p-ニトロアニソールのマウスを用いた経口投与による 13 週 間 毒 性 試 験 (混 餌 試 験)報 告 書

試験番号:0370

APPENDIX

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APPENDIX A 1

CLINICAL OBSERVATION: SUMMARY, MOUSE: MALE

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

Administration Week-day

ANIMAL : MOUSE Crj:BDF1

Group Name

Control 2500 ppm

5000 ppm

10000 ppm

20000 ppm 30000 ppm 0

0

0

0

0

0

REPORT TYPE: A1 14

STUDY NO.: 0370

SEX : MALE

Clinical sign

OCTITION STOLL	di dup Manio	MOIII III	SHOTINI "	OUN Way											
		17	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9–7	10-7	11-7	12-7	13-7	14-7
															,
DEATH	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
•	30000 ppm	0	0	2	4	5	5	5	5	5	5	5	5	5	5
UNCHBACK POSITION	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
	30000 ppm	0	0	1	0	0	0	0	0	0	0	0	0	0	0
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
	30000 ppm	0	0	1	0	0	0	0	0	0	0	0	0	0	0
TUM	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	1	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
	30000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
IRREGULAR BREATHING	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
	30000 ppm	0	0	1	0	0	0	0	0	0	0	0	0	0	0

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ABNORMAL RESPIRATION

0

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0

PAGE: 1

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 14

SEX : MALE

PAGE: 2

Clinical sign	Group Name	Admini	stration W	eek-day											
		1-7	2-7	3-7	4-7	5–7	6-7	7-7	8-7	9–7	10-7	11-7	12-7	13-7	14-7
YELLOW URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
TELEON VILLE	2500 ppm	0	0	0	0	0	0	Õ	10	10	10	10	10	10	10
	5000 ppm	ő	Ô	Ö	Ö	Ö	Õ	ŏ	10	10	10	10	10	10	10
	10000 ppm	Ô	0	0	0	0	0	0	10	10	10	10	10	10	10
	20000 ppm	0	10	10	10	10	10	10	10	10	10	10	10	10	10
	30000 ppm	0	10	8	6	5	5	5	5	5	5	5	5	5	5
MALL STOOL	Contral	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
	30000 ppm	0	0	1	0	0	0	0	0	0	0	0	0	0	0

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APPENDIX A 2

CLINICAL OBSERVATION: SUMMARY, MOUSE: FEMALE

CLINICAL OBSERVATION (SUMMARY) ALL ANIMALS

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 14

STUDY NO.: 0370

linical sign	Group Name	Admini	stration W	eek-day									•• ••		~~~
ermout Sign	or bup ramo	1-7	2-7	3-7	4-7	5-7	6-7	7–7	8–7	9-7	10-7	11-7	12-7	13-7	14-7
		_				_	_					_		_	
DEATH	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
	30000 ppm	0	1	4	7	7	7	7	7	7	7	7	7	7	7
UNCHBACK POSITION	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
	30000 ppm	0	0	2	0	0	0	0	0	0	0	0	0	0	0
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
	30000 ppm	0	0	3	0	0	0	0	0	0	0	0	0	0	0
RREGULAR BREATHING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	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
	30000 ppm	0	0	1	0	0	0	0	0	0	0	0	0	0	0
ABNORMAL RESPIRATION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	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
	30000 ppm	0	0	1	0	0	0	0	0	0	0	0	0	0	0
YELLOW URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	2500 ppm	0	0	0	0	0	0	0	10	10	10	10	10	10	10
	5000 ppm	0	0	0	0	0	0	0	10	10	10	10	10	10	10
	10000 ppm	0	Ŏ	Õ	Ô	0	Ö	0	10	10	10	10	10	10	10
	20000 ppm	Ö	10	10	10	10	10	10	10	10	10	10	10	10	10

CLINICAL OBSERVATION (SUMMARY)

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1 14

ALL ANIMALS

SEX : FEMALE

PAGE : 4

Clinical sign	Group Name	o Name Administration Week-day													
		1-7	2-7	3-7	4-7	5-7	6-7	7–7	8-7	9-7	10-7	11-7	12-7	13-7	14-7
SMALL 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
	30000 ppm	0	0	1	0	0	0	0	0	0	0	0	0	0	0

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APPENDIX B 1

BODY WEIGHT CHANGES: SUMMARY, MOUSE: MALE

ANIMAL : MOUSE Crj:BDF1

UNIT : g
REPORT TYPE : A1 14

SEX : MALE

BODY WEIGHT CHANGES ALL ANIMALS

(SUMMARY)

PAGE: 1

roup Name	Administrati	an week					
	0	1	2	3	4	5	6
Control	23.2± 0.6	23.8± 0.5	24.4± 1.1	25.8± 0.8	26.9± 0.9	27.1± 0.9	28.2± 1.2
2500 ppm	23.1± 0.6	23.6± 0.9	24.2± 0.8	25.2± 0.8	25.9± 1.2	26.8± 1.3	27.6± 1.6
5000 ppm	23.1± 0.6	23.5± 0.9	24.1± 1.0	25.5± 1.1	26.4± 1.4	27.5± 1.5	28.1± 1.6
10000 ppm	23.1± 0.7	23.9± 0.8	24.3± 0.9	25.7± 0.8	26.1± 1.1	26.8± 1.3	27.1± 1.2
20000 ppm	23.2± 0.6	23.7± 0.7	22.3± 0.9**	24.9± 1.0	25.6± 1.9	25.8± 1.3	26.4± 1.0*
30000 ppm	23.1± 0.7	23.1± 0.8	18.2± 0.8**	17.3± 1.5**	18.1± 1.8**	20.1± 1.6**	21.3± 1.7**
Significant difference;	*: P ≤ 0.05	**: P ≦ 0.01		Test of Dunnett			
HAN260)	· · · · · · · · · · · · · · · · · · ·						

ANIMAL : MOUSE Crj:BDF1
UNIT : g

REPORT TYPE : A1 14

SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)

PAGE: 2

ALL ANIMALS

oup Name	Administration	week					
	7	8	9	10	11	12	13
C. down	00.01.1.0	00.04-1.4	00.74 1.7	20.04.17	31.1± 1.6	31.3± 1.5	21 04 1 5
Control	28.0± 1.2	28.9± 1.4	29.7± 1.7	30.0± 1.7	31.11 1.0	51.5.L 1.U	31.9± 1.5
2500 ppm	27.3± 1.5	28.2± 1.9	28.5± 2.4	28.9± 2.1	29.9± 2.1	29.9± 2.1	30.8± 2.5
5000 ppm	27.4± 1.5	28.3± 1.8	28.8± 2.3	29.2± 2.4	30.1± 2.4	30.0± 2.3	30.7± 2.4
10000 ppm	26.6± 1.3	27.8± 1.4	28.1± 1.4	28.1± 1.5	28.8± 1.7*	28.7± 1.6**	28.9± 2.3**
20000 ppm	25.9± 1.1**	26.8± 0.9*	27.0± 0.9**	27.3± 1.0**	27.3± 1.0**	27.3± 1.0**	28.0± 1.0**
30000 ppm	22.4± 1.4**	22.7± 1.6**	23.7± 1.9**	24.2± 1.1**	24.4± 1.4**	24.2± 1.4**	24.6± 1.3**
Significant differenc	ce; *:P≦0.05	**: P ≤ 0.01		Test of Dunnett			
(AN260)	· .						

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ANIMAL : MOUSE Crj:BDF1
UNIT : g

REPORT TYPE: A1 14

BODY WEIGHT CHANGES ALL ANIMALS

(SUMMARY)

Group Name	Administration week		
	14		
			'
Control	32.4± 1.5		
2500 ppm	31.5± 2.7		
5000 ppm	31.6± 2.4		
10000 ppm	29.5± 2.7		
10000 ppiii	20.02		
20000 ppm	28.3± 0.9**		
30000 ppm	25.0± 1.8**		
Significant differ	ence; *: P ≤ 0.05 **: P ≤ 0.01	Test of Dunnett	
(HAN260)			BAISS

APPENDIX B 2

BODY WEIGHT CHANGES: SUMMARY, MOUSE: FEMALE

ANIMAL : MOUSE Crj:BDF1

UNIT : g
REPORT TYPE : A1 14

SEX : FEMALE

BODY WEIGHT CHANGES ALL ANIMALS (SUMMARY)

PAGE: 4

roup Name	Administrati	on week					
	0	1	2	3	4	5	6
Control	18.3± 0.4	18.4± 0.6	19.0± 0.6	19.7± 0.5	19.6± 0.7	21.1± 0.9	21.0± 0.8
2500 ppm	18.3± 0.4	18.5± 0.4	19.1± 0.8	19.8± 0.5	20.2± 0.4	20.6± 0.9	21.1± 0.6
5000 ppm	18.3± 0.4	18.5± 0.7	19.1± 0.6	19.8± 0.5	20.1± 0.6	20.7± 0.5	21.6± 0.8
10000 ppm	18.3± 0.4	18.7± 0.6	19.0± 0.5	19.8± 0.6	20.3± 0.6	20.8± 0.6	21.6± 0.7
20000 ppm	18.3± 0.4	18.5± 0.8	17.3± 0.6**	19.8± 1.0	21.0± 0.9**	21.6± 1.1	21.4± 1.0
30000 ppm	18.3± 0.4	18.5± 0.8	14.5± 0.9**	12.9± 1.4*	16.2± 0.9**	18.0± 2.1	19.6± 2.0*
Significant difference;	*: P ≤ 0.05	** : P ≤ 0.01		Test of Dunnett			
IAN260)							

ANIMAL : MOUSE Crj:BDF1

UNIT : g

REPORT TYPE : A1 14

BODY WEIGHT CHANGES ALL ANIMALS

(SUMMARY)

SEX : FEMALE PAGE : 5

up Name	Administratio	on week					
	7	8	9	10	11	12	13
Control	20.7± 0.6	21.3± 1.1	21.3± 0.7	22.1± 1.1	21.5± 0.8	22.1± 1.1	22.3± 1.1
2500 ppm	20.9± 0.8	21.3± 1.1	21.2± 0.7	21.8± 1.0	21.7± 1.3	21.6± 0.8	22.0± 1.0
5000 ppm	20.2± 0.4	21.3± 1.0	21.5± 0.4	22.0± 0.5	21.7± 0.7	22.3± 1.0	22.5± 0.6
10000 ppm	20.9± 0.8	22.1± 0.8	21.8± 0.8	22.2± 0.7	22.8± 1.1	22.7± 1.0	23.4± 0.5*
20000 ppm	20.6± 1.1	21.4± 1.1	21.7± 0.9	21.7± 0.9	21.8± 0.7	22.0± 1.0	22,2± 1.0
30000 ppm	20.7± 1.8	22.2± 1.4	22.3± 1.3	22.5± 1.4	22.4± 1.4	22.2± 0.7	22.5± 0.8
Significant difference;	*: P ≤ 0.05	**: P ≤ 0.01		Test of Dunnett			

BAIS3 (HAN260)

ANIMAL : MOUSE Crj:BDF1

UNIT : g

REPORT TYPE : A1 14

SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)

