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

APPENDIX

 $(A1-1\sim A7-4)$

2週間試験:ラット/0179;マウス/0180

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APPENDIX A 1-1

CLINICAL OBSERVATION (TWO-WEEK STUDY: SUMMARY)

RAT: MALE

STUDY NO.: 0179
ANIHAL: RAT F344
REPORT TYPE: A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

7

PAGE: 1

Clinical sign	Group Name	Admini	stration We	ek-day											
		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	2-7
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
ALL OFFICIAL OF			_												
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	40000 ppm	0	0	0	0	0	0	3	4	4	4	7	7	7	7
OILED PERI GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	40000 ppm	0	0	0	0	0	0	1	1	1	0	0	0	0	0
LIGO-STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ô	Ö
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ô	0
	20000 ppm	0	0	0	0	0	0	0	0	0	Ö	Ö	Ō	Ô	Ō
	40000 ppm	0	0	10	10	10	10	10	10	10	10	4	1	0	0

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APPENDIX A 1-2

CLINICAL OBSERVATION (TWO-WEEK STUDY: SUMMARY)

RAT: FEMALE

STUDY NO.: 0179
ANIMAL: RAT F344
REPORT TYPE: A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

PAGE: 2

Clinical sign	Group Name	Adminis	stration We	ek-day											
		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	2-7
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
ILOERECTION	Control	0	0	0	0	0	0	0	٥	0	0	٥	٥	٨	0
***************************************	2500 ppm	0	n	0	0	0	0	0	٥	0	0	٥	0	٥	0
	5000 ppm	0	0	0	0	0	0	٨	0	n	0	n	۸	٨	٥
	10000 ppm	0	0	0	Ô	0	0	0	0	0	0	0	n	n	٥
	20000 ppm	0	Ö	Ö	Ö	Ŏ	0	Ô	0	0	0	0	0	0	0
	40000 ppm	0	0	0	0	0	0	4	5	5	5	5	5	5	5
.IGO-STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	40000 ppm	0	0	10	10	10	10	10	10	10	10	5	2	2	0

(HAN190)

APPENDIX A 1-3

CLINICAL OBSERVATION (TWO-WEEK STUDY: SUMMARY)

MOSUE: MALE

STUDY NO. : 0180
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : MALE

PAGE: 1

SEA . MALE															1 NOL •
Clinical sign	Group Name	Admini:	stration We	eek-day											
		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	2-7
	***************************************	1	1	1	1	1	1	1	1	1	1	1	1	1	1
															_
DEATH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	•	
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	1	1 7	1 7	7	1 7	7	1 7	1 7
	20000 ppm	0	0	0	1	3	5	6	1	1	1	I	,	ľ	1
LOCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	. 0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	1	0	0	0	0	. 0	0	0	0
	20000 ppm	0	0	0	0	0	1	0	0	0	0	0	0	0	0
PRONE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	1	2	0	0	1	0	0	0	0	0	0
LATERAL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	0	Ö	Ö	Ö	Ö	0	Ö	0	0	Ö	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	i	0	0	0	0	0	0	0
	20000 ppm	0	0	0	.0	0	2	1	0	. 0	0	0	0	0	0
HUNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
TOTAL TOTAL	1250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	n	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	۸	0	0	0	0	0	0	0	0	٥	0	٥	0	0
	10000 ppm 10000 ppm	0	0	0	10	7	•	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	9	7	3 5	3	2	2	1	0	0	0	0
	ZOOOO PPIII	V	v	v	Ð	,	J	J	4	4	1	v	v	V	V

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STUDY NO. : 0180
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

PAGE: 2

Clinical sign	Group Name	Adminis	stration We	eek-day											
		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	2-7
***************************************			I	1	1	1	1	1	<u> </u>	1	1	I		<u> </u>	1
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	. 0	0	0	0
	1250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	10	10	5	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	9	7	5	3	2	2	2	2	2	2	1
MALL STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	- 0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	10	10	8	3	1	1	0	0	0	0	0
	20000 ppm	0	0	0	8	7	7	4	3	2	2	2	2	2	2
LIGO-STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	10	10	10	10	10	10	8	5	1	0	0	0	0	0
	20000 ppm	10	10	10	10	9	7	5	4	3	2	2	2	2	1

(HAN190)

APPENDIX A 1-4

CLINICAL OBSERVATION (TWO-WEEK STUDY: SUMMARY)

MOSUE: FEMALE

STUDY NO. : 0180
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : FEMALE

PAGE: 3

Clinical sign	Group Name	Admini:	stration W	eek-day											
		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	2-7
		1	1	1	1	1	1	1	1	1	1	1	1	1	1
EATH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	1	1	1	1	1	1	1	1	1	1
	20000 ppm	0	0	0	1	3	4	4	5	6	6	6	6	6	6
OCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0	0	0	0	0	. 0	0	. 0	0	0
	1250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	. 0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	1	0	0	0	Ö	0	0	0	Ô	0	0
	20000 ppm	0	0	0	6	2	2	2	1	0	0	0	0	0	0
PRONE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	Ô	0	0	0	0	Ö	0	0	Ô	0	0	0	0	0
	10000 ppm	Ō	0	Ö	0	1	Ö	0	Ö	Ô	0	0	0	0	0
	20000 ppm	Ö	Ö	Ö	Ö	ō	1	0	1	Ö	Ö	0	Ö	0	0
ATERAL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0.	0
	1250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	Ö	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	Õ	Ô	Ô	0	0	0	0	0	0
	10000 ppm	0	0	Ö	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	Ö	Ō	ő	1	2	Ö	Ö	Ö	1	Ö	Ö	0	ő	ő
UNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	Ö	0	0	0	ŏ	Ŏ	ő	Ŏ	0	0	0	0	Ô	0
	5000 ppm	Õ	Ö	Ö	Ô	Ŏ	0	0	ő	0	Ô	0	0	0	0
	10000 ppm	Ö	Ö	Ŏ	6	5	Ö	Ö	Ö	Ö	Ö	0	0	Ö	ő
	20000 ppm	Ö	Ô	0	9	7	6	6	1	0	0	0	0	0	0

