ビフェニルのラット及びマウスを用いた経口投与によるがん原性予備試験(混餌試験)報告書

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 $(B1-1\sim C2)$

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APPENDIX B 1-1

CLINICAL OBSERVATION (THIRTEEN—WEEK STUDY: SUMMARY)

MOUSE: FEMALE

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

STUDY NO.: 0186
ANIMAL: MOUSE BDF1
REPORT TYPE: A1 13

SEX : FEMALE

linical sign	Group Name		stration We								···				
		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	
		1	1	1	1	. 1	1	1	1	1	1	1	1	1	
EATH	Control	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	
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	8000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	16000 ppm	0	0	1	1	1	1	1	1	1	1	1	1	1	
UNCHBACK POSITION	Control	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	
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	4000 ppm	0	0	0	0	0	0	0	1	0	0	0	0	0	
	8000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	10000 ppm	0	0	1	0	0	0	0	0	0	0	0	0	0	
	16000 ppm	Ö	Ŏ	0	0	Ŏ	0	0	0	0 .	0	0	0	0	
PILOERECTION	Control	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	
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	4000 ppm	0	0	0	0	0	0	0	1	0	0	0	0	0	
	8000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	10000 ppm	0	0	1	0	0	0	0	0	0	0	0	0	0	
	16000 ppm	0	0	ō	0	0	0	0	0	0	0	0	0	0	
RREGULAR BREATHING	Control	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	
	2000 ppm	0	0	0	0	0	0	0	. 0	0	0	0	0	0	
	4000 ppm	0	0	0	0	0	0	0	1	0	0	0	0	0	
	8000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	16000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
ABNORMAL RESPIRATION	Control	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	
	2000 ppm	0	0 .	0	0	0	0	0	0	0	0	0	0	0	
	4000 ppm	0	0	0	0	0	0	0	1	0	0	0	0	0	
	mqq 0008	0	0	0	0	0	0	0	0	0	0	0	0	0	
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	16000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	

(HAN190)

BAIS 2

STUDY NO. : 0186 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

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	
		1	1	1	1	1	1	1	1	1	1	1	1	1	
OLIGO-STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	
	mqq 003	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	
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	8000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	10000 ppm	0	0	1	0	0	0	0	0	0	0	0	0	0	
	16000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
(HAN190)	······														BAIS

APPENDIX B 2-1

BODY WEIGHT CHANGES (THIRTEEN—WEEK STUDY:SUMMARY)

RAT: MALE

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STUDY NO. : 0185 ANIMAL : RAT F344

UNIT : g

REPORT TYPE : A1 13

SEX : MALE

BODY WEIGHT CHANGES ALL ANIMALS

(SUMMARY)

Group Name Administration week-day_ 4-7 5-7 6-7 3-7 1-7 2-7 0-0 246± 18 264± 19 125± 5 153± 8 182± 11 208± 14 227 ± 16 Control 227 ± 13 247 ± 14 265± 15 6 $181 \pm$ 9 207± 12 $125 \pm$ 4 152± 1000 ppm 243± 12 259± 14 224土 10 $125\pm$ 151± 7 180± 10 206± 10 2000 ppm 4 218± 16 234± 18 249± 19 175± 11 198± 13 4000 ppm $125\pm$ 5 148± 7 243士 7** $229 \pm$ $125\pm$ 5 142士 4** 169士 6** 191± 7** $210 \pm$ 8* 6* 8000 ppm 147土 164士 10** 181± 13** 195± 14** 211± 14** 16000 ppm $125\pm$ 4 127士 4** 6** Significant difference : $*: P \le 0.05$ Test of Dunnett

** : $P \leq 0.01$

(HAN260)

BAIS 2

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STUDY NO. : 0185 ANIMAL : RAT F344 UNIT : g

BODY WEIGHT CHANGES ALL ANIMALS

(SUMMARY)

REPORT TYPE : A1 13

SEX : MALE

up Name	Admin	istration	week-day												
	7–7		8-7		9-7	-	10-7		11-7		12-7		13-7		
Control	275±	22	287±	22	301±	25	313±	24	321±	24	328±	25	335±	26	
1000 ppm	277±	17	289±	17	300±	17	313±	17	322±	17	331±	18	340±	20	
2000 ppm	269±	17	282±	18	294±	19	303±	19	313±	20	319±	21	326±	22	
4000 ppm	256±	19	270±	20	279±	20*	288±	21*	294±	20**	302±	20*	308±	20*	
8000 ppm	247±	17**	262±	9**	274±	9**	285±	9**	291±	10**	298±	10**	304±	12**	
16000 ppm	221±	14**	231±	14**	242±	12**	252±	13**	257±	13**	264±	14**	270±	13**	
Significant differenc	ce; *:P≦	0.05	**: P ≤ 0.	01			Test of D	unnett							
260)															Е

APPENDIX B 2-2

BODY WEIGHT CHANGES (THIRTEEN—WEEK STUDY: SUMMARY)

RAT: FEMALE

STUDY NO. : 0185 ANIMAL : RAT F344

UNIT : g
REPORT TYPE : A1 13

SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS

Name	Adminis	tration	week-day											
·	0-0		1-7		2-7		3-7		4-7		5–7		6-7	
Control	103±	4	118±	4	130±	4	141±	5	148±	6	157±	6	166±	7
1000 ppm	103±	4	117±	4	129±	5	138±	6	143±	6	151±	7	160±	8
2000 ppm	103±	4	117±	4	129±	4	137±	6	144±	6	152±	7	160±	7
4000 ppm	103±	4	113±	3**	125±	4*	132±	5**	140±	6*	148±	6*	156±	7**
8000 ppm	104±	4	110±	3**	122±	3**	130±	5**	137±	6**	144±	7**	151±	6**
16000 ppm	103±	4	103±	2**	115±	4**	123±	5**	130±	6**	137±	7**	143±	7**
Cignificant differen		05	** • D < ^ 1				Toot of N	ionott						
Significant difference 260)	e; *: P ≤ 0.	.05	**: P ≤ 0.0)1			Test of Du	nnett						

STUDY NO. : 0185 ANIMAL : RAT F344

UNIT : g
REPORT TYPE : A1 13

SEX : FEMALE

BODY WEIGHT CHANGES ALL ANIMALS

(SUMMARY)

ıp Name	Admini	stration	week-day											
	7-7		8-7		9–7		10-7		11-7		12-7		13-7	
Control	169士	7	174±	9	180±	9	184±	10	188±	8	189±	9	192±	8
1000 ppm	162±	9	168±	7	174±	8	179±	8	183±	8	185±	9	187±	8
2000 ppm	162±	8	168±	7	173±	7	177±	7	182±	9	180±	12	189±	9
4000 ppm	157±	7**	162±	7**	167±	7**	172±	8**	175±	8**	172±	11**	179±	7**
8000 ppm	152±	6**	157±	7**	160±	7**	164±	7**	165±	7**	169±	8**	172±	8**
16000 ppm	147±	8**	150±	8**	154±	8**	158±	8**	160±	7**	163±	7**	166土	7**
Significant differenc	pe: *:P≤(). 05	**:P≦0.0)]			Test of D	unnett						
1260)	.e, *•r≥(.00	** · r ≥ v.v	, i			Test of M	##1 6 [[

APPENDIX B 2-3

BODY WEIGHT CHANGES (THIRTEEN—WEEK STUDY:SUMMARY)

MOSUE: MALE

STUDY NO. : 0186

ANIMAL : MOUSE BDF1

UNIT : g
REPORT TYPE : A1 13

SEX : MALE

BODY WEIGHT CHANGES ALL ANIMALS

(SUMMARY)

oup Name	Administration	n week-day					
	0-0	1-7	2-7	3–7	4-7	5-7	6-7
Control	23.3± 0.7	23.9± 0.7	25.0± 1.2	25.9± 1.5	26.8± 1.2	27.6± 1.2	28.2± 1.0
500 ppm	23.3± 0.7	24.1± 0.6	25.6± 0.5	26.1± 0.5	27.2± 0.7	28.0± 0.9	28.4± 0.9
2000 ppm	23.3± 0.7	23.6± 0.9	25.2± 0.9	25.9± 1.0	26.7± 1.2	27.6± 1.4	28.0± 1.6
4000 ppm	23.3± 0.7	22.9± 0.8*	24.6± 0.8	25.2± 0.9	25.9± 0.8	26.6± 0.8	27.2± 0.9
8000 ppm	23.4± 0.7	22.8± 0.7*	21.7± 2.2**	22.7± 2.1**	23.8± 2.8*	24.4± 3.4*	24.8± 3.1**
10000 ppm	23.3± 0.7	23.2± 0.8	21.9± 2.0**	22.7± 1.1**	24.1± 1.2**	25.5± 1.0*	24.9± 1.7**
16000 ppm	23.3± 0.7	22.5± 1.7*	22.1± 0.5**	20.0± 0.7**	21.8± 1.0**	22.7± 1.0**	23.0± 0.8**
Significant differe	nce; *: P ≦ 0.05	** : P ≤ 0.01		Test of Dunnett			
N260)							

BAIS 2

STUDY NO. : 0186

ANIMAL : MOUSE BDF1

UNIT : g

REPORT TYPE: A1 13

SEX : MALE

(HAN260)

BODY WEIGHT CHANGES ALL ANIMALS

(SUMMARY)

PAGE: 2 Group Name Administration week-day_ 7-7 8-7 9-7 10-7 11-7 12 - 713-7 Control 28.2± 1.2 26.2± 1.6 29.0± 1.1 26.7± 1.2 30.2 ± 1.2 31.1± 1.6 32.5 ± 2.2 500 ppm 28.7 ± 1.2 25.4 ± 1.4 29.7± 1.1 26.6± 1.1 30.0± 1.1 30.9 ± 1.3 31.5 ± 1.6 2000 ppm 28.1± 1.7 25.5± 1.6 29.2± 1.8 25.8± 1.6 30.0 ± 2.0 30.8 ± 2.2 31.4 ± 2.3 4000 ppm 27.0± 0.6 24.0± 0.7* 27.8± 0.7 25.1± 1.3* 28.1± 0.8** 29.0± 0.7* 29.5± 0.7 8000 ppm 24.6± 3.0** 25.4 2.1 ** 24.0± 1.4** 25.7± 1.6** 27.1± 2.2** 26.6± 2.2** 10000 ppm 24.1± 1.3** 22.1± 1.8** 25.7± 1.5** 23.5± 1.0** 27.6± 1.4** 27.0± 1.8** 27.6± 1.4** 16000 ppm 22.7± 1.2** 20.5± 1.5** 22.8± 1.5** 21.1 ± 1.3** 23.8 ± 1.2** 24.1± 1.4** 24.4± 1.4** Significant difference; $*: P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett

BAIS 2

APPENDIX B 2-4

BODY WEIGHT CHANGES (THIRTEEN—WEEK STUDY: SUMMARY)

MOSUE: FEMALE

STUDY NO. : 0186

ANIMAL : MOUSE BDF1

UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES ALL ANIMALS (SUMMARY)

	Administration 0–0						
		1-7	2-7	3-7	4-7	5-7	6-7
Control	18.8± 0.6	18.9± 0.8	19.7± 0.8	20.0± 0.9	20.7± 1.0	20.9± 1.0	21.9± 1.2
500 mag 003	18.8± 0.6	19.0± 0.6	19.9± 0.8	20.1± 1.0	21.1± 0.9	21.3± 0.6	21.9± 1.1
2000 ppm	18.8± 0.6	18.7± 0.7	19.8± 0.8	19.6± 0.5	20.6± 0.7	20.9± 0.8	21.7± 0.8
4000 ppm	18.8± 0.6	18.5± 0.7	19.6± 0.7	19.6± 0.7	20.4± 0.7	20.5± 0.8	21.6± 0.6
mqq 0008	18.8± 0.5	18.7± 0.5	18.7± 0.8	19.6± 0.6	20.1± 0.6	20.4± 0.4	21.0± 0.5
10000 ppm	18.8± 0.5	18.3± 0.9	16.8± 1.0**	17.5± 2.5**	19.2± 0.8**	19.9± 1.3	18.8± 0.9**
16000 ppm	18.8± 0.5	18.1± 0.6	17.4± 1.3**	15.6± 1.1**	17.2± 1.0**	18.6± 1.0**	18.6± 1.0**
Significant difference	; *: P ≤ 0.05	**: P ≤ 0.01		Test of Dunnett			

BAIS 2

STUDY NO. : 0186

ANIMAL : MOUSE BDF1

UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES

ALL ANIMALS

PAGE: 4

oup Name	Administration	week-day					
	7-7	8-7	9-7	10-7	11-7	12-7	13-7
Control	22.0± 1.1	20.2± 0.8	22.9± 0.9	20.4± 1.2	23.5± 1.1	23.6± 1.1	23.9± 1.2
500 ppm	22.3± 0.9	18.0± 1.2**	23.7± 1.0	20.0± 1.0	23.5± 0.8	23.6± 1.0	24.2± 1.3
2000 ppm	22.4± 0.9	18.3± 1.2*	23.5± 0.8	20.6± 1.6	23.5± 1.0	23.4± 1.3	24.3± 1.1
4000 ppm	22.2± 0.6	18.8± 2.2	23.0± 0.8	19.7± 1.2	22.9± 0.6	22.9± 1.0	23.3± 0.9
mag 0008	21.0± 0.8	18.2± 1.5*	22.1± 0.6	19.9± 0.9	22.1± 0.5**	22.3± 0.7*	22.4± 0.6**
10000 ppm	19.8± 1.1**	18.3± 1.6*	21.1± 1.2**	19.4± 1.1	21.5± 1.4**	21.1± 1.2**	21.9± 1.1**
16000 ppm	18.7± 0.9**	17.5± 1.0**	19.0± 1.3**	18.4± 0.9**	20.1± 0.8**	20.3± 0.8**	20.5± 0.8**
Significant difference	; *: P ≤ 0.05	**: P ≤ 0.01		Test of Dunnett			

(SUMMARY)

(HAN260)

BAIS 2

APPENDIX B 3-1

FOOD CONSUMPTION CHANGES (THIRTEEN—WEEK STUDY: SUMMARY)

RAT: MALE

STUDY NO. : 0185 ANIMAL : RAT F344 UNIT : g
REPORT TYPE : AI 13 FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

SEX : MALE

PAGE: 1

1-7(7) 13.4± 0.8 13.1± 0.6 12.8± 0.6	week-day(effecti∪e)	3-7(7) 15.5± 1.4 15.3± 1.2	4-7(7) 15.4± 1.4 15.3± 1.2	5-7(7) 15.8± 1.3	6-7(7) 15.4± 1.3	7-7(7)
13.1± 0.6						
	14.4± 0.9	15.3± 1.2	15.3± 1.2	15.8+ 1.0	15 64 0 0	
12.8+ 0.6				10.02 1.0	15.6± 0.8	15.5± 0.9
	14.1± 1.0	15.2± 1.1	15.1± 1.0	15.6± 1.1	15.2± 1.3	15.1± 2.1
12.2± 0.8	13.9± 1.2	14.4± 1.4	14.3± 1.3	14.7± 1.6	14.3± 1.5	14.4± 1.5
11.1± 1.6**	13.6± 0.6	14.3± 0.6	14.4± 0.9	14.6± 0.6	14.2± 0.6	14.3± 0.9
8.6± 0.7**	12.3± 0.7**	12.6± 1.0**	12.7± 1.2**	12.7士 1.5**	12.8± 1.1**	12.9士 1.2**
• D < 0.05	ν+ • D < 0.01		Took of Divinity			
1	11.1± 1.6** 8.6± 0.7**	11.1± 1.6** 13.6± 0.6 8.6± 0.7** 12.3± 0.7**	11.1± 1.6** 13.6± 0.6 14.3± 0.6 8.6± 0.7** 12.3± 0.7** 12.6± 1.0**	11.1± 1.6** 13.6± 0.6 14.3± 0.6 14.4± 0.9 8.6± 0.7** 12.3± 0.7** 12.6± 1.0** 12.7± 1.2**	11.1± 1.6** 13.6± 0.6 14.3± 0.6 14.4± 0.9 14.6± 0.6 8.6± 0.7** 12.3± 0.7** 12.6± 1.0** 12.7± 1.2** 12.7± 1.5**	11.1± 1.6** 13.6± 0.6 14.3± 0.6 14.4± 0.9 14.6± 0.6 14.2± 0.6 8.6± 0.7** 12.3± 0.7** 12.6± 1.0** 12.7± 1.2** 12.7± 1.5** 12.8± 1.1**

STUDY NO.: 0185 ANIMAL: RAT F344

UNIT : g
REPORT TYPE : A1 13

SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

PAGE: 2

oup Name	Administration 8–7(7)	week-day(effective) 9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)	
Control	15.6± 1.3	16.1± 1.7	15.9± 1.2	15.6± 1.1	15.1± 1.1	15.4± 1.0	
1000 ppm	16.2± 1.1	15.9± 1.3	16.4± 1.2	15.7± 0.8	15.5± 0.9	15.7± 1.1	
2000 ppm	15.9± 1.3	15.6± 1.1	14.5± 2.4	15.7± 1.6	15.2± 1.3	15.1± 1.4	
4000 ppm	15.2± 1.5	15.0± 1.3	15.1± 1.3	14.6± 1.6	14.9± 1.5	14.7± 1.4	
8000 ppm	14.9± 0.7	15.2± 0.6	15.5± 0.4	14.9± 0.7	15.1± 0.6	15.0± 0.7	
16000 ppm	13.5± 1.0**	14.0± 0.9**	14.5± 1.0	13.8± 0.7**	14.1± 1.2	14.0± 1.0*	
Significant difference;	*: P ≤ 0.05	**: P ≤ 0.01		Test of Dunnett			

(HAN260)

BAIS 2

APPENDIX B 3-2

FOOD CONSUMPTION CHANGES (THIRTEEN—WEEK STUDY: SUMMARY)

RAT: FEMALE

STUDY NO.: 0185 ANIMAL: RAT F344

UNIT : g
REPORT TYPE : A1 13

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

SEX : FEMALE

PAGE: 3

oup Name	Administrati	on week-day(effective)					•
	1-7(7)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	11.2± 0.6	11.3± 0.6	11.7± 0.6	11.1± 0.7	11.8± 0.9	10.9± 0.7	11.2± 0.8
1000 ppm	10.7± 0.6	11.1± 0.8	11.5± 0.8	10.4± 0.7	10.7± 0.7*	10.7± 0.8	10.6± 0.8
2000 ppm	12.7± 2.3	11.1± 0.5	11.1± 0.9	10.7± 0.7	11.3± 1.2	11.6± 2.9	11.4± 2.4
4000 ppm	9.9± 0.5	10.4± 0.4**	10.2± 0.5**	10.3± 0.5*	10.7± 0.5*	10.3± 1.0	10.2± 0.7
8000 ppm	9.7± 1.7*	10.1± 0.4**	10.0± 0.6**	10.0± 0.6**	10.0生 0.5**	9.9± 0.4*	9.7± 0.4**
16000 ppm	8.4± 2.5**	9.8± 0.5**	9.6生 0.4**	9.5± 0.6**	9.3± 0.7**	9.6± 1.2**	9.5± 1.0**
Significant difference	; *:P≦0.05	**: P ≤ 0.01		Test of Dunnett			

