アントラセン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

# **APPENDIXES**

(B1-1~C2)13 週間試験:ラット/0220;マウス/0221

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# APPENDIX A 1-1

# BODY WEIGHT CHANGES (TWO-WEEK STUDY:SUMMARY)

RAT : MALE

BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS

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STUDY NO.: 0193 ANIMAL : RAT F344 UNIT : g REPORT TYPE : A1 2 SEX : MALE

PAGE: 1

Group Name	Λdmini	stratio	n week-day											 
	0-0		1-1		1-3		1-7		2-3		2-7		·	 
Control	120±	4	123±	5	130±	5	147±	5	159±	5	171±	5		
mag 08	120±	4	122±	5	130±	5	146±	5	158±	5	169±	6		
400 ppm	120±	4	122±	5	129±	5	145±	7	157±	8	168±	9		
2000 mag	120±	4	121±	5	129±	5	145±	5	$157\pm$	6	$167\pm$	6		
10000 ppm	120±	4	118±	5	126±	4	142±	4	154±	3	165±	4		
50000 mga	120±	4	117±	3*	123±	4**	140±	5**	152±	6*	161±	8**		
											<u></u>			 
Significant differer	nce; *:P≦(	.05	** : P ≦ 0.0	1			Test of Du	Innett						
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# APPENDIX A 1-2

# BODY WEIGHT CHANGES (TWO-WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO.: 0193 ANIMAL : RAT F344 UNIT : g REPORT TYPE : A1 2 SEX : FEMALE

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BODY WEIGHT CHANGES (SUNMARY) ALL ANIMALS

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oup Name	Admini	stratic	n week-day										
	0-0		1-1		1-3		1-7		2-3		2-7		
Control	99土	3	101±	3	105±	4	113±	4	120±	4	$124\pm$	4	
10 mag	99±	3	101±	3	106±	3	114±	4	120±	5	125±	6	
400 ppm	99±	3	100±	3	105±	4	114±	5	121±	5	$127\pm$	4	
2000 ppm	99±	3	99±	3	103±	2	112±	3	117±	4	121±	4	
10000 ppm	99±	3	96±	3**	101士	3*	110±	5	116土	4	121±	4	
50000 mag	99±	2	94±	3**	$97\pm$	3**	107±	3**	11 <b>3</b> ±	5**	117±	3**	
								<u></u>					
Significant difference	; *:P≦0	.05	** : P ≦ 0.0	1			Test of Du	nnett					
IAN260)											,		

# APPENDIX A 1-3

# BODY WEIGHT CHANGES(TWO-WEEK STUDY:SUMMARY)

MOSUE : MALE

BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS

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STUDY NO. : 0194 ANIMAL : MOUSE BDF1 UNIT ; g REPORT TYPE : A1 2 SEX : MALE

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roup Name	Administratio	on week-day			· · · · · · · · · · · · · · · · · · ·		
	. 0-0	1-1	1-3	1-7	2-3	2-7	
Control	23.5± 0.8	23.2± 1.0	22.7± 1.0	23.7± 1.1	23.7± 1.1	24.7土 1.0	
mqq 08	23.6± 0.8	23.1± 1.0	22.9± 0.9	23.6± 0.8	23.9± 0.9	24.4± 1.2	
400 ppm	23.5± 0.8	23.3± 0.9	22.9± 0.9	23.7± 1.1	23.9± 0.9	24.5± 1.0	
2000 ppm	23.5± 0.8	23.3± 1.2	23.1± 1.1	$23.6 \pm 1.1$	$23.5 \pm 1.3$	24.2± 1.1	
10000 ppm	23.5± 0.8	23.3± 0.8	22.9± 0.8	23.3± 0.8	23.3± 0.8	24.0± 0.8	
50000 ppm	23.5± 0.8	22.2± 1.0	22.3± 1.1	22.4± 0.9*	22.6± 0.9	22.6± 1.3**	
Significant difference ;	*:P≦ 0.05	** : P ≦ 0.01		Test of Dunnett			
(HAN260)							

# APPENDIX A 1-4

## BODY WEIGHT CHANGES (TWO-WEEK STUDY: SUMMARY)

MOSUE: FEMALE

BODY WEIGHT CHANGES (SUMMARY) ALL ANIMALS

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STUDY NO. : 0194 ANIMAL : MOUSE BDF1 UNIT : g REPORT TYPE : A1 2 SEX : FEMALE

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roup Name	Administratio	n week-day					
	0-0	1-1	1–3	1-7	2-3	2-7	
Control	18.9± 0.6	18.7± 0.6	18.4± 0.6	18.9± 0.7	18.9± 0.5	19.3± 0.6	
80 mqq 08	18.9± 0.6	18.8± 0.8	18.6± 0.6	18.8± 0.5	19.4± 0.8	19.8± 0.6	
400 ppm	18.9± 0.6	18.5± 0.6	18.3± 0.9	18.6± 0.8	19.8± 0.6*	19.3± 0.6	
2000 ppm	18.9± 0.6	18.5± 0.5	18.3± 0.6	18.5± 0.8	19.0± 0.6	19.3± 0.7	
10000 maa	18.9± 0.7	18.2± 0.7	18.1± 0.8	18.5± 0.7	18.8± 0.7	18.5± 0.8*	
50000 mag	18.9± 0.6	17.7± 0.6**	17.6± 0.7*	18.0± 0.6	18.4± 0.7	18.3± 0.4**	
Significant difference;	* : P ≤ 0.05	** : P ≤ 0.01		Test of Dunnett			
(HAN260)							

# APPENDIX A 2-1

# FOOD CONSUMPTION CHANGES (TWO-WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0193 ANIMAL : RAT F344 UNIT : g REPORT TYPE : A1 2 SEX : MALE

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### FOOD CONSUNPTION CHANGES (SUMMARY) ALL ANIMALS

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oup Name	Administration	week-day(effective)_				
· · · · · · · · · · · · · · · · · · ·	1-3(3)	1-7(4)	2-3(3)	2-7(4)		
Control	12.3± 0.6	13.4± 0.5	12.8± 0.6	13.4± 0.4		
80 mag	12.5± 0.7	13.4± 0.6	12.9± 0.8	13.1± 1.1		
400 maa	12.0± 0.8	13.1± 0.9	12.8± 0.9	13.2± 0.9		
2000 ppm	11.4± 0.7*	12.8± 0.6	12.8± 0.8	13.2± 0.8		
10000 mqq	10.3± 0.7**	12.8± 0.5	12.7± 0.5	13.0± 0.6		
50000 ppm	9.4± 0.6**	12.8± 0.7	13.1± 0.6	13.4± 1.0		
Significant differend	ce; ∗:P≤0.05	** : P ≤ 0.01		Test of Dunnett		
IIAN260)				·····	· · · · · · · · · · · · · · · · · · ·	

# APPENDIX A 2-2

# FOOD CONSUMPTION CHANGES (TWO-WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO.: 0193 ANIMAL : RAT F344 UNIT : g REPORT TYPE : A1 2 SEX : FEMALE

### FOOD CONSUNPTION CHANGES (SUMMARY) ALL ANIMALS

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oup Name	Administration	n week-day(effective)			 	
	1-3(3)	1-7(4)	2-3(3)	2-7(4)		
Control	10 1 - 0 5		1054 00			
	10.1± 0.5	11.1± 0.6	10.5± 0.6	10.8± 0.9		
mqq 08	10.5± 0.5	11.3± 0.7	10.9± 0.7	11.4± 0.7		
400 ppm	10.2± 0.6	10.9± 0.6	11.0± 0.6	11.5± 0.6		
2000 ppm	9.0± 0.3	10.3± 0.5*	10.2± 0.5	10.5± 0.6		
10000 ppm	8.0± 0.4**	10.1± 0.6**	10.2± 0.4	10.4± 0.8		
50000 ppm	6.5± 0.9**	9.9± 0.4**	9.9± 0.6	10.0± 0.6*		
Significant difference	; *:P≦0.05	** : P ≦ 0.01		Test of Dunnett		
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# APPENDIX A 2-3

# FOOD CONSUMPTION CHANGES (TWO-WEEK STUDY: SUMMARY)

MOSUE : MALE

STUDY NO. : 0194 ANIMAL : MOUSE BDF1 UNIT : g REPORT TYPE : A1 2 SEX : MALE

### FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

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PAGE : 1

roup Name	Administrati	on week-day(effective)	0.0(0)	0.7(1)		
	1-3(3)	1-7(4)	2-3(3)	2-7(4)		
Control	4.9± 0.4	5.4± 0.5	4.7± 0.2	5.1± 0.4		
100 mag	4.4± 0.3	4.9± 0.3	4.3± 0.3	5.0± 0.8	· · · · ·	
400 ppm	4.9± 0.7	5.3± 0.8	4.6± 0.6	4.9± 0.4		
2000 mag	5.1± 0.6	5.3± 0.6	4.5± 0.5	4.8± 0.4		
10000 ppm	4.6± 0.5	5.1± 0.8	4.4± 0.4	4.8± 0.4		
50000 ppm	4.5± 0.5	5.1± 0.7	4.3± 0.5	4.6± 0.5		
Significant difference ;	*:P≦ 0.05	** : P ≦ 0.01		Test of Dunnett		
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# APPENDIX A 2-4

# FOOD CONSUMPTION CHANGES(TWO-WEEK STUDY: SUMMARY)

MOSUE : FEMALE

STUDY NO. : 0194 ANIMAL : MOUSE BDF1 UNIT : g REPORT TYPE : A1 2 SEX : FEMALE

### FOOD CONSUNPTION CHANGES (SUMMARY) ALL ANIMALS

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roup Name	Administrati	on week-day(effective)			
	1-3(3)	1-7(4)	2-3(3)	2-7(4)	 
Control	4.3± 0.5	4.6± 0.5	4.1± 0.6	4.5± 0.4	
זוסס 80	4.8± 0.8	4.7± 0.4	4.4± 0.9	4.4± 0.3	
400 mag	4.5± 0.6	4.7± 0.7	4.4± 0.4	4.5± 0.3	
2000 ppm	4.2± 0.5	4.5± 0.4	4.1± 0.4	4.4± 0.2	
10000 mqq 00001	4.0± 0.4	4.2± 0.5	3.9± 0.4	4.0± 0.3**	
50000 ppm	3.9± 0.8	4.5± 0.8	4.0± 0.6	4.1± 0.5*	
				······································	 
Significant difference ;	*:P≦ 0.05	** : P ≦ 0.01		Test of Dunnett	
HAN260)					 

# APPENDIX A 3-1

# CHEMICAL INTAKE CHANGES (TWO-WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO.: 0193 ANIMAL: RAT F344 UNIT: g/kg/day REPORT TYPE: A1 2 SEX: MALE

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CHEMICAL INTAKE CHENGES (SUNMARY) ALL ANIMALS

Administration (weeks) Group Name 2 1 Control 0.000± 0.000  $0.000 \pm 0.000$  $0.007 \pm 0.000$ 80 ppm 0.006± 0.001 400 ppm 0.036± 0.002 0.031± 0.001 2000 ppm 0.177± 0.007  $0.158 \pm 0.006$ 10000 ppm 0.897± 0.029  $0.791 \pm 0.039$ 50000 ppm 4.595± 0.170 4.138± 0.144

