± 82± 17

Significant difference; $*: P \leq 0.05$

**: $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 3

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (14W)

ANIMAL : RAT F344/DuCrj

MEASURE. TIME : 1 SEX : MALE

REPORT TYPE : A1

roup Name	NO. of Animals	PHOSPHOI mg/dl	LIPID	GOT I U / A	!	GPT I U/1		LDH IU/A	2	ALP IU/£		G-GTP IU/l		CPK IU/&	?
Control	10	115±	10	76±	13	43±	5	176±	32	238±	17	1±	1	101生	9
250 ppm	10	121±	10	92±	34	50±	14	203±	70	237±	19	1±	1	95±	8
500 ppm	10	118±	5	75±	10	42±	3	176±	28	229±	15	1±	1	101±	13
1000 ppm	10	126±	7*	74±	10	41±	6	178±	27	228±	15	2±	1	96±	7
2000 ppm	10	129±	8**	63±	9	34±	3**	160±	38	221±	16	2±	1	98±	18
3000 ppm	10	128±	8**	64±	5	33±	3**	157±	36	226±	17	1±	1	106±	12

(HCL074)

BAIS 3

SEX : MALE

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (14W)

ANIMAL : RAT F344/DuCrj MEASURE. TIME : 1

REPORT TYPE : A1

PAGE: 3

oup Name	NO. of Animals	UREA NI mg∕dl	TROGEN	CREATIN mg/dl	IINE	SODIUM m Eq / 2		POTASSI m Eq /		CHLORIDE m Eq / 1		CALCIUM mg/dl	ſ	INORGAN mg∕dl	VIC PHOSPHORU
Control	10	18.2±	1.4	0.5±	0.0	142±	1	4.3±	0.5	107±	1	10.3±	0. 2	6.1±	0, 7
250 ppm	10	18.2±	1.0	0.5±	0.0	142±	1	4.3±	0.4	107±	1	10.3±	0. 2	6.0±	0.6
500 ppm	10	19.2±	1.8	0.5±	0.0	141±	1	4.3±	0.3	107±	1	10.2±	0.2	5.9±	0.6
1000 ppm	10	19.7±	3.7	0.5±	0.1	140±	1**	4.5±	0.3	105±	1	10.2±	0.2	6.0±	0.5
2000 ppm	10	21.7±	3.0*	0.5±	0.1	140±	1**	4.5±	0.3	106±	1	10.2±	0.2	6.0±	0.6
3000 ppm	10	24.4±	3.9**	0.5±	0.1	140±	1**	4.6±	0.4	106±	1	10.1±	0.2	6.1±	0.5

(HCL074) BAIS 3

APPENDIX G 2

BIOCHEMISTRY: SUMMARY, RAT: FEMALE

ANIMAL : RAT F344/DuCrj

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (14W)

MEASURE. TIME: 1

SEX : FEMALE

REPORT TYPE : A1

PAGE: 4

roup Name	NO. of Animals	TOTAL P	PROTEIN	ALBUMIN g/dl		A/G RAT	,IO	T-BILIR mg/dl	UBIN	GLUCOSE mg/dl		T-CHOLES mg∕dℓ	TEROL	TRIGLYCE mg/dl	RIDE
Control	10	6.1±	0. 2	3.8±	0.1	1.6±	0.1	0, 14±	0.01	135±	10	71±	5	18±	3
250 ppm	10	6.1±	0.1	3.8±	0.1	1.6±	0.1	0.14±	0. 02	133±	12	68±	5	16±	3
500 ppm	10	5.9±	0.1**	3.6±	0.2	1.6±	0.1	0.14±	0.01	137±	11	65±	5*	18±	3
1000 ppm	10	5.8±	0.2**	3.6±	0.1	1.7±	0.1	0.14±	0. 01	133±	9	63±	5**	19±	4
2000 ppm	10	5.6±	0.2**	3.5±	0.1**	1.6±	0.1	0.14±	0.01	134±	8	55±	5**	21±	5
3000 ppm	8	5.5±	0.1**	3.4±	0.1**	1.7±	0.1	0.15±	0.01	139±	12	54±	6**	16±	2

(HCL074) BAIS 3

BIOCHEMISTRY (SUMMARY)

ANIMAL : RAT F344/DuCrj

ALL ANIMALS (14W)

MEASURE. TIME : 1

SEX : FEMALE

REPORT TYPE : A1

PAGE: 5

roup Name	NO. of Animals	PHOSPHO mg/dl	LIPID	GOT I U / L		GPT I U/l		LDH IU/J	2	ALP IU/A		G-GTP I U/l		CPK IU/l	
Control	10	132±	7	67±	16	36±	14	221±	77	163±	10	2±	1	111±	23
250 ppm	10	128±	9	72±	15	38±	11	285±	154	172±	16	2±	1	124±	40
500 ppm	10	121±	8*	71±	9	$34\pm$	4	289±	77	160±	10	2±	1	121±	19
1000 ppm	10	120±	11*	64±	7	31±	3	230±	74	165±	18	1±	1	118±	28
2000 ppm	10	108±	7**	72±	12	30±	4	273±	116	179±	24	2±	1	141±	40
3000 ppm	8	103±	12**	88±	5**	36±	3	299±	59	242±	30**	3±	1	147±	19

(HCL074) BAIS 3

ANIMAL : RAT F344/DuCrj

MEASURE. TIME: 1

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (14W)

up Name	NO. of Animals	UREA NI mg∕dl	TROGEN	CREATIN mg/dl	TINE	SODIUM m Eq / l		POTASSI m Eq /		CHLORIDE m Eq / L		CALCIUM mg/dl	[INORGAN mg/dl	IC PHOSPHORU
Control	10	18.5±	1.6	0.5±	0,0	141±	1	4.2±	0.4	107±	1	10.0±	0.1	5.5±	1. 2
250 ppm	10	19.1±	1.8	0.5±	0.1	140±	1	4.4±	0.3	108±	2	10.0±	0.2	5.6±	1. 2
500 ppm	10	18.5±	2.5	0.5±	0.1	140±	1	4.4±	0.4	108±	1	9.8±	0.2	5.4±	1.0
1000 ppm	10	19.8±	3.3	0.5±	0.0	139±	1*	4.5±	0.4	108±	1	9.8±	0.2	5.7±	0.8
2000 ppm	10	26.5±	7. 4**	0.5±	0.1	139±	1**	4.6±	0.5	108±	2	9.7±	0.2	5.7±	0.5
3000 ppm	8	31.5±	4.0**	0.5±	0.0	140±	1	4.4±	0.5	110±	1**	9.5±	0.3**	5.8±	0.5