ALL ANIMALS

Graup Name	Administration w 14	eek			
				 	 W.
Control	22.4± 0.9				
2500 ppm	22.1± 0.9				
5000 ppm	22.8± 0.8				
10000 ppm	23.5± 0.5*				
20000 ppm	22.3± 0.8				
30000 ppm	22.4± 0.9				
Significant difference ;	*: P ≤ 0.05 **	: P ≤ 0.01	Cest of Dunnett		
(HAN260)				······································	 BAIS3

PAGE : 6

APPENDIX C 1

FOOD CONSUMPTION CHANGES: SUMMARY, MOUSE: MALE

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

ANIMAL : MOUSE Crj:BDF1
UNIT : g

STUDY NO. : 0370

REPORT TYPE : A1 14

SEX : MALE

PAGE: 1

roup Name	Administration	week-day(effective)	<u> </u>			nt-t		
	1-7(7)	2–7 (7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7–7(7)	
Control	4.2± 0.3	3.8± 0.5	4.2± 0.4	3.9± 0.5	4.0± 0.5	4.0± 0.4	4.1± 0.2	
2500 ppm	4.0± 0.3	3.7± 0.4	4.0± 0.4	4.0± 0.4	3.9± 0.3	4.0± 0.4	3.9± 0.3	
5000 ppm	4.1± 0.2	3.8± 0.3	4.0± 0.2	4.0± 0.3	4.0± 0.3	4.0± 0.3	3.8± 0.3	
10000 ppm	4.0± 0.2	3.8± 0.3	3.9± 0.5	3.8± 0.5	3.8± 0.4	3.9± 0.4	3.9± 0.4	
20000 ppm	4.2± 0.4	3.9± 1.2	4.7± 1.1	4.2± 1.2	4.4± 1.0	4.3± 1.1	4.4± 0.8	
30000 ppm	3.9± 0.3	2.0± 0.4**	2.4± 0.6**	3.1± 1.1	3.7± 1.1	4.1± 1.3	4.5± 1.4	
				m				
Significant differen	nce; *: P ≤ 0.05	** : P ≤ 0.01		Test of Dunnett				RA

(HAN260) BAIS3 FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

PAGE: 2

STUDY NO. : 0370

ANIMAL : MOUSE Crj:BDF1

UNIT : g
REPORT TYPE : A1 14
SEX : MALE

3.9± 0.3 4.0± 0.4 4.1± 0.3	4.1± 0.4 4.0± 0.3	4.1± 0.3 4.0± 0.3	4.2± 0.3 4.1± 0.4	3.9± 0.3	4.0± 0.4	4.1± 0.3
	4.0± 0.3	4.0± 0.3	4.1± 0.4	204 04		
4.1± 0.3				3.9± 0.4	4.0± 0.4	4.2± 0.3
	3.9± 0.6	4.0± 0.4	4.0± 0.3	3.8± 0.3	4.0± 0.4	4.2± 0.3
4.0± 0.4	4.0± 0.3	3.9± 0.4	4.1± 0.3	4.0± 0.4	3.7± 0.5	4.1± 0.4
4.6± 0.9	4.3± 0.5	4.2± 0.6	4.1± 0.5	4.2± 0.8	4.3± 0.7	4.4± 0.7
4.5± 1.5	4.5± 1.7	4.2± 1.1	4.0± 1.0	4.1± 1.2	4.8± 0.9*	4.8± 0.9
*: P ≤ 0.05	**: P ≤ 0.01		Test of Dunnett			
- ×	4.5± 1.5	4.5± 1.5 4.5± 1.7	4.5± 1.5 4.5± 1.7 4.2± 1.1	4.5± 1.5 4.5± 1.7 4.2± 1.1 4.0± 1.0	4.5± 1.5 4.5± 1.7 4.2± 1.1 4.0± 1.0 4.1± 1.2	4.5± 1.5 4.5± 1.7 4.2± 1.1 4.0± 1.0 4.1± 1.2 4.8± 0.9*

BAIS 3 (HAN260)

APPENDIX C 2

FOOD CONSUMPTION CHANGES : SUMMARY, MOUSE : FEMALE (13-WEEK STUDY)

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

STUDY NO. : 0370

ANIMAL : MOUSE Crj:BDF1

UNIT : g
REPORT TYPE : A1 14
SEX : FEMALE

oup Name	Administration	week-day(effective)								
	1-7(7)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)			
Control	3.7± 0.5	3.5± 0.3	3.5± 0.3	3.5± 0.2	3.6± 0.3	3.5± 0.3	3.5± 0.1			
2500 ppm	3.6± 0.3	3.4± 0.3	3.4± 0.2	3.3± 0.2	3.6± 0.2	3.5± 0.3	3.5± 0.2			
5000 ppm	3.6± 0.1	3.4± 0.2	3.4± 0.2	3.5± 0.2	3.6± 0.3	3.5± 0.3	3.5± 0.2			
10000 ppm	3.6± 0.2	3.3± 0.2	3.5± 0.4	3.5± 0.4	3.6± 0.4	3.6± 0.4	3.5± 0.5			
20000 ppm	3.5± 0.2	3.3± 0.7	3.8± 0.7	3.5± 0.7	3.4± 0.8	3.1± 0.3**	3.2± 0.4			
30000 ppm	3.5± 0.2	3.0± 1.3	3.1± 2.2	3.5± 1.5	3.0± 0.8	3.2± 0.6	3.4± 0.6			
Significant differen	nce; *: P ≤ 0.05	**: P ≤ 0.01		Test of Dunnett						
111000)				•						

(HAN260)

BAIS3

PAGE: 3

ANIMAL : MOUSE Crj:BDF1

UNIT : g
REPORT TYPE : A1 14

SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)

ALL ANIMALS

oup Name	Administration	week-day(effective)					
	8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)	14-7(7)
Control	3.7± 0.2	3.7± 0.2	3.8± 0.3	3.7± 0.2	3.7± 0.3	3.8± 0.2	3.7± 0.2
2500 ppm	3.7± 0.3	3.7± 0.2	3.7± 0.3	3.8± 0.3	3.5± 0.3	3.7± 0.4	3.7± 0.2
5000 ppm	3.8± 0.3	3.8± 0.2	3.7± 0.2	3.8± 0.4	3.8± 0.3	3.8± 0.4	3.8± 0.3
10000 ppm	3.7± 0.5	3.6± 0.4	3.7± 0.5	3.9± 0.6	3.7± 0.5	3.9± 0.5	3.7± 0.5
20000 ppm	3.4± 0.4	3.4± 0.3*	3.5± 0.5	3.7± 0.5	3.6± 0.7	3.7± 0.5	3.6± 0.3
30000 ppm	3.3± 0.3	3.3± 0.7	3.5± 0.7	4.1± 1.7	4.1± 2.1	4.3± 2.0	3.9± 1.2
Significant difference	; *: P ≤ 0.05	**: P ≤ 0.01		Test of Dunnett			
IAN260)							

PAGE: 4

APPENDIX D 1

CHEMICAL INTAKE CHANGES: SUMMARY, MOUSE: MALE

ANIMAL : MOUSE Crj:BDF1

UNIT : g/kg/day
REPORT TYPE : A1 14

SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)

ALL ANIMALS

PAGE: 1

Administration	(weeks)								
2	3	4	5	6	7	8			
0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000			
0.383± 0.037	0.398± 0.034	0.387± 0.030	0.362± 0.026	0.367± 0.024	0.359± 0.021	0.353± 0.020			
0.790± 0.083	0.776± 0.039	0.762± 0.031	0.722± 0.056	0.707± 0.026	0.702± 0.047	0.718± 0.029			
1.571± 0.097	1.528± 0.164	1.441± 0.144	1.419± 0.118	1.439± 0.117	1.456± 0.108	1.454± 0.106			
3.487± 1.021	3.799± 0.815	3.227± 0.782	3.381± 0.755	3.233± 0.835	3.402± 0.631	3.452± 0.684			
3.329± 0.644	4.130± 0.840	5.148± 1.441	5.420± 1.423	5.639± 1.454	5.958± 1.566	5.919± 1.779			
	2 0.000± 0.000 0.383± 0.037 0.790± 0.083 1.571± 0.097 3.487± 1.021	2 3 0.000± 0.000 0.000± 0.000 0.383± 0.037 0.398± 0.034 0.790± 0.083 0.776± 0.039 1.571± 0.097 1.528± 0.164 3.487± 1.021 3.799± 0.815	2 3 4 0.000± 0.000 0.000± 0.000 0.000± 0.000 0.383± 0.037 0.398± 0.034 0.387± 0.030 0.790± 0.083 0.776± 0.039 0.762± 0.031 1.571± 0.097 1.528± 0.164 1.441± 0.144 3.487± 1.021 3.799± 0.815 3.227± 0.782	2 3 4 5 0.000± 0.000 0.000± 0.000 0.000± 0.000 0.000± 0.000 0.383± 0.037 0.398± 0.034 0.387± 0.030 0.362± 0.026 0.790± 0.083 0.776± 0.039 0.762± 0.031 0.722± 0.056 1.571± 0.097 1.528± 0.164 1.441± 0.144 1.419± 0.118 3.487± 1.021 3.799± 0.815 3.227± 0.782 3.381± 0.755	2 3 4 5 6 0.000± 0.000 0.000± 0.000 0.000± 0.000 0.000± 0.000 0.000± 0.000 0.383± 0.037 0.398± 0.034 0.387± 0.030 0.362± 0.026 0.367± 0.024 0.790± 0.083 0.776± 0.039 0.762± 0.031 0.722± 0.056 0.707± 0.026 1.571± 0.097 1.528± 0.164 1.441± 0.144 1.419± 0.118 1.439± 0.117 3.487± 1.021 3.799± 0.815 3.227± 0.782 3.381± 0.755 3.233± 0.835	2 3 4 5 6 7 0.000± 0.000 0.000± 0.000 0.000± 0.000 0.000± 0.000 0.000± 0.000 0.000± 0.000 0.383± 0.037 0.398± 0.034 0.387± 0.030 0.362± 0.026 0.367± 0.024 0.359± 0.021 0.790± 0.083 0.776± 0.039 0.762± 0.031 0.722± 0.056 0.707± 0.026 0.702± 0.047 1.571± 0.097 1.528± 0.164 1.441± 0.144 1.419± 0.118 1.439± 0.117 1.456± 0.108 3.487± 1.021 3.799± 0.815 3.227± 0.782 3.381± 0.755 3.233± 0.835 3.402± 0.631			

(HAN300)

BAIS 3

CHEMICAL INTAKE CHANGES (SUMMARY) ALL ANIMALS

ANIMAL : MOUSE Crj:BDF1 UNIT : g/kg/day
REPORT TYPE : Al 14

SEX : MALE

PAGE: 2

Group Name	Administration	(weeks)					
	9	10	11	12	13	14	
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	
2500 ppm	0.350± 0.020	0.346± 0.023	0.339± 0.027	0.328± 0.032	0.325± 0.021	0.333± 0.024	
5000 ppm	0.675± 0.097	0.683± 0.033	0.668± 0.032	0.642± 0.025	0.647± 0.046	0.665± 0.030	
10000 ppm	1.426± 0.099	1.385± 0.086	1.411± 0.111	1.378± 0.109	1.266± 0.121	1.384± 0.142	
20000 ppm	3.147± 0.414	3.053± 0.449	3.040± 0.367	3.064± 0.555	3.060± 0.463	3.110± 0.468	
30000 ppm	5.776± 1.957	5.179± 1.273	5.003± 1.134	5.097± 1.383	5.916± 1.390	5.820± 1.244	