(HAN190)

STUDY NO. : 0180
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : FEMALE

PAGE: 4

Clinical sign	Group Name	Admini	stration W	eek-day											
		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	2-7
· · · · · · · · · · · · · · · · · · ·		1	1	1	1	1	1	1	1	1	1	1	1	1	1
OILED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	. 0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	2	1	0	0	0	0	0	0	0	0	0
ILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	6	5	3	2	1	1	0	0	0	0	0
	20000 ppm	0	0	0	. 9	7	6	6	4	0	0	0	0	0	0
RREGULAR BREATHING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	1	1	1	0	0	0	0	0	0
BNORMAL RESPIRATION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	Ō	0.
	20000 ppm	0	0	0	0	0	1	1	1	0	0	0	0	Ō	Ō
MALL STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	0	0	0	0	0	0	0	Ö	Õ	Ö	0	Ŏ	0	0
	2500 ppm	0	0	0	Ö	Ö	Ö	Ö	Ö	0	0	0	0	0	0
	5000 ppm	Õ	0	0	Õ	0	0	0	0	0	0	0	0	0	0
	10000 ppm	Ŏ	Ő	ő	4	4	6	4	4	0	0	0	0	0	0
	20000 ppm	Ŏ	Ö	0	9	8	7	6	6	4	0	0	0	0	0

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STUDY NO. : 0180
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

SEX : FEMALE

PAGE: 5

Clinical sign	Group Name	Admini	stration W	eek-day											
		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	2-7 1
OLIGO-STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	5000 ppm	1	1	1	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	10	10	9	8	8	7	4	4	0	0	0	0	0	0
	20000 ppm	10	10	10	10	9	7	6	6	5	4	4	4	4	0

(HAN190)

APPENDIX A 2-1

BODY WEIGHT CHANGES (TWO-WEEK STUDY:SUMMARY)

RAT: MALE

STUDY NO.: 0179

ANIMAL : RAT F344

UNIT : g

REPORT TYPE : A1 2

SEX : MALE

(HAN260)

BODY WEIGHT CHANGES (SUMMARY)

ALL ANIMALS

oup Name	Admini	stration	week-day											
	0-0		1-1		1-2		1-4		1-7		2-4		2-7	
Control	125±	5	130±	5	136±	4	147±	5	162±	6	183±	6	199±	9
2500 ppm	125±	5	125±	7	135±	5	146±	6	161±	7	179±	6	194士	7
5000 ppm	125±	5	125±	5	133±	6	143±	7	159±	6	178±	6	192±	7
10000 ppm	125±	5	116±	4**	118±	5**	131±	5**	146±	6**	161±	6**	175±	7**
20000 ppm	125±	5	111±	4**	108±	1**	113±	6**	126±	6**	140±	7**	151±	7**
40000 ppm	125±	5	109±	4**	104土	4**	93±	6**	93±	5**	97±	7**	102±	8**
Significant differer	nce; *:P≦(0.05	**: P ≤ 0.0	1			Test of Du	nnett						

BAIS 2

PAGE: 1

APPENDIX A 2-2

BODY WEIGHT CHANGES (TWO-WEEK STUDY: SUMMARY)

RAT: FEMALE

STUDY NO. : 0179

ANIMAL : RAT F344

UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

BODY WEIGHT CHANGES ALL ANIMALS

(SUMMARY)

PAGE: 2

oup Name	Admini	stration	n week-day											
	0-0		1-1		1-2		1-4		1-7		2-4		2-7	
Control	103±	3	106±	3	109±	3	113±	3	121±	4	126±	3	135±	4
2500 ppm	103±	3	105±	4	108±	4	112±	4	121±	4	125±	5	133±	5
5000 ppm	103±	3	100土	3**	104±	3**	110±	4	116±	5*	122±	4	130±	4
10000 ppm	103±	3	94土	3**	96±	3**	103±	3**	111±	2**	118±	3**	124±	4 **
20000 ppm	103±	3	93±	3**	91±	3**	94±	2**	101±	3**	110±	4**	117±	5**
40000 ppm	103±	3	90±	3**	85±	3**	81 ±	4**	80±	4**	84±	4**	88±	5**
												,		
Significant differenc	e; *:P≦(0.05	**: P ≤ 0.0)1			Test of Du	ınnett						

(HAN260)

APPENDIX A 2-3

BODY WEIGHT CHANGES(TWO-WEEK STUDY:SUMMARY)

MOSUE : MALE

STUDY NO. : 0180
ANIMAL : MOUSE BDF1

UNIT : g
REPORT TYPE : A1 2

SEX : MALE

BODY WEIGHT CHANGES

ALL ANIMALS

(SUMMARY)

PAGE: 1

oup Name	Administratio	an week-day					
	0-0	1-1	1-2	1-4	1-7	2-4	2-7
Control	22.9± 0.9	22.5± 1.1	22.8± 1.3	22.8± 1.1	23.1± 1.2	24.7± 1.4	24.2± 1.8
1250 ppm	22.9± 0.9	22.2± 1.1	22.8± 1.1	23.0± 1.0	23.4± 1.0 ·	24.7± 1.0	24.5± 1.0
2500 ppm	22.8± 1.0	22.2± 1.1	22.5± 0.8	22.8± 0.8	23.2± 0.9	24.4± 1.0	24.3± 1.0
5000 ppm	22.9± 0.9	21.1± 0.9**	21.2± 1.1**	21.8± 1.1	22.4± 0.7	24.0± 1.1	24.0± 1.0
10000 ppm	22.9± 0.9	19.5± 0.8**	18.2± 0.7**	17.0± 0.8**	17.5± 1.0**	20.1± 1.5**	21.3± 1.3**
20000 ppm	22.9± 0.9	19.4± 0.7**	17.7± 0.8**	15.8± 1.0**	15.1± 1.2**	16.9± 2.9**	18.2± 3.4*
Significant difference;	*: P ≤ 0.05	**: P ≤ 0.01		Test of Dunnett			