(HCL074) BAIS 3

APPENDIX H 1

URINALYSIS: SUMMARY, RAT: MALE

URINALYSIS

ANIMAL : RAT F344/DuCrj

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : A1

Group Name NO. of Glucose____ Ketone body Bilirubin Protein____ - + 2+ 3+ CHI Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI $-\pm + 2 + 3 + 4 + CHI$ $-\pm + 2 + 3 + 4 +$ CHI $-\pm + 2 + 3 + 4 + CHI$ Control 10 0 0 0 0 6 4 0 0 4 6 0 0 10 0 0 0 0 0 0 5 5 0 0 0 10 0 0 0 250 ppm 7 3 0 0 7 3 0 0 0 7 3 0 0 0 10 0 0 0 10 0 0 0 10 0 0 0 0 0 500 ppm 10 0 0 0 4 6 0 0 10 0 0 0 0 0 0 9 1 0 0 0 10 0 0 0 1000 ppm 10 0 0 8 2 0 0 4 6 0 0 10 0 0 0 0 0 1 6 3 0 0 0 10 0 0 0 0 0 1 9 0 0 2000 ppm 10 10 0 0 0 0 0 0 6 4 0 0 0 10 0 0 0 0 0 6 4 3000 ppm 10 0 0 0 1 7 2 0 0 4 5 1 0 10 0 0 0 0 0 0 9 1 0 0 0 10 0 0 0

PAGE: 1

Significant difference ; *: $P \le 0.05$ **: $P \le 0.01$ Test of CHI SQUARE

(HCL101) BAIS 3

ANIMAL : RAT F344/DuCrj

MEASURE. TIME: 1

SEX : MALE REPORT TYPE : A1

PAGE: 2 Group Name NO. of Occult blood Urobilinogen - \pm + 2+ 3+ CHI ± + 2+ 3+ 4+ CHI Animals Control 10 10 0 0 0 0 10 0 0 0 0 250 ppm 10 0 0 0 0 10 10 0 0 0 0 500 ppm 10 10 0 0 0 0 10 0 0 0 0 1000 ppm 10 9 0 0 0 1 10 0 0 0 0 2000 ppm 10 10 0 0 0 0 10 0 0 0 0 3000 ppm 10 9 0 0 0 1 10 0 0 0 0 Significant difference ; $*: P \leq 0.05$ ** : $P \leq 0.01$ Test of CHI SQUARE

URINALYSIS

(HCL101) BAIS 3

APPENDIX H 2

URINALYSIS : SUMMARY, RAT : FEMALE

URINALYSIS

ANIMAL : RAT F344/DuCrj

MEASURE. TIME: 1

SEX : FEMALE

REPORT TYPE : A1

PAGE: 3

roup Name	NO. of	Ha								P:	rote	in_			_	G1	ucos	se			Ket	one	bod	у.			Bi	liru	bin	
	Animals	5. 0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	_	- ±	+	2+	3+ 4	+ CHI	_	±	+ 2	+ 3+	4+ CHI				-	+ 4+	CHI			2+ 3+	CHI
Control	10	0	0	0	0	0	7	3		1	0 1	7	2	0)	10	0	0	0 0	0	10	0	0	0 1	0 0		10	0	0 (1
250 ppm	10	0	0	0	0	0	6	4		1	0 1	8	1	0	0	10	0	0	0 0	0.	9	1	0	0 1	0 0		10	0	0 ()
500 ppm	10	0	0	0	0	2	6	2		1	0 0	7	3	0	0	10	0	0	0 0	0	9	1	0	0	0 0		10	0	0 0)
1000 ppm	10	0	0	0	0	0	9	1		1	0 0	7	3	0	0	10	0	0	0 0	0	7	3	0	0	0 0		10	0	0 ()
2000 ppm	10	0	0	0	2	2	5	1		ı	0 0	3	7	0	0	10	0	0	0 0	0	5	5	0	0	0 0	**	10	0	0 ()
3000 ppm	8	0	0	2	0	4	2	0	**		0 0	2	6	0	0	8	0	0	0 0	0	2	6	0	0	0 0	**	8	0	0 ()

(HCL101) BAIS 3

URINALYSIS

ANIMAL : RAT F344/DuCrj

MEASURE. TIME: 1

SEX : FEMALE

REPORT TYPE : A1

PAGE: 4 NO. of Group Name Occult blood Urobilinogen Animals $- \pm + 2 + 3 +$ CHI \pm + 2+ 3+ 4+ CHI 10 Control 10 0 0 0 0 10 0 0 0 0 250 ppm 10 10 0 0 0 0 10 0 0 0 0 500 ppm 10 10 0 0 0 0 10 0 0 0 0 1000 ppm 10 10 0 0 0 0 10 0 0 0 0 2000 ppm 10 10 0 0 0 0 10 0 0 0 0 3000 ppm 8 8 0 0 0 0 8 0 0 0 0 Significant difference ; $*: P \le 0.05$ ** : $P \leq 0.01$ Test of CHI SQUARE

(HCL101) BAIS 3

APPENDIX I 1

GROSS FINDINGS: SUMMARY, RAT: MALE ALL ANIMALS

ANIMAL : RAT F344/DuCrj

GROSS FINDINGS (SUMMARY) ALL ANIMALS (0- 14W)

REPORT TYPE : A1

SEX : MALE

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	250 ppm 10 (%)	500 ppm 10 (%)	1000 ppm 10 (%)
liver	herniation		1 (10)	1 (10)	1 (10)	0 (0)
kidney	hydronephrosis		0 (0)	0 (0)	0 (0)	1 (10)
(HPT080)						BAIS 3

ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

GROSS FINDINGS (SUMMARY)

SEX : MALE

ALL ANIMALS (0- 14W)

Organ	Findings	Group Name NO. of Animals	2000 ppm 10 (%)	3000 ppm 10 (%)
liver	herniation		1 (10)	2 (20)
kidney	hydronephrosis		0 (0)	0 (0)
···				
(HPT080)				BAIS

APPENDIX I 2

GROSS FINDINGS : SUMMARY, RAT : FEMALE ALL ANIMALS

ANIMAL : RAT F344/DuCrj

GROSS FINDINGS (SUMMARY) ALL ANIMALS (0- 14W)

REPORT TYPE : A1

(HPT080)

SEX : FEMALE

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	250 ppm 10 (%)	500 ppm 10 (%)	1000 ppm 10 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
gl stomach	erosion		0 (0)	0 (0)	0 (0)	0 (0)
liver	herniation		1 (10)	0 (0)	1 (10)	1 (10)
kidney	nodule		1 (10)	0 (0)	0 (0)	0 (0)
ovary	cyst		1 (10)	0 (0)	0 (0)	0 (0)

BAIS 3

STUDY NO. : 0351 ANIMAL : RAT F

: RAT F344/DuCrj

REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)

ALL ANIMALS (0- 14W)

Group Name 2000 ppm 3000 ppm 10 (%) 10 (%) Findings_ NO. of Animals Organ_ 0 (0) 1 (10) thymus atrophic gl stomach erosion 0 (0) 1 (10) liver herniation 3 (30) 1 (10) 0 (0) 0 (0) kidney nodule ovary cyst 0 (0) 0 (0)

PAGE: 4

(HPT080) BAIS 3

APPENDIX I 3

GROSS FINDINGS: SUMMARY, RAT: FEMALE: SACRIFICED ANIMALS

ANIMAL : RAT F344/DuCrj

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (14W)

REPORT TYPE : A1

SEX : FEMALE

Group Name Control 250 ppm 500 ppm 1000 ppm 0rgan____ Findings____ NO. of Animals 10 (%) 10 (%) 10 (%) 10 (%)

Organ	Findings	NO. of Animals	10 (%)	10 (%)	10 (%)	10 (%)
liver	herniation		1 (10)	0 (0)	1 (10)	1 (10)
kidney	nodule		1 (10)	0 (0)	0 (0)	0 (0)
ovary	cyst		1 (10)	0. (0)	0 (0)	0 (0)

