アセト酢酸メチルのラットを用いた経口投与 による2週間毒性試験(混水試験)報告書

試験番号: 0419

APPENDIXES

APPENDIXES

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APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, RAT : MALE

ANIMAL : RAT F344/DuCrj REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Admini	stration W	eek-day	
		1-4	1-7	2-4	2-7
PILOERECTION	Control	0	0	0	0
	2500 ppm	0	0	0	0
	5000 ppm	0	0	0	0
	10000 ppm	0	0	0	0
	20000 ppm	0	0	0	0
	40000 ppm	2	2	4	0
SMALL STOOL	Control	0	0	0	0
	2500 ppm	0	0	0	0
	5000 ppm	0	0	0	0
	10000 ppm	0	0	0	Ō
	20000 ppm	4	0	0	0
	40000 ppm	5	5	5	0
OLIGO-STOOL	Control	0	0	0	0
	2500 ppm	0	0	Õ	0
	5000 ppm	0	Ô	0	0
	10000 ppm	0	0	Ő	0
	20000 ppm	0	0	0	0
	40000 ppm	5	1	ů	0
	10000 ppm	0	1	U	v

(HAN190)

BAIS 3

PAGE: 1

APPENDIX A 2

 ${\tt CLINICAL\ OBSERVATION}: {\tt SUMMARY}, \ {\tt RAT}: {\tt FEMALE}$

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	TIGHT, ILL	stration W	een day	
		1-4	1-7	2-4	2-7
				·	
PILOERECTION	Control	0	٥	0	0
TIDOBRECTION		0	0	0	0
	2500 ppm	0	•	0	0
	5000 ppm	0	0	0	0
	10000 ppm	0	0	0	0
	20000 ppm	0	0	0	0
	40000 ppm	4	3	3	0
SOILED PERI GENITALIA	Control	0	^	0	^
SOILED TEXT GENTIALIA	Control	0	0	0	0
	2500 ppm	0	0	0	0
	5000 ppm	0	0	0	0
	10000 ppm	0	0	0	0
	20000 ррш	0	0	0	0
	40000 ppm	1	. 0	0	0
SMALL STOOL	Cantra 1		0	0	0
SMALE STOOL	Control	0	0	0	0
	2500 ppm	0	Ü	Ţ	0
	5000 ppm	0	0	0	0
	10000 ppm	0	0	0	0
	20000 ppm	4	0	2	0
	40000 ppm	5	4	3	2
OLIGO-STOOL	Control	0	0	0	0
22100 01000	2500 ppm	0	0	0	0
	5000 ppm	0	0	0	0
	10000 ppm	0	0	0	
	20000 ppm	0	0		0
	40000 ppm	-		0	0
	40000 ppm	5	1	1	0

(HAN190)

BAIS 3

PAGE: 2

APPENDIX B 1

BODY WEIGHT CHANGES : SUMMARY, RAT : MALE

ANIMAL : RAT F344/DuCrj

UNIT : g

REPORT TYPE : A1 2

BODY WEIGHT CHANGES (SUMMARY)

ALL ANIMALS

SEX : MALE

PAGE: 1

oup Name	Adminis	stration	week-day									
	0-0		1-4		1-7		2-4		2-7			
Control	132±	4	152±	7	166±	7	186±	10	196±	10		
2500 ppm	131±	5	148±	5	160±	7	178±	8	189±	7		
5000 թթա	131±	4	146±	4	159±	6	178±	8	188±	8		
10000 ppm	131±	5	146±	6	159±	7	175±	8	186±	8		
20000 ррт	131±	5	136±	5**	153±	6*	169±	6*	181±	6 *		
40000 ppm	132±	4	110±	1**	120±	10**	143±	11**	157±	9**		
					,							
Significant differen	nce; *: P ≦ 0.	. 05	**: P ≤ 0.0	1			Test of Du	mett				

(HAN260)

APPENDIX B 2

BODY WEIGHT CHANGES: SUMMARY, RAT: FEMALE

ANIMAL : RAT F344/DuCrj

UNIT : g

REPORT TYPE : A1 2

SEX : FEMALE

BODY WEIGHT CHANGES ALL ANIMALS

(SUMMARY)

PAGE: 2

oup Name	Administration week-day										
	0-0		1-4		1-7		2-4		2-7		
											` `
Control	99±	3	109±	2	116±	2	123±	2	128±	3	
2500 ppm	99±	3	108±	5	113±	6	122±	4	127±	5	
5000 թթա	99±	3	107±	4	113±	5	121±	5	126±	6	
10000 ppm	99±	3	107±	3	112±	3	122±	3	127±	3	
10000 pp.m.	**-	v	241.—	v	115—	Ū	120		10. —		
20000 ppm	99±	2	103±	2	109±	4	117生	5	121±	4	
40000 ppm	99±	3	83±	7**	95±	10**	109±	6**	117±	8**	
Significant difference	; *: P ≤ 0	05	**: P ≤ 0.0	·1	···		Test of Du	unatt		*	

(HAN260)

APPENDIX C 1

WATER CONSUMPTION CHANGES : SUMMARY, RAT : MALE

ANIMAL : RAT F344/DuCrj

UNIT : g

REPORT TYPE : A1 2

WATER CONSUMPTION CHANGES (SUMMARY)

ALL ANIMALS

roup Name	Administration	week-day(effective)			
	1-4(4)	1-7(3)	2-4(4)	2-7(3)	
Control	18.9± 1.5	19.4± 1.1	20.1± 1.5	19.8± 1.4	
2500 ppm	15.6± 1.1**	15.3± 1.6	15.4± 1.4**	15.1± 1.1**	
5000 ррш	15.1± 1.1**	15.5± 1.4	15.3± 1.2**	14.4± 0.7**	
10000 ppm	13.7± 0.8**	14.2± 0.8*	14.7± 1.0**	14.2± 0.5**	
20000 ppm	10.2± 1.4**	13.6± 0.5**	13.0± 0.4**	13.2± 0.4**	
40000 ррт	3.1± 1.0**	9.3± 3.2**	12.6± 2.0**	12.6± 0.6 * *	

(HAN260)

APPENDIX C 2

WATER CONSUMPTION CHANGES: SUMMARY, RAT: FEMALE

ANIMAL : RAT F344/DuCrj

UNIT : g

REPORT TYPE : A1 2

SEX : FEMALE

WATER 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	14.9± 0.6	15.9± 1.6	16.9± 1.4	16.7± 1.6	
2500 ppm	12.4± 0.6	11.6± 0.9	12.3± 1.3**	12.2± 1.8	
5000 ppm	11.5± 1.2	11.2± 1.2	10.6± 0.9**	10.7± 0.6	
10000 ppm	10.6± 0.4*	10.5± 0.4*	11.1± 0.8**	10.2± 0.3**	
20000 ppm	9.4± 0.4**	10.4± 0.7**	10.3± 0.6**	9.9± 0.9**	
40000 ppm	3.6± 1.5**	10.1± 3.3*	11.0± 1.1**	9.7± 1.2**	
Significant difference;	* : P ≤ 0.05	** : P ≤ 0.01		Test of Dunnett	
(417000)					

(HAN260)

APPENDIX D 1

FOOD CONSUMPTION CHANGES: SUMMARY, RAT: MALE

ANIMAL : RAT F344/DuCrj

UNIT : g

REPORT TYPE : A1 2

FOOD CONSUMPTION CHANGES (SUMMARY)

ALL ANIMALS

roup Name	1-4(4)	week-day(effective) 1-7(3)			
		11(3)	2-4(4)	2-7 (3)	
Control	14.7± 1.2	15.9± 1.3	16.2± 1.5	16.6± 1.5	
2500 ppm	13.9± 0.9	15.0± 1.1	14.8± 1.3	15.2± 0.7	
5000 ррт	13.2± 0.8*	14.6± 1.2	14.9± 0.5	14.8± 0.6	
10000 ррт	12.7± 0.8**	14.2± 0.6	14.4± 0.4	14.6± 0.4	
20000 ррт	11.5± 0.7**	13.3± 0.4**	13.6± 0.8**	14.0± 0.4*	
40000 ppm	7.1± 0.6**	7.9± 1.7**	12.5± 1.6**	13.6± 0.4**	
Significant difference	; *: P ≤ 0.05 :	** : P ≤ 0.01		Test of Dunnett	