(HAN300)

BAIS 3

APPENDIX D 2

CHEMICAL INTAKE CHANGES: SUMMARY, MOUSE: FEMALE

STUDY NO. : 0370 ANIMAL : MOUSE Crj:BDF1
UNIT : g/kg/day CHEMICAL INTAKE CHANGES (SUMMARY)

ALL ANIMALS

REPORT TYPE : A1 14

SEX : FEMALE

PAGE: 3

Group Name		(weeks)					0
	2	3	4	5	6	7	8
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
2500 ppm	0.444± 0.033	·0.435± 0.026	0.412± 0.027	0.440± 0.031	0.412± 0.031	0.422± 0.018	0.435± 0.020
5000 ppm	0.885± 0.059	0.862± 0.053	0.858± 0.043	0.876± 0.068	0.821± 0.042	0.862± 0.048	0.896± 0.050
10000 ppm	1.714± 0.112	1.781± 0.172	1.702± 0.182	1.719± 0.213	1.654± 0.183	1.681± 0.193	1.681± 0.161
20000 ppm	3.856± 0.841	3.836± 0.714	3.291± 0.595	3.125± 0.679	2.871± 0.206	3.082± 0.260	3.160± 0.244
30000 ppm	6.263± 2.635	7.052± 4.799	6.332± 2.459	4.936± 0.802	4.889± 0.510	4.957± 0.583	4.470± 0.384

BAIS 3 (HAN300)

CHEMICAL INTAKE CHANGES (SUMMARY) ALL ANIMALS

ANIMAL : MOUSE Crj:BDF1
UNIT : g/kg/day
REPORT TYPE: A1 14

SEX : FEMALE

PAGE: 4

roup Name	Administration	(weeks)					
	9	10	11	12	13	14	
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	
2500 ppm	0.434± 0.035	0.419± 0.025	0.435± 0.029	0.409± 0.031	0.423± 0.035	0.413± 0.019	
5000 ppm	0.876± 0.050	0.843± 0.041	0.865± 0.071	0.845± 0.045	0.833± 0.084	0.824± 0.045	
10000 ppm	1.666± 0.162	1.689± 0.208	1.707± 0.257	1.650± 0.207	1.666± 0.187	1.560± 0.224	
20000 ppm	3.096± 0.243	3.255± 0.366	3.420± 0.466	3.284± 0.555	3.309± 0.405	3.249± 0.264	
30000 ppm	4.466± 0.670	4.633± 0.667	5.373± 2.009	5.458± 2.714	5.756± 2.506	5.242± 1.396	

(HAN300)

BAIS 3

APPENDIX E 1

HEMATOLOGY: SUMMARY, MOUSE: MALE

ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1

REPORT TYPE : A1

HEMATOLOGY (SUMMARY) ALL ANIMALS (15W)

PAGE: 1 SEX : MALE PLATFLET

roup Name	NO. of Animals	RED BLO	OOD CELL	HEMOGLOBIN g/dl		HEMATOCRIT %		MCV f Q		MCH pg		MCHC		PLATELET 1 0 ³ /μ ^g	
Control	10	10.69±	0.28	15.5±	0.3	49.8±	1.3	46.6±	0.5	14.5±	0.2	31.1±	0.4	1368±	87
2500 ppm	9	10.76±	0.28	15.5±	0.2	49.9±	1.0	46.4±	0.5	14.5±	0.3	31.2±	0.5	1382±	105
5000 ppm	10	10.70±	0,30	15.7±	0.3	50.3±	1.5	47.0±	0.7	14.6±	0.2	31.1±	0.6	1369±	158
10000 ppm	9	10.49±	0.34	15.6±	0.5	49.4±	1.7	47.1±	0.7	14.9±	0.3*	31.5±	0.4	1456±	96
20000 ppm	10	9.63±	0.36**	15.5±	0.7	45.2±	1.6**	46.9±	0.5	16.1±	0.4**	34.2±	0.6**	1514±	65*
30000 ppm	5	10.23±	0.38*	14.9±	0.3	46.7±	1.2**	45.6±	0.6*	14.6±	0.3	31.9±	0.3*	1528±	95*

BAIS3

(HCL070)

ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1
SEX : MALE REPOR

REPORT TYPE : A1

HEMATOLOGY (SUMMARY) ALL ANIMALS (15W)

obn - mbb	nai on a																
Group Name	NO. of Animats	WBC 1 0³∕		Dif N-BAND	ferentia	UWBC (%	5)	EOSINO		BASO		МОМО		LYMPHO		OTHER	
Control	10	1.23±	0.48	1±	1	17±	3	2±	1	0±	0	4±	2	77±	4	0±	0
2500 ppm	9	1,47±	0.59	l±	1	15±	5	1±	1	0土	0	4 ±	3	79±	6	0±	0
5000 ppm	. 10	1.22±	0.50	0±	1	16±	5	1±	1	0±	0	3±	1	80±	5	0±	0
10000 ppm	9	1.43±	0.70	1±	2	17±	5	1±	1	0±	0	3±	2	78±	5	0±	0
20000 ppm	10	1,28±	0.61	1±	2	16±	5	0±	1	0±	0	2±	2	81±	5	0±	0
30000 ppm	5	0.71±	0.39	0±	0	14±	4	1±	1	0±	0	6±	2	79±	3	0±	0
Significan	t difference	; *:P;	≤ 0.05	**: P ≦	0.01			Test	of Duni	nett							
(HCL070)				· · · · ·												,	BAIS 3

PAGE: 2

APPENDIX E 2

HEMATOLOGY: SUMMARY, MOUSE: FEMALE

HEMATOLOGY (SUMMARY) ALL ANIMALS (15W)

STUDY NO. : 0370

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1

SEX : FEMALE

REPORT TYPE : A1

MCH MCHC PLATELET RED BLOOD CELL HEMOGLOBIN HEMATOCRIT MCV Group Name NO. of g/dl 1 03/µl Animals 1 06/µl g/dl % f Q рg 45.9± 14.5± 0.2 31.5± 0.5 1223± 77 Control 10 11.05± 0.37 $16.0 \pm$ 0.6 50.7± 1.9 0.5 $1307 \pm$ 120 11.08± 0.26 $16.1 \pm$ 0.4 51.0± 1.4 46.0士 0.4 14.5± 0.2 31.6± 0.4 2500 ppm 10 14.7生 0.2 $31.9 \pm$ 0.6 1322士 92 50.0± 46.0± 0.8 5000 ppm 10 10.89± 0.28 16.0± 0.4 1.2 0.3** 31.6± 0.5 $1358 \pm$ 102* 10.69± 0.37* 15.9± 0.5 50.3± 1.4 47.0± 0.7** $14.8 \pm$ 10 10000 ppm $32.7 \pm$ 0.3** $1385 \pm$ 84** 47.7± 0.6** 15.6士 0.2** 9.82± 0.24** $15.3 \pm$ 0.4* 46.8± 1.2** 20000 ppm 10 $43.5 \pm$ 1.0** 45.8± 0.8 $15.0 \pm$ 0.2** $32.7 \pm$ 0.5** 1430 ± 15** 30000 ppm 9.49士 0.16** $14.2 \pm$ 0.1** ** : $P \leq 0.01$ Test of Dunnett Significant difference: $*: P \leq 0.05$

PAGE: 3

(HCL070) BAIS 3

ANIMAL : MOUSE Crj:BDF1

MEASURE, TIME: 1 SEX: FEMALE REPORT TYPE : A1 HEMATOLOGY (SUMMARY) ALL ANIMALS (15W)

Group Name	NO. of Animals	WBC 1 O³/		Did N-BAND	fferentia	L WBC (% N-SEG	6)	EOSINO		BASO		ОИОМ		LYMPHO		OTHER	
Control	10	1.24±	0.45	1±	1	17±	8	1±	1	0±	0	3±	2	80±	8	0±	0
2500 ppm	10	1.19±	0.79	0±	0	17±	10	1±	2	0±	0	3±	2	78±	10	0±	0
5000 ppm	10	1.27±	0.43	0±	1	18±	5	1±	1	0±	0	4±	4	77±	5	0±	0
10000 ppm	10	1.10±	0.53	1±	3	18±	7	1±	1	0±	0	2±	2	78±	8	0±	0
20000 ppm	10	1.58±	0.40	0±	1	15±	5	1±	1	0±	0	4±	2	80±	6	0±	0
30000 ppm	3	3.52±	2.58	0±	. 1	13±	2	1±	1	0±	0	4±	2	81±	3	0±	0
Significan	t difference :	; *:P:	≦ 0.05	**: P ≦	0.01			Test	of Dunr	nett							
(HCL070)					 				············	<u> </u>			.	· · · · · · · · · · · · · · · · · · ·			BAISS

PAGE: 4

(HCL070)

APPENDIX F 1

BIOCHEMISTRY: SUMMARY, MOUSE: MALE

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1 SEX: MALE

REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (15W)

Group Name	NO. of Animals	TOTAL P	ROTEIN	g∕dø ALBUMIN		A/G RAT	.10	T-BILI mg/dl		GLUCOSE mg∕dl		T-CHOLE	STEROL	TRIGLYC mg/dl	ERIDE
Control	10	4.7±	0.2	2.7±	0.1	1.3±	0.1	0.16±	0.02	171±	23	79±	10	52士	18
2500 ppm	10	4.9±	0.2	2.8±	0.2	1.3±	0.1	0.16±	0.01	172±	37	81±	13	52±	31
5000 ppm	10	5.0±	0.2**	2.9±	0.1**	1.4±	0.1	0.16±	0.02	184±	28	81土	6	45±	15
10000 ppm	10	5.1±	0.2**	2.9±	0.1*	1.3±	0.1	0.18±	0.04	183±	45	103±	21	42±	19
20000 ppm	10	5.4±	0.2**	3.1±	0.1**	1.4±	0.1	0.17±	0.01	242土	52**	189±	17**	82±	32*
30000 ppm	5	5.8±	0.2**	3.4±	0.1**	1.4±	0.0	0.18±	0.01	308±	47**	262±	17**	65±	23

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

(HCL074)

BAIS3

ANIMAL : MOUSE Crj:BDF1

MEASURE, TIME: 1

REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (15W)

SEX : MALE

PAGE: 2

roup Name	NO. of Animals	PHOSPHO mg/dl	LIPID -	GOT I U / L		GPT IU/0	ļ.	IU/s	2	ALP IU/0		G-GTP IU∕£		CPK IU/0	
Control	10	172±	17	43±	6	19±	3	194±	29	130±	11	2±	1	61±	16
2500 ppm	10	169±	23	44±	5	19±	3	209±	66	136±	10	1±	1	65±	28
5000 ppm	10	164±	11	42±	4	19±	3	204±	47	139±	8	2±	1	64±	17
10000 ppm	10	183±	31	45±	9	24士	7	269±	119	147±	20	1±	1	78±	36
20000 ppm	10	293士	28**	47±	7	35±	10**	230±	52	177±	19**	1±	1	82±	32
30000 ppm	5	387±	22**	137±	52**	146±	57**	386±	86**	285±	21**	4±	2**	120±	59