(HPT080)

BAIS 3

ANIMAL : RAT F344/DuCrj

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (14W)

REPORT TYPE : A1

SEX : FEMALE

Organ	Findings	Group Name 2000 ppm NO. of Animals 10 (%)	3000 ppm 8 (%)	
liver	herniation	3 (30)	1 (13)	
idney	nodule	0 (0)	0 (0)	
ovary	cyst	0 (0)	0 (0)	
(HPT080)				BAIS

APPENDIX I 4

GROSS FINDINGS: SUMMARY, RAT: FEMALE

DEAD AND MORIBUND ANIMALS

ANIMAL : RAT F344/DuCrj

GROSS FINDINGS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 14W)

REPORT TYPE : A1 SEX : FEMALE

Organ	Findings	Group Name NO. of Animals	Control 0 (%)	250 ppm 0 (%)	500 ppm 0 (%)	1000 ppm 0 (%)
ıymus	atrophic		- (-)	- (-)	- (-)	- (-)
stomach	erosion		- (-)	- (-)	- (-)	- (-)

ANIMAL : RAT F344/DuCrj

GROSS FINDINGS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 14W)

REPORT TYPE : A1 SEX : FEMALE

Organ	Findings	Group Name NO. of Animals	2000 ppm 0 (%)	3000 ppm 2 (%)	
thymus	atrophic		- (-)	1 (50)	
gl stomach	erosion		- (-)	1 (50)	
(HPT080)					BAIS

APPENDIX J 1

ORGAN WEIGHT, ABSOLUTE: SUMMARY, RAT: MALE (13-WEEK STUDY)

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1 SEX : MALE UNIT: g ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (14W)

PAGE: 1

oup Name	NO. of Animals	Body	Weight	ТНҮМ	US	ADRE	NALS	TEST	ES	HEAR	T	LUNG	S
Control	10	294±	13	0.251±	0.038	0.053±	0.007	3.129±	0.111	0.917±	0.056	1.043±	0.029
250 ppm	10	296±	15	0.266±	0.032	0.060±	0.011	3.139±	0. 103	0.911±	0.064	1.019±	0. 044
500 ppm	10	290±	10	0.259±	0.042	0.052±	0.008	3.020±	0.218	0.911±	0.062	1.026±	0. 046
1000 ppm	10	276±	14*	0.238±	0.032	0.054±	0.011	3.035±	0.071	0.890±	0.066	0.984±	0. 022**
2000 ppm	10	256±	14**	0.204±	0.022**	0.052±	0,006	3.021±	0.114	0.818±	0.074**	0.956±	0. 035**
3000 ppm	10	232±	17**	0.178±	0.021**	0.048±	0.007	2.951±	0.151*	0.772±	0.078**	0.925±	0.057**

(HCL040)

BAIS 3

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1 SEX : MALE

UNIT: g

ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (14W)

PAGE: 2

oup Name	NO. of Animals	KIDI	NEYS	SPL	EEN	LIV	ER	BRA		
Control	10	1.827±	0.090	0.567±	0.024	7.468±	0.389	1.881±	0. 056	
250 ppm	10	1.805±	0.112	0.571±	0.032	7.617±	0.490	1.883±	0. 040	
500 ppm	10	1.782±	0.066	0.579±	0. 035	7.503±	0.356	1.894±	0. 043	
1000 ppm	10	2.176±	1. 188	0.549±	0.025	7.554±	0.534	1.855±	0, 047	
2000 ppm	10	1.754±	0.071	0.509±	0.037**	7.386±	0.736	1.824±	0. 054*	
3000 ppm	10	1.673±	0.114**	0.475±	0.032**	7.035±	0.670	1.766±	0. 050**	

(HCL040)

BAIS 3

APPENDIX J 2

ORGAN WEIGHT, ABSOLUTE: SUMMARY, RAT: FEMALE (13-WEEK STUDY)

ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (14W)

STUDY NO. : 0351

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1

SEX : FEMALE UNIT: g

oup Name	NO. of Animals	Body W	eight	тнум	js 	ADREN	IALS	OVAR	IES	HEAR	<u>. </u>	LUNG	
Control	10	169±	8	0.213±	0. 022	0.059±	0.008	0.116±	0.019	0.628±	0.052	0.776±	0.049
250 ppm	10	161±	5	0.202±	0.029	0.059±	0.007	0.109±	0.010	0.609±	0.037	0.763±	0.032
500 ppm	10	158±	9**	0.187±	0.018*	0.057±	0.005	0.109±	0.016	0.593±	0.044	0.731±	0. 034*
1000 ppm	10	153±	7**	0.187±	0.020*	0.055±	0.006	0.102±	0.011	0.568±	0.035**	0.730±	0.024*
2000 ppm	10	139±	8 **	0.162±	0.013**	0.051±	0.004*	0.090±	0.007**	0.533±	0.033**	0.690±	0, 029**
3000 ppm	8	114±	9**	0.108±	0, 015**	0.047±	0.006**	0.064±	0.009**	0.452±	0.043**	0.603±	0. 028**

PAGE: 3

BAIS 3 (HCL040)

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1 SEX : FEMALE UNIT: g ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (14W)

PAGE: 4

oup Name	NO. of Animals	KIDi	NEYS	SPLI	BEN	LIVI	ER	BRA		
Control	10	1.215±	0. 129	0.392±	0. 031	4.118±	0. 230	1.765±	0.050	
250 ppm	10	1.134±	0.038	0.376±	0.020	3.893±	0.145	1.718±	0.051	
500 ppm	10	1.148±	0. 067	0.372±	0.020	3.832±	0.143	1.723±	0.033	
1000 ppm	10	1.162±	0.029	0.361±	0.015*	3.756±	0.123*	1.708±	0.066	
2000 ppm	10	1.181±	0.039	0.324±	0.020**	3.589±	0.175**	1.656±	0.035**	
3000 ppm	8	1.075±	0. 055**	0.255±	0.029**	3.062±	0. 377**	1.612±	0.053**	

(HCL040)

BAIS 3

APPENDIX K 1

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : MALE

(13-WEEK STUDY)

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1 SEX : MALE

UNIT: %

ORGAN WEIGHT: RELATIVE (SUMMARY)

SURVIVAL ANIMALS (14W)

roup Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	294± 13	0.085± 0.011	0.018± 0.003	1.064± 0.033	0.311± 0.013	0.355± 0.016
250 ppm	10	296± 15	0.090± 0.010	0.020± 0.004	1.060± 0.038	0.307± 0.015	0.344± 0.018
500 ppm	10	290± 10	0.089± 0.014	0.018± 0.002	1.042± 0.079	0.314± 0.017	0.354± 0.013
1000 ppm	10	276± 14*	0.086± 0.008	0.020± 0.004	1.103± 0.046	0.323± 0.014	0.358± 0.016
2000 ppm	10	256± 14**	0.080± 0.007	0.021± 0.002	1.184± 0.070**	0.319± 0.017	0.375± 0.015*
3000 ppm	10	232± 17**	0.077± 0.009	0.021± 0.002	1.273± 0.061**	0.332± 0.020*	0.399± 0.016**

(HCL042)