APPENDIX D 2

FOOD CONSUMPTION CHANGES: SUMMARY, RAT: FEMALE

ANIMAL : RAT F344/DuCrj

UNIT : g

REPORT TYPE : A1 2

FOOD CONSUMPTION CHANGES (SUMMARY)

ALL ANIMALS

coup Name	Administration	week-day(effective)_			
	1-4(4)	1-7(3)	2-4(4)	2-7 (3)	
Control	10.9 ± 0.2	11.5 ± 0.4	11.1± 0.2	11.5± 0.5	
2500 ppm	10.7± 0.7	10.9± 0.7	10.9± 0.7	11.3± 0.7	
5000 ppm	10.0± 0.8	10.5± 1.1	10.0± 0.8	10.4生 0.9	•
10000 ppm	9.9 ± 0.4	10.3± 0.3	10.5± 0.6	10.2± 0.4	
20000 ppm	9.1± 0.2**	10.0± 0.2*	10.1± 0.7	9.8± 0.7*	
40000 ppm	5.2± 1.2**	7.9± 2.0**	10.1± 0.9	10.1± 1.2*	
Significant difference	; *: P ≤ 0.05	** : P ≤ 0.01		Test of Dunnett	

(HAN260)

APPENDIX E 1

CHEMICAL INTAKE CHANGES: SUMMARY, RAT: MALE

CHEMICAL INTAKE CHANGES (SUMMARY) ALL ANIMALS

ANIMAL : RAT F344/DuCrj UNIT : g/kg/day

REPORT TYPE : A1 2

PAGE: 1 SEX : MALE

Group Name	Administration 1-4	(Week-Day)	2-4	2-7
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000 ± 0.000
2500 ppm	0.263± 0.014	0.238± 0.020	0.217± 0.013	0.200± 0.012
5000 ррт	0.517± 0.029	0.486± 0.029	0.430± 0.019	0.382± 0.026
10000 ppm	0.939± 0.027	0.893± 0.035	0.839± 0.052	0.761± 0.031
20000 ррш	1.491± 0.161	1.779± 0.081	1.540± 0.064	1. 454± 0. 075
40000 ppm	1.107± 0.364	3.030± 0.818	3.520 ± 0.341	3.202± 0.199

(DOC/ANI)

APPENDIX E 2

CHEMICAL INTAKE CHANGES: SUMMARY, RAT: FEMALE

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

SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)

ALL ANIMALS

oup Name	Administration	Administration (Week-Day)								
	1-4	1-7	2-4	2-7						
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000						
2500 ррш	0.288± 0.008	0.256± 0.012	o. 252± 0. 019	0.239± 0.028						
5000 שעט	0.539± 0.040	0.493± 0.036	0.440± 0.024	0.426± 0.013						
10000 ррш	0.991± 0.035	0.937± 0.020	0.906± 0.051	0.800± 0.015						
20000 ppm	1.827± 0.118	1.913± 0.135	1.759± 0.100	1.635± 0.152						
40000 ppm	1.714± 0.601	4. 197± 1. 176	4. 041± 0. 479	3.328± 0.294						

APPENDIX F 1

HEMATOLOGY : SUMMARY, RAT : MALE

ANIMAL : RAT F344/DuCrj

HEMATOLOGY (SUMMARY) ALL ANIMALS (2W)

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : A1

PAGE: 1

roup Name	NO. of Animals	RED BLOOD CELL 1 O ⁵ /µl	HEMOGLOBIN g/dl	HEMATOCR %	IT	MCV f &		MCH pg		MCHC g/dl		PLATELE 1 O³/µ	
Control	5	7.97± 0.14	15.2± 0.4	44. l±	1.2	55.3±	0.8	19.0±	0.2	34.3±	0.3	948±	40
2500 ppm	5	7.99± 0.12	15.3± 0.3	43.9±	0.5	55.0±	0.2	19.1±	0.3	34.7±	0.6	907±	32
5000 ppm	5	8.01± 0.29	15.1± 0.3	44.0±	1.1	55.0±	0.8	18.9±	0.3	34.4±	0.3	919±	76
10000 ppm	5	7.99± 0.23	15.2± 0.4	43.9±	0.9	54.9±	0.4	19.1±	0. 1	34.7±	0.3	886±	64
20000 ррш	5	7.89± 0.20	14.9± 0.3	43.2±	1.2	54.7±	0.5	18.9±	0. 2	34.6±	0.6	876±	50
40000 ppm	5	7.79± 0.26	14.9± 0.4	42.8±	1.2	54.9±	0.3	19.1±	0.2	34.8±	0.3	809±	116

(HCL070)

ANIMAL : RAT F344/DuCrj

HEMATOLOGY (SUMMARY) ALL ANIMALS (2W)

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : A1

roup Name	NO. of Animals	RETICULO	OCYTE	PROTHROM s e c	BIN TIME	APTT sec		 	/ma_	 	
Control	5	32±	5	13.9±	0.2	21. 4±	1.5				
2500 ppm	5	27±	3	13.9±	0.4	21.1±	0. 9				
5000 ppm	5	35±	12	13.6±	0.1	18.3±	1.6				
10000 ppm	5	31±	7	13.7±	0.4	19.5±	2. 7				
20000 թթա	5	26±	5	13.8±	0. 5	19.0±	3. 3				
40000 ppm	5	37±	9	14.3±	0.4	21.3±	1.2				

(IICL070)

BAIS 3

PAGE: 2

ANIMAL : RAT F344/DuCrj

HEMATOLOGY (SUMMARY) ALL ANIMALS (2W)

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : A1

PAGE: 3

roup Name	NO. of Animals	WBC 1 0³∕µ	l	Dif N-BAND	ferential	WBC (% N-SEG	5)	EOSINO		BAS0		MONO		LYMPHO		OTHER	
Control	5	3. 36±	0. 38	0±	0	18±	2	1±	1	0±	0	3±	1	78±	3	0±	1
2500 ppm	5	3.47±	0. 41	0±	1	15±	2	1±	1	0±	0	3±	2	80±	2	0±	0
5000 ppm	5	3.63±	1. 40	1±	1	18±	5	1±	1	0±	0	3±	1	77±	6	0±	0
10000 ppm	5	3.64±	0.35	0±	1	18±	2	1±	1	0±	0	3±	1	78±	3	0±	0
20000 թթա	5	3.87±	0.55	0±	0	20±	5	1±	1	0±	0	3±	1	76±	5	0±	0
40000 ppm	5	3.10±	1. 11	1±	1	22±	4	1±	1	0±	0	3±	1	73±	5	· 0±	I
Significant	difference;	*: P ≤	0.05	**: P ≦	0.01	,		Test	of Dunn	ett							

(HCL070)

APPENDIX F 2

HEMATOLOGY : SUMMARY, RAT : FEMALE

ANIMAL : RAT F344/DuCrj

HEMATOLOGY (SUMMARY) ALL ANIMALS (2W)

