1,4 - ジクロロ - 2 - ニトロベンゼン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:0302

APPENDIX

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APPENDIX A 1

CLINICAL OBSERVATION: SUMMARY, MOUSE: MALE

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)

ALL ANIMALS

SEX : MALE

PAGE: 1

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	
V24 TV															
EATH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	
	1481 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	2222 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	3333 ppm	0	0	1	1	1	1	1	1	1	1	1	1	1	
	5000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	7500 ppm	0	2	3	3	3	3	4	4	4	4	4	4	4	
ILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	
	1481 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	2222 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	
	3333 ppm	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	
	7500 ppm	0	1	0	3	3	4	3	2	1	0	0	0	0	
ELLOW URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	
	1481 ppm	9	9	9	9	9	9	9	9	9	9	9	9	9	
	2222 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10	
	3333 ppm	10	10	9	9	9	9	9	9	9	9	9	9	9	
	5000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10	
	7500 ppm	10	8	7	7	7	7	6	6	6	6	6	6	6	

(HAN190)

APPENDIX A 2

CLINICAL OBSERVATION: SUMMARY, MOUSE: FEMALE

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 13

SEX : FEMALE

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
DEATH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	1481 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	2222 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	3333 ppm	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
	7500 ppm	0	0	1	2	2	2	3	4	4	4	4	4	4
ILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	1481 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	2222 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	3333 ppm	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
	7500 ppm	0	0	1	3	3	2	2	1	1	1	0	0	0
VELLOW URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	1481 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	2222 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	3333 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	5000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	7500 ppm	10	10	9	8	8	8	7	6	6	6	6	6	6

(HAN190)

APPENDIX B 1

BODY WEIGHT CHANGES :SUMMARY, MOUSE : MALE (13-WEEK STUDY)

STUDY NO. : 0302 ANIMAL : MOUSE Crj:BDF1

UNIT : g

REPORT TYPE : A1 13

SEX : MALE

BODY WEIGHT CHANGES ALL ANIMALS

(SUMMARY)

roup Name	Administration	week					
	0	1	2	3	4	5	6
Control	22.6± 0.7	20.3± 0.9	21.6± 0.7	21.1± 1.0	24.1± 1.0	25.3± 0.7	24.6± 0.7
1481 ppm	22.5± 0.7	20.7± 1.1	22.3± 0.9	21.9± 1.1	24.4± 0.8	25.7± 0,9	25.0± 0.8
2222 ppm	22.6± 0.7	20.6± 0.8	21.9± 0.6	21.2± 1.0	24.3± 0.8	25.7± 1.1	25.5± 1.2
3333 ppm	22.6± 0.7	21.3± 1.1	21.7± 1.0	22.1± 0.7	24.6± 1.0	25.5± 0.9	25.2± 0.9
5000 ppm	22.6± 0.7	21.2± 0.6	21.0± 1.0	20.5± 1.2	24.2± 1.4	25.6± 1.5	25.6± 1.7
7500 ppm	22.6± 0.7	18.1± 0.5**	17.2± 1.2**	17.0± 1.1**	15.5± 1.3**	15.0± 1.3**	15.2± 1.1**
Significant differe	ence; *: P ≤ 0.05	** : P ≤ 0.01		Test of Dunnett			

(HAN260)

BAIS 3

PAGE: 1

ANIMAL : MOUSE Crj:BDF1

UNIT : g

REPORT TYPE : A1 13

SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)

ALL ANIMALS

Group Name Administration week_ 7 8 9 10 11 12 13 Control 26.0 ± 1.1 22.3± 1.1 27.1 \pm 1.1 27.2 ± 1.1 28.5 ± 1.2 29.5 ± 1.6 30.3 ± 1.4 1481 ppm 26.0 ± 1.2 24.0± 1.9 27.2 ± 1.1 26.9 ± 1.3 28.4 \pm 1.3 29.8 ± 1.5 30.1 ± 1.8 2222 ppm 26.7± 1.2 24.3± 1.6* 27.2± 1.0 27.3± 1.1 28.6 ± 1.3 29.4± 1.4 29.9 ± 1.8 3333 ppm 25.9 ± 0.9 24.9± 1.2** 27.1± 0.8 27.4± 0.9 28.3 \pm 1.2 29.1 \pm 1.4 29.7 \pm 1.5 5000 ppm 26.1 \pm 1.4 24.5± 1.8* 27.2 ± 1.2

 27.1 ± 0.9

16.9± 2.0**

28.4 \pm 1.0

18.2± 2.2**

 28.7 ± 1.1

19.1± 2.3**

 29.0 ± 1.2

20.0± 2.6**

Significant difference; $*: P \leq 0.05$ ** : P ≤ 0.01 Test of Dunnett

16.6± 1.5**

(HAN260)