BAIS 3 (HCL074)

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1

REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (15W)

SEX : MALE PAGE: 3

Group Name	NO. of Animals	UREA NI mg/dl		SODIUM mEq/2		POTASSI mEq/		CHLORIDE mEq/Q		CALCIUM mg/dl		INORGAN mg/dl	NIC PHOSPHORUS
Control	10	23.8±	3.6	151±	1	4.8±	0.5	123±	2	8.5±	0.5	√7.7±	0.5
2500 ppm	10	26.0±	5.2	152±	1	4.7±	0.6	122±	3	8.8±	0.3	8.1±	0.8
5000 ppm	10	29.4±	5.4	152±	1	4.7±	0.5	122±	2	8.8±	0.2	7.7±	0.9
10000 ppm	10	32.2±	6.5**	151±	1	4.6±	0.7	122±	2	8.7±	0.3	7.5±	1.2
20000 ppm	10	30.7±	3.6*	150±	2	4.3±	0.5	120±	2*	9.1±	0.2**	6.9±	0.6
30000 ppm	5	31.8±	3.1*	149±	1**	4.6±	0.3	116±	2**	9.4±	0.1**	7.8±	0.5
Significant	defference;	*: P ≤ (0.05	**: P ≤ 0.01	L			Test of Dunr	nett				

BAIS3 (HCL074)

APPENDIX F 2

BIOCHEMISTRY: SUMMARY, MOUSE: FEMALE

SEX : FEMALE

STUDY NO.: 0370
ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1

REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (15W)

oup Name	NO. of Animals	TOTAL P	PROTEIN	albumin g∕d1		A/G RAT	.10	T-BILI mg/dl		GLUCOSE mg/dl		T-CHOLE mg/dl	STEROL	TRIGLYCI mg/dl	ERIDE
Control	10	5.0±	0.1	3.1±	0.1	1.6±	0.1	0.15±	0.01	147±	22	77±	4	35±	17
2500 ppm	10	5.0±	0.1	3.1±	0.1	1.6±	0.1	0.14±	0.01	143±	18	69±	9	24±	8
5000 ppm	10	5.0±	0.2	3.0±	0.1	1.6±	0.1	0.15±	0.01	159±	28	81±	12	24±	11
10000 ppm	10	5.0±	0.2	3.1±	0.1	1.6±	0.1	0.14±	0.01	167±	25	100土	7*	26±	12
20000 ppm	10	5.2±	0.1**	3.1±	0.1	1.5±	0.0**	0.14±	0.01	226±	26**	192±	17**	48±	18
30000 ppm	3	5.7±	0.2**	3.4±	0.1**	1.5±	0.1	0.16±	0.01	261±	7**	208±	12**	58±	9

PAGE: 4

BAIS 3 (HCL074)

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (15W)

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1

SEX : FEMALE REPORT TYPE : A1

PAGE: 5

coup Name	NO. of Animals	PHOSPHO mg/dl	LIPID	GOT IU/1		GPT IU/1		IU/s	1	ALP IU/0		G-GTP IU/l		CPK IU/Q	ļ
Control	10	160±	10	50±	5	19±	3	188±	20	197±	14	2±	2	84±	39
2500 ppm	10	142±	22	52±	7	25±	15	209±	30	202±	14	1±	1	95±	2,8
5000 ppm	10	158±	26	51±	8	20±	3	203±	37	200土	23	1±	1	104±	63
10000 ppm	10	178±	12	50±	10	24±	6	204±	57	196±	19	2±	1	90±	33
20000 ppm	10	313±	27**	75±	18**	47±	12**	225±	30*	201±	13	2±	1	88±	27
30000 ppm	3	347±	15**	202±	97*	182±	81**	405±	141**	201±	20	7±	1**	118±	61

(HCL074)

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME : 1 SEX : FEMALE

REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (15W)

NO. of UREA NITROGEN SODIUM POTASSIUM CHLORIDE CALCIUM INORGANIC PHOSPHORUS Group Name mEq/Q Animals mg/dl mEq/l mEq/lmg/dl mg/dl Control 10 18.1± 2.4 151± 1 4.7± 0.3 $121\pm$ 2 8.8± 0.2 $6.9 \pm$ 1.2 20.6± 2.5 $151 \pm$ $4.8 \pm$ 0.3 122± 8.6± 0.2 6.7± 0.7 2500 ppm 10 2 1 8.8± $6.5 \pm$ 5000 ppm 10 $20.9 \pm$ 2.2 $151 \pm$ 2 $4.7\pm$ 0.2 $122\pm$ 0.2 0.6 2 4.7± 2 8.9± 0.2 $6.3 \pm$ 0.7 10000 ppm 10 22.4± 2.5** $151 \pm$ 0.4 123± $9.2 \pm$ $6.5 \pm$ 0.7 20000 ppm 10 $25.0 \pm$ 4.0** 150± 1 $4.2 \pm$ 0.5** 120± 2 0.2** 26.1± 2.1** 149± 2 $5.4\pm$ 0.7 $9.5 \pm$ 0.2** $6.4\pm$ 0.8 30000 ppm $116\pm$ 2** Significant defference; $*: P \leq 0.05$ **: $P \leq 0.01$ Test of Dunnett

PAGE: 6

(HCL074) BAIS 3

APPENDIX G 1

URINALYSIS: SUMMARY, MOUSE: MALE

URINALYSIS

**: $P \leq 0.01$

STUDY NO. : 0370

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : A1

Significant difference ; $*: P \leq 0.05$

Occult blood Group Name NO. of pH_ Protein_ Glucase_ Ketone body 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI - ± + 2+ 3+ 4+ CHI $-\pm+2+3+4+$ CHI $-\pm + 2 + 3 + 4 + CHI$ $-\pm + 2 + 3 + CHI$ Animals 10 0 0 0 0 1 9 0 0 0 0 Control 10 0 0 1 8 1 0 0 0 10 0 0 0 10 0 0 0 0 0 10 0 0 0 0 2 8 0 0 0 0 2500 ppm 10 0 0 10 0 0 0 10 0 0 0 0 0 0 0 7 3 0 0 10 0 0 0 0 0 4 6 0 0 0 0 10 0 0 0 0 5000 ppm 10 0 0 10 0 0 0 0 0 3 7 0 0 0 0 10 0 0 0 0 10000 ppm 10 3 2 0 0 0 10 0 0 0 9 0 0 0 0 20000 ppm 9 1 1 0 0 0 0 1 8 0 0 0 9 0 0 0 0 0 4 5 0 0 0 0 4 0 0 0 0 4 0 0 0 0 0 0 4 0 0 0 0 30000 ppm 0 2 1 1 0 0 0 0 4 0 0 0

PAGE: 1

(HCL101) BAIS 3

Test of CHI SQUARE

URINALYSIS

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : A1

Group Name	NO. of Animals	Urabilinagen ± + 2+ 3+ 4+ CHI		
Control	10	10 0 0 0 0		
2500 ppm	10	10 0 0 0 0		
5000 ppm	10	10 0 0 0 0		
10000 ppm	10	10 0 0 0 0		
20000 ppm	9	9 0 0 0 0		
30000 ppm	4	4 0 0 0 0		
Significan	t difference	; *: $P \le 0.05$ **: $P \le 0.01$	Test of CHI SQUARE	
(HCL101)				BAIS3

APPENDIX G 2

URINALYSIS: SUMMARY, MOUSE: FEMALE

URINALYSIS

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1

SEX : FEMALE

REPORT TYPE : A1

PAGE: 3

oup Name	NO. of	p	-							-	Pro		_				luco	-						body						blo		
	Animals	5	.0	6.0	6.5	7,0	7.	5 8	.0 8.	5 CHI	-	± ·	+ 2	+ 3+	· 4+ CH	I	- ±	+	2+ :	3+ 4+	CHI		±	+ 2-	3+	4+	CHI		±	+ 2	2+ 3+	СН
Control	10		0	1	3	2	2	3	2 0		0	5	5	0 0	0		10 (0	0	0 0		0	8	2 (0	0		10	0	0	0 0	
2500 ppm	10		0	0	1	3	4	l .	2 0		0	5	5	0 0	0		LO (0	0	0 0		1	8	1 (0	0		10	0	0	0 0	
5000 ppm	10		0	0	1	4	3	3	2 0		0	6	4	0 0	0		10 (0	0	0 0		1	9	0 (0	0		10	0	0	0 0	
10000 ppm	10		0	1	6	2	1		0 0		0	8	2	0 0	0		10 (0	Ó	0 0		1	9	0	0	0		10	0	0	0 0	
20000 ppm	10		0	6	3	1	C)	0 0		1	8	1	0 0	0		10 () 0	0	0 0		1	9	0	0	0		10	0	0	0 0	
30000 ppm	3		0	3	0	0	C)	0 0		0	2	1	0 0) 0		3 () 0	0	0 0		0	3	0 (0 0	0		3	0	0	0 0	
Significant	difference	•	*:	P <	0.0	5	**	k : P	[,] ≤ 0.	01					T	est of	CHI	SOU	ARE													
DISHITICANL		, 		. ==	. 0.0				= 0.	· · · · · · · · · · · · · · · · · · ·						05. 01	oni	q.∪														

(HCL101) BAIS 3

URINALYSIS

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1

SEX : FEMALE

REPORT TYPE : A1

Group Name	NO. of Animals	Urobilingen ± + 2+ 3+ 4+ CHI		
Control	10	10 0 0 0 0		
2500 ppm	10	10 0 0 0 0	•	
5000 ppm	10	10 0 0 0 0		·
10000 ppm	10	10 0 0 0 0		
20000 ppm	10	10 0 0 0 0		
30000 ppm	3	3 0 0 0 0		
Significan	t difference	; *: P ≤ 0.05 **: P ≤ 0.01	Test of CHI SQUARE	
(HCL101)				BAIS 3

APPENDIX H 1

GROSS FINDINGS: SUMMARY, MOUSE: MALE ALL ANIMALS

ANIMAL : MOUSE Crj:BDF1

GROSS FINDINGS (SUMMARY)

REPORT TYPE : A1

: MALE

ALL ANIMALS (0- 15W)

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)
IPT080)						B/

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : MALE GROSS FINDINGS (SUMMARY) ALL ANIMALS (0- 15W)

Organ	Findings_	Group Name NO. of Animals	20000 ppm 10 (%)	30000 ppm 10 (%)	
thymus	atrophic		0 (0)	5 (50)	
(HPT080)					

APPENDIX H 2

GROSS FINDINGS: SUMMARY, MOUSE: FEMALE ALL ANIMALS

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : FEMALE GROSS FINDINGS (SUMMARY) ALL ANIMALS (0- 15W)

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)
(HPT080)						<u>,</u>

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)

ALL ANIMALS (0- 15W)

SEX	: FEMALE				PAGE: 4
Organ	Findings	Group Name NO. of Animals	20000 ppm 10 (%)	30000 ppm 10 (%)	
thymus	atrophic		0 (0)	7 (70)	
(HPT080)			1		BAIS3

APPENDIX H 3

GROSS FINDINGS : SUMMARY, MOUSE : MALE

DEAD AND MORIBUND ANIMALS

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 15W)