MEASURE. TIME: 1

SEX: FEMALE

REPORT TYPE : A1

PAGE: 4

roup Name	NO. of Animals	RED BLO 1 0 ⁵ / μ.		HEMOGLO g/dl	DBIN	HEMATOC %	RIT	MCV f &		MCH pg		MCHC g∕dl		PLATELE 1 O³∕µ	
Control	5	7. 95±	0.50	15.3±	0.8	43.4±	1.6	54.6±	1. 4	19.3±	0.3	35.3±	0.4	873±	120
2500 ppm	5	8.06±	0. 21	15.7±	0.4	43.9±	1.3	54.5±	0.5	19.4±	0.3	35.7±	0.5	826±	44
5000 ppm	5	8.05±	0. 21	15.5±	0.4	43.8±	1.3	54.4±	0.4	19.2±	0.3	35.3±	0.3	746±	84
10000 ppm	5	8.14±	0. 27	15.8±	0.5	44. 4±	1. 4	54.5±	0.3	19.4±	0. 3	35.6±	0.5	830±	58
20000 ppm	5	8. 18±	0.09	15.7±	0.2	44. 2±	0. 5	54.1±	0.4	19.1±	0. 2	35.4±	0.4	761±	38
40000 ppm	3	8.12±	0.12	15.5±	0.2	43.9±	0. 5	54.2±	0.7	19.0±	0. 2	35.2±	0.2	693±	105*

(HCL070)

ANIMAL : RAT F344/DuCrj

HEMATOLOGY (SUMMARY) ALL ANIMALS (2W)

20.7 \pm 1.0

 20.8 ± 3.6

MEASURE. TIME: 1

SEX : FEMALE

REPORT TYPE : A1

RETICULOCYTE NO. of PROTHROMBIN TIME ΛΡΤΤ Group Name Animals s e c s e c Control 5 14土 4 14.0± 0.6 18.3 \pm 2.3 $27\pm$ $14.4\pm$ 0.3 19.4± 2.8 2500 ppm 5 5* 19.3± 2.0 5 $20\pm$ 6 14.5 \pm 0.4 5000 ppm 5 $23\pm$ 3 $14.7 \pm$ 0.2* 19.9 \pm 1.6 10000 ppm

Significant difference; $*: P \leq 0.05$

5

3

 $15\pm$

 $21\pm$

6

7

**: $P \leq 0.01$

 $14.9 \pm$

14.3± 0.3

0.1**

Test of Dunnett

(HCL070)

20000 ppm

40000 ppm

BAIS 3

PAGE: 5

ANIMAL : RAT F344/DuCrj

HEMATOLOGY (SUMMARY) ALL ANIMALS (2W)

MEASURE. TIME :- 1 SEX : FEMALE

REPORT TYPE : A1

PAGE: 6

NO. of Animals	WBC 1 O³∕µl		Dif N-BAND	ferentia	1 WBC (% N-SEG	,)	EOSINO		BASO		MONO		LYMPHO		OTHER	
5	2.75± 1	1. 16	0±	0	20±	5	1±	1	0±	0	3±	2	76±	4	0±	0
5	3.03± 1	1. 00	1±	1	21±	4	2±	1	0±	0	3±	2	74±	4	0±	0
. 5	2.58± (0. 61	0±	0	19±	4	1±	0	0±	0	3±	1	78±	4	0±	1
5	2.56± (0. 87	0±	1	17±	3	1±	1	0±	0	4±	1	78±	3	0±	0
5	3.50± (0. 48	0±	1	18±	2	1±	1	0±	0	4±	2	77±	2	0±	0
3	2.74±	1. 37	0±	1	16±	7	1±	1	0±	0	5±	1	76±	5	1±	1
difference :	*: P ≤ (0, 05	**:P≤	0. 01			Test	of Dunn	ett							-
	Animals 5 5 5 5 3	Animals $10^{3} / \mu \ell$ 5 $2.75 \pm$ 5 $3.03 \pm$ 5 $2.58 \pm$ 6 $2.56 \pm$ 6 $3.50 \pm$ 3 $2.74 \pm$	Animals $10^{3}/\mu \ell$ 5 2.75 ± 1.16 5 3.03 ± 1.00 5 2.58 ± 0.61 5 2.56 ± 0.87 5 3.50 ± 0.48	Animals $1 \text{ O}^3 / \mu \ell$ N-BAND $5 2.75 \pm 1.16 0 \pm$ $5 3.03 \pm 1.00 1 \pm$ $5 2.58 \pm 0.61 0 \pm$ $5 2.56 \pm 0.87 0 \pm$ $5 3.50 \pm 0.48 0 \pm$ $3 2.74 \pm 1.37 0 \pm$	Animals $10^{3} / \mu \ell$ N-BAND 5 2.75 ± 1.16 0 ± 0 5 3.03 ± 1.00 1 ± 1 5 2.58 ± 0.61 0 ± 0 5 2.56 ± 0.87 0 ± 1 5 3.50 ± 0.48 0 ± 1 3 2.74 ± 1.37 0 ± 1	Animals $10^3/\mu\ell$ N-BAND N-SEG 5 2.75± 1.16 0± 0 20± 5 3.03± 1.00 1± 1 21± 5 2.58± 0.61 0± 0 19± 5 2.56± 0.87 0± 1 17± 5 3.50± 0.48 0± 1 18± 3 2.74± 1.37 0± 1 16±	Animals $10^{8}/\mu\ell$ N-BAND N-SEG 5 2.75± 1.16 0± 0 20± 5 5 3.03± 1.00 1± 1 21± 4 5 2.58± 0.61 0± 0 19± 4 5 2.56± 0.87 0± 1 17± 3 5 3.50± 0.48 0± 1 18± 2 3 2.74± 1.37 0± 1 16± 7	Animals $1 \ 0^3 / \mu \ell$ N-BAND N-SEG EOSINO 5 2.75 \pm 1.16 0 \pm 0 20 \pm 5 1 \pm 5 3.03 \pm 1.00 1 \pm 1 1 21 \pm 4 2 \pm 5 2.58 \pm 0.61 0 \pm 0 19 \pm 4 1 \pm 5 2.56 \pm 0.87 0 \pm 1 17 \pm 3 1 \pm 5 3.50 \pm 0.48 0 \pm 1 18 \pm 2 1 \pm 3 2.74 \pm 1.37 0 \pm 1 16 \pm 7 1 \pm 1 \pm 1.37	Animals $1 \ 0^3 / \mu \ell$ N-BAND N-SEG EOSINO 5 2.75 \pm 1.16 0 \pm 0 20 \pm 5 1 \pm 1 5 3.03 \pm 1.00 1 \pm 1 1 21 \pm 4 2 \pm 1 5 2.58 \pm 0.61 0 \pm 0 19 \pm 4 1 \pm 0 5 2.56 \pm 0.87 0 \pm 1 17 \pm 3 1 \pm 1 5 3.50 \pm 0.48 0 \pm 1 18 \pm 2 1 \pm 1 3 2.74 \pm 1.37 0 \pm 1 16 \pm 7 1 \pm 1	Animals 1 0³/μℓ N-BAND N-SEG EOSINO BASO 5 2.75± 1.16 0± 0 20± 5 1± 1 0± 5 3.03± 1.00 1± 1 21± 4 2± 1 0± 5 2.58± 0.61 0± 0 19± 4 1± 0 0± 5 2.56± 0.87 0± 1 17± 3 1± 1 0± 5 3.50± 0.48 0± 1 18± 2 1± 1 0± 3 2.74± 1.37 0± 1 16± 7 1± 1 0±	Animals $1 \ 0^3 / \mu \ell$ N-BAND N-SEG EOSINO BASO $\frac{1}{2} \ \frac{1}{2} \ \frac{1}{$	Animals $1.0^3 / \mu \ell$ N-BAND N-SEG EOSINO BASO MONO 5 2.75 \pm 1.16 $0\pm$ 0 $20\pm$ 5 $1\pm$ 1 $0\pm$ 0 $3\pm$ 5 $3.03\pm$ 1.00 $1\pm$ 1 $21\pm$ 4 $2\pm$ 1 $0\pm$ 0 $3\pm$ 5 $2.58\pm$ 0.61 $0\pm$ 0 $19\pm$ 4 $1\pm$ 0 $0\pm$ 0 $3\pm$ 5 $2.58\pm$ 0.87 $0\pm$ 1 $17\pm$ 3 $1\pm$ 1 $0\pm$ 0 $4\pm$ 5 $3.50\pm$ 0.48 $0\pm$ 1 $18\pm$ 2 $1\pm$ 1 $0\pm$ 0 $4\pm$ 3 $2.74\pm$ 1.37 $0\pm$ 1 $16\pm$ 7 $1\pm$ 1 $0\pm$ 0 $5\pm$	Animals 1 0³/μℓ N-BAND N-SEG EOSINO BASO MONO 5 2.75± 1.16 0± 0 20± 5 1± 1 0± 0 3± 2 5 3.03± 1.00 1± 1 21± 4 2± 1 0± 0 3± 2 5 2.58± 0.61 0± 0 19± 4 1± 0 0± 0 3± 1 5 2.56± 0.87 0± 1 17± 3 1± 1 0± 0 4± 1 5 3.50± 0.48 0± 1 18± 2 1± 1 0± 0 4± 2 3 2.74± 1.37 0± 1 16± 7 1± 1 0± 0 5± 1	Animals $1.0^3 / \mu \ell$ N-BAND N-SEG EOSINO BASO MONO LYMPHO 5 2.75± 1.16 0± 0 20± 5 1± 1 0± 0 3± 2 76± 5 3.03± 1.00 1± 1 21± 4 2± 1 0± 0 3± 2 74± 5 2.58± 0.61 0± 0 19± 4 1± 0 0± 0 3± 1 78± 5 2.56± 0.87 0± 1 17± 3 1± 1 0± 0 4± 1 78± 5 3.50± 0.48 0± 1 18± 2 1± 1 0± 0 4± 2 77± 3 2.74± 1.37 0± 1 16± 7 1± 1 0± 0 5± 1 76±	Animals 1 0³/μℓ N-BAND N-SEG EOSINO BASO MONO LYMPHO 5 2.75± 1.16 0± 0 20± 5 1± 1 0± 0 3± 2 76± 4 5 3.03± 1.00 1± 1 21± 4 2± 1 0± 0 3± 2 74± 4 5 2.58± 0.61 0± 0 19± 4 1± 0 0± 0 3± 1 78± 4 5 2.56± 0.87 0± 1 17± 3 1± 1 0± 0 4± 1 78± 3 5 3.50± 0.48 0± 1 18± 2 1± 1 0± 0 4± 2 77± 2 3 2.74± 1.37 0± 1 16± 7 1± 1 0± 0 5± 1 76± 5	Animals 1 0³ / μ2 N-BAND N-SEG EOSINO BASO MONO LYMPHO OTHER 5 2.75± 1.16 0± 0 20± 5 1± 1 0± 0 3± 2 76± 4 0± 5 3.03± 1.00 1± 1 21± 4 2± 1 0± 0 3± 2 74± 4 0± 5 2.58± 0.61 0± 0 19± 4 1± 0 0± 0 3± 1 78± 4 0± 5 2.56± 0.87 0± 1 17± 3 1± 1 0± 0 4± 1 78± 3 0± 5 3.50± 0.48 0± 1 18± 2 1± 1 0± 0 4± 2 77± 2 0± 3 2.74± 1.37 0± 1 16± 7 1± 1 0± 0 5± 1 76± 5 1±

