N,N-ジメチルホルムアミドのラット及びマウスを用いた 吸 入 に よ る が ん 原 性 予 備 試 験 報 告 書

APPENDIX

(A1-1~A12)

2週間試験:ラット/0263;マウス/0264

APPENDIXES

- APPENDIX A 1-1 CLINICAL OBSERVATION (TWO-WEEK STUDY:SUMMARY)
 RAT:MALE
- APPENDIX A 1-2 CLINICAL OBSERVATION (TWO-WEEK STUDY:SUMMARY)
 RAT:FEMALE
- APPENDIX A 2-1 BODY WEIGHT CHANGES (TWO-WEEK STUDY:SUMMARY)
 RAT:MALE
- APPENDIX A 2-2 BODY WEIGHT CHANGES (TWO-WEEK STUDY:SUMMARY)
 RAT:FEMALE
- APPENDIX A 2-3 BODY WEIGHT CHANGES (TWO-WEEK STUDY:SUMMARY)
 MOUSE:MALE
- APPENDIX A 2-4 BODY WEIGHT CHANGES (TWO-WEEK STUDY:SUMMARY)
 MOUSE:FEMALE

)

- APPENDIX A 3-1 FOOD CONSUMPTION CHANGES (TWO-WEEK STUDY: SUMMARY)
 RAT:MALE
- APPENDIX A 3-2 FOOD CONSUMPTION CHANGES (TWO-WEEK STUDY:SUMMARY)
 RAT:FEMALE
- APPENDIX A 3-3 FOOD CONSUMPTION CHANGES (TWO-WEEK STUDY:SUMMARY)
 MOUSE:MALE
- APPENDIX A 3-4 FOOD CONSUMPTION CHANGES (TWO-WEEK STUDY:SUMMARY)
 MOUSE:FEMALE
- APPENDIX A 4-1 HEMATOLOGY (TWO-WEEK STUDY:SUMMARY)
 RAT:MALE
- APPENDIX A 4-2 HEMATOLOGY (TWO-WEEK STUDY:SUMMARY)
 RAT:FEMALE
- APPENDIX A 4-3 HEMATOLOGY (TWO-WEEK STUDY: SUMMARY)
 MOUSE: MALE
- APPENDIX A 4-4 HEMATOLOGY (TWO-WEEK STUDY:SUMMARY)
 MOUSE:FEMALE

APPENDIXES (CONTINUED)

- APPENDIX A 5-1 BIOCHEMISTRY (TWO-WEEK STUDY: SUMMARY)
 RAT:MALE
- APPENDIX A 5-2 BIOCHEMISTRY (TWO-WEEK STUDY:SUMMARY)
 RAT:FEMALE
- APPENDIX A 5-3 BIOCHEMISTRY (TWO-WEEK STUDY: SUMMARY)
 MOUSE: MALE
- APPENDIX A 5-4 BIOCHEMISTRY (TWO-WEEK STUDY: SUMMARY)
 MOUSE: FEMALE
- APPENDIX A 6-1 GROSS FINDINGS (TWO-WEEK STUDY:SUMMARY)
 RAT:MALE:SACRIFICED ANIMALS
- APPENDIX A 6-2 GROSS FINDINGS (TWO-WEEK STUDY: SUMMARY)
 RAT: FEMALE: SACRIFICED ANIMALS

)

- APPENDIX A 6-3 GROSS FINDINGS (TWO-WEEK STUDY:SUMMARY)
 RAT:MALE:DEAD AND MORIBUND ANIMALS
- APPENDIX A 6-4 GROSS FINDINGS (TWO-WEEK STUDY:SUMMARY)
 RAT:FEMALE:DEAD AND MORIBUND ANIMALS
- APPENDIX A 6-5 GROSS FINDINGS (TWO-WEEK STUDY:SUMMARY)
 MOUSE:MALE:SACRIFICED ANIMALS
- APPENDIX A 7-1 ORGAN WEIGHT (TWO-WEEK STUDY: SUMMARY), ABSOLUTE RAT: MALE
- APPENDIX A 7-2 ORGAN WEIGHT (TWO-WEEK STUDY: SUMMARY), ABSOLUTE RAT: FEMALE
- APPENDIX A 7-3 ORGAN WEIGHT (TWO-WEEK STUDY: SUMMARY), ABSOLUTE MOUSE: MALE
- APPENDIX A 7-4 ORGAN WEIGHT (TWO-WEEK STUDY: SUMMARY), ABSOLUTE MOUSE: FEMALE
- APPENDIX A 8-1 ORGAN WEIGHT (TWO-WEEK STUDY: SUMMARY), RELATIVE RAT: MALE
- APPENDIX A 8-2 ORGAN WEIGHT (TWO-WEEK STUDY: SUMMARY), RELATIVE RAT: FEMALE
- APPENDIX A 8-3 ORGAN WEIGHT (TWO-WEEK STUDY: SUMMARY), RELATIVE MOUSE: MALE
- APPENDIX A 8-4 ORGAN WEIGHT (TWO-WEEK STUDY: SUMMARY), RELATIVE MOUSE: FEMALE

APPENDIXES (CONTINUED)

- APPENDIX A 9-1 HISTOLOGICAL FINDINGS:NON-NEOPLASTIC LESIONS (TWO-WEEK STUDY:SUMMARY)
 RAT:MALE:SACRIFICED ANIMALS
- APPENDIX A 9-2 HISTOLOGICAL FINDINGS:NON-NEOPLASTIC LESIONS (TWO-WEEK STUDY:SUMMARY)
 RAT:FEMALE:SACRIFICED ANIMALS
- APPENDIX A 9-3 HISTOLOGICAL FINDINGS:NON-NEOPLASTIC LESIONS (TWO-WEEK STUDY:SUMMARY)
 RAT:MALE:DEAD AND MORIBUND ANIMALS
- APPENDIX A 9-4 HISTOLOGICAL FINDINGS:NON-NEOPLASTIC LESIONS (TWO-WEEK STUDY:SUMMARY)
 RAT:FEMALE:DEAD AND MORIBUND ANIMALS
- APPENDIX A 9-5 HISTOLOGICAL FINDINGS:NON-NEOPLASTIC LESIONS (TWO-WEEK STUDY:SUMMARY)
 MOUSE:MALE:SACRIFICED ANIMALS
- APPENDIX A 9-6 HISTOLOGICAL FINDINGS:NON-NEOPLASTIC LESIONS (TWO-WEEK STUDY:SUMMARY)
 MOUSE:FEMALE:SACRIFICED ANIMALS
- APPENDIX A 10-1 IDENTITY OF N.N-DIMETHYLFORMAMIDE (TWO-WEEK STUDIES)
- APPENDIX A 10-2 STABILITY OF N,N-DIMETHYLFORMAMIDE (TWO-WEEK STUDIES)
- APPENDIX A 11-1 CONCENTRATION OF N,N-DIMETHYLFORMAMIDE IN INHALATION CHAMBER (TWO-WEEK STUDIES)
- APPENDIX A 11-2 ENVIRONMENT OF INHALATION CHAMBER (TWO-WEEK STUDIES)

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APPENDIX A 12 METHODS FOR HEMATOLOGY AND BIOCHEMISTRY (TWO-WEEK STUDIES)

APPENDIX A 1-1

CLINICAL OBSERVATION (TWO-WEEK STUDY: SUMMARY)

RAT: MALE

STUDY NO.: 0263 ANIMAL: RAT F344 REPORT TYPE: A1 2 CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

PAGE: 1

Clinical sign	Graup Name	Adminis	stration We	eek-day					····							
		0-0	1-1	1-2	1-3	1-4	1-5	1-6	1-7	2-1	2-2	2-3	2-4	2-5	2-6	
		1	1	1	1	1	1	1	1	1	1	1	1	1	1	
OCONOTOR MOVEMENT DECR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
OOOHOTON HOTERENT PEON	100 ppm	0	0	0	0	0	0	0	0	0	0	0	Ō	0	0	
	200 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	400 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	800 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	1600 ppm	0	0	0	3	1	0	0	0	0	0	0	1	1	0	
UNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	100 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	200 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	400 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	800 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	1	1	0	
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	100 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	200 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	400 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	mqq 008	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	2	2	0	

(HAN190) BAIS 3

STUDY NO.: 0263 ANIMAL: RAT F344 REPORT TYPE: A1 2 CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

SEX : MALE

Clinical sign Group Name Administration Week-day 2-7 1 LOCOMOTOR MOVEMENT DECR Control 0 100 ppm 0 0 200 ppm 400 ppm 0 mqq 008 0 1600 ppm 0 HUNCHBACK POSITION Control 100 ppm 0 200 ppm 400 ppm 0 800 ppm 0 1600 ppm 0 PILOERECTION Control 0 100 ppm 200 ppm 0 400 ppm 800 ppm 0 1600 ppm 0

(HAN190)

BAIS 3

PAGE: 2

APPENDIX A 1-2

CLINICAL OBSERVATION (TWO-WEEK STUDY: SUMMARY)

RAT: FEMALE

STUDY NO.: 0263 ANIMAL: RAT F344 REPORT TYPE: A1 2

CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

SEX : FEMALE

PAGE: 3

Clinical sign	Group Name	∆dmini:	stration We	eek-day											
		0-0 1	1-1 1	1-2 1	1-3 1	1-4 1	1-5 1	1-6 1	1-7 1	2-1 1	2-2 1	2-3 1	2-4 1	2-5 1	2-6 1
TOCONOLOG HONDALIA DECID									_	_					
LOCONOTOR MOVEMENT DECR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	100 ppm	0	0	0	0	0	0	0	U	0	Ü	U	V	0	0
	200 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	400 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	mqq 008	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	3	0	0	0	0	0	0	0	0	0	0

(HAN190)

APPENDIX A 2-1

BODY WEIGHT CHANGES (TWO-WEEK STUDY:SUMMARY)

RAT: MALE

STUDY NO.: 0263

ANIMAL : RAT F344

UNIT : g

REPORT TYPE : A1 2

SEX : MALE

BODY WEIGHT CHANGES ALL ANIMALS

(SUMMARY)

PAGE: 1 Group Name Administration week-day_ 1-7 0-0 1-1 2-7 122± 3 144± 5 Control 124± 3 168± 9 100 ppm 122± 4 125± 5 146± 8 175± 15 200 ppm $123\pm$ 3 125± 3 149± 176± 13 122士 122± 4 142士 400 ppm 4 6 165± 8 800 ppm 122± 4 121士 4 130士 7** 147士 10** 109± 7** 1600 ppm 122± 3 121± 3 109士 13** Significant difference; $*:P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett

(IIAN260)

APPENDIX A 2-2

BODY WEIGHT CHANGES (TWO-WEEK STUDY: SUMMARY)

RAT: FEMALE

STUDY NO.: 0263 ANIMAL : RAT F344 UNIT : g

REPORT TYPE : A1 2

BODY WEIGHT CHANGES ALL ANIMALS

(SUMMARY)

SEX : FEMALE

pup Name	Admini	strati	on week-day					
	0-0		1-1		1-7		2-7	
Contral	101±	4	102±	4	112±	5	125±	6
100 ppm	100±	4	102±	3	114士	4	127±	4
200 ppm	100±	3	101±	3	111±	3	123±	3
400 ppm	100±	2	98±	3	107±	4*	116±	4**
mqq 008	100±	4	98±	3	103±	4**	110±	6**
1600 ppm	99±	3	97±	4*	89±	5**	94士	3**
Significant difference	e; *:P≦0	.05	** : P ≤ 0.0)1			Test of Dur	nett

(HAN260)

BAIS3

PAGE: 2

APPENDIX A 2-3

BODY WEIGHT CHANGES(TWO-WEEK STUDY:SUMMARY)

MOSUE: MALE

STUDY NO. : 0264

ANIMAL : MOUSE BDF1

UNIT : g
REPORT TYPE : A1 2

SEX : MALE

BODY WEIGHT CHANGES ALL ANIMALS

(SUMMARY)

PAGE: 1

lame	Administratio	n week-day			
	0-0	1-1	1-7	2-7	
Control	22.9± 1.0	22.8± 0.9	24.0± 1.0	25.1± 1.3	
Mag 001	22.8± 0.9	22.4± 1.0	23.4± 0.9	24.6± 1.2	
mdd 000	22.3± 1.0	22.2± 0.7	23.4± 1.1	24.7± 1.1	
400 ppm	22.4± 1.0	22.2± 0.9	23.6± 1.1	25.1± 1.1	
800 ppm	22.5± 0.8	21.6± 0.8*	22.9± 1.1	24.0± 1.1	
Mag 000	22.9± 1.0	21.6± 0.9*	22.6± 0.9*	23.3± 1.0**	
gnificant difference;	$*:P \leq 0.05$	$** : P \leq 0.01$		Test of Dunnett	

(HAN260)

APPENDIX A 2-4

BODY WEIGHT CHANGES (TWO-WEEK STUDY: SUMMARY)

MOSUE: FEMALE

STUDY NO.: 0264

ANIMAL : MOUSE BDF1

UNIT : g

REPORT TYPE : A1 2

SEX : FEMALE

BODY WEIGHT CHANGES ALL ANIMALS

(SUMMARY)

PAGE: 2 Group Name Administration week-day_ 0-0 1-1 1-7 2-7 Control 17.9 ± 0.7 18.0 ± 1.0 18.7± 1.1 20.4± 1.0 100 ppm 17.7± 1.1 18.6± 1.0 17.8± 0.8 20.0 ± 0.6 200 ppm 17.8± 0.5 17.7± 0.4 18.5± 0.5 20.2± 0.7 400 ppm 17.8± 0.8 17.8± 0.8 19.0± 0.8 20.6± 1.3 800 ppm 18.1± 0.8 17.6± 1.0 17.9± 0.7 19.4± 0.9 1600 ppm 18.0± 0.9 16.6± 1.0** 18.2± 1.1 18.8± 0.9** Significant difference; $*: P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett (HAN260)