SEX : MALE

Organ	Findings	Group Name NO. of Animals	Control 0 (%)	2500 ppm 0 (%)	5000 ppm 0 (%)	10000 ppm 0 (%)
thymus	atrophic		- (-)	- (-)	- (-)	- (-)
(HPT080)						BAISS

ANIMAL : MOUSE Crj:BDF1

GROSS FINDINGS (SUMMARY) DEAD AND MORIBUND ANIMALS (0- 15W)

REPORT TYPE : A1 SEX : MALE

Organ	Findings	Group Name NO. of Animals	20000 ppm 0 (%)	30000 ppm 5 (%)	
thymus	atrophic		- (-)	5 (100)	
(UDTAGA)					BYICS

(HPT080)

BAIS3

APPENDIX H 4

GROSS FINDINGS: SUMMARY, MOUSE: FEMALE

DEAD AND MORIBUND ANIMALS

ANIMAL : MOUSE Crj:BDF1

GROSS FINDINGS (SUMMARY) DEAD AND MORIBUND ANIMALS (0- 15W)

REPORT TYPE : A1

: FEMALE

Organ	Findings	Group Name NO. of Animals	Control 0 (%)	2500 ppm 0 (%)	5000 ppm 0 (%)	10000 ppm 0 (%)
thymus	atrophic		- (-)	- (-)	- (-)	- (-)
HPT080)						Bai

STUDY NO. : 0370
ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 15W)

SEX	: FEMALE				PAGE: 4
0rgan	Findings	Group Name NO. of Animals	20000 ppm 0 (%)	30000 ppm 7 (%)	
thymus	atrophic		- (-)	7 (100)	
(HPT080)					BAIS 3

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APPENDIX I 1

ORGAN WEIGHT, ABSOLUTE: SUMMARY, MOUSE: MALE

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : MALE UNIT: g

ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (15W)

PAGE: 1

roup Name	NO. of Animals	Bady Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	30.0± 1.9	0.035± 0.007	0.017± 0.005	0.195± 0.018	0.159± 0.018	0.159± 0.009
2500 ppm	10	29.2± 2.6	0.032± 0.005	0.014± 0.004	0.222± 0.015	0.149± 0.011	0.157± 0.009
5000 ppm	10	29.0± 2.5	0.034± 0.008	0.014± 0.003	0.226± 0.032	0.153± 0.012	0.159± 0.014
10000 ppm	10	27.6± 1.8*	0.030± 0.006	0.014± 0.003	0.210± 0.045	0.151± 0.013	0.159± 0.012
20000 ppm	10	26.0生 1.2**	0.030± 0.004	0.013± 0.004	0.218± 0.025	0.139± 0.013**	0.155± 0.005
30000 ppm	5	23.2± 1.8**	0.032± 0.003	0.014± 0.003	0.207± 0.023	0.119± 0.009**	0.140± 0.007**

(HCL040)

ANIMAL : MOUSE Crj:BDF1

ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (15W)

REPORT TYPE : A1 SEX : MALE UNIT: g

PAGE: 2

roup Name	NO. of Animals			SPLEEN LIVE		ER BRAIN				
Control	10	0.412±	0.032	0.043±	0.005	1.078±	0.073	0.441±	019	
2500 ppm	10	0.406±	0.030	0.045±	0.004	1.132±	0.076	0.441±	015	
5000 ppm	10	0.420±	0.035	0.047±	0.003	1.178±	0.080	0.447±	022	
10000 ppm	10	0.410±	0.027	0.051±	0.004*	1.318±	0.100**	0.453±	016	
20000 ppm	10	0.385±	0.017	0.092±	0.018**	1.925±	0.214**	0.435±	012	
30000 ppm	5	0.329±	0.021**	0.057±	0.011*	2.508±	0.287**	0.424±	014	

APPENDIX I 2

ORGAN WEIGHT, ABSOLUTE: SUMMARY, MOUSE: FEMALE

STUDY NO. : 0370 ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : FEMALE UNIT: g

ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (15W)

PAGE: 3

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	20.5± 1.1	0.038± 0.006	0.015± 0.004	0.041± 0.019	0.120± 0.008	0.150± 0.008
2500 ppm	10	19.6± 0.7	0.036± 0.005	0.014± 0.005	0.032± 0.006	0.121± 0.009	0.148± 0.011
5000 ppm	10	20.2± 0.8	0.035± 0.005	0.012± 0.002	0.036± 0.007	0.122± 0.007	0.153± 0.010
10000 ppm	10	20.2± 0.5	0.034± 0.003	0.013± 0.003	0.034± 0.006	0.120± 0.006	0.149± 0.010
20000 ppm	10	20.5± 0.9	0.036± 0.005	0.014± 0.003	0.033± 0.011	0.120± 0.010	0.147± 0.010
mpp 00008	3	20.9± 0.9	0.042± 0.010	0.014± 0.001	0.037± 0.008	0.127± 0.017	0.145± 0.008
Significant	difference;	*: P ≤ 0.05 **	: P ≤ 0.01	Test	of Dunnett		

(HCL040)

BAIS 3

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1

SEX : FEMALE UNIT: g

ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (15W)

PAGE: 4

	Animals		ieys 	SPLI	CEM	LIV	ER .	BRA			·····	
Control	10	0.282±	0.017	0.050±	0.006	0.878±	0.061	0.448土	0.014			
2500 ppm	10	0.279±	0.017	0.046±	0.006	0.823±	0.050	0.451±	0.015	,		
5000 ppm	10	0.280±	0.011	0.051±	0.005	0.895±	0.048	0.457±	0.019			
10000 ppm	10	0.283±	0.016	0.055±	0.006	0.980±	0.059	0.466±	0.013			•
20000 ppm	10	0.279±	0.013	0.083±	0.011**	1.489±	0.127**	0.442±	0.018			
30000 ppm	3	0.295±	0.010	0.080±	0.008**	2.116±	0.121**	0.424±	0.017			
Significant	t difference;	*: P ≤ 0.0)5 **	: P ≤ 0.01			Tes	st of Dunnet	t	4-4000-000-0		

(HCL040)

BAIS 3

APPENDIX J 1

ORGAN WEIGHT, RELATIVE: SUMMARY, MOUSE: MALE

ORGAN WEIGHT:RELATIVE (SUMMARY) SURVIVAL ANIMALS (15W)

STUDY NO. : 0370

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1
SEX : MALE
UNIT: %

UNIT: %

roup Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS	
Control	10	30.0± 1.9	0.115± 0.022	0.056± 0.015	0.652± 0.070	0.530± 0.046	0.531± 0.031	
2500 ppm	10	29.2± 2.6	0.109± 0.013	0.048± 0.015	0.765± 0.064	0.512± 0.027	0.541± 0.039	
5000 ppm	10	29.0± 2.5	0.116± 0.024	0.049± 0.009	0.783± 0.132*	0.529± 0.026	0.550± 0.034	
10000 ppm	10	27.6± 1.8*	0.109± 0.025	0.050± 0.013	0.758± 0.146	0.549± 0.041	0.577± 0.032*	
20000 ppm	10	26.0± 1.2**	0.114± 0.016	0.050± 0.016	0.839± 0.094**	0.535± 0.055	0.597± 0.033**	
30000 ppm	5	23.2士 1.8**	0.139± 0.018	0.062± 0.022	0.895± 0.130**	0.514± 0.031	0.603± 0.046**	
Significant	: difference ;	*: P ≤ 0.05 **	: P ≤ 0.01	Tes	at of Dunnett			
'ugi o to'								

PAGE: 1

(HCL042) BAIS 3

ORGAN WEIGHT: RELATIVE (SUMMARY) SURVIVAL ANIMALS (15W)

STUDY NO.: 0370 ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1
SEX : MALE

UNIT: % PAGE: 2

roup Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	
Control	10	1.375± 0.109	0.142± 0.013	3.590± 0.116	1.473± 0.092	
2500 ppm	10	1.396± 0.094	0.154± 0.013	3.889± 0.227	1.517± 0.112	
5000 ppm	10	1.454± 0.119	0.164± 0.012	4.067± 0.177	1.548± 0.131	
10000 ppm	10	1.488± 0.096	0.183± 0.015**	4.792± 0.431**	1.646± 0.089**	
20000 ppm	10	1.482± 0.076	0.352± 0.061**	7.385± 0.631**	1.673± 0.065**	
30000 ppm	5	1.419± 0.096	0.245± 0.038**	10.776± 0.670**	1.830± 0.118**	

BAIS 3 (HCL042)

APPENDIX J 2

ORGAN WEIGHT, RELATIVE: SUMMARY, MOUSE: FEMALE

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : FEMALE UNIT: %

ORGAN WEIGHT: RELATIVE (SUMMARY) SURVIVAL ANIMALS (15W)

PAGE: 3

roup Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS	
Control	10	20.5± 1.1	0.185± 0.023	0.072± 0.016	0.198± 0.081	0.583± 0.029	0.732± 0.030	
2500 ppm	10	19.6± 0.7	0.184± 0.029	0.074± 0.024	0.161± 0.033	0.618± 0.034	0.757± 0.041	
5000 ppm	10	20.2± 0.8	0.172± 0.025	0.059± 0.012	0.175± 0.031	0.605± 0.033	0.758± 0.049	
10000 ppm	10	20.2± 0.5	0.167± 0.018	0.062± 0.015	0.165± 0.028	0.592± 0.028	0.734± 0.050	
20000 ppm	10	20.5± 0.9	0.174± 0.022	0.066± 0.014	0.160± 0.053	0.587± 0.056	0.718± 0.041	
mqq 0000E	3	20.9± 0.9	0.199± 0.040	0.067± 0.002	0.177± 0.036	0.613± 0.104	0.697± 0.029	
Significant	: difference;	*: P ≤ 0.05 **	: P ≤ 0.01	Tes	et af Dunnett	i e e e e		
HCL042)								В

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT: RELATIVE (SUMMARY) SURVIVAL ANIMALS (15W)

PAGE: 4

roup Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	
Control	10	1.373± 0.045	0.245± 0.023	4.280± 0.153	2.189± 0.094	
2500 ppm	10	1.425± 0.072	0.234± 0.030	4.198± 0.149	2.305± 0.101	
5000 ppm	10	1.385± 0.059	0.251± 0.020	4.428± 0.224	2.264± 0.146	
10000 ppm	10	1.397± 0.071	0.271± 0.026	4.841± 0.240**	2.302± 0.072	
20000 ppm	10	1.366± 0.088	0.403± 0.044**	7.265± 0.367**	2.161± 0.063	
30000 ppm	3	1.413± 0.071	0.383± 0.026**	10.136± 0.160**	2.034± 0.110	

(HCL042) BAIS 3

APPENDIX K 1

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY

MOUSE: MALE: ALL ANIMALS

(13-WEEK STUDY)

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 15W)