(HCL070)

APPENDIX G 1

BIOCHEMISTRY: SUMMARY, RAT: MALE

ANIMAL : RAT F344/DuCrj

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

MEASURE. TIME : 1

SEX : MALE

REPORT TYPE : A1

PAGE: 1

roup Name	NO. of Animals	TOTAL P g/dl		ALBUMIN g/dl		A/G RAT	10	T-BIL11 mg/dl		GLUCOSE mg/dl		T-CHOLES	TEROL	PHOSPHOI mg/dl	LIPID
Control	5	5.8±	0. 2	3.6±	0.1	1.7生	0.1	0.13±	0.01	227±	20	66±	3	145±	6
2500 ppm	5	5.7±	0. 1	3.6±	0. 1	1.7±	0.1	0.14±	0.03	213±	10	66±	2	145±	9
5000 ppm	5	5.7±	0. 1	3.6±	0.1	1.7生	0.1	0.14±	0.02	227±	23	64±	2	138生	7
10000 ppm	5	5.5±	0.2*	3.5±	0.1	1.7±	0. 1	0.13±	0.01	216±	6	65±	2	139±	5
20000 ррт	5	5.5±	0.0**	3.4±	0.0**	1.7±	0. 1	0.14±	0.02	212±	8	65±	3	142±	7
40000 ppm	5	5.3±	0.1**	3.4±	0.1**	1.7±	0.1	0.15±	0.02	201±	14	78±	6	165±	13**

(IICL074)

ANIMAL : RAT F344/DuCrj

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (2W)

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : A1

PAGE: 2

roup Name	NO. of Animals	GOT IU/l		GPT IU/l		LDH IU/	2	G-GTP IU/l		CPK IU/l	!	UREA Ni mg/dl	TROGEN	CREATIN mg/dl	INE
Control	5	60±	9	32±	5	262±	56	1±	1	163±	27	18.3±	4. 2	0.4±	0. 1
2500 ppm	5	58生	3	30±	2	303±	105	1±	1	185±	40	18.7±	2.8	0.4±	0. 1
5000 ppm	5	56±	4	30±	2	290±	76	1±	1	177±	40	18.9±	1. 7	0.4±	0.1
10000 ppm	5	54±	3	27±	1	308±	117	1±	1	15 4 ±	35	18.6±	2. 4	0.4±	0.0
20000 ррш	5	55±	5	28±	2	314±	143	1±	1	164±	70	16.8±	2. 9	0.4±	0. 1
40000 ppm	5	57±	2	29±	2	281±	73	1±	1	165±	33	17.5±	2.0	0.4±	0. 1

(IICL074)

BIOCHEMISTRY (SUMMARY)

ANIMAL : RAT F344/DuCrj

ALL ANIMALS (2W)

MEASURE. TIME: 1 SEX: MALE

REPORT TYPE : A1

PAGE: 3

roup Name	NO. of Animals	SODIUM m Eq / L		POTASSI mEq/1		chloride m Eq / l		calciuw mg∕dl	I	INORGAN mg∕dl	IC PHOSPHORUS
Control	5	139±	1	3.7±	0.3	101生	1	10.6±	0. 1	7.9±	0.8
2500 ppm	5	138±	1	3.9±	0.4	101土	2	10.7±	0.2	6.9±	0.9
5000 ppm	5	138±	2	4.0±	0.2	101±	1	10.5±	0.3	7.3±	1. 2
10000 ppm	5	138±	1	3.8±	0.4	101±	1	10.6±	0.2	7.1±	1.1
20000 ppm	5	137±	1	4.2±	0.5	102±	1	10.3±	0.3	6.7±	1.2
40000 ppm	5	139±	2	4.5±	0.5*	102±	1	10.8±	0. 2	6.5±	1.1

(HCL074)

APPENDIX G 2

BIOCHEMISTRY: SUMMARY, RAT: FEMALE

ANIMAL : RAT F344/DuCrj

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (2W)

MEASURE. TIME: 1

SEX : FEMALE

REPORT TYPE : A1

PAGE: 4

roup Name	NO. of Animals	TOTAL F g/dl		 ALBUMIN g/dl	· · · · · · · · · · · · · · · · · · ·	A/G RAT		T-BILI mg/dl		GLUCOSE mg/dl		T-CHOLES mg/dl	STEROL	PHOSPHOL mg/dl	IPID
Control	.5	5.5±	0.1	3.5±	0.1	1.7±	0.1	0.15±	0.02	216±	8	72±	4	141±	7
2500 ppm	5	5.5±	0.2	3.4±	0. 1	1.7±	0. 1	0.14±	0. 04	204生	14	73±	5	145±	8
5000 ppm	5	5.3±	0.1	3.3±	0.1	1.7±	0. 1	0.13±	0. 01	208±	9	74±	4	140±	5
10000 ppm	5	5.3±	0.2	3.4±	0.1	1.7±	0.0	0.13±	0.01	204±	8	72±	2	145±	6
20000 ррш	5	5.3±	0.1	3.3±	0. 1	1.6±	0. 1	0.14±	0. 01	200±	3	74±	2	148±	6
40000 ppm	4	5.3±	0.2	3.3±	0.2	1.7±	0. 1	0.16±	0.03	206±	4	82±	3**	166±	5**