(HAN260)

BAIS 2

STUDY NO. : 0185

ANIMAL : RAT F344

UNIT ; g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

PAGE: 4

roup Name	Administration 8-7(7)	week-day(effective) 9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)	
Control	11.4± 0.6	11.5± 0.7	11.7± 1.0	11.8± 1.3	11.1± 0.8	11.5± 0.9	
1000 ppm	11.2± 0.5	11.4± 0.6	11.3± 0.5	11.3± 0.6	10.8± 0.8	11.1± 0.8	
2000 ppm	11.3± 1.1	12.7± 3.1	11.4± 1.0	12.7± 2.8	11.5± 1.6	12.6± 3.8	
4000 ppm	10.9± 0.8	11.0± 0.8	11.3± 1.3	10.6± 0.8	11.0± 1.0	11.0± 1.2	
8000 ppm	10.2± 0.5*	10.6± 2.0	10.2± 0.6*	9.5± 0.5**	10.2± 0.6	10.0± 0.4**	
16000 ppm	10.1± 2.7**	10.1± 2.4**	10.6± 4.5	10.5± 3.7**	11.5± 6.2	10.3± 2.9**	
Significant differenc	ce; *: P ≦ 0.05	**: P ≤ 0.01		Test of Dunnett			

(HAN260)

BAIS 2

APPENDIX B 3-3

FOOD CONSUMPTION CHANGES (THIRTEEN—WEEK STUDY: SUMMARY)

MOSUE: MALE

STUDY NO. : 0186 Δ

ANIMAL : MOUSE BDF1

UNIT : g

10000 ppm

4.9± 0.4**

5.7± 0.4*

REPORT TYPE : A1 13

SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)

ALL ANIMALS

Administration week-day(effective) Group Name 3-7(7) 4-7(7) 5-7(7) 6-7(7) 7-7(7) 1-7(7)2-7(7)

PAGE: 1

Control 6.0 ± 0.5 5.0 ± 0.6 5.1± 0.6 5.1 ± 0.5 5.5 ± 0.8 5.1± 0.4 4.6 ± 0.3 500 ppm 5.1± 0.4** 5.0 ± 0.3 5.0 ± 0.4 5.1± 0.4 6.0 ± 0.5 4.9 ± 0.3 5.1 ± 0.3 2000 ppm 5.0± 0.4** 5.0± 0.3 5.7 ± 0.4 5.2 ± 0.3 5.2 ± 0.4 5.0 ± 0.2 4.8 ± 0.2

4.9± 0.5 4000 ppm 5.2± 0.4* 5.0 ± 0.4 5.0 ± 0.4 4.8 ± 0.3 5.8 ± 0.4 5.3 ± 0.4

mag 0008 5.0± 0.5** 5.0± 1.1 5.3 ± 0.6 5.4± 0.7 5.0 ± 0.8 6.5± 1.7 5.6± 0.9

5.7± 0.7

16000 ppm 5.1± 0.9** 5.5± 0.9* 5.4± 0.7 5.5 ± 0.8 5.5 ± 0.7 6.2± 1.1 5.7 ± 0.7

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

 5.0 ± 0.5

6.3± 0.9

 5.6 ± 0.7

4.6± 0.5

(HAN260) BAIS 2 STUDY NO. : 0186

ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

PAGE: 2

Group Name	Administrati	on week-day(effective)					
	8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)	
Control	4.3± 0.4	5.0± 0.3	4.1± 0.4	5.5± 0.5	5.4± 0.4	5.5± 0.3	
500 ppm	4.0± 0.5	5.9± 0.4**	4.0± 0.2	5.4± 0.3	5.4± 0.3	5.0± 0.3	
2000 ppm	4.5± 0.4	5.5± 0.3	4.0± 0.3	5.8± 0.4	5.6± 0.5	5.2± 0.5	
4000 ppm	4.0± 0.4	5.5± 0.5	4.2± 0.3	5.6± 0.8	5.8± 0.5	5.2± 0.4	
8000 ppm	4.1± 0.4	6.2± 0.9**	4.7± 0.6	5.5± 0.7	5.7± 0.6	5.4± 0.4	
10000 ppm	4.5± 0.7	6.1± 0.7**	4.3± 0.3	5.8± 0.3	5.6± 0.9	5.2± 0.5	
16000 ppm	4.6± 0.5	5.7± 0.7*	4.7± 0.3**	5.9± 0.7	5.7± 0.9	5.5± 1.0	
Significant difference;	*: P ≤ 0.05	** : P ≤ 0.01		Test of Dunnett			

(HAN260)

BAIS 2

APPENDIX B 3-4

FOOD CONSUMPTION CHANGES (THIRTEEN-WEEK STUDY: SUMMARY)

MOSUE: FEMALE

STUDY NO. : 0186

ANIMAL : MOUSE BDF1

UNIT : g

REPORT TYPE : A1 13

SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)

ALL ANIMALS

Control 5.1± 0.3 4.1 ± 0.3 5.0± 0.6 5.4 ± 0.7 5.3 ± 0.8 5.9 ± 0.8 5.1± 0.9 500 ppm 5.1 ± 0.5 4.3± 0.4 4.7± 0.3 5.2 ± 0.4 5.9 ± 0.8 5.6± 0.4 5.8± 0.8 2000 ppm 4.5 ± 0.4 4.0± 0.2 4.5± 0.4 5.9± 0.4* 4.9± 0.4 5.6 ± 0.6 5.6 ± 0.4 4000 ppm 4.9± 0.7 4.1± 0.4 4.7± 0.4 4.8± 0.4 5.7± 0.7 5.6 ± 0.5 5.9± 0.5* 8000 ppm 4.9± 0.6 4.6± 0.4 5.1± 0.6 5.0 ± 0.5 6.1± 0.7 5.7 ± 0.5 5.2± 0.5 10000 ppm 4.7± 0.5 5.4± 0.7** 6.0± 0.8 $5.3\pm\ 1.2$ 6.4± 0.9* 6.0 ± 0.9 5.2± 0.5 16000 ppm 5.5 ± 0.8 6.2± 0.5** 6.5± 1.1* 6.0 ± 0.8 7.9± 1.0** 6.6 ± 0.7 5.7 ± 1.0

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

(HAN260)

BAIS 2

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STUDY NO. : 0186

ANIMAL : MOUSE BDF1

UNIT : g
REPORT TYPE : A1 13

SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

roup Name	Administrati	on week-day(effective)					
	8-7(7)	9–7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)	
Control	4.4± 0.4	5.3± 0.5	4.4± 0.5	6.2± 0.7	5.7± 0.6	5.9± 1.0	
500 ppm	3.9± 0.3	6.6± 0.5**	4.3± 0.6	6.4± 0.6	5.8± 0.7	5.7± 0.3	
2000 ppm	4.3± 0.4	6.4± 0.7**	4.2± 0.4	6.2± 0.7	5.7± 0.7	5.3± 0.6	
4000 ppm	4.0± 0.5	6.1± 0.6	4.0± 0.3	5.8± 0.8	5.7± 0.5	5.3± 0.5	
8000 ppm	4.1± 0.4	6.3± 0.8*	4.3± 0.4	6.1± 0.8	5.9± 0.8	5.4± 0.5	
10000 ppm	4.4± 1.0	6.2± 0.9*	4.0± 0.6	6.0± 1.0	6.1± 0.8	5.2± 0.8	
16000 ppm	4.7± 0.6	5.7± 0.6	4.7± 0.5	6.5± 1.1	6.9± 1.0**	6.4± 1.1	
Significant difference;	*: P ≤ 0.05	** : P ≤ 0.01		Test of Dunnett			

(HAN260)

BAIS 2

APPENDIX B 4-1

CHEMICAL INTAKE CHANGES (THIRTEEN—WEEK STUDY: SUMMARY)

RAT: MALE

STUDY NO. : 0185

ANIMAL : RAT F344

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

SEX : MALE

CHEMICAL INTAKE CHENGES (SUMMARY)

ALL ANIMALS

PAGE: 1

6	7	
	7	
0.000± 0	0.000 ±	0.000
0.059± 0	0.001 0.056±	0.002
0.117± 0	0.006 0.113±	0.013
0.230± 0	0.224±	0.010
0.469± 0	0.464±	0.029
0.972± 0	0.032 0.935±	0.049
	0.230± (0.230± 0.010 0.224± 0.469± 0.015 0.464±

(HAN300) BAIS 2

STUDY NO. : 0185 ANIMAL : RAT F344
UNIT : g /kg / d a y
REPORT TYPE : A1 13
SEX : MALE

ALL ANIMALS

CHEMICAL INTAKE CHENGES (SUMMARY)

PAGE: 2

roup 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
1000 ppm	0.056± 0.002	0.053± 0.002	0.052± 0.002	0.049± 0.001	0.047± 0.001	0.046± 0.002
2000 ppm	0.113± 0.005	0.106± 0.004	0.096± 0.015	0.100± 0.006	0.095± 0.008	0.093± 0.004
4000 ppm	0.226± 0.010	0.215± 0.009	0.210± 0.009	0.198± 0.013	0.197± 0.011	0.190± 0.011
8000 ppm	0.454± 0.013	0.444± 0.011	0.434± 0.007	0.410± 0.013	0.404± 0.013	0.394± 0.013
16000 ppm	0.934± 0.027	0.927± 0.036	0.922± 0.044	0.860± 0.028	0.855± 0.050	0.830± 0.038

(HAN300)

BAIS 2

APPENDIX B 4-2

CHEMICAL INTAKE CHANGES (THIRTEEN—WEEK STUDY: SUMMARY)

RAT: FEMALE

STUDY NO. : 0185 ANIMAL : RAT F344 CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

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

SEX : FEMALE

PAGE: 3

Administration 1 .000 ± 0.000 ± 0.004	0.000± 0.000 0.086± 0.004	0.000± 0.000 0.083± 0.004	0.000± 0.000 0.072± 0.003	5 0.000± 0.000 0.071± 0.003	0.000± 0.000 0.067± 0.003	7 0.000± 0.000 0.065± 0.002
.092± 0.004	0.086± 0.004					
		0.083± 0.004	0.072± 0.003	0.071± 0.003	0.067± 0.003	0.065± 0.002
.217± 0.036	0.172± 0.005	0.162± 0.009	0.149± 0.007	0.149± 0.013	0.145± 0.037	0.141± 0.031
.349± 0.021	0.334± 0.010	0.309± 0.015	0.293± 0.015	0.290± 0.015	0.264± 0.026	0.261± 0.013
0.706± 0.128	0.664± 0.020	0.617± 0.037	0.584± 0.025	0.555± 0.016	0.524± 0.016	0.508± 0.021
.304± 0.380	1.360± 0.042	1.248土 0.044	1.174± 0.042	1.081± 0.074	1.065± 0.124	1.034± 0.074
٠.	706± 0.128	706± 0.128 0.664± 0.020	706± 0.128 0.664± 0.020 0.617± 0.037	706± 0.128 0.664± 0.020 0.617± 0.037 0.584± 0.025	706± 0.128	706± 0.128

(HAN300)

CHEMICAL INTAKE CHENGES (SUMMARY) ALL ANIMALS

ANIMAL : RAT F344 UNIT : g/kg/day
REPORT TYPE : A1 13

STUDY NO. : 0185

SEX : FEMALE

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	
1000 ppm	0.067± 0.002	0.066± 0.003	0.063± 0.003	0.062± 0.004	0.059± 0.004	0.059± 0.004	
2000 ppm	0.134± 0.008	0.147± 0.036	0.129± 0.008	0.139± 0.031	0.127± 0.015	0.134± 0.041	
4000 ppm	0.269± 0.018	0.263± 0.018	0.263± 0.025	0.243± 0.015	0.257± 0.025	0.244± 0.025	
8000 ppm	0.518± 0.017	0.531± 0.098	0.500± 0.016	0.460± 0.013	0.484± 0.022	0.467± 0.017	
16000 ppm	1.062± 0.229	1.047± 0.187	1.074± 0.446	1.043± 0.327	1.120± 0.551	0.990± 0.242	

PAGE: 4

BAIS 2 (HAN300)

APPENDIX B 4-3

CHEMICAL INTAKE CHANGES (THIRTEEN—WEEK STUDY: SUMMARY)

MOSUE: MALE

CHEMICAL INTAKE CHENGES (SUMMARY) ALL ANIMALS

ANIMAL : MOUSE BDF1 UNIT : g/kg/day REPORT TYPE : Al 13

SEX : NALE

PAGE: 1

Administration 1 0.000± 0.000	(weeks)2 0.000± 0.000	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
0.106± 0.008	0.098± 0.006	0.097± 0.007	0.094± 0.005	0.108± 0.011	0.087± 0.006	0.089± 0.003
0.424± 0.029	0.398± 0.017	0.389± 0.028	0.363± 0.020	0.416± 0.032	0.373± 0.028	0.370± 0.040
0.914± 0.079	0.808± 0.061	0.791± 0.054	0.733± 0.039	0.874± 0.037	0.778± 0.050	0.727± 0.065
0.877± 0.085	1.963± 0.217	1.935± 0.332	1.716± 0.425	2.275± 1.234	1.879± 0.709	1.703± 0.764
0.852± 0.064	2.616± 0.331	2.522± 0.378	2.058± 0.227	2.473± 0.409	2.264± 0.365	1.905± 0.256
0.905± 0.129	1.953± 0.288	4.390± 0.680	4.049± 0.409	4.381± 0.885	3.961± 0.591	3.924± 0.714
	0.424± 0.029 0.914± 0.079 0.877± 0.085 0.852± 0.064	0.424 ± 0.029	0.424 ± 0.029	0.424 ± 0.029	0.424 ± 0.029	0.424 ± 0.029

(IIAN300)

ANIMAL : MOUSE BDF1
UNIT : g/kg/day
REPORT TYPE : A1 13

SEX : MALE

CHEMICAL INTAKE CHENGES (SUMMARY)

ALL ANIMALS

PAGE: 2

oup Name	 Admini	stration	(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
500 ppm	0.079±	0.009	0.099±	0.007	0.074±	0.004	0.090±	0.005	0.087±	0.004	0.080±	0.005
2000 ppm	0.351±	0.033	0.374±	0.019	0.307±	0.019	0.388±	0.030	0.362±	0.032	0.331±	0.026
4000 ppm	0.669±	0.066	0.789±	0.063	0.669±	0.041	0.790±	0.109	0.803±	0.065	0.706±	0.057
8000 ppm	1.527±	0.313	1.966±	0.455	1.559±	0.219	1.731±	0.338	1.727±	0.288	1.593±	0.203
10000 ppm	2.029±	0.246	2,395±	0.374	1.838±	0.195	2.095±	0.100	2.078±	0.372	1.881±	0.186
16000 ppm	3.595±		4.013±	0.614	3.599±	0.425	3.943±	0.547	3,826±	0.711	3.663±	0.770

(HAN300)

APPENDIX B 4-4

CHEMICAL INTAKE CHANGES (THIRTEEN—WEEK STUDY: SUMMARY)

MOUSE: FEMALE

ANIMAL : MOUSE BDF1
UNIT : g/kg/day
REPORT TYPE : A1 13
SEX : FEMALE

CHEMICAL INTAKE CHENGES (SUMMARY)

ALL ANIMALS

PAGE: 3

Group 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
500 ppm	0.135± 0.014	0.107± 0.010	0.117± 0.008	0.122± 0.011	0.139± 0.017	0.128± 0.007	0.130± 0.015
2000 ppm	0.482± 0.044	0.403± 0.023	0.462± 0.048	0.479± 0.044	0.539± 0.073	0.514± 0.038	0.530± 0.043
4000 ppm	1.059± 0.142	0.846± 0.072	0.952± 0.096	0.941± 0.089	1.115± 0.134	1.027± 0.098	1.065± 0.110
8000 ppm	1.056± 0.143	1.944± 0.172	2.086± 0.220	2.002± 0.165	2.375± 0.306	2.177± 0.205	1.984± 0.199
10000 ppm	1.028± 0.127	3.226± 0.486	3.502± 0.760	2.794± 0.674	3.245± 0.524	3.173± 0.499	2.621± 0.318
16000 ppm	1.218± 0.185	2.876± 0.242	6.817土 1.282	5.585± 0.965	6.825± 1.115	5.745± 0.868	4.918± 0.988

(HAN300)

ANIMAL : MOUSE BDF1 UNIT : g/kg/day REPORT TYPE : A1 13

SEX : FEMALE

CHEMICAL INTAKE CHENGES (SUMMARY)

ALL ANIMALS

PAGE: 4

Administration	(weeks)					
8	9	10	11	12	13	
0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	
0.107± 0.005	0.139± 0.012	0.106± 0.013	0.137± 0.011	0.123± 0.011	0.118± 0.007	
0.465± 0.037	0.548± 0.054	0.413± 0.035	0.532± 0.066	0.486± 0.060	0.440± 0.057	
0.846± 0.056	1.054± 0.109	0.812± 0.068	1.008± 0.135	0.989± 0.089	0.900± 0.085	
1.826± 0.227	2.273± 0.264	1.722± 0.184	2.214± 0.300	2.133± 0.253	1.941± 0.174	
2,407± 0,528	2.968± 0.548	2.089± 0.330	2.809± 0.485	2.882± 0.442	2.400± 0.423	
4.273± 0.462	4.860± 0.717	4.073± 0.507	5.181± 0.940	5.438± 0.951	5.015± 0.943	
	8 0.000± 0.000 0.107± 0.005 0.465± 0.037 0.846± 0.056 1.826± 0.227 2.407± 0.528	0.000± 0.000 0.000± 0.000 0.107± 0.005 0.139± 0.012 0.465± 0.037 0.548± 0.054 0.846± 0.056 1.054± 0.109 1.826± 0.227 2.273± 0.264 2.407± 0.528 2.968± 0.548	8 9 10 0.000± 0.000 0.000± 0.000 0.000± 0.000 0.107± 0.005 0.139± 0.012 0.106± 0.013 0.465± 0.037 0.548± 0.054 0.413± 0.035 0.846± 0.056 1.054± 0.109 0.812± 0.068 1.826± 0.227 2.273± 0.264 1.722± 0.184 2.407± 0.528 2.968± 0.548 2.089± 0.330	8 9 10 11 0.000± 0.000 0.000± 0.000 0.000± 0.000 0.000± 0.000 0.107± 0.005 0.139± 0.012 0.106± 0.013 0.137± 0.011 0.465± 0.037 0.548± 0.054 0.413± 0.035 0.532± 0.066 0.846± 0.056 1.054± 0.109 0.812± 0.068 1.008± 0.135 1.826± 0.227 2.273± 0.264 1.722± 0.184 2.214± 0.300 2.407± 0.528 2.968± 0.548 2.089± 0.330 2.809± 0.485	8 9 10 11 12 0.000± 0.000 0.000± 0.000 0.000± 0.000 0.000± 0.000 0.000± 0.000 0.107± 0.005 0.139± 0.012 0.106± 0.013 0.137± 0.011 0.123± 0.011 0.465± 0.037 0.548± 0.054 0.413± 0.035 0.532± 0.066 0.486± 0.060 0.846± 0.056 1.054± 0.109 0.812± 0.068 1.008± 0.135 0.989± 0.089 1.826± 0.227 2.273± 0.264 1.722± 0.184 2.214± 0.300 2.133± 0.253 2.407± 0.528 2.968± 0.548 2.089± 0.330 2.809± 0.485 2.882± 0.442	8 9 10 11 12 13 0.000± 0.000 0.000± 0.000 0.000± 0.000 0.000± 0.000 0.000± 0.000 0.000± 0.000 0.107± 0.005 0.139± 0.012 0.106± 0.013 0.137± 0.011 0.123± 0.011 0.118± 0.007 0.465± 0.037 0.548± 0.054 0.413± 0.035 0.532± 0.066 0.486± 0.060 0.440± 0.057 0.846± 0.056 1.054± 0.109 0.812± 0.068 1.008± 0.135 0.989± 0.089 0.900± 0.085 1.826± 0.227 2.273± 0.264 1.722± 0.184 2.214± 0.300 2.133± 0.253 1.941± 0.174 2.407± 0.528 2.968± 0.548 2.089± 0.330 2.809± 0.485 2.882± 0.442 2.400± 0.423