APPENDIX A 3-1

FOOD CONSUMPTION CHANGES (TWO-WEEK STUDY: SUMMARY)

RAT: MALE

STUDY NO.: 0263

ANIMAL : RAT F344

UNIT ; g
REPORT TYPE : A1 2

SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

PAGE: 1

Group Name	Administration 1-7(7)	week-day(effective) 2-7(7)	
Control	14.6± 0.6	14.8± 0.7	
100 ppm	14.4± 1.0	16.2± 1.8	
200 ppm	15.0± 1.0	16.1± 2.0	
400 ppm	13.1± 0.7**	14.2± 0.7	
Mqq 008	11.8± 0.5**	12.5± 0.8*	
1600 ppm	6.7± 1.1**	7.2± 2.3**	
Significant differer	nce; *; P ≦ 0.05	** : P ≤ 0.01	Test of Dunnett

(HAN260)

APPENDIX A 3-2

FOOD CONSUMPTION CHANGES (TWO-WEEK STUDY: SUMMARY)

RAT: FEMALE

STUDY NO.: 0263 ANIMAL : RAT F344

UNIT : g REPORT TYPE: A1 2 FOOD CONSUMPTION CHANGES (SUMMARY)

ALL ANIMALS

SEX: FEMALE

PAGE: 2 Group Name Administration week-day(effective)_ 1-7(7) 2-7(7) Control 12.0 ± 0.9 11.6± 0.8 100 ppm 11.8± 0.3 11.8 ± 0.5 200 ppm 11.5± 0.5 11.9± 0.5 400 ppm 10.4± 0.7* 9.9± 0.6** 800 ppm 9.4± 0.7** 9.3± 0.7** 5.8± 1.1** 7.5± 0.9** 1600 ppm Test of Dunnett Significant difference : $*: P \leq 0.05$ ** : $P \leq 0.01$

(HAN260)

APPENDIX A 3-3

FOOD CONSUMPTION CHANGES (TWO-WEEK STUDY: SUMMARY)

MOSUE: MALE

STUDY NO.: 0264

ANIMAL : MOUSE BDF1

UNIT : g
REPORT TYPE : A1 2

FOOD CONSUMPTION CHANGES (SUMMARY)

ALL ANIMALS

Name	∧dministration	week-day(effective)		
	1-7(7)	2-7(7)		
Control	4.2± 0.3	4.2± 0.3		
100 ppm	4.1± 0.3	4.4± 0.4		
200 ppm	4.1± 0.3	4.4± 0.2		
400 ppm	3.9± 0.3	4.3± 0.5		
Maja 008	3.6± 0.3**	3.6± 0.2**		
1600 ppm	3.5± 0.2**	4.0± 0.4		
Significant difference		** : P ≦ 0.01	Test of Dunnett	

APPENDIX A 3-4

FOOD CONSUMPTION CHANGES(TWO-WEEK STUDY: SUMMARY)

MOSUE: FEMALE

STUDY NO.: 0264

ANIMAL : MOUSE BDF1

UNIT : g

REPORT TYPE : A1 2

SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

oup Name	Administration (1–7(7)	week-day(effecti∪e) 2-7(7)		
Control	3.5± 0.4	3.8± 0.2		
100 ppm	3.4± 0.2	3.7± 0.2		
200 ppm	3.4± 0.2	3.8± 0.2		
400 ppm	3.4± 0.2	3.6± 0.4		
mag 008	3.1± 0.2**	3.4± 0.2**		
1600 ppm	2.9± 0.3**	3.6± 0.3		
Significant differer	nce; *:P≦0.05 *	* : P ≤ 0.01	Test of Dunnett	

(IIAN260)

BAIS 3

PAGE: 2

APPENDIX A 4-1

HEMATOLOGY (TWO-WEEK STUDY: SUMMARY)

RAT: MALE

STUDY NO.: 0263 ANIMAL: RAT F344

SAMPLING DATE: 002-7
SEX: MALE REPORT TYPE: A1

HEMATOLOGY (SUMMARY) SURVIVAL ANIMALS (2)

oup Name	NO. of Animals	RED BL	DOD CELL	g ∕dl	BIN	HEMATOC %	CRIT	MCV f &		MCH pg		MCHC g∕dશ		PLATELE 1 0°/1	
Control	5	7.68±	0.33	14.1±	0.6	41.6±	1.7	54.2±	0.5	18.4±	0.1	33.9±	0.1	779±	78
100 ppm	5	7.70±	0.38	13.9±	0.6	41.6±	1.6	54.0±	0.7	18.1±	0.2	33,5±	0.2	946±	69
200 ppm	5	7,63±	0.33	13.8±	0.6	40.9±	1.4	53.6±	0.5	18.1±	0.2	33.8±	0.5	933±	100
400 ppm	5	7.76±	0.34	14.1±	0.5	41.5±	1.7	53.6±	0.6	18.2±	0.3	33.9±	0.6	821±	85
mqq 008	5	8.24±	0.38	14.9±	0.4	43.3±	1.6	52,6±	0.6*	18.1±	0.3	34.4±	0.5	883±	54
1600 ppm	5	7.28±	0.94	13.1±	1.5	39.5±	3.9	54.5±	2.1	18.1±	0.4	33.2±	0.8	682±	652

(IICL070)

BAIS 3

PAGE: 1

STUDY NO.: 0263 ANIMAL : RAT F344

SAMPLING DATE: 002-7 SEX: MALE REPORT TYPE : A1 HEMATOLOGY (SUMMARY) SURVIVAL ANIMALS (2)

SEX : MALE	REPORT T	TYPE : A1			PAGE: 2
Group Name	NO. of Animals	RETICULOCYTE ‰	PROTHROMBIN TIME	APTT sec	

Toda Namo	Animals	%i		s e c		sec	
Control	5	56±	15	12.3±	0.2	18.1±	0.4
100 ppm	5	63±	9	11.9±	0.2	18.1±	0.9
200 ppm	5	59±	13	11.9±	0.2	18.8±	0.3
400 ppm	5	54±	8	12.3±	0.3	19.1±	0.5
maq 008	5	47±	10	14.3±	0.7	19.4±	2.9
1600 ppm	5	83±	19*	12.7±	1.1	17.2±	2.6
Significant	difference;	*: P ≤ 0	.05	** : P ≤ 0.01			Test of Dunnett

(IICL070)

STUDY NO.: 0263 ANINAL: RAT F344

SAMPLING DATE: 002-7

HEMATOLOGY (SUMMARY)
SURVIVAL ANIMALS (2)

SEX : MALE

REPORT TYPE : A1

Group Name NO. of WBC Differential WBC (%) Animals 1 03/11.8 N-BAND N-SEG EOSINO BASO MONO LYMPHO OTHERS Control 5 2.47 ± 0.86 $0\pm$ 24士 11 $1\pm$ 0± 1 4± $70 \pm$ 2 10 $1\pm$ 1 100 ppm 5 0± 2.14士 0.79 0 $24\pm$ 12 1± 0土 1 0 $4\pm$ 70± 11 1± 1 200 ppm 5 2.26 ± 0.70 0土 0 $21\pm$ 5 0土 1 0土 0 $3\pm$ 2 75± 6 1± 1 400 ppm 5 1.94± 0.30 0± 0 19± 4 0± 0 0± 0 $3\pm$ $77 \pm$ 5 $1 \pm$ 2 5 Mqq 008 2.35± 1.18 1± 1 31± 5 1± 1 0± 0 $3\pm$ 2 64± 6 0± 0 1600 ppm 5 2.49± 0.80 $0\pm$ 32± 0± $0\pm$ 4土 $62 \pm$ $2\pm$ 1 Significant difference; $*:P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett

(IICL070)

BAIS 3

PAGE: 3

APPENDIX A 4-2

HEMATOLOGY (TWO-WEEK STUDY: SUMMARY)

RAT: FEMALE

STUDY NO. : 0263 ANIMAL : RAT F344

HEMATOLOGY (SUMMARY) SURVIVAL ANIMALS (2)

SAMPLING DATE: 002-7

REPORT TYPE : A1

SEX : FEMALE PAGE: 4

DUD Name	NO. of Animals	RED BLOOD CELL 1 O°/µ²	B ∕qγ B √qγ	HEMATOCRIT %	MCV f Q	MCH pg	MCHC g∕d%	PLATELET 1 Ο³ / με	
Control	5	8.05± 0.19	15.1± 0.7	43.5± 1.0	54.0± 0.4	18.7± 0.4	34.7± 0.8	641± 77	
100 ppm	5	8.06± 0.17	15.0± 0.3	43.4± 1.2	53.8± 0.6	18.6± 0.2	34.5± 0.3	749± 140	
200 ppm	5	8.13± 0.07	15.0± 0.1	43.8± 0.2	53.8± 0.3	18.5± 0.1	34.4± 0.1	749± 48	
400 ppm	5	8.30± 0.24	15.1± 0.5	44.0± 1.3	53.0± 0.3*	18.2± 0.2	34.4± 0.4	707± 114	
800 ppm	5	8.49± 0.18	15.7± 0.6	45.0± 1.1	53.0± 0.2*	18.5± 0.4	34.9± 0.6	705± 61	
1600 ppm	3	7.60± 1.20	14.1± 2.0	43.0± 5.4	56.8± 4.1	18.5± 0.5	32.7± 1.4	714± 569	
Significant	difference;	* : P ≤ 0.05	** : P ≤ 0.01		Test of Dunnett				

(HCL070)

STUDY NO.: 0263 ANIMAL: RAT F344

SAMPLING DATE: 002-7
SEX: FEMALE REPORT TYPE: A1

HEMATOLOGY (SUMMARY) SURVIVAL ANIMALS (2)

Group Name NO. of RETICULOCYTE PROTHROMBIN TIME APTT ‰ Animals sec s e c Control 5 $28\pm$ 6 12.1± 0.3 16.9± 0.7 100 ppm 5 34± 9 $12.1 \pm$ 0.2 17.6± 0.2 200 ppm 5 $41 \pm$ 10 $12.0 \pm$ 0.1 $17.5 \pm$ 0.7 400 ppm 5 $27 \pm$ 3 $12.5 \pm$ 0.1 $18.1 \pm$ 0.4* mqq 008 5 $27 \pm$ 2 $14.0 \pm$ 19.2± 0.9** 1.0* 1600 ppm 3 144士 146* 12.0± 0.3 16.4± 1.0 Significant difference : $*: P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett

(HCL070)

BAIS3

PAGE: 5

STUDY NO.: 0263 ANIMAL : RAT F344

SAMPLING DATE: 002-7

HEMATOLOGY (SUMMARY) SURVIVAL ANIMALS (2)

SEX : FEMALE REPORT TYPE : A1

oup Name	NO. of Animals	₩BC 1 O³/		Dif N-BAND	ferentia	L WBC (% N-SEG	6)	EOSINO		BASO		MONO		LYMPHO	·	OTHERS	
Control	5	2.40±	1.11	0±	0	21±	3	2±	1	0±	0	3±	1	73±	3	1±	
100 ppm	5	3.25±	1.49	0±	0	22±	6	1±	1	0±	0	4±	3	71±	2	Ι±	
200 ppin	5	2.41±	0.67	0±	0	22生	4	1±	1	0±	0	3±	2	73±	3	0±	
400 ppm	5	1.55±	0.52	0±	0	23±	9	1±	1	0±	0	3±	1	72±	8	1±	
mqq 008	5	1.17±	0.16	0±	1	30±	5	1±	1	0±	0	4±	3	64±	6	1±	
1600 ppm	3	2.16±	0.99	0±	0	36±	18	1±	1	0±	0	6±	2	51±	13*	6±	
Significant	difference;	* : P :	≦ 0.05	** : P ≤	0.01			Test	of Dunr	ett							<u></u>
L070)																· · · · · · · · · · · · · · · · · · ·	BA

PAGE: 6

APPENDIX A 4-3

HEMATOLOGY (TWO-WEEK STUDY: SUMMARY)

MOSUE: MALE

STUDY NO. : 0264

ANIMAL : MOUSE BDF1

SAMPLING DATE: 002-7 SEX: MALE

: MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY) SURVIVAL ANIMALS (2)

	10.00.11.00.10.														* 1,02		
anb Nawe	NO. of Animals	RED BLOOD CELL 1 O ⁶ /μ ^g		HEMOGLOBIN g∕d≬		HEMATOCRIT %		MCV f Q			MCH Pg		MCHC g∕dl		PLATELET 1 O³ / με		
Control	5	10.79±	0.39	16.3±	0.4	51.5±	2.4	47.7±	0.7	15.1±	0.2	31.6±	0.7	1193±	79		
100 ppm	5	10.47±	0.31	15.7±	0.5	49.5±	1.5	47.3±	0.5	15.1±	0.2	31.8±	0.5	1298±	106		
200 ppm	5	10.47±	0.32	15.8土	0.3	49.3±	2.2	47.1±	1.0	15.0±	0.2	32.0±	0.9	1324±	99		
400 ppm	5	10.54±	0.32	15.8±	0.6	49.5±	2.0	46.9±	0.7	15.0±	0.1	32.0±	0.3	1431±	119**		
mqq 008	5	11.04±	0.54	16.7±	0.8	52.3±	3,2	47.4±	0.6	15.1±	0.0	31,9±	0.5	1271±	84		
1600 ppm	5	11.30±	0.37	17.2±	0.6	52.4±	2.0	46.4±	0.6	15.2±	0.2	32.8±	0.3	1375±	69*		