7500 ppm

15.3± 1.4**

15.3± 1.2**

BAIS 3

PAGE: 2

APPENDIX B 2

BODY WEIGHT CHANGES: SUMMARY, MOUSE: FEMALE

ANIMAL : MOUSE Crj:BDF1

UNIT : g

REPORT TYPE : A1 13

SEX : FEMALE

BODY WEIGHT CHANGES ALL ANIMALS (SUMMARY) ٠٠....

oup Name	Administration	week					
	0	1	2	3	4 &	5	6
Control	18.9± 0.5	18.3± 0.7	19.0± 0.6	18.1± 2.1	20.4± 0.9	20.1± 1.0	21.1± 0.8
1481 ppm	18.9± 0.5	18.7± 0.7	19.1± 0.9	18.9± 1.1	21.0± 0.9	21.0± 0.7	21.8± 0.8
2222 ppm	18.9± 0.5	18.8± 0.8	19.6± 0.7	19.0± 1.3	20.9± 0.6	21.3± 0.5*	21.5± 0.4
3333 mag 8888	18.9± 0.5	18.3± 0.7	19.2± 0.9	18.3± 1.5	20.9± 0.8	21.3± 1.1*	21.9± 1.0
5000 ppm	18.9± 0.5	17.7± 1.3	18.7± 0.5	18.6± 1.3	20.9± 0.5	21.0± 0.7	21.6± 0.5
7500 ppm	18.9± 0.5	15.8± 1.0**	14.7± 1.3**	13.7± 1.2**	13.7± 1.4**	14.5± 1.3**	15.3± 1.7*
Significant differe	ence; *: P ≤ 0.05	** : P ≤ 0.01		Test of Dunnett			

(HAN260)

BAIS 3

PAGE: 3

ANIMAL : MOUSE Crj:BDF1

UNIT : g

REPORT TYPE : A1 13

SEX : FEMALE

BODY WEIGHT CHANGES ALL ANIMALS (SUMMARY)

PAGE: 4

oup Name	Administration	week					
	7	8	9	10	11	12	13
Control	21.2± 0.8	18.9± 1.0	22.6± 1.2	22.0 ± 0.7	22.7 \pm 0.9	23.3± 1.0	23.9± 0.8
1481 ppm	22.0± 0.9	19.7± 1.7	22.8± 1.3	22.9± 1.0	23.8± 1.1	24.7± 1.4*	24.9± 0.9
2222 ppm	21.4± 0.6	19.6± 1.2	23.1± 0.7	22.7 ± 0.4	23.8± 1.3	24.1± 0.8	25.0± 0.5
3333 ppm	22.1± 0.9	19.4 \pm 1.2	23.6± 1.1	23.2± 1.0*	23.8± 1.1	24.7± 1.4*	25.7± 1.4**
5000 ppm	20.8 ± 2.0	19.1± 1.2	22.6± 1.0	22.5± 0.7	23.8± 0.5	24.6± 0.8	24.5± 0.8
7500 ppm	15.5± 1.9*	15.7± 1.3**	17.3± 1.7**	16.8± 1.6	18.3± 1.2**	18.3± 1.6**	18.7± 2.0
Significant differe	ence; $*: P \leq 0.05$	** : P ≤ 0.01		Test of Dunnett			

(HAN260)

APPENDIX C 1

FOOD CONSUMPTION CHANGES: SUMMARY, MOUSE: MALE

ANIMAL : MOUSE Crj:BDF1

UNIT : g

REPORT TYPE : A1 13

SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)

ALL ANIMALS

PAGE: 1

roup Name	Administration 1-7(7)	week-day(effective) 2-7(7)	3-7(7)	4-7 (7)	5-7 (7)	6-7(7)	7-7(7)
Control	3.6± 0.3	3.1± 0.4	2.9± 0.3	4.9± 0.4	4.5± 0.6	3.7± 0.5	3.8± 0.3
1481 ppm	3.9± 0.4	3.5± 0.4	3.5± 0.3**	4.9± 0.4	4.5± 0.4	3.7± 0.3	4.2± 0.3
2222 ppm	3.7± 0.2	3.3± 0.2	3.0± 0.4	5.0± 0.4	4.6± 0.5	4.1± 0.4	4.4± 0.3*
3333 ppm	3.9± 0.4	3.3± 0.3	3.2± 0.2	4.6± 0.3	4.5± 0.3	3.8± 0.3	4.2± 0.3
5000 ppm	3.7± 0.3	2.9± 0.4	2.8± 0.4	4.7± 0.4	4.3± 0.6	3.7± 0.4	4.0± 0.4
7500 ppm	4.1± 0.3**	3.3± 0.5	2.8± 0.3	3.3± 0.2**	3.1± 0.5**	3.3± 0.5	3.0± 0.6**

Significant difference; $*: P \le 0.05$ **: $P \le 0.01$

Test of Dunnett

(HAN260)

ANIMAL : MOUSE Crj:BDF1

UNIT : g

REPORT TYPE : A1 13

FOOD CONSUMPTION CHANGES (SUMMARY)