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APPENDIX A 3-2

# CHEMICAL INTAKE CHANGES (TWO-WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO. : 0193 ANIMAL : RAT F344 UNIT : g∕kg⁄day REPORT TYPE : A1 2 SEX : FEMALE		CHEMICAL INTAKE CHENGES (SUMMARY) ALL ANIMALS	
			PAGE : 2
Group Name	Administration		
	1	2	
Control	$0.000 \pm 0.000$	0.000± 0.000	
80 ppm	0.008± 0.000	0.007± 0.000	
400 ppm	0.038± 0.001	0.036± 0.002	
2000 ppm	0.184± 0.007	0.173± 0.007	
10000 ppm	0.915± 0.030	0.861± 0.040	
50000 ppm	4.603± 0.138	4.257土 0.277	

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APPENDIX A 3-3

# CHEMICAL INTAKE CHANGES (TWO-WEEK STUDY: SUMMARY)

MOSUE : MALE

STUDY NO.: 0194 ANIMAL : MOUSE BDF1 UNIT : g/kg/day REPORT TYPE : A1 2 SEX : MALE			CHEMICAL INTAKE CHENC ALL ANIMALS	JES (SUMMARY)		
Group Name	Administration	n (weeks)		····		PAGE : 1
		2		······	 	
	<u>,</u>				 	
Control	0.000± 0.000	0.000± 0.0	000			
80 maa	0.017± 0.001	0.017± 0.0	003			
400 ppm	0.089± 0.012	0.080± 0.0	008			
2000 ppm	0.446± 0.051	0.400± 0.0	030			
10000 ppm	2.182± 0.297	1.990± 0.1	157			
	2.102± 0.201	1.550 ± 0.	107		· .	
50000 ppm	11.498± 1.878	10.235± 1.0	082			

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APPENDIX A 3-4

# CHEMICAL INTAKE CHANGES (TWO-WEEK STUDY: SUMMARY)

MOSUE : FEMALE

STUDY NO.: 0194 ANIMAL : MOUSE BDF1 UNIT : g/kg/day REPORT TYPE : A1 2 SEX : FEMALE			CHEMICAL INTAKE CHENGES ALL ANIMALS	S (SUMMARY)		PAGE : 2
Group Name	Administratio	n (weeks)			 	· · · · · · · · · · · · · · · · · · ·
	1	2				u
· · · · · · · · · · · · · · · · · · ·					 	
Control	0.000± 0.000	0.000± 0.00	00			
maga 08	0.020± 0.002	0.018± 0.00	01			
400 ppm	0.102± 0.012	0.094± 0.00	05			
2000 ppm	0.483± 0.060	0.451± 0.03	24			
10000	9 901 1 0 001	0.1001.001				
10000 ppm	2.291± 0.281	2.179± 0.1	69			
50000 ppm	$12.532 \pm 1.950$	11.168± 1.1	19			
	15.005 2. 1.000	11.100 - 1.1	1.6			

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APPENDIX A 4-1

# HEMATOLOGY (TWO-WEEK STUDY: SUMMARY)

RAT: MALE

### STUDY NO. : 0193 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE

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# HEMATOLOGY(1) (SUMMARY) SURVIVAL ANIMALS (2)

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| oup Name  | NO. of<br>Animals | RED BL.<br>1 O <sup>6</sup> /µ | OOD CELL | lienogi<br>g∕dl | OBIN  | HENATO<br>% | CRIT  | NCV<br>f @ |     | MCH<br>pg |     | MCHC<br>g∕dl | <u></u> | РІ.АТЕІ.<br>1 0³∕µ |     |
|-----------|-------------------|--------------------------------|----------|-----------------|-------|-------------|-------|------------|-----|-----------|-----|--------------|---------|--------------------|-----|
| Contral   | 5                 | 8.00±                          | 0.16     | 14.9±           | 0.1   | 43.2±       | 0.8   | 54.0±      | 0.2 | 18.7±     | 0.4 | 34.6±        | 0.7     | $990 \pm$          | 34  |
| 80 ppm    | 5.                | 7.83±                          | 0.18     | 14.7±           | 0.4   | 42.2±       | 0.9   | $53.9\pm$  | 0.3 | 18.7士     | 0.2 | 34.7±        | 0.4     | $970\pm$           | 134 |
| 400 ppm   | 5                 | 7.74土                          | 0.06     | $14.5\pm$       | 0.1   | 41.5±       | 0.3*  | 53.6±      | 0.3 | 18.7±     | 0.1 | 35.0±        | 0.2     | $990\pm$           | 53  |
| 2000 ppm  | 5                 | 7.62±                          | 0.12**   | 14.1±           | 0.2*  | 41.0±       | 0.5** | 53.8±      | 0.6 | 18.5±     | 0.3 | 34.4±        | 0.4     | 1068±              | 51  |
| 10000 ppm | 5                 | 7.48±                          | 0.24**   | $13.9\pm$       | 0.4** | 40.4±       | 1.2** | 54.0土      | 0.3 | 18.7±     | 0.3 | 34.5±        | 0.5     | $1057\pm$          | 74  |
| 50000 ppm | 5                 | 7.61±                          | 0.19**   | 14.0±           | 0.2** | 41.1±       | 0.9** | 54.0土      | 0.1 | 18.5±     | 0.2 | 34.2±        | 0.3     | 1086士              | 38  |

(IICL070)

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STUDY NO. : 0193 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE

### HEMATOLOGY(1) (SUMMARY) SURVIVAL ANIMALS ( 2)

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| roup Name   | NO. of<br>Animals | RETICU<br>‰ | LOCYTE | PROTHING<br>sec | DMBIN TIME | APTT<br>sec |      | · · · · · · · · · · · · · · · · · · · | <br>   | <br> | <br>   |
|-------------|-------------------|-------------|--------|-----------------|------------|-------------|------|---------------------------------------|--------|------|--------|
| Control     | 5                 | 52±         | 13     | 12.5±           | 0.2        | 20.0土       | 1.1  |                                       |        |      |        |
| 80 maga     | 5                 | 51±         | 8      | 12.3±           | 0.3        | 20.6±       | 1.1  |                                       |        |      |        |
| 400 ppm     | 5                 | 52±         | 13     | 12.6土           | 0.2        | 20.8土       | 0.6  |                                       |        |      |        |
| 2000 ppm    | 5                 | 65±         | 8      | 12.4±           | 0.1        | 21.3±       | 1.2  |                                       |        |      |        |
| 10000 pom   | 5                 | $59\pm$     | 10     | 12.3±           | 0.4        | 22.0土       | 1.7  |                                       |        |      |        |
| 50000 ppm   | 5                 | 67 ±        | 4      | 12.1±           | 0.4        | 22.3±       | 1.3* |                                       |        |      |        |
| Significant | difference ;      | * : P ≦ 0   | .05    | ** : P ≦ 0.0    | 1          |             |      | Test of Dunnett                       | <br>•- | <br> | <br>   |
| (IICL070)   |                   |             |        |                 |            |             |      |                                       | <br>   |      | BAIS 2 |

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STUDY NO. : 0193 ANIKAL. : RAT F344 REPORT TYPE : A1 SEX : MALE

NO. of

WBC

Differential WBC

Group Name

## IVENATOLOGY (2) (SUMMARY)

### SURVIVAL ANIMALS ( 2)

(%)

Animals 1 0<sup>3</sup>/µl N-BAND N-SEG EOSINO BASO NONO LYNPHO OTHER Control 5 3.49± 0.30 0± 0 14土 3 1土 1 0土 0 1土 81± 3 0土 0 1 80 ppm 5 3.48± 0.68 0± 1 14土 3 1土 1 0± 0 4士 1  $81\pm$ 5  $0\pm$ 0 400 ppm 5 2.95± 0.25 0土 0 17土 3 1± 0 0上 0 3± ì 79± 4 0土 0 2000 ppm 5 3.45± 0.27 0± 0 19土 4 1土 1 0± 0 3土 2 78± 4 0土 0 10000 ppm 5 3.88士 0.96 1土 I 16土 4 1± 1 0土 0 1土 78土 1 5 0土 0 50000 ppm 5 4.08土 1.25 0± 0 18上 3 11 0 0土 0  $3\pm$ 1 78± 4 0± 0 Significant difference ;  $*: P \leq 0.05$ \*\* : P ≦ 0.01 Test of Dunnett .

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(JCL71A)

BAIS 2

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APPENDIX A 4-2

# HEMATOLOGY(TWO-WEEK STUDY: SUMMARY)

RAT: FEMALE

STUDY NO. : 0193 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FENALE

### HEMATOLOGY(1) (SUMMARY) SURVIVAL ANIMALS ( 2)

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| oup Name  | NO. of<br>Animals | RED B<br>1 06/ | LOOD CELL<br>H | lienogi<br>g∕d¢ |       | ПЕМАТС<br>% | CRIT  | NCV<br>F e |     | NCH<br>Pg | - 112 - 112 - 112 - 112 | NCHC<br>g / ell |       | РІАТЕІ.<br>1 0 <sup>3</sup> ∕µ. |      |
|-----------|-------------------|----------------|----------------|-----------------|-------|-------------|-------|------------|-----|-----------|-------------------------|-----------------|-------|---------------------------------|------|
| Control   | 5                 | 8.16±          | 0.17           | 15.5士           | 0.3   | 43.8土       | 0.8   | $53.6\pm$  | 0.1 | 19.0土     | 0.1                     | 35.4±           | 0.4   | 833±                            | 58   |
| 80 ppm    | 5                 | 8.14±          | 0.06           | 15.6±           | 0.2   | 43.8±       | 0.4   | 53.8土      | 0.3 | 19.1土     | 0.3                     | 35.6±           | 0.5   | 840 土                           | 50   |
| 400 ppm   | 5                 | $7.52\pm$      | 0.09**         | 14.3±           | 0.2** | 40.3±       | 0.6** | $53.6\pm$  | 0.3 | 19.0±     | 0.2                     | 35.3±           | 0.3   | 900±                            | 86   |
| 2000 ppm  | 5                 | 7.35±          | 0.11**         | $13.9\pm$       | 0.2** | $39.5\pm$   | 0.4** | $53.8\pm$  | 0.3 | 18.9±     | 0.3                     | 35.1±           | 0.4   | 930±                            | 58   |
| 10000 ppm | 5                 | 7.48±          | 0.29**         | 13.8±           | 0.4** | 40.1±       | 1.4** | 53.7±      | 0.3 | 18.4土     | 0.4*                    | 34.4±           | 0.6** | 985土                            | 144* |
| 50000 ppm | 5                 | 7.35±          | 0.13**         | 13.7士           | 0.3** | 39.4±       | 0.6** | 53.6±      | 0.3 | 18.7±     | 0.3                     | 34.8±           | 0.4   | 952士                            | 47   |

(HCL070)

BAIS 2

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STUDY NO. : 0193 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE

## HENATOLOGY(1) (SUMMARY)

### SURVIVAL ANIMALS (2)

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| Group Name  | NO. of<br>Animals | RETICULOCYTE<br>‰ |      | PROTHROMBIN TIME<br>S C C |       | APTT<br>sec |     |                 | <br>          |                    | <br> | ····· |
|-------------|-------------------|-------------------|------|---------------------------|-------|-------------|-----|-----------------|---------------|--------------------|------|-------|
| Control     | 5                 | 33±               | 3    | 12.6±                     | 0.3   | 18.8±       | 0.7 |                 |               |                    |      |       |
| maga 08     | 5                 | 33±               | 5    | 12.6±                     | 0.2   | 19.6上       | 1.1 |                 |               |                    |      |       |
| 400 ppm     | 5                 | $56\pm$           | 6**  | 12.3±                     | 0.4   | 18.5±       | 0.8 |                 |               |                    |      |       |
| 2000 ppm    | 5                 | 82±               | 4**  | 12.4±                     | 0.2   | 19.7土       | 2.8 |                 |               |                    |      |       |
| 10000 ppm   | 5                 | 80±               | 10** | 12.3±                     | 0.1   | 20.6±       | 1.9 |                 |               |                    |      |       |
| 50000 ppm   | 5                 | 89土               | 10** | 12.0±                     | 0.2** | 20.9±       | 1.9 |                 |               |                    |      |       |
| Significant | difference ;      | * : P ≦ 0         | .05  | ** : P ≦ 0.(              | )]    |             |     | Test of Dunnett |               | -16 <del>-16</del> | <br> |       |
| IICL.070)   |                   |                   |      |                           | ••••• |             |     |                 | <br>· · · · · |                    | <br> | BAL   |

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STUDY NO. : 0193 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE

NO. of

WBC

Group Name

### HENATOLOGY(2) (SUMMARY)

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Differential WBC

### SURVIVAL ANIMALS (2)

(%)

Animals 107/118 N-BAND N-SEG EOSINO BASO MONO 1.1'812110 OTHER Control 5 3.47± 0.93 0土 1 20土 7 2上 2 0土 0 5土 2 71士 7 0土 0 80 ppm 5 3.09± 0.61 0土 1 21土 2 2土 1 0土 0 5土 1 71土 3 0土 0 400 ppm 5 2.86 ± 0.22 1± 21土 1 6 2上 1 0上 0 4土 2 72士 5 0土 0 2000 ppm 5 3.47± 0.92 0± 0 18± 2 1土 1  $0\pm$ 0 5± 2 76± 3 0± 0 10000 ppm 5 3.19± 1.54 0土 16土 1 4 1土 1 0土 0 4士 1  $79\pm$ 5 0± 0 50000 ppm 5 3.12± 0.86 1± 1 19上 4 1± 1 0土 0 1土 1  $75\pm$ 4 0土 0 ... Significant difference ;  $*: P \leq 0.05$ \*\* : P ≦ 0.01 Test of Dunnett . (JCL71A)

BAIS 2

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APPENDIX A 4-3

HEMATOLOGY (TWO-WEEK STUDY: SUMMARY)

MOSUE : MALE

STUDY NO. : 0194 ANIMAL. : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE

# HEMATOLOGY(1) (SUMMARY)

# SURVIVAL ANIMALS ( 2)

Group Name NO. of RED BLOOD CELL HEMOGLOBIN HEMATOCRIT NCV MCH ACHC PLATELET Animals  $1.0^{6}/\mu e$ g/dl % ſl g/df 1 0<sup>3</sup>/µl рg Control 5 10.91± 0.38  $16.3 \pm$ 0.7 49.0± 2.5 45.0土 1.4 14.9土  $33.2\pm$  $1323\pm$ 0.7 1.0 5980 ppm 5 10.79± 0.26  $16.4 \pm$ 0.7  $49.4 \pm$ 1.7 45.8土 0.8 15.2土 0.5  $33.3\pm$ 0.8  $1334\pm$ 126 400 ppm 5 10.70± 0.32  $16.3 \pm$ 0.5 49.0土 1.2 45.8士 0.5  $15.3 \pm$ 0.3  $33.3 \pm$ 0.6 1334土 40 2000 ppm 5 10.80± 0.13 16.2± 0.3  $49.4 \pm$ 0.9 45.8土 1.1 15.0土 0.2  $32.7 \pm$ 0.9 1326土 95 10000 ppm 5 10.28± 0.27\*\*  $15.7 \pm$ 0.4 47.1土 45.8± 0.5 1.3  $15.3 \pm$ 0.1  $33.4\pm$ 0.2  $1477 \pm$ 83\* 50000 ppm 5 10.07± 0.17\*\* 15.2士 0.1\* 45.9± 1.4\* 45.6± 0.9 15.1± 0.2  $33.1\pm$ 0.9 70\*\*  $1681\pm$ • • Significant difference ;  $*: P \leq 0.05$ \*\* : P ≦ 0.01 Test of Dunnett

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BAIS 2

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PAGE : 1

STUDY NO. : 0194 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE

NO. of

WBC

Group Name

# IIEMATOLOGY (2) (SUMMARY)

# SURVIVAL ANIMALS ( 2)

(%)

Differential WBC

Animals 103/118 N-BAND N-SEG EOSINO BASO MONO LYMPHO OTHER Control 5 1.86± 0.65 2± 1  $13\pm$ 5 1土 1 0± 0  $2\pm$ 1 81± 5 0± 0 80 ppm 5 1.81± 0.47 2土 3 1  $16\pm$  $2\pm$ 3 0± 0  $3\pm$ 78± 1 -4 0± 0 400 ppm 5  $2.92 \pm 1.78$ 1土 1 11土 2 1土 1 0土 0 3土 0 84士 4 0± 0 2000 ppm 5 2.29± 1.25 2土 1 16土 6 1土 1 0土 0 2土 1 79土 6 0± 0 10000 ppm 5 1.72± 0.77 4土 3 17土 4 1:1: 1 0土 0 3土 1 75 土 3 0土 0 50000 ppm 5 1.13± 0.28 4土 2  $26\pm$ 4\*\* 2上 3 0土 0  $3\pm$  $65\pm$ 1 6\*\* 0土 0 • • Significant difference ;  $*: P \leq 0.05$ \*\* : P ≦ 0.01 Test of Dunnett (JCL71A)

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BAIS 2

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## PAGE : 1

APPENDIX A 4-4

HEMATOLOGY (TWO-WEEK STUDY: SUMMARY)

MOSUE : FEMALE

STUDY NO. : 0194 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : FEMALE

# HEMATOLOGY(1) (SUMMARY)

# SURVIVAL ANIMALS (2)

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Group Name NO. of RED BLOOD CELL HEMOGLOBIN HEMATOCRIT NCHC MCV MCII PLATELET Animals  $1.0^{6}/\mu$ g/dl % ſℓ рg g/dl  $1.0^{3}/\mu^{2}$ Control 5 10.52± 0.26 15.8土 0.2 47.3土 1.5 45.0土 0.5  $15.0 \pm$ 1099士 0.4  $33.5\pm$ 1.0 42 80 ppm 5 10.52± 0.19  $15.9 \pm$ 0.2 47.3土 1.0 44.9土 0.5  $15.1 \pm$ 0.3  $33.6\pm$ 0.5 1146± 66 400 ppm 5 10.20± 0.36  $15.5 \pm$ 0.6 46.2± 1.6 45.3土 0.2  $15.2 \pm$ 0.3  $33.6 \pm$ 0.5 1155土 107 2000 ppm 5 9.99土 0.32\*  $15.2 \pm$ 0.2\* 45.1士 0.9 45.2土 0.9  $15.2 \pm$ 0.4  $33.7\pm$ 0.5 1144土 84 10000 ppm 5 10.02± 0.26\*  $15.3 \pm$ 0.3 45.5上 1.6 45.4土  $15.3 \pm$  $33.6\pm$ \*\*08 0.6 0.3 0.9  $1322\pm$ 50000 ppm 5 9.61± 0.26\*\* 14.7土 0.4\*\* 43.7主 1.3\*\* $45.5 \pm$ 0.4  $15.2 \pm$ 0.1  $33.6 \pm$ 0.3 1419土 69\*\* Significant difference :  $*: P \leq 0.05$ \*\* : P ≦ 0.01 Test of Dunnett

(IICL070)

BAIS 2

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PAGE : 2

STUDY NO. : 0194 ANIMAL : NOUSE BDF1 REPORT TYPE : A1 SEX : FEMALE

NO. of

WBC

Differential WBC

Group Name

# HEMATOLOGY(2) (SUMMARY)

# SURVIVAL ANIMALS (2)

(%)

Animals 1 03/12 N-BAND N-SEG EOSINO BASO MONO LYMPHO OTHER Control 5 1.49± 0.37 2± 1 10± 2 2± i 0土 0 3土 2 84士 4 0土 0 80 ppm 5 1.05± 0.23 1± 1 13士 3 1土  $0\pm$ 1 0 2土  $82\pm$ 2 1 0土 0 400 ppm 5 1.37± 0.40 2± 2 11± 3 2土 1 0± 0 3± 1 82士 4 0土 0 2000 ppm 5 1.10± 0.56 2土 1 12± 4 1± 0 0± 0  $3\pm$ 2 82土 5 0± 0 10000 ppm 5 0.72± 0.13\*  $3\pm$ 13± 1 6 2土 1 0土 0  $3\pm$ 5 1 78± 0± 0 50000 ppm 5 0.56± 0.09\*\* 5± 3 15土 5 1± 3 0土 0  $3\pm$ 1 76士 10 0± 0 ••• Significant difference :  $*: P \leq 0.05$ \*\* : P ≦ 0.01 Test of Dunnett

(JCL71A)

BAIS 2

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APPENDIX A 5-1

# BIOCHEMISTRY (TWO-WEEK STUDY: SUMMARY)

RAT: MALE

STUDY NO. : 0193 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE

## BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS ( 2)

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PAGE : 1

| roup Name | NO. of<br>Animals | TOTAL F<br>g / dl | PROTEIN | ALBUNTA<br>g / dl |       | ∆/G RAT | 017 | T−B11.1<br>mg∕dl |      | GLUCOSE<br>mg/-10 |    | T-CHOLES<br>mg/dl | TEROL | PHOSPHO<br>mg/df | JPID |
|-----------|-------------------|-------------------|---------|-------------------|-------|---------|-----|------------------|------|-------------------|----|-------------------|-------|------------------|------|
| Control   | 5                 | 5.8±              | 0.1     | 3.3±              | 0.1   | 1.4±    | 0.1 | 0.28±            | 0.17 | 184±              | 8  | 61 土              | 3     | 114土             | 9    |
| 80 ppm    | 5                 | 5.7±              | 0.1     | $3.3\pm$          | 0.1   | 1.4±    | 0.1 | 0.28±            | 0.13 | 177土              | 5  | $59\pm$           | 3     | 111±             | 8    |
| 400 ppm   | 5                 | $5.5\pm$          | 0.2**   | 3.1±              | 0.1** | 1.4±    | 0.1 | 0.37±            | 0.14 | 174土              | 13 | $50\pm$           | 2     | 108±             | 10   |
| 2000 ppm  | 5                 | 5.5±              | 0.1**   | 3.1±              | 0.1** | 1.3±    | 0.0 | 0.34±            | 0.13 | 179±              | 19 | 61±               | 5     | 109士             | 10   |
| 10000 ppm | 5                 | 5.6±              | 0.1*    | 3.2土              | 0.1   | 1.3±    | 0.1 | 0.33±            | 0.10 | 180土              | 22 | 62土               | 3     | 113士             | 9    |
| 50000 ppm | 5                 | 5.7±              | 0.1     | 3.3±              | 0.0   | 1.3±    | 0.1 | 0.26土            | 0.14 | $170 \pm$         | 12 | 66±               | 3     | 115±             | 5    |