PAGE: 1

(IICLO70) BAIS 3

STUDY NO.: 0264

ANIMAL : MOUSE BDF1

SAMPLING DATE: 002-7

SEX : MALE

REPORT TYPE : A1

HEMATOLOGY (SUMMARY) SURVIVAL ANIMALS (2)

up Name	NO. of Animals	WBC 1 O³∕		Dif N-BAND	ferential	. WBC (% N-SEG	5)	EOSINO		BASO		MONO		LYMPHO		OTHERS	
Control	5	2.19±	0.92	0±	1	10±	1	1±	1	0±	0	2±	1	87土	1	0±	
100 ppm	5	2.93±	1.48	0±	1	9±	2	1±	1	0±	0	2±	1	87±	2	0±	
200 ppm	5	2.46±	1.01	Ο±	0	12±	2	0±	1	0±	0	2±	1	86±	2	ο±	
400 ppm	5	3.21±	1.45	0±	1	15±	5	2±	1	0±	0	3±	2	79±	6*	1±	
mag 008	5	3.37±	1.71	0±	0	10±	2	1±	1	0±	0	1±	1	86±	2	0±	
1600 ppm	5	3,94±	1.19	0±	0	21±	19	1±	1	0±	0	3±	1	74±	18	0±	

(HCL070)

BAIS3

PAGE : 2

APPENDIX A 4-4

HEMATOLOGY (TWO-WEEK STUDY: SUMMARY)

MOSUE: FEMALE

STUDY NO.: 0264

HEMATOLOGY (SUMMARY) SURVIVAL ANIMALS (2)

ANIMAL: MOUSE BDF1

SAMPLING DATE: 002-7
SEX: FEMALE

REPORT TYPE : A1

PAGE: 3

up Name	NO. of Animals	RED BLO 1 0°/µ	OD CELL	g∕dl g∕dl	BIN	HEMATOC %	RIT	MCV f Q		MCH Pg		MCHC g∕dl		PLATELE 1 O³/μ:	
Control	5	10.13±	0.57	15.6±	0.5	47.9±	3.0	47.3±	1.1	15.4±	0.9	32.7±	1.8	932±	61
100 ppm	5	10.52±	0.26	15.8±	0.7	49.4±	2,1	46.9±	0.9	15.0±	0.3	32.0±	0.3	1174±	74**
200 ppm	5	10.28±	0.28	15.9±	0.6	48.1±	1.1	46.8±	0,5	15.4±	0.8	33.0±	1.4	1254±	95**
400 ppm	5	10.25±	0.37	15.4±	0.6	47.7±	1.8	46,5±	0.3	15.1±	0.1	32.4±	0.2	1283±	65**
mag 008	5	10.75±	0,42	16.3±	0.6	50.2±	2.0	46.7±	0.2	15.2±	0.1	32.5±	0.3	1202±	81**
1600 ppm	5	10.86±	0.37*	16.8±	0.9*	50.1±	1.8	46.2±	1.0	15.5±	0,5	33.5±	1.4	1265±	113**

(HCL070)

BAIS 3

STUDY NO. : 0264
ANIMAL : MOUSE BDF1

HEMATOLOGY (SUMMARY) SURVIVAL ANIMALS (2)

SAMPLING DATE: 002-7

SEX: FEMALE REPORT TYPE: A1

oup Name	NO. of Animals	WBC 1 O³∕µl		Dif N-BAND	ferentia	L WBC (% N-SEG	6)	EOSINO		BASO		MONO		LYMPHO		OTHERS	
Control	5	2.13± 0	0.78	0±	1	9±	2	Ι±	1	0±	0	3±	1	86±	2	0±	0
100 ppm	5	3.17± 1	1.63	1±	1	10±	2	0±	1	0±	0	2±	0	87±	2	0±	0
200 ppm	5	2.42± 1	1.24	0±	0	10±	1	2±	1	0±	0	Ζ±	1	86士	2	0±	0
400 ppm	5	3.06± 1	1.45	1±	2	10±	1	2±	2	0±	0	2±	1	85±	4	0±	0
800 ppm	5	4.10± 1	1.59	0±	0	11±	3	2±	1	0±	0	2±	1	85±	3	0±	0
1600 ppm	5	3.28± 0	0.32	1±	1	27±	11**	2±	2	0±	0	3±	1	66±	12*	1±	1
Significant	difference ;	*; P ≦ (0.05	**:P≦	0.01			Test	of Dunr	nett							
CL070)																	BAISS

APPENDIX A 5-1

BIOCHEMISTRY (TWO-WEEK STUDY: SUMMARY)

RAT: MALE

STUDY NO.: 0263 ANIMAL : RAT F344 BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (2)

SAMPLING DATE: 003-1

SEX : MALE

PAGE: 1 REPORT TYPE : A1

oup Name	NO. of Animals	TOTAL P	ROTEIN	ALBUMIN g∕dl		A/G RAT	10	T-BILII		GLUCOSE mg/dl		T-CHOLE: mg∕dl	STEROL	PHOSPHOI mg/dl	LIPID
Control	5	5.9±	0.1	3.6±	0.1	1.5±	0.0	0.23±	0.02	190±	8	58±	3	120±	3
100 ppm	5	6.1±	0.1	3.7±	0.1	1.5±	0.0	0.25士	0.02	190土	7	72±	4	145土	8
200 ppm	5	6.1±	0.1	3.7±	0.1	1.5±	0.0	0.27±	0.04	186士	7	75±	3	148士	11
400 ppm	5	6.0±	0.2	3,6±	0.2	1.5±	0.1	0.28±	0,03	178±	5*	82±	4*	152±	6*
Mag 008	5	6.1±	0.1	3.7±	0.1	1.5±	0.1	0.34±	0.08	162±	5**	92±	4**	147±	3
1600 ppm	5	6.1±	0.9	3.7±	0.5	1.5±	0.0	0.68±	0.39**	156±	6**	129±	21**	255±	16**
Significant	defference ;	* : P ≦ 0	.05	**: P ≤ 0.0	1			Test of Du	nnett						

BAIS3 (HCL074)

STUDY NO.: 0263 ANIMAL : RAT F344 BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (2)

SAMPLING DATE: 003-1

PAGE : 2 SEX : MALE REPORT TYPE : A1

roup Name	NO. of Animals	GOT I U / !	e	GPT IU/0	,	LDH IU/	2	G−GTP IU∕£		CPK I U / Q		UREA NI mg∕dl	TROGEN	CREATIN mg∕dl	INE
Control	5	59±	4	21±	2	177±	29	0±	1	154±	27	14.2±	2.3	0.4±	0.1
100 ppm	5	66±	10	25±	5	172±	14	1±	1	139±	7	14.8±	2.9	0.3±	0.1
200 ppm	5	62±	10	26±	5	168±	32	0±	1	128±	15	13.4±	0.9	0.4±	0.1
400 ppm	5	64土	8	26 ±	4	176±	34	1±	1	134±	17	14.0±	3.6	0.4±	0.0
Mqq 008	5	188±	83*	170±	107**	266±	73	1±	0	152±	32	19.3±	2.9	0.3±	0.1
1600 ppm	5	452±	290**	232±	131**	469±	605	16±	10**	150±	38	15.7±	4.1	0.3±	0.1
Significant	defference;	*: P ≦ (0.05 *	* : P ≤ 0.0	1			Test of Dun	nett						

(HCL074)

BAIS3

STUDY NO. : 0263 ANIMAL : RAT F344 BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (2)

SAMPLING DATE: 003-1 SEX : MALE

REPORT TYPE : A1

PAGE: 3

up Name	NO. of Animals	SODIUM mEq/Q		POTASSII mEq/l		CHLORIDE mEq/Q		CALCIUM mg∕dl		INORGAN mg∕dl	NIC PHOSPHORUS
Control	5	141±	1	4.1±	0.3	105±	1	10.8士	0.3	7.5±	1.6
100 ppm	5	142±	1	4.3±	0.2	105±	2	10.7±	0.5	7.5±	1.4
200 ppm	5	142±	2	4.2±	0.2	106±	1	10.7±	0.5	7,9±	1.3
400 ppm	5	141±	1	4.4±	0.1	106±	1	10.9±	0.3	7.1±	1.2
mqq 008	5	140±	1	4.6±	0.2*	106±	2	10.4±	0.4	8.1±	1.4
1600 ppm	5	143±	1*	4.6±	0,2*	107±	3	11.1±	0.4	6.5±	1.4
Significant	defference;	*: P ≤ 0.	.05	** : P ≦ 0.0	1			Test of Dur	nnett		
L074)											BA

APPENDIX A 5-2

BIOCHEMISTRY (TWO-WEEK STUDY: SUMMARY)

RAT: FEMALE

STUDY NO. : 0263 ANIMAL : RAT F344 BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (2)

SAMPLING DATE: 003-1

SEX : FEMALE REPORT TYPE : A1

PAGE : 4

100 ppm 5 5.8± 0.1 3.5± 0.1 1.5± 0.1 0.36± 0.09 188± 6 93± 3 168± 7 200 ppm 5 5.9± 0.1 3.6± 0.1 1.6± 0.1 0.37± 0.11 184± 10 98± 8 171± 15 400 ppm 5 5.7± 0.1 3.4± 0.1 1.5± 0.1 0.60± 0.17 165± 14** 100± 7 165± 15 800 ppm 5 5.9± 0.2 3.6± 0.1 1.6± 0.1 0.52± 0.37 171± 7** 120± 3** 187±	up Name	NO. of Animals	TOTAL PI g∕dl	ROTEIN	ALBUMIN g∕dl		A/G RAT	10	T-BILI mg∕d0		GLUCOSE mg∕dl		T-CHOLES	STEROL	PHOSPHOI mg/dl	JPID
200 ppm 5 5.9± 0.1 3.6± 0.1 1.6± 0.1 0.37± 0.11 184± 10 98± 8 171± 13 400 ppm 5 5.7± 0.1 3.4± 0.1 1.5± 0.1 0.60± 0.17 165± 14** 100± 7 165± 13 800 ppm 5 5.9± 0.2 3.6± 0.1 1.6± 0.1 0.52± 0.37 171± 7** 120± 3** 187± 7 1600 ppm 3 6.1± 0.7 3.7± 0.5 1.5± 0.1 0.58± 0.13 153± 3** 128± 15** 248± 23	Control	5	5.8±	0.1	3.5±	0.1	1,6±	0.1	0.36±	0.05	192±	7	71±	4	137±	8
400 ppm 5 5.7± 0.1 3.4± 0.1 1.5± 0.1 0.60± 0.17 165± 14** 100± 7 165± 15** 800 ppm 5 5.9± 0.2 3.6± 0.1 1.6± 0.1 0.52± 0.37 171± 7** 120± 3** 187± 1600 ppm 3 6.1± 0.7 3.7± 0.5 1.5± 0.1 0.58± 0.13 153± 3** 128± 15** 248± 25*	100 ppm	5	5,8±	0.1	3,5±	0.1	1.5±	0.1	0.36±	0.09	188±	6	93±	3	168±	7**
800 ppm 5 5.9± 0.2 3.6± 0.1 1.6± 0.1 0.52± 0.37 171± 7** 120± 3** 187± 7** 1600 ppm 3 6.1± 0.7 3.7± 0.5 1.5± 0.1 0.58± 0.13 153± 3** 128± 15** 248± 25**	200 ppm	5	5.9±	0.1	3.6±	0.1	1.6±	0.1	0.37±	0.11	184±	10	98士	8	171±	12**
1600 ppm 3 6.1± 0.7 3.7± 0.5 1.5± 0.1 0.58± 0.13 153± 3** 128± 15** 248± 23	400 ppm	5	5.7±	0.1	3.4±	0.1	1.5±	0.1	0.60±	0.17	165±	14**	100±	7	165士	13**
	Mqq 008	5	5.9±	0.2	3.6±	0.1	1.6±	0.1	0.52±	0.37	171±	7**	120±	3**	187±	7**
Significant defference : *: $P \le 0.05$ **: $P \le 0.01$ Test of Dunnett	1600 ppm	3	6.1±	0.7	3.7±	0.5	1.5±	0.1	0,58±	0.13	153±	3**	128±	15**	248±	23**
	Significant	defference ;	*: P ≤ 0	.05	** : P ≤ 0.0	1			Test of Du	nnett						<u></u>

(HCL074) BAIS3 STUDY NO.: 0263 ANIMAL: RAT F344 BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (2)

SAMPLING DATE: 003-1

SEX : FEMALE

REPORT TYPE : A1

Group Name NO. of GOT GPT LDII G-GTP CPK UREA NITROGEN CREATININE IU/Q Animals IU∕2 IU∕Q IU/l IU/l ing/dl mg/dl $60 \pm$ 3 20± 2 $227 \pm$ 42 1± $139 \pm$ 22 15.8± 3.4 0.4± 0.0 Control 5 0 5 1± 9 0.3± 0.0 100 ppm $59\pm$ 4 $21\pm$ 2 $225 \pm$ 29 142± 15.9± 2.2 $24\pm$ 2 248士 59 1土 141土 16 14.9± 2.8 0.4± 0.0 200 ppm 5 $62 \pm$ 4 1 400 ppm 5 $65 \pm$ 5 $25\pm$ 3 261± 68 1± 1 143士 27 14.6± 4.4 0.4± 0.1 Mgg 008 5 135士 95** 98** 309± 89 $2\pm$ 144± 17 19.5± 5.8 0.4 0.0 $101 \pm$ 3 157± $79\pm$ 72* $233 \pm$ 77 14士 9* 144士 28 15.6± 4.3 0.4± 0.1 1600 ppm 140*

Significant defference : $*: P \leq 0.05$

** : $P \le 0.01$

Test of Dunnett

PAGE: 5

(HCLO74) BAIS 3

STUDY NO.: 0263 ANIMAL : RAT F344

SAMPLING DATE: 003-1

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (2)

SEX : FEMALE REPORT TYPE : A1

oup Name	NO, of Animals	SODIUM mEq/Q		POTASSIUM mEq/Q	4	CHLORIDE mEq/2		CALCIUM mg∕dl		INORGAN mg∕dl	NIC PHOSPHORUS
Control	5	141±	1	3.9±	0.3	108±	1	10.5±	0.4	6,1±	1.1
100 ppm	5	142±	2	4.0±	0.3	109±	1	10.5±	0.4	6.8±	1.1
200 ppm	5	142±	1	3.7±	0.4	109±	1	10.6±	0.4	6.5±	1.0
400 ppm	5	141±	1	4.1±	0.2	108士	1	10.2±	0.2	6.6±	1.4
800 ppm	5	142±	2	4.0±	0.2	108±	1	10.4±	0.3	7.4±	1.0
1600 ppm	3	141±	1	4.3±	0.3	108±	4	11.5±	0.7**	6.2±	0,2
Significant	defference;	* ; P ≦ 0	. 05	** : P ≤ 0.01				Test of Dur	nett		
CI 074)	, ,,=					······································					RATI