(IICL074)

ANIMAL : RAT F344/DuCrj

MEASURE. TIME: 1 SEX: FEMALE

REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (2W)

PAGE: 5

roup Name	NO. of Animals	GOT IU/L	!	GPT IU/L		LDH IU/I	2	G-GTP IU/l		CPK IU/s	2	UREA NI mg/dl	TROGEN	CREATIN mg/dl	INE
Control	5	57±	3	26±	1	410±	125	1±	1	225±	109	17.6±	3. 4	0.4±	0.0
2500 ppm	5	65±	12	30±	5	430±	241	2±	1	240土	127	18.8±	0. 7	0.4±	0.0
5000 ppm	5	58±	4	27±	2	397±	215	$2\pm$	1	178±	54	18.7±	2. 0	0.4±	0.0
10000 ppm	5	58±	2	27±	1	336±	87	1±	1	165±	40	19.3±	2. 2	0.4±	0. 1
20000 ррт	5	61±	3	27±	2	443±	169	1±	1	217±	70	19.2±	1.9	0. 4±	0.0
40000 ppm	4	62±	2	30±	2	385±	69	1±	1	197生	25	20.2±	2.0	0.4±	0. 1

(HCL074)

ANIMAL : RAT F344/DuCrj MEASURE. TIME : 1

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (2W)

SEX : FEMALE

REPORT TYPE : A1

PAGE: 6

roup Name	NO. of Animals	SODIUM m Eq / 2		POTASSI m Eq/		CHLORIDE m Eq / l		CALCIUM mg/dl		INORGAN mg/dl	TIC PHOSPHORUS
Control	5	137±	1	3.7±	0. 3	104±	1	10.0±	0. 2	6.9±	1. 2
2500 ppm	5	136±	2	4.0±	0. 4	103±	2	10.0±	0.2	6.4±	1. 5
5000 ppm	5	136±	1	4.0±	0.6	104±	1	9.9±	0.3	6.1±	0.7
10000 ppm	5	137±	1	3.9±	0.2	103生	1	10.0生	0.2	6.0±	1. 1
20000 ppm	5	137±	1	4.0±	0. 4	104±	1	9.9±	0.2	6.1±	1.0
40000 ppm	4	137±	1	3.8±	0.0	103±	1	10.1±	0.2	5.8±	1. 4
Significant	difference;	*: P ≤ 0.	05	**: P ≤ 0.(01			Test of Dun	nett		

(HCL074)

APPENDIX H 1

GROSS FINDINGS : SUMMARY, RAT : MALE : ALL ANIMALS

(2-WEEK STUDY)

ANIMAL : RAT F344/DuCrj

GROSS FINDINGS (SUMMARY) ALL ANIMALS (0- 2W)

REPORT TYPE : A1

SEX : MALE

Organ	Findings	Group Name NO. of Animals	Control 5 (%)	2500 ppm 5 (%)	5000 ppm 5 (%)	10000 ppm 5 (%)
liver	herniation		0 (0)	0 (0)	0 (0)	1 (20)
 HPT080)						

ANIMAL : RAT F344/DuCrj

GROSS FINDINGS (SUMMARY)

REPORT TYPE : A1

SEX : MALE

ALL ANIMALS (0- 2W)

SEX	: MALE				PAGE: 2
Organ	Findings	Group Name NO. of Animals	20000 ppm 5 (%)	40000 ppm 5 (%)	
liver	herniation		1 (20)	1 (20)	
(HPT080)					BAIS 3

APPENDIX H 2

GROSS FINDINGS : SUMMARY, RAT : FEMALE : ALL ANIMALS

(2-WEEK STUDY)

ANIMAL : RAT F344/DuCrj

GROSS FINDINGS (SUMMARY)

REPORT TYPE : A1

SEX : FEMALE

ALL ANIMALS (0- 2W)

Organ	Findings	Group Name NO. of Animals	Control 5 (%)	2500 ppm 5 (%)	5000 ppm 5 (%)	10000 ppm 5 (%)
liver	herniation		1 (20)	0 (0)	0 (0)	1 (20)
HPT080)						

ANIMAL : RAT F344/DuCrj

GROSS FINDINGS (SUMMARY)

REPORT TYPE : A1

SEX : FEMALE

ALL ANIMALS (0- 2W)

3EA	- FEMALE				PAGE: 4
Organ	_ Findings	Group Name NO. of Animals	20000 ppm 5 (%)	40000 ppm 5 (%)	
liver	herniation		0 (0)	0 (0)	
(HPT080)			- <u></u>		BAIS 3

APPENDIX I 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE

(2-WEEK STUDY)

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1

SEX : MALE UNIT: g ORGAN WEIGHT: ABSOLUTE (SUMMARY)

SURVIVAL ANIMALS (2W)

roup Name	NO. of Animals	Body Weig	ht 	TIIYMU	JS	ADREI	NALS	TEST	ES	HEAR	r 	LUNG	S
Control	5	196± 10		0.355±	0.038	0.041±	0.002	2. 445±	0. 149	0.696±	0.066	0.809±	0.050
2500 ppm	5	189± 7		0.340±	0.022	0.042±	0.005	2. 329±	0. 161	0.657±	0.042	0.801±	0.024
5000 ppm	5	188± 8	1	0.338±	0. 027	0.043±	0.003	2. 434±	0. 133	0.693±	0.024	0.797±	0.031
10000 ppm	5	186± 8	:	0.352±	0.036	0.045±	0.002	2.367±	0. 131	0.667±	0.057	0.829±	0.081
20000 ppm	5	181± 6	*	0.315±	0.030	0.038±	0.003	2. 345±	0.143	0.625±	0.019	0.759±	0. 028
40000 ppm	5	157± 9:	**	0.301±	0.051	0.042±	0.004	2.265±	0.068	0.569±	0. 052**	0.697±	0.041**

(HCL040)

BAIS 3

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1 SEX : MALE UNIT: g ORGAN WEIGHT: ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2W)

PAGE: 2

up Name	NO. of Animals	KIDN	NEYS	SPL	EEN	LIV	ER	BRA	IN		
Control	5	1.427±	0.095	0 . 44 5±	0.020	7.868±	0. 472	1.756±	0. 022		
2500 ppm	5	1. 443±	0. 074	0.439±	0. 020	7. 474±	0. 369	1. 731±	0. 025		
5000 ppm	5	1.450±	0.083	0.432±	0. 025	7. 209±	0.331*	1.746±	0.018		
10000 ppm	5	1. 423±	0.066	0.436±	0. 024	7.098±	0. 346*	1.717±	0.046		
20000 ppm	5	1.411±	0.042	0. 424±	0. 013	6. 722±	0.301**	1.713±	0. 047		
40000 ppm	5	1.322±	0.084	0.370±	0. 021**	6.138±	0.379**	1.677±	0.063		
Significant	difference;	*: P < 0 (05 **	: P ≤ 0.01			Tes	t of Dunnet	f.	 	
51gn111cant	difference ,	* · P \(\) 0. (05 ++	· r ≥ 0.01				or or bunner	L	 	

(HCL040)

APPENDIX I 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT: ABSOLUTE (SUMMARY)