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX

Findings	Group Name No. of Animals on Study Grade 1	10 2	3	4 %)	1 2	10	(%)	1 (%)			<u>4</u> (%)	(1	10 2	3	<u>4</u> (%)
rtem]																
eosinophilic change:respiratory epith		0	0						0	0	0 (0)			-	0	0 0)
respiratory metaplasia:olfactory epit	thelium C						0 (0)	0 (0)	0 (0)	0 (0)	0 (0)			0 0) (0 0) (0 0)
respiratory metaplasia:gland							0 (0)	(0)	(0)	(0)	0 (0)			0 (0 (0
system]																
congestion		0	0			<10> 0 0 0) (0)	0 (0)		0	0	0 (0)		0 (0	0	0
atrophy		0	0		0 (<10> 0 0 0) (0)			0	0	0 (0)		0 (0	0	0 0)
atrophy		0	0					(0)	0	0	0 (0)			0	0	0
		No. of Animals on Study Grade 1 Findings (%) Stem] eosinophilic change:respiratory epithelium (0) respiratory metaplasia:olfactory epithelium (0) respiratory metaplasia:gland (0) system] congestion (0) atrophy (0)	No. of Animals on Study 10 Grade 1 2 (%) (%) (%)	No. of Animals on Study 10 Grade 1 2 3 (%) (%) (%) (%) (%) (%) (%) (%) (%) (%)	No. of Animals on Study	No. of Animals on Study 10 1 2 3 4 1 2 3 4	No. of Animals on Study	No. of Animals on Study 10								

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 15W)

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1

SEX : MALE

0rgan	Group Name No. of Anima Grade	20000 ppm Ls on Study 10 1 2 3 4 (%) (%) (%) (%)	30000 ppm 10 1 2 3 4 (%) (%) (%) (%)		
[Respiratory :	system]				
nasal cavit	eosinophilic change:respiratory epithelium	<10> 0 0 0 0 (0) (0) (0) (0)	1 0 0 0 (10) (0) (0) (0)		
	respiratory metaplasia:olfactory epithelium	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)		
	respiratory metaplasia:gland	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)		
[Hematopoieti	c system]				
bone marrow	congestion	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 4 0 0 0 (40) (0) (0) (0)		
thymus	atrophy	<10> 0 0 0 0 (0) (0) (0) (0)	(10) 0 0 5 0 * (0) (0) (50) (0)		
spleen	atrophy		<10> 0 5 0 0 * (0) (50) (0) (0)		
Grade <a>a> b (c) Significant o	1: Slight 2: Moderate 3: Marked a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 difference; *: $P \le 0.05$ **: $P \le 0.01$ Test	4: Severe		·	

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0- 15W)

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1

SEX : MALE

Organ	Findings	Group Name Control No. of Animals on Study 10 Grade 1 2 3 4 (%) (%) (%) (%)	2500 ppm 10 1 2 3 4 (%) (%) (%) (%)	5000 ppm 10 1 2 3 4 (%) (%) (%) (%)	10000 ppm 10 1 2 3 4 (%) (%) (%) (%)
[Hematopoieti	c system]				
spleen	extramedullary hematopoiesis	(10) 0 0 0 0 (0) (0) (0) (0)	(0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)
[Digestive sy	rstem]				
liver	granulation	(0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	1 0 0 0 (10) (0) (0) (0)
	hepatocellular hypertrophy:central	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0)	5 0 0 0 * (50) (0) (0) (0)
[Urinary syst	tem]				
kidney	vacuolic change:proximal tubule	7 0 0 0 (70) (0) (0) (0)	5 0 0 0 (50) (0) (0) (0)	5 0 0 0 (50) (0) (0) (0)	1 0 0 0 * (10) (0) (0) (0)
[Reproductive	ə system]				
epididymis	debris of spermatic elements	(10) 0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	(10) 0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)
Grade <a>> b (c) Significant	a: Number of animals examined at the b: Number of animals with lesion c: b / a * 100	3 : Marked 4 : Severe site ≤ 0.01 Test of Chi Square			

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 15W)

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1

SEX : MALE PAGE: 4

Organ	Findings	Group Name 20000 ppm No. of Animals on Study 10 Grade 1/2 3 4 (%) (%) (%) (%) (%)	$\begin{array}{cccccccccccccccccccccccccccccccccccc$	
[Hematopoieti	c system]			
spleen	extramedullary hematopoiesis	6 0 0 0 * (60) (0) (0) (0)	3 0 0 0 (30) (0) (0) (0)	
[Digestive sy	vstem]			
liver	granulation	0 0 0 0 (0) (0) (0) (0)	(10) 0 0 0 0 (0) (0) (0) (0)	
	hepatocellular hypertrophy:central	2 8 0 0 ** (20) (80) (0) (0)	0 5 0 0 * (0) (50) (0) (0)	
[Urinary sys	tem]			
kidney	vacuolic change:proximal tubule	0 0 0 0 *** (0) (0) (0) (0)	<10> 0 0 0 0 ** (0) (0) (0) (0)	
[Reproductive	ə system]			
epididymis	debris of spermatic elements	0 0 0 0 (0) (0) (0) (0)	1 0 0 0 (10) (0) (0) (0)	
Grade (a > b (c) Significant	1: Slight 2: Moderate 3 a: Number of animals examined at the s b: Number of animals with lesion c: b / a * 100 difference; *: P ≤ 0.05 **: P:			

(HPT150)

APPENDIX K 2

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY

MOUSE: FEMALE: ALL ANIMALS

(13-WEEK STUDY)

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0- 15W)

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1
SEX : FEMALE

STUDY NO. : 0370

Organ	Group Nam No. of An Grade Findings	Control mals on Study 10 10 (%) (%) (%) (%)	2500 ppm 10 1 2 3 4 (%) (%) (%) (%)	5000 ppm 10 1 2 3 4 (%) (%) (%) (%)	10000 ppm 10 1 2 3 4 (%) (%) (%) (%)
[Respiratory	system]				
nasal ca∪it	eosinophilic change:respiratory epithelium	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)
	respiratory metaplasia:gland	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 (0) (0)	0 0 0 0 0 0 (0) (0)
Hematopoieti	ic system]				
one marrow	congestion	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)
thymus	atrophy	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	(10) 0 0 0 0 (0) (0) (0) (0)	(10) 0 0 0 0 (0) (0) (0) (0)
pleen	atrophy	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)
	extramedullary hematopolesis	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0) (0)	1 0 0 0 0 (10) (10) (10) (10)	0 0 0 0 0 (0) (0)
Grade (a > b	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			

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 15W)

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX

: FEMALE

0rgan	No	Dup Name 20000 ppm or of Animals on Study 10 ade 1 2 3 4 (%) (%) (%) (%)	30000 ppm 10 1 2 3 4 (%) (%) (%) (%)	
[Respiratory	system]			
nasal cavit	eosinophilic change:respiratory epitheli	3 0 0 0 (30) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	
	respiratory metaplasia:gland	1 0 0 0 0 (10) (10) (10)	0 0 0 0 0 (0) (0)	
[Hematopoieti	c system]			
bone marrow	congestion	<10> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	6 0 0 0 * (60) (0) (0) (0)	
thymus	atrophy	0 0 0 0 (0) (0) (0) (0)	<10> 0 1 6 0 ** (0) (10) (60) (0)	~7
spleen	atrophy	<10> 0 0 0 0 (0) (0) (0) (0)	<10> 0 7 0 0 ** (0) (70) (0) (0)	
	extramedullary hematopoiesis	6 0 0 0 * (60)(0)(0)(0)	3 0 0 0 (30) (0) (0) (0)	
Grade <a>> b c c) Significant c	1: Slight 2: Moderate 3: a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 difference; $*: P \le 0.05$ **: $P \le 0.05$			

(HPT150)

BAIS3

SEX

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 15W)

ANIMAL : MOUSE Crj:BDF1 REPORT TYPE : A1

: FEMALE

PAGE: 7

0rgan	Findings	Group Name Control No. of Animals on Study 10 Grade 1 2 3 4 (%) (%) (%) (%)	2500 ppm 10 1 2 3 4 (%) (%) (%) (%)	5000 ppm 10 1 2 3 4 (%) (%) (%) (%)	10000 ppm 10 1 2 3 4 (%) (%) (%) (%)
[Digestive	system]				
liver	hepatocellular hypertrophy:central	(0) (0) (0) (0)	(0)(0)(0)(0)	(10) 0 0 0 0 (0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)
	amphophilic cell focus	0 0 0 0 0 0 0 0 0 0 0 0 0 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	vstem]				
kidney	basophilic change	(0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	1 0 0 0 (10) (0) (0) (0)
Grade <a>> b (c) Significant	1: Slight 2: Moderate a: Number of animals examined at the s b: Number of animals with lesion c: b / a * 100 t difference; *: P ≤ 0.05 **: P:				
(HPT150)		·			BA

ANIMAL : MOUSE Crj:BDF1

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- 15W)

REPORT TYPE : A1

SEX : FEMALE

Organ		p Name 20000 ppm of Animals on Study 10 e 1 2 3 4 (%) (%) (%) (%)	30000 ppm 10 1 2 3 4 (%) (%) (%) (%)	
Digestive	system]			
Liver	hepatocellular hypertrophy:central	(10) 9 0 0 0 *** (90) (0) (0) (0)	(10) 0 3 0 0 (0) (30) (0) (0)	
	amphophilic cell focus	3 0 0 0 0 (30) (0) (0) (0)	1 0 0 0 0 (10) (10) (10)	
[Urinary s	ystem]			
cidney	basophilic change	0 0 0 0 (0) (0) (0) (0)	(10) 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 t difference; *: P ≤ 0.05 **: P ≤ 0.0			
(HPT150)				

APPENDIX K 3

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY

MOUSE: MALE: DEAD AND MORIBUND ANIMALS

(13-WEEK STUDY)

SEX : MALE

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 15W)

)rgan	Graup Na. at Grade Findings	Name Control Animals on Study 0 1 2 3 4 (%) (%) (%) (%)	2500 ppm 0 . 1 2 3 4 (%) (%) (%) (%)	5000 ppm 0 1 2 3 4 (%) (%) (%) (%)	10000 ppm 0 1 2 3 4 (%) (%) (%) (%)
[Hematopoieti	c system]				
oone marrow	congestion	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	< 0> (-) (-) (-) (-)
hymus	atrophy	< 0> (-) (-) (-) (-)	< 0> (-) (-) (-) (-)	< 0> (-) (-) (-) (-)	< 0> (-) (-) (-) (-)
pleen	atrophy	< 0> (-) (-) (-) (-)	< 0> (-) (-) (-) (-)	< 0> (-) (-) (-) (-)	< 0> (-) (-) (-) (-:
Reproductive	ə system]				
epididymis	debris of spermatic elements	(-) (-) (-) (-)	(-) (-) (-)	< 0> (-) (-) (-) (-)	< 0> (-) (-) (-) (-)
Grade (a> b	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			

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 15W)

ANIMAL : MOUSE Crj:BDF1

(HPT150)

REPORT TYPE : A1

: MALE

SEX PAGE: 2 Group Name 20000 ppm 30000 ppm No. of Animals on Study 0 5 Grade 3 3 (%) (%) (%) Organ_ Findings [Hematopoietic system] < 0> < 5> bone marrow 4 0 0 0 congestion (-) (-) (-) (-) (80) (0) (0) (0) < 0> < 5> thymus 0 0 5 0 atrophy (-) (-) (-) (-) (0)(0)(100)(0) < 0> < 5> spleen 0 5 0 0 atrophy (-) (-) (-) (-) (0) (100) (0) (0) [Reproductive system] epididymis < 0> < 5> debris of spermatic elements 1 0 0 0 (-) (-) (-) (-) (20) (0) (0) (0) 1 : Slight Grade 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