(HCL074)

BAIS3

APPENDIX A 5-3

BIOCHEMISTRY (TWO-WEEK STUDY: SUMMARY)

MOUSE: MALE

STUDY NO.: 0264

ANIMAL : MOUSE BDF1
SAMPLING DATE : 003-1

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (2)

SEX : MALE

REPORT TYPE: A1

Group Name NO. of TOTAL PROTEIN ALBUMIN A/G RATIO T-BILIRUBIN GLUCOSE T-CHOLESTEROL GOT g/dl Animals g/dl mg/dl mg/dl mg/dl IU/Q Control 5 $5.3\pm$ 0.2 $2.9 \pm$ 0.2 1.2± 0.1 0.31± 0.04 26 $311 \pm$ 88± 10 $35\pm$ 3 100 ppm 5 $5.1\pm$ 0.3 2.8士 0.2 1.3± 0.1 0.28± 0.09 $306 \pm$ 9 85± 13 36± 3 200 ppm 5 $5.0 \pm$ 0.2 2.9± 0.1 1.4土 0.1* 0.31± 0.05 309± 18 89± 6 33± 2 400 ppm 5 $5.4 \pm$ 0.3 $3.0 \pm$ 0.1 $1.3 \pm$ 0.0 0.34± 0.09 $277 \pm$ 17 $103 \pm$ 39± 6 8 Mqq 008 5 $5.3 \pm$ 0.3 $3.0 \pm$ 0.2 $1.3 \pm$ 0.0 0.40± 0.17 $303 \pm$ 22 89± 10 42士 10 1600 ppm 5 5.4± 0.2 $3.2\pm$ 0.1* $1.5\pm$ 0.1** 0.42 ± 0.16 $291 \pm$ 15 $108\pm$ 6** $246 \pm$ 348* Significant defference; $*:P \leq 0.05$ ** : $P \le 0.01$ Test of Dunnett

PAGE: 1

(IICLO74) BAIS 3

STUDY NO. : 0264 ANIMAL : MOUSE BDF1

SAMPLING DATE: 003-1

SURVIVAL ANIMALS (2)

BIOCHEMISTRY (SUMMARY)

SEX : MALE

REPORT TYPE : A1

up Name	NO. of Animals	GPT IU/	0	LDH I U/	Q	CPK IU/	Q	UREA NI mg∕dl		SODIUM mEq/Q		POTASSI mEq/		CIILOR I DE m Eq / Q	
Control	5	16±	2	236±	50	150±	133	20.6±	4.2	151±	2	4.8±	0.7	119±	5
100 ppm	5	20±	4	230±	52	126±	81	23.2±	4.9	150±	1	4.5±	0.7	119±	3
200 ppm	5	19±	2	197±	19	86土	23	20.7±	3.2	150±	2	4.4±	0.4	121±	1
400 ppm	5	26±	5	280±	148	. 71±	24	23.0±	2.8	152±	1	4.8±	0.5	121±	1
mag 008	5	23±	5	381±	270	202±	219	21.5±	4.5	150±	2	5.6±	1.0	116±	5
1600 ppm	5	367±	585**	1479±	2493	114±	102	19.1±	3.3	150±	1	5.0±	0.6	117±	5

PAGE: 2

(HCL074) BAIS 3

STUDY NO. : 0264 ANIMAL : MOUSE BDF1

SAMPLING DATE: 003-1 SEX : MALE REPORT TYPE : A1 BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (2)

up Name	NO. of Animals	mg∕d£ CVFCINW		INORGANI mg∕dl	IIC PIIOSPIIORUS
Control	5	9.4±	0.5	8.7±	1.1
100 ppm	5	9.2±	0.2	8.1±	1.0
200 ppm	5	9.6±	0.5	6.8±	2.1
400 ppm	5	10.2生	0.5*	7.2±	1.4
800 ppm	5	9.8±	0.2	7.8±	2.0
1600 ppm	5	10.0±	0.3	8.7±	0.7

(HCL074)

BAIS 3

APPENDIX A 5-4

BIOCHEMISTRY (TWO-WEEK STUDY: SUMMARY)

MOUSE: FEMALE

STUDY NO. : 0264 ANIMAL : MOUSE BDF1

SAMPLING DATE: 003-1

BIOCHEMISTRY (SUMMARY) SURVIVAL ANIMALS (2)

SEX : FEMALE REPORT TYPE : A1

up Name	NO. of Animals	TOTAL, P g∕d¢	PROTEIN	g∕dl MLBUMIN		A/G RAT	10	T-BILI mg∕dl		GLUCOSE mg∕dl		T-CHOLES	STEROL	GOT IU/	Q
Control	5	5.1±	0.2	3.2±	0.2	1.6±	0.1	0.32±	0.04	284±	19	78±	7	46±	3
100 ppm	5	5.1±	0.3	3.1±	0.2	1.5±	0.0	0.41±	0.15	293±	20	96±	8**	45±	4
mqq 00S	5	5.3±	0.3	3,2±	0.2	1.6±	0.1	0.37±	0.07	291士	15	97±	6**	45±	5
400 ppm	5	5.2±	0.2	3.1±	0.1	1.5±	0.1	0.34±	0.03	264±	13	94±	7**	42±	5
mqq 008	5	5,1±	0.1	3,2±	0.0	1.6±	0.1	0.27±	0.11	287±	30	85±	6	48±	5
1600 ppm	5	5.5±	0.3	3.5±	0.2*	1.7±	0.1	0.52±	0,26	231±	28**	128±	9**	3452±	3478

PAGE: 4

(IICLO74) BAIS 3

STUDY NO.: 0264
ANIMAL: MOUSE BDF1

SAMPLING DATE: 003-1

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

SEX : FEMALE REPORT TYPE : A1

Group Name NO. of GPT LDII CPK UREA NITROGEN SODIUM POTASSIUM CHLORIDE Animals IU∕ Q IU/Q IU/l mg/dl mEq/Q mEq∕ Q mEq/Q Control 5 $22\pm$ 4 $277 \pm$ 33 94± 32 $18.2 \pm$ 1.5 $149 \pm$ 5.0 ± 0.6 117± 3 100 ppm 5 22± $281 \pm$ 89± 28 18.3± 1.1 150± 2 4.8± 0.8 $121 \pm$ 5 200 ppm 5 $25\pm$ 3 242± 45 ± 83 40 $19.0 \pm$ 0.9 $149 \pm$ 2 4.8± 0.7 $120 \pm$ 1 400 ppm 5 26± 6 $197 \pm$ 20 61± 15 $19.8 \pm$ 3.9 150± 2 4.8± 0.4 122± 3 800 ppm 5 $33\pm$ 7* $273 \pm$ $122 \pm$ 71 $16.4 \pm$ 2.6 150± 2 5.0 ± 0.5 119± 2 1600 ppm 5 4627± 4361** 15692 ± 17575 142± 49 $20.0 \pm$ 3.9 $149 \pm$ 1 5.2± 0.8 $113 \pm$ 5 Significant defference : $*: P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett

(IICL074)

BAIS 3

STUDY NO.: 0264 ANIMAL : MOUSE BDF1

SAMPLING DATE: 003-1

SURVIVAL ANIMALS (2)

SEX: FEMALE REPORT TYPE : A1

Group Name NO. of INORGANIC PHOSPHORUS CALCIUM Animals mg/dl mg/dl Control 5 9.2± 0.3 7.6± 1.7 100 ppm 5 9.7± 0.5 8.2± 2.0 200 ppm 5 9.8± 0.4 6.4± 1.3 400 ppm 5 0.5 10.0± 6.7± 1.2 800 ppm 5 $9.4 \pm$ 0.3 6.8± 1.9 1600 ppm 9.6± 0.5 9.1± 1.2 Significant defference; $*:P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett (HCL074)

PAGE: 6

BIOCHEMISTRY (SUMMARY)

BAIS 3

APPENDIX A 6-1

GROSS FINDINGS (TWO-WEEK STUDY: SUMMARY)

RAT: MALE: SACRIFICED ANIMALS

STUDY NO. : 0263

ANIMAL : RAT F344

REPORT TYPE : A1 SEX : MALE GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (2W)

PAGE: 1

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	100 ppm 10 (%)	200 ppm 10 (%)	400 ppm 10 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
.iver	red zone		0 (0)	0 (0)	0 (0)	0 (0)
	herniation		1 (10)	0 (0)	0 (0)	0 (0)
	accentuation of lobular structure		0 (0)	0 (0)	0 (0)	0 (0)

(HPT080)

BAIS3

STUDY NO. : 0263 ANIMAL : RAT F344 REPORT TYPE : A1

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (2W)

SEX : MALE

Group Name 1600 ppm mqq 008 Organ___ Findings_ 7 (%) NO. of Animals 10 (%) thymus atrophic 0 (0) 6 (86) Liver red zone 0 (0) 3 (43) herniation 0 (0) 0 (0) 0 (0) accentuation of lobular structure 6 (86) (HPT080) BAIS 3

APPENDIX A 6-2

GROSS FINDINGS (TWO-WEEK STUDY: SUMMARY)

RAT: FEMALE: SACRIFICED ANIMALS

STUDY NO. : 0263 ANIMAL : RAT F344 REPORT TYPE : A1

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (2W)

SEX : FEMALE

Group Name Contral 100 ppm 200 ppm 400 ppm Organ__ Findings_ 10 (%) NO. of Animals 10 (%) 10 (%) 10 (%) thymus atrophic 0 (0) 0 (0) 0 (0) 0 (0) liver red zane 0 (0) 0 (0) 0 (0) 0 (0) herniation 0 (0) 0 (0) 1 (10) 1 (10) accentuation of lobular structure 0 (0) 0 (0) 0 (0) 0 (0)

(IIPT080)

BAIS 3

STUDY NO. : 0263 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (2W)

PAGE: 4

Organ	Findings	Group Name 800 ppm NO. of Animals 10 (%)	1600 ppm 3 (%)	
thymus	atrophic	0 (0)	3 (100)	
liver	red zone	0 (0)	2 (67)	
	herniation	0 (0)	0 (0)	
	accentuation of lobular structure	0 (0)	3 (100)	
(HPT080)				BAICS

(HPT080)

BAIS 3

APPENDIX A 6-3

GROSS FINDINGS (TWO-WEEK STUDY: SUMMARY)

RAT: MALE: DEAD AND MORIBUND ANIMALS

STUDY NO. : 0263 ANIMAL : RAT F344

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

REPORT TYPE : A1 SEX : MALE

PAGE: 1

0rgan	Findings	Group Name NO. of Animals	Control 0 (%)	100 ppm 0 (%)	200 ppm 0 (%)	400 ppm 0 (%)
i∪er	red zone		- (-)	- (-)	- (-) - (-)	- (-)
	accentuation of lobular structure		- (-)	- (-)	- (-)	- (-)
estis	red		- (-)	- (-)	- (-)	- (-)

STUDY NO. : 0263 ANIMAL : RAT F344 REPORT TYPE : A1

SEX

: MALE

GROSS FINDINGS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 2W)

1600 ppm 3 (%) mag 008 Group Name 0 (%) Findings_ NO. of Animals Organ____ - (-) liver red zone 3 (100) - (-) 3 (100) accentuation of lobular structure - (-) 2 (67) testis red (HPT080) BAIS 3

APPENDIX A 6-4

GROSS FINDINGS (TWO-WEEK STUDY: SUMMARY)

RAT: FEMALE: DEAD AND MORIBUND ANIMALS

STUDY NO. : 0263 ANIMAL : RAT F3

: RAT F344

REPORT TYPE : A1 SEX : FEMALE GROSS FINDINGS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 2W)

Group Name Control 100 ppm 200 ppm 400 ppm Organ_ Findings_ NO. of Animals 0 (%) 0 (%) 0 (%) 0 (%) - (-) - (-) - (-) - (-) lung red zane - (-) - (-) - (-) - (-) liver red zone - (-) - (-) - (-) - (-) accentuation of lobular structure - (-) - (-) - (-) - (-) abdominal c hemorrhage - (-) - (-) - (-) - (-) ascites - (-) - (-) - (-) - (-) pleural fluid thoracic ca

(IIPT080)

BAIS 3

STUDY NO. : 0263 ANIMAL : RAT F344

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

REPORT TYPE : A1

SEX : FEMALE

Organ	Findings		800 ppm (%)	1600 ppm 7 (%)	
			····		
lung	red zone	-	(-)	3 (43)	
liver	red zane	-	(-)	6 (86)	
	accentuation of lobular structure	-	(-)	5 (71)	
abdominal c	hemorrhage	-	(-)	2 (29)	
	ascites	-	(-)	2 (29)	
thoracic ca	pleural fluid	_	(-)	3 (43)	
(HPT080)					BAIS3

APPENDIX A 6-5

GROSS FINDINGS (TWO-WEEK STUDY: SUMMARY)

MOUSE: MALE: SACRIFICED ANIMALS

STUDY NO. : 0264

ANIMAL : MOUSE BDF1
REPORT TYPE : A1

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (2W)

N 2

SEX : MALE

	NO. of Animals 10) (%)	10 (%)	10 (9	6) 	10	(%)
Lack zone	C) (0)	0 (0)	1 (10)	0	(0)
vdranephrasis	0	(0)	0 (0)	0 (0)	2	(20)

STUDY NO. : 0264

ANIMAL : MOUSE BDF1

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (2W)

~--

REPORT TYPE : A1

SEX : MALE

Organ	Findings	Group Name NO. of Animals	10	800 ppm (%)	1600 ppm 10 (%)	
spleen	black zone		1	(10)	1 (10)	
kidney	hydronephrosis		0	(0)	0 (0)	
(IIPT080)						BAIS 3