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ANIMAL : RAT F344 SURVIVAL ANIMALS (2) REPORT TYPE : A1 SEX : MALE PAGE : 2 Group Name NO. of GOT GPT LDII CPK CREATININE G-GTP UREA NITROGEN Animals 111/0 IU/e IU/0 IU/l IU/l mg∕d£ mg / dl Control 5  $57\pm$ 4 17士 1 336土 180 1土 0 198土 77 16.0± 2.1 0.4土 0.0 80 ppm 5  $57\pm$ 1  $17\pm$ 33 1  $253\pm$ 1土 1 171土 44  $15.2 \pm$ 1.5 0.4土 0.0 400 ppm 5 57± 3 15士 1  $323\pm$ 112 1土 . 0 158± 15.5土 0.1± 0.0 32 2.1 2000 ppm 5 58士 5 15土 1  $253\pm$ 108 比 0  $149\pm$ 36  $15.9 \pm$ 0.4± 0.0 1.4 10000 ppm 5 57± 4  $15\pm$  $276 \pm$ 84 1 1土 0 185士 104 16.0± 2.5 0.1± 0.0 50000 ppm 5 53± 4  $13\pm$ ]\*\* 260± 115 1± 0 140土 34  $17.6 \pm$ 2.7 0.4± 0.0 . . Significant difference ;  $*: P \leq 0.05$ \*\* : P ≦ 0.01 Test of Dunnett . (IICL074) BAIS 2

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BIOCHEMISTRY (SUMMARY)

STUDY NO. : 0193

STUDY NO. : 0193 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE

# BIOCHEMISTRY (SUMMARY)

SURVIVAL ANIMALS ( 2)

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| Group Name  | NO. of<br>Animals | SODIUM<br>mEq∕ℓ |    | POTASSIU<br>mEq / Ø |     | CHLORIDE<br>mEq 🖊 l |   | CALCIUM<br>mg/dl |      | I NORGAN<br>mg/dl | HC PHOSPHORUS |
|-------------|-------------------|-----------------|----|---------------------|-----|---------------------|---|------------------|------|-------------------|---------------|
| Control     | 5                 | 140土            | 1  | 3.8±                | 0.2 | 105±                | 2 | 10.8士            | 0.2  | 8.1±              | 0.8           |
| 80 ppm      | 5                 | 140土            | 1  | $3.8\pm$            | 0.3 | $105\pm$            | 2 | 10.9±            | 0.2  | 8.6±              | 0.9           |
| 400 ppm     | 5                 | 140±            | 2  | $3.9\pm$            | 0.3 | 106±                | 1 | 10.7±            | 0.3  | 8.1±              | 0.9           |
| 2000 ppm    | 5                 | 140±            | 2  | $3.7\pm$            | 0.4 | 105土                | 1 | 10.8土            | 0.2  | 8.4土              | 0.7           |
| 10000 ppm   | 5                 | 141土            | 2  | 4.0±                | 0.4 | 105±                | I | 10.8±            | 0.2  | 8.5±              | 0.7           |
| 50000 ppm   | 5                 | 141土            | 2  | $3.9\pm$            | 0.3 | 104土                | 1 | 11.0土            | 0.2  | 8.4±              | 0.5           |
| Significant | difference ;      | *:P≦0.          | 05 | ** : P ≦ 0.01       |     |                     |   | Test of Dun      | nett | ·····             |               |

(IICL074)

BAIS 2

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APPENDIX A 5-2

# BIOCHEMISTRY (TWO-WEEK STUDY: SUMMARY)

RAT: FEMALE

STUDY NO. : 0193 ANIMAL : RAT F344 REPORT TYPE : AI SEX : FEMALE

NO. of

Animals

TOTAL PROTEIN

g/dl

ALBUMIN

g/dl

Group Name

# BIOCHENISTRY (SUMMARY)

# SURVIVAL ANIMALS ( 2)

A/G RATIO

T-BILIRUBIN

mg / dl

GLUCOSE

mg / dl

T-CHOLESTEROL

mg / els

| Significant o | difference ; | *:P≦0 | .05   | ** : P ≦ 0.0 | 1   |      |     | Test of Du | nett  |       |    |     |     |      | BAI  |
|---------------|--------------|-------|-------|--------------|-----|------|-----|------------|-------|-------|----|-----|-----|------|------|
| 50000 ppm     | 5            | 6.0±  | 0.1** | 3.4±         | 0.1 | 1.3± | 0.1 | 0.85±      | 0.02* | 176 土 | 8  | 83土 | 5** | 142± | 11** |
| 10000 ppm     | 5            | 5.7±  | 0.0   | $3.3\pm$     | 0.0 | 1.4± | 0.0 | 0.71±      | 0,16  | 180土  | 9  | 81士 | 6** | 140土 | 10** |
| mqq 000S      | 5            | 5.6±  | 0.1   | $3.3\pm$     | 0.1 | 1.4± | 0.0 | 0.64±      | 0.11  | 170土  | 18 | 72± | 2   | 124土 | 6    |
| 400 ppm       | 5            | 5.5±  | 0.1   | $3.3\pm$     | 0.1 | 1.4± | 0.1 | $0.55\pm$  | 0.13  | 172士  | 16 | 71± | 5   | 127上 | 9    |
| 80 ppm        | 5            | 5.7±  | 0.1   | 3.3±         | 0.1 | 1.4± | 0.1 | $0.57\pm$  | 0.11  | 190土  | 17 | 70土 | 3   | 125上 | 6    |
| Control       | 5            | 5.7±  | 0.2   | 3.3±         | 0.1 | 1.5± | 0.1 | 0.58±      | 0.03  | 185±  | 14 | 64± | 2   | 114土 | 4    |

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## PAGE: 4

PHOSPHOLIPID

mg/dl

STUDY NO. : 0193 ANIMAL. : RAT F344 REPORT TYPE : A1 SEX : FEMALE

# BIOCHEMISTRY (SUMMARY)

# SURVIVAL ANIMALS (2)

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Group Name NO. of GOT GPT LDII G-GTP CPK UREA NITROGEN CREATININE Animals IU/l IU/e IU/l IU/l IU∕ℓ ng∕dl mg / dl Control 5 60土 4 16士 1 372土 89 1± 1 178± 12 18.8士 2.1 0.4土 0.0 80 ppm 5 57士 4 16士 2  $288\pm$ 88 2土 0 175土 69 16.9± 3.30.4± 0.0 400 ppm 5 58土 2  $15\pm$ 1 343士 71 1土 0  $181\pm$ 71  $16.9 \pm$ 3.10.4土 0.0 2000 ppm 5 62± 6 14土 1 469土 239 2土 1 188土 63 19.0± 1.8 0.1土 0.0 10000 ppm 5 59± 2 14土 58 1 383士  $2\pm$ 0  $240 \pm$ 109 16.8土 2.1 0.4± 0.0 50000 ppm 5  $54\pm$ 3 13士 1\*\*  $387\pm$ 70  $3\pm$ 0  $193\pm$ 52 18.1± 1.7 0.4± 0.1 Significant difference ;  $*: P \leq 0.05$ \*\* : P ≦ 0.01 Test of Dunnett (IICL074)

BAIS 2

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### PAGE : 5

STUDY NO. : 0193 ANIMAL : RAT F344 REPORT TYPE : A1

# BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (2)

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SEX : FEMALE

Group Name	NO. of Animals	SODIUM mEq⁄¢		POTASSI mEq / l		CIII.ORIDE mEg∕¢		CALCIUM mg/ell	·	INORGAN mg/df	HC PHOSPHORUS
Control	5	142±	4	3.7±	0.4	109±	1	10.4±	0.4	6.9±	1.3
80 ppm	5	141土	3	3.6±	0.1	107土	1	10.6±	0.1	7.3±	1.4
400 ppm	5	141±	2	$3.9\pm$	0.3	106士	2	10.8土	0.1	7.7士	0.8
2000 ppm	5	140±	2	$3.9\pm$	0.4	$106\pm$	2*	10.8±	0.4	7.6±	1.0
10000 ppm	5	142土	1	3.6±	0.3	106±	1*	10.8±	0.4	7.1±	0.7
50000 ppm	5	142±	2	$3.8\pm$	0.2	106土	2	11.2±	0.3**	7.7土	1.0
Significant	difference ;	*:P≦0.	05	** : P ≦ 0.01				Test of Duni		· · · · · · · · · · · · · · · · · · ·	

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APPENDIX A 5-3

BIOCHEMISTRY (TWO-WEEK STUDY: SUMMARY)

MOSUE : MALE

STUDY NO. : 0194 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE

# BIOCHEMISTRY (SUMMARY)

# SURVIVAL ANIMALS ( 2)

Group Name NO. of TOTAL PROTEIN ALBUMIN A/G RATIO . T-BILIRUBIN GLUCOSE T-CHOLESTEROL GOT Animals g / તેર g/dl mg / d.£ ng∕d£ mg / df IU/l Control 5  $5.3\pm$  0.3 2.7土 0.2 1.1土 0.0 0.35± 0.18  $291\pm$ 18  $90\pm$ 7  $35\pm$ 80 ppm 5 5.3± 0.4  $2.7\pm$ 0.2 1.1土 0.1 0.31± 0.12 300土 24 96土 9  $39\pm$ 400 ppm 5 5.3± 0.2  $2.7\pm$ 0.1 1.1± 0.1 0.28± 0.03 7  $299\pm$ 11 94±  $33\pm$ 2000 ppm 5 5.6± 0.2  $2.9\pm$ 0.1  $1.1 \pm$ 0.1 0.30± 0.03 298士 60  $95\pm$ 7 36士 10000 ppm 5 5.4± 0.2 2.9土 0.1 1.2士 0.0 0.33± 0.02  $320\pm$ 17  $90\pm$ 5  $35\pm$ 50000 ppm 5 5.7土 0.3 3.0土 0.1\* 1.1± 0.1 0.45± 0.10  $265 \pm$ 25 87 土 8 34± \$ + Significant difference :  $*: P \leq 0.05$ \*\* : P ≦ 0.01 Test of Dunnett

(IICL074)

BAIS 2

PAGE : 1

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STUDY NO. : 0194 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE

# BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (2)

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Sroup Name	NO. of Animals	GPT IU∕e		LDII IU/(	2	CPK IU/e		UREA N mg/de	ITROGEN	SODIUM mEq/e		POTASSI mEq/		CHLORIDF mEq / l	
Control	5	15±	2	222±	28	47±	10	24.1士	4.0	150土	1	4.2±	0.2	117上	1
80 ppm	5	16±	3	266±	88	72±	33	25.1±	2.8	151±	Z	4.5±	0.1	116土	4
400 ppm	5	13土	2	197土	12	43±	11	23.6土	4.0	150土	1	4.4土	0.4	115±	4
2000 ppm	5	17±	5	$235\pm$	48	61±	32	24.9±	3.6	151±	3	1.1±	0.6	118±	1
10000 ppm	5	16土	3	239±	31	48土	11	24.2比	2.3	149±	2	3.8土	0.5	117土	2
50000 ppm	5	12上	4	322±	110	63±	38	26.0土	6.2	152±	5	4.0±	0.5	117土	2
Significant	difference ;	*:P≦0.	.05	** : P ≦ 0.0	1	····		Test of Du	nett	•••					

(IICL074)

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PAGE : 2

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STUDY NO. : 0194 ANIMAL : HOUSE BDF1 REPORT TYPE : A1 SEX : HALE

NO. of

Animals

CALCIUM

ng∕dl

Group Name

## BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (2)

SUNATANI,

INORGANIC PHOSPHORUS

ng∕dl

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Significant	difference ;	*:P≦(	). 05	** : P ≦ 0.01	Test of Dunnett	• •	
50000 ppm	5	9.5±	0.2	8.3± 1.8			
10000 ppm	5	9.4±	0.2	8.1± 1.3			
2000 ppm	5	9.4±	0.3	8.5± 0.4			
400 ppm	5	9.2±	0.3	8.6± 1.7			
80 ppm	5	9.3±	0.3	8.6± 2.1			
Control	5	9.3±	0.2	8.4± 2.1			

PAGE : 3

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APPENDIX A 5-4

BIOCHEMISTRY (TWO-WEEK STUDY: SUMMARY)

MOSUE : FEMALE

STUDY NO. : 0194 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : FENALE

# BIOCHENISTRY (SUMMARY)

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# SURVIVAL ANIMALS ( 2)

Group Name NO. of TOTAL PROTEIN ALBUNIN A/G RATIO T-BILIRUBIN GLUCOSE T-CHOLESTEROL GOT Animals g/dl g/dl mg / d.f mg/df ng / dl IU/l Control 5 5.2± 0.2 2.9± 0.1 1.3± 0.0 0.32± 0.10  $191\pm$ 22  $65\pm$ 4 45土 80 ppm 5 5.1± 0.3  $2.9\pm$ 0.2  $1.3 \pm$ 0.0 0.27± 0.08  $215\pm$ 46  $65\pm$ 3 40土 400 ppm 5 5.1± 0,3  $2.9\pm$ 0.1  $1.3\pm$ 0.1 0.31± 0.13  $200\pm$ 41 68± 3 42土 2000 ppm 5 5.2士 0.3  $2.9\pm$ 0.2 1.3± 0.1 0.30± 0.08  $202 \pm$ 58 65士 9 43士 10000 ppm 5 5.4± 0.3 3.0± 0.2 1.3± 0.1 0.31± 0.08 185士 50 58± 7 41土 50000 ppm 5 5.1± 0.2 2.9± 0.1 1.3土 0.1 0.38土 0.13  $185\pm$ 36 52± 5\*\*  $41\pm$ Test of Dunnett

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

(IICL074)

BAIS 2

PAGE : 4

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STUDY NO. : 0194 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : FEMALE

# BIOCHENISTRY (SUMMARY)

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# SURVIVAL ANIMALS ( 2)

# PAGE : 5

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oup Name	NO. of Animals	GPT IU∕ℓ		LDII IU/@		CPK IU/e	·	URIEA NI mg/cll		SODIUN mEg⁄¢		POTASSI mEg/		CHLORIDI mEg/l	
Control	5	19±	4	276±	56	69±	38	23.8士	6.7	153±	3	4.6±	0.6	117土	. 1
80 ppm	5	14±	5	257±	66	60土	18	25.2±	4.6	152土	3	4.0±	0.4	119±	3
400 ppm	5	13±	4	277±	70	56±	17	23.7±	3.3	153±	4	4.3±	0.2	116土	1
2000 ppm	5	15±	2	260土	39	67土	36	22.8±	3.8	153±	3	4.2±	0.6	117土	3
10000 ppm	5	20±	3	$311\pm$	44	62土	25	21.4土	3.9	155土	2	4.6±	0.7	116±	2
50000 ppm	5	19±	3	$331\pm$	64	47±	16	24.2±	4.6	154土	3	3.9±	0.3	118±	2

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STUDY NO. : 019 ANIMAL : MOU REPORT TYPE : A SEX : FEMALE	ISE BDF1			BIOCHE SURVIV	EMISTRY (SUMMARY) VAL ANIMALS (2)	
Group Name	NO. of Animals	CALCIU mg/dl		1NORGANIC PHOSPHORUS		PAGE : 6
Control	5	8.9±	0.1	8.5± 0.9		
80 ppm	5	8.9±	0.2	7.3± 1.2		
400 ppm	5	8.9±	0.3	7.4± 1.9		
2000 ppm	5	$8.9\pm$	0.4	7.5± 0.8		
10000 ppm	5	9.2±	0.3	8.4± 1.2		
50000 ppm	5	9.0±	0.4	7.6± 1.1		
Significant (NCL.074)	difference :	*:P≦(	).05	** : P ≤ 0.01	Tost of Dunnott ,	
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APPENDIX A 6-1

GROSS FINDINGS (TWO-WEEK STUDY: SUMMARY)

RAT : MALE : SACRIFICED ANIMALS

STUDY NO. ANIMAL REPORT TYPE SEX	: 0193 : RAT F344 : A1 : MALE	GROSS FINDINGS (SUMMARY) ALL ANIMALS (O- 2W)				PAGE : 1
0rgan	Findings	Group Name NO. of Animals	Control 10 (%)	80 ppm 10 (%)	400 ppm 10 (%)	2000 ppm 10 (%)
thymus	red zone		0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
liver	herniation		0 ( 0)	0 ( 0)	1 (10)	0 ( 0)

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STUDY NO. : 0193	GROSS FINDINGS (SUMMARY)
ANIMAL : RAT F344	ALL ANIMALS (0- 2W)
REPORT TYPE : A1	
SEX : NALE	

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PAGE :	2
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Organ	Findings	Group Name NO. of Animals	10000 ppm 10 (%)	50000 ppm 10 (%)	,
thymus Liver	red zone herniation		1 (10) 0 (0)	0 ( 0) 0 ( 0)	

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BAIS 2

APPENDIX A 6-2

GROSS FINDINGS (TWO-WEEK STUDY: SUMMARY)

RAT : FEMALE : SACRIFICED ANIMALS

STUDY NO. : 0193 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE	GROSS FINDINGS (SUMMARY) ALL ANIMALS (O- 2W)			PAGE
Organ Findings	Group Name Control NO. of Animals 10 (%)	maq 08 10 (%)	400 mag 10 (%)	2000 ppm 10 (%)
liver herniation	0 ( 0)	0 ( 0)	1 (10)	0 ( 0)

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STUDY NO. : 0193 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE	GROSS FINDINGS (SUMMARY) ALL ANIMALS (O- 2W)		PAGE : 4
OrganFindings	Group Name 10000 ppm NO. of Animals 10 (%)	50000 ppm 10 (%)	
liver herniation	0 ( 0)	1 (10)	
(HPT080)			BAIS 2

APPENDIX A 6-3

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

ANIMAL REPORT TYPE	: 0194 : MOUSE BDF1 : A1 : MALE	GROSS FINDINGS (SUMMARY) ALL ANIMALS (O- 2W)				PAGE : 1
0rgan	Findings	Group Name NO. of Animals	Control 10 (%)	80 DDM 10 (%)	400 ppm 10 (%)	2000 ppm 10 (%)
spleen	black zone		0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)
kidney	hydronephrasis		0 ( 0)	1 (10)	0 ( 0)	0 ( 0)

(HPT080)

BAIS 2

ANIMAL REPORT TYPE	: 0194 : MOUSE BDF1 : A1 : MALE		IDINGS (SUNMARY) LS (0- 2W)			PAGE : 2
0rgan	Findings	·	Group Name NO. of Animals	10000 ppm 10 (%)	50000 ppm 10 (%)	
spleen	black zone			0 ( 0)	1 (10)	
kidney	hydronephrosis			0 ( 0)	1 (10)	

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(HPT080)

BAIS 2

APPENDIX A 6-4

# GROSS FINDINGS (TWO-WEEK STUDY: SUMMARY) MOUSE: FEMALE : SACRIFICED ANIMALS

ANIMAL REPORT TYPE	: 0194 : MOUSE BDF1 : A1 : FEMALE	GROSS FINDINGS (SUMMARY) ALL ANIMALS (0- 2W)						
0rgan	Findings		Group Name NO. of Animals	Control 10 (%)	מסק 80 10 (%)	400 ppm 10 (%)	2000 pom 10 (%)	
spleen	black zone			0 ( 0)	0 ( 0)	0 ( 0)	2 (20)	
(HPT080)					· · · · · · · · · · · · · · · · · · ·		BAIS 2	

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STUDY NO. : 0194 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : FEMALE	GROSS FINDINGS (SUMMARY) ALL ANIMALS (O- 2W)	PAGE : 4
Organ Findings	Group Name 10000 ppm 50000 ppm NO. of Animals 10 (%) 10 (%)	
spleen black zone	0 ( 0) 2 ( 20)	
(HPT080)		BAIS 2

# APPENDIX A 7-1

# ORGAN WEIGHT (TWO-WEEK STUDY: SUMMARY), ABSOLUTE

RAT: MALE

STUDY NO. : 0193 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE UNIT: g

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

roup Name	NO, of Animals	Body N	Weight	ТНҮМ	US	ADRE	NALS	TEST	ES	HEAR	Г	LUNG	S	
Control	5	171±	5	0.374±	0.020	0.030土	0.001	$2.077\pm$	0.090	0.625±	0.041	0.777±	0.040	
mag 08	5	171±	4	0.372±	0.017	0.031±	0.003	$2.045\pm$	0.063	0.620土	0.013	0.758±	0.031	
400 ppm	5	165±	6	0.372±	0.025	0.033±	0.005	1.932±	0.184	$0.597\pm$	0.039	0.768±	0.044	
2000 ppm	5	167±	9	0.364±	0.019	0.037土	0.004	$2.081\pm$	0.256	0.584±	0.034	0.802±	0.060	
10000 ppm	5	166土	4	$0.374\pm$	0.029	0.032±	0.005	2.014±	0.187	0.611±	0.043	0.764±	0.034	
50000 ppm	5	158±	8*	$0.365\pm$	0.036	0.035±	0.007	1.900±	0.195	0.580±	0.013	0.757±	0.010	

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PAGE : 1

STUDY NO. : 0193 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE UNIT: g

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

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roup Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	
Control	5	1.360± 0.029	0.392± 0.018	6.816± 0.398	1.710± 0.039	
80 ppm	5	1.365± 0.098	0.409± 0.015	6.673± 0.469	1.683± 0.032	
400 ppm	5	1.382± 0.066	0.427± 0.017*	6.583± 0.569	1.692土 0.027	
2000 ppm	5	1.422± 0.104	0.451± 0.014**	7.440± 0.859	1.698± 0.043	
10000 ppm	5	1.430± 0.117	0.457± 0.016**	8.246上 0.532**	1.682土 0.057	
50000 ppm	5	1.421± 0.112	0.429± 0.024*	8.921± 0.718**	1.693土 0.053	