(HAN260)

APPENDIX A 2-4

BODY WEIGHT CHANGES (TWO-WEEK STUDY: SUMMARY)

MOSUE: FEMALE

STUDY NO. : 0180

ANIMAL : MOUSE BDF1

UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

BODY WEIGHT CHANGES ALL ANIMALS (SUMMARY)

PAGE: 2

p Name	Administration	week-day					
	0-0	1-1	1-2	1-4	1-7	2–4	2-7
Control	18.8± 0.6	18.4± 0.8	18.5± 0.7	18.4± 0.8	18.8± 0.8	20.0± 0.8	19.8± 0.8
1250 ppm	18.9± 0.6	18.2± 0.7	18.4± 0.9	18.6± 0.6	18.8± 0.8	19.9± 0.9	19.9± 0.7
2500 ppm	18.9± 0.6	18.2± 0.7	18.2± 0.8	18.5± 0.8	18.4± 0.9	19.6± 0.9	19.6± 1.0
5000 ppm	18.8± 0.6	17.3± 0.6**	17.5± 0.5*	17.9± 0.4	18.6± 0.5	19.4± 0.7	19.4± 0.7
10000 ppm	18.9± 0.6	15.9± 0.6**	14.8± 0.8**	14.1± 1.7**	15.4生 1.5**	17.4生 1.0**	18.3± 1.1**
20000 ppm	18.8± 0.6	15.4± 0.4**	13.8± 0.5**	12.5± 0.9**	12.8± 1.6**	15.2± 1.6**	16.6± 1.0**
							
Significant difference	ce; *: P ≤ 0.05	**: P ≤ 0.01	•	Test of Dunnett			
N260)	1.776.1.2						

APPENDIX A 3-1

FOOD CONSUMPTION CHANGES (TWO-WEEK STUDY: SUMMARY)

RAT: MALE

Δ

STUDY NO. : 0179 ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

PAGE: 1

p Name	Administration	week-day(effective)			
****	1-4(4)	1-7(3)	2-4(4)	2-7(3)	
Control	14.3± 0.6	15.0± 0.9	14.6± 0.7	16.2± 1.1	
2500 ppm	13.6± 1.2	14.9± 0.9	13.9± 0.9	15.9± 1.1	
5000 ppm	12.3± 0.7	14.3± 0.7	13.6± 0.6*	15.6± 0.8	
10000 ppm	10.0± 3.9**	13.3± 0.9**	13.0± 0.8**	14.7± 0.9**	
20000 ppm	6.2± 2.1**	11.0± 0.8**	11.7± 0.9**	13.0± 1.0**	
40000 ppm	5.6± 7.7**	7.1± 1.6**	7.0± 0.4**	8.6± 0.9**	
	Time.				
Significant difference	; *: P ≤ 0.05	**: P ≤ 0.01		Test of Dunnett	
¥260)			· · · · · · · · · · · · · · · · · · ·		

APPENDIX A 3-2

FOOD CONSUMPTION CHANGES (TWO-WEEK STUDY: SUMMARY)

RAT: FEMALE

STUDY NO. : 0179 ANIMAL : RAT F344

UNIT : g
REPORT TYPE : A1 2 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

PAGE: 2

oup Name	Administration 1–4(4)	week-day(effective) 1-7(3)	2-4(4)	2-7(3)	
,					·
Control	11.2± 0.6	11.3± 0.5	10.1± 0.5	11.5± 0.6	
2500 ppm	10.7± 0.6	11.2± 0.4	9.6± 0.3	11.5± 0.7	
5000 ppm	9.5± 0.9	10.6± 0.6	9.5± 0.6	11.3± 0.5	
10000 ppm	7.0± 1.3**	10.3± 0.5	9.5± 0.6	11.2± 1.8	
20000 ppm	4.9士 1.3**	9.2± 0.6**	9.1± 0.5**	10.1± 0.9*	
40000 ppm	4.2± 4.8**	8.3± 5.1**	8.6± 7.0**	7.9± 0.7**	
· · · · · · · · · · · · · · · · · · ·	*****				
Significant differenc	e; *:P≦0.05	**: P ≤ 0.01		Test of Dunnett	
AN260)		•			

APPENDIX A 3-3

FOOD CONSUMPTION CHANGES (TWO-WEEK STUDY: SUMMARY)

MOSUE: MALE

STUDY NO. : 0180

ANIMAL : MOUSE BDF1

UNIT : g

REPORT TYPE : A1 2

SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)

ALL ANIMALS

Group Name Administration week-day(effective) 1-4(4)1-7(3)2-4(4) 2-7(3) Control 4.5± 0.4 4.7 ± 0.5 4.7± 0.6 4.3± 0.6 1250 ppm 4.6± 0.4 4.6± 0.3 4.5± 0.4 4.6± 0.4 2500 ppm 4.5± 0.7 4.9± 0.6 4.5± 0.6 4.6± 0.6 5000 ppm 4.8± 0.9 5.8± 0.9 5.0± 0.7 4.9± 0.5 10000 ppm 3.5± 1.0 5.9± 1.1 7.8土 1.8** 7.3± 1.1** 20000 ppm 2.7± 1.4* 3.7 ± 2.4 $6.1\pm\ 3.6$ 6.9 ± 3.2