(HAN300)

APPENDIX B 5-1

HEMATOLOGY (THIRTEEN-WEEK STUDY: SUMMARY)

RAT: MALE

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STUDY NO. : 0185 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE

HEMATOLOGY(1) (SUMMARY) SURVIVAL ANIMALS (14)

PAGE: 1

up Name	NO. of Animals	RED BI	LOOD CELL	g∕dl HEMOGI		HEMATO %	CRIT	MCV f e		MCH Pg		MCHC g∕d£		PLATELI 1 Ο³ / μ:	
Control	10	9.56±	0.28	16.4±	0.4	45.8±	1.2	47.9±	0.5	17.1±	0.3	35.8±	0.5	765±	28
1000 ppm	10	9.38±	0.25	16.3±	0.3	45.4±	1.6	48.4±	0.8	17.4±	0.3	35.9±	0.9	720±	42
2000 ppm	10	9.29±	0.22*	16.1±	0.3	45.1±	1.2	48.6±	0.7*	17.3±	0.4	35.7±	0.7	729±	49
4000 ppm	10	9.06±	0.14**	16.0±	0.2*	44.6±	0.7	49.2±	0.5**	17.7±	0.2**	35.9±	0.4	762±	70
mag 0008	10	8.91±	0.18**	15.8±	0.3**	44.1±	1.1*	49.5±	0.4**	17.7±	0.2**	35.7±	0.6	819±	71
16000 ppm	10	8.83±	0.28**	15.7±	0.3**	43.8±	1.4**	49.6±	0.6**	17.8±	0.4**	35.8±	0.9	856±	61**

(HCL070)

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STUDY NO. : 0185 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE HEMATOLOGY(2) (SUMMARY) SURVIVAL ANIMALS (14)

PAGE: 1

up Name	NO. of Animals	WBC 1 Ο ³ / μ.	l	Differentia N-BAND	l WBC	(%) N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHER	
Control	10	3.84±	1.57	0±	0	28±	7	2±	1	0±	0	5±	1	64±	8	1±	1
1000 ppm	10	5.37±	1.66	ο±	0	26±	5	2±	1	0±	0	4±	1	68±	5	1±	1
2000 ppm	10	4.42±	1.42	1±	1	28±	5	1±	1	0±	0	4±	1	65±	6	1±	2
4000 ppm	10	4.36±	1.66	0±	0	30士	8	1±	1	0±	0	3±	1	65±	7	1±	1
8000 ppm	10	5.51±	1.96	0±	1	26士	8	2±	1	0±	0	4±	1	66±	8	2±	2
16000 ppm	10	4.74±	1.65	0±	0	24±	5	2±	1	0±	0	4±	1	69±	6	1±	1

(JCL71A)

APPENDIX B 5-2

HEMATOLOGY (THIRTEEN-WEEK STUDY: SUMMARY)

RAT: FEMALE

STUDY NO. : 0185 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE

HEMATOLOGY(1) (SUMMARY) SURVIVAL ANIMALS (14)

		цl	g/dl	OBIN	HEMAT(%		MCV f ℓ		MCH Pg		MCHC g∕dl		PLATEL 1 O³/μ	
10	8.55±	0.17	15.9±	0.3	43.9±	1.2	51.4±	0.6	18.6±	0.2	36.2±	0.7	807±	74
10	8.46±	0.24	15.7±	0.5	43.7±	1.4	51.7±	0.6	18.6±	0.3	36.0±	0.6	782士	99
10	8.41±	0.21	15.7±	0.3	43.5±	1.4	51.7±	0.6	18.7±	0.2	36.2±	0.6	834±	56
9	8.33±	0.29	15.6±	0.5	42.9±	1.4	51.5±	0.5	18.8±	0.4	36.4±	0.7	845±	62
10	8.14±	0.28**	15.2±	0.4**	41.9±	1.2**	51.5±	0.9	18.6±	0.3	36.1±	0.7	823±	96
10	8.17±	0.19**	14.9±	0.5**	41.7±	1.0**	51.1±	1.1	18.2±	0.4*	35.7±	1.2	834±	86
ifference :	*: P ≦	0.05 *	*: P ≤ 0.0	01			Test of Dur	nett			2			
	10 10 9 10	10 8.46± 10 8.41± 9 8.33± 10 8.14± 10 8.17±	10 8.46± 0.24 10 8.41± 0.21 9 8.33± 0.29 10 8.14± 0.28** 10 8.17± 0.19**	10 8.46± 0.24 15.7± 10 8.41± 0.21 15.7± 9 8.33± 0.29 15.6± 10 8.14± 0.28** 15.2± 10 8.17± 0.19** 14.9±	10 8.46± 0.24 15.7± 0.5 10 8.41± 0.21 15.7± 0.3 9 8.33± 0.29 15.6± 0.5 10 8.14± 0.28** 15.2± 0.4** 10 8.17± 0.19** 14.9± 0.5**	10 8.46± 0.24 15.7± 0.5 43.7± 10 8.41± 0.21 15.7± 0.3 43.5± 9 8.33± 0.29 15.6± 0.5 42.9± 10 8.14± 0.28** 15.2± 0.4** 41.9± 10 8.17± 0.19** 14.9± 0.5** 41.7±	10 8.46± 0.24 15.7± 0.5 43.7± 1.4 10 8.41± 0.21 15.7± 0.3 43.5± 1.4 9 8.33± 0.29 15.6± 0.5 42.9± 1.4 10 8.14± 0.28** 15.2± 0.4** 41.9± 1.2** 10 8.17± 0.19** 14.9± 0.5** 41.7± 1.0**	10 8.46± 0.24 15.7± 0.5 43.7± 1.4 51.7± 10 8.41± 0.21 15.7± 0.3 43.5± 1.4 51.7± 9 8.33± 0.29 15.6± 0.5 42.9± 1.4 51.5± 10 8.14± 0.28** 15.2± 0.4** 41.9± 1.2** 51.5± 10 8.17± 0.19** 14.9± 0.5** 41.7± 1.0** 51.1±	10 8.46± 0.24 15.7± 0.5 43.7± 1.4 51.7± 0.6 10 8.41± 0.21 15.7± 0.3 43.5± 1.4 51.7± 0.6 9 8.33± 0.29 15.6± 0.5 42.9± 1.4 51.5± 0.5 10 8.14± 0.28** 15.2± 0.4** 41.9± 1.2** 51.5± 0.9 10 8.17± 0.19** 14.9± 0.5** 41.7± 1.0** 51.1± 1.1	10 8.46± 0.24 15.7± 0.5 43.7± 1.4 51.7± 0.6 18.6± 10 8.41± 0.21 15.7± 0.3 43.5± 1.4 51.7± 0.6 18.7± 9 8.33± 0.29 15.6± 0.5 42.9± 1.4 51.5± 0.5 18.8± 10 8.14± 0.28** 15.2± 0.4** 41.9± 1.2** 51.5± 0.9 18.6± 10 8.17± 0.19** 14.9± 0.5** 41.7± 1.0** 51.1± 1.1 18.2±	10 8.46± 0.24 15.7± 0.5 43.7± 1.4 51.7± 0.6 18.6± 0.3 10 8.41± 0.21 15.7± 0.3 43.5± 1.4 51.7± 0.6 18.7± 0.2 9 8.33± 0.29 15.6± 0.5 42.9± 1.4 51.5± 0.5 18.8± 0.4 10 8.14± 0.28** 15.2± 0.4** 41.9± 1.2** 51.5± 0.9 18.6± 0.3 10 8.17± 0.19** 14.9± 0.5** 41.7± 1.0** 51.1± 1.1 18.2± 0.4*	10 8.46 \pm 0.24 15.7 \pm 0.5 43.7 \pm 1.4 51.7 \pm 0.6 18.6 \pm 0.3 36.0 \pm 10 8.41 \pm 0.21 15.7 \pm 0.3 43.5 \pm 1.4 51.7 \pm 0.6 18.7 \pm 0.2 36.2 \pm 9 8.33 \pm 0.29 15.6 \pm 0.5 42.9 \pm 1.4 51.5 \pm 0.5 18.8 \pm 0.4 36.4 \pm 10 8.14 \pm 0.28** 15.2 \pm 0.4** 41.9 \pm 1.2** 51.5 \pm 0.9 18.6 \pm 0.3 36.1 \pm 10 8.17 \pm 0.19** 14.9 \pm 0.5** 41.7 \pm 1.0** 51.1 \pm 1.1 18.2 \pm 0.4* 35.7 \pm	10 8.46 \pm 0.24 15.7 \pm 0.5 43.7 \pm 1.4 51.7 \pm 0.6 18.6 \pm 0.3 36.0 \pm 0.6 10 8.41 \pm 0.21 15.7 \pm 0.3 43.5 \pm 1.4 51.7 \pm 0.6 18.7 \pm 0.2 36.2 \pm 0.6 9 8.33 \pm 0.29 15.6 \pm 0.5 42.9 \pm 1.4 51.5 \pm 0.5 18.8 \pm 0.4 36.4 \pm 0.7 10 8.14 \pm 0.28** 15.2 \pm 0.4** 41.9 \pm 1.2** 51.5 \pm 0.9 18.6 \pm 0.3 36.1 \pm 0.7 10 8.17 \pm 0.19** 14.9 \pm 0.5** 41.7 \pm 1.0** 51.1 \pm 1.1 18.2 \pm 0.4* 35.7 \pm 1.2 11 11 11 11 11 11 11 11 11 11 11 11 11	10 8.46 \pm 0.24 15.7 \pm 0.5 43.7 \pm 1.4 51.7 \pm 0.6 18.6 \pm 0.3 36.0 \pm 0.6 782 \pm 10 8.41 \pm 0.21 15.7 \pm 0.3 43.5 \pm 1.4 51.7 \pm 0.6 18.7 \pm 0.2 36.2 \pm 0.6 834 \pm 9 8.33 \pm 0.29 15.6 \pm 0.5 42.9 \pm 1.4 51.5 \pm 0.5 18.8 \pm 0.4 36.4 \pm 0.7 845 \pm 10 8.14 \pm 0.28** 15.2 \pm 0.4** 41.9 \pm 1.2** 51.5 \pm 0.9 18.6 \pm 0.3 36.1 \pm 0.7 823 \pm 10 8.17 \pm 0.19** 14.9 \pm 0.5** 41.7 \pm 1.0** 51.1 \pm 1.1 18.2 \pm 0.4* 35.7 \pm 1.2 834 \pm 11 11 11 11 11 11 11 11 11 11 11 11 11

BAIS 2

PAGE: 2

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STUDY NO.: 0185
ANIMAL: RAT F344
REPORT TYPE: A1
SEX: FEMALE

HEMATOLOGY(2) (SUMMARY) SURVIVAL ANIMALS (14)

PAGE: 2

up Name	NO. of Animals	WBC 1 O³∕µ	ıl	Differentia N-BAND	al WBC	(%) N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHER	
Control	10	2.54±	0.56	0±	1	26±	4	2±	1	0±	0	4±	1	67±	4	1±	1
1000 ppm	10	2.50±	0.71	0±	0	27±	6	2±	1	0±	0	3±	1	67±	7	1±	2
2000 ppm	10	2.65±	0.93	0±	1	30±	6	2±	1	0±	0	4±	1	61±	6	1±	1
4000 ppm	9	3,11±	1.22	0±	0	25±	5	1±	1	0土	0	4±	1	68±	6	2±	1
mqq 0008	10	3.63±	1.40	0±	0	22±	4	1±	1	0±	0	4±	1	. 71±	4	1±	1
16000 ppm	10	3.43±	2.19	0±	0	23±	6	2±	1	0±	0	4±	2	71±	6	1±	1

BA125

APPENDIX B 5-3

HEMATOLOGY (THIRTEEN-WEEK STUDY: SUMMARY)

MOSUE: MALE

ANIMAL : MOUSE BDF1

REPORT TYPE : A1

HEMATOLOGY(1) (SUMMARY) SURVIVAL ANIMALS (14)

SEX : MALE

PAGE: 1

oup Name	NO. of Animals	RED BLOOD CELL 1 O ⁶ /με	HEMOGLOBIN g∕dl	HEMATOCRIT %	MCV f e	MCH pg	MCHC g ∕dl	PLATELET 1 Ο³ / μℓ
Control	9	10.49± 0.43	15.6± 0.6	46.1± 1.4	43.9± 1.0	14.9± 0.3	34.0± 0.7	1486± 98
500 ppm	10	10.12± 0.34	15.2± 0.7	44.7± 2.1	44.2± 1.0	15.0± 0.3	34.0± 0.7	1380± 90
2000 ppm	10	10.31± 0.24	15.4± 0.4	44.9± 1.3	43.5± 0.7	15.0± 0.3	34.3± 0.3	1424± 104
4000 ppm	10	10.36± 0.34	15.4± 0.6	45.2± 1.7	43.6± 0.6	14.9± 0.4	34.2± 0.8	1489± 106
8000 ppm	9	10.69± 0.56	15.7± 0.6	46.3± 1.8	43.4± 1.1	14.6± 0.4	33.8± 0.8	1515± 86
10000 ppm	10	10.57± 0.32	15.7± 0.4	46.5± 1.2	43.9± 0.6	14.9± 0.4	33.8± 0.5	1562± 116
16000 ppm	10	10,69± 0,38	15.7± 0.6	46.5± 1.6	43.5± 0.9	14.7± 0.6	33.8± 0.9	1464± 113
Significant	difference;	*: P ≤ 0.05	**: P ≤ 0.01		Test of Dunnett			
CL070)								1

(HCLO70)

STUDY NO. : 0186
ANIMAL : MOUSE RDET

ANIMAL : MOUSE BDF1
REPORT TYPE : A1

SEX : MALE

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HEMATOLOGY(2) (SUMMARY) SURVIVAL ANIMALS (14)

PAGE: 1

roup Name	NO. of Animals	WBC 1 O³∕µ	Q.	Differentia N-BAND	al WBC	(%) N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHER	
Control	9	1.20±	0.68	0±	1	18±	5	1±	1	0±	0	4土	1	77±	5	0±	0
500 ppm	10	1.08±	0.75	1±	1	17±	4	2±	1	0±	0	4±	1	77±	4	0±	0
2000 ppm	10	1.06±	0.40	0±	0	21±	6	1±	2	0±	0	3±	1	74±	6	0±	0
4000 ppm	10	0.75±	0.62	1生	1	19±	5	1±	1	0±	0	3±	1	76±	6	ο±	0
8000 ppm	9	0.75±	0.50	0±	0	19±	6	0±	1	0±	0	3±	1	77±	7	0±	0
10000 ppm	10	1.30±	0.72	0±	0	17±	3	1±	0	0±	0	3±	1	79±	4	0±	0
16000 ppm	10	0.80±	0.60	0±	0	24士	8	0±	1	0±	0	3±	1	72±	8	0±	0
Significant	difference;	*: P ≤ 0	.05	**: P ≤ 0	.01			1	Cest of	Dunnett							
JCL71A)						-					• • • • • • • • • • • • • • • • • • • •		-				

APPENDIX B 5-4

HEMATOLOGY (THIRTEEN-WEEK STUDY: SUMMARY)

MOSUE: FEMALE

ANIMAL : MOUSE BDF1
REPORT TYPE : A1 SEX: FEMALE

-7

HEMATOLOGY(1) (SUMMARY) SURVIVAL ANIMALS (14)