ALL ANIMALS

roup Name	Administration	week-day(effective)					
	8-7(7)	9-7(7)	10-7(7)	11-7 (7)	12-7 (7)	13-7 (7)	
Control	3.4± 0.5	5.4± 0.6	4.1± 0.5	4.6± 0.5	4.8± 0.8	4.7± 0.5	
1481 ppm	3.6± 0.4	5.0± 0.5	4.2± 0.4	4.4± 0.4	4.8± 0.5	4.6± 0.6	
2222 ppm	3.8± 0.4	5.0± 0.5	4.6± 0.7	4.9± 0.8	4.9± 0.7	4.9± 0.7	
3333 ppm	3.7± 0.2	4.7± 0.5*	3.9± 0.3	4.1± 0.4	4.4± 0.4	4.3± 0.5	
5000 ppm	3.6± 0.4	4.4± 0.4**	4.1± 0.7	4.4± 0.5	4.3± 0.4	4.2± 0.5	
7500 ppm	3.1± 0.4	3.6± 0.6**	3.8± 0.5	4.2± 0.5	4.6± 1.0	4.8± 1.1 ?	
					<u> </u>		

^{?:} Significant test is not applied, because No. of data in this group is less than 3.

(HAN260)

APPENDIX C 2

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

ANIMAL : MOUSE Crj:BDF1

UNIT : g

REPORT TYPE : A1 13

SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

PAGE: 3

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	4.0± 0.3	3.2± 0.2	2.6± 0.4	4.4± 0.6	3.9± 0.5	4.0± 0.3	4.1± 0.3
1481 ppm	4.2± 0.2	3.2± 0.3	2.7± 0.3	4.5± 0.3	4.0± 0.2	4.1± 0.4	4.3± 0.2
2222 ppm	4.0± 0.3	3.4 ± 0.4	2.8± 0.4	4.4± 0.5	4.0± 0.4	4.1± 0.4	4.3± 0.4
3333 ppm	3.8± 0.1	3.4± 0.3	2.9± 0.4	4.5± 0.5	3.9± 0.2	4.0± 0.3	4.3± 0.2
5000 ppm	4.0± 0.3	3.6± 0.3*	3.1± 0.3*	4.3± 0.4	4.0± 0.3	3.7± 0.2	4.1± 0.3
7500 ppm	4.1± 0.5	3.3± 0.5	2.5± 0.3	3.1± 1.0*	3.6± 0.8	3.4± 0.6**	3.4± 0.4**
Significant difference	ze; *:P≦0.05	** : P ≤ 0,01		Test of Dunnett			

(HAN260)

ANIMAL : MOUSE Crj:BDF1

UNIT : g

REPORT TYPE : A1 13

SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY) ALL ANIMALS

PAGE: 4

up Name		week-day(effective)		·		
	8-7 (7)	9–7 (7)	10-7(7)	11-7 (7)	12-7 (7)	13-7 (7)
Control	3.5± 0.4	4.9± 0.5	3.8± 0.6	4.7± 0.8	4.7± 0.6	4.8± 0.7
1481 ppm	3.3± 0.3	4.9± 0.5	4.1± 0.4	4.9± 0.7	5.2± 0.5	5.0± 0.6
2222 ppm	3.3± 0.3	5.1± 0.7	3.9± 0.3	4.8± 0.8	4.9± 0.9	4.8± 0.6
3333 ppm	3.1± 0.3	5.0± 0.3	3.8± 0.3	4.2± 0.4	4.6± 0.4	4.5± 0.6
5000 ppm	3.0± 0.3*	5.1± 0.4	3.8± 0.6	4.3± 0.9	4.4± 0.7	4.2± 0.5
7500 ppm	2.6± 0.6**	3.7± 0.8**	3.2 ± 0.7	3.5± 0.7*	3.3± 0.6**	4.0± 1.1

(HAN260)

APPENDIX D 1

CHEMICAL INTAKE CHANGES: SUMMARY, MOUSE: MALE

ANIMAL : MOUSE Crj:BDF1
UNIT : g/kg/day

REPORT TYPE : A1 13

SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)

ALL ANIMALS

PAGE: 1

Group Name	Administration	(weeks)				:	
	1	2	3	4	5	6	7
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
1481 ppm	0.282± 0.021	0.230± 0.025	0.234± 0.018	0.301± 0.024	0.260± 0.018	0.222± 0.017	0.240± 0.011
2222 ppm	0.396± 0.028	0.335± 0.021	0.318± 0.035	0.459± 0.038	0.397± 0.039	0.361± 0.031	0.362± 0.023
3333 ppm	0.605± 0.075	0.516± 0.058	0.488± 0.023	0.619± 0.036	0.595± 0.048	0.507± 0.041	0.541± 0.034
5000 ppm	0.883± 0.074	0.692± 0.073	0.671± 0.091	0.971± 0.104	0.848± 0.115	0.714± 0.071	0.765± 0.080
7500 ppm	1.706± 0.139	1.439± 0.207	1.247± 0.073	1.649± 0.103	1.605± 0.282	1.626± 0.241	1.553± 0.220