APPENDIX A 7-1

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

RAT: MALE

STUDY NO. : 0263 ANIMAL : RAT F344 REPORT TYPE : A1 ORGAN WEIGHT: ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2)

SEX : MALE UNIT: g

Group Name NO. of Body Weight THYMUS ADRENALS TESTES HEART LUNGS Animals Control 5 173± 9 0.319± 0.046 0.034± 0.005 2.007 ± 0.215 0.646± 0.036 0.736± 0.041 100 ppm 177± 13 0.309± 0.042 0.033± 0.004 2.138 ± 0.213 0.649 ± 0.036 0.763± 0.038 200 ppm 5 174± 14 0.314 ± 0.033 0.031 ± 0.005 2.028± 0.304 0.636± 0.047 0.732± 0.064 400 ppm 5 168± 7 0.284± 0.029 2.148± 0.211 0.630 ± 0.010 0.748± 0.054 Mqq 008 5 149± 11* 0.234± 0.040* 0.036± 0.005 0.699± 0.065 1.953± 0.199 0.561± 0.043** 1600 ppm 5 110± 13** 0.064± 0.059** 0.037± 0.010 1.438± 0.377** 0.475± 0.020** 0.637± 0.044* Significant difference; $*: P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett

(HCL040)

BAIS 3

STUDY NO.: 0263 ANIMAL: RAT F344 REPORT TYPE: A1

SEX : MALE UNIT: g ORGAN WEIGHT: ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2)

PAGE: 2

up Name	NO. of Animals	KIDI	VEYS	SPLI	EEN	LIV	ER	BRA		
Control	5	1.247±	0.075	0.376±	0.049	6.788±	0.748	1.645±	0.076	
100 ppm	5	1.311±	0.095	0.380±	0.042	7.842±	0.801	1.672±	0.039	
200 ppm	5	1.306±	0.035	0.393±	0.049	7.777±	0.936	1.595±	0.093	
400 ppm	5	1.335±	0.079	0.371±	0.022	7.363±	0.637	1.640±).112	
mag 008	5	1.237±	0.115	0.343±	0.038	6.354±	0.659	1.619±).070	
1600 ppm	5	1.242±	0.085	0.289±	0.027**	7.842±	0.483	1.547±	0.043	

(HCL040)

APPENDIX A 7-2

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

RAT: FEMALE

STUDY NO.: 0263
ANIMAL: RAT F344

REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

PAGE : 3

p Name	NO. of Animals	Body W	Weight	ТНУМ	JS 	ADRE	NALS	OVAR	IES	HEAR	ľ	LUNG	S
Cantrol	5	124±	3	0.267±	0.042	0,041±	0,008	0.058±	0.009	0.481±	0.025	0.595±	0.046
100 ppm	5	129±	4	0.279±	0.022	0.044±	0.005	0.061±	0.010	0.515±	0,012	0.621±	0.034
200 mag	5	123±	4	0.256±	0.024	0.041±	0.006	0.062±	0,010	0.505±	0.032	0.594±	0.049
400 ppm	5	114±	4**	0,235±	0.017	0.039±	0.010	0.058±	0.009	0.460±	0.025	0.551±	0.051
MQQ 008	5	113±	6**	0.212±	0.028*	0.038±	0.005	0.047±	0.009	0.464±	0.040	0.568±	0.036
1600 ppm	3	94±	3**	0.044±	0.010**	0.035±	0.003	0.048±	0,003	0.418±	0.025*	0.621±	0.034

(IICL040)

STUDY NO.: 0263
ANIMAL: RAT F344
REPORT TYPE: A1
SEX: FEMALE

UNIT: g

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

PAGE: 4

up Name	NO. of Animals	KIDN	NEYS	SPLI	GEN	LIV	ER	BRAI		
Control	5	0.932±	0.038	0.267±	0.015	4.453±	0.427	1.527±	0.088	
100 ppm	5	1.019±	0.029*	0.282±	0.011	5.122±	0.159	1.557±	0.046	
200 ppm	5	0.986±	0.051	0.279±	0.016	4.810±	0.225	1.551±	0.069	
400 ppm	5	0.945±	0.062	0.265±	0.019	4.266±	0.339	1.543±	0.072	
800 ppm	5	0.950±	0.039	0,258±	0.009	4.483±	0.265	1,537±	0.034	
1600 ppm	3	1.007±	0.013	0.230±	0.027*	5.947±	1.338	1.471±).105	

(IICL040)

APPENDIX A 7-3

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

MOUSE: MALE

STUDY NO. : 0264

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : MALE

SEX : MAL UNIT: g ORGAN WEIGHT: ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2)

PAGE: 1

oup Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	5	24.3± 1.3	0.051± 0.010	0.011± 0.001	0.177± 0.018	0.115± 0.012	0.138± 0.010
100 ppm	5	24.9± 1.3	0.043± 0.011	0.009± 0.002	0.171± 0.023	0.125± 0.021	0.142± 0.007
200 ppm	5	24.7± 1.1	0.044± 0.006	0.009± 0.002	0.177± 0.011	0.116± 0.007	0.138± 0.010
400 ppm	5	24.8± 0.7	0.039± 0.008	0.010± 0.002	0.167± 0.035	0.119± 0.014	0.136± 0.014
800 ppm	5	23.7± 0.7	0.039± 0.007	0.008± 0.002	0.175± 0.018	0.111± 0.015	0.140± 0.020
1600 ppm	5	23.0± 0.7	0.026± 0.009**	0.008± 0,002	0.158± 0.013	0.108± 0.005	0.155± 0.009
Significant	difference;	*: P ≤ 0.05 **	: P ≤ 0.01	Test	of Dunnett		
CI 040)	·	•					b

(HCL040)

STUDY NO.: 0264

ANIMAL : MOUSE BDF1

REPORT TYPE : A1

SEX : MALE UNIT: g

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

PAGE: 2

up Name	NO. of Animals	KIDN	NEYS	SPLI	EEN	LIV	ER	BRA		
Control	5	0.362±	0.027	0.047±	0.006	1.278±	0.057	0.424±	0.008	
100 ppm	5	0.399±	0.041	0.043±	0.006	1.422±	0.159	0.419±	0.013	
200 ppm	5	0.390±	0.035	0.045±	0.007	1.470±	0.149	0.438±	0.008	
400 ppm	5	0.398±	0.047	0.048±	0.007	1.628±	0.160**	0.426±	0.015	
mqq 008	5	0.383±	0.028	0.046±	0.009	1.375±	0.121	0.420±	0.017	
1600 ppm	5	0.374±	0.018	0,039±	0.008	1,478±	0.062	0.416±	0.011	
Significant	difference;	*: P ≤ 0.0	05 **	: P ≤ 0.01			T€	est of Dunnet		
CL040)						,				

APPENDIX A 7-4

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

MOUSE: FEMALE

STUDY NO.: 0264

ANIMAL : MOUSE BDF1

REPORT TYPE: A1
SEX: FEMALE
UNIT: g

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

PAGE: 3

5	20.0± 0.9	0.064± 0.006	0.010± 0.003	0.017± 0.004	0.093± 0.008	0.125± 0.008
5	19.7± 0.5	0.063± 0.011	0.009± 0.002	0.013± 0.005	0.093± 0.004	0.128± 0.009
5	20.0± 0.8	0.055± 0.007	0.011± 0.003	0.015± 0.004	0.094± 0.004	0.122± 0.008
5	20.8± 1.0	0.059± 0.005	0.010± 0.002	0.014± 0.003	0.101± 0.006	0.133± 0.014
5	19.6± 0.6	0.057± 0.007	0.009± 0.002	0.014± 0.001	0.096± 0.007	0.133± 0.020
5	18.7± 0.9*	0.030± 0.004**	0.009± 0.003	0.014± 0.004	0.091± 0.010	0.146± 0.013
	5 5	5 20.0± 0.8 5 20.8± 1.0 5 19.6± 0.6	5 20.0± 0.8 0.055± 0.007 5 20.8± 1.0 0.059± 0.005 5 19.6± 0.6 0.057± 0.007	5 20.0± 0.8 0.055± 0.007 0.011± 0.003 5 20.8± 1.0 0.059± 0.005 0.010± 0.002 5 19.6± 0.6 0.057± 0.007 0.009± 0.002	5 20.0± 0.8 0.055± 0.007 0.011± 0.003 0.015± 0.004 5 20.8± 1.0 0.059± 0.005 0.010± 0.002 0.014± 0.003 5 19.6± 0.6 0.057± 0.007 0.009± 0.002 0.014± 0.001	5

(HCL040)

STUDY NO.: 0264

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : FEMALE UNIT: g

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

PAGE: 4

up Name	NO. of Animals	KID	NEYS	SPLI	EEN	LIV	ER	BRA		
Control	5	0.254±	0.008	0.051±	0.004	1.011±	0.105	0.413±	.023	
100 ppm	5	0.248±	0.012	0.049±	0.005	1.067±	0.055	0.405±	.020	
200 ppm	5	0.246±	0.014	0.047±	0.007	1.166±	0.112	0.408±	.016	
400 ppm	5	0.271±	0.012	0.053±	0.005	1.273±	0.095**	0.414±	.014	
800 ppm	5	0.261±	0.021	0.050±	0,006	1.146士	0.109	0.436±	.021	
1600 ppm	5	0.264±	0.019	0,053±	0.013	1,282±	0.141**	0.399±	.015	

(HCL040)

APPENDIX A 8-1

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

RAT: MALE

STUDY NO.: 0263 ANIMAL: RAT F344

REPORT TYPE : A1
SEX : MALE
UNIT: %

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

PAGE: 1

oup Name	NO. of Animals		Veight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS	
Control	5	173±	9	0.184± 0.024	0.020± 0.002	1.160± 0.096	0.374± 0.016	0.427± 0.021	
100 ppm	5	177±	13	0.174± 0.016	0.019± 0.002	1.209± 0.109	0.367± 0.014	0.432± 0.015	
200 ppm	5	174士	14	0.181± 0.018	0.018± 0.003	1.159± 0.100	0.365± 0.013	0.420± 0.023	
400 ppm	5	168±	7	0.170± 0.021	0.024± 0.005	1.280± 0.088	0.377± 0.010	0.446± 0.029	
Mqq 008	5	149±	11*	0.156± 0.019	0.024± 0.002	1.305± 0.053	0.376± 0.018	0.467± 0.010	
1600 ppm	5	110±	13**	0.054± 0.043**	0.035± 0.013	1.297± 0.220	0.437± 0.052	0.585± 0.042**	

(IICL042)

STUDY NO.: 0263 ANIMAL: RAT F344

REPORT TYPE : A1
SEX : MALE
UNIT: %

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

PAGE: 2

oup Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	
Control	5	0.721± 0.013	0.217± 0.018	3.919± 0.241	0.953± 0.039	
100 ppm	5	0.741± 0.026	0.214± 0.008	4.424± 0.161	0.948± 0.064	
200 ppm	5	0.753± 0.045	0,225± 0.013	4.452± 0.199*	0.921± 0.098	
400 ppm	5	0.797± 0.042	0.221± 0.008	4.387± 0.206	0.979± 0.068	
Mqq 008	5	0.827± 0.023*	0.229± 0.011	4.245± 0.145	1.087± 0.063	
1600 ppm	5	1.152± 0.201**	0.264± 0.019**	7.262± 1.194**	1.428± 0.181**	
Significant	difference;	*: P ≤ 0.05 **:	P ≤ 0.01	Test	of Dunnett	

(IICL042)

APPENDIX A 8-2

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

RAT: FEMALE

STUDY NO.: 0263 ANIMAL: RAT F344 REPORT TYPE: A1

SEX : FEMALE UNIT: %

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

PAGE: 3

up Name	NO. of Animals		Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	5	124±	3	0.216± 0.032	0.033± 0.006	0.047± 0.006	0.389± 0.023	0.481± 0.036
100 ppm	5	129±	4	0.217± 0.018	0.034± 0.005	0.048± 0.007	0.401± 0.011	0.483± 0.025
200 ppm	5	123±	4	0.209± 0.019	0.034± 0.005	0.051± 0.009	0.412± 0.028	0.484 ± 0.026
400 ppm	5	114±	4**	0.207± 0.017	0.034± 0.008	0.051± 0.010	0.404± 0.022	0.484± 0.042
mqq 008	5	113±	6**	0.188± 0.019	0.034± 0.006	0.041± 0.006	0.412± 0.026	0.505± 0.029
1600 ppm	3	94±	3**	0.047± 0.011**	0.038± 0.004	0.052± 0.005	0.445± 0.027	0.661± 0.057**

(IICL042)

STUDY NO.: 0263 ANIMAL : RAT F344 REPORT TYPE : A1

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

SEX: FEMALE UNIT: %

PAGE: 4 Group Name NO. of KIDNEYS SPLEEN LIVER BRAIN Animals Control 5 0.754 ± 0.013 0.216 ± 0.008 3.597 ± 0.267 1.236 ± 0.076 100 ppm 5 0.793 ± 0.033 0.219 ± 0.004 3.984 ± 0.096 1.213 ± 0.074 200 ppm 0.804 ± 0.033 0.228 ± 0.008 3.926 ± 0.196 1.265 ± 0.035 400 ppm 5 0.831 ± 0.043** 0.233 ± 0.013 3.744 ± 0.184 1.356 ± 0.031 800 ppm 5 0.844生 0.021** 0.229 ± 0.008 3.981 ± 0.098 1.368± 0.088* 1600 ppm 3 1.072± 0.026** 0.246 ± 0.036 6.318± 1.319** 1.567± 0.149** Significant difference; $*:P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett (HCL042)