PAGE: 2

10.08±	0.66												
	*****	15.6±	0.6	45.3±	2.7	44.9±	1.0	15.5±	0.9	34.6±	1.5	1218±	195
10.40±	0.47	15.8±	0.7	45.7±	2.2	44.0±	0.5*	15.3±	0.5	34.7±	0.8	1378±	102
10.38±	0.38	15.8±	0.5	45.9±	1.7	44.2±	0.6	15.2±	0.4	34.4±	1.0	1296±	140
10.49±	0.29	15.8±	0.5	45.8±	0.8	43.7±	0.7**	15.1±	0.3	34.5±	0.5	1312±	90
10.63±	0.42	15.7±	0.3	46.0±	1.6	43.3±	0.9**	14.8±	0.6*	34.3±	1.2	1371±	155*
10.54±	0.33	15.7±	0.6	45.7±	1.9	43.3±	0.6**	14.9±	0.4	34.5±	0.7	1377±	68
10.72±	0.42	15.7±	0.5	46.4±	1.4	43.3±	1.0**	14.7±	0.4**	33.9±	0.8	1304±	64
	10.38± 10.49± 10.63± 10.54±	10.38 ± 0.38 10.49 ± 0.29 10.63 ± 0.42 10.54 ± 0.33	$10.38\pm$ 0.38 $15.8\pm$ $10.49\pm$ 0.29 $15.8\pm$ $10.63\pm$ 0.42 $15.7\pm$ $10.54\pm$ 0.33 $15.7\pm$	$10.38\pm$ 0.38 $15.8\pm$ 0.5 $10.49\pm$ 0.29 $15.8\pm$ 0.5 $10.63\pm$ 0.42 $15.7\pm$ 0.3 $10.54\pm$ 0.33 $15.7\pm$ 0.6	$10.38\pm$ 0.38 $15.8\pm$ 0.5 $45.9\pm$ $10.49\pm$ 0.29 $15.8\pm$ 0.5 $45.8\pm$ $10.63\pm$ 0.42 $15.7\pm$ 0.3 $46.0\pm$ $10.54\pm$ 0.33 $15.7\pm$ 0.6 $45.7\pm$	$10.38\pm$ 0.38 $15.8\pm$ 0.5 $45.9\pm$ 1.7 $10.49\pm$ 0.29 $15.8\pm$ 0.5 $45.8\pm$ 0.8 $10.63\pm$ 0.42 $15.7\pm$ 0.3 $46.0\pm$ 1.6 $10.54\pm$ 0.33 $15.7\pm$ 0.6 $45.7\pm$ 1.9	$10.38\pm$ 0.38 $15.8\pm$ 0.5 $45.9\pm$ 1.7 $44.2\pm$ $10.49\pm$ 0.29 $15.8\pm$ 0.5 $45.8\pm$ 0.8 $43.7\pm$ $10.63\pm$ 0.42 $15.7\pm$ 0.3 $46.0\pm$ 1.6 $43.3\pm$ $10.54\pm$ 0.33 $15.7\pm$ 0.6 $45.7\pm$ 1.9 $43.3\pm$	10.38 ± 0.38 15.8 ± 0.5 45.9 ± 1.7 44.2 ± 0.6 10.49 ± 0.29 15.8 ± 0.5 45.8 ± 0.8 $43.7\pm 0.7**$ 10.63 ± 0.42 15.7 ± 0.3 46.0 ± 1.6 $43.3\pm 0.9**$ 10.54 ± 0.33 15.7 ± 0.6 45.7 ± 1.9 $43.3\pm 0.6**$	$10.38\pm$ 0.38 $15.8\pm$ 0.5 $45.9\pm$ 1.7 $44.2\pm$ 0.6 $15.2\pm$ $10.49\pm$ 0.29 $15.8\pm$ 0.5 $45.8\pm$ 0.8 $43.7\pm$ $0.7**$ $15.1\pm$ $10.63\pm$ 0.42 $15.7\pm$ 0.3 $46.0\pm$ 1.6 $43.3\pm$ $0.9**$ $14.8\pm$ $10.54\pm$ 0.33 $15.7\pm$ 0.6 $45.7\pm$ 1.9 $43.3\pm$ $0.6**$ $14.9\pm$	10.38 ± 0.38 15.8 ± 0.5 45.9 ± 1.7 44.2 ± 0.6 15.2 ± 0.4 10.49 ± 0.29 15.8 ± 0.5 45.8 ± 0.8 $43.7\pm 0.7**$ 15.1 ± 0.3 10.63 ± 0.42 15.7 ± 0.3 46.0 ± 1.6 $43.3\pm 0.9**$ $14.8\pm 0.6*$ 10.54 ± 0.33 15.7 ± 0.6 45.7 ± 1.9 $43.3\pm 0.6**$ 14.9 ± 0.4	$10.38\pm$ 0.38 $15.8\pm$ 0.5 $45.9\pm$ 1.7 $44.2\pm$ 0.6 $15.2\pm$ 0.4 $34.4\pm$ $10.49\pm$ 0.29 $15.8\pm$ 0.5 $45.8\pm$ 0.8 $43.7\pm$ $0.7**$ $15.1\pm$ 0.3 $34.5\pm$ $10.63\pm$ 0.42 $15.7\pm$ 0.3 $46.0\pm$ 1.6 $43.3\pm$ $0.9**$ $14.8\pm$ $0.6*$ $34.3\pm$ $10.54\pm$ 0.33 $15.7\pm$ 0.6 $45.7\pm$ 1.9 $43.3\pm$ $0.6**$ $14.9\pm$ 0.4 $34.5\pm$	$10.38\pm \ 0.38$ $15.8\pm \ 0.5$ $45.9\pm \ 1.7$ $44.2\pm \ 0.6$ $15.2\pm \ 0.4$ $34.4\pm \ 1.0$ $10.49\pm \ 0.29$ $15.8\pm \ 0.5$ $45.8\pm \ 0.8$ $43.7\pm \ 0.7**$ $15.1\pm \ 0.3$ $34.5\pm \ 0.5$ $10.63\pm \ 0.42$ $15.7\pm \ 0.3$ $46.0\pm \ 1.6$ $43.3\pm \ 0.9**$ $14.8\pm \ 0.6*$ $34.3\pm \ 1.2$ $10.54\pm \ 0.33$ $15.7\pm \ 0.6$ $45.7\pm \ 1.9$ $43.3\pm \ 0.6**$ $14.9\pm \ 0.4$ $34.5\pm \ 0.7$	$10.38\pm$ 0.38 $15.8\pm$ 0.5 $45.9\pm$ 1.7 $44.2\pm$ 0.6 $15.2\pm$ 0.4 $34.4\pm$ 1.0 $1296\pm$ $10.49\pm$ 0.29 $15.8\pm$ 0.5 $45.8\pm$ 0.8 $43.7\pm$ $0.7***$ $15.1\pm$ 0.3 $34.5\pm$ 0.5 $1312\pm$ $10.63\pm$ 0.42 $15.7\pm$ 0.3 $46.0\pm$ 1.6 $43.3\pm$ $0.9**$ $14.8\pm$ $0.6*$ $34.3\pm$ 1.2 $1371\pm$ $10.54\pm$ 0.33 $15.7\pm$ 0.6 $45.7\pm$ 1.9 $43.3\pm$ $0.6**$ $14.9\pm$ 0.4 $34.5\pm$ 0.7 $1377\pm$

(HCL070)

ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

HEMATOLOGY(2) (SUMMARY) SURVIVAL ANIMALS (14)

PAGE: 2

1.23± 0.75 1.36± 0.81	0± 0±	0	15±	4										
1.36± 0.81	0土			•	2±	1	0±	0	4±	2	78±	5	0±	0
		0	17±	7	2±	1	0±	0	3±	1	78±	6	0±	0
1.06± 0.53	0±	1	15±	4	1±	1	0±	0	3±	1	81±	5	0±	0
0.98± 0.94	0±	0	16±	5	1±	1	0±	0	3±	1	80±	3	0±	0
1.14± 0.62	0±	0	17±	4	1±	1	0±	0	4±	1	78±	5	0±	0
1.08± 0.85	0±	0	18±	5	1±	1	0±	0	4±	1	77±	6	0±	0
0.92± 0.45	0±	1	17±	6	1±	1	0±	0	4±	1	78±	6	0±	0
0	.92± 0.45 P ≤ 0.05													

(JCL71A)

APPENDIX B 6-1

BIOCHEMISTRY (THIRTEEN-WEEK STUDY: SUMMARY)

RAT: MALE

STUDY NO.: 0185 ANIMAL: RAT F344

REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (14)

SEX : MALE

oup Name	NO. of Animals	TOTAL F		& ∕qf ∀TBNWIN		A/G RAT	TIO	T-BILI mg/dl		GLUCOSE ™g∕dl		T-CHOLES	STEROL	TRIGLYC mg/dl	ERIDE
Control	10	6.7±	0.2	3.8±	0.1	1.3±	0.1	0.21±	0.04	206±	19	61±	4	79±	23
1000 ppm	10	6.8±	0.2	3.9±	0.1	1.3±	0.0	0.21±	0.03	207±	23	64±	4	99±	20
2000 ppm	10	6.8±	0.2	3.9±	0.1	1.4±	0.1	0.21±	0.03	204±	28	69±	6*	87±	24
4000 ppm	10	6.8±	0.3	4.0±	0.1**	1.4±	0.1*	0.18±	0.02	195±	21	77±	6**	69±	29
mqq 0008	10	7.0±	0.2	4.1±	0.1**	1.4±	0.1*	0.18±	0.02	200±	19	86±	9**	58±	11
16000 ppm	10	7.0±	0.2	4.1±	0.1**	1.4±	0.1**	0.20±	0.03	185±	15	89±	6**	58±	11
Significant o	lifference;	*: P ≤ 0	.05	**: P ≤ 0.0	1		·	Test of Du	nnett						
L074)															

BAIS 2

PAGE: 1

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STUDY NO. : 0185 ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (14)

oup Name	NO. of Animals	PHOSPHO mg/dl	LIPID	GOT IU/l		GPT IU/e		LDH IU/4	?	ALP IU/4		G-GTP IU/l		CPK IU/0	
Contral	10	111±	6	92±	29	29±	8	220±	72	308±	16	1±	1	93生	16
1000 ppm	10	119±	6	99±	21	29±	4	224±	54	323±	23	1±	1	93±	21
2000 ppm	10	125±	12	87±	24	25±	6	198±	47	319±	19	1±	1	80±	9
4000 ppm	10	134土	7**	94士	40	25±	7	203±	91	321±	18	1±	1	79±	6
8000 ppm	10	142±	14**	88±	30	24±	5	212±	59	324±	25	1±	1	86±	9
16000 ppm	10	149士	8**	64±	17	20±	4**	191±	61	322±	25	2±	1	87±	13
Significant o	difference :	*: P ≤ 0	.05 *	*: P ≤ 0.0	1			Test of Dun	nett						
L074)															

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STUDY NO. : 0185 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (14)

oup Name	NO. of Animals	UREA NI	TROGEN	CREATIN mg/dl	INE	SODIUM mEq∕ℓ		POTASSI mEq/		CHLORIDE mEq/l		CALCIUI mg∕dl		INORGAN mg/dl	VIC PHOSPHORU
Control	10	18.0±	2.0	0.5±	0.1	143±	1	3.2±	0.3	106±	1	10.5±	0.1	5.1±	0.7
1000 ppm	10	18.2±	1.3	0.5±	0.0	143±	1	3.2±	0.2	105±	1	10.5±	0.2	5.2±	0.6
2000 ppm	10	17.4±	1.2	0.5±	0.1	143±	1	3.3±	0.3	106±	1	10.5±	0.2	4.9±	0.7
4000 ppm	10	18.9±	1.2	0.5±	0.0	142±	1	3.4±	0.3	107±	1	10.6±	0.2	4.9±	0.7
mqq 0008	10	20.0±	2.2	0.5±	0.1	142±	1	3.5±	0.3	106±	1	10.7±	0.1**	5.0±	0.4
16000 ppm	10	19.5±	1.9	0.5±	0.0	141±	1**	3.8±	0.3**	104±	1**	10.7±	0.2*	5.1±	0.5

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(HCL074) BAIS 2

APPENDIX B 6-2

BIOCHEMISTRY(THIRTEEN-WEEK STUDY: SUMMARY)

RAT: FEMALE

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STUDY NO. : 0185 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (14)

oup Name	NO. of Animals	TOTAL I		albumin g∕dl		A/G RAT	210	T-BILI mg/dl		GLUCOSE mg∕dl		T-CHOLES	TEROL		RIGLYCE g/dl	RIDE
Control	10	6.5±	0.2	3.6±	0.1	1.3±	0.1	0.22±	0.03	147土	18	76±	6	;	35±	4
1000 ppm	10	6.5±	0.3	3.7±	0.1	1.3±	0.1	0.26±	0.10	157±	13	76±	8	:	37±	4
2000 ppm	10	6.7±	0.3	3.7±	0.2	1.3±	0.1	0.22±	0.08	155±	18	79±	6	:	36±	5
4000 ppm	9	6.5±	0.3	3.7±	0.2	1.3±	0.1	0.22±	0.04	152±	15	81±	5	;	32±	3
mqq 0008	10	6.6±	0.2	3.8±	0.1*	1.4±	0.1*	0.23±	0.09	159±	13	88±	7**	:	29±	4*
16000 ppm	10	6.6±	0.2	3.8±	0.1**	1.4±	0.0**	0.23±	0.06	155±	23	104土	4**		32±	6
Significant o	difference;	*: P ≦ ().05	**: P ≦ 0.0	1			Test of Du	nnett		· · · · · · · · · · · · · · · · · · ·					
L074)																1

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STUDY NO. : 0185 ANIMAL : RAT F344 REPORT TYPE : A1 SEX: FEMALE

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (14)

Group Name NO. of PHOSPHOLIPID LDH IU/e GOT GPT ALP G-GTP CPK Animals mg/dl IU/e IU/l IU/l IU∕ℓ IU∕ℓ Control 10 $133 \pm$ 12 10 $70\pm$ $21\pm$ 7 $241\pm$ 152 $222 \pm$ 24 1土 100土 1 24 1000 ppm 10 $135 \pm$ 10 $65\pm$ 10 $19\pm$ 4 $249 \pm$ 116 $225\pm$ 26 $1\pm$ 1 104士 29 2000 ppm 10 136± 9 66± 7 $20\pm$ 5 206士 77 $223 \pm$ 20 $1\pm$ 98± 25 1 4000 ppm 9 137± 8 $75\pm$ 13 $23\pm$ 9 $300 \pm$ 71 $221\pm$ 27 1土 1 117士 17 8000 ppm 10 $144 \pm$ 9 $68\pm$ 6 $20\pm$ 3 $287 \pm$ 104 217± 21 $2\pm$ 1 109± 28 16000 ppm 10 $163 \pm$ 9** 62± 7 $19\pm$ 3 $296 \pm$ 143 $242\pm$ 35 $3\pm$ 1** 109± 29 Significant difference : $*: P \le 0.05$ **: $P \leq 0.01$ Test of Dunnett

(HCL074)

BAIS 2

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STUDY NO.: 0185
ANIMAL: RAT F344
REPORT TYPE: A1
SEX: FEMALE

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (14)

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oup Name	NO. of Animals	urea n mg/dl	TROGEN	CREATIN mg/dl		SODIUM mEq∕ℓ		POTASS mEq/		CHLORIDI mEq∕ℓ		mg/dl	<u> </u>	INORGAN mg/dl	IIC PHOSPHORUS
Control	10	16.2±	1.5	0.4±	0.0	144±	1	3.4±	0.3	109±	1	10.0±	0.3	4.6±	0.8
1000 ppm	10	15.6±	2.4	0.4±	0.1	143±	1 .	3.5±	0.2	109±	2	10.0±	0.4	4.5±	1.0
2000 ppm	10	15.5±	2.0	0.5±	0.1	144土	1	3.2±	0.2	109±	2	10.2±	0.1	4.5±	1.0
4000 ppm	9	17.3±	1.4	0.4±	0.1	143±	1	3.4±	0.2	109±	1	10.1±	0.2	4.7±	1.1
8000 ppm	10	18.6±	1.6*	0.4±	0.1	142±	1	3.4±	0.3	108±	1	10.2±	0.1	4.8±	0.8
16000 ppm	10	18.5±	2.2*	0.4±	0.1	141±	1**	4.1±	0.8**	107±	3	10.4±	0.4	5.1±	1.1

(HCL074)

APPENDIX B 6-3

BIOCHEMISTRY (THIRTEEN-WEEK STUDY: SUMMARY)

MOSUE: MALE

STUDY NO.: 0186
ANIMAL: MOUSE BDF1
REPORT TYPE: A1
SEX: MALE

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (14)

oup Name	NO. of Animals	g/dl g/dl	PROTEIN	ALBUMIN g∕dl		A/G RAT	010	T-BILI mg/dl		GLUCOSE mg∕dl		T-CHOLE	STEROL	TRIGLYC mg/dl	ERIDE
Control	10	5.4±	0.3	2.9±	0.1	1.1±	0.1	0.39±	0.17	234±	53	84±	12	64±	13
500 ppm	10	5.2±	0.3	2.8±	0.2	1.2±	0.0	0.36±	0.10	180±	62	78±	5	60±	12
2000 ppm	10	5.4±	0.2	2.9±	0.1	1.2±	0.0*	0.37±	0.14	186±	52	85±	7	64±	23
4000 ppm	10	5.4±	0.2	3.0±	0.1	1.3±	0.1**	0.38±	0.20	189±	63	88±	8	56±	22
8000 ppm	9	5.6±	0.2	3.1±	0.1**	1.2±	0.1**	0.38±	0.11	164±	40	99±	10**	53±	14
10000 ppm	10	5.5±	0.2	3.0±	0.1	1.3±	0.1**	0.44±	0.11	176±	48	92±	6	58±	14
16000 ppm	10	5.6±	0.3	3.2±	0.2**	1.3±	0.1**	0.43±	0.20	186±	32	101±	3**	42±	4**
Significant	difference;	*: P ≤ 0	0.05	**: P ≤ 0.0	1		 	Test of Du	nett						

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STUDY NO. : 0186

ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (14)

PAGE: 2

roup Name	NO. of Animals	GOT IU/4	?	GPT IU∕ℓ		LDH IU/	e	ALP IU/4	e	CPK I U/	e	UREA N		SODIUM mEq/l	
Control	10	40±	7	11±	2	216±	22	194±	17	43±	5	28.3±	7.7	153±	1
500 ppm	10	46±	13	12±	2	232±	71	192±	19	53±	28	28.8±	5.3	153±	3
2000 ppm	10	42±	6	12±	2	212±	14	201±	18	43±	9	28.4±	4.2	153±	2
4000 ppm	10	41±	7	12±	3	225±	45	215±	18	49±	17	27.9±	4.9	153±	2
8000 ppm	9	45±	9	12±	2	236±	69	269±	56**	58±	22	29.2±	5.1	154±	1
10000 ppm	10	43±	7	13±	2	226士	44	241±	15**	67±	26	27.6±	4.4	154±	. 1
16000 ppm	10	59±	17**	15±	2**	305±	93	348±	31**	154±	123**	28.5±	4.1	155±	3
Significant	difference;	*: P ≤ 0	.05 *:	*: P ≤ 0.01				Test of Duni	nett						

ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (14)

PAGE: 3

roup Name	NO. of Animals	POTASS: mEq/		CHLORIDE mEq/l		CALCIUM mg/dl		INORGAN mg/dl	IC PHOSPHORUS	·	
Control	10	4.3±	0.5	122±	3	9.0±	0.4	7.3±	1.0		-
500 ppm	10	4.5±	0.4	122士	2	8.8±	0.2	7.8±	1.6		
2000 ppm	10	4.3±	0.4	122±	2	8.9±	0.3	7.5±	1.0		
4000 ppm	10	4.3±	0.2	123±	2	8.9±	0.1	7.4±	1.1		
mqq 0008	9	4.1±	0.5	122±	2	9.2±	0.2	8.0±	1.6		
10000 ppm	10	4.4±	0.2	123±	3	9.0±	0.3	7.9±	1.0		
16000 ppm	10	4.0±	0.7	124±	2	9.0±	0.2	7.6±	1.5		
Significant	difference;	*: P ≦ (0.05	**: P ≤ 0.01				Test of Dur	nett		
CL074)											BA

APPENDIX B 6-4

BIOCHEMISTRY (THIRTEEN-WEEK STUDY: SUMMARY)

MOSUE: FEMALE

STUDY NO. : 0186
ANIMAL : MOUSE BDF1
REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (14)