BAIS 3

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1 SEX : MALE

UNIT: %

ORGAN WEIGHT: RELATIVE (SUMMARY) SURVIVAL ANIMALS (14W)

ıp Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	
Control	10	0.621± 0.018	0.193± 0.009	2.537± 0.053	0.640± 0.029	
250 ppm	10	0.609± 0.021	0.193± 0.011	2.569± 0.070	0.636± 0.025	
500 ppm	10	0.615± 0.025	0.199± 0.009	2.585± 0.060	0.653± 0.031	
1000 ppm	10	0.797± 0.464**	0.199± 0.007	2.740± 0.106**	0.675± 0.032	
2000 ppm	10	0.686± 0.029**	0.199± 0.010	2.882± 0.155**	0.715± 0.050**	
3000 ppm	10	0.720± 0.019**	0.205± 0.006*	3.023± 0.118**	0.763± 0.041**	

PAGE: 2

BAIS 3 (HCL042)

APPENDIX K 2

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1 SEX : FEMALE UNIT: % ORGAN WEIGHT: RELATIVE (SUMMARY) SURVIVAL ANIMALS (14W)

PAGE: 3

oup Name	NO. of Animals	Body V	/eight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	169±	8	0.126± 0.013	0.035± 0.004	0.068± 0.012	0.371± 0.029	0.459± 0.016
250 ppm	10	161±	5	0.125± 0.017	0.036± 0.004	0.068± 0.005	0.377± 0.024	0.473± 0.013
500 ppm	10	158土	9**	0.118± 0.010	0.036± 0.003	0.069± 0.010	0.376± 0.023	0.464± 0.024
1000 ppm	10	153±	7**	0.123± 0.012	0.036± 0.004	0.067± 0.009	0.372± 0.029	0.478± 0.016
2000 ppm	10	139±	8**	0.117± 0.012	0.037± 0.004	0.065± 0.004	0.385± 0.024	0.500± 0.039**
3000 ppm	8	114±	9**	0.095± 0.010**	0.041± 0.003**	0.057± 0.007*	0.398± 0.016	0.533± 0.033**

(HCL042)

BAIS 3

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1 SEX : FEMALE UNIT: % ORGAN WEIGHT: RELATIVE (SUMMARY) SURVIVAL ANIMALS (14W)

PAGE: 4

oup Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	
Control	10	0.718± 0.067	0.231± 0.012	2.493± 0.051	1.045± 0.044	
250 ppm	10	0.702± 0.018	0.233± 0.007	2.412± 0.042	1.065± 0.043	
500 ppm	10	0.727± 0.022	0.236± 0.010	2.428± 0.065	1.093± 0.059	
1000 ppm	10	0.761± 0.030**	0.236± 0.009	2.459± 0.084	1.118± 0.038**	
2000 ppm	10	0.854± 0.030**	0.234± 0.010	2.593± 0.067**	1.199± 0.057**	
3000 ppm	8	0.948± 0.048**	0.224± 0.011	2.690± 0.169**	1.426± 0.110**	

(HCL042)

BAIS 3

APPENDIX L 1

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY

RAT: MALE: ALL ANIMALS

(13-WEEK STUDY)

SEX

: 0351

ANIMAL : RAT F344/DuCrj

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 14W)

REPORT TYPE : A1

: MALE

TIDD INTIBIDO (

Group Name Control 250 ppm 500 ppm 1000 ppm No. of Animals on Study 10 10 10 10 Grade Findings_ (%) (%) (%) (%) (%) (%) {Respiratory system} nasal cavit <10> <10> <10> <10> inflammation:respiratory epithelium 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (10) (0) (0) (0) duct ectasia:olfactory gland 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) lung <10> <10> <10> <10> accumulation of foamy cells 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (10) (0) (0) (0) {Circulatory system} heart <10> <10> <10> <10> inflammatory cell nest 0 0 0 0 0 0 0 0 (10) (0) (0) (0) (0)(0)(0)(0) (10) (0) (0) (0) (10) (0) (0) (0) {Digestive system} liver <10> <10> <10> <10> herniation 0 0 0 0 0 0 0 0 0 0 (10) (0) (0) (0) (10) (0) (0) (0) (10) (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 Significant difference; * : $P \le 0.05$ **: $P \le 0.01$ Test of Chi Square

(HPT150)

BAIS3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

: RAT F344/DuCrj ALL ANIMALS (0- 14W)

ANIMAL REPORT TYPE : A1

SEX : MALE

Organ	Findings	Group Name No. of Animals on Study Grade (%)	2000 ppm 10 2 3 4 (%) (%) (%)	3000 ppm 10 1 2 3 4 (%) (%) (%) (%)	
{Respiratory	system)				
nasal cavit	inflammation:respiratory epithelium	0 (0)	<10> 0 0 0 (0) (0) (0)	<10> 0 0 0 0 0 0 0 0 0 0	
	duct ectasia:olfactory gland	1 (10)	0 0 0 0 (0) (0)	7 0 0 0 ** (70) (0) (0) (0)	
	necrosis:olfactory epithelium	0 (0)	0 0 0 0 (0) (0)	1 0 0 0 0 (10) (10) (10)	
lung	accumulation of foamy cells	(0)	<10> 0 0 0 (0) (0) (0)	1 0 0 0 (10) (0) (0) (0)	
{Circulatory	system)				
heart	inflammatory cell nest	0 (0)	<10> 0 0 0 (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	
{Digestive sy	stem)				
liver	herniation	1 (10)	<10> 0 0 0 0 0 0	<10> 2 0 0 0 (20) (0) (0) (0)	

1 : Slight 2 : Moderate Grade 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b: Number of animals with lesion b

c:b/a*100

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

(HPT150)

BAIS3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0- 14W)

: RAT F344/DuCrj ANIMAL REPORT TYPE : A1

SEX : MALE

PAGE: 3

Organ	_ Findings	Group Name Control No. of Animals on Study 10 Grade 1 2 3 4 (%) (%) (%) (%)	250 ppm 10 1 2 3 4 (%) (%) (%) (%)	500 ppm 10 1 2 3 4 (%) (%) (%) (%)	1000 ppm 10 1 2 3 4 (%) (%) (%) (%)
{Digestive	system)				
liver	granulation	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	1 0 0 0 (10) (0) (0) (0)	1 0 0 0 (10) (0) (0) (0)
	perivascular inflammation	2 0 0 0 0 (20) (0) (0) (0)	3 0 0 0 0 (30) (30) (0) (0)	1 0 0 0 (10) (0) (0) (0)	3 0 0 0 0 (30) (30) (0) (0)
{Urinary sy	vstem)				
ridney	basophilic change	0 0 0 0 0 (0) (0) (0)	2 0 0 0 (20) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	2 0 0 0 (20) (0) (0) (0)
	eosinophilic body	2 8 0 0 (20) (80) (0) (0)	1 9 0 0 (10) (90) (0) (0)	7 3 0 0 (70) (30) (0) (0)	4 5 0 0 (40) (50) (0) (0)
	hydronephrosis	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 0 (0)	0 0 1 0 (0) (10) (0)
	mineralization:papilla	0 0 0 0 0 (0) (0)	1 0 0 0 (10) (0) (0) (0)	1 0 0 0 (10) (0) (0) (0)	0 0 0 0 0 (0)
	degeneration:papilla	0 0 0 0 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: Number of animals examined at the site < a > b: Number of animals with lesion b