APPENDIX A 8-3

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

MOUSE: MALE

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

STUDY NO.: 0264
ANIMAL: MOUSE BDF1

REPORT TYPE: A1
SEX: MALE
UNIT: %

Group Name NO. of Body Weight THYMUS ADRENALS TESTES HEART LUNGS

di pup raile	Animals	(g)	THINOS	nDnennLo	TESTES	nean1	Lundo	····································
Control	5	24.3± 1.3	0.208± 0.038	0.044± 0.005	0.726± 0.043	0.472± 0.045	0.568± 0.045	
100 ppm	5	24.9± 1.3	0.173± 0.043	0.037± 0.009	0.685± 0.075	0.498± 0.061	0.572± 0.038	
200 ppm	5	24.7± 1.1	0.178± 0.030	0.037± 0.008	0.715± 0.044	0.468± 0.016	0.558± 0.041	
400 ppm	5	24.8± 0.7	0.158± 0.028	0.040± 0.008	0.675± 0.147	0.479± 0.054	0.550± 0.048	
mqq 008	5	23.7± 0.7	0.163± 0.025	0.032± 0.007	0.740± 0.071	0.468± 0.055	0.588± 0.072	
1600 ppm	5	23.0± 0.7	0.114± 0.036**	0.037± 0.011	0.685± 0.064	0.469± 0.023	0.673± 0.049*	
Significant	difference;	* : P ≤ 0.05 **	: P ≤ 0.01	Tes	et of Dunnett			

PAGE: 1

(HCL042) BAIS 3

STUDY NO.: 0264

ANIMAL : MOUSE BDF1

REPORT TYPE : A1

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

SEX : MALE UNIT: %

up Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	
Control	5	1.485± 0.064	0.194± 0.027	5.263± 0.367	1.745± 0.077	
100 ppm	5	1.597± 0.093	0.173± 0.025	5.695± 0.459	1.682± 0.100	
200 ppm	5	1.575± 0.084	0.183± 0.025	5.940± 0.470	1.776± 0.071	
400 ppm	5	1.608± 0.193	0.196± 0.027	6.568± 0.528**	1.722± 0.055	
mqq 008	5	1.616± 0.087	0.195± 0.034	5.797± 0.355	1.773± 0.079	
1600 ppm	5	1.624± 0.088	0.170± 0.034	6.430± 0.459**	1.807± 0.077	

(IICL042)

BAIS3

PAGE : 2

APPENDIX A 8-4

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

MOUSE: FEMALE

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

STUDY NO. : 0264
ANIMAL : MOUSE BDF1
REPORT TYPE : A1

SEX : FEMALE UNIT: %

⊅ Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS	
Control	5	20.0± 0.9	0.322± 0.027	0.051± 0.013	0.086± 0.021	0.465± 0.032	0.622± 0.024	
100 ppm	5	19.7± 0.5	0.320± 0.057	0.047± 0.010	0.066± 0.025	0.473± 0.024	0.647± 0.040	
200 ppm	5	20.0± 0.8	0.276± 0.028	0.053± 0.013	0.074± 0.019	0.471± 0.017	0.611± 0.041	
400 ppm	5	20.8± 1.0	0.283± 0.026	0.048± 0.011	0.068± 0.016	0.489± 0.038	0.641± 0.074	
800 ppm	5	19.6± 0.6	0.291± 0.034	0.046± 0.007	0.072± 0.003	0.488± 0.025	0.678± 0.099	
1600 ppm	5	18.7± 0.9*	0.159± 0.028**	0.046± 0.015	0.074± 0.022	0.487± 0.033	0.782± 0.058**	

PAGE: 3

(HCL042) BAIS 3

STUDY NO.: 0264

ANIMAL : MOUSE BDF1
REPORT TYPE : A1

SEX : FEMALE UNIT: %

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

PAGE: 4

NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN		
5	1,268± 0.056	0.253± 0.014	5.039± 0.386	2.067± 0.213		
5	1.257± 0.074	0.248± 0.025	5.411± 0.393	2.053± 0.093		
5	1.228± 0.039	0.235± 0.033	5.821± 0.470*	2.039± 0.072		
5	1.306± 0.077	0.255± 0.020	6.135± 0.436**	2.001± 0.133		
5	1.334± 0.071	0.254± 0.022	5.843± 0.384*	2.227± 0.108		
5	1.415± 0.071**	0.281± 0.060	6.863± 0.626**	2.142± 0.090		
	Animals 5 5 5 5 5	5 1.268± 0.056 5 1.257± 0.074 5 1.228± 0.039 5 1.306± 0.077 5 1.334± 0.071	Animals 5 1.268± 0.056 0.253± 0.014 5 1.257± 0.074 0.248± 0.025 5 1.228± 0.039 0.235± 0.033 5 1.306± 0.077 0.255± 0.020 5 1.334± 0.071 0.254± 0.022	Animals 5 1.268 ± 0.056 0.253 ± 0.014 5.039 ± 0.386 5 1.257 ± 0.074 0.248 ± 0.025 5.411 ± 0.393 5 1.228 ± 0.039 0.235 ± 0.033 5.821 ± 0.470* 5 1.306 ± 0.077 0.255 ± 0.020 6.135 ± 0.436** 5 1.334 ± 0.071 0.254 ± 0.022 5.843 ± 0.384*	Animals Sharm 5 1.268± 0.056 0.253± 0.014 5.039± 0.386 2.067± 0.213 5 1.257± 0.074 0.248± 0.025 5.411± 0.393 2.053± 0.093 5 1.228± 0.039 0.235± 0.033 5.821± 0.470* 2.039± 0.072 5 1.306± 0.077 0.255± 0.020 6.135± 0.436** 2.001± 0.133 5 1.334± 0.071 0.254± 0.022 5.843± 0.384* 2.227± 0.108	Animals Dam 5 1.268 ± 0.056 0.253 ± 0.014 5.039 ± 0.386 2.067 ± 0.213 5 1.257 ± 0.074 0.248 ± 0.025 5.411 ± 0.393 2.053 ± 0.093 5 1.228 ± 0.039 0.235 ± 0.033 5.821 ± 0.470* 2.039 ± 0.072 5 1.306 ± 0.077 0.255 ± 0.020 6.135 ± 0.436** 2.001 ± 0.133 5 1.334 ± 0.071 0.254 ± 0.022 5.843 ± 0.384* 2.227 ± 0.108

(HCL042)

APPENDIX A 9-1

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

RAT: MALE: SACRIFICED ANIMALS

STUDY NO. : 0263 ANIMAL : RAT F344 HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (2W)

REPORT TYPE : A1

SEX : MALE

PAGE: 1

Organ		Do Name Control of Animals on Study 2 9 1 2 3 4 (%) (%) (%) (%)	100 ppm 2 1 2 3 4 (%) (%) (%) (%)	200 ppm 2 1 2 3 4 (%) (%) (%) (%)	400 ppm 2 1 2 3 4 (%) (%) (%) (%)
[Hematopoie	tic system]				
thymus	atrophy	<pre></pre>	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)
[Digestive :	system]				
liver	herniation	2> 1 0 0 0 (50) (0) (0) (0)	<pre></pre>	(2> 0 0 0 0 (0) (0) (0) (0)	<pre></pre>
	necrosis:facal	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
	necrosis:single cell	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
	fibrosis	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
[Reproducti	ue system]				
testis	germ cell necrosis	<pre></pre>	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	<pre></pre>
Grade (a) b (c)	1: Slight 2: Moderate 3: Ma a: Number of animals examined at the site b: Number of animals with lesion c: b/a*100	rked 4 : Severe			RAIS

STUDY NO. : 0263

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (2W)

ANIMAL : RAT F344 REPORT TYPE : A1

SEX : MALE

Group Name mag 008 1600 ppm No. of Animals on Study 2 2 2 3 Findings (%) (%) (%) (%) (%) (%) 0rgan [Hematopoietic system] thymus < 2> < 2> 0 0 0 0 1 0 1 0 atrophy (0)(0)(0)(0) (50) (0) (50) (0) [Digestive system] liver < 2> 0 0 0 0 0 0 0 0 herniation (0)(0)(0)(0) (0)(0)(0)(0) necrosis:focal 0 0 0 0 0 2 0 0 (0)(0)(0)(0) (0)(100)(0)(0) 2 0 0 0 necrosis:single cell 0 0 0 0 (100) (0) (0) (0) (0)(0)(0)(0) fibrosis 0 0 0 0 0 2 0 0 (0)(0)(0)(0) (0)(100)(0)(0) [Reproductive system]

testis

germ cell necrosis

< 2> < 2> 0 0 0 0 1 1 0 0 (0)(0)(0)(0) (50) (50) (0) (0)

Grade 1 : Slight

2 : Moderate

3 : Marked

4 : Severe

b

a: Number of animals examined at the site

(c)

b: Number of animals with lesion c:b/a*100

(HPT150)

(a)

BAIS3

PAGE: 2

STUDY NO. : 0263 ANIMAL : RAT F344 HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (2W)

REPORT TYPE : A1 SEX : MALE

PAGE: 3

	(%)	(%) (%	5) (%)	(%)	2 (%)	3 4 (%) (%)	<u>1</u> (%)	(%)	3 (%)	(%)	<u>1</u> (%	2) (%			<u>4</u> (%)
vstem]															
decreased:sperma	(0) (0 (0) +	0	0 0	(0) (0	0	0		0	(0
debris of spermatic elements	(0) (0 (0)	0 (0 0 0 0) (0)	(0)	0 (0 0) (0)) (0 0)
- · - · · · -															
	decreased:sperma debris of spermatic elements : Slight 2: Moderate 3: Number of animals examined at the sit Number of animals with lesion	decreased:sperma 0 (0) (debris of spermatic elements 0 (0) (: Slight 2: Moderate 3: Marked 4: Severe: Number of animals examined at the site: Number of animals with lesion	Careased:sperma Careased:s	decreased:sperma	decreased: sperma	decreased:sperma	decreased:sperma	Compared Compared	decreased: sperma	decreased: sperma 0 0 0 0 0 0 0 0 0	decreased: sperma \[\begin{array}{c ccccccccccccccccccccccccccccccccccc	decreased:sperma	decreased: sperma \[\begin{array}{c ccccccccccccccccccccccccccccccccccc	decreased: sperma 0 0 0 0 0 0 0 0 0	decreased: sperma \[\begin{array}{c ccccccccccccccccccccccccccccccccccc

(IIPT150)

STUDY NO. : 0263 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

PAGE: 4

SACRIFICED ANIMALS (2W)

Group Name mag 008 1600 ppm No. of Animals on Study 2 2 2 3 (%) Organ__ Findings_ (%) (%) (%) (%) (%) (%) [Reproductive system] epididymis < 2> < 2> decreased:sperma 0 0 0 0 0 0 1 0 (0)(0)(0)(0) (0) (0) (50) (0) debris of spermatic elements 0 0 0 0 1 1 0 0 (0)(0)(0)(0) (50) (50) (0) (0) Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe a: Number of animals examined at the site (a) b b: Number of animals with lesion c : b / a * 100(c) (IIPT150) BAIS3

APPENDIX A 9-2

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

RAT: FEMALE: SACRIFICED ANIMALS

STUDY NO. : 0263 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (2W)

PAGE : 5

ndings	Group Name No. of Animals on Study Grade 1 (%) (%	Control 2 3 4 (%) (%)	100 ppm 2 1 2 3 4 (%) (%) (%) (%)	200 ppm 2 1 2 3 4 (%) (%) (%) (%)	400 ppm 2 1 2 3 4 (%) (%) (%) (%)
tem]					
-aphy	0	< 2> 0 0 0 0 0 0 (0) (0)	<pre></pre>	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)
n]					
crosis:focal	0 (< 2> 0 0 0 0) (0) (0)	2> 0 0 0 0 (0) (0) (0) (0)	(2> 0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)
anulation		0 0 0	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
crease in mitosis	0	< 2>) 0 0)) (0) (0)	<pre></pre>	<pre></pre>	0 0 0 0 (0) (0) (0) (0)
crosis:focal	0 (0 0 0	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
Slight 2: Moderate Number of animals examined at the Number of animals with lesion o / a * 100					
Vumber Vumber	of animals examined at the of animals with lesion	2 : Moderate 3 : Marked 4 : Severe of animals examined at the site of animals with lesion	of animals examined at the site of animals with lesion	2: Moderate 3: Marked 4: Severe of animals examined at the site of animals with lesion	2: Moderate 3: Marked 4: Severe of animals examined at the site of animals with lesion

STUDY NO. : 0263 ANIMAL : RAT F344 REPORT TYPE : A1

: FEMALE

SEX

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

PAGE: 6

Group Name 800 ppm 1600 ppm No. of Animals on Study 2 2 Grade Findings_ (%) (%) (%) [Hematopoietic system] thymus < 2> < 2> atrophy 0 0 0 0 0 2 0 0 (0)(0)(0)(0) (0)(100)(0)(0) [Circulatory system] heart < 2> < 2> necrosis:focal 0 0 0 0 1 0 0 0 (0)(0)(0)(0) (50) (0) (0) (0) granulation 0 0 0 0 (0) (0) (0) (0) (50) (0) (0) (0) [Digestive system] liver < 2> < 2> increase in mitosis 0 0 0 0 0 1 0 0 (0) (0) (0) (0) (0)(50)(0)(0) necrosis:focal 0 0 0 0 0 2 0 0 (0)(0)(0)(0) (0)(100)(0)(0) Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe (a) a: Number of animals examined at the site b b: Number of animals with lesion (c) c:b/a*100

(HPT150)

STUDY NO. : 0263 ANIMAL : RAT F344 REPORT TYPE : A1

SEX : FEMALE

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

PAGE: 7

		Group Name No. of Animals on Study Grade 1	Cont 2 2	trol 3 4	1 2	100 ppm 2 3 4	1	20 2 2	0 ppm 3 4		1	40 2 2	0 ppm	4
gan	Findings	(%)	(%)	(%) (%)	(%) (%) (%) (%)	(%)	(%)	(%) (%)		(%)	(%)	(%)	(%)
igestive sy	vstem]													
ver	necrasis:single cell	(0)		0 0 0 0) (0)	0 0	< 2> 0 0) (0) (0)	0 (0)	< 2 0 (0) (0 0	(0	< 2 0 0) (0	0 (0)
	fibrosis	0 (0)		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)