Test of Dunnett

(HAN260)

Significant difference : $*: P \le 0.05$

**: $P \leq 0.01$

BAIS 2

PAGE: 1

APPENDIX A 3-4

FOOD CONSUMPTION CHANGES(TWO-WEEK STUDY: SUMMARY)

MOSUE: FEMALE

STUDY NO. : 0180

ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

PAGE: 2

up Name	Administration 1-4(4)	week-day(effective) 1-7(3)	2-4(4)	2-7(3)	
<u> </u>					
Control	4.3± 0.3	4.6± 0.3	4.2± 0.6	4.2± 1.0	
1250 ppm	4.4± 0.8	4.7± 0.6	4.4± 0.2	4.5± 0.6	
2500 ppm	4.2± 0.5	4.7± 0.6	4.1± 0.5	4.6± 0.6	
5000 ppm	5.6± 1.6	6.0± 0.7*	4.4± 0.7	4.4± 0.8	
10000 ppm	3.6± 1.2	7.6± 2.7*	6.8± 1.6**	5.7± 1.0**	
20000 ppm	2.1± 0.9**	3.4± 1.5	5.5± 2.8	6.4± 1.4**	
Significant difference;	*: P ≤ 0.05 *	*: P ≤ 0.01		Test of Dunnett	

(HAN260)

APPENDIX A 4-1

CHEMICAL INTAKE CHANGES (TWO-WEEK STUDY: SUMMARY)

RAT: MALE

STUDY NO. : 0179

ANIMAL : RAT F344

UNIT : g/kg/day
REPORT TYPE : A1 2
SEX : MALE

CHEMICAL INTAKE CHENGES (SUMMARY)

ALL ANIMALS

roup Name	Administration ((weeks)2	 	
Control	0.000± 0.000	0.000± 0.000	 	
2500 ppm	0.231± 0.006	0.204± 0.008		
5000 ppm	0.448± 0.020	0.406± 0.018		
10000 ppm	0.913± 0.040	0.841± 0.035		
20000 ppm	1.747± 0.066	1.722± 0.080		
40000 ppm	3.049± 0.655	3.377± 0.305		

(HAN300)

BAIS 2

PAGE: 1

APPENDIX A 4-2

CHEMICAL INTAKE CHANGES (TWO-WEEK STUDY: SUMMARY)

RAT: FEMALE

STUDY NO. : 0179

ANIMAL : RAT F344
UNIT : g/kg/day
REPORT TYPE : A1 2
SEX : FEMALE

CHEMICAL INTAKE CHENGES (SUMMARY)

ALL ANIMALS

Group Name Administration (weeks) 2 Control 0.000± 0.000 0.000± 0.000 2500 ppm 0.231± 0.005 0.215± 0.008 5000 ppm 0.455± 0.017 0.433± 0.021 10000 ppm 0.930± 0.049 0.899± 0.122	
2500 ppm 0.231± 0.005 0.215± 0.008 5000 ppm 0.455± 0.017 0.433± 0.021	
2500 ppm 0.231± 0.005 0.215± 0.008 5000 ppm 0.455± 0.017 0.433± 0.021	
5000 ppm 0.455± 0.017 0.433± 0.021	
10000 ppm $0.930\pm\ 0.049$ $0.899\pm\ 0.122$	
20000 ppm 1.806± 0.096 1.733± 0.111	
40000 ppm $4.190\pm\ 2.663$ $3.591\pm\ 0.359$	

(HAN300)

APPENDIX A 4-3

CHEMICAL INTAKE CHANGES (TWO-WEEK STUDY: SUMMARY)

MOSUE: MALE

STUDY NO. : 0180

ANIMAL : MOUSE BDF1 UNIT : g/kg/day
REPORT TYPE : A1 2

CHEMICAL INTAKE CHENGES (SUMMARY)

ALL ANIMALS

SEX : MALE			PAGE:
Group Name	Administration 1	(weeks)2	
	1	4	
Control	0.000± 0.000	0.000± 0.000	
1250 ppm	0.244± 0.020	0.234± 0.022	
2500 ppm	0.525± 0.054	0.473± 0.063	
5000 ppm	1.293± 0.206	1.025± 0.107	
10000 ppm	3.463± 0.601	3.422± 0.495	
20000 ppm	6.431± 4.426	7.680± 3.978	

(HAN300)

APPENDIX A 4-4

CHEMICAL INTAKE CHANGES (TWO-WEEK STUDY: SUMMARY)

MOSUE: FEMALE

CHEMICAL INTAKE CHENGES (SUMMARY) ALL ANIMALS

ANIMAL : MOUSE BDF1
UNIT : g/kg/day
REPORT TYPE : A1 2

SEX : FEMALE

PAGE: 2

-oup Name	Administration	(weeks)2				
	•	<u></u>	 		 	
Control	0.000± 0.000	0.000± 0.000				
1250 ppm	0.312± 0.035	0.283± 0.039				
2500 ppm	0.637± 0.065	0.584± 0.061				
5000 ppm	1.612± 0.193	1.129± 0.194				
10000 ppm	5.369± 1.794	3.168± 0.672				·
20000 ppm	5.737± 2.047	7.681± 1.493		•		

(HAN300)

BAIS 2

APPENDIX A 5-1

GROSS FINDINGS (TWO-WEEK STUDY: SUMMARY)

RAT: MALE: SACRIFICED ANIMALS

 Δ

ANIMAL : RAT F344
REPORT TYPE : A1 : MALE

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (2W)