(HAN300)

ANIMAL : MOUSE Crj:BDF1
UNIT : g/kg/day
REPORT TYPE : A1 13

CHEMICAL INTAKE CHANGES (SUMMARY)

ALL ANIMALS

Group Name	Administ	tration (weeks)										
	8		9		10	•	11		12		13		
Control	0.000± 0	0.000	0.000± 0.	000 0.	000±	0.000	0.000±	0.000	0.000±	0.000	0.000±	0.000	
1481 ppm	0.222± 0	0.017	0.273± 0.	029 0.	229±	0.017	0.230±	0.016	0.239±	0.018	0.227±	0.020	
2222 ppm	0.348± 0	0.029	0.405± 0.	042 0.	372±	0. 053	0.378±	0.055	0.371±	0.048	0.360±	0.048	
3333 ppm	0.495± 0	0.026	0.572± 0.	062 0.	480±	0.034	0.485±	0.039	0.499±	0.049	0.486±	0.045	
5000 ppm	0.725± 0	0. 069	0.811± 0.	077 0.	753±	0. 129	0.772±	0.092	0.743±	0. 075	0.724±	0.080	·
7500 ppm	1.506± 0	0. 125	1.604± 0.	184 1.	837±	0.308	1.782±	0. 078	1.861±	0.306	1,992±	0. 214	

(HAN300) BAIS 3

APPENDIX D 2

CHEMICAL INTAKE CHANGES: SUMMARY, MOUSE: FEMALE

ANIMAL : MOUSE Crj:BDF1 UNIT : g/kg/day

REPORT TYPE : A1 13

SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)

ALL ANIMALS

Group Name	Administration	(weeks)					
	1	2	3	4	5	6	7
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
1481 ppm	0.330± 0.017	0.246± 0.016	0.213± 0.015	0.315± 0.021	0.280± 0.021	0.278± 0.024	0.287± 0.010
2222 ppm	0.467± 0.033	0.386± 0.044	0.324 ± 0.031	0.473± 0.049	0.416± 0.035	0.423± 0.035	0.442± 0.049
3333 ppm	0.698± 0.041	0.587± 0.049	0.536± 0.064	0.722± 0.073	0.611± 0.043	0.604± 0.066	0.644± 0.055
5000 ppm	1.153± 0.165	0.972± 0.089	0.824± 0.070	1.029± 0.120	0.962± 0.063	0.851± 0.061	0.997± 0.135

 1.937 ± 0.304 1.676 ± 0.304 1.352 ± 0.211 1.850 ± 0.527 1.870 ± 0.514 1.675 ± 0.420 1.692 ± 0.360

(HAN300)

7500 ppm

BAIS 3

PAGE: 3

CHEMICAL INTAKE CHANGES (SUMMARY) ALL ANIMALS

ANIMAL : MOUSE Crj:BDF1 UNIT : g/kg/day REPORT TYPE : A1 13

SEX : FEMALE

PAGE: 4

Group Name	Administration	(weeks)				
	8	9	10	11	12	13
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
***************************************	3,333	0.000 0.000	0.0002 0.000	0.000± 0.000	0.000 = 0.000	0.000 = 0.000
1481 ppm	0.248± 0.009	0.315 ± 0.022	0.262 ± 0.025	0.303 ± 0.036	0.313± 0.031	0.299 ± 0.041
2222 ppm	0.377± 0.036	0.488± 0.068	0.377± 0.034	0.447± 0.071	0.447± 0.084	0.428± 0.056
3333 ppm	0.525± 0.052	0.702± 0.051	0.549± 0.062	0.593± 0.052	0.619± 0.065	0.581± 0.080
5000 ppm	0.777± 0.059	1.121± 0.083	0.842± 0.131	0.891± 0.174	0.887± 0.133	0.863± 0.111
7500 ppm	1.258± 0.287	1.596± 0.343	1.421± 0.350	1.444± 0.341	1.375± 0.322	1.673± 0.692

(HAN300)

APPENDIX E 1

HEMATOLOGY: SUMMARY, MOUSE: MALE

STUDY NO. : 0302 ANIMAL : MOUSE Crj:BDF1

HEMATOLOGY (SUMMARY) ALL ANIMALS (14W)