STUDY NO. : 0263 ANIMAL. : RAT F344

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (2W)

REPORT TYPE : A1 : FEMALE

(HPT150)

Group Name mag 008 1600 ppm No. of Animals on Study 2 2 2 3 2 3 4 Findings___ (%) (%) (%) (%) (%) (%) [Digestive system] liver < 2> < 2> 0 0 0 0 1 1 0 0 necrosis:single cell (50) (50) (0) (0) (0)(0)(0)(0) fibrosis 0 0 0 0 1 1 0 0 (0) (0) (0) (0) (50) (50) (0) (0) Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe (a) a: Number of animals examined at the site b b: Number of animals with lesion (c) c:b/a * 100

BAIS3

PAGE: 8

APPENDIX A 9-3

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

RAT: MALE: DEAD AND MORIBUND ANIMALS

STUDY NO. : 0263 ANIMAL : RAT F344 REPORT TYPE : A1

: MALE

SEX

(HPT150)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

PAGE: 1

BAIS3

DEAD AND MORIBUND ANIMALS (0- 2W)

Group Name Control 100 ppm 200 ppm 400 ppm No. of Animals on Study 0 0 0 0 2 3 4 Grade 2 3 4 2 3 (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) Findings [Hematopoietic system] < 0> bone marrow congestion (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) hemorrhage (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) ∜ ⟨ 0⟩ < 0> < 0> < 0> thymus hemorrhage (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) karyorrhexis < 0> < 0> < 0> < 0> spleen karyorrhexis [Circulatory system] heart hemorrhage Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe a: Number of animals examined at the site (a) b b: Number of animals with lesion (c) c:b/a*100

STUDY NO. : 0263 ANIMAL : RAT F344

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 2W)

REPORT TYPE : A1 SEX : MALE

0rgan	Findings	Group Name 800 ppm No. of Animals on Study 0 Grade 1 2 3 4 (%) (%) (%) (%)	1600 ppm 1 1 2 3 4 (%) (%) (%) (%)	
[Nematopoieti	c system]			
bone marrow	cangestion	< 0> (-) (-) (-) (-)	<pre></pre>	
	hemorrhage	(-) (-) (-) (-)	1 0 0 0 0 (100) (-0) (-0)	
thymus	hemorrhage	<pre></pre>	<pre></pre>	
	karyorrhexis	(-) (-) (-) (-)	0 0 1 0 (0) (100) (0)	
spleen	karyorrhexis	(-) (-) (-) (-)	\(\ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \ \	
[Circulatory	system]			
heart	hemarrhage	(-) (-) (-) (-)	<pre></pre>	
Grade <a>> b (c)	1: Slight 2: Moder a: Number of animals exami b: Number of animals with c: b / a * 100	ned at the site		

(IIPT150)

PAGE: 2

STUDY NO. : 0263 ANIMAL : RAT F344 HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

REPORT TYPE : A1

SEX : MALE

PAGE: 3

)rgan	N		rol 3 4 1 (%)	100 ppm 0 2 3 4 (%) (%) (%)	200 ppm 0 1 2 3 4 (%) (%) (%)	400 ppm 0 1 2 3 4 (%) (%) (%) (%)
Digestive sy	vstem]					
iver		· < 0>		< 0>	< 0>	< 0>
	necrasis:central	(-) (-) (-) (-) (-)	(-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
Reproductive	system]					
estis	hemorrhage	< 0>		< 0>	< 0>	< 0>
	TOURDET ENDINGE	(-) (-) (-) (-)	(-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
	germ cell necrosis	(-) (-) (-) (-) (-)		(-) (-) (-) (-)	(-) (-) (-) (-)
oididymis		< 0>		< 0>	< 0>	< 0>
	debris of spermatic elements	(-) (-) (-) (-) (-)	(-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
rade a > b	1: Slight 2: Moderate 3: a: Number of animals examined at the sit b: Number of animals with lesion c: b / a * 100	Marked 4 : Severe e				

STUDY NO. : 0263 ANIMAL : RAT F344 HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

REPORT TYPE : A1

SEX : MALE

Organ		p Name 800 ppm of Animals on Study 0 e 1 2 3 4 (%) (%) (%) (%)	1600 ppm 1 1 2 3 4 (%) (%) (%) (%)	
[Digestive s	ystem]			
liver	necrasis:central	(-) (-) (-)	0 0 1 0 (0) (0) (100) (0)	
(Reproductiv	e system]			
testis	hemorrhaga	(-) (-) (-) (-)	(1) 1 0 0 0 (100) (0) (0) (0)	
	germ cell necrosis	(-) (-) (-) (-)	1 0 0 0 (100) (0) (0) (0)	
epididymis	debris of spermatic elements	(-) (-) (-) (-)	<pre></pre>	
Grade (a > b (c)	1: Slight 2: Moderate 3: Ma a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	rked 4 ; Severe		
(IIPT150)				· · · · · · · · · · · · · · · · · · ·

APPENDIX A 9-4

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

RAT: FEMALE: DEAD AND MORIBUND ANIMALS

STUDY NO. : 0263 ANIMAL : RAT F344 REPORT TYPE : A1

SEX : FEMALE

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

PAGE: 5

Organ	Group No. of Grade Findings	Name Control Animals on Study 0 1 2 3 4 (%) (%) (%) (%)	100 ppm 0 1 2 3 4 (%) (%) (%) (%)	200 ppm 0 1 2 3 4 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)
[Respiratory	system]				
lung	congestion	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	< 0> (-) (-) (-) (-)
[Hematopoieti	ic system]				
bone marrow	congestion	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
	hemorrhage	(-) (-) (-) (-)	(-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
thymus	hemorrhage	< 0> (-) (-) (-) (-)	(0) (-) (-) (-) (-)	< 0> (-) (-) (-) (-)	< 0> (-) (-) (-) (-)
	karyarrhexis	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
spleen	karyorrhexis	< 0> 	< 0> (-) (-) (-) (-)	(-) (-) (-)	(-) (-) (-) (-)
Grade <a> b (c)	1: Slight 2: Moderate 3: Mark a: Number of animals examined at the site b: Number of animals with lesion c:b/a*100	red 4: Sovere			

(HPT150)

STUDY NO. : 0263 ANIMAL : RAT F344

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 2W)

REPORT TYPE : A1 SEX : FEMALE

Group Name mag 008 1600 ppm No. of Animals on Study 0 1 2 3 4 2 3 Findings (%) (%) (%) (%) (%) (%) (%) [Respiratory system] < 0> < 1> < 1> 0 0 0 lung congestion (-) (-) (-) (-) (100) (0) (0) (0) [Hematopoietic system] bone marrow < 1> 0 1 0 0 congestion (-) (-) (-) (-) (0)(100)(0)(0) hemorrhage 1 0 0 0 (-) (-) (-) (100) (0) (0) (0) thymus < 0> < 1> 1 0 0 0 hemorrhage (-) (-) (-) (100) (0) (0) (0) karyorrhexis 0 0 1 0 (-) (-) (-) (0)(0)(100)(0) spleen < 0> < 1> 1 0 0 0 karyorrhexis (-) (-) (-) (100) (0) (0) (0) Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe (a) a: Number of animals examined at the site b: Number of animals with lesion b (c) c:b/a*100(HPT150)

BAIS3

STUDY NO. : 0263 ANIMAL : RAT F344 REPORT TYPE : A1

SEX : FEMALE

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

0rgan		p Name Control of Animals on Study 0 0 e 1 2 3 4 (%) (%) (%) (%)	100 ppm 0 1 2 3 4 (%) (%) (%) (%)	200 ppm 0 1 2 3 4 (%) (%) (%) (%)	400 ppm 0 1 2 3 4 (%) (%) (%) (%)
[Circulator:	y system]				
heart		< 0>	< 0>	< 0>	< 0>
	hemorrhage	(-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-)
[Digestive :	system]				
iver	necrosis:central	< 0>	< 0>	< 0>	< 0>
	Hed usts contract	(-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-)	(-) (-) (-) (-)
Nervous sy:	stem]				
rain	hemorrhage	< 0>	< 0>	< 0>	< 0>
	nemorrnage	(-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
rade a > b c)	1: Slight 2: Moderate 3: Ma a: Number of animals examined at the site b: Number of animals with lesion c:b/a*100	rked 4 : Severe			
(HPT150)					

STUDY NO. : 0263 ANIMAL : RAT F344

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 2W)

REPORT TYPE : A1 SEX : FEMALE

0rgan	Group Nam No. of Ar Grade Findings	ne 800 ppm nimals on Study 0 1 2 3 4 (%) (%) (%) (%)	1600 ppm 1 1 2 3 4 (%) (%) (%) (%)	
(Circulatory	v system]			
heart	hemorrhage	< 0> (-) (-) (-) (-)	1 0 0 0 (100) (0) (0) (0)	
[Digestive s	system]			
liver	necrasis:central	(-) (-) (-)	0 0 1 0 (0) (0) (100) (0)	
(Nervous sys	stem]			
brain	hemorrhage	(-) (-) (-) (-)	1 0 0 0 (100) (0) (0) (0)	
Grade (a) b (c)	1: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	4 : Severe		
(IIPT150)				

APPENDIX A 9-5

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

MOUSE: MALE: SACRIFICED ANIMALS

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

REPORT TYPE : A1

: MALE

PAGE: 1 SEX Group Name Control 100 ppm 200 ppm 400 ppm No. of Animals on Study 2 2 2 2 Grade 3 Organ Findings [Respiratory system] lung < 2> < 2> < 2> < 2> 1 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 hemorrhage (0)(0)(0)(0) (0) (0) (0) (0) (50) (0) (0) (0) (0)(0)(0)(0) [Hematopoietic system] < 2> thymus < 2> < 2> 0 0 0 0 0 0 0 0 0 0 0 0 atrophy 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0) (0) (0) (0) (0)(0)(0)(0) [Digestive system] Liver < 2> < 2> < 2> < 2> 0 0 0 0 necrosis:focal 0 0 0 0 1 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (50) (0) (0) (0) (0)(0)(0)(0) necrosis:single cell 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) 0 2 0 0 degeneration:central 0 0 0 0 0 0 0 0 1 1 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (50) (50) (0) (0) (0) (100) (0) (0) Grade 1: Slight 2 : Moderate 3 : Marked 4 : Severe <a>> a: Number of animals examined at the site b b: Number of animals with lesion (c) c : b / a * 100

(HPT150)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (2W)

REPORT TYPE : A1 SEX : MALE

YPE: A1

Organ	No	roup Name 800 ppm b. of Animals on Study 2 rade 1 2 3 4 (%) (%) (%) (%)	1600 ppm 2 1 2 3 4 (%) (%) (%) (%)	
[Respirator	y system]			
lung	hemorrhage	\(\langle 2 \rangle \) 1	<pre></pre>	
[Nematopoie	tic system]			
thymus	atrophy	<pre></pre>	2 0 0 0 (100) (0) (0) (0)	
[Digestive	system]			
liver	necrosis:focal	<pre></pre>	<pre></pre>	
	necrosis:single cell	0 0 0 0 0 (0)	1 1 0 0 (50) (50) (0) (0)	
	degeneration:central	0 2 0 0 0 (0) (100) (0) (0)	0 1 1 0 (0) (50) (50) (0)	
Grade <a>> b (c)	1: Slight 2: Moderate 3: a: Number of animals examined at the site b: Number of animals with lesion c: b/a*100	Marked 4 : Severe e		

(HPT150)

STUDY NO. : 0264

ANIMAL : MOUSE BDF1 REPORT TYPE : A1

SEX : MALE

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

[Digestive system] liver granulation Grade 1: Slight 2: Moderate 3: Marked 4: Severe 4 > a: Number of animals examined at the site b b: Number of animals with lesion	Organ	Ī	Group Name No. of Animals on Study Grade 1 (%)	Control 2 2 3 (%) (%)	<u>4</u> (%)	1 (%)	10 2 (%)	0 ppm 3 (%)	<u>4</u> (%)	<u>1</u> (%)		mad 00 2 <u>3</u> (%)	<u>4</u> (%)	1 (%)	2 (%)	100 ppm 2 3 (%)	<u>4</u> (%)
Sight 2: Moderate 3: Marked 4: Severe	Digestive	svstaml		, 44 44 , , , , , , , , , , , , , , , ,													
granulation		5.5 5.5m <u>.</u>		<i>(</i> 2)			/ 2	,			,	2			,	27	
<pre>a : Number of animals examined at the site</pre>	1106	granulation	1 (50) (0 0			0	0	-	1 (50)	0	0	•		0	0	0 (0)
(c) c:b/a*100	⟨a⟩ b	a: Number of animals examined at the sibs: Number of animals with lesion											···········				

STUDY NO. : 0264 ANIMAL

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

: MOUSE BDF1

REPORT TYPE : A1

SEX : MALE SACRIFICED ANIMALS (2W)

PAGE: 4 Group Name mag 008 1600 ppm No. of Animals on Study 2 2 2 3 4 (%) (%) (%) (%) (%) Findings_ [Digestive system] liver < 2> < 2> 2 0 0 0 granulation 1 0 0 0 (100) (0) (0) (0) (50) (0) (0) (0) Grade 1: Slight 2 : Moderate 3 : Marked 4 : Severe (a) a: Number of animals examined at the site b b: Number of animals with lesion (c) c:b/a*100(HPT150) BAIS3

APPENDIX A 9-6

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

MOUSE: FEMALE: SACRIFICED ANIMALS

STUDY NO. : 0264

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

ANIMAL : MOUSE BDF1
REPORT TYPE : A1

SEX : FEMALE

Organ	Group Name No. of Ani Grade Findings	Control mals on Study 2 1 2 3 4 (%) (%) (%) (%)	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$	200 ppm 2 1 2 3 4 (%) (%) (%) (%)	400 ppm 2 1 2 3 4 (%) (%) (%) (%)
[Respirato	ry system]				
lung	hemorrhage	2> 1 0 0 0 (50) (0) (0) (0)	<pre></pre>	<pre></pre>	<pre></pre>
	pleuritis	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 (0) (0)
[Hematopoi	etic system]				
thymus	atrophy	<pre></pre>	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	<pre></pre>
[Circulato	ry system]				
heart	inflammation	<pre></pre>	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	<pre></pre>
[Digestive	system]				
liver	necrosis:single cell	<pre></pre>	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	<pre></pre>
Grade <a> b (c)	1: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	4 : Se∪ere			