APPENDIX K 4

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY

MOUSE: FEMALE: DEAD AND MORIBUND ANIMALS

(13-WEEK STUDY)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 15W)

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1

SEX

: FEMALE

AI PEMAI E

Organ		Sup Name Control of Animals on Study 0 ide 1/2 3 4 (%) (%) (%) (%)	2500 ppm 0 1 2 3 4 (%) (%) (%) (%)	5000 ppm 0 1 2 3 4 (%) (%) (%) (%)	10000 ppm 0 1 2 3 4 (%) (%) (%) (%)
Hematopoieti	c system]				
oone marrow	cangestian	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
nymus	atrophy	< 0> (-) (-) (-) (-)	< 0> (-) (-) (-) (-)	< 0> (-) (-) (-) (-)	< 0> (-) (-) (-) (-)
eleen	atrophy	(-) (-) (-) (-)	< 0> (-) (-) (-) (-)	< 0> (-) (-) (-) (-)	< 0> (-) (-) (-) (-)
rade a > b c)	1: Slight 2: Moderate 3: 1 a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100	farked 4 : Severe			

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 15W)

ANIMAL : MOUSE Cri:BDF1 REPORT TYPE : A1

SEX : FEMALE

PAGE: 4 Group Name 20000 ppm 30000 ppm No. of Animals on Study 0 7 2 3 3 (%) (%) Findings_

[Hematopoietic system]

bone marrow

congestion

< 0> < 7> 6 0 0 0 (-) (-) (-) (-) (86) (0) (0) (0)

thymus

atrophy

< 0> < 7> 0 1 6 0 (-) (-) (-) (-) (0)(14)(86)(0)

spleen

atrophy

< 0> < 7> 0 7 0 0 (-) (-) (-) (0) (100) (0) (0)

Grade 1 : Slight

2 : Moderate

(a) a: Number of animals examined at the site

3 : Marked

4 : Severe

b b: Number of animals with lesion

(c) c:b/a * 100

(HPT150)

BAIS3

APPENDIX K 5

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY

MOUSE: MALE: SACRIFICED ANIMALS

(13-WEEK STUDY)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (15W)

ANIMAL : MOUSE Crj:BDF1 REPORT TYPE : A1

: MALE

(HPT150)

mag 00001 2500 ppm 5000 ppm Control Group Name 10 10 10 No. of Animals on Study 10 Findings_ [Respiratory system] <10> (10) <10> nasal cavit 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 eosinophilic change:respiratory epithelium (10) (0) (0) (0) (0) (0) (0) (0) (0)(0)(0)(0) (0)(0)(0)(0) 0 0 0 0 respiratory metaplasia:olfactory epithelium (0)(0)(0)(0) (0)(0)(0)(0) (0) (0) (0) (0) (10) (0) (0) (0) 0 0 0 0 1 0 0 0 0 0 0 0 respiratory metaplasia:gland (0)(0)(0)(0) (0)(0)(0)(0) (10) (0) (0) (0) (0)(0)(0)(0) [Hematopoietic system] <10> spleen 0 0 0 0 0 0 0 0 0 0 0 0 extramedullary hematopoiesis (0)(0)(0)(0) (0)(0)(0)(0)(0) (0)(0)(0)(0) [Digestive system] <10> Liver 0 0 0 0 1 0 0 0 0 0 0 0 0 0 0 granulation (0)(0)(0)(0) (0)(0)(0)(0) (10) (0) (0) (0) (0)(0)(0)(0) 3 : Marked 4 : Severe Grade 1 : Slight 2 : Moderate a: Number of animals examined at the site (a) b b: Number of animals with lesion c:b/a*100(c) Significant difference ; * : $P \le 0.05$ ** : $P \le 0.01$ Test of Chi Square

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (15W)

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1

SEX : MALE

30000 ppm 20000 ppm Group Name No. of Animals on Study 10 (%) Findings_ [Respiratory system] < 5> <10> nasal cavit 1 0 0 0 0 0 0 0 eosinophilic change:respiratory epithelium (0) (0) (0) (0) (20) (0) (0) (0) respiratory metaplasia:olfactory epithelium (0)(0)(0)(0) (0)(0)(0)(0) 0 0 0 0 respiratory metaplasia:gland (0)(0)(0)(0) (0)(0)(0)(0) [Hematopoietic system] <10> < 5> spleen 3 0 0 0 * 6 0 0 0 * extramedullary hematopoiesis (60) (0) (0) (0) (60) (0) (0) (0) [Digestive system] <10> < 5> Liver 0 0 0 0 0 0 0 granulation (0)(0)(0)(0) (0)(0)(0)(0) Grade 1: Slight 2 : Moderate 3 : Marked 4 : Severe a: Number of animals examined at the site <a>> b b: Number of animals with lesion (c) c:b/a*100

(HPT150)

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

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (15W)

ANIMAL : MOUSE Crj:BDF1 REPORT TYPE : A1

: MALE SEX

		Group Name No. of Animals on Study Grade 1	Co: 1: 2	ntral 0 3	4	1	2500 10 2) ppm) 3	4	1	500 1 2	0 ppm 0	4	7	1000	0 ppm 0 3	Λ
Organ	Findings	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
Digestive s	ystem]																
.i∪er	hepatocellular hypertrophy:central	0 (0)	(0)	0> (0)	0 (0)	(0)	<10 0 (0)		0 0)	(0)		0> (0)	0 (0)	5 (50)	0	0> (0)	0 * (0)
Urinary sys	rtem]																
cidney	vacuolic change:proximal tubule	7 (70)	(1 0 (0)	0	0 (0)	5 (50)	(0)	0	0 0)	5 (50)	0	0> 0 (0)	0 (0)	1 (10)	0	0> 0 (0)	0 * (0)
irade (a> b (c)	1: Slight 2: Moderate a: Number of animals examined at the b: Number of animals with lesion c: b / a * 100 difference; *: P ≤ 0.05 **: P						•				··· ·· · · · · · · · · · · · · · · · ·						

(HPT150)

BAIS3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (15W)

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1

SEX : MALE

Organ	Group No. o Grade Findines		0 ppm 5 3 4 (%) (%)
[Digestive	system]		
liver	hepatocellular hypertrophy:central	2 8 0 0 ** 0 5 (20) (80) (0) (0) (0) (100)	5> 0 0 *** (0) (0)
[Urinary s	vstem]		
kidney	vacuolic change:proximal tubule	<pre></pre>	
Grade (a> b (c) Significan	1: Slight 2: Moderate 3: Maria: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 t difference; $*: P \le 0.05$ **: $P \le 0.01$		
(HPT150)			BAIS

APPENDIX K 6

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY

MOUSE: MALE: SACRIFICED ANIMALS

(13-WEEK STUDY)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (15W)

ANIMAL : MOUSE Crj:BDF1 REPORT TYPE : A1

:	FEMAL	E
---	-------	---

Organ		Group Name No. of Animals on Study Grade <u>1</u>	Control 10 2 3 (%) (%) (2500 ppm 10 1 2 3 4 (%) (%) (%) (%)	5000 ppm 10 1 2 3 4 (%) (%) (%) (%)	10000 ppm 10 10 1 2 3 4 (%) (%) (%)
[Respiratory s	system]					
nasal cavit	easinophilic change:respiratory epithe	lium 0 (0)	<10> 0 0 (0) (0) ((10) 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 (0) (0) (0) (0)	(10) 0 0 0 0 (0) (0) (0) (0)
	respiratory metaplasia:gland	0 (0)	0 0 (0) (0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0)
[Hematopoieti	c system]					
spleen	extramedullary hematopoiesis	0 (0)	<10> 0 0 (0) (0) ((10) 0 0 0 0 (0) (0) (0) (0)	1 0 0 0 (10) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)
[Digestive sy	rstem]					
liver	hepatocellular hypertrophy:central	0 (0)	<10> 0 0 (0) (0) ((10> 0 0 0 0 0 0 0 0 0 0	0 0 0 0 (0) (0) (0) (0)	(10) 0 0 0 0 (0) (0) (0) (0)
	amphophilic cell focus	0 (0)	0 0 0	0 0 0 0 0	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0)

Grade

1 : Slight

2 : Moderate

3 : Marked

4 : Severe

< a >

b

a : Number of animals examined at the site

b: Number of animals with lesion

(c)

c:b/a * 100

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

(HPT150)

BAIS3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (15W)

ANIMAL : MOUSE Crj:BDF1 REPORT TYPE : A1

: FEMALE

Organ		Group Name No. of Animals on Study Grade $\frac{1}{(\%)}$	20000) ppm) 3 (%)	<u>4</u> (%)	<u>1</u> (%)	30000 3 2 (%)		<u>4</u> (%)			
[Respiratory	system]											
nasal cavit	eosinophilic change:respiratory epithe		0 (0)	0	0 (0)	0 (0) (< 3 0 0 (0				
	respiratory metaplasia:gland	(10)	0 (0)	0 (0)	0 (0)	(0) (0 (0 (0 (0)			
[Hematopoieti	c system]											
spleen	extramedullary hematopoiesis	6 (60)		0		3 (100) (< 3 0 (0) (0	0 **			
Digestive sy	rstem]											
iver	hepatocellular hypertrophy:central	(80) 8	(0)	0	0 ** (0)	0 (0) (< 3 3 (100) (0	0 **			
	amphophilic cell focus	3 (30)	0 (0)	0	0	1 (33)	0 (0 (0) (0 (0)	•		
Grade (a) b (c)	1: Slight 2: Moderate 3 a: Number of animals examined at the si b: Number of animals with lesion c: b/a * 100 difference; *: P ≤ 0.05 **: P ≤			1-11-1								

(HPT150)

BAIS3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (15W)

ANIMAL : MOUSE Crj:BDF1 REPORT TYPE : A1

SEX				P	AGE :	7
		 	 			_

Organ	Group No. o Grade Findines	of Animals on Study 10	3 4 %) (%) 1 (%)	2500 ppm 10 2 3 4 (%) (%) (%)	5000 pp 10 1 2 3 (%) (%) (%	4_	10000 ppm 10 1 2 3 4 (%) (%) (%) (%)
[Urinary s	ystem]						
kidney	basophilic change	0 0 (0) (0) (0 0 0 0	<10> 0 0 0 (0) (0) (0)	<10> 0 0 0 (0) (0) (0	•	1 0 0 0 (10) (0) (0) (0)
Grade <a>> b (c) Significan	1: Slight 2: Moderate 3: Mar a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 t difference; *: P ≤ 0.05 **: P ≤ 0.01						·

(HPT150)

BAIS3

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (15W)

ANIMAL : MOUSE Crj:BDF1

Organ	Findings	Group Name 20000 ppm No. of Animals on Study 10 Grade 1 2 3 4 (%) (%) (%) (%)	30000 ppm 3 1 2 3 4 (%) (%) (%) (%)	———
[Urinary s	system]			
kidney	basophilic change	<10> 0 0 0 0 (0) (0) (0) (0)	<pre></pre>	
Grade (a) b (c) Significan	1 : Slight 2 : Moderate a : Number of animals examined at b : Number of animals with lesion c : b / a * 100 at difference : * : P ≤ 0.05 **			
		: P ≤ 0.01 Test of Chi Square	·8-19	······

APPENDIX L 1

IDENTITY AND IMPURITY OF p-NITROANISOLE

IN THE 13-WEEK FEED STUDY

IDENTITY AND IMPURITY OF p-NITROANISOLE IN THE 13-WEEK FEED STUDY

Test Substance

: p-Nitroanisole (Wako Pure Chemical Industries, LTD.)