MEASURE. TIME : 1

SEX : MALE

REPORT TYPE : A1

PAGE: 1

roup Name	NO. of Animals	RED BL	OOD CELL	HEMOGLO g/dl		HEMATOO %	CRIT	MCV f l		MCH pg		MCHC g/dl		PLATELE 1 0 ³ /µ	
Control	10	10.88±	0. 27	16.2±	0.3	51,1±	1.0	47.0±	0, 5	14.9±	0. 2	31.7±	0.2	1433±	52
1481 ppm	9	10.64±	0.31	16.0±	0.3	50.8±	1.4	47.8±	0.7	15.1±	0.3	31.5±	0.5	1269±	90**
2222 ppm	10	10.44±	0.29*	16.0±	0.5	50.6±	1.8	48.5±	0.9**	15.3±	0.2**	31.5±	0.5	1239±	121**
3333 ppm	9	10.36±	0.31**	15.8±	0.3	49.8±	1.5	48.0±	0.7	15.2±	0.3	31.7±	0.5	1289±	82*
5000 ppm	10	10.14±	0.31**	15.4±	0.4**	48.8±	1.8*	48.1±	1.4**	15.2±	0.3	31.6±	0.6	1311±	132*
7500 ppm	6	10.19±	0.38**	15.4±	0.5**	47.8±	2. 3**	46.9±	1.4	15.1±	0.3	32.2±	0.8	1367±	84

(HCL070)

ANIMAL : MOUSE Crj:BDF1

HEMATOLOGY (SUMMARY) ALL ANIMALS (14W)

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : A1

PAGE: 2

Group Name	NO. of Animals	METHEMOGL %	OBIN CONTRACTOR OF THE PROPERTY OF THE PROPERT	
Control	10	0.3±	0.0	
1481 ppm	9	0.3±	0.1	
2222 ppm	10	0.3±	0.1	
3333 ppm	9	0.4±	0.2	
5000 ppm	10	0.6±	0.6	
7500 ppm	6	1.6±	1.2**	

Significant difference; *: P ≤ 0.05

** : P ≤ 0.01

Test of Dunnett

(HCL070)

ANIMAL : MOUSE Crj:BDF1

HEMATOLOGY (SUMMARY) ALL ANIMALS (14W)

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : A1

PAGE: 3

roup Name	NO. of Animals	₩BC 1 0 ³ ⁄		Dif N-BAND	fferentia	1 WBC (% N-SEG	b)	EOSINO		BAS0		MONO		LYMPHO		OTHERS	
<i>a</i>			0.50	•	•	40.1											
Control	10	1.74±	0.78	0±	0	13±	3	1±	1	0±	0	4±	2	81±	5	0±	0
1481 ppm	9	2.11±	1.26	0±	0	16±	4	1±	1	0±	0	4±	1	79±	5	0±	0
2222 ppm	10	1.42±	0.75	0±	0	15±	4	0±	0	0±	0	4±	2	80±	5	0±	0
3333 ppm	9	1.53±	0.85	1±	1	19±	8	1±	1	0±	0	3±	1	78±	9	0±	0
5000 ppm	10	1.76±	0.80	1±	1	15±	6	0±	0	0±	0	3±	1	81±	6	0±	0
7500 ppm	6	0.65±	0.36	0±	1	30±	8**	0±	1	0±	0	4±	2	66±	7**	0 ±	0

(HCL070)

APPENDIX E 2

HEMATOLOGY: SUMMARY, MOUSE: FEMALE

ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1

HEMATOLOGY (SUMMARY) ALL ANIMALS (14W)

SEX : FEMALE

REPORT TYPE : A1

PAGE: 4

Group Name	NO. of Animals	RED BL	OOD CELL µl	HEMOGLO g/dl	DBIN	HEMATO(%	CRIT	MCV f 2		MCH pg		MCHC g/dl		PLATELE 1 O³/µ	
Control	10	10.71±	0. 26	16.2±	0.4	49.9±	1.4	46.6±	0, 5	15.1±	0.2	32.4±	0.5	1282±	49
1481 ppm	10	10.55±	0.46	16.4±	0.4	50.8±	1.9	48.2±	0.6*	15.5±	0.5	32.3±	0.9	1172±	72*
2222 ppm	10	10.48±	0.33	16.2±	0.6	50.7±	1.7	48.4 \pm	0.4**	15.4±	0.4	32.0±	0.8	1153±	103**
3333 ppm	10	10.23±	0.45*	15.9±	0.6	49.6±	2.0	48.5±	0.6**	15.6±	0.4*	32.1±	0.9	1270±	87
5000 ppm	10	10.31±	0.23	16.0±	0.4	50.4±	1.0	48.9±	0.6**	15.5±	0.3	31.8±	0.5	1238±	74
7500 ppm	6	9.54±	0.44**	15.1±	0.5**	44.6±	3. 2**	46.7±	1.3	15.9±	0.6**	34.0±	1.8	1207±	120

(HCL070)

ANIMAL : MOUSE Crj:BDF1

HEMATOLOGY (SUMMARY) ALL ANIMALS (14W)

MEASURE. TIME: 1

SEX : FEMALE

REPORT TYPE : A1

A V VO A VOCA CONTINUES ON V

roup Name	NO. of Animals	METHEMOGI %	LOBIN
Control	10	0.3±	0.1
1481 ppm	10	0.3±	0.1
2222 ppm	10	0.3±	0.1
3333 ppm	10	0.4±	0.2
5000 ppm	10	0.4±	0.3
7500 ppm	6	1.4±	0.7**