SURVIVAL ANIMALS (2W)

roup Name	NO. of Animals	Body W	Veight	ТНҮМ	US	ADRE	NALS	OVAR	IES	HEAR	Т	LUNG	S
Control	5	128±	3	0.292±	0.023	0.047±	0.003	0.089±	0.006	0.492±	0. 031	0.646±	0. 026
2500 ppm	5	127±	5	0.281±	0. 022	0.046±	0.004	0.085±	0.011	0.512±	0.061	0.666±	0.064
5000 ppm	5	126土	6	0.286±	0. 027	0.044±	0.004	0.072±	0.008	0.488±	0. 028	0.639±	0. 028
10000 ppm	5	127±	3	0.292±	0.017	0.045±	0.002	0.073±	0.008	0.484±	0. 030	0.633生	0.049
20000 ppm	5	121±	4	0.274±	0.013	0.044±	0.004	0.079±	0.018	0.475±	0. 010	0.636±	0.010
40000 ppm	5	117±	8**	0.277±	0.039	0.043±	0. 006	0.059±	0.010**	0.453±	0.032	0.579±	0.018

(HCL040)

BAIS 3

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1

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

SEX : FEMALE UNIT: g

Group Name NO. of KIDNEYS SPLEEN LIVER BRAIN Animals 0.986 ± 0.053 0.320 ± 0.010 4.776± 0.231 1.618± 0.048 Control 4.711± 0.331 1.625 ± 0.026 2500 ppm 5 1.046± 0.057 0.356 ± 0.057 5000 рри 1.015± 0.050 0.318± 0.026 4.475± 0.261 1.629 ± 0.031 1.048± 0.017 0.323 ± 0.019 4.541± 0.281 1.626± 0.046 10000 ppm 20000 ppm 4.384± 0.228 1.598± 0.021 1.052 ± 0.035 0.303 ± 0.013 40000 ppm 5 1.023± 0.020 0.288 ± 0.022 4.349± 0.327 1.568 ± 0.046 Significant difference; $*: P \leq 0.05$ $**: P \leq 0.01$ Test of Dunnett

(HCL040)

BAIS 3

APPENDIX J 1

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : MALE

(2-WEEK STUDY)

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1

SEX : MALE UNIT: %

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

coup Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	5	196± 10	0.180± 0.010	0.021± 0.002	1.246± 0.075	0.354± 0.025	0.412± 0.022
2500 ppm ·	5	189± 7	0.180± 0.008	0.022± 0.003	1.234± 0.093	0.348± 0.019	0.424± 0.011
5000 ppm	5	188± 8	0.179± 0.008	0.023± 0.002	1.294± 0.091	0.368± 0.018	0.424± 0.027
10000 ppm	5	186± 8	$0.189\pm\ 0.013$	0.024± 0.001	1.270± 0.056	0.357± 0.019	0.444± 0.030
20000 ppm	5	181± 6*	0.174± 0.014	0.021± 0.002	1.294± 0.051	0.345± 0.010	0.4i9± 0.009
40000 ppm	5	157± 9**	0.190± 0.023	0.027± 0.003**	1.444± 0.091**	0.362± 0.026	0.444± 0.027

(HCL042)

BAIS 3

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1

SEX : MALE UNIT: %

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

PAGE: 2

roup Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	
Control	5	0.727± 0.021	0.227± 0.006	4.006± 0.109	0.896± 0.047	
2500 ррш	5	0.763 ± 0.017	0.232± 0.009	3.954± 0.104	0.917± 0.031	
5000 ppm	5	0.769± 0.020	0.230± 0.007	3.827± 0.088	0.928± 0.039	
10000 ppm	5	0.763± 0.022	0.234± 0.006	3.808± 0.111	0.922± 0.017	
20000 ppm	5	0.779± 0.026*	0.234± 0.009	3.710± 0.129**	0.946± 0.012*	
40000 ppm	5	0.842± 0.043**	0.236± 0.007	3.906± 0.148	1.070± 0.080**	

(HCL042)

APPENDIX J 2

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1 SEX : FEMALE UNIT: % ORGAN WEIGHT: RELATIVE (SUMMARY) SURVIVAL ANIMALS (2W)

PAGE: 3

roup Name	NO. of Animals	Body W	Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	5	128±	3	0.228± 0.019	0.037± 0.002	0.069± 0.005	0.384± 0.025	0.504± 0.024
2500 ppm	5	127±	5	0.221± 0.016	0.036± 0.002	0.066± 0.008	0.402± 0.034	0.524± 0.040
5000 ppm	5	126±	6	0.227 ± 0.015	0.035± 0.003	0.057± 0.005 0.388± 0.018		0.508± 0.015
10000 ppm	5	127±	3	0.230± 0.015	0.035± 0.002	0.058± 0.006	0.381± 0.023	0.498 ± 0.034
20000 ppm	5	121±	4	0.226± 0.012	0.036± 0.003	0.065± 0.014	0.392± 0.007	0.526± 0.027
40000 ppm	5	117±	8**	0.237± 0.024	0.037± 0.003	0.051± 0.009**	0.388± 0.014	0.498± 0.035

(HCL042)

ANIMAL : RAT F344/DuCrj

REPORT TYPE : A1 SEX : FEMALE UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN	
Control	5	0.768± 0.036	0.249± 0.008	3.721± 0.188	1.260± 0.043	
2500 ppm	5	0.823± 0.025*	0.280± 0.044	3.706± 0.135	1.280± 0.033	
5000 ppm	5	0.806± 0.011	0.252± 0.014	3.551± 0.118	1.295± 0.057	
10000 ppm	5	0.825± 0.014*	0.255± 0.011	$3.574\pm\ 0.162$	1. 281± 0. 031	
20000 ppm	5	0.869± 0.040**	0.250± 0.008	3.616± 0.090	1.320± 0.065	
40000 ppm	5	0.880± 0.057**	0.247± 0.008	3.729± 0.111	1.351± 0.120	
Significan	t difference ;	*: P ≤ 0.05 **:	P ≤ 0.01	Tes	t of Dunnett	
(HCL042)						PA.

(HCL042)

BAIS 3

APPENDIX K 1

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY

RAT: MALE: ALL ANIMALS

(2-WEEK STUDY)

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) ALL ANIMALS (0- $2 \mbox{W})$

STUDY NO. : 0419 ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

REPORT TYPE SEX	: MALE			·	PAGE :
Organ	Findings	Group Name Control No. of Animals on Study 5 Grade 1 2 3 4 (%) (%) (%) (%)	2500 ppm 5 1 2 3 4 (%) (%) (%) (%)	5000 ppm 5 1 2 3 4 (%) (%) (%) (%)	10000 ppm 5 1 2 3 4 (%) (%) (%) (%)
{Digestive s	ystem) .				
liver	herniation	< 5> 0 0 0 0 (0) (0) (0) (0)	<pre></pre>	< 5> 0 0 0 0 (0) (0) (0) (0)	(5> 1 0 0 0 (20) (0) (0) (0)
{Urinary sys	tem}				
kidney	eosinophilic body	2 0 0 0 0 (40) (0) (0) (0)	<pre></pre>	<pre></pre>	2 0 0 0 (40) (0) (0)
{Endocrine s	ystem}				
pituitary	Rathke pouch	0 0 0 0 0 (0) (0) (0)	<pre></pre>	2 0 0 0 (40) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)
thyroid	ultimobranchial body remanet	<pre></pre>	< 5> 0 0 0 0 (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	<pre></pre>
{Reproductiv	re system)				
prostate	lymphocytic infiltration	< 5> 2 0 0 0 (40) (0) (0) (0)	<pre></pre>	< 5> 0 0 0 0 (0) (0) (0) (0)	(5) 1 0 0 0 (20) (0) (0) (0)
Grade < a > b (c)	1: Slight 2: Moderate a: Number of animals examined at the b: Number of animals with lesion c: b/a * 100	3 : Marked 4 : Severe site			
(IIPT150)					В

ANIMAL : RAT F344/DuCrj

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0- 2W)