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PAGE : 2

## APPENDIX A 7-2

## ORGAN WEIGHT (TWO-WEEK STUDY: SUMMARY), ABSOLUTE

RAT: FEMALE

STUDY NO. : 0193 ANIMAL. : RAT F344 REPORT TYPE : A1 SEX : FEMALE UNIT: g

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

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PAGE : 3

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Group Name	NO. of Animals	Body I	Wəight	ТНҮМ	US	ADRE	NALS	OVAR	IES	HEAR	T	LUNG	5
Control	5	124±	4	0.302±	0.021	0.035±	0.007	0.079±	0.009	0.483±	0.018	$0.635\pm$	0.026
80 ppm	5	125 土	8	0,308±	0.016	0.038±	0.005	0.082±	0.011	0.484±	0.028	0.670±	0.053
400 ppm	5	128土	3	0.322±	0.024	0.040±	0.005	0.081±	0.015	0.486±	0.018	0.673±	0.053
2000 ppm	5	121±	6	$0.294\pm$	0.036	0.038±	0.007	0.077±	0.014	0.483±	0.045	0.660±	0.043
10000 ppm	5	120±	4	0.292±	0.040	0.038±	0.006	0.065±	0.011	0,455±	0.014	0.626±	0.014
50000 ppm	5	119±	3	$0.266\pm$	0.018	0.041±	0.007	0.076 $\pm$	0.005	0.458±	0.014	$0.595\pm$	0.010
Significan	t difference ;	*:P≦0.(	)5	** : P ≦ 0.01	u_		Tes	t of Dunnett	ł		##*****		
IICL040)											~~~~		

STUDY NO. : 0193 ANTHAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE UNIT: g

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

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Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	
Control	5	1.039± 0.061	0.304± 0.015	4.425± 0.307	1.622± 0.015	
mag 08	5	1.112± 0.065	0.316± 0.012	4.777± 0.460	1.622± 0.041	
400 ppm	5	1.127± 0.036	0.361± 0.016**	5.058± 0.331*	1.601土 0.034	
maga 000\$	5	1.077± 0.058	0.397± 0.022**	5.036土 0.406	1.607± 0.027	
10000 ppm	5	i.078± 0.064	0.382± 0.035**	5.737± 0.396**	1.586土 0.028	
50000 ppm	5	1.016± 0.048	0.372± 0.027**	6.225± 0.179**	1.605士 0.012	
Significan	t difference ;		* : P ≦ 0.01	Te:	st of Dunnett ,	
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## APPENDIX A 7-3

## ORGAN WEIGHT (TWO-WEEK STUDY: SUMMARY), ABSOLUTE

MOUSE: MALE

STUDY NO. : 0194 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE UNIT: g

NO. of

Animals

Rody Weight

Group Name

## ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIYAL ANIMALS (2)

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#### TILYMUS ADRENALS TESTES HEART LUNGS

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Significant IICL040)	difference ;	*:P≦0.05 **	: P ≦ 0.01		Test of Dunnett	1		
50000 ppm	5	22.4± 1.7	0.037± 0.006**	0.010± 0.003	0.171± 0.8	015 0.115±	0.012 0.138±	0.024
10000 ppm	5	24.2± 0.4	0.049± 0.006	0.008± 0.001	0.164± 0.	024 0.132±	0.013 0.145±	0.009
2000 ppm	5	24.6± 1.4	0.053± 0.011	0.003± 0.001	0.164土 0.4	051 0.125±	0.013 0.135±	0.008
400 ppm	5	24.1± 1.3	0.048± 0.008	0.009± 0.001	0.163± 0.	015 0.129±	0.010 0.143±	0.010
80 ppm	5	24.5± 1.4	0.051± 0.006	0.008± 0.002	0.165± 0.	026 0.116±	0.015 0.137±	0.011
Control	5	24.8± 1.3	0.054± 0.004	0.008± 0.002	0.178± 0.1	011 0.129±	0.011 0.148±	0.016

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PAGE : I

STUDY NO. : 0194 ANIMAL : HOUSE BDF1 REPORT TYPE : A1 SEX : MALE UNI

## ORGAN WEIGHT:ABSOLUTE (SUNMARY) SURVIVAL ANIMALS (2)

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Control 80 ppm 400 ppm	5 5	0.355± 0.024 0.353± 0.024		1.166± 0.117	0.429± 0.019 ·	
	5	0.353± 0.024	0.046± 0.005			
400 ppm				1.220± 0.113	0.432± 0.021	
	5	0.351± 0.018	0.047± 0.006	1.237± 0.112	0.424± 0.011	
2000 pepin	5	0.345± 0.023	0.045± 0.005	1.270土 0.189	0.425± 0.017	
10000 maa	5	0.356± 0.018	0.047土 0.005	1.397土 0.075	0.131± 0.016	
50000 ppm	5	0.347± 0.043	0.048± 0.007	1.311± 0.158	0.427± 0.008	
Significant dif	ifference ;	* : P ≦ 0.05	** : P ≦ 0.01	T	est of Dunnett ,	 

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## APPENDIX A 7-4

## ORGAN WEIGHT (TWO-WEEK STUDY: SUMMARY), ABSOLUTE

MOUSE: FEMALE

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

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PAGE : 3

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Group Name	NO. of Animals	Body Weight	THYNUS	ADRENALS	OVARIES	HEART	1.UNGS
Control	5	19.5± 0.7	0.065± 0.009	0.012± 0.002	0.022± 0.003	0.105± 0.008	0.148± 0.012
80 ppm	5	19.8土 0.5	0.064± 0.005	0.011± 0.001	0.024± 0.005	0.105± 0.011	0.134土 0.007
400 ppm	5	18.8± 0.4	0.058土 0.007	0.010± 0.001	0.019± 0.003	0.103± 0.008	0.129± 0.012
2000 ppm	5	19.1± 0.7	0.065± 0.006	0.010± 0.001	0.017± 0.003	0.104± 0.012	0.129± 0.014
10000 ppm	5	18.4± 1.0	0.059± 0.009	0.011± 0.003	0.020± 0.004	0.095± 0.009	0.136± 0.013
50000 ppm	5	18.1± 0.5*	0.054± 0.007	0.011± 0.002	0.017± 0.002	0.101± 0.022	0.129± 0.006
Significan	t difference ;	*:P≦0.05 **	: P ≦ 0.01	Test	of Dunnett		
IICI.040)					•• •• •• ••		

STUDY NO. : 0104 ANIMAL : MOUSE BDF1 REPORT TYPE : A1

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

SEX : FEHALE UNIT: g

PAGE : 4

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Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	
Control	5	0.260± 0.016	0.052± 0.005	0.811± 0.070	0.428土 0.017	
80 ppm	5	0.244± 0.020	0.050± 0.004	0.850土 0.116	0.441± 0.010	
400 ppm	5	0.262± 0.018	0.048± 0.005	0.849上 0.038	0.441± 0.015	
2000 ppm	5	0.255± 0.019	0.047± 0.005	0.924土 0.141	0.433± 0.016	
10000 ppm	5	0.255± 0.030	0.050± 0.009	0.880± 0.150	0.451± 0.013	
50000 ppm	5	0.248± 0.023	0.055± 0.005	0.945土 0.117	0.427± 0.013	
Significan	t difference ;	*:P≦0.05 **	: P ≦ 0.01	Τe	st of Dunnett ,	
IICL040)			9 Av			

## APPENDIX A 8-1

## ORGAN WEIGHT (TWO-WEEK STUDY: SUMMARY), RELATIVE

RAT: MALE

STUDY NO. : 0193 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE UNIT: %

#### ORGAN WEIGHT: RELATIVE (SUMMARY)

SURVIVAL ANIMALS (2)

PAGE : 1 Group Name NO. of Body Weight THYMUS ADRENALS HEART LUNGS TESTES Animals (g) Control 5 171± 5 0.219± 0.017 0.018土 0.001 1.212土 0.058  $0.364 \pm 0.018$ 0.453± 0.021 80 ppm 5 171± 4 0.217± 0.012 0.018± 0.002 1.196± 0.031 0.363土 0.016 0.444 0.016 400 ppm 5 165士 6 0.225± 0.014 0.020土 0.003  $1.169 \pm 0.090$ 0.362± 0.016 0.465± 0.026 2000 ppm 5 167土 9 0.219± 0.017 0.022士 0.002\*  $1.243 \pm 0.103$ 0.350± 0.008 0.480土 0.016 10000 ppm 5 166± 4  $0.226 \pm 0.018$  $0.019 \pm 0.003$ 1.212土 0.097  $0.368 \pm 0.024$ 0.460土 0.021 50000 ppm 5 158士 8\* 0.231± 0.024 0.022± 0.004\* 1.202± 0.104 0.367± 0.013  $0.480 \pm 0.032$ • • Significant difference :  $*: P \leq 0.05$ \*\* : P ≤ 0.01 Test of Dunnett ,

(IICL.042)

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STUDY NO. : 0193 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE UNIT: %

#### ORGAN WEIGHT: RELATIVE (SUMMARY)

SURVIVAL ANIMALS ( 2)

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Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	
Control	5	0.794± 0.021	0.229± 0.004	3.975士 0.147	0.998土 0.030	
10 mag	5	0.798± 0.039	0.239± 0.010	3.900± 0.184	0.985± 0.022	
400 ppm	5	0.836± 0.032	0.259土 0.005**	3.982± 0.275	1.025 ± 0.039	
mqq 000S	5	0.851± 0.024	0.271± 0.013**	4.444主 0.283*	1.019± 0.046	
10000 ppm	5	0.861± 0.054*	0.276土 0.009**	4.967± 0.278**	1.013± 0.025	
50000 ppm	5	0.899± 0.039**	0.272± 0.014**	5.640土 0.206**	1.072± 0.029**	
Significan	t difference ;	*:P≦0.05 **:	P ≤ 0.01	Test	: of Dunnett	
ICI.042)						ВА

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## APPENDIX A 8-2

## ORGAN WEIGHT (TWO-WEEK STUDY: SUMMARY), RELATIVE

RAT: FEMALE

STUDY NO. : 0193 ANIMAL : RAT F344 REPORT TYPE : AI SEX : FENALE UNIT: %

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

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iroup Name	NO. of Animals	Body W (	loight g)	THYMUS	ADRENALS	OVARTES	HEART	LUNGS	
Control	5	124±	4	0.244± 0.018	0.028± 0.006	0.064± 0.007	0.389± 0.017	0.512土 0.022	
80 ppm	5	125±	8	0.247± 0.013	0.031± 0.007	0.066土 0.009	0.388± 0.015	0.537± 0.035	
400 ppm	5	128±	3	0.251± 0.015	0.031± 0.004	0.063± 0.013	0.380± 0.013	0.527士 0.051	
2000 ppm	5	121±	6	0.242土 0.022	0.031± 0.006	0.063± 0.010	0.399± 0.031	0.545± 0.024	
10000 ppm	5	120±	4	0.242± 0.031	0.032± 0.005	0.055± 0.009	0.378± 0.017	0.520± 0.010	
50000 ppm	5	119±	3	0.223± 0.014	0.035± 0.005	0.063± 0.003	0.385± 0.017	0.500± 0.016	
Significan	t difference :	*:P≦0.0	15 *1	a : P ≦ 0,01	Те	st of Dunnett ,			
IICL042)						<u>.</u>			