(HCL070)

BAIS 3

PAGE: 5

ANIMAL : MOUSE Crj:BDF1

HEMATOLOGY (SUMMARY) ALL ANIMALS (14W)

MEASURE. TIME: 1

SEX : FEMALE

REPORT TYPE : A1

PAGE: 6

NO. of Animals	₩BC 1 0³/		Dif N-BAND	ferentia	l WBC (% N-SEG	6)	EOSINO		BAS0		MONO		LYMPHO		OTHERS	
10	1.45±	0.37	0±	0	16±	5	1±	1	0±	0	$3\pm$	2	80±	6	0±	į
10	1.55±	0.67	0±	0	15±	4	1±	1	0±	0	4±	2	81±	4	0±	
10	1.51±	0.74	0±	0	15±	6	1±	1	0±	0	4±	2	80±	5	0±	
10	1.87±	0.68	0±	0	13±	3	1±	1	0±	0	4±	2	82±	4	0±	
10	1.57±	0.39	0±	0	18生	7	0±	1	0±	0	4 ±	2	77±	6	0±	
6	1.20±	0. 53	1±	1	23±	19	0±	1	0±	0	4±	3	72±	19	0±	
difference ;	* : P =	≤ 0.05	**: P ≦	0.01			Test	of Dunn	ıett							
	10 10 10 10 10 6	Animals 10 ³ / 10 1.45± 10 1.55± 10 1.51± 10 1.87± 10 1.57± 6 1.20±	Animals $10^3 / \mu \ell$ 10 1.45 ± 0.37 10 1.55 ± 0.67 10 1.51 ± 0.74 10 1.87 ± 0.68 10 1.57 ± 0.39	Animals $1 \text{ O}^3 / \mu \ell$ N-BAND $10 1.45 \pm 0.37 0 \pm$ $10 1.55 \pm 0.67 0 \pm$ $10 1.51 \pm 0.74 0 \pm$ $10 1.87 \pm 0.68 0 \pm$ $10 1.57 \pm 0.39 0 \pm$ $6 1.20 \pm 0.53 1 \pm$	Animals $10^3 / \mu \ell$ N-BAND $10 1.45 \pm 0.37 0 \pm 0$ $10 1.55 \pm 0.67 0 \pm 0$ $10 1.51 \pm 0.74 0 \pm 0$ $10 1.87 \pm 0.68 0 \pm 0$ $10 1.57 \pm 0.39 0 \pm 0$ $6 1.20 \pm 0.53 1 \pm 1$	Animals $10^{9}/\mu\ell$ N-BAND N-SEG $10 1.45\pm 0.37 0\pm 0 16\pm 10 1.55\pm 0.67 0\pm 0 15\pm 10 1.51\pm 0.74 0\pm 0 15\pm 10 1.87\pm 0.68 0\pm 0 13\pm 10 1.57\pm 0.39 0\pm 0 18\pm 6 1.20\pm 0.53 1\pm 1 23\pm 10$	Animals $10^{3}/\mu\ell$ N-BAND N-SEG 10 1.45 ± 0.37 0 ± 0 16 ± 5 10 1.55 ± 0.67 0 ± 0 15 ± 4 10 1.51 ± 0.74 0 ± 0 15 ± 6 10 1.87 ± 0.68 0 ± 0 13 ± 3 10 1.57 ± 0.39 0 ± 0 18 ± 7 6 1.20 ± 0.53 1 ± 1 23 ± 19	Animals 1 0³ / μℓ N-BAND N-SEG EOSINO 10 1.45± 0.37 0± 0 16± 5 1± 10 1.55± 0.67 0± 0 15± 4 1± 10 1.51± 0.74 0± 0 15± 6 1± 10 1.87± 0.68 0± 0 13± 3 1± 10 1.57± 0.39 0± 0 18± 7 0± 6 1.20± 0.53 1± 1 23± 19 0±	Animals 1 0³ / μℓ N-BAND N-SEG EOSINO 10 1.45± 0.37 0± 0 16± 5 1± 1 10 1.55± 0.67 0± 0 15± 4 1± 1 10 1.51± 0.74 0± 0 15± 6 1± 1 10 1.87± 0.68 0± 0 13± 3 1± 1 10 1.57± 0.39 0± 0 18± 7 0± 1 6 1.20± 0.53 1± 1 23± 19 0± 1	Animals 1 0³ / μℓ N-BAND N-SEG EOSINO BASO 10 1.45± 0.37 0± 0 16± 5 1± 1 0± 10 1.55± 0.67 0± 0 15± 4 1± 1 0± 10 1.51± 0.74 0± 0 15± 6 1± 1 0± 10 1.87± 0.68 0± 0 13± 3 1± 1 0± 10 