SEX : FEMALE

0.2 1.5 \pm 0.1 0.52 \pm 0.12 171 \pm 38 72 \pm 13 49 \pm 9 0.1 1.5 \pm 0.1 0.42 \pm 0.16 163 \pm 31 78 \pm 9* 47 \pm 5 0.1* 1.5 \pm 0.0 0.40 \pm 0.13 189 \pm 31 83 \pm 7** 47 \pm 9 0.1* 1.5 \pm 0.1 0.56 \pm 0.17 173 \pm 20 96 \pm 8** 44 \pm 5 0.1 1.5 \pm 0.1 0.49 \pm 0.19 167 \pm 29 90 \pm 6** 42 \pm 7 0.1** 1.5 \pm 0.1 0.46 \pm 0.13 146 \pm 19 101 \pm 9** 34 \pm 6**	iroup Name	NO. of Animals	TOTAL F		&∖q _l yrBnWIy	N	A/G RAT	LIO	mg∕dl T-BILI		GLUCOSE mg/dl		T-CHOLES	TEROL	TRIGLYCI mg/dl	ERIDE
0.1 1.5± 0.1 0.42± 0.16 163± 31 78± 9* 47± 5 0.1* 1.5± 0.0 0.40± 0.13 169± 31 83± 7** 47± 9 0.1* 1.5± 0.1 0.56± 0.17 173± 20 96± 8** 44± 5 0.1 1.5± 0.1 0.49± 0.19 167± 29 90± 6** 42± 7 0.1** 1.5± 0.1 0.46± 0.13 146± 19 101± 9** 34± 6**	Control	9	5.2±	0.3	3.1±	0.2	1.4±	0.1	0.42±	0.06	189±	17	66±	5	49±	10
0.1* 1.5± 0.0 0.40± 0.13 169± 31 83± 7** 47± 9 0.1* 1.5± 0.1 0.56± 0.17 173± 20 96± 8** 44± 5 0.1 1.5± 0.1 0.49± 0.19 167± 29 90± 6** 42± 7 0.1** 1.5± 0.1 0.46± 0.13 146± 19 101± 9** 34± 6**	500 ppm	10	5.4±	0.3	3.2±	0.2	1.5±	0.1	0.52±	0.12	171土	38	72±	13	49±	9
0.1* 1.5± 0.1 0.56± 0.17 173± 20 96± 8** 44± 5 0.1 1.5± 0.1 0.49± 0.19 167± 29 90± 6** 42± 7 0.1** 1.5± 0.1 0.46± 0.13 146± 19 101± 9** 34± 6**	2000 ppm	10	5.5±	0.2	3.3±	0.1	1.5±	0.1	0.42±	0.16	163±	31	78±	9*	47±	5
0.1 1.5± 0.1 0.49± 0.19 167± 29 90± 6** 42± 7 0.1** 1.5± 0.1 0.46± 0.13 146± 19 101± 9** 34± 6**	4000 ppm	10	5.6±	0.2**	3.3±	0.1*	1.5±	0.0	0.40±	0.13	169±	31	83±	7**	47±	9
0.1** 1.5± 0.1 0.46± 0.13 146± 19 101± 9** 34± 6**	mqq 0008	10	5.5±	0.2	3.3±	0.1*	1.5±	0.1	0.56±	0.17	173±	20	96±	8**	44±	5
	10000 ppm	10	5.5±	0.2*	3.3±	0.1	1.5±	0.1	0.49±	0.19	167±	29	90±	6**	42±	7
1 Toot of Dispositi	16000 ppm	9	5.5±	0.2*	3.4±	0.1**	1.5±	0.1	0.46±	0.13	146±	19	101±	9**	34±	6**
1 sect of pullett	Significant	difference;	*: P ≤ 0).05 *	*: P ≤ 0.0	1			Test of Du	nnett						

PAGE: 4

STUDY NO.: 0186
ANIMAL: MOUSE BDF1
REPORT TYPE: A1
SEX: FEMALE

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (14)

roup Name	NO. of Animals	GOT IU/@	?	GPT IU∕ℓ		LDH IU/e		ALP IU/0		CPK IU/	ę	UREA NI mg/dl	TROGEN	SODIUM mEq/l	
Control	9	45±	3	12±	3	249±	39	276±	23	55±	20	21.1±	1.5	153±	2
500 ppm	10	50±	9	14±	5	257±	74	274±	37	59±	35	18.5±	2.7	153±	2
2000 ppm	10	52±	15	14±	2	261±	37	289±	31	64±	24	20.4±	4.0	153±	1
4000 ppm	10	53±	10	15±	3	270±	34	300±	32	83±	22	21.0土	3.2	153±	2
8000 ppm	10	52±	6	14±	2	253±	78	334±	27**	111±	165	21.4±	2.0	153±	1
10000 ppm	10	50±	9	12±	1	255±	66	324±	39*	59±	26	20.2±	2.8	153±	2
16000 ppm	9	59±	6**	16±	3**	270±	43	480±	59**	83±	30	22.4±	3.5	155±	2
Significant	difference;	*: P ≤ 0	.05 *	*: P ≤ 0.01				Test of Dun	nett						
ICL074)						-	·								BA

PAGE: 5

STUDY NO. : 0186 ANIMAL : MOUSE BDF1
REPORT TYPE : A1 BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (14)

SEX : FEMALE

Group Name	NO. of Animals	POTASSIUM mEq∕ℓ		CHLORIDE mEq∕ℓ		mg∕48 CALCIUM	mg∕dl Tg/dl		IC PHOSPHORUS	
Control	9	4.7±	0.5	122±	3	8.8±	0.2	6.3±	1.5	
500 ppm	10	4.4±	0.6	123±	3	8.9±	0.3	7.0±	0.9	
2000 ppm	10	4.7±	0.3	121±	4	8.9±	0.3	7.3±	0.9	
4000 ppm	10	4.6±	0.5	121±	3	9.0±	0.4	6.6±	0.8	
8000 ppm	10	4.4±	0.4	122±	2	9.1±	0.2	6.2±	0.6	
10000 ppm	10	4.1±	0.5*	124士	2	9.1±	0.3	6.0±	1.0	
16000 ppm	9	4.2±	0.3	122±	3	9.1±	0.3	6.2±	1.2	
Significant	difference;	*: P ≤ 0	0.05	**: P ≤ 0.01				Test of Dun	nett	DATO

(HCL074)

BAIS 2

PAGE: 6

APPENDIX B 7-1

URINALYSIS (THIRTEEN—WEEK STUDY: SUMMARY)

RAT: MALE

 Δ

STUDY NO. : 0185

ANIMAL : RAT F344
SAMPLING DATE : 013-6

URINALYSIS

		Hq								Protein				Glucose		Keto	ne ba	dy_			Bili	rubin		
	Animals	5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	- ± + :	2+ 3-	+ 4+	CHI	- ± + 2+ 3+ 4	+ CHI	- : 	<u>+</u>	2+ 3	+ 4+	CHI		+ 2+	3+ C	HI
Control	10	0	0	0	0	0	8	2		0 0 7	3	0 0		10 0 0 0 0	0	1	9 0	0	0 0		10	0 0	0	
1000 ppm	10	0	0	0	0	2	8	0		0 0 7	3	0 0		10 0 0 0 0	0	1	9 0	0	0 0		10	0 0	0	
2000 ppm	10	0	0	0	0	0	9	1		0 0 7	3	0 0		10 0 0 0 0	0	1	9 0	0	0 0		10	0 0	0	
4000 ppm	10	0	0	0	0	3	6	1		0 0 7	3	0 0		10 0 0 0 0	0	5	5 0	0	0 0		10	0 0	0	
Mqq 0008	10	0	0	0	2	8	0	0	**	0 0 10	0	0 0		10 0 0 0 0	0	10	0 0	0	0 0	**	10	0 0	0	
16000 ppm	10	0	0	0	2	8	0	0	**	0 3 7	0	0 0	*	10 0 0 0 0	0	10	0 0	0	0 0	**	10	0 0	0	

STUDY NO. : 0185

ANIMAL : RAT F344

SAMPLING DATE: 013-6 SEX: MALE

REPORT TYPE : A1

URINALYSIS

TOUR Name	NO. of Animals	0ccult blood ± + 2+ 3+ CHI	Urobilinogen ± + 2+ 3+ 4+ CHI		
Control	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		
4000 ppm	10	8 1 1 0 0	10 0 0 0 0		
mqq 0008	10	9 1 0 0 0	10-0-0-0		
16000 ppm	10	9 0 1 0 0	10 0 0 0 0		
Significent	difference	; *: P ≤ 0.05 **	: P ≤ 0.01	Test of CHI SQUARE	
CL103)					BA

BAIS 2

APPENDIX B 7-2

URINALYSIS (THIRTEEN—WEEK STUDY: SUMMARY)

RAT: FEMALE

STUDY NO. : 0185

ANIMAL : RAT F344

URINALYSIS

SAMPLING DATE: 013-6
SEX: FEMALE REPORT TYPE: A1
PAGE: 3

roup Name	NO. of	_Hq								Prote	in				Gl	UCOS	:e				Ket	nna	bady_			Bil	irubi	n		-
	Animals	5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	- ±		2+	3+ 4+	CHI				2+ 3-	+ 4+	CHI			- 2+		+ CHI		+ 2+		CHI	
Control	10	0	0	0	0	3	7	0		0 9	9 1	0	0 0		10	0	0	0 (0 0		10	0	0 0	0	0	10	0 0	0		
1000 ppm	10	0	0	0	1	2	7	0		0 8	3 2	0	0 0		10	0	0	0	0 0		9	1	0 0	0	0	10	0 0	0		
2000 ppm	10	0	0	0	0	5	5	0		0 8	9 1	0	0 0		10	0	0	0	0 0		10	0	0 0	0	0	10	0 0	0		
4000 ppm	10	0	0	0	0	7	3	0		0 10	0	0	0 0		10	0	0	0	0 0		10	0	0 0	0	0	10	0 0	0		
mqq 0008	10	0	0	0	1	6	3	0		0 10	0	0	0 0		10	0	0	0	0 0		10	0	0 0	0	0	10	0 0	0		
16000 ppm	10	0	0	1	3	6	0	0	**	0 10	0	0	0 0		10	0	0	0	0 0		10	0	0 0	0	0	10	0 0	0		
											-																			
Significent	difference	; *	: P ≦	≦ 0.05	5	** :	P ≦	0.01						Tes-	t of C	HI S	SQUA	RE												
ICI 103)															-		_													

(JCL103)

STUDY NO. : 0185

ANIMAL : RAT F344

SAMPLING DATE: 013-6

URINALYSIS

SEX : FEMALE	REPORT	TYPE : A1		PAGE: 4
Group Name	NO. of Animals	Occult blood — ± + 2+ 3+ CHI	Urobilinogen ± + 2+ 3+ 4+ CHI	
	10	10.000		
Control	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	
4000 ppm	10	10 0 0 0 0	10 0 0 0 0	
Mqq 0008	10	10 0 0 0 0	10 0 0 0 0	
16000 ppm	10	10 0 0 0 0	10 0 0 0 0	
Significent	difference	; *: P ≤ 0.05 **	P ≤ 0.01 Test of CHI SQI	UARE
(JCL103)				BAIS 2

APPENDIX B 7-3

URINALYSIS (THIRTEEN—WEEK STUDY: SUMMARY)

MOSUE: MALE

URINALYSIS

STUDY NO. : 0186
ANIMAL : MOUSE BDF1 SAMPLING DATE: 013-6

SEX : MALE

REPORT TYPE : A1

PAGE: 1

coup Name	NO. of	_Hq				_			P	rot	ein				GL	JCOS	e			Ket	tone	bod	v			00	cnl.	t bl	.ood		
	Animals	5.0	6.0	6.5	7.0	7.5	8.0	8.5 CHI					- 3+	· 4+ CHI			_	2+ 3-	+ 4+ CHI			+ 2		4+	CHI				2+ 3	+ CH1	i
Control	10	0	0	1	4	4	1	0		0	0	5 5	5 0	0	10	0	0	0 (0 0	5	5	0	0 0	0		10	0	0	0	0	
500 ppm	10	0	0	4	5	1	0	0		0	0	3 6	6 1	. 0	10	0	0	0 (0 0	6	4	0	0 0	0		10	0	0	0	0	
2000 ppm	10	0	1	4	1	3	1	0		0	0	4 6	3 0	0 .	10	0	0	0 (0 0	2	8	0	0 0	0		10	0	0	0	0	
4000 ppm	10	0	0	3	2	3	2	0		0	0	2 8	3 0	0	10	0	0	0	0 0	5	5	0	0 0	0		10	0	0	0	0	
8000 ppm	9	0	1	2	5	1	0	0		0	0	3 6	3 0	0	9	0	0	0	0 0	6	3	0	0 0	0		9	0	0	0	0	
10000 ppm	10	0	0	6	2	2	0	0		0	0	5 8	5 0	0	10	0	0	0	0 0	4	6	0	0 0	0		9	9 1	0	0	0	
16000 ppm	10	0	1	1	2	5	1	0		0	1	7 2	2 (0	10	0	0	0	0 0	7	3	0	0 0	0		10	0	0	0	0	
	+~-												•							· · ·						-					
Significent	t difference	; *:	P ≦	€ 0.05	5	** ;	P ≦	0.01						Tes	t of C	HI S	SQUA	RE													
JCL104)																															

(JCL104)

STUDY NO. : 0186

URINALYSIS

ANIMAL : MOUSE BDF1
SAMPLING DATE : 013-6

SEX : MALE

REPORT TYPE : A1

Group Name NO. of Urobilinogen ± + 2+ 3+ 4+ CHI Animals Control 10 10 0 0 0 0 500 ppm 10 10 0 0 0 0 2000 ppm 10 10 0 0 0 0 4000 ppm 10 10 0 0 0 0 8000 ppm 9 9 0 0 0 0 10000 ppm 10 10 0 0 0 0 16000 ppm 10 10 0 0 0 0 Significant difference ; $*: P \leq 0.05$ ** : $P \leq 0.01$ Test of CHI SQUARE

(JCL104)

BAIS 2

APPENDIX B 7-4

URINALYSIS (THIRTEEN—WEEK STUDY: SUMMARY)

MOSUE: FEMALE

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STUDY NO.: 0186

URINALYSIS

ANIMAL : MOUSE BDF1 SAMPLING DATE: 013-6 SEX: FEMALE

REPORT TYPE : A1

PAGE: 3

oup Name	NO. of	Hq								Prot	ein					Glu	COS	3			Ke	tone	bod s	dν				0ccı	ılt	bloo	nd	
	Animals	5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI		_		3+ 4	+	CHI			+ 2+	- 3+	4+ CHI					3+ 4+	C	HI				- 3+	CHI
																												·				
Control	10	0	0	8	2	0	0	0		0	4 6	0	0	0		10	0	0 (0	0	4	6	0	0	0 0)		10	0	0 (0	
500 ppm	10	0	5	5	0	0	0	0	*	0	0 10	0	0	0	*	10	0	0 (0	0	5	5	0	0	0 0)		10	0	0 (0	
2000 ppm	10	0	3	4	1	2	0	0		0	4 8	0	0	0		10	0	0 (0	0	8	2	0	0	0 0)		10	0	0 (0	
4000 ppm	10	0	5	3	2	0	0	0	*	0	5 5	0	0	0		10	0	0 (0	0	9	1	0	0	0 0) *	:	10	0	0 (0 0	
mqq 0008	10	0	1	8	1	0	0	0		0	5 5	0	0	0		10	0	0	0 0	0	10	0	0	0	0 () *	*	10	0	0	0 0	
10000 ppm	10	0	4	2	4	0	0	0	*	0	7 3	3 0	0	0		10	0	0	0 0	0	10	0	0	0	0 () *	*	10	0	0	0 0	
16000 ppm	9	0	0	1	2	4	2	0	**	0	7 2	2 0	0	0		9	0	0	0 0	0	7	2	0	0	0 ()		9	0	0	0 0	

(JCL104)

STUDY NO. : 0186

URINALYSIS

ANIMAL : MOUSE BDF1 SAMPLING DATE: 013-6

SEX : FEMALE

REPORT TYPE : A1

PAGE: 4 Group Name NO. of Urabilinagen ± + 2+ 3+ 4+ CHI Animals Control 10 10 0 0 0 0 500 ppm 10 10 0 0 0 0 2000 ppm 10 10 0 0 0 0 4000 ppm 10 10 0 0 0 0 mqq 0008 10 10 0 0 0 0 10000 ppm 10 10 0 0 0 0 16000 ppm 9 9 0 0 0 0 Significent difference ; $*: P \leq 0.05$ ** : $P \leq 0.01$ Test of CHI SQUARE

(JCL104)

APPENDIX B 8-1

GROSS FINDINGS (THIRTEEN—WEEK STUDY: SUMMARY)

RAT: MALE: SACRIFICED ANIMALS

1

STUDY NO. : 0185 ANIMAL : RAT F344

REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (14W)

PAGE: 1

Organ	Findings	Group Name NO. of Animals 1	Control 0 (%)	1000 ppm 10 (%)	2000 ppm 10 (%)	4000 ppn 10 (%)
liver	herniation		0 (0)	0 (0)	0 (0)	0 (0)
kidney	white patch/zone		0 (0)	0 (0)	0 (0)	0 (0)
	white zone		0 (0)	0 (0)	0 (0)	0 (0)
	elevated		0 (0)	0 (0)	0 (0)	0 (0)

(HPT080)

STUDY NO. : 0185 ANIMAL : RAT F344
REPORT TYPE : A1 SEX : MALE

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (14W)

PAGE: 2

Organ	Findings	Group Name NO. of Animals	10	8000 ppm (%)	1(16000 ppm) (%)	
liver	herniation		0	(0)		. (10)	
kidney	white patch/zone		0	(0)	;	(10)	
	white zone		1	(10)	() (0)	
	elevated		1	(10)	() (0)	
(HPT080)							BAIS 2

APPENDIX B 8-2

GROSS FINDINGS (THIRTEEN—WEEK STUDY: SUMMARY)

RAT: FEMALE: SACRIFICED ANIMALS

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STUDY NO. : 0185 ANIMAL : RAT F344

REPORT TYPE : A1 : FEMALE SEX

GROSS FINDINGS (SUMMARY)

SACRIFICED ANIMALS (14W)

1000 ppm 10 (%) 2000 ppm 10 (%) Group Name Control 10 (%) 4000 ppm 10 (%) Organ___ Findings_ NO. of Animals cyst 0 (0) 0 (0) 1 (10) 0 (0) ovary (HPT080) BAIS 2

STUDY NO. : 0185 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (14W)

APPENDIX B 8-3

GROSS FINDINGS (THIRTEEN—WEEK STUDY: SUMMARY)

MOSUE: FEMALE DEAD AND MORIBUND ANIMALS

STUDY NO. : 0186

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : FEMALE

GROSS FINDINGS (SUMMARY) DEAD AND MORIBUND ANIMALS (0- 14W)

Organ	Findings	Group Name NO. of Animals	Control 0 (%)	500 ppm 0 (%)	2000 ppm 0 (%)	4000 ppm 0 (%)
skin/app	absence		- (-)	- (-)	- (-)	- (-)
thymus	atrophic		- (-)	- (-)	- (-)	- (-)
whole body	wasting		- (-)	- (-)	- (-)	- (-)
(HPT080)						BAIS 2

STUDY NO. : 0186

ANIMAL : MOUSE BDF1

REPORT TYPE : A1
SEX : FEMALE

(HPT080)

GROSS FINDINGS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 14W)

Group Name 8000 ppm 10000 ppm 16000 ppm 0 (%) 0 (%) 0rgan_ Findings_ NO. of Animals 1 (%) skin/app - (-) absence - (-) 1 (100) - (-) thymus - (-) atrophic 1 (100) - (-) - (-) whole body wasting 1 (100)