REPORT TYPE : A1 SEX : MALE

PAGE: 2

		Group Name 20000 ppm No. of Animals on Study 5 Grade _1 2 3 4	40000 ppm 5 1 2 3 4
Organ	Findings	(%) (%) (%)	(%) (%) (%)
{Digestive sy	vstem)		
liver	herniation	<pre></pre>	<pre></pre>
{Urinary syst	cem}		
kidney	eosinophilic body	<pre></pre>	<pre></pre>
{Endocrine sy	vstem)		
pituitary	Rathke pouch	<pre></pre>	<pre></pre>
thyroid	ultimobranchial body remanet	0 0 0 0 (0) (0) (0) (0)	2 0 0 0 (40) (0) (0) (0)
{Reproductive	e system)		
prostate	lymphocytic infiltration	<pre></pre>	< 5> 2 0 0 0 (40) (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	: Marked 4 : Severe te	
(III)mı = a\			

(IIPT150)

APPENDIX K 2

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY

RAT : FEMALE : ALL ANIMALS

(2-WEEK STUDY)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0- 2W)

ANIMAL : RAT F344/DuCrj REPORT TYPE : A1

SEX : FEMALE

Organ	И	roup Name to. of Animals on Study trade	Con 5 2 (%)	3 (%)	<u>4</u> (%)	<u>1</u> (%)	2500 5 2 (%)	3 (%)	<u>4</u> (%)	1 (%)		5000 5 2 %)	ppm 3 (%)	<u>4</u> (%)	<u>1</u> (%)	2	3 (%)	4
Respiratory	system)																	
lung	osseous metaplasia	1 (20)	< 5 0 (0) (0	0 (0)	0 (0) (< 5 0 0) (0	0	, 0 (0)	(< 5) 0 0) (0	0	0 (0)	0	< 5> 0) (0)	
	focal hyperplasia	0 (0)	0 (0) (0 0)	0	1 (20) (0	0 (0) (0	(0)	(0 0) (0	0 (0)	0 (0)		0 (0)	
Hematopoieti	c system)																	
ymph node	hemorrhage	1 (20)	< 5 0 (0) (0	0	0 (0) (< 5 0 0) (0	0	0 (0)	(< 5) 0 0) (0	0 (0)	0 (0)	0	< 5> 0) (0)	
Digestive sy	vstem)																	
iver	hermiation	1 (20)	0 (0) (0	0	0 (0) (0		0 (0)		< 50 0 0) (0 0)	0 (0)	1 (20	0	< 5> 0) (0	
	granulation	0 (0)	0 (0) (0 0)	0 (0)	1 (20) (0	0 (0) (0	1 (20)		0 0) (0	0 (0)	0 (0)		0 (0)	
rade a > b c)	1: Slight 2: Moderate 3: a: Number of animals examined at the sit b: Number of animals with lesion c: b / a * 100	Marked 4: Severe e	3															

(HPT150)

BAIS3

ANIMAL : RAT F344/DuCrj

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0- 2W)

REPORT TYPE : AI SEX : FEMALE

)rgan	Group M No. of Grade	Animals on Study 5 1 2 3 4 (%) (%) (%)	40000 ppm 5 1 2 3 4 (%) (%) (%)	
(Respiratory	system)			
ung	osseous metaplasia	< 5> 0 0 0 0 (0) (0) (0) (0)	<pre></pre>	
	focal hyperplasia	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0)	
(Hematopoieti	ic system)			
lymph node	hemorrhage	< 5> 0 0 0 0 (0) (0) (0) (0)	< 5> 0 0 0 0 (0) (0) (0) (0)	
Digestive sy	ystem)			
liver	herniation	< 5> 0 0 0 0 (0) (0) (0) (0)	< 5> 0 0 0 0 (0) (0) (0) (0)	
	granulation	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0) (0)	
Grade (a > b (c)	1: Slight 2: Moderate 3: Marke a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	d 4: Severe	· · · · · · · · · · · · · · · · · · ·	

(HPT150)

BAIS3

ANIMAL : RAT F344/DuCrj

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

REPORT TYPE : A1

SEX : FEMALE

Organ	No	roup Name on of Animals on Study rade 1 (%)	Control 5 2 3 (%) (%)	<u>4</u> (%)	<u>1</u> (%)		<u>4</u> <u>1</u> (%)	5000 ppt 5 2 3 (%) (%)	4_	10000 ppm 5 1 2 3 4 (%) (%) (%) (%)
{Urinary sys	stem)									
kidney	mineralization:cortico-medullary junctic		< 5> 0 0 (0) (0)	0 (0)	2 (40) (< 5> 0 0 0) (0) (0 1 (20)	< 5> 0 0 (0) (0)		<pre></pre>
{Endocrine	system}									
pituitary	Rathke pouch	0 (0)	< 5> 0 0 (0) (0)	0 (0)	0 (0) (< 5> 0 0 0) (0) (0 1 (20)	< 5> 0 0 (0) (0	0 (0)	<pre></pre>
thyroid	ultimobranchial body remanet	0 (0)	< 5> 0 0 (0) (0)	0 (0)	0 (0) (< 5> 0 0 0) (0) (0 0	< 5> 0 0 (0) (0		<pre></pre>
Grade < a > b (c)	1: Slight 2: Moderate 3: a: Number of animals examined at the site b: Number of animals with lesion c: b/a * 100	Marked 4: Severe								

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0- 2W)

: RAT F344/DuCrj REPORT TYPE : A1

ANIMAL.

SEX : FEMALE

> Group Name 20000 ppm 40000 ppm No. of Animals on Study 5

Grade (%) (%) (%) (%) Findings_

{Urinary system}

kidney mineralization:cortico-medullary junction

< 5> < 5> 0 0 0 0 0 0 0 (20) (0) (0) (0) (0)(0)(0)(0)

{Endocrine system}

pituitary

Rathke pouch

< 5> < 5> 0 0 0 0 0 0 (0) (0) (0) (0) (0)(0)(0)(0)

thyroid

ultimobranchial body remanet

< 5> < 5> 0 0 0 0 0 0 0 (0) (0) (0) (0) (0)(0)(0)(0)

Grade < a > 1 : Slight

2 : Moderate

3 : Marked

4 : Severe

a: Number of animals examined at the site

b

b: Number of animals with lesion

(c) c:b/a*100

(HPT150)

BAIS3

APPENDIX L 1

IDENTITY OF METHYL ACETOACETATE

IN THE 2-WEEK DRINKING WATER STUDY

IDENTITY OF METHYL ACETOACETATE IN THE 2-WEEK DRINKING WATER STUDY

Test Substance

: Methyl Acetoacetate (Tokyo Kasei Kogyo Co., Ltd.)

Lot No.

: GI01

1. Spectral Data

Mass Spectrometry

Instrument

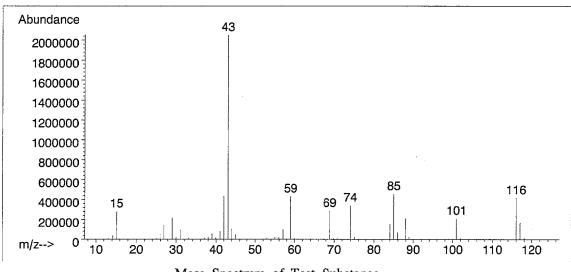
: Hewlett Packard 5989B Mass Spectrometer

Ionization

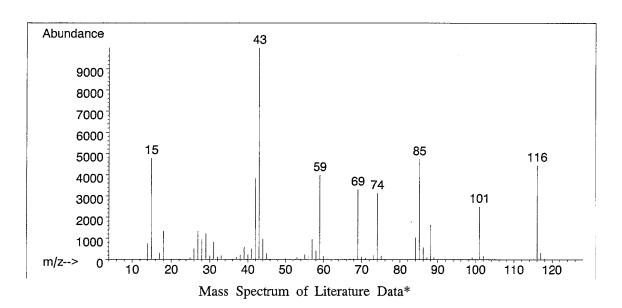
: EI (Electron Ionization)

Ionization Voltage

: 70eV



Mass Spectrum of Test Substance



Results: The mass spectrum was consistent with literature spectrum.

(*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition.