1.57± 0.39 0± 0 18± 7 0± 1 0± 6 1.20± 0.53 1± 1 23± 19 0± 1 0±	Animals $1 \ 0^3 / \mu \ell$ N-BAND N-SEG EOSINO BASO 10 1.45 ± 0.37 0 ± 0 16 ± 5 1 ± 1 0 ± 0 10 1.55 ± 0.67 0 ± 0 15 ± 4 1 ± 1 0 ± 0 10 1.51 ± 0.74 0 ± 0 15 ± 6 1 ± 1 0 ± 0 10 1.87 ± 0.68 0 ± 0 13 ± 3 1 ± 1 0 ± 0 10 1.57 ± 0.39 0 ± 0 18 ± 7 0 ± 1 0 ± 0 6 1.20 ± 0.53 1 ± 1 23 ± 19 0 ± 1 0 ± 0	Animals $10^{3}/\mu \ell$ N-BAND N-SEG EOSINO BASO MONO 10 1.45± 0.37 0± 0 16± 5 1± 1 0± 0 3± 10 1.55± 0.67 0± 0 15± 4 1± 1 0± 0 4± 10 1.51± 0.74 0± 0 15± 6 1± 1 0± 0 4± 10 1.87± 0.68 0± 0 13± 3 1± 1 0± 0 4± 10 1.57± 0.39 0± 0 18± 7 0± 1 0± 0 4± 6 1.20± 0.53 1± 1 23± 19 0± 1 0± 0 4±	Animals 1 0 ³ /μℓ N-BAND N-SEG EOSINO BASO MONO 10 1.45± 0.37 0± 0 16± 5 1± 1 0± 0 3± 2 10 1.55± 0.67 0± 0 15± 4 1± 1 0± 0 4± 2 10 1.51± 0.74 0± 0 15± 6 1± 1 0± 0 4± 2 10 1.87± 0.68 0± 0 13± 3 1± 1 0± 0 4± 2 10 1.57± 0.39 0± 0 18± 7 0± 1 0± 0 4± 2 6 1.20± 0.53 1± 1 23± 19 0± 1 0± 0 4± 3	Animals $10^{3}/\mu\ell$ N-BAND N-SEG EOSINO BASO MONO LYMPHO $10 1.45\pm 0.37 0\pm 0 16\pm 5 1\pm 1 0\pm 0 3\pm 2 80\pm 10 1.55\pm 0.67 0\pm 0 15\pm 4 1\pm 1 0\pm 0 4\pm 2 81\pm 10 1.51\pm 0.74 0\pm 0 15\pm 6 1\pm 1 0\pm 0 4\pm 2 80\pm 10 1.87\pm 0.68 0\pm 0 13\pm 3 1\pm 1 0\pm 0 4\pm 2 82\pm 10 1.57\pm 0.39 0\pm 0 18\pm 7 0\pm 1 0\pm 0 4\pm 2 77\pm 6 1.20\pm 0.53 1\pm 1 23\pm 19 0\pm 1 0\pm 0 4\pm 3 72\pm 10 1.57\pm 0.58 1\pm 1 1 10\pm 1 10\pm 10 10\pm 10 10$	Animals 103/µl N-BAND N-SEG EOSINO BASO MONO LYMPHO 10 1.45± 0.37 0± 0 16± 5 1± 1 0± 0 3± 2 80± 6 10 1.55± 0.67 0± 0 15± 4 1± 1 0± 0 4± 2 81± 4 10 1.51± 0.74 0± 0 15± 6 1± 1 0± 0 4± 2 80± 5 10 1.87± 0.68 0± 0 13± 3 1± 1 0± 0 4± 2 82± 4 10 1.57± 0.39 0± 0 18± 7 0± 1 0± 0 4± 2 77± 6 6 1.20± 0.53 1± 1 23± 19 0± 1 0± 0 4± 3 72± 19	Animals 1 0³/μ2 N-BAND N-SEG EOSINO BASO MONO LYMPHO OTHERS 10 1.45± 0.37 0± 0 16± 5 1± 1 0± 0 3± 2 80± 6 0± 10 1.55± 0.67 0± 0 15± 4 1± 1 0± 0 4± 2 81± 4 0± 10 1.51± 0.74 0± 0 15± 6 1± 1 0± 0 4± 2 80± 5 0± 10 1.87± 0.68 0± 0 13± 3 1± 1 0± 0 4± 2 82± 4 0± 10 1.57± 0.39 0± 0 18± 7 0± 1 0± 0 4± 2 77± 6 0± 6 1.20± 0.53 1± 1 23± 19 0± 1 0± 0 4± 3 72± 19 0±

(HCL070)

APPENDIX F 1

BIOCHEMISTRY: SUMMARY, MOUSE: MALE

ANIMAL : MOUSE Crj:BDF1

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (14W)