BAIS 2

APPENDIX B 8-4

GROSS FINDINGS (THIRTEEN—WEEK STUDY: SUMMARY)

MOSUE: MALE: SACRIFICED ANIMALS

STUDY NO. : 0186

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : MALE GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (14W)

PAGE: 1

Organ	Findings	Group Name Control NO. of Animals 10 (%)	500 ppm 10 (%)	2000 ppm 10 (%)	4000 ppm 10 (%)
spleen	black zone	0 (0)	1 (10)	0 (0)	0 (0)
Liver	dark	0 (0)	0 (0)	0 (0)	0 (0)
kidney	white zone	1 (10)	1 (10)	0 (0)	0 (0)
	hydronephrosis	1 (10)	0 (0)	0 (0)	0 (0)

(HPT080)

Δ,

STUDY NO. : 0186

ANIMAL : MOUSE BDF1

REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)

SACRIFICED ANIMALS (14W)

Organ	Findings	Group Name NO. of Animals	mqq 0008 (%) 9	10000 ppm 10 (%)	16000 ppm 10 (%)
spleen	black zone		0 (0)	0 (0)	1 (10)
liver	dark		9 (100)	10 (100)	10 (100)
idney	white zone		1 (11)	0 (0)	0 (0)
	hydranephrosis		1 (11)	0 (0)	0 (0)

APPENDIX B 8-5

GROSS FINDINGS (THIRTEEN—WEEK STUDY: SUMMARY)

MOSUE: FEMALE: SACRIFICED ANIMALS

STUDY NO. : 0186

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : FEMALE GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (14W)

PAGE: 3

Organ	Findings	Group Name Control NO. of Animals 10 (%)	500 ppm 10 (%)	2000 ppm 10 (%)	4000 ppm 10 (%)
pleen	black zone	0 (0)	2 (20)	0 (0)	0 (0)
ver	dark	0 (0)	0 (0)	0 (0)	0 (0)
wary	cyst	0 (0)	0 (0)	0 (0)	0 (0)

STUDY NO. : 0186 ANIMAL : MOUSE BDF1

REPORT TYPE: A1

(HPT080)

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (14W)

SEX : FEMALE

Organ	Findings	Group Name NO. of Animals	8000 ppm 10 (%)	10000 ppm 10 (%)	16000 ppm 9 (%)	
spleen	black zone		1 (10)	1 (10)	0 (0)	
liver	dark		9 (90)	8 (80)	9 (100)	
ovary	cyst		0 (0)	1 (10)	0 (0)	

BAIS 2

APPENDIX B 9-1

ORGAN WEIGHT (THIRTEEN-WEEK STUDY: SUMMARY), ABSOLUTE

RAT: MALE

STUDY NO. : 0185 ANIMAL : RAT F344 REPORT TYPE : A1

SEX : MALE UNIT: g

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

PAGE: 1

up Name	NO. of Animals	Body W	Weight	ТНУИ	Z	ADREI	NALS	TESTI	25	HEAR	r	LUNG	S
Control	10	315±	25	0.231±	0.025	0.049±	0.006	2.879±	0.105	0.947±	0.077	1.012±	0.081
1000 ppm	10	320±	19	0.256±	0.035	0.051±	0.004	2.876±	0.083	0.944±	0.059	1.025±	0.079
2000 ppm	10	307±	20	0.231±	0.026	0.051±	0.005	2.865±	0.111	0.925±	0.068	1,016±	0,083
4000 ppm	10	289±	20*	0,195±	0.027**	0.050±	0.004	2.809±	0.254	0.882±	0.084	0.967±	0.091
8000 ppm	10	285±	11**	0.198±	0.015*	0.052±	0.007	2.837±	0.209	0.844±	0.041**	0.963±	0.064
16000 ppm	10	252±	12**	0.170±	0.015**	0.047±	0.004	2.866±	0.085	0.787±	0.038**	0.879±	0.052**

(HCL040)

STUDY NO. : 0185 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE

UNIT: g

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

PAGE: 2

up Name	NO. of Animals	KIDNEYS		SPLEEN		LIVER		BRA		
Control	10	1.838±	0.109	0.524±	0.046	7.688±	0.851	1.859±	.046	
1000 ppm	10	1.910±	0.090	0.536±	0.023	8.403±	0.520	1.886±	.071	
2000 ppm	10	1.868±	0.148	0.498±	0.033	8.346±	0.911	1.891±	.052	
4000 ppm	10	1.895±	0.148	0.500±	0.050	8.393±	0.754	1.874±	.045	
8000 ppm	10	1.935±	0.060	0.481±	0.023*	8.985±	0.412**	1.916±	.162	
16000 ppm	10	1.931±	0.097	0.445±	0.029**	8.784±	0.481**	1.799±	. 057	

(HCL040)

APPENDIX B 9-2

ORGAN WEIGHT (THIRTEEN-WEEK STUDY: SUMMARY), ABSOLUTE

RAT: FEMALE

STUDY NO. : 0185 ANIMAL : RAT F344 REPORT TYPE : A1
SEX : FEMALE

UNIT: g

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

PAGE: 3

Name	NO. of Animals	Body W	leight	ТНҮМ	JS	ADRE	NALS	OVAR	IES	HEAR	r	LUNG	S
Control	10	182±	8	0.187±	0.025	0.052±	0.003	0.097±	0.016	0.625±	0.027	0.762±	0.035
1000 ppm	10	176±	8	0.187±	0.016	0.052±	0.004	0.091±	0.011	0.618±	0.020	0.747±	0.026
2000 ppm	10	178±	9	0.189±	0.013	0.053±	0.004	0.115±	0.089	0.624±	0.027	0.759±	0.052
4000 ppm	10	168±	7**	0.176±	0.014	0.054±	0.003	0.094±	0.015	0.580±	0.030**	0.771±	0.046
mqq 0008	10	161±	8**	0.169±	0.015	0.051±	0.005	0.081±	0.012	0.548±	0.039**	0.718±	0.046
16000 ppm	10	156±	8**	0.162±	0.016**	0.046±	0.006**	0.074±	0.006**	0.535±	0.029**	0.696±	0.046**

STUDY NO.: 0185 ANIMAL: RAT F344

REPORT TYPE : A1
SEX : FEMALE
UNIT: g

Δ

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

PAGE: 4

up Name	NO. of Animals	KIDNE	YS	SPLE	EEN	LIVI	ER	BRA	
Control	10	1.189±	0.038	0.356±	0.019	4.266±	0.329	1.749±	0.070
1000 ppm	10	1.185±	0.031	0.340±	0.028	4.234±	0.210	1.747±	0.029
2000 ppm	10	1.162±	0.054	0.349±	0.030	4.310±	0.236	1.730±).031
4000 ppm	10	1.145±	0.083	0.350±	0.034	4.466±	0.419	1.763±	0.038
8000 ppm	10	1.140±	0.078	0.330±	0.033	4.663±	0.190*	1.716±	0.045
16000 ppm	10	1.171±	0.080	0.327±	0.036	5.117±	0.469**	1.761±	0.046

(HCL040)

APPENDIX B 9-3

ORGAN WEIGHT (THIRTEEN-WEEK STUDY: SUMMARY), ABSOLUTE

MOUSE: MALE

STUDY NO. : 0186

ANIMAL : MOUSE BDF1

REPORT TYPE : A1

SEX : MALE UNIT: g ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (14)

PAGE: 1

oup Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	29.4± 1.6	0.035± 0.009	0.013± 0.004	0.190± 0.027	0.140± 0.017	0.157± 0.014
500 ppm	10	28.7± 1.5	0.036± 0.006	0.011± 0.002	0.193± 0.023	0.135± 0.009	0.150± 0.013
2000 ppm	10	28.7± 2.3	0.036± 0.007	0.011± 0.004	0.188± 0.026	0.140± 0.012	0.153± 0.007
4000 ppm	10	26.9± 0.6	0.033± 0.004	0.011± 0.002	0.202± 0.020	0.134± 0.010	0.149± 0.007
8000 ppm	9	24.4± 1.9**	0.030± 0.005	0.010± 0.002	0.209± 0.021	0.127± 0.007	0.144± 0.012*
10000 ppm	10	25.1± 1.5**	0.033± 0.007	0.012± 0.004	0.197± 0.035	0.126± 0.010*	0.143± 0.006*
16000 ppm	10	21.9± 1.2**	0.028± 0.006	0.010± 0.002	0.190± 0.026	0.113± 0.012**	0.135± 0.009**

(HCL040)

STUDY NO. : 0186

ANIMAL : MOUSE BDF1

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

SEX: MALI UNIT: g

roup Name	NO. of Animals	KIDN	NEYS	SPLEEN		LIVER		BRA		
Control	10	0.521±	0.376	0.047±	0.007	1.044±	0.053	0.444±	0.015	
500 ppm	10	0.416±	0.030	0.040±	0.008	1.044±	0.052	0.443±	0.021	
2000 ppm	10	0.406±	0.023	0.043±	0.004	1.066±	0.082	0.441±	0.019	
4000 ppm	10	0.399±	0.020	0.044±	0.005	1.099±	0.042	0.445±	0.019	
8000 ppm	9	0.372±	0.027	0.045±	0.008	1.090±	0.094	0.438±	0.013	
10000 ppm	10	0.371±	0.015	0.043±	0.006	1.084±	0.052	0.427±	0.025	
16000 ppm	10	0.325±	0.026**	0.042±	0.008	1.077±	0.044	0.423±	0.013	

(HCL040)

BAIS 2

APPENDIX B 9-4

ORGAN WEIGHT (THIRTEEN-WEEK STUDY: SUMMARY), ABSOLUTE

MOUSE: FEMALE

STUDY NO. : 0186

ANIMAL : MOUSE BDF1
REPORT TYPE : A1

SEX: FEMALE
UNIT: g

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

PAGE: 3

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	21.4± 1.1	0.042± 0.005	0.011± 0.002	0.018± 0.005	0.114± 0.007	0.143± 0.008
500 ppm	10	21.7± 1.5	0.041± 0.007	0.012± 0.002	0.019± 0.003	0.115± 0.009	0.145± 0.011
2000 ppm	10	21.5± 1.3	0.044± 0.007	0.013± 0.002	0.019± 0.004	0.116± 0.011	0.146± 0.012
4000 ppm	10	20.7± 0.8	0.041± 0.005	0.013± 0.001	0.021± 0.005	0.109± 0.008	0.143± 0.010
Mqq 0008	10	20.3± 0.7	0.041± 0.004	0.012± 0.002	0.018± 0.004	0.106± 0.008	0.136± 0.009
10000 ppm	10	19.4± 1.0**	0.039± 0.005	0.012± 0.002	0.022± 0.009	0.105± 0.010	0.132± 0.005*
16000 ppm	9	18.6± 0.5**	0.041± 0.004	0.011± 0.003	0.020± 0.005	0.090± 0.007**	0.132± 0.010
Significant	difference;	*: P ≤ 0.05 **:	P ≤ 0.01	Test	of Dunnett		

(HCL040)

STUDY NO. : 0186
ANIMAL : MOUSE BDF1

REPORT TYPE : A1

SEX : FEMALE

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

UNIT: g

roup Name	NO. of Animals	KIDNEY	YS	SPLI	EEN	LIV	ER	BRA	N .	
Control	10	0.284± (0.015	0.051±	0.004	0.854±	0.038	0.448±	0.019	
500 ppm	10	0.288± (0.014	0.052±	0.005	0.883±	0.063	0.446±	0.015	
2000 ppm	10	0.289± (0.015	0.049±	0.007	0.874±	0.051	0.454±	0.024	
4000 ppm	10	0.273± 0	0.013	0.051±	0.006	0.899±	0.055	0.447±	0.016	
8000 ppm	10	0.268± (0.020	0.051±	0.008	0.996±	0.050**	0.454±	0.022	
10000 ppm	10	0.258± (0.013**	0.046±	0.009	0.897±	0.074	0.446±	0.010	
16000 ppm	9	0.253± (0.012**	0.045±	0.007	1.009±	0.064**	0.424±	0.013*	
Significant	difference;	*: P ≦ 0.05	** :	P ≦ 0.01			Tes	t of Dunnet		

(HCL040)

BAIS 2

APPENDIX B 10-1

ORGAN WEIGHT (THIRTEEN-WEEK STUDY: SUMMARY), RELATIVE

RAT: MALE

STUDY NO. : 0185

ANIMAL : RAT F344

REPORT TYPE : A1
SEX : MALE
UNIT: %

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

PAGE: 1

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.0	315±	25	0.073± 0.007	0.016± 0.001	0.917± 0.056	0.301± 0.017	0.322± 0.025
0	320±	19	0.080± 0.009	0.016± 0.001	0.901± 0.042	0.296± 0.016	0.321± 0.017
0	307±	20	0.075± 0.006	0.017± 0.002	0.936± 0.042	0.302± 0.011	0.332± 0.020
0	289±	20*	0.067± 0.008	0.017± 0.002	0.972± 0.082	0.305± 0.017	0.334± 0.025
0	285±	11**	0.069± 0.003	0.018± 0.002*	0.996± 0.070*	0.296± 0.013	0.338± 0.021
0	252±	12**	0.068± 0.006	0.019± 0.002**	1.139± 0.046**	0.313± 0.017	0.349± 0.015*
.0		307± 289± 285±	307± 20 289± 20* 285± 11**	307 ± 20 0.075 ± 0.006 $289\pm 20*$ 0.067 ± 0.008 $285\pm 11**$ 0.069 ± 0.003 $252\pm 12**$ 0.068 ± 0.006	307± 20 0.075± 0.006 0.017± 0.002 289± 20* 0.067± 0.008 0.017± 0.002 285± 11** 0.069± 0.003 0.018± 0.002* 252± 12** 0.068± 0.006 0.019± 0.002**	307± 20 0.075± 0.006 0.017± 0.002 0.936± 0.042 289± 20* 0.067± 0.008 0.017± 0.002 0.972± 0.082 285± 11** 0.069± 0.003 0.018± 0.002* 0.996± 0.070* 252± 12** 0.068± 0.006 0.019± 0.002** 1.139± 0.046**	307 ± 20 0.075 ± 0.006 0.017 ± 0.002 0.936 ± 0.042 0.302 ± 0.011 $289\pm 20*$ 0.067 ± 0.008 0.017 ± 0.002 0.972 ± 0.082 0.305 ± 0.017 $285\pm 11**$ 0.069 ± 0.003 $0.018\pm 0.002*$ $0.996\pm 0.070*$ 0.296 ± 0.013 $252\pm 12**$ 0.068 ± 0.006 $0.019\pm 0.002**$ $1.139\pm 0.046**$ 0.313 ± 0.017

(HCL042)

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STUDY NO. : 0185 ANIMAL : RAT F344 REPORT TYPE : A1

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

SEX : MALE UNIT: %

up Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	
Control	10	0.584± 0.028	0.166± 0.005	2.437± 0.162	0.593± 0.046	
1000 ppm	10	0.598± 0.025	0.168± 0.009	2.627± 0.054	0.591± 0.028	
2000 ppm	10	0.609± 0.019	0.162± 0.008	2.715± 0.144	0.618± 0.035	
4000 ppm	10	0.655± 0.027**	0.173± 0.021	2.898± 0.122**	0.650± 0.047*	
8000 ppm	10	0.679± 0.016**	0.169± 0.006	3.152± 0.062**	0.673± 0.066**	
16000 ppm	10	0.766士 0.028**	0.177± 0.007*	3.486± 0.130**	0.715± 0.037**	

(HCL042)

BAIS 2

APPENDIX B 10-2

ORGAN WEIGHT (THIRTEEN-WEEK STUDY: SUMMARY), RELATIVE

RAT: FEMALE

STUDY NO. : 0185 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE UNIT: %

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

roup Name	NO. of Animals	Bady W	eight g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS	
Control	10	182±	8	0.103± 0.011	0.029± 0.002	0.053± 0.007	0.344± 0.016	0.420± 0.020	
1000 ppm	10	176土	8	0.107± 0.010	0.029± 0.002	0.052± 0.007	0.352± 0.017	0.425± 0.016	
2000 ppm	10	178±	9	0.107± 0.007	0.030± 0.003	0.064± 0.048	0.352± 0.017	0.427± 0.022	
4000 ppm	10	168±	7**	0.105± 0.006	0.032± 0.002*	0.056± 0.010	0.346± 0.013	0.459± 0.017**	
mqq 0008	10	161±	8**	0.105± 0.007	0.032± 0.003*	0.050± 0.006	0.341± 0.020	0.447± 0.020*	
16000 ppm	10	156土	8**	0.104± 0.007	0.030± 0.003	0.047± 0.003	0.344± 0.027	0.447± 0.022*	
Significant	difference;	*: P ≤ 0.0	5 **	: P ≤ 0.01	Tes	t of Dunnett			
CL042)	····								BA

STUDY NO. : 0185 ANIMAL : RAT F344
REPORT TYPE : A1 SEX : FEMALE UNIT: %

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

PAGE: 4

oup Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	
Control	10	0.655± 0.032	0.196± 0.013	2.349± 0.164	0.963± 0.037	
1000 ppm	10	0.675± 0.038	0.193± 0.011	2.408± 0.115	0.994± 0.043	
2000 ppm	10	0.655± 0.027	0.196± 0.015	2.427± 0.115	0.976± 0.046	
4000 ppm	10	0.682± 0.039	0.208± 0.015	2.663± 0.240*	1.052± 0.041**	
mqq 0008	10	0.709± 0.027**	0.205± 0.013	2.903± 0.054**	1.069± 0.035**	
16000 ppm	10	0.751± 0.027**	0.210± 0.015	3.282± 0.209**	1.132± 0.054**	

(HCL042)

APPENDIX B 10-3

ORGAN WEIGHT (THIRTEEN-WEEK STUDY: SUMMARY), RELATIVE

MOUSE: MALE

4.