Group Name Control 5000 ppm 10000 ppm 2500 ppm Findings__ 10 (%) 10 (%) 10 (%) 10 (%) Organ____ NO. of Animals 0 (0) 0 (0) 0 (0) 0 (0) thymus atrophic (HPT080)

BAIS 2

Δ

STUDY NO. : 0179
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name NO. of Animals	20000 ppm 10 (%)	40000 ppm 10 (%)	
thymus	atrophic		0 (0)	2 (20)	
(HPT080)					BAIS 2

APPENDIX A 5-2

GROSS FINDINGS (TWO-WEEK STUDY: SUMMARY)

RAT: FEMALE: SACRIFICED ANIMALS

 Δ

STUDY NO. : 0179 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (2W)

0rgan	Findings	Group Name NO. of Animals	Control 10 (%)	2500 ppm 10 (%)	5000 ppm 10 (%)	10000 ppm 10 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
iver	herniation		0 (0)	0 (0)	0 (0)	0 (0)

Δ

STUDY NO. : 0179 ANIMAL : RAT F344 REPORT TYPE : A1 SEX : FEMALE

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (2W)

0rgan	Findings	Group Name NO. of Animals	20000 ppm 10 (%)	40000 ppm 10 (%)	
thymus	atrophic		0 (0)	1 (10)	
Liver	herniation		1 (10)	0 (0)	
(HPT080)					BAIS 2

APPENDIX A 5-3

GROSS FINDINGS (TWO-WEEK STUDY: SUMMARY)

MOUSE: MALE: DEAD AND MORIBUND ANIMALS

STUDY NO. : 0180 ANIMAL : MOUSE BDF1 REPORT TYPE : A1
SEX : MALE

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

5000 ppm 0 (%) Group Name Contral 1250 ppm 2500 ppm Findings_ NO. of Animals 0 (%) 0 (%) 0 (%) - (-) - (-) - (-) - (-) thymus atrophic - (-) - (-) - (-) - (-) whale bady wasting

PAGE: 1

(HPT080) BAIS 2

 Δ

STUDY NO. : 0180

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : MALE

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

Group Name 20000 ppm 10000 ppm Findings_ NO. of Animals 1 (%) 7 (%) Organ____ thymus 0 (0) 1 (14) atrophic whale body wasting 1 (100) 4 (57) (HPT080) BAIS 2

APPENDIX A 5-4

GROSS FINDINGS (TWO-WEEK STUDY: SUMMARY)

MOUSE: FEMALE: DEAD AND MORIBUND ANIMALS

Δ

STUDY NO. : 0180

ANIMAL

: MOUSE BDF1 REPORT TYPE : A1
SEX : FEMALE

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

Group Name

NO. of Animals

- (-)

- (-)

Findings_

atrophic

wasting

2500 ppm 0 (%) Control 1250 ppm 0 (%) 0 (%)

- (-)

- (-) - (-)

- (-) - (-) - (-)

(HPT080)

thymus

whate body

BAIS 2

PAGE: 3

5000 ppm

0 (%)

ANIMAL : MOUSE BDF1

REPORT TYPE : A1 SEX : FEMALE

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

Organ	Findings	Group Name NO. of Animals	10000 ppm 1 (%)	20000 ppm 6 (%)	
thymus	atrophic		0 (0)	2 (33)	
whole body	wasting		1 (100)	5 (83)	
(HPT080)					BAIS 2

APPENDIX A 5-5

GROSS FINDINGS (TWO-WEEK STUDY: SUMMARY)

MOUSE: MALE: SACRIFICED ANIMALS

STUDY NO. : 0180 ANIMAL : MOUSE BDF1

REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (2W)

0rgan	Findings	Group Name Contro NO. of Animals 10 (%)	1250 ppm 10 (%)	2500 ppm 10 (%)	5000 ppm 10 (%)
thymus	atrophic	0 (0)	0 (0)	0 (0)	0 (0)
leen	black zone	1 (10)	0 (0)	0 (0)	0 (0)
idney	hydronephrosis	1 (10)	0 (0)	0 (0)	0 (0)

Δ

STUDY NO. : 0180

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (2W) ANIMAL : MOUSE BDF1 REPORT TYPE : A1
SEX : MALE

Findings	Group Name NO. of Animals	10000 ppm 9 (%)	20000 ppm 3 (%)		
atrophic		0 (0)	1 (33)		
black zone		0 (0)	0 (0)		
hydronephrosis		0 (0)	0 (0)		
-					BAIS 2
	atrophic black zone	atrophic black zone	### No. of Animals 9 (%) atrophic 0 (0) black zone 0 (0)	Findings	Findings NO. of Animals 9 (%) 3 (%) atrophic 0 (0) 1 (33) black zone 0 (0) 0 (0)

APPENDIX A 5-6

GROSS FINDINGS (TWO-WEEK STUDY: SUMMARY)

MOUSE: FEMALE: SACRIFICED ANIMALS

ANIMAL : MOUSE BDF1

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (2W)

REPORT TYPE : A1 SEX : FEMALE SEX

Organ	Findings_	Group Name NO. of Animals	Control 10 (%)	1250 ppm 10 (%)	2500 ppm 10 (%)	5000 ppm 10 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
oleen	black zone		0 (0)	1 (10)	0 (0)	0 (0)
ouary	cyst		0 (0)	0 (0)	1 (10)	0 (0)

 \triangle

STUDY NO. : 0180

ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name NO. of Animals	10000 ppm 9 (%)	20000 ppm 4 (%)	
thymus	atrophic		1 (11)	1 (95)	
			1 (11)	1 (25)	
spleen	black zone		0 (0)	0 (0)	
ovary	cyst		0 (0)	0 (0)	
(HPT080)	· · · · · · · · · · · · · · · · · · ·				BAIS 2