(c)

c:b/a*100

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

ANIMAL

: RAT F344/DuCrj

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 14W)

REPORT TYPE : A1 SEX : MALE

3000 ppm Group Name 2000 ppm No. of Animals on Study 10 10 (%) (%) (%) (%) (%) Findings_ Organ__ {Digestive system} liver <10> <10> granulation 0 0 (0)(0)(0)(0) (0)(0)(0)(0) 3 perivascular inflammation 0 0 0 1 0 0 (30) (0) (0) (0) (10) (0) (0) (0) {Urinary system} kidney <10> <10> basophilic change 0 0 0 0 0 0 (10) (0) (0) (0) (0)(0)(0)(0) eosinophilic body 0 * 0 0 1 (80) (20) (0) (0) (80) (10) (0) (0) hydronephrosis 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) mineralization:papilla 0 1 (10) (0) (0) (0) (10) (0) (0) (0) degeneration:papilla 0 0 0 (10) (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:b/a*100

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

(HPT150)

ь

BAIS3

: RAT F344/DuCrj

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 14W)

ANIMAL REPORT TYPE : A1

SEX

: MALE

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

PAGE: 5 Group Name 250 ppm 500 ppm Control 1000 ppm No. of Animals on Study 10 10 10 10 Findings_ (%) (%) (%) (%) (%) (%) (%) (%) (%) {Urinary system} urin bladd <10> <10> <10≻ simple hyperplasia: transitional epithelium 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) nodular hyperplasia:transitional epithelium (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) {Endocrine system} thyroid <10> <10> <10> <10> ultimobranchial body remanet 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (10) (0) (0) (0) {Reproductive system} testis <10> <10> <10> <10> atrophy 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(10)(0)(0) (0)(0)(0)(0) {Special sense organs/appendage} Harder gl <10> <10> <10> inflammation 0 0 0 0 0 0 1 0 0 4 (10) (0) (0) (0) (0)(0)(0)(0) (10) (0) (0) (0) (40) (0) (0) (0) 1 : Slight 2 : Moderate 3 : Marked Grade 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

ANIMAL : RAT F344/DuCrj

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0- 14W)

REPORT TYPE : A1

SEX : MALE

Organ	Group Nam No. of Am Grade Findings	ne 2000 ppm nimals on Study 10 1 2 3 4 (%) (%) (%) (%)	3000 ppm 10 1 2 3 4 (%) (%) (%) (%)		
{Urinary sys	stem)				
urin bladd	simple hyperplasia∶transitional epithelium	<10> 1 1 0 0 (10) (10) (0) (0)	<10> 1 2 0 0 (10) (20) (0) (0)		
	nodular hyperplasia:transitional epithelium	0 0 0 0 0 (0) (0)	2 0 0 0 0 (20) (0) (0) (0)		
{Endocrine s	system}				
thyroid	ultimobranchial body remanet	<10> 2 0 0 0 (20) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	,	
{Reproductiv	ve system)				
testis	atrophy	<10> 0 0 0 0 0 0 0 0 0 0 0	<10> 0 0 0 0 (0) (0) (0) (0)		
{Special sen	nse organs/appendage)				
Harder gl	inflammation	<10> 3 1 0 0 (30) (10) (0) (0)	3 2 0 0 (30) (20) (0) (0)		
Grade <a>> b (c) Significant	1: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 difference; *: $P \le 0.05$ **: $P \le 0.01$	4 : Severe Test of Chi Square			
(tipm+ = 0)				- "	

(HPT150)

APPENDIX L 2

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY

RAT: FEMALE: ALL ANIMALS

(13-WEEK STUDY)

ANIMAL

SEX

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

: RAT F344/DuCrj

REPORT TYPE : A1 : FEMALE ALL ANIMALS (0- 14W)

Group Name Control 250 ppm 500 ppm 1000 ppm No. of Animals on Study 10 10 10 10 Findings_ (%) (%) (%) (%) Organ__ (%) (%) (%) (%) (%) {Respiratory system} nasal cavit <10> <10> <10> <10> inflammation:respiratory epithelium 0 0 0 0 0 (0)(0)(0)(0) (20) (0) (0) (0) (10) (0) (0) (0) (30) (0) (0) (0) duct ectasia:olfactory gland 0 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) necrosis:olfactory epithelium 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) lung <10> <10> <10> <10> perivascular inflammation 0 0 0 0 0 0 0 0 (10) (0) (0) (0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0) accumulation of foamy cells 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 <10> <10> <10> <10> congestion 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)

Significant difference; *: P ≤ 0.05 **: P ≤ 0.01 Test of Chi Square

ANIMAL : RAT F344/DuCrj

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0- 14W)

REPORT TYPE : A1

SEX : FEMALE

Organ		Group Name 2000 ppm No. of Animals on Study 10 Grade 1 2 3 4 (%) (%) (%) (%)	3000 ppm 10 1 2 3 4 (%) (%) (%) (%)	
{Respiratory	system}			
nasal cavit	inflammation:respiratory epithelium	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	
	duct ectasia:olfactory gland	0 0 0 0 0 (0) (0)	3 0 0 0 (30) (0) (0) (0)	
	necrosis:olfactory epithelium	1 0 0 0 0 (10) (0) (0)	6 0 0 0 *	
lung	perivascular inflammation	<00 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	
	accumulation of foamy cells	1 0 0 0 0 (10) (10) (10)	0 0 0 0 0 (0) (0) (0)	
{Hematopoietic	c system}	•		
bone marrow	congestion	<10> 0 0 0 0 0 0 0 0 0 0 0	<10> 0 2 0 0 (0) (20) (0) (0)	
<a>> b (c)	1: Slight 2: Moderate 3 a: Number of animals examined at the si b: Number of animals with lesion c: b / a * 100 ifference; *: P ≤ 0.05 **: P ≤			,

(HPT150)

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1 SEX : FEMALE ALL ANIMALS (0- 14W)

PAGE: 9

Organ	N	roup Name Control o. of Animals on Study 10 rade 1 2 3 4 (%) (%) (%) (%)	250 ppm 10 1 2 3 4 (%) (%) (%) (%)	500 ppm 10 1 2 3 4 (%) (%) (%) (%)	1000 ppm 10 1 2 3 4 (%) (%) (%) (%)
{Hematopoiet	tic system)				
one marrow	granulation	<10> 0 1 0 0 0 (10) (0) (0)	1 3 0 0 (10) (30) (0) (0)	0 2 0 0 (0) (20) (0) (0)	0 1 0 0 (0) (10) (0) (0)
hymus	atrophy	(10) 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	(0) (0) (0) (0) (0) (0) (0) (0)
Circulatory	y system}				
əart	inflammatory cell nest	(10> 0 0 0 0 (0) (0) (0) (0)	1 0 0 0 (10) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)
)igestive s	system)				
iver	herniation	(10) 1 0 0 0 (10) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	1 0 0 0 (10) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)
	granulation	1 0 0 0 (10) (0) (0) (0)	2 0 0 0 (20) (20) (0) (0)	1 0 0 0 (10) (0) (0) (0)	0 0 0 0 0 (0) (0)
rade a > b c)	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)