STUDY NO. : 0186

ANIMAL : MOUSE BDF1

REPORT TYPE : A1
SEX : MALE
UNIT: %

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

PAGE: 1

roup Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	29.4± 1.6	0.117± 0.031	0.045± 0.013	0.645± 0.080	0.477± 0.069	0.534± 0.065
500 ppm	10	28.7± 1.5	0.126± 0.021	0.037± 0.008	0.673± 0.081	0.473± 0.036	0.525± 0.055
2000 ppm	10	28.7± 2.3	0.125± 0.024	0.040± 0.012	0.659± 0.103	0.488± 0.036	0.534± 0.048
4000 ppm	10	26.9± 0.6	0.122± 0.015	0.041± 0.006	0.751± 0.078	0.499± 0.034	0.556± 0.026
8000 ppm	9	24.4± 1.9**	0.121± 0.019	0.042± 0.009	0.862± 0.110**	0.523± 0.037	0.592± 0.025
10000 ppm	10	25.1± 1.5**	0.131± 0.026	0.047± 0.016	0.786± 0.137*	0.501± 0.037	0.570± 0.036
16000 ppm	10	21.9± 1.2**	0.127± 0.025	0.045± 0.009	0.869± 0.112**	0.515± 0.047	0.618± 0.020**

(HCL042)

STUDY NO. : 0186 ANIMAL : MOUSE BDF1

REPORT TYPE : A1

SEX : MALE UNIT: %

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

PAGE: 2

TOUR Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	
Control	10	1.815± 1.456	0.159± 0.030	3.556± 0.230	1.511± 0.080	
500 ppm	10	1.452± 0.098	0.138± 0.025	3.638± 0.092	1.549± 0.106	
2000 ppm	10	1.415± 0.071	0.151± 0.017	3.709± 0.076	1.542± 0.142	
4000 ppm	10	1.484± 0.074	0.163± 0.019	4.092± 0.127*	1.657± 0.067*	
8000 ppm	9	1.531± 0.154	0.182± 0.023	4.468± 0.113**	1.805± 0.150**	
10000 ppm	10	1.483± 0.089	0.171± 0.023	4.324± 0.171**	1.707± 0.143**	
16000 ppm	10	1.485± 0.083	0.191± 0.030*	4.931± 0.113**	1.938± 0.093**	

(HCL042)

APPENDIX B 10-4

ORGAN WEIGHT (THIRTEEN-WEEK STUDY: SUMMARY), RELATIVE

MOUSE: FEMALE

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STUDY NO. : 0186 ANIMAL : MOUSE BDF1

REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

PAGE: 3

roup Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS	
Control	10	21.4± 1.1	0.194± 0.018	0.051± 0.007	0.086± 0.023	0.532± 0.022	0.669± 0.027	
500 ppm	10	21.7± 1.5	0.187± 0.026	0.054± 0.010	0.088± 0.012	0.529± 0.056	0.666± 0.036	
2000 ppm	10	21.5± 1.3	0.204± 0.028	0.060± 0.010	0.087± 0.016	0.538± 0.051	0.679± 0.038	
4000 ppm	10	20.7± 0.8	0.199± 0.022	0.062± 0.005	0.101± 0.024	0.527± 0.044	0.691± 0.052	
mqq 0008	10 -	20.3± 0.7	0.203± 0.017	0.057± 0.008	0.091± 0.018	0.524± 0.041	0.672± 0.032	
10000 ppm	10	19.4± 1.0**	0.199± 0.019	0.061± 0.014	0.115± 0.048	0.545± 0.049	0.681± 0.030	
16000 ppm	9	18.6± 0.5**	0.221± 0.021	0.060± 0.014	0.105± 0.028	0.482± 0.042	0.707土 0.048	

(HCL042)

STUDY NO. : 0186 ANIMAL : MOUSE BDF1 REPORT TYPE : A1

REPORT TYPE : SEX : FEMALE UNIT: %

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

PAGE: 4

-oup Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	
Control	10	1.327± 0.071	0.239± 0.020	3.989± 0.194	2.095± 0.122	
500 ppm	10	1.331± 0.076	0.239± 0.019	4.065± 0.201	2.060± 0.170	
2000 ppm	10	1.345± 0.078	0.226± 0.030	4.063± 0.192	2.115± 0.116	
4000 ppm	10	1.323± 0.081	0.249± 0.030	4.354± 0.205**	2.166± 0.125	
8000 ppm	10	1.324± 0.061	0.254± 0.036	4.917± 0.145**	2.240± 0.081*	
10000 ppm	10	1.333± 0.052	0.238± 0.039	4.631± 0.194**	2.308± 0.119**	
16000 ppm	9	1.359± 0.066	0.239± 0.038	5.411± 0.270**	2.274± 0.079**	

(HCL042)

APPENDIX B 11-1

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS

(THIRTEEN-WEEK STUDY: SUMMARY)

RAT: MALE: SACRIFICED ANIMALS

STUDY NO. : 0185

ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (14W)

organ	Findings	No. of Animals 10 <1> <2> <3> <4> (%) (%) (%) (%)	10 <1> <2> <3> <4> (%) (%) (%) (%)	10 <1> <2> <3> <4> (%) (%) (%) (%)	4000 ppm 10 <1> <2> <3> <4> (%) (%) (%) (%) (%)
		(6) (6) (6)		(4) (4) (4)	(8) (8) (8)
Respiratory s	ystem]				
asal cauit	respiratory metaplasia:gland	4 0 0 0 (40) (0) (0) (0)	3 0 0 0 0 (30) (0) (0) (0)	6 0 0 0 0 (60) (0) (0)	3 0 0 0 0 (30) (0) (0) (0)
ung	osseous metaplasia	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0)	2 0 0 0 0 (20) (0) (0) (0)
Circulatory s	vstem]				
eart	granulation	0 0 0 0 0 (0) (0)	1 0 0 0 (10) (0) (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
Digestive sys	tem]				
iver	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 0 0 0 0 (0) (0)
	swelling of livor coll	(0) (0) (0) (0)	0 0 0 0 0 0 (0) (0)	1 0 0 0 (10) (0) (0) (0)	0 0 0 0 0 (0) (0)
Urinary system	n]				
idney	basophilic change	0 0 0 0 0 (0) (0) (0)	2 0 0 0 (20) (0) (0) (0)	2 0 0 0 0 (20) (0) (0)	3 0 0 0 (30) (0) (0) (0)
	easinaphilic body	0 10 0 0 (0) (100) (0) (0)	0 10 0 0 (0) (100) (0) (0)	2 7 0 0 (20) (70) (0) (0)	1 9 0 0 (10) (90) (0) (0)
	hyaline cast	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 0 (10) (0) (0) (0)
	mineralization:cortico-medullary junction	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0)	1 2 0 0 (10) (20) (0) (0)
ignificant di	fference; *: P ≤ 0.05 **: P ≤ 0.01	Test of Chi Square <1>:Slig	ht <2>:Moderate <	:3>:Marked <4>:Severe	

STUDY NO. : 0185 ANIMAL : RAT F344

REPORT TYPE : A1
SEX : MALE SEX

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (14W)

gan	Findings	Group Name 8000 ppm No. of Animals 10 <1> <2> <3> <4>	16000 ppm 10 · · · · · · · · · · · · · · · · · · ·	
Respiratory s	system]			
asal cavit	respiratory metaplasia:gland	2 0 0 0 (20) (0) (0) (0)	2 0 0 0 (20) (0) (0) (0)	
ing	osseous metaplasia	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	
Circulatory s	system]			
eart	granulation	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	
)igestive sys	stem]	•		
i ver	granulation	1 0 · 0 0 (10) (10) (10) (10)	0 0 0 0 0 (0) (0) (0)	
	swelling of liver cell	7 0 0 0 ** (70) (0) (0) (0)	10 0 0 0 *** (100) (0) (0) (0)	·
Jrinary syste	em]			
idney	basophilic change	7 3 0 0 ** (70) (30) (0) (0)	0 10 0 0 ** (0) (100) (0) (0)	
	easinophilic body	1 8 1 0 (10) (80) (10) (0)	2 8 0 0 (20) (80) (0) (0)	
	hyaline cast	0 2 0 0 (0) (20) (0) (0)	1 4 0 0 * (10) (40) (0) (0)	
	mineralization:cortico-medullary junction	3 3 0 0 * (30) (30) (0) (0)	5 1 0 0 * (50) (10) (0) (0)	

STUDY NO. : 0185 ANIMAL : RAT F344 REPORT TYPE : A1

: MALE

SEX

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

PAGE: 3

Organ	Findings	Group Name Control No. of Animals 10 <1> <2> <3> <4 (%) (%) (%) (%)		2000 ppm 10 <1> <2> <3> <4> (%) (%) (%) (%)	4000 ppm 10 <1> <2> <3> <4> (%) (%) (%) (%)
[Urinary syst	em]				
kidney	mineralization: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)
	dilatation:tubular lumen	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
	desquamation:pelvis	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0		0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0)
urin bladd	mineralization	0 0 0 0 0 0 0 0 0 0 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 sy	stem]				
pituitary	cyst	0 0 0 0 0		0 0 0 0 0 (0) (0)	1 0 0 0 (10) (0) (0) (0)
[Reproductive	system]				
testis	atrophy	0 0 0 0 0		0 0 0 0 0 (0) (0)	0 0 1 0 (0) (10) (0)
prostate	lymphocytic infiltration	1 0 0 0 0 10 10 10 10 10 10 10 10 10 10		0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
Significant d	lifference; *: P ≤ 0.05 **: P	≤ 0.01 Test of Chi Square <1>:5	light <2>:Moderate <	3>:Marked <4>:Severe	
(HPT150)					ВА

STUDY NO. : 0185 ANIMAL : RAT F344 REPORT TYPE : A1

[Urinary system]

kidney

urin bladd

[Endocrine system]

: MALE

Findings_

mineralization

SEX

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (14W)

Group Name mqq 0008 16000 ppm No. of Animals 10 10 <1> ⟨2⟩ ⟨3⟩ ⟨4⟩ <1> ⟨2⟩ ⟨3⟩ ⟨4⟩ (%) (%) (%) (%) (%) (%) (%) (%) mineralization:papilla 3 2 0 * (10) (0) (0) (0) (30) (20) (0) (0) dilatation:tubular lumen 3 0 0 * (0)(0)(0)(0) (20) (30) (0) (0) desquamation:pelvis 0 0 0 0 2 3 0 0 * (0)(0)(0)(0) (20) (30) (0) (0) 2 0 0 0 0 0 0 0 (20) (0) (0) (0) (0)(0)(0)(0)

pituitary	cyst	(1	1 (0)	0 0)	(0 0)	(0 0)	(0	(0 0)	(0 0)		0
[Reproductive	system]															
testis	atrophy	(0 0)	0 0)	(1 10)		0 0)	(0 0)	(0 0)	(0 0)		0 0)
prostate	lymphocytic infiltration	(0 0)	0 0)		0 0)		0 0)	(0		0 0)	(0 0)	(0 0)

Significant difference; * : $P \le 0.05$ ** : $P \le 0.01$ Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

(HPT150)

BAIS2

APPENDIX B 11-2

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS

(THIRTEEN-WEEK STUDY: SUMMARY)

RAT: FEMALE: SACRIFICED ANIMALS

STUDY NO. : 0185 ANIMAL : RAT F344 REPORT TYPE : A1

SEX

(HPT150)

: FEMALE

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS (SUMMARY)

PAGE: 5

BAIS2

SACRIFICED ANIMALS (14W)

Group Name Control 1000 ppm 2000 ppm 4000 ppm No. of Animals 10 10 10 10 ⟨2⟩ ⟨3⟩ ⟨4⟩ <1> ⟨2⟩ ⟨3⟩ ⟨4⟩ (2) (3) (4) <2> 〈3〉 〈4〉 (1) (1) (%) (%) (%) (%) 0rgan____ Findings_ (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) [Respiratory system] nasal cavit inflammation:squamous epithelium 0 0 0 0 1 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (10) (0) (0) (0) respiratory metaplasia:gland 0 0 2 0 0 0 0 (20) (0) (0) (0) (20) (0) (0) (0) (20) (0) (0) (0) (30) (0) (0) (0) lung osseous metaplasia (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) [Hematopoietic system] bone marrow granulation 0 2 0 2 (10) (20) (0) (0) (0)(20)(0)(0) (10) (20) (0) (0) (20) (0) (0) (0) spleen deposit of hemosiderin 3 0 0 0 4 0 (40) (0) (0) (0) (30) (0) (0) (0) (20) (0) (0) (0) (20) (0) (0) (0) [Digestive system] inflammation: foreign body tangue 0 1 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(10)(0)(0) Liver granulation (10) (10) (0) (0) (20) (10) (0) (0) (20) (0) (0) (0) (0)(10)(0)(0) swelling of liver cell 0 0 0 0 0 0 0 0 0 0 0 0 1 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (10) (0) (0) (0) [Urinary system] kidney basophilic change 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) Significant difference; $*:P \le 0.05$ $**:P \le 0.01$ Test of Chi Square <1>:Slight <2>:Moderate <4>:Severe <3>: Marked

STUDY NO. : 0185 ANIMAL : RAT F344

REPORT TYPE : A1
SEX : FEMALE

(HPT150)

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS (SUMMARY)

PAGE: 6

BAIS2

SACRIFICED ANIMALS (14W)

Group Name 8000 ppm 16000 ppm No. of Animals 10 10 <1> <2> ⟨3⟩ **<4>** ⟨2⟩ ⟨3⟩ ⟨4⟩ Findings (%) (%) (%) (%) (%) (%) (%) (%) [Respiratory system] nasal cavit inflammation:squamous epithelium 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) respiratory metaplasia:gland (40)(0)(0)(0) (30) (0) (0) (0) lung osseous metaplasia 1 0 0 0 (10) (0) (0) (0) (0)(0)(0)(0) [Hematopoietic system] bone marrow granulation (10) (0) (0) (0) (0)(0)(0)(0) spleen deposit of hemosiderin 3 0 0 (30) (0) (0) (0) (40) (0) (0) (0) [Digestive system] tongue inflammation: foreign body (0) (0) (0) (0) (0)(0)(0)(0) Liver granulation (0)(0)(0)(0) (0)(0)(0)(0) swelling of liver cell 8 0 0 0 ** 10 0 0 0 ** (80) (0) (0) (0) (100) (0) (0) (0) [Urinary system] kidney basophilic change 0 (10) (0) (0) (0) (10) (10) (0) (0) Significant difference; $*: P \le 0.05$ $**: P \le 0.01$ Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

STUDY NO. : 0185 ANIMAL : RAT F344 REPORT TYPE : A1

: FEMALE

SEX

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS (SUMMARY)

PAGE: 7

BAIS2

SACRIFICED ANIMALS (14W)

Group Name 4000 ppm Control 1000 ppm 2000 ppm No. of Animals 10 10 10 10 <1> <2> <3> <2> <3> <4> 〈2〉 〈3〉 〈4〉 ⟨2⟩ ⟨3⟩ ⟨4⟩ <4> <1> <1> <1> (%) (%) Findings_ (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) [Urinary system] kidney hyaline cast 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0) (0) (0) (0) (0)(0)(0)(0) (0)(0)(0)(0) mineralization:cortico-medullary junction 4 6 0 0 (60) (30) (0) (0) (40) (60) (0) (0) (30) (60) (0) (0) (40) (60) (0) (0) dilatation:tubular lumen 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) desquamation:pelvis 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) [Reproductive system] DUALLA cyst 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(10)(0)(0) (0)(0)(0)(0) [Special sense organs/appandage] Harder gl lymphocytic infiltration 0 1 0 0 (0)(10)(0)(0) (0) (10) (0) (0) (0)(0)(0)(0) (0)(0)(0)(0) Significant difference; * : $P \le 0.05$ ** : $P \le 0.01$ Test of Chi Square <1>:Slight <3>:Marked <2>:Moderate <4>:Severe (HPT150)

STUDY NO. : 0185 ANIMAL : RAT F344

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

SACRIFICED ANIMALS (14W)

Group Name Mqq 0008 16000 ppm No. of Animals 10 10 〈2〉 〈3〉 〈4〉 <1> <2> <3> <4> <1> Findings (%) (%) (%) (%) (%) (%) (%) (%) [Urinary system] kidney hyaline cast 2 0 0 0 1 5 0 0 * (20) (0) (0) (0) (10) (50) (0) (0) mineralization:cortico-medullary junction 4 5 0 0 (40) (50) (0) (0) (20) (40) (0) (0) dilatation:tubular lumen 0 0 0 0 -1 2 0 0 (0)(0)(0)(0) (10) (20) (0) (0) desquamation:pelvis 1 0 0 0 3 4 0 0 ** (10) (0) (0) (0) (30) (40) (0) (0) [Reproductive system] ovary cyst (0)(0)(0)(0) (0)(0)(0)(0) [Special sense organs/appandage] lymphocytic infiltration Harder gl 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) Significant difference; $*: P \le 0.05$ $**: P \le 0.01$ Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe (HPT150) BAIS2

APPENDIX B 11-3

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS

(THIRTEEN-WEEK STUDY: SUMMARY)

MOUSE: MALE: SACRIFICED ANIMALS

STUDY NO. : 0186

ANIMAL : MOUSE BDF1
REPORT TYPE : A1 SEX : MALE

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

0rgan	Findings	Group Name No. of Animals <1> (%)	Control 10 (2> (3> (%) (%)	<4> (%)	<1> (%)	500 10 <2> (%)	<pre>ppm <3> (%)</pre>	<4> (%)	<1> (%)	200 (2) (%)	0 ppm 0 (3> (%)	<4> (%)	<1> (%)			<4>
[Respiratory :	system]															
nasal cavit	eosinophilic change: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)	1 (10)	(0)	0 (0)	0 (0)
[Hematopoietio	c system]															
spleen	deposit of melanin	0 (0) (0 0	0 (0)	1 (10) (0	0	0	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Digestive sy	stem]															
stomach	hyperplasia:forestomach	0 (0) (0 0	0 (0)	0 (0) (0	0	0 (0)	0 (0)	0	0 (0)	0 (0)	(0)	(0)	(0)	(0)
Liver	granulation	4 (40) (0 0 0) (0)	0 (0)	3 (30) (0 0) (0	0 (0)	5 (50)	0 (0)	0 (0)	0 (0)	5 (50)	0 (0)	0 (0)	0 (0)
	swelling of liver cell	0 (0) (0 0	0 (0)	0 (0) (0 0) (0 0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Urinary syst	em]															
<idney< td=""><td>basophilic change</td><td>1 (10) (</td><td>0 0</td><td>0 (0)</td><td>0 (0) (</td><td>0</td><td>0 0)</td><td>0</td><td>0 (0)</td><td>0 (0)</td><td>0 (0)</td><td>0 (0)</td><td>1 (10)</td><td>(0)</td><td>0 (0)</td><td>(0)</td></idney<>	basophilic change	1 (10) (0 0	0 (0)	0 (0) (0	0 0)	0	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	(0)	0 (0)	(0)
	hyaline cast	0 (0) (0 0 0) (0)	0 (0)	0 (0) (0 0) (0	0 (0)	0 (0)	0	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	osseous metaplasia	0 (0) (0 0	0 (0)	0 (0) (0 0) (0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	(0)	0 (0)	0 (0)	0 (0)
	inflammatory polyp	0 (0) (0 1 0) (10)	0 (0)	(0) (0	0 (0)	0 (0)	0 (0)	0	0 (0)	0 (0).	0 (0)	0 (0)	0 (0)	0 (0)
Significant d	ifference; *: P ≤ 0.05 **: P ≤ 0.01	. Test of Chi Square		1>:Slight		>:Mode			(3>:Marked			Severe				

 Δ

STUDY NO. : 0186

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : MALE HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (14W)