PAGE : 3

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STUDY NO. : 0193 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE UNIT: %

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

roup Name	NO. of Animals	K I DNEYS	SPLEEN	LIVER	BRAIN	
Control	5	0.836± 0.042	0.245± 0.014	3.561± 0.187	1.307土 0.048	
80 ppm	5	0.892± 0.047	0.254± 0.015	3.824土 0.203	1.304土 0.090	
400 ppm	5	0.880± 0.011	0.282± 0.016**	3.949± 0.200**	1.251± 0.034	
2000 ppm	5	0.890± 0.033	0.328± 0.013**	4.158主 0.200**	1,330主 0.059	
10000 ppm	5	0.895± 0.034	0.317± 0.024**	4.761土 0.172**	1.318± 0.032	
50000 ppm	5	0.854± 0.034	0.313± 0.017**	5.231土 0.037**	1.350± 0.049	

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## APPENDIX A 8-3

## ORGAN WEIGHT (TWO-WEEK STUDY: SUMMARY), RELATIVE

MOUSE: MALE

STUDY NO. : 0194 ANIMAL : NOUSE BDF1 REPORT TYPE : A1 SEX : MALE UNIT: %

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

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PAGE : 1

Group Name	NO. of Animals	Body Weight (g)	TIIYNUS	ADRENALS	TESTES	HEART	LUNGS	
Control	5	24.8± 1.3	0.217± 0.017	0.033± 0.009	0.721± 0.068	$0.522 \pm 0.039$	0.599± 0.078	
80 ppm	5	24.5± 1.4	0.210± 0.027	0.031± 0.007	0.676土 0.121	0.472± 0.040	0.561± 0.049	
400 ppm	5	24.1± 1.3	0.201± 0.037	0.036± 0.006	0.676± 0.042	0.536土 0.066	0.591± 0.030	
2000 ppm	5	24.6± 1.4	0.216± 0.041	0.036土 0.006	0.658土 0.187	0.507土 0.055	0.547± 0.033	
10000 ppm	5	24.2± 0.4	0.204± 0.024	0.034土 0.004	0.677± 0.097	0.546± 0.054	0.602± 0.037	
50000 ppm	5	22.4± 1.7	0.165± 0.016	0.043± 0.011	0.767± 0.069	0.515± 0.061	0.616± 0.095	
Significan	t difference ;	* : P ≤ 0.05 **	: P ≦ 0.01	Tes	t of Dunnett .			
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#### ORGAN WEIGHT:RELATIVE (SUMMARY) SURVIVAL ANIMALS ( 2)

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iroup Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	
Control	5	1.434± 0.097	0.194± 0.022	4.713± 0.467	1.736± 0.099	
80 ppm	5	1.441± 0.056	0.188± 0.014	4.982± 0.388	1.764± 0.064	
400 ppm	5	1.456土 0.069	0.194± 0.020	5.127± 0.415	1.760± 0.073	
2000 ppm	5	1.400土 0.060	0.183± 0.017	5.148± 0.698	1.727± 0.076	
10000 ppm	5	1.472± 0.070	0.194± 0.020	5.784± 0.283**	1.784± 0.064	
50000 ppm	5	. 1.561± 0.283	0.213± 0.026	5.851± 0.274**	1.918土 0.148*	
Significan	t difference ;	*:P≦0.05 **:	₽ ≦ 0.01	Tost	of Dunnott	
lici.042)					· · · · · · · · · · · · · · · · · · ·	B

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PAGE : 2

## APPENDIX A 8-4

## ORGAN WEIGHT (TWO-WEEK STUDY: SUMMARY), RELATIVE

MOUSE: FEMALE

STUDY NO. : 0194 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : FEMALE UNIT: %

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

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PAGE : 3

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Foup Name	NO. of Animals	Body Weight (g)	TIIYMUS	ADRENALS	OVARIES	HEART	LUNGS	
Control	5	19.5± 0.7	0.334土 0.035	0.060± 0.008	0.114± 0.015	0.538± 0.022	0.763± 0.071	
80 ppm	5	19.8± 0.5	0.321± 0.023	0.056± 0.004	0.119± 0.026	0.529± 0.046	0.676± 0.035	
400 ppm	5	18.8± 0.4	0.312± 0.034	0.055± 0.007	0.103± 0.016	0.549± 0.034	0.685± 0.064	
2000 ppm	Б	19.1± 0.7	0.342± 0.030	0.052± 0.009	0.088土 0.019	0.546± 0.061	0.677± 0.058	
10000 ppm	5	18.4± 1.0	0.318± 0.032	0.060± 0.016	0.106± 0.020	0.517± 0.025	0.738± 0.052	
50000 ppm	5	18.1± 0.5*	0.301± 0.034	0.062± 0.008	0.092± 0.010	0.559± 0.110	0.713士 0.046	
Significan	t difference ;	*:P≦0.05 **	: P ≦ 0.01	Tos	st of Dunnott .			
IICL042)					14 Wester Herrich an an aite sa			E

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

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roup Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	
Control	5	1.335± 0.075	0.268± 0.017	4.165± 0.326	2.203± 0.083	
80 ppm	5	1.228± 0.098	0.253± 0.016	4.277± 0.510	2.222± 0.085	
400 ppm	5	1.391± 0.082	0.257± 0.022	4.514土 0.501	2.346± 0.112	
2000 ppm	5	1.336± 0.099	0.245± 0.027	4.832± 0.627	2.272± 0.079	
10000 ppm	5	1.381± 0.092	0.268± 0.038	4.755± 0.534	2.453土 0.124**	
50000 ppm	5	1.375± 0.112	0.304± 0.032	5.225± 0.562*	2.363± 0.094	

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PAGE : 4

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# APPENDIX A 9-1 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (TWO-WEEK STUDY: SUMMARY)

RAT : MALE : SACRIFICED ANIMALS

#### STUDY NO. : 0193 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE

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

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		Group Name Control No. of Animals 2	80 ppm 2	400 ppm 2	2000 ppm 2
)rgan	Findings	<1><2><3><4>     (%)   (%)   (%)	<1> <2> <3> <4> (%) (%) (%) (%) (%)	<1> <2> <3> <4> (%) (%) (%) (%)	<1> <2> <3> <4> (%) (%) (%) (%) (%)
lematopoie	tic system]				
pleen	engorgement of erythrocyte	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 (0)(0)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (50)(0)(0)(0)
Digestive	system]				
iver	herniation	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 (0)(0)(0)(0)(0)	1 0 0 0 (50)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)
	swelling:central	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	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 sy	stem]				
idney	eosinophilic body	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (50)(0)(0)(0)	1 1 0 0 (50)(50)(0)(0)	0 2 0 0 ( 0) (100) ( 0) ( 0)
Endocrine	system]				
ituitary	Rathke pouch	1 0 0 0 (50)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)

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#### STUDY NO. : 0193 ANIMAL : RAT F344 PEDOPT TYPE : A1

#### REPORT TYPE : A1 SEX : MALE

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

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PAGE: 2

Organ	Findings	Group Name 10000 ppm No. of Animals 2 <1> <2> <3> <4> (%) (%) (%) (%)	50000 ppm 2 <1> <2> <3> <4> (%) (%) (%) (%)	
[Hematopoie1	tic system]			
spleen	engorgement of erythracyte	1 0 0 0 (50)(0)(0)(0)	2 0 0 0 (100) ( 0) ( 0) ( 0)	
[Digestive s	system]			
liver	herniation	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	
	swelling:central	2 0 0 0 (100) ( 0) ( 0) ( 0)	2 0 0 0 (100) ( 0) ( 0) ( 0)	
[Urinary sys	stem]			
kidney	eosinophilic body	0 2 0 0 ( 0) (100) ( 0) ( 0)	0 2 0 0 ( 0) (100) ( 0) ( 0)	
[Endocrine :	system]			
pituitary	Rathke pouch	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	

(HPT150)

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## APPENDIX A 9-2

# HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

RAT : FEMALE : SACRIFICED ANIMALS

STUDY NO. : 0193 ANIMAL : RAT F344 REPORT TYPE : A1

: FEMALE

SEX

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

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PAGE : 3

		Group Name No. of Anima	ls	Con	rol !				ppm 2				ppm 2			200	0 ppm 2	
Organ	Findings		<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)			
[Respiratory :	system]																	
nasal ca∪it	respiratory metaplasia:gland	(	0 0) (	0	0	0 ( 0)	0 ( 0) (	0 0)	0	0 ( 0)	1 (50)	0 ( 0)	0 ( 0)	( (				
[llematopoietic	c system]																	
bone marrow	erythropoiesis:increased	(	0 0) (	0	0 ( 0)	0 (0)	0 ( 0) (	0 0)	0	0 (0)	0 ( 0)	0 ( 0)	0 ( 0)	( (				
spleen	engargement of erythracyte	(	0 0) (	0 ( 0)	0 0)	0 ( 0)	0 ( 0) (	0 0)	0 ( 0)	0 ( 0)	1 (50)	0 ( 0)	0 ( 0)	( (				
(Digestive sys	stem]																	
liver	herniation	(	0 0)	0 (0)	0	0 ( 0)	1 (50) (	0 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	(				
	granulation	(	0 0)	0 (0)	0	0 ( 0)	0 ( 0) (	0 0)	0 ( 0)	0 ( 0)	1 (50)	0 ( 0)	0 ( 0)	( (				
	swelling:central	(	0 0)	0 ( 0)	0 ( 0)	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]																	
kidney	basophilic change	(	0 0)	0 ( 0)	1 (50) (	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	0 ( 0)	(						
	mineralization:cortico-medullary junction	(	0 0)	2 (100)	0 ( 0)	0 ( 0)	0 ( 0)	2 (100)	0 ( 0)	0 ( 0)	0 ( 0) (	2 (100)	0 ( 0)	0	0 ( 0)	-	0 ( 0)	(

(IIPT150)

STUDY NO. : 0193 ANIMAL : RAT F344 REPORT TYPE : A1

#### ; FEMALE SEX

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

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PAGE: 4

		Group Name 10000 ppm No. of Animals 2 <1> <2> <3> <4>	50000 ppm 2 <1> <2> <3> <4>	
0rgan	Findings	(%) (%) (%) (%)	(%) (%) (%)	·
[Respiratory	system]			
nasal cavit	respiratory metaplasia:gland	0 0 0 0 (0)(0)(0)(0)	1 0 0 0 (50)(0)(0)(0)	
[Hematopoieti	c system]			
bone marrow	erythropoiesis:increased	1 0 0 0 (50)(0)(0)(0)	2 0 0 0 (100) ( 0) ( 0) ( 0)	
spleen	engargement of erythrocyte	1 0 0 0 (50)(0)(0)(0)	1 1 0 0 (50) (50) (0) (0)	
[Digestive sy	stem]			
liver	herniation	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	
	granulation	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	
	swelling:central	2 0 0 0 (100) ( 0) ( 0) ( 0)	2 0 0 0 (100) ( 0) ( 0) ( 0)	
[Urinary syst	em]			
kidney	basophilic change	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	
	mineralization:cortico-medullary junction	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	