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1 SEX : FEMALE HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0- 14W)

PAGE: 10

Organ	Findings	Group Name 2000 ppm No. of Animals on Study 10 Grade 1 2 3 4 (%) (%) (%)	3000 ppm 10 1 2 3 4 (%) (%) (%) (%)	
{Hematopoietio	c system}			
bone marrow	granulation	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 0 0 0 0 0 0 0 0 0	
thymus	atrophy	<10> 0 0 0 0 0 0 0 0 0 0 0	<10> 0 1 1 0 (0) (10) (10) (0)	
{Circulatory	system)			
heart	inflammatory cell nest	0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 (0) (0) (0) (0)	
{Digestive sys	stem}			
liver	herniation	3 0 0 0 (30) (0) (0) (0)	1 0 0 0 (10) (0) (0) (0)	
	granulation	0 0 0 0 0 (0) (0)	2 0 0 0 (20) (0) (0)	
<a>> b (c)	1: Slight 2: Moderate 3 a: Number of animals examined at the s b: Number of animals with lesion c: b / a * 100 ifference; *: P ≤ 0.05 **: P ≤			

(HPT150)

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0- 14W)

ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

SEX

: FEMALE

PAGE: 11

Organ	N	roup Name Control fo. of Animals on Study 10 rade 1 2 3 4 (%) (%) (%) (%)	250 ppm 10 1 2 3 4 (%) (%) (%) (%)	500 ppm 10 1 2 3 4 (%) (%) (%) (%)	1000 ppm 10 10 1 2 3 4 (%) (%) (%)
{Digestive	system)				
liver	perivascular inflammation	3 0 0 0 (30) (0) (0) (0)	3 0 0 0 (30) (0) (0) (0)	4 0 0 0 (40) (0) (0) (0)	1 0 0 0 (10) (0) (0) (0)
{Urinary sy	rstem)				
kidney	mineralization:cortico-medullary juncti	on 2 0 0 0 (20) (0) (0) (0)	6 0 0 0 (60) (0) (0) (0)	3 0 0 0 (30) (0) (0) (0)	2 0 0 0 (20) (0) (0) (0)
	mineralization:papilla	4 0 0 0 0 (40) (40) (60) (60)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
	degeneration:papilla	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0) (0)
{Endocrine	system)				
thyroid	ultimobranchial body remanet	<10> 0 0 0 0 0 0 0 0 0 0 0	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	1 0 0 0 (10) (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 t difference: $*: P \le 0.05$ **: $P \le 0.05$				

(HPT150)

BAIS3

ANIMAL : RAT F344/DuCrj

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 14W)

REPORT TYPE : A1 SEX : FEMALE

Organ	No.	oup Name 2000 ppm of Animals on Study 10 ade 1 2 3 4 (%) (%) (%) (%)	3000 ppm 10 1 2 3 4 (%) (%) (%) (%)	
{Digestive	system}			
liver	perivascular inflammation	5 0 0 0 (50) (0) (0) (0)	1 0 0 0 (10) (0) (0) (0)	
{Urinary sy	stem}			
kidney	mineralization:cortico-medullary junction	\(\lambda 10 \rangle \) \(10 \rangle \) \(2 0 0 0 (20) (0) \qua	<10> 1 0 0 0 (10) (0) (0) (0)	
	mineralization:papilla	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	
	degeneration:papilla	5 0 0 0 * (50) (0) (0) (0)	6 0 0 0 * (60) (0) (0) (0)	
{Endocrine	system)			
thyroid	ultimobranchial body remanet	<10> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<10> 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 ≤ 0.05 **: P ≤ 0			
(HPT150)				BAIS3

(HPT150)

STUDY NO. : 0351 ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1

SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) — ALL ANIMALS (0- 14W)

Organ	Findings	Group Name No. of Animals on Study Grade 1 (%)	Control 10 2 3 4 (%) (%) (%)	250 ppm 10 1 2 3 4 (%) (%) (%) (%)	500 ppm 10 1 2 3 4 (%) (%) (%) (%)	1000 ppm 10 1 2 3 4 (%) (%) (%) (%)
{Special sens	se organs/appendage)					
Harder gl	inflammation	3 (30)	<10> 1 0 0 (10) (0) (0)	<10> 1 2 0 0 (10) (20) (0) (0)	<10> 1 1 1 0 (10) (10) (10) (0)	2 1 1 0 (20) (10) (10) (0)
Grade	1: Slight 2: Moderate a: Number of animals examined at b: Number of animals with lesion	3: Marked 4: Severe the site	9			

BAIS3

(HPT150)

: RAT F344/DuCrj

ANIMAL REPORT TYPE : A1

SEX : FEMALE HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

PAGE: 14

BAIS3

ALL ANIMALS (0- 14W)

Group Name 2000 ppm 3000 ppm No. of Animals on Study 10 10 3 Grade (%) (%) (%) (%) (%) (%) Findings___ Organ____ {Special sense organs/appendage} Harder gl <10> <10> 3 1 0 inflammation 3 5 0 0 (30) (30) (10) (0) (30) (50) (0) (0) 4 : Severe Grade 1 : Slight 2 : Moderate 3 : Marked < a > a : Number of animals examined at the site b: Number of animals with lesion b (c) c:b/a*100 Significant difference; $*: P \le 0.05$ $**: P \le 0.01$ Test of Chi Square

APPENDIX L 3

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY

RAT: FEMALE: SACRIFICED ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0351 ANIMAL : RAT F344/DuCrj

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (14W)

REPORT TYPE : A1

SEX : FEMALE PAGE: 7

Organ	į	Group Name Control No. of Animals on Study 10 Grade 1 2 3 4 (%) (%) (%) (%)	250 ppm 10 1 2 3 4 (%) (%) (%) (%)	500 ppm 10 1 2 3 4 (%) (%) (%) (%)	1000 ppm 10 1 2 3 4 (%) (%) (%) (%)
{Respiratory	system}				
nasal cavit	inflammation:respiratory epithelium	(10) 0 0 0 0 (0) (0) (0) (0)	2 0 0 0 (20) (0) (0) (0)	1 0 0 0 (10) (0) (0) (0)	3 0 0 0 (30) (0) (0) (0)
	duct ectasia:olfactory gland	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0)
	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)
lung	perivascular inflammation	(10) (10) (10) (10) (10) (10)	0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)
	accumulation of foamy cells	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
{Hematopoieti	c system}				
bone marrow	granulation	(10) 0 1 0 0 (0) (10) (0) (0)	1 3 0 0 (10) (30) (0) (0)	0 2 0 0 0 0 (20) (0) (0)	<10> 0 1 0 0 (0) (10) (0) (0)
<a>> b (c)	1: Slight 2: Moderate 3 a: Number of animals examined at the si b: Number of animals with lesion c: b / a * 100 ifference; *: P ≤ 0.05 **: P ≤				

(HPT150)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1

SEX : FEMALE

SACRIFICED ANIMALS (14W)