PAGE: 2 Group Name Mqq 0008 10000 ppm 16000 ppm No. of Animals 9 10 10 <2> <3> <2> ⟨3⟩ <2> <3> <1> **〈4〉** <1> (4) <1> (4) Organ_ Findings (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) [Respiratory system] nasal cavit eosinophilic change:olfactory epithelium 0 0 0 0 0 (0)(0)(0)(0) (10) (0) (0) (0) (10) (0) (0) (0) [Hematopoietic system] spleen deposit of melanin 0 0 0 1 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(10)(0)(0) [Digestive system] stomach hyperplasia: forestomach 0 0 (0)(0)(0)(0) (0)(10)(0)(0) (0)(0)(0)(0) Liver granulation 5 0 0 0 0 0 3 0 0 0 (56) (0) (0) (0) (40) (0) (0) (0) (30) (0) (0) (0) swelling of liver cell 0 0 ** 10 0 ** 10 0 0 ** . (100) (0) (0) (0) (100) (0) (0) (0) (100) (0) (0) (0) [Urinary system] kidney basophilic change 2 0 0 0 (11) (0) (0) (0) (30) (0) (0) (0) (20) (0) (0) (0) hyaline cast 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (40) (0) (0) (0) osseous metaplasia 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (10) (0) (0) (0) inflammatory polyp 0 (0)(0)(11)(0) (0)(0)(0)(0) (0)(0)(0)(0)

<1>:Slight

<2>: Moderate

<3>:Marked

<4>:Severe

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

 \triangle

STUDY NO. : 0186

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : MALE HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (14W)

		Group Name Control No. of Animals 10	500 ppm 10	2000 ppm 10	4000 ppm 10					
rgan	Findings	<1> <2> <3> <4> (%) (%) (%) (%)	<1> <2> <3> <4> (%) (%) (%) (%)	<1> <2> <3> <4> (%) (%) (%) (%)	<1> <2> <3> <4>(%) (%) (%) (%)					
rinary sys	tem]									
dney	vacuolization of proximal tubule	3 0 0 0 0 (30) (30) (30) (30)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	1 0 0 0 0 (10) (0) (0)					
	hydronephrosis	0 0 1 0 (0) (0) (10) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)					
	mineralization:papilla	0 0 0 0 0 (0) (0)	1 0 0 0 (10) (0) (0) (0)	1 0 0 0 0 (10) (0) (0)	1 0 0 0 0 (10) (10) (10)					
	desquamation:pelvis	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0) (0)					

STUDY NO. : 0186

ANIMAL : MOUSE BDF1

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

SACRIFICED ANIMALS (14W)

Group Name Mqq 0008 10000 ppm 16000 ppm No. of Animals 9 10 10 <1> <2> <3> <4> <1> <2> <3> <4> <1> 〈2〉 〈3〉 〈4〉 (%) (%) Findings_ (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) [Urinary system] kidney vacuolization of proximal tubule 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) hydronephrosis 0 0 0 0 (0) (0) (11) (0) (0)(0)(0)(0) (0)(0)(0)(0) mineralization:papilla 1 0 0 0 0 0 0 0 0 0 0 0 (0) (0) (0) (0) (11) (0) (0) (0) (0)(0)(0)(0) desquamation:pelvis 0 0 0 0 0 0 0 0 8 0 0 0 ** (0)(0)(0)(0) (0)(0)(0)(0) (80) (0) (0) (0) Significant difference ; * : $P \le 0.05$ ** : $P \le 0.01$ Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe (HPT150) BAIS2

APPENDIX B 11-4

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS

(THIRTEEN-WEEK STUDY: SUMMARY)

MOUSE: FEMALE: SACRIFICED ANIMALS

STUDY NO. : 0186

ANIMAL : MOUSE BDF1

REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS (SUMMARY)

PAGE: 5

SACRIFICED ANIMALS (14W)

0rgan	Findings	Group Name No. of Animals <1> (%)		<3>	<4> (%)	<1> (%)	500 10 <2> (%)	mqq () (%)	<4> (%)	<1> (%)	200 (2> (%)	0 ppm 0 <3> (%)	<4> (%)	<12 (%)	> <2		s> <	<4> (%)
[Respiratory s	system]																	
nasal cavit	eosinophilic change:olfactory epithelium	1 (10)	0 (0) (0 (0 0)	1 (10)	0	0 (0) (0	0 (0) (0 0)	0 (0)	0 (0)	1 (10)) (0
	eosinophilic change:respiratory epithelium	0 (0) (0 (0) (0 (0 0)	1 (10) (0 (0)	0 (0) (0 0)	(0) (0 0)	0 (0)	0 (0)	3 (30)) (0
[Hematopoietio	: system]																	
spleen	deposit of melanin	0 (0) (0 (0) (0 (0 0)	(0) (2 (20)	0 (0) (0 0)	0 (0) (0 0)	0 (0)	0 (0)	(0)) ((0 0)
[Digestive sys	rtem]																	
liver	necrosis:focal	0 (0)	0 (0) (0 (0 0)	1 (10) (0 (0)	0 (0) (0 0)	0 (0) (0 0)	0 (0)	0 (0)	(0)) (C		0 0)
	granulation	5 (50)	0 (0) (0 0) (0 0)	5 (50)	1 (10)	0 (0)	0 0)	3 (30) (0 0)	0 (0)	0 (0)	4 (40)) (C		0 0)
	eosinophilic fine granular change:liver cell	(0)	0 (0) (0 (0	(0) (0 (0)	0 (0)	0 0)	(0) (0 0)	0 (0)	0 (0)	(0)		((0 0)
[Urinary syste	om]																	
cidney	basophilic change	0 (0) (0 (0) (0 (0 0)	0 (0) (0 (0)	0 (0) (0 0)	0 (0) (0 0)	0 (0)	0 (0)	0 (0)	0 (0) (0
	hyaline cast	0 (0)	0 (0) (0 (0 0)	1 (10)	0	0 (0) (0 0)	0 (0) (0 0)	0 (0)	0 (0)	(0)) ((0 0)
	mineralization:papilla	1 (10)	0 (0) (0 (0 0)	0 (0) (0	0 (0 0)	0 (0) (0 0)	0 (0)	0 .	(0)) (0 0)
Significant di	fference; *: $P \le 0.05$ **: $P \le 0.01$	Test of Chi Square		Z13	>:Slight		:Mode			<3>:Marked			Seuere					

STUDY NO. : 0186

ANIMAL : MOUSE BDF1

REPORT TYPE : A1

(HPT150)

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

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

SEX : FEMALE PAGE: 6 Group Name 8000 ppm 10000 ppm 16000 ppm No. of Animals 10 10 9 ⟨3⟩ 〈2〉 〈3〉 <1> (2> ⟨2⟩ ⟨3⟩ ⟨4⟩ (%) (%) (%) Findings (%) (%) (%) (%) (%) (%) (%) (%) (%) [Respiratory system] nasal cavit eosinophilic change:olfactory epithelium (10) (0) (0) (0) (0)(0)(0)(0) (0)(0)(0)(0) easinophilic change:respiratory epithelium 1 0 0 0 0 0 0 0 (10) (0) (0) (0) (0)(0)(0)(0) (0)(0)(0)(0) [Hematopoietic system] deposit of melanin spleen (0)(10)(0)(0) (0)(10)(0)(0) (0)(0)(0)(0) [Digestive system] Liver necrosis:focal 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (10) (0) (0) (0) (0)(0)(0)(0) granulation 0 6 0 0 5 0 0 0 (60) (0) (0) (0) (60) (0) (0) (0) (56) (0) (0) (0) eosinophilic fine granular change: liver cell 2 0 (0)(0)(0)(0) (0)(0)(0)(0) (78) (22) (0) (0) [Urinary system] kidney basophilic change 0 0 0 0 0 1 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(11)(0)(0) hyaline cast (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) mineralization:papilla 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0)

<1>:Slight

<2>:Moderate

<3>:Marked

<4>:Severe

STUDY NO. : 0186 ANIMAL : MOUSE BDF1

REPORT TYPE : A1
SEX : FEMALE

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

	Group Name No. of Animals	1:			500 ppm 10						4000 ppm 10						
ganFindings	(%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)		1> %)	<2> (%)	<3> (%)	<4 (%
Jrinary system]																	
idney desquamation:pelvis	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	(0)	0 (0)	0 (0)	0 (0) (0 0)	0 (0) (0 0)		0 0) (0	0	0 (
ervous system]																	
pinal cord epidermal cyst	1 (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

STUDY NO. : 0186

SEX

ANIMAL : MOUSE BDF1

: FEMALE

REPORT TYPE : A1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

PAGE: 8

SACRIFICED ANIMALS (14W)

Group Name 8000 ppm 10000 ppm 16000 ppm No. of Animals 10 10 9 <1> ⟨2⟩ ⟨3⟩ ⟨4⟩ <1> 〈2〉 〈3〉 〈4〉 〈2〉 〈3〉 〈4〉 <1> (%) (%) (%) Findings (%) (%) (%) 0rgan_ (%) (%) (%) (%) (%) (%) [Urinary system] kidney desquamation:pelvis 1 0 0 0 0 0 0 0 (10) (0) (0) (0) (0)(0)(0)(0) (11) (0) (0) (0) [Nervous system] spinal cord epidermal cyst 0 0 0 0 (0) (0) (0) (0) (0)(0)(0)(0) (0)(0)(0)(0) Significant difference; $*: P \le 0.05$ $**: P \le 0.01$ Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe (HPT150) BAIS2

APPENDIX B 12-1

IDENTITY AND PURITY OF BIPHENYL PERFORMED AT THE JAPAN BIOASSAY LABORATORY (THIRTEEN-WEEK STUDY)

IDENTITY AND PURITY OF BIPHENYL PERFORMED AT THE JAPANBIOASSAY LABORATORY (THIRTEEN-WEEK STUDIES)

Lot no. DSK6646

1. Spectral data

Mass Spectrometry

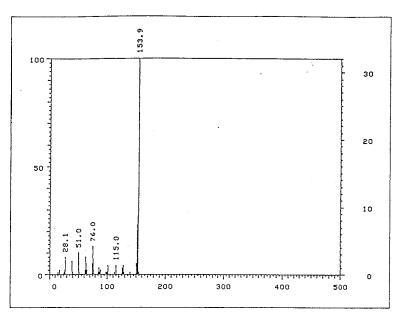
Instrument:

Hitachi M-80B

Ionization:

EI(Electron Ionization)

Ionization Voltage: 70eV



Mass Spectrum of BIPHENYL

Result:

Molecule Weight

Theoretical Value

154.1(Calculated)

Determined

153.9

ULTRA VIOLET SPECTRUM

Instrument: SHIMADZU UV-240

Cell: 1 mm Cell

Solvent:

Methanol

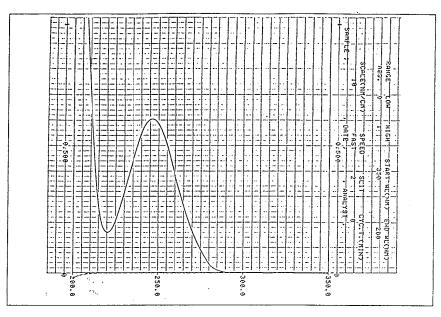
Slit:

2 nm

Range:

0 - 1

Concentration(mg/l): 50



Ultra Violet Spectrum of BIPHENYL

Results:

Determined

Literature Value

(Sadtler handbook by Sadtler Research Laboratories, Inc.)

Wave Length

246.5

246.5

(nm)

2. Gas Chromatography

Instrument:

Hewlett Packard 5890A

Column:

Methyl Silicone(0.2mm $\phi \times 50$ m)

Column Temperature:

180°C

Flow Rate:

1 ml/min

Detector:

FID(Hydrogen Flame Ionization)

Injection Volume: 1 μ 1

Results: Only major peak(except solvent peek)

Peak No.	Retention Time(min)	Retention Time Relative to Major Peak	AREA (percent of major peak)
1	3.27	1.00	100

^{3.} Conclusions: The result of the Mass spectrum agreed with the theoretical value and the ultra violet spectrum agreed with the literature values. Gas chromtography indicated only the major peak.

APPENDIX B 12-2

STABILITY OF BIPHENYL AT THE JAPAN BIOASSAY LABORATORY (THIRTEEN-WEEK STUDY)

STABILITY OF BIPHENYL AT THE JAPAN BIOASSAY LABORATORY (THIRTEEN-WEEK STUDIES)

Lot no.DSK6646

1. Sample storage: Biphenyl were stored for about 13 weeks at 5°C.

2. Gas Chromatography

Instrument:

Hewlett Packard 5890A

Column:

Methyl Silicone(0.2mm $\phi \times 50$ m)

Column Temperature: 180°C

Flow Rate:

1 ml/min

Detector:

FID(Hydrogen Flame Ionization)

Injection Volume: 1 μ 1

Results: Only major peak(except solvent peek)

Date	Retention Time(min)	Retention Time Relative to Major Peak	Area (percent of Major peak)
11/01/91	3.27	1.00	100
03/02/92	3.268	1.00	100

3. Conclusions: Gas chromatography indicates only the major peak. Consequently, Biphenyl was stable as the chemical when stored for about 13 weeks at 5°C.

APPENDIX B 12-3

ANALYSYS OF BIPHENYL CONCENTRATION IN FORMULATED DIETS OF THE THIRTEEN —WEEK STUDIES

ANALYSIS OF BIPHENYL CONCENTRATION IN FORMULATED DIETS OF THE THIRTEEN-WEEK STUDIES

(Rat)

	Concentration of	BIPHENYL in feed	for Target Concent	ration(ppm)
1000 (a)	2000 (a)	4000 (a)	8000 (a)	16000 (a)
1080.2(110.4)	1983.2(99.2)	4383.2(97.9)	8925.6(111.6)	16744.1(104.7)

(Mouse)

Concentration of BIPHENYL in feed for Target Concentration(ppm)																							
 500	(a)	2000	(a)	4000	(а)	8000	(a)	10000	(a)	16000	(a)
555.	8(1	10.	4)	1983.	2(99.	2)	4383.	2(1	09.	6)	8925.	6(1	11.	6)	10598.	5(1	.06.	0)	16744.	1(1	04.	7)

⁽a) Determined as a percent of target concentration

APPENDIX B 12-4

STABILITY OF BIPHENYL IN FORMULATED DIETS OF THE THIRTEEN - WEEK STUDIES

STABILITY OF BIPHENYL IN FORMULATED DIETS OF THE THIRTEEN-WEEK STUDIES

(Rat)

	Concentration of BIPHENYL in feed for Target Concentration(ppm)					
Date Mixed	500 (a)	16000 (a)				
10/29/91	471.3	17720.3				
11/05/91	478.6(101.5)	15082.6(85.1)				

(Mouse)

Conc	ncentration of BIPHENYL in feed for Target Concentration(ppm)						
Date Mixed	500 (a)	16000 (a)					
10/29/91	471.3	17720.3					
11/05/91	491.4(104.3)	14411.1(81.3)					
	•						

⁽a) Determined as a percent of target concentration

APPENDIX C 1

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALSYS

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS

Item	Method	Unit
Hematology		
Red blood cell (RBC)	Light scattering method 1)	×10°/μ1
Hemoglobin (Hgb)	Cyanmethemoglobin method 1)	g/dl
Hematocrit (Hct)	Calculated as RBC×MCV/10 1)	%
Mean corpuscular volume (MCV)	Light scattering method 1)	fl
Mean corpuscular hemoglobin (MCH)	Calculated as Hgb/RBC×10 1)	Pg
Mean corpuscular hemoglobin		
concentration (MCHC)	Calculated as Hgb/Hct×100 1)	g/dl
Platelet	Light scattering method 1)	×10³/μ1
White blood cell (WBC)	Light scattering method 1)	×10³/μ1
Differential WBC	Pattern recognition method 2)	%
	(May-Grunwald-Giemsa staining)	
Biochemistry		
Total protein (TP)	Biuret method ³⁾	g/dl
Albumin (Alb)	BCG method 3)	g/dl
A/G ratio	Calculated as Alb/ (TP-Alb) 3)	
T-bilirubin	Michaelson method ³⁾	mg/dl
Glucose	Enzymatic method (HK·G-6-PDH) 3)	mg/dl
T-cholesterol	Enzymatic method (CEH·COD·POD) 3)	mg/dl
Triglyceride	Enzymatic method (GK·GPO·POD) 3)	mg/dl
Phospholipid	Enzymatic method (PLD·COD·POD) 3)	mg/dl
Glutamic oxaloacetic transaminase (GOT)	Karmen method ³⁾	IU/1
Glutamic pyruvic transaminase (GPT)	Karmen method ³⁾	IU/1
Lactate dehydrogenase (LDH)	Wroblewski-LaDue method 3)	IU/1
Alkaline phosphatase (ALP)	GSCC method 3)	IU/1
γ-Glutamyl transpeptidase (G-GTP)	L-γ-Glutamyl-p-nitroanilide substrate	IU/1
	method 3)	-0, -
Creatine phosphokinase (CPK)	GSCC method ³⁾	IU/1
Urea nitrogen	Enzymatic method (Urease·GLDH) 3)	mg/dl
Creatinine	Jaffe method 3)	mg/dl
Sodium	Flame photometry 4)	mEq/l
Potassium	Flame photometry 4)	mEq/l
Chloride	Coulometric titration 4)	mEq/l
Calcium	OCPC method 3)	mg/dl
Inorganic phosphorus	Enzymatic method (SPL·PGM·G-6-PDH) 3)	mg/dl
Urinalysis pH, Protein, Glucose, Ketone body, Bilirubin, Occult blood, Urobilinogen	Urinalysis reagent paper method ⁵⁾	

- 1) Automatic blood cell analyzer (Technicon H·1: Technicon Instruments Corporation, USA)
- 2) Automatic blood cell differential analyzer (Hitachi 8200 : Hitachi, Ltd., Japan)
- 3) Automatic analyzer (Hitachi 705 : Hitachi, Ltd., Japan)
- 4) Flame photometer (Hitachi 750 : Hitachi, Ltd., Japan)
- 5) Ames reagent strips for urinalysis (Multistix, Uro-Labstix: Miles Sankyo Co., Ltd., Japan)

APPENDIX C 2

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

UNITS AND DECIMNAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

F		1	
	TEST ITEM	DECIMAL PLACE	UNIT
HEMATOLOGY	Red blood cell	2	× 10 ⁶ / μ 1
	Hemoglobin	1	g/dl
	Hematocrit	1	%
	MCV	1	f1
	MCH	1	pg
	MCHC	1	g/dl
	Platelet	0	× 10 ³ / μ 1
	White blood cell	2	$\times 10^3/\mu 1$
	Differntial WBC	0	%
BIOCHEMISTRY	Total protein	1	g/dl
	Albumin	1	g/dl
	A/G ratio	1	
	T-bilirubin	2	mg/dl
	Glucose	0	mg/dl
	T-cholesterol	0	mg/dl
	Triglyceride	0	mg/dl
	Phospholipid	0	mg/dl
	GOT	0	IU/1
	GPT	0	IU/I
	LDH	0	IU/1
	ALP	0	IU/1
	γ-GTP	0	IU/1
	CPK	0	IU/1
	Urea nitrogen	1	mg/dl
	Creatinine	1	mg/dl
	Sodium	0	mEq/1
	Potassium	1	mEq/1
	Chloride	0	mEq/l
	Calcium	1	mg/dl
	Inorganic phosphorus	1	mg/dl