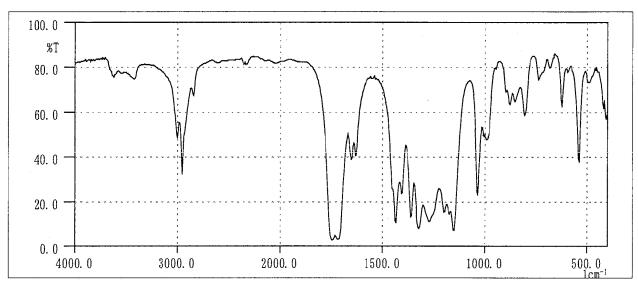
John Wiley and Sons, Inc. (U.S.), Entry Number 12752)

Infrared Spectrometry

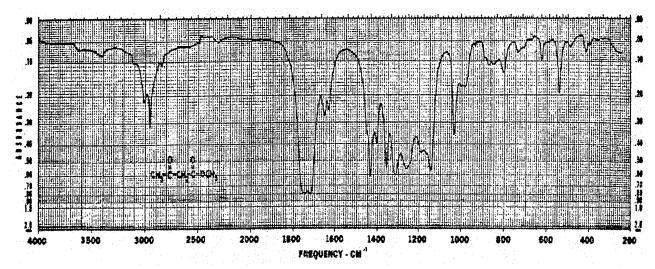
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 2 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.), p.766)

2. Conclusions: The test substance was identified as methyl acetoacetate, by the mass spectrum and the infrared spectrum.

APPENDIX L 2

STABILITY OF METHYL ACETOACETATE

IN THE 2-WEEK DRINKING WATER STUDY

STABILITY OF METHYL ACETOACETATE IN THE 2-WEEK DRINKING WATER STUDY

Test Substance

: Methyl Acetoacetate (Tokyo Kasei Kogyo Co., Ltd.)

Lot No.

: GI01

1. Sample

: This lot was used from 2000.10.27 to 2000.11.10. 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 : 100 °C (1 min) \rightarrow (10 °C/min) \rightarrow 190 °C

Flow Rate

: 1 mL/min

Detector

: FID (Flame Ionization Detector)

Injection Volume

: 1 µL

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
2000.10.04	1	6.853	100
2000.11.22	1	6.819	100

Results: Gas chromatography indicated one major peak (peak No.1) analyzed at 2000.10.4 and one major peak (peak No.1) analyzed at 2000.11.22. No new trace impurity peak in the test substance analyzed at 2000.11.22 was detected.

3. Conclusions: The test substance was stable for about 7 weeks in a dark place at room temperature.

APPENDIX L 3

CONCENTRATION OF METHYL ACETOACETATE IN FORMULATED WATER IN THE 2-WEEK DRINKING WATER STUDY

CONCENTRATION OF METHYL ACETOACETATE IN FORMULATED WATER IN THE 2-WEEK DRINKING WATER STUDY

Target Concentration								
Date Analyzed	2500ª	5000	10000	20000	40000			
2000.10.27	2520 (101) ^b	5050 (101)	10000 (100)	18800 (94.0)	39700 (99.3)			

a ppm b %

Analytical Method

: The samples were analyzed by gas chromatography.

Instrument

: Hewlett Packard 5890A Gas Chromatograph

Column

: INNOWAX (0.2 mm ϕ × 50 m)

Column Temperature

: 100 °C (1 min) \rightarrow (10 °C/min) \rightarrow 190 °C

Flow Rate

: 1 mL/min

Detector

: FID (Flame Ionization Detector)

Injection Volume

: 1 μL

APPENDIX L 4

STABILITY OF METHYL ACETOACETATE IN FORMULATED WATER IN THE 2-WEEK DRINKING WATER STUDY

STABILITY OF METHYL ACETOACETATE IN FORMULATED WATER IN THE 2-WEEK DRINKING WATER STUDY

		Target Concentration					
Date Prepared	Date Analyzed	2500°	40000				
2000.10.02	2000.10.02	2590 (100) ^b	39000 (100)				
	2000.10.06°	2510 (96.9)	41200 (106)				
	2000.10.12°	2540 (98.1)	40300 (103)				

a ppm

Analytical Method : The samples were analyzed by gas chromatography.

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : INNOWAX (0.2 mm ϕ × 50 m)

Column Temperature : 100 °C (1 min) \rightarrow (10 °C/min) \rightarrow 190 °C

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 µL

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

^c Animal room samples

APPENDIX M 1

METHODS FOR HEMATOLOGY AND BIOCHEMISTRY

IN THE 2-WEEK DRINKING WATER STUDY OF METHYL ACETOACETATE

METHODS FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK DRINKING WATER STUDY OF METHYL ACETOACETATE

Item	Method
Hematology	
Red blood cell (RBC)	Light scattering method 1)
Hemoglobin (Hgb)	Cyanmethemoglobin method 1)
Hematocrit (Hct)	Calculated as RBC×MCV/10 1)
Mean corpuscular volume (MCV)	Light scattering method 1)
Mean corpuscular hemoglobin (MCH)	Calculated as Hgb/RBC×10 1)
Mean corpuscular hemoglobin concentration (MCHC)	Calculated as Hgb/Hct×100 1)
Platelet	Light scattering method 1)
Reticulocyte	Pattern recognition method 3)
	(New methyleneblue staining)
Prothrombin time	Quick one stage method 2)
Activated partial thromboplastin time (APTT)	Ellagic acid activaterd method 2)
White blood cell (WBC)	Light scattering method 1)
Differential WBC	Pattern recognition method 3)
	(Wright staining)
Biochemistry	
Total protein (TP)	Biuret method 4)
Albumin (Alb)	BCG method 4)
A/G ratio	Calculated as Alb/(TP-Alb) 4)
T-bilirubin	Alkaline azobilirubin method 4)
Glucose	GlcK·G-6-PDH method 4)
T-cholesterol	CE · COD · POD method 4)
Phospholipid	PLD·ChOD·POD method 4)
Glutamic oxaloacetic transaminase (GOT)	JSCC method ⁴⁾
Glutamic pyruvic transaminase (GPT)	JSCC method 4)
Lactate dehydrogenase (LDH)	SFBC method 4)
γ -Glutamyl transpeptidase (γ -GTP)	L- γ -Glutamyl-p-nitroanilide method 4)
Creatine phosphokinase (CPK)	JSCC method 4)
Urea nitrogen	Urease · GLDH method 4)
Creatinine	Jaffe method 4)
Sodium	Ion selective electrode method 4)
Potassium	Ion selective electrode method 4)
Chloride	Ion selective electrode method 4)
Calcium	OCPC method 4)
Inorganic phosphorus	PNP·XOD·POD method 4)

- 1) Automatic blood cell analyzer (Technicon H·1: Bayer Corporation)
- 2) Automatic coagulometer (Sysmex CA-5000: Sysmex Corporation)
- 3) Automatic blood cell differential analyzer (MICROX HEG-120NA: OMRON Corporation)
- 4) Automatic analyzer (Hitachi 7070: Hitachi, Ltd.)

APPENDIX N 1

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY
IN THE 2-WEEK DRINKING WATER STUDY OF METHYL ACETOACETATE

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK DRINKING WATER STUDY OF METHYL ACETOACETATE

Item	Unit	Decimal Place
Hematology		
Red blood cell (RBC)	$\times 10^6/\mu$ L	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
Reticulocyte	%	1
Prothrombin time	sec	1
Activated partial thromboplastin time (APTT)	sec	1
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
Phospholipid	mg/dL	0
Glutamic oxaloacetic transminase (GOT)	IU/L	0
Glutamic pyruvic transaminase (GPT)	IU/L	0
Lactate dehydrogenase (LDH)	IU/L	0
γ -Glutamyl transpeptidase (γ -GTP)	IU/L	0
Creatine phosphokinase (CPK)	IU/L	0
Urea nitrogen	mg/dL	1
Creatinine	mg/dL	1
Sodium	mEq/L	0
Potassium	mEq/L	1
Chloride	mEq/L	0
Calcium	mg/dL	1
Inorganic phosphorus	mg/dL	1