Organ	1	Froup Name 2000 ppm No. of Animals on Study 10 Frade 1 2 3 4 (%) (%) (%) (%)	3000 ppm 8 1 2 3 4 (%) (%) (%) (%)	
{Respiratory	evetom)			
nasal cavit	inflammation:respiratory epithelium	<10> 0 0 0 0 0 0 0 0 0 0 0	<pre></pre>	
	duct ectasia:olfactory gland	0 0 0 0 0 (0) (0)	3 0 0 0 0 (38) (0) (0) (0)	
	necrosis:olfactory epithelium	1 0 0 0 (10) (0) (0) (0)	6 0 0 0 ** (75) (0) (0) (0)	
lung	perivascular inflammation	<10> 0 0 0 0 0 0 0 0 0 0 0	<pre></pre>	
	accumulation of foamy cells	1 0 0 0 (10) (0) (0) (0)	0 0 0 0 0 (0) (0) (0)	
{Hematopoieti	c system}			-
bone marrow	granulation	<10> 0 0 0 0 0 0 0 0 0 0 0	<pre></pre>	
Grade <a>> b (c) Significant d	1: Slight 2: Moderate 3 a: Number of animals examined at the si b: Number of animals with lesion c: b / a * 100 ifference; *: P ≤ 0.05 **: P ≤			

(HPT150)

ANIMAL : RAT F344/DuCrj

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (14W)

REPORT TYPE : A1

(HPT150)

SEX : FEMALE

PAGE: 9

BAIS3

Organ	Group Name No. of Ani Grade	Control mals on Study 10 1 2 3 4 (%) (%) (%) (%)	250 ppm 10 1 2 3 4 (%) (%) (%) (%)	500 ppm 10 1 2 3 4 (%) (%) (%) (%)	1000 ppm 10 1 2 3 4 (%) (%) (%) (%)
{Circulato	ry system}				
heart	inflammatory cell nest	0 0 0 0 (0) (0) (0) (0)	1 0 0 0 (10) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)
{Digestive	system)				
liver	herniation	1 0 0 0 (10) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	1 0 0 0 (10) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)
	granulation	1 0 0 0 (10) (0) (0) (0)	2 0 0 0 0 (20) (0) (0)	1 0 0 0 (10) (0) (0) (0)	0 0 0 0 0 (0) (0)
	perivascular inflammation	3 0 0 0 0 (30) (0) (0)	3 0 0 0 0 (30) (0) (0)	4 0 0 0 (40) (0) (0)	1 0 0 0 0 (10) (0) (0)
{Urinary s	ystem)				
kidney	mineralization:cortico-medullary junction	2 0 0 0 (20) (0) (0) (0)	6 0 0 0 (60)(0)(0)(0)	3 0 0 0 (30) (0) (0) (0)	2 0 0 0 (20) (0) (0) (0)
Grade <a> b (c) Significan	1: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 at difference; *: P ≤ 0.05 **: P ≤ 0.01 T	4 : Severe			

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (14W)

ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

SEX : FEMALE

Organ	Group N No. of Grade Findings	ame 2000 ppm Animals on Study 10 1 2 3 4 (%) (%) (%) (%)	3000 ppm 8 1 2 3 4 (%) (%) (%) (%)	
{Circulatory	y system)			
heart	inflammatory cell nest	<10> 0 0 0 0 (0) (0) (0) (0)	< 8> 0 0 0 0 (0) (0) (0) (0)	
{Digestive s	system}			
liver	herniation	3 0 0 0 (30) (0) (0) (0)	<pre></pre>	
	granulation	0 0 0 0 0 (0) (0)	2 0 0 0 (25) (0) (0) (0)	
	perivascular inflammation	5 0 0 0 (50) (0) (0) (0)	1 0 0 0 (13) (0) (0) (0)	
{Urinary sys	stem}			
kidney	mineralization:cortico-medullary junction	<10> 2 0 0 0 (20) (0) (0) (0)	<pre></pre>	
Grade <a>> b (c) Significant	1: Slight 2: Moderate 3: Market a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 difference; *: P ≤ 0.05 **: P ≤ 0.01	d 4: Severe Test of Chi Square		
(HPT150)				BAIS3

SEX

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (14W)

ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

: FEMALE

Group Name Control 250 ppm 500 ppm 1000 ppm No. of Animals on Study 10 10 10 10 Grade 3 Organ__ Findings_ (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) {Urinary system} kidney <10> <10> <10> <10> mineralization:papilla 0 0 0 0 (40) (0) (0) (0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) degeneration:papilla 0 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0) (0) (0) (0) (0)(0)(0)(0) {Endocrine system} thyroid <10> <10> <10> <10> ultimobranchial body remanet 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (10) (0) (0) (0) {Special sense organs/appendage} Harder gl <10> <10> <10> <10> inflammation 0 0 2 0 0 (30) (10) (0) (0) (20) (10) (10) (0) (10) (20) (0) (0) (10) (10) (10) (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 b (c) c:b/a*100 Significant difference ; * : $P \le 0.05$ ** : $P \le 0.01$ Test of Chi Square

(HPT150)

BAIS3

(HPT150)

: RAT F344/DuCrj

ANIMAL REPORT TYPE : A1 SEX : FEMALE HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (14W)

3000 ppm Group Name 2000 ppm No. of Animals on Study 10 8 3 Grade (%) (%) (%) (%) Organ____ Findings___ {Urinary system} kidney <10> < 8> mineralization:papilla 0 0 (0)(0)(0)(0) (0)(0)(0)(0) degeneration:papilla 5 0 0 0 * 6 0 0 0 ** (50) (0) (0) (0) (75) (0) (0) (0) {Endocrine system} thyroid <10> < 8> 0 0 ultimobranchial body remanet 0 0 0 0 0 (0) (0) (0) (0) (0)(0)(0)(0) {Special sense organs/appendage} Harder gl <10> < 8> inflammation 1 0 (30) (30) (10) (0) (38) (63) (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 Significant difference ; * : P \leq 0.05 ** : P \leq 0.01 Test of Chi Square

BAIS3

APPENDIX L 4

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY

RAT: FEMALE: DEAD AND MORIBUND ANIMALS

(13-WEEK STUDY)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : RAT F344/DuCri

REPORT TYPE : A1 : FEMALE SEX

DEAD AND MORIBUND ANIMALS (0- 14W)

PAGE: 1 Group Name Control 250 ppm 500 ppm 1000 ppm No. of Animals on Study 0 0 0 0 Grade Findings_ {Hematopoietic system} bone marrow < 0> congestion (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) thymus < 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

: 0351

ANIMAL : RAT F344/DuCrj

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

PAGE: 2

DEAD AND MORIBUND ANIMALS (0- 14W)

REPORT TYPE : A1
SEX : FEMALE

Group Name 2000 ppm 3000 ppm No. of Animals on Study 0 2 Grade Findings_ (%) (%) {Hematopoietic system} bone marrow < 0> < 2> 0 2 0 0 congestion (-) (-) (-) (-) (0) (100) (0) (0) thymus < 0> < 2> 0 1 1 0 atrophy (-) (-) (-) (0) (50) (50) (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 M 1

IDENTITY OF o-PHENYLENEDIAMINE DIHYDROCHLORIDE IN THE 13-WEEK DRINKING WATER STUDY

IDENTITY OF o-PHENYLENEDIAMINE DIHYDROCHLORIDE IN THE 13-WEEK DRINKING WATER STUDY

Test Substance

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

Lot No.