Lot No.

: ACG7156

1. Spectral data

Mass Spectrometry

Instrument

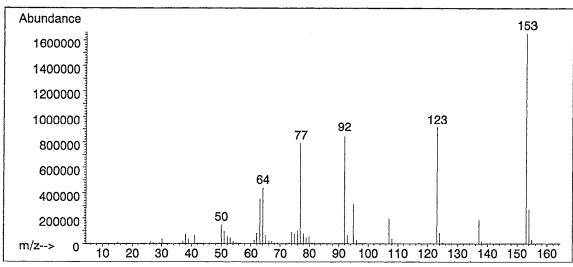
: Hewlett Packard 5989B Mass Spectrometer

Ionization

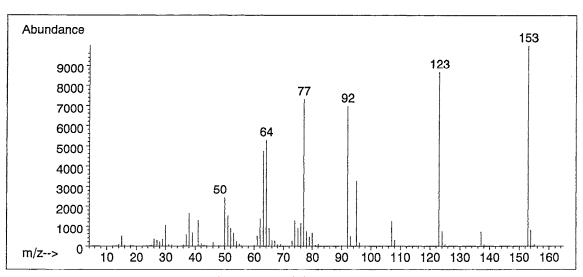
: EI (Electron Ionization)

Ionization Voltage

: 70eV



Mass Spectrum of Test Substance



Mass Spectrum of Literature Data*

Results: The mass spectrum was consistent with literature spectrum.

(*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition. John Wiley and Sons, Inc. (U.S.), Entry Number 38330)

Infrared Spectrometry

Instrument

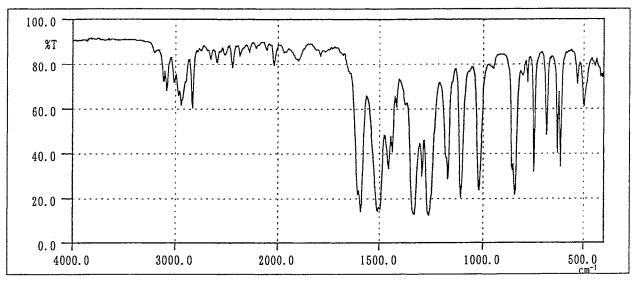
: Shimadzu FTIR-8200PC Infrared Spectrometer

Cell

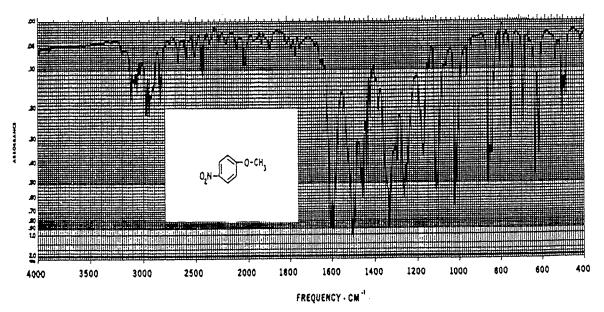
: KBr Liquid Cell

Resolution

: 2.0 cm⁻¹



Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data*

Results: The infrared spectrum was consistent with literature spectrum.

(*William W. Simons (1978) The Sadtler Handbook of Infrared Spectra. Sadtler Research Laboratories, Inc. (U.K.), pp.443)

2. Impurity

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : INNOWAX (0.2 mm ϕ × 50 m)

Column Temperature : 80 $^{\circ}$ C \rightarrow (15 $^{\circ}$ C/min) \rightarrow 280 $^{\circ}$ C (5 min)

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μ L

Sample Name	Peak No.	Area (%)	Peak Name
Test Substance	1	0.01	m-Chloronitrobenzene
	2	99.99	p-Nitroanisole

Results: Gas chromatography indicated one major peak (peak No.2) and one impurity. It was identified only by comparing its gas chromatograph with that of m-chloronitrobenzene (peak No.1) in the p-nitroanisole, the amount in the test substance were 0.01%.

3. Conclusions: The test substance was identified as p-nitroanisole, by the mass spectrum and the infrared spectrum. Gas chromatography indicated one major peak (peak No.2) and one impurity. It was identified only by comparing its gas chromatograph with that of m-chloronitrobenzene, the amount in the test substance were 0.01%.

APPENDIX L 2

STABILITY OF p-NITROANISOLE IN THE 13-WEEK FEED STUDY

STABILITY OF p-NITROANISOLE IN THE 13-WEEK FEED STUDY

Test Substance : p-Nitroanisole (Wako Pure Chemical Industries, LTD.)

Lot No. : ACG7156

1. Sample : This lot was used from 1998.11.6 to 1999.2.8. Test substance was stored in a

dark place at room temperature.

2. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : INNOWAX (0.2 mm ϕ × 50 m)

Column Temperature : 80 $^{\circ}$ C \rightarrow (15 $^{\circ}$ C/min) \rightarrow 280 $^{\circ}$ C (5 min)

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μL

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
1998.10.26	1 2	10.248 13.132	0.01 99.99
1999.02.24	1 2	10.251 13.139	0.01 99.99

Results: Gas chromatography indicated one major peak (peak No.2) and one impurity (peak No.1 < 0.02% of total area) analyzed at 1998.10.26 and one major peak (peak No.2) and one impurity (peak No.1 < 0.02% of total area) analyzed at 1999.2.24. No new trace impurity peak in the test substance analyzed at 1999.2.24 was detected.

4. Conclusions: The test substance was stable for about 4 months in a dark place at room temperature.

APPENDIX L 3

CONCENTMOUSEION OF p-NITROANISOLE IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

CONCENTRATION OF p-NITROANISOLE IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

Target Concentration							
Date Analyzed	2500ª	5000	10000	20000	30000		
1998.10.29	2430 (97.2) ^b	4760 (95.2)	9430 (94.3)	19200 (96.0)	29500 (98.3)		

^a ppm

Analytical method

: The samples were analyzed by the high performance liquid chromatography.

Instrument

: Hewlett Packard 1090 High Performance Liquid Chromatograph

Column

: TSK GEL ODS-80TM (4.6 mm ϕ \times 15 cm)

Column Temperature

: Room Temperature

Flow Rate

: 1 mL/min

Mobile Phase

: Distilled Water : Acetonitrile = 1 : 1

Detector

: UV (295 nm)

Injection Volume

: 20 μL

ь %

APPENDIX L 4

STABILITY OF p-NITROANISOLE IN FORMULATED DIETS

IN THE 13-WEEK FEED STUDY

STABILITY OF p-NITROANISOLE IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

		oncentration	
Date Prepared	Date Analyzed	300ª	40000
1998.09.24	1998.09.24	314 (100) ^b	40500 (100)
	1998.10.02°	264 (*84.1)	37700 (93.1)
	1998.10.29 ^d	304 (96.8)	39400 (97.3)

a ppm

Analytical method : The samples were analyzed by the high performance liquid chromatography.

Instrument : Hewlett Packard 1090 High Performance Liquid Chromatograph

Column : TSK GEL ODS-80TM (4.6 mm ϕ × 15 cm)

Column Temperature: Room Temperature

Flow Rate : 1 mL/min

Mobile Phase : Distilled Water : Acetonitrile = 1 : 1

Detector : UV (295 nm)

Injection Volume : 20 μL

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

^c Animal room samples

d Cold storage samples

APPENDIX M 1

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALSIS IN THE 13-WEEK FEED STUDY OF p-NITROANISOLE

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS IN THE 13-WEEK FEED STUDY OF $\ensuremath{p\mbox{-}}$ NITROANISOLE

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)	
White blood cell (WBC)	Light scattering method 1)	
Differential WBC	Pattern recognition method 2)	
	(Wright staining)	
Biochemistry		
Total protein (TP)	Biuret method 3)	
Albumin (Alb)	BCG method 3)	
A/G ratio	Calculated as Alb/(TP-Alb) 3)	
T-bilirubin	Alkaline azobilirubin method 3)	
Glucose	GlcK·G-6-PDH method 3)	
T-cholesterol	CE•COD•POD method 3)	
Triglyceride	LPL·GK·GPO·POD method 3)	
Phospholipid	PLD·ChOD·POD method 3)	
Glutamic oxaloacetic transaminase (GOT)	JSCC method 3)	
Glutamic pyruvic transaminase (GPT)	JSCC method 3)	
Lactate dehydrogenase (LDH)	SFBC method 3)	
Alkaline phosphatase (ALP)	GSCC method 3)	
γ -Glutamyl transpeptidase (γ -GTP)	L-γ-Glutamyl-p-nitroanilide method ³⁾	
Creatine phosphokinase (CPK)	JSCC method 3)	
Urea nitrogen	Urease • GLDH method 3)	
Sodium	Ion selective electrode method 3)	
Potassium	Ion selective electrode method 3)	
Chloride	Ion selective electrode method 3)	
Calcium	OCPC method 3)	
Inorganic phosphorus	PNP·XOD·POD method 3)	
Urinalysis		
pH,Protein,Glucose,Ketone body,Occult Blood,	Urinalysis reagent paper method 4)	
Urobilinogen		

- 1) Automatic blood cell analyzer (Technicon H·1: Bayer Corporation)
- 2) Automatic blood cell differential analyzer (MICROX HEG-120NA: OMRON Corporation)
- 3) Automatic analyzer (Hitachi 7070: Hitachi, Ltd.)
- 4) Ames reagent strips for urinalysis (Uro-Labstix: Bayer Corporation)

APPENDIX N 1

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK FEED STUDY OF p-NITROANISOLE

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK FEED STUDY OF p-NITROANISOLE

Item	Unit	Decimal place
Hematology		
Red blood cell (RBC)	×10 ⁶ /μL	2
Hemoglobin	g/dL	1
Hematocrit	%	1
Mean corpuscular volume (MCV)	fL	1
Mean corpuscular hemoglobin (MCH)	pg	1
Mean corpuscular hemoglobin concentration (MCHC)	g/dL	1
Platelet	$\times 10^3/\mu L$	0
White blood cell (WBC)	$\times 10^3/\mu L$	2
Differential WBC	%	0
Biochemistry		
Total protein	g/dL	1
Albumin	g/dL	1
A/G ratio	_	1
T-bilirubin	mg/dL	2
Glucose	mg/dL	0
T-cholesterol	mg/dL	0
Triglyceride	mg/dL	0
Phospholipid	mg/dL	0
Glutamic oxaloacetic transminase (GOT)	IU/L	0
Glutamic pyruvic transaminase (GPT)	IU/L	0
Lactate dehydrogenase (LDH)	IU/L	0
Alkaline phosphatase (ALP)	IU/L	0
γ-Glutamyl transpeptidase (γ-GTP)	IU/L	0
Creatine phosphokinase (CPK)	IU/L	0
Urea nitrogen	mg/dL	1
Sodium	mEq/L	0
Potassium	mEq/L	1
Chloride	mEq/L	0
Calcium	mg/dL	1
Inorganic phosphorus	mg/dL	1