APPENDIX A 6-1

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

RAT: MALE: SACRIFICED ANIMALS

STUDY NO. : 0179 ANIMAL : RAT F344

REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

PAGE: 1

SACRIFICED ANIMALS (2W)

Owene	Finding.	Group Name Control No. of Animals 2 <1> <2> <3> <4>	2500 ppm 2 <1> <2> <3> <4>	5000 ppm 2 <1> <2> <3> <4>	10000 ppm 2 <1> <2> <3> <4>
Organ	Findings	(%) (%) (%)	(%) (%) (%) (%)	(%) (%) (%) (%)	(%) (%) (%) (%)
[Hematopoieti	ic system]				
oone marrow	hypoplasia	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)
thymus	atrophy	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	tem]				
kidney	basophilic change	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0)
	hyaline cast	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
	desquamation:pelvis	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0)
[Endocrine sy	ystem]				
adrena L	increased lipid:cortex	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
[Reproductive	e system]				
testis	atrophy	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
<12	>:Slight <2>:Moderate <3	>:Marked <4>:Severe			
(HPT150)					

ANIMAL : RAT F344 REPORT TYPE : A1 SEX : MALE

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS (SUMMARY)

PAGE: 2

SACRIFICED ANIMALS (2W)

Group Name 20000 ppm 40000 ppm No. of Animals 2 2 <1> 〈2〉 〈3〉 〈4〉 (1) <2> <3> <4> 0rgan_ Findings (%) (%) (%) (%) (%) (%) (%) (%) [Hematopoietic system] bone marrow hypoplasia 0 0 2 0 0 (100) (0) (0) (0) (0)(100)(0)(0) thymus atrophy 0 0 0 0 (0)(0)(0)(0) (50) (0) (0) (0) [Urinary system] kidney basophilic change (0)(0)(0)(0) (100) (0) (0) (0) hyaline cast (0)(0)(0)(0) (50) (0) (0) (0) desquamation:pelvis 0 0 0 0 2 0 0 0 (0)(0)(0)(0) (100) (0) (0) (0) [Endocrine system] adrenal increased lipid:cortex 0 2 (0)(0)(0)(0) (100) (0) (0) (0) [Reproductive system] testis atrophy 0 0 0 0 0 2 0 0 (0)(0)(0)(0) (0) (100) (0) (0) <1>:Slight <2>:Moderate <3>:Marked <4>:Severe (HPT150) BAIS2

APPENDIX A 6-2

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

RAT: FEMALE: SACRIFICED ANIMALS

ANIMAL : RAT F344 REPORT TYPE : A1 : FEMALE SEX

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

		Group Name Control No. of Animals 2	2500 ppm 2	5000 ppm 2	10000 ppm 2
rgan	Findings	<1> <2> <3> <4> (%) (%) (%) (%) (%)	<1> <2> <3> <4> (%) (%) (%) (%) (%)	<1> <2> <3> <4> (%) (%) (%) (%)	<1> <2> <3> <4> (%) (%) (%) (%) (%)
Hematopoietio	c system]				
one marrow	hypoplasia	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)
[Digestive sys	stem]				
stomach	dilated glands	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)
[Urinary syste	em]				
cidney	basophilic change	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)
	mineralization:cortico-medullary junction	1 0 0 0 (50) (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)
	dilatation:tubular lumen	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
	desquamation:pelvis	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 0 (0) (0)
(Endocrine sy	stem]				
pituitary	Rathke pouch	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)
<1>	:Slight <2>:Moderate <3>:Marked	<4>:Severe			
(HPT150)					

STUDY NO. : 0179 ANIMAL : RAT F344

REPORT TYPE : A1
SEX : FEMALE

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

0rgan	Findings	Group Name 20000 ppm No. of Animals 2 <pre><1> <2> <3> <4></pre> <pre></pre> (%) (%) (%) (%)	40000 ppm 2 <1> <2> <3> <4> (%) (%) (%) (%)	
[Hematopoietio	c system]			
bone marrow	hypoplasia	1 1 0 0 0 (50) (50) (0)	0 2 0 0 (0) (100) (0) (0)	
[Digestive sy	stem]			
stomach	dilated glands	0 0 0 0 0 (0) (0)	1 0 0 0 (50) (0) (0) (0)	
[Urinary syste	em]			
kidney	basophilic change	1 0 0 0 0 (50) (50) (60)	1 0 0 0 (50) (0) (0) (0)	
	mineralization:cortico-medullary junction	1 0 0 0 (50) (0) (0) (0)	0 0 0 0 0 (0) (0) (0)	
	dilatation:tubular lumen	0 0 0 0 0 (0) (0)	1 0 0 0 (50) (0) (0) (0)	
	desquamation:pelvis	(0) (0) (0) (0)	2 0 0 0 0 (100) (0) (0) (0)	
[Endocrine sy:	stem]			
pituitary	Rathke pouch	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0) (0)	
<1>	:Slight <2>:Moderate <3>:Marked	<4>:Seuere		
(HPT150)				

APPENDIX A 6-3

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

MOUSE: MALE: DEAD AND MORIBUND ANIMALS

 Δ

STUDY NO. : 0180

ANIMAL : MOUSE BDF1

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

PAGE: 1

DEAD AND MORIBUND ANIMALS (0- 2W)

Group Name 1250 ppm Control 2500 ppm 5000 ppm No. of Animals 0 0 0 0 <1> <2> ⟨3⟩ 〈2〉 〈3〉 〈4〉 <2> <3> (2) (3) (4) (%) (%) (%) (%) (%) (%) (%) (%) Organ____ Findings_ (%) (%) (%) (%) (%) (%) (%) [Hematopoietic system] spleen atrophy (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) [Digestive system] liver atrophy (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) necrosis:focal (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) <1>:Slight <2>: Moderate <3>:Marked <4>:Severe (HPT150) BAIS2 Δ