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APPENDIX A 9-3

## HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

MOUSE: MALE : SACRIFICED ANIMALS

STUDY NO. : 0194 ANIMAL : MOUSE BDF1 REPORT TYPE : A1 SEX : MALE	HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 2W) PAGE : 1									
Organ Findings	Group Name Control No. of Animals 2 <1> <2> <3> <4> (%) (%) (%) (%)	80 ppm 2 <1> <2> <3> <4> (%) (%) (%) (%)	400 ppm 2 <1> <2> <3> <4> (%) (%) (%) (%)	2000 ppm 2 <1> <2> <3> <4> (%) (%) (%) (%)						
[Hematopoietic system]										
spleen extramedullary hematopoiesis	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 (0)(0)(0)(0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)						
(Urinary system)										
kidney hydronephrasis	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	0 0 0 0 0 0 ( 0) ( 0) ( 0)						
<1>:Slight <2>:Noderate <3>:Na	rked <4>:Severe									
(IIPT150)		·····		BAIS						

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ANIMAL : : REPORT TYPE : :	0194 IOUSE BDF1 ALE	HISTOLOGICAL FINDINGS : NON- ALL ANIMALS (0- 2W)	NEOPLASTIC LESIONS (SUMMARY)	PAGE : 2
0rgan	Findings	Group Name 10000 ppm No. of Animals 2 <1> <2> <3> <4> (%) (%) (%) (%)	50000 ppm 2 <1> <2> <3> <4> (%) (%) (%) (%)	
(Hematopoietic	system]			
spleen	extramedullary hematopoiesis	0 0 0 0 ( 0) ( 0) ( 0) ( 0)	1 0 0 0 (50)(0)(0)(0)	
[Urinary syste	n]			

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## APENDIX A 9-4

## HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

MOUSE: FEMALE :SACRIFICED ANIMALS

STUDY NO.:0194ANIMAL:MOUSE BDF1REPORT TYPE:A1SEX:FEMALE

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

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PAGE : 3

		Group Name No. of Animals	;	Cont 2					80 p 2	pm			400 2	ppm			2000	ppm 2	
)rgan	Findings			<2> (%)	<3> (%)	<4> (%)	<1> (%)		2> %)	<3> (%)	<4> (%)	<1) (%)	<2> (%)	<3> (%)	<4> (%)	(1> (%)	<2> (%)	<3> (%)	<4> (%)
ilematopo i e	tic system]																		
pleen	deposit of melanin		0 0) (	0 0) (	0 ( 0)	0 ( 0)	0 ( 0)	(	0 0) (	0 0) (	0 0)	0 ( 0	0 0) (	0 0)	0 ( 0)	0 0) (	0 0)	0 ( 0)	0 ( 0)
	extramedullary hematopoiesis		0 0) (	0 0) (	0 ( 0)	0 ( 0)	0 ( 0)		0 0) (	0 0) (	0 0)	0 ( 0)	0 0) (	0 0)	0 ( 0)	0 0) (	0 0)	0 ( 0)	0 ( 0)

(HPT150)

BAIS2

STUDY NO. ANIMAL REPORT TYP: SEX	: 0194 : MOUSE BDF1 E : A1 : FEMALE	HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (O- 2W)	PAGE : 4
0rgan	_ Findings	Group Name 10000 ppm 50000 ppm   No. of Animals 2 2   <1><2><3><4>< <1><2><3><4>   (%) (%) (%) (%) (%)	
[Hematopoi	etic system]		
spleen	deposit of melanin	0 0 0 0 1 0 0 0 ( 0) ( 0) ( 0) ( 0) ( 50) ( 0) ( 0) ( 0)	
	extramedullary hematopoiesis	0 0 0 0 2 0 0   ( 0) ( 0) ( 0) ( 0) ( 0)	
	<1>:Slight <2>:Moderate <3>:Mar	-ked <4>:Severe	

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(HPT150)

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APPENDIX A 10-1

IDENTITY AND PURITY OF ANTHRACENE PERFORMED AT THE JAPAN BIOASSAY LABORATORY (TWO-WEEK STUDY) IDENTITY AND PURITY OF ANTHRACENE PERFORMED AT THE JAPAN BLOASSAY LABORATORY (TWO-WEEK STUDIES)

Lot no. 304P4138

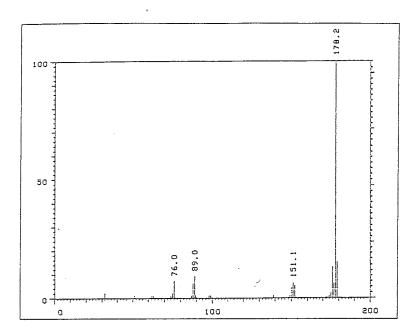
1. Spectral data

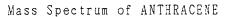
(1) Mass Spectrometry

Instrument: Hitachi M-80B

Ionization Voltage: 70eV

Ionization: EI(Electron Ionization)





Result:

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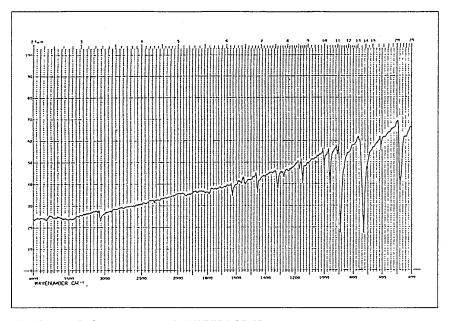
Molecular Weight

Theoretical Value	178.1(Calculated)
Literature Values	178(Sadtler Handbook by Sadtler Research Laboratories, Inc.)
Determined	178.2

#### (2) Infrared Spectrometry

Instrument	:	Hitachi 270-30
Cell	:	KBr(Wafer)

Slit : Medium



Infrared Spectrum of ANTHRACENE

Results:

#### Wave Number( $CM^{-1}$ )

Determines

460~ 490

 $700 \sim 750$  $860 \sim 900$ 

940~ 970

990~1010

1130~1160

1300~1330

 $1440 \sim 1470$ 

1610~1640

3030~3080

#### Literature Values

 $460 \sim 490$   $700 \sim 750$   $860 \sim 900$   $940 \sim 970$   $990 \sim 1010$   $1130 \sim 1160$   $1300 \sim 1330$   $1440 \sim 1470$   $1530 \sim 1550$   $1610 \sim 1640$   $3010 \sim 3050$ (Sadtler Handbook by Sadtler Research Laboratories, Inc.)

2. Conclusions: The result of the mass spectrum agreed with the theoretical value and the Infrared spectrum agreed with the literature values.

## APPENDIX A 10-2

## STABILITY OF ANTHRACENE AT THE JAPAN BIOASSAY LABORATORY (TWO-WEEK STUDY)

STABILITY OF ANTHRACENE AT THE JAPAN BIOASSAY LABORATORY(TWO-WEEK STUDIES) Lot no. 304P4138

1. Sample storage: Anthracene were stored for about 6 weeks at 5°C.

2. Gas Chromatography

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Instrument:	Hewlett Packard 5890A
Column:	Methyl Silicone(0.2mm $\phi$ × 30m)
Column Temperature:	170°C
Flow Rate:	l ml/min
Detector:	FID(Hydrogen Flame Ionization)
Injection Volume:	$1 \mu 1$

Results: Major peak and six impurities

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				AREA
Date	Peak No.	Retention Time(min)	AREA (measurement)	(percent of total peak)
07/29/92	1	4.175	83	0.0148
	2	10.792	753	0.134
	3	14.135	7278	1.30
	4	19.67	2881	0.514
	5	20.532	540751	96.4
	6	21.133	1655	0.295
	7	22.297	7640	1.36
09/14/92	1	5.125	78	0.0158
	2	10.738	646	0.131
	3	14.067	6254	1.27
	4	19.563	2508	0.508
	5	20.405	476164	96.4
	6	21.015	1446	0.293
	7	22.18	6768	1.37

 Conclusions: Gas chromtography indicated six impurities with concentration totaling <3.6% of the major peak.</li>

Consequently, Anthracene was stable as the chemical when stored for about 6 weeks at  $5\,^\circ\text{C}.$ 

## APPENDIX A 10-3

## ANALYSYS OF BIPHENYL CONCENTRATION IN FORMULATED DIETS

OF THE TOW-WEEK STUDIES

#### ANALYSIS OF ANTHRACENE CONCENTRATION AND HOMOGENEITY IN FORMULATED DIETS OF THE TWO-WEEK STUDIES

(Rat)(MOUSE)

		Concentrati	on of Anthracer	ne in feed for	Target Concentrat:	ion(ppm)
Date	80 ( a ( b	) 400		)00 ( a ) ( b )	10000 ( a ) ( b )	50000 ( a ) ( b )
08/18/92	70.8(88. (7.		(97.3) 19 (2.0)	)80 ( 99.0 ) ( 1.4)	9920 ( 99.2) ( 4.1)	50300 ( 101 ) ( 1.1 )

(a) Percent of target concentration

(b) Homogeneity(C.V.(%) n=7)

Analytical method: The sample were analyzed by the Gas Chromatography.

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Instrument:Hewlett Packard 5890AColumn:Methylsilicon ( $0.2 \text{mm} \phi \times 30 \text{m}$ )Column Temperature:260°CFlow Rate:1m1/minDetector:FIDInjection Volume:1 $\mu$ 1

## APPENDIX A 10-4

## STABILITY OF ANTHRACENE IN FORMULATED DIETS

OF THE TOW-WEEK STUDIES

#### STABILITY OF ANTHRACENE IN FORMULATED DIETS OF THE TWO-WEEK STUDIES

#### (Rat)(Mouse)

	С	onc	cent	ratio	n of An	thı	race	ne	in feed	fo	r Ta	rget	Concent	rat	tion(	(ppm)					
Date	80	(	а	)	400	(	а	)	200	0 (	а	)	10000	(	а	)	50000	(	a	)	
07/15/92(b)	69.	1(	100	)	372	(	100	)	193	0 (	100	)	10200	(	100	)	50100	(	100	))	
07/23/92(c)	90.	5(	131	)	461	(	124	)	201	0 (	104	)	10700	(	105	)	53100	(	106	3)	
08/06/92(d)	78.	8(	114	)	374	(	101	)	199	0 (	103	)	9600	(	94.	1)	48600	(	97	7.0)	

(a) Percent of concentration on preparation day

(b) Date of preparation

(c) Formulated diets were stored for 8 days at room temperature $(24 \pm 2^{\circ}C)$ .

(d) Formulated diets were stored for about 3 weeks at 8°C.

Analytical method: The sample were analyzed by the Gas Chromatography.

Instrument:Hewlett Packard 5890AColumn:Methylsilicon ( $0.2mm \phi \times 30m$ )Column Temperature:260°CFlow Rate:1m1/minDetector:FIDInjection Volume:1 $\mu$ l