: WTE0491

1. Spectral Data

Mass Spectrometry

Instrument

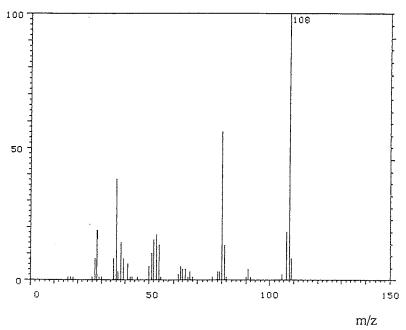
: Hitachi M-80B Mass Spectrometer

Ionization

: EI (Electron Ionization)

Ionization Voltage

: 70eV



Mass Spectrum of Test Substance

Determined Value Fragment Peak (m/z) Calculated Value
Fragment Peak (m/z)

108

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

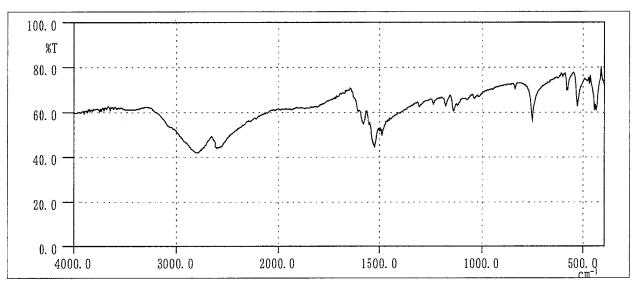
Results: The mass spectrum was consistent with calculated spectrum.

Infrared Spectrometry

Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr

Resolution : 2 cm⁻¹



Infrared Spectrum of Test Substance

Determined Values	Literature Values*
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
$1010 \sim 1050$	1010~1050
1050~1160	$1050 \sim 1160$
1160~1200	1160~1200
1250~1280	$1250\sim 1280$
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.

APPENDIX M 2

STABILITY OF o-PHENYLENEDIAMINE DIHYDROCHLORIDE IN THE 13-WEEK DRINKING WATER STUDY

STABILITY OF o-PHENYLENEDIAMINE DIHYDROCHLORIDE IN THE 13-WEEK DRINKING WATER STUDY

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

Lot No. : WTE0491

1. Sample : This lot was used from 1998.2.23 to 1998.5.27. Test substance was stored

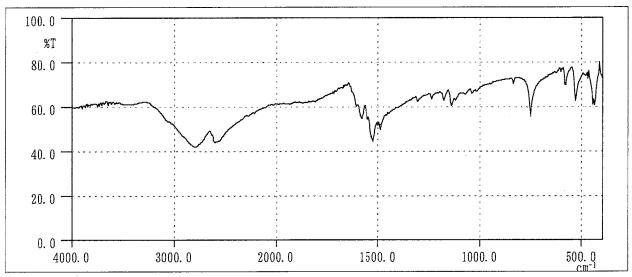
in cold storage in a dark place.

2. Infrared Spectrometry

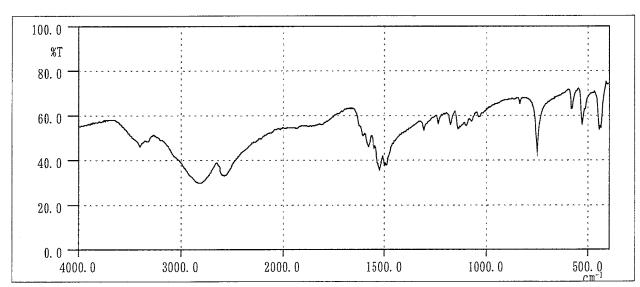
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr

Resolution : 2 cm⁻¹



Infrared Spectrum of Test Substance (date analyzed: 1998.02.18)



Infrared Spectrum of Test Substance (date analyzed: 1998.06.10)

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 µL

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
1998.02.18	1	3.022	100
1998.06.10	1	2.917	100

Results: High performance liquid chromatography indicated one major peak (peak No.1) analyzed on 1998.2.18 and one major peak (peak No.1) analyzed on 1998.6.10. No new trace impurity peak in the test substance analyzed on 1998.6.10 was detected.

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

APPENDIX M 3

CONCENTRATION OF o-PHENYLENEDIAMINE DIHYDROCHLORIDE IN FORMULATED WATER IN THE 13-WEEK DRINKING WATER STUDY

CONCENTRATION OF o-PHENYLENEDIAMINE DIHYDROCHLORIDE IN FORMULATED WATER IN THE 13-WEEK DRINKING WATER STUDY

Target Concentration					
Date Analyzed	250ª	500	1000	2000	3000
1998.02.23	248 (99.2) ^b	488 (97.6)	1010 (101)	2030 (102)	2990 (99.7)

^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 μL

APPENDIX M 4

STABILITY OF o-PHENYLENEDIAMINE DIHYDROCHLORIDE IN FORMULATED WATER IN THE 13-WEEK DRINKING WATER STUDY

STABILITY OF o-PHENYLENEDIAMINE DIHYDROCHLORIDE IN FORMULATED WATER IN THE 13-WEEK DRINKING WATER STUDY

		Target Concer	ntration
Date Prepared	Date Analyzed	250ª	3000
1998.02.09	1998.02.09	251 (100) ^b	2970 (100)
	1998.02.13°	238 (94.8)	2880 (97.0

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 \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 μL

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

^c Animal room samples

APPENDIX N 1

METHODS FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK DRINKING WATER STUDY OF o-PHENYLENEDIAMINE DIHYDROCHLORIDE

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS IN THE 13-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)
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 17
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) (1)
T-bilirubin	Alkaline azobilirubin method 4)
Glucose	Enzymatic method (GLK·G-6-PDH)
T-cholesterol	Enzymatic method (CE·COD·POD) 4)
Triglyceride	Enzymatic method (LPL·GK·GPO·POD) 4)
Phospholipid	Enzymatic method (PLD·COD·POD) 4)
Glutamic oxaloacetic transaminase (GOT)	IFCC method 49
Glutamic pyruvic transaminase (GPT)	IFCC method 4)
Lactate dehydrogenase (LDH)	Wroblewski-LaDue method 4)
Alkaline phosphatase (ALP)	p-Nitrophenylphosphate 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
Potassium	Ion selective electrode method
Chloride	Ion selective electrode method 4)
Calcium	OCPC method 4)
Inorganic phosphorus	Enzymatic method (PNP·XOD·POD) 4)
Urinalysis	
pH,Protein,Glucose,Ketone body,Bilirubin,Occult Blood,	Urinalysis reagent paper method 5)
Urobilinogen	

- 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) Ames reagent strips for urinalysis (Multistix: Bayer-Sankyo Co.,Ltd.)

APPENDIX O 1

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK DRINKING WATER STUDY OF o-PHENYLENEDIAMINE DIHYDROCHLORIDE

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-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	$\times 10^3/\mu \mathrm{L}$	0
Reticulocyte	‰	0
Prothrombin time	sec	1
Activated partial thromboplastin time (APTT)	sec	1
White blood cell (WBC)	$\times 10^3/\mu L$	2
Differential WBC	%	0
Biochemistry		
Total protein	g/dL	1
Albumin	g/dL	1
A/G ratio	_	1
T-bilirubin	mg/dL	2
Glucose	mg/dL	0
T-cholesterol	mg/dL	0
Triglyceride	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
Alkaline phosphatase (ALP)	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