STUDY NO. : 0180

ANIMAL : MOUSE BDF1

REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name 10000 ppm 20000 ppm No. of Animals 1 2 <pre></pre>	
[11;	±:		
	tic system]		
spleen	atrophy	0 0 0 0 1 1 0 0 (0) (0) (50) (50) (0) (0)	
[Digestive	system]		
liver	atrophy	0 1 0 0 0 2 0 0 (0) (100) (0) (0) (0) (100) (0) (0	
	necrosis:focal	1 0 0 0 2 0 0	
		(100) (0) (0) (100) (0) (0) (0)	
<	<pre><1>:Slight <2>:Moderate <3.</pre>	:Marked <4>:Seuere	
(HPT150)			

APENDIX A 6-4

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

MOUSE: FEMALE: DEAD AND MORIBUND ANIMALS

Δ

STUDY NO. : 0180

ANIMAL : MOUSE BDF1

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

PAGE: 3

DEAD AND MORIBUND ANIMALS (0- 2W)

Group Name Control 1250 ppm 2500 ppm 5000 ppm No. of Animals 0 0 0 0 ⟨2⟩ ⟨3⟩ ⟨4⟩ <1> <2> <3> <4> (2) (3) (4) <1> <2> <3> <4> <1> <1> Organ_ Findings_ (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) [Hematopoietic system] thymus atrophy (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) spleen atrophy (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) [Digestive system] liver atrophy (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) necrosis:central (-) (-) (-) (-) (-) (-) (-) necrosis:focal (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) <1>:Slight <2>:Moderate <3>:Marked <4>:Severe (HPT150) BAIS2

ANIMAL : MOUSE BDF1

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

DEAD AND MORIBUND ANIMALS (0- 2W)

Group Name 10000 ppm 20000 ppm No. of Animals 2 1 <1> <2> <3> <4> <1> <2> <3> <4> (%) (%) (%) (%) 0rgan__ Findings_ (%) (%) (%) (%) [Hematopoietic system] thymus atrophy 0 0 0 0 0 1 0 0 (0) (0) (0) (0) (0)(50)(0)(0) spleen atrophy 1 0 0 0 2 0 0 0 (100) (0) (0) (0) (100) (0) (0) (0) [Digestive system] liver atrophy 0 1 0 0 0 1 0 0 (0)(50)(0)(0) (0) (100) (0) (0) 0 0 0 0 0 1 0 0 necrosis:central (0)(0)(0)(0) (0)(50)(0)(0) necrosis:focal 0 0 0 0 1 0 0 0 (0)(0)(0)(0) (50) (0) (0) (0) <1>:Slight <2>:Moderate <3>:Marked <4>:Severe (HPT150)

BAIS2

APPENDIX A 6-5

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

MOUSE: MALE: SACRIFICED ANIMALS

STUDY NO. : 0180 ANIMAL : MOUSE BDF1

REPORT TYPE : A1
SEX : MALE

PAGE: 1

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

Organ	Findings	Group Name Control No. of Animals 2	1250 ppm 2	2500 ppm 2	5000 ppm 2
		(%) (%) (%) (%)		<1> <2> <3> <4> (%) (%) (%) (%)	<1> <2> <3> <4> (%) (%) (%) (%) (%)
Digestive	system]				
liver	swelling	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)
	necrosis: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 0 0 (0) (0) (0)
	granulation	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]				
kidney	basophilic change	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
[Reproducti	ue system]				
epididymis	spermatogenic granuloma	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 0 (50) (50) (0) (0)
[Musculoske	letal system]				
muscle	necrosis	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>:Moderate <3>	:Marked <4>:Severe			
(HPT150)					

ANIMAL : MOUSE BDF1

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

PAGE: 2

SACRIFICED ANIMALS (2W)

Group Name 10000 ppm 20000 ppm No. of Animals 2 2 <1> ⟨2⟩ ⟨3⟩ ⟨4⟩ 〈2〉 〈3〉 〈4〉 <1> Findings_ (%) (%) (%) (%) Organ_ (%) (%) (%) (%) [Digestive system] Liver swelling 2 0 0 0 2 0 0 0 (100) (0) (0) (0) (100) (0) (0) (0) necrosis: focal 2 0 0 0 (0)(0)(0)(0) (100) (0) (0) (0) granulation 2 0 0 0 0 1 0 0 (100) (0) (0) (0) (0)(50)(0)(0) [Urinary system] kidney basophilic change 0 0 0 0 (0)(0)(0)(0) (50) (0) (0) (0) [Reproductive system] epididymis spermatogenic granuloma 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) [Musculoskeletal system] muscle necrosis 0 0 0 0 1 0 0 0 (0)(0)(0)(0) (50) (0) (0) (0) <1>:Slight <2>:Moderate <3>:Marked <4>:Severe (HPT150) BAIS2

APPENDIX A 6-6

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

MOUSE: FEMALE: SACRIFICED ANIMALS

Δ

STUDY NO. : 0180 ANIMAL : MOUSE BDF1

REPORT TYPE : A1

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (2W)

SEX : FEMALE

		Group Name Control No. of Animals 2	1250 ppm 2	2500 ppm 2	5000 ppm 2
Organ	Findings	<1> <2> <3> <4> (%) (%) (%) (%) (%)	<1> <2> <3> <4> (%) (%) (%) (%)	<1> <2> <3> <4> (%) (%) (%) (%)	(1) (2) (3) (4) (%) (%) (%) (%)
[Digestive :	system]				
stomach	intestinal metaplasia	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)
liver	swelling	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)
	necrosis: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 0 (0) (0)
	granulation	0 0 0 0 0 (0) (0) (0)	1 0 0 0 (50) (0) (0) (0)	1 0 0 0 (50) (0) (0) (0)	0 0 0 0 0 (0) (0)
· · · · · · · · · · · · · · · · · · ·	1>:Slight <2>:Moderate <3>:M	(0) (0) (0) (0) farked <4>:Severe	(50) (0) (0) (0)	(50) (0) (0) (0)	
(HPT150)					Bi