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (2W)

REPORT TYPE : A1

SEX : FEMALE

PAGE: 6

Organ	No	roup Name 800 ppm b. of Animals on Study 2 rade 1 2 3 4 (%) (%) (%) (%)	1600 ppm 2 1 2 3 4 (%) (%) (%) (%)	a.
[Respiratory	y system]			
lung	hemorrhage	<pre></pre>	<pre></pre>	
	pleuritis	0 0 0 0 0 (0) (0)	1 0 0 0 0 (50) (0) (0)	
[Hematopoie	tic system]			
thymus	atrophy	<pre></pre>	(2> 1	
[Circulator	y system]			
heart	inflammation	2> 1 0 0 0 (50) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	
[Digestive :	system]			
liver	necrosis:single cell	0 0 0 0 (0) (0) (0) (0)	<pre></pre>	
Grade <a> b (c)	1: Slight 2: Moderate 3: a: Number of animals examined at the sit b: Number of animals with lesion c:b/a*100	Marked 4 : Severe e		·

(HPT150)

BAIS3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (2W)

REPORT TYPE : A1

SEX : FEMALE

Organ	Group No. o Grade Findings	f Animals on Study 2	100 ppm 2 1 2 3 4 (%) (%) (%)	200 ppm 2 1 2 3 4 (%) (%) (%) (%)	400 ppm 2 1 2 3 4 (%) (%) (%) (%)
[Digestive	system]				
liver	degeneration:central	0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	2 0 0 0 (100) (0) (0) (0)	0 2 0 0 0 0) (100) (0) (0)
	granulation	2 0 0 0 (100) (0) (0) (0)	2 0 0 0 (100) (0) (0) (0)	2 0 0 0 (100) (0) (0) (0)	1 0 0 0 (50) (0) (0) (0)
Grade < a > b (c)	1: Slight 2: Moderate 3: Mar a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	ked 4: Severe			
(IIPT150)					BA

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

REPORT TYPE : A1

SEX : FEMALE

Organ		o Name 800 ppm of Animals on Study 2 e 1 2 3 4 (%) (%) (%) (%) (%)	1600 ppm 2 1 2 3 4 (%) (%) (%) (%)	
[Digestive	system]			
liver	degeneration:central	2 > 0 0 0 0 (100) (0) (0) (0)	2> 1 1 0 0 (50) (50) (0) (0)	
	granulation	2 0 0 0 (100) (0) (0) (0)	0 0 0 0 0 (0) (0)	
Grade <a> b (c)	1: Slight 2: Moderate 3: Ma a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	rked 4 : Severe		
(IIPT150)				BAIS

APPENDIX A 10-1

IDENTITY OF N,N-DIMETHYLFORMAMIDE (TWO-WEEK STUDY)

IDENTITY OF N, N-DIMETHYLFORMAMIDE(TWO-WEEK STUDIES)

Lot no. PTE4986

1. Spectral data

Mass Spectrometry

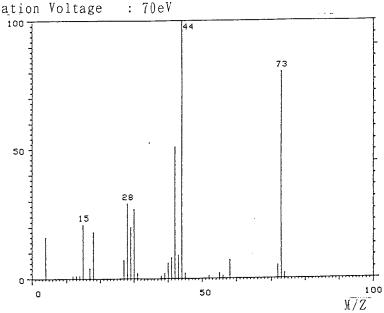
Instrument

: Hitachi M-80B Mass Spectrometer

Ionization

: EI Electron Ionization)

Ionization Voltage 100 7



Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with literature spectrum.

Determine	be	<u>Values</u>
Fragment	Ре	ak(M/Z)

15 28 44(Base Peak) 73

<u>Literature Values*</u> Fragment Peak(M/Z)

15 28 44(Base Peak) (*EPA/NIH Mass Spectral Data Base (1978) Vol. 1, p. 20.)

Infrared Spectrometry

Instrument

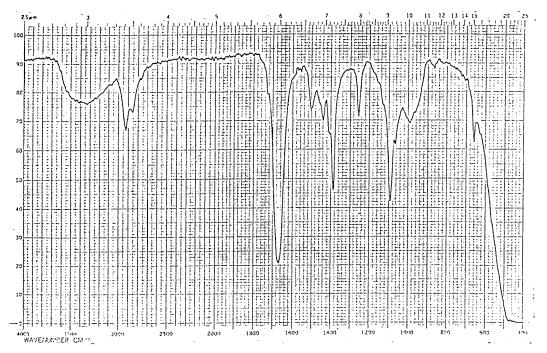
: Hitachi 270-30 Infrared Spectrometer

Cell

: KBr

Slit

: Medium



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

Determined Values Wave Number(cm ⁻¹) 650~ 680 850~ 890	Literature Values* Wave Number(cm ⁻¹) 650~ 680 850~ 890
920~1030	
$1030 \sim 1150$	$1030 \sim 1150$
$1220 \sim 1280$	$1220 \sim 1280$
$1350 \sim 1430$	$1350 \sim 1430$
$1430 \sim 1480$	1430~1480
$1480 \sim 1540$	$1480 \sim 1540$
$1600 \sim 1760$	$1600 \sim 1760$
2800~3000	2800~3000
3100~3650	$3100 \sim 3700$
	(*Performed by the WAKO PURE
	CHEMICAL INDUSTRIES, LTD.)

2. Conclusions: The test substance was identified as $\it N, N-Dimethylformamide$, by the mass spectrum and the infrared spectrum.

APPENDIX A 10-2

STABILITY OF N,N-DIMETHYLFORMAMIDE (TWO-WEEK STUDY)

STABILITY OF N, N-DIMETHYLFORMAMIDE (TWO-WEEK STUDIES)

Lot no. PTE4986

1. Sample: This lot was used from 1994.3.22 to 1994.4.12. Test substance was stored at room temperature.

2. Infrared Spectrometry

Instrument

: Hitachi 270-30 Infrared Spectrometer

Cell

: KBr

Slit

: Medium

Results: The result of infrared spectrum did not change when before and after studies.

1994.03.09(date analyzed)	1994.04.13(date analyzed)
Wave Number(cm ⁻¹)	Wave Number(cm ⁻¹)
650~ 680	650~ 680
850~ 890	850~ 890
920~1030	920~1030
1030~1150	$1030 \sim 1150$
$1220 \sim 1280$	$1220 \sim 1280$
$1350 \sim 1430$	$1350 \sim 1430$
$1430 \sim 1480$	$1430 \sim 1480$
$1480 \sim 1540$	$1480 \sim 1540$
$1600 \sim 1760$	$1600 \sim 1760$
2800~3000	2800~3000
$3100 \sim 3650$	$3100 \sim 3650$

3. Gas Chromatography

Instrument:

Hewlett Packard 5890A Gas Chromatograph

Column:

INNOWax(0.2mm $\phi \times 50$ m)

Column Temperature: 150°C

Flow Rate:

1 ml/min

Detector:

FID(Flame Ionization Detector)

Injection Volume: 1 μ 1

Results: Gas chromatography indicated one major peak(peak No.1) analyzed at 1994.3.9 and one major peak(peak No.1) analyzed at 1994.4.13. No new treace impurity peak in the test substance analyzed at 1994.4.13 was detected.

Date	Peak	No.	Retention Time(min)	Area Count	
1994.03. (date an		1	6.012	28976	
1994.04. (date an		1	6.012	29129	

^{4.} Conclusions: The test substance was stable for about 1 months in the dark at room temperature.

APPENDIX A 11-1

STABILITY OF BIPHENYL AT THE JAPAN BIOASSAY LABORATORY

(TWO-WEEK STUDY)

CONCENTRATION OF N, N-DIMETHYLFORMAMIDE

IN INHALTION CHAMBER

(RAT:TWO-WEEK STUDY)

	Concentration (ppm)				
Group Name	Mean \pm S.D.				
Control	0.0 ± 0.0				
100ppm	96.5 ± 3.1				
200ppm	197.6 \pm 4.6				
400ppm	392.2 ± 10.2				
800ppm	779.1 ± 18.7				
1600ppm	1554.4 ± 40.4				

CONCENTRATION OF N, N-DIMETHYLFORMAMIDE

IN INHALTION CHAMBER

(MOUSE: TWO-WEEK STUDY)

	Concentration (ppm)			
Group Name	Mean \pm S.D.			
Control	0.0 ± 0.0			
100ppm	101.1 \pm 1.8			
200ppm	203.6 ± 5.0			
400ppm	407.9 ± 6.1			
800ppm	806.6 ± 9.8			
1600ppm	1623.8 ± 17.7			

APPENDIX A 11-2 ENVIRONMENT OF INHALATION CHAMBER (TWO-WEEK STUDY)

ENVIRONMENT OF INHALATION CHAMBER (RAT: TWO-WEEK STUDY)

Group Name	Temperat Mean ±		Humidi Mean ±		Ventilati Mean			Room Air Change(time/h) Mean
Control	23.0 ±	0.1	54.6 ±	1.1	211.7	<u>+</u>	0.7	12.0
100ppm	$22.4 \pm$	0.3	$53.7 \pm$	2.1	211.8	<u>+</u>	0.9	12.0
200ppm	$22.7 \pm$	0.2	$53.3 \pm$	2.6	210.8	<u>+</u>	0.9	11.9
400ppm	$22.7 \pm$	0.2	48.7 ±	2.4	212.5	<u>+</u>	0.7	12.0
800ppm	$23.3 \pm$	0.3	48.0 ±	3.2	211.9	<u>+</u>	1.1	12.0
1600ppm	22.4 <u>+</u>	0.1	49.1 ±	3.4	212.8	<u>±</u>	1.5	12.0

ENVIRONMENT OF INHALATION CHAMBER (MOUSE: TWO-WEEK STUDY)

Group Name	Temperature Mean ± S.D	• • • • • • • • • • • • • • • • • • • •	Ventilation Rate(L/min) Mean ± S.D.	Room Air Change(time/h) Mean
Control	21.9 ± 0.2	53.5 ± 1.2	104.8 ± 0.5	12.1
100ppm	21.9 ± 0.2	50.9 ± 1.9	104.7 ± 1.1	12.1
200ppm	22.1 ± 0.1	50.2 ± 1.8	105.1 ± 1.4	12.1
400ppm	22.4 ± 0.1	48.8 ± 2.0	104.5 ± 0.6	12.1
800ppm	23.1 ± 0.1	46.8 ± 1.9	104.3 ± 1.1	12.0
1600ppm	22.7 ± 0.1	43.7 ± 1.7	104.0 ± 1.5	12.0

${\bf APPENDIX~A~12}$ ${\bf METHODS~FOR~HEMATOLOGY~AND~BIOCHEMISTRY}$

METHODS FOR HEMATOLOGY AND BIOCHEMISTRY (TWO-WEEK STUDIES)

Item	Method
Hematology	
Red blood cell (RBC)	Light scattering method 1)
Hemoglobin (Hgb)	Cyanmethemoglobin method 1)
Hematocrit (Hct)	Calculated as RBC × MCV/10 1)
Mean corpuscular volume (MCV)	Light scattering method 1)
Mean corpuscular hemoglobin (MCH)	Calculated as Hgb/RBC×10 1)
Mean corpuscular hemoglobin concentration (MCHC)	Calculated as Hgb/Hct×100 1)
Platelet	Light scattering method 1)
Reticulocyte	Pattern recognition method 3)
	(New methyleneblue staining)
Prothrombin time	Quick one stage method 2)
Activated partial thromboplastin time (APTT)	Ellagic acid activated method 2)
White blood cell (WBC)	Light scattering method 1)
Differential WBC	Pattern recognition method 3)
	(May-Grunwald-Giemsa staining)
Biochemistry	
Total protein (TP)	Biuret method 4)
Albumin (Alb)	BCG method 4)
A/G ratio	Calculated as Alb/(TP-Alb) 4)
T-bilirubin	Michaelson method 4)
Glucose	Enzymatic method (HK·G-6-PDH) 4)
T-cholesterol	Enzymatic method (CEH·COD·POD) 4)
Triglyceride	Enzymatic method (GK·GPO·POD) 4)
Phospholipid	Enzymatic method (PLD·COD·POD) 4)
Glutamic oxaloacetic transaminase (GOT)	Karmen method 4)
Glutamic pyruvic transaminase (GPT)	Karmen method 4)
Lactate dehydrogenase (LDH)	Wroblewski-LaDue method 4)
Alkaline phosphatase (ALP)	GSCC method 4)
γ -Glutamyl transpeptidase (G-GTP)	$L-\gamma$ -Glutamyl-p-nitroanilide substrate method 4)
Creatine phosphokinase (CPK)	GSCC method 4)
Urea nitrogen	Enzymatic method (Urease GLDH) 4)
Creatinine	Jaffe metod 4)
Sodium	Flame photometry 5)
Potassium	Flame photometry 5)
Chloride	Coulometric titration 5)
Calcium	OCPC method 4)
Inorganic phosphorus	Enzymatic method (SPL.PGM.G-6-PDH) 4)

- 1) Automatic blood cell analyzer (Technicon H-1: Technicon Instruments Corporation, USA)
- 2) Automatic coagulometer (Sysmex CA-5000 : Toa Medical Electronics Co., Ltd., Japan)
- 3) Automatic blood cell differential analyzer (Hitachi 8200 : Hitachi, Ltd., Japan)
- 4) Automatic analyzer (Hitachi 705 : Hitachi, Ltd., Japan)
- 5) Flame photometer (Hitachi 750 : Hitachi, Ltd., Japan)