PAGE: 3

STUDY NO. : 0180

ANIMAL : MOUSE BDF1

REPORT TYPE : A1

SEX : FEMALE

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS (SUMMARY)

PAGE: 4

SACRIFICED ANIMALS (2W)

		Group Name 10000 ppm No. of Animals 2	20000 ppm 2	
0rgan	Findings	<1> <2> <3> <4> (%) (%) (%) (%)	<1> <2> <3> <4> (%) (%) (%) (%)	
(Digestive :	system]			
stomach	intestinal metaplasia	0 0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0) (0)	
liver	swelling	2 0 0 0 (100) (0) (0) (0)	2 0 0 0 (100) (0) (0) (0)	
	necrosis:focal	0 0 0 0 0 (0) (0)	2 0 0 0 (100) (0) (0) (0)	
	granulation	0 1 0 0 (0) (50) (0) (0)	1 0 0 0 (50) (0) (0) (0)	
<	(1>:Slight <2>:Moderate <3>	:Marked <4>:Severe		
(HPT150)				BAI

APPENDIX A 7-1

IDENTITY AND PURITY OF BIPHENYL

PERFORMED AT THE JAPAN BIOASSAY LABORATORY

(TWO-WEEK STUDY)

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

Lot no. DSQ3708

1. Spectral data

Mass Spectrometry

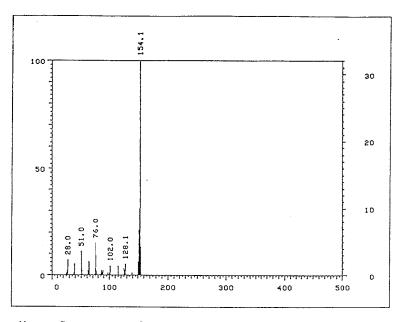
Instrument:

Hitachi M-80B

Ionization:

EI(Electron Ionization)

Ionization Voltage: 70eV



Mass Spectrum of BIPHENYL

Result:

Molecule Weight

Theoretical Value

154.1(Calculated)

Determined

154.1

ULTRA VIOLET SPECTRUM

Instrument:

SHIMADZU UV-240

Cell: 1 mm Cell

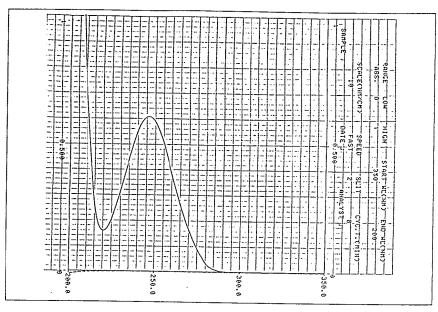
Solvent: Methanol

Slit:

2 nm

Range: 0-1

Concentration(mg/l): 50



Ultra Violet Spectrum of BIPHENYL

Results:	Determined	<u>Literature Value</u>
		(Sadtler handbook by Sadtler Research Laboratories, Inc.)
Wave Length	246.5	246.5

2. Gas Chromatography

Instrument: Hewlett Packard 5890A

Column:

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

Column Temperature: 180°C

Flow Rate:

1 ml/min

Detector: FID(Hydrogen Flame Ionization)

Injection Volume: 1 μ l

Results: Only major peak(except solvent peak)

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

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

APPENDIX A 7-2

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

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

Lot no. DSQ3708

1. Sample storage: Biphenyl were stored for about 2 weeks at 5°C.

2. Gas Chromatography

Instrument: Hewlett Packard 5890A

Column:

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

Column Temperature: 180°C

Flow Rate:

1 ml/min

Detector:

FID(Hydrogen Flame Ionization)

Injection Volume: 1 μ l

Results: Only major peak(except solvent peak)

Date	Retention Time(min)	Retention Time Relative to Major Peak	Area (percent of Major peak)
08/30/91	3.27	1.00	100
10/14/91	3.27	1.00	100

3. Conclusions: Gas chromatography indicates only the major peak. Consequently, Biphenyl was stable as the chemical when stored for about 2 weeks at 5°C.

APPENDIX A 7-3 ANALYSYS OF BIPHENYL CONCENTRATION IN FORMULATED DIETS OF THE TOW-WEEK STUDIES

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

(Rat)

C	Concentration of	BIPHENYL in	feed for Tar	get Concentration	(ppm)
2500 (a)	5000 (a) 10000	(a)	20000 (a)	40000 (a)
2572.9(102.9)	4461.1(89	.2) 9138.	1(91.4)	19843.3(99.2)	40182.0(100.5)

(Mouse)

Concentration of BIPHENYL in feed for Target Concentration(ppm)				
1250 (a)	2500 (a)	5000 (a)	10000 (a)	20000 (a)
1220.0(97.6)	2572.9(102.9)	4461.1(89.2)	9138.1(91.4)	19843.3(99.2)

⁽a) Determined as a percent of target concentration

APPENDIX A 7-4 STABILITY OF BIPHENYL IN FORMULATED DIETS OF THE TOW-WEEK STUDIES

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

(Rat)(Mouse)

	Concentration of BIPHENYL in feed	for Target Concentration(ppm)
Date Mixed	1250 (a)	40000 (a)
08/26/91	1177.7	37454.5
09/02/91	1097.8(93.2)	37763.7(100.8)

⁽a) Determined as a percent of target concentration