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : A1

PAGE: 1

roup Name	NO. of Animals	TOTAL E	PROTEIN	ALBUMII g/dl		A/G RA	OIT	T-BILI mg/dl		GLUCOSE mg/dl		T-CHOLE mg/dl	STEROL	TRIGLYC mg/dl	ERIDE
Control	10	5.1±	0.2	2.9±	0.1	1.3±	0.1	0.19±	0.02	215±	53	84±	10	23±	8
1481 ppm	9	5.1±	0.2	3.0±	0.1	1.4±	0. 1	0.19±	0.01	194±	51	128±	10	30±	12
2222 ppm	10	5.3±	0.2	3.0±	0.1	1.3±	0. 1	0.18±	0.02	176±	36	145±	15*	33±	6
3333 ppm	9	5.4±	0,1*	3.1±	0.1*	1.4±	0. 1	0.18±	0.02	208±	47	178±	13**	47±	21**
5000 ppm	10	5.5±	0.3**	3.1±	0.2**	1.3±	0.1	0.19±	0.02	208±	24	203±	24**	42±	13**
7500 ppm	6	5.9±	0. 2**	3.6±	0.2**	1,6±	0.1**	0.25±	0.06*	192±	24	248±	9**	29±	6

(HCL074)

ANIMAL : MOUSE Crj:BDF1

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (14W)

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : A1

PAGE: 2

roup Name	NO. of Animals	PHOSPHO mg/dl	LIPID	GOT IU/A	2	GPT IU/A	2	LDH IU/A	?	ALP IU/A	!	G-GTP IU/A		CPK IU/A	!
Control	10	161±	20	43±	5	19±	4	261±	71	182±	9	1±	1	46±	12
1481 ppm	9	229±	19**	54±	6	54±	10	277±	44	188±	12	1±	1	52±	14
2222 ppm	10	251±	25**	54土	7	58±	10	319±	46	195土	15	1±	1	72±	34
3333 ppm	9	303±	22**	63±	12**	82生	13**	327±	49	201±	23	2±	1	70±	22
5000 ppm	10	336±	39**	70±	11**	94±	20**	368±	59**	230±	25**	5±	4*	119±	72**
7500 ppm	6	403±	15**	116±	34**	201±	56**	550±	67**	513±	65**	61±	23**	114±	27**

(HCL074)

ANIMAL : MOUSE Crj:BDF1
MEASURE. TIME : 1

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (14W)

SEX : MALE

REPORT TYPE : A1

PAGE: 3

oup Name	NO. of Animals	UREA NI mg∕dl	TROGEN	SODIUM mEq∕ l		POTASS1 m Eq /		CHLORIDE m Eq / &		CALCIUM mg/dl		INORGAI mg/dl	NIC PHOSPHORUS
Control	10	26.5±	4. 2	152±	2	4.7±	0.4	123±	2	8.7±	0.2	6.6±	1.5
1481 ppm	9	27.4±	5.9	152±	2	4.3±	0.5	123±	2	8.9±	0.3	7.2±	0.8
2222 ppm	10	29.0±	4.3	153±	2	4.7±	0.4	123±	2	9.1±	0.3**	7.8±	1.4
3333 ppm	9	30.7±	6.6	152±	2	4.4±	0.3	122±	2	9.1±	0.2*	7.6±	1.5
5000 ppm	10	31.2±	6.3	152±	2	4.3±	0.4	121±	3	9.3±	0.2**	7.3±	1.4
7500 ppm	6	30.4±	4. 1	154±	2	4.1±	0.3*	120±	2	9.1±	0.3*	7.8±	1.1

(HCL074) BAIS 3

APPENDIX F 2

BIOCHEMISTRY: SUMMARY, MOUSE: FEMALE

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1

SEX: FEMALE

REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (14W)

PAGE: 4 Group Name NO. of TOTAL PROTEIN ALBUMIN T-BILIRUBIN TRIGLYCERIDE A/G RATIO GLUCOSE T-CHOLESTEROL Animals g/dl g/dl mg/dl mg/dl mg/dl mg/dl Control 10 $5.1\pm$ 0.1 $3.1\pm$ 0.1 1.7± 0.1 0.19± 0.03 156± 28 71± 5 19± 5 1481 ppm 10 $5.2\pm$ 0.2 $3.3\pm$ 0.1* 1.7± 0.1 0.20 ± 0.04 $181 \pm$ 23 $114\pm$ 7 $28\pm$ 9 2222 ppm 10 $5.3\pm$ 0.2* $3.3\pm$ 0.1 1.7 ± 0.2 0.19 ± 0.04 184± 28 136± 17* 36± 15** 3333 ppm 10 5.2± 0.1 $3.2\pm$ 0.1 1.7± 0.1 0.18 ± 0.02 175± 21 $156\pm$ $37\pm$ 8** 11** 5000 ppm 10 $5.4\pm$ 0.1** $3.2\pm$ 0.1 1.6± 0.1 0.18± 0.01 $182 \pm$ 23 184土 12** $37 \pm$ 10** 7500 ppm 6 $6.0 \pm$ 0.2** 3.7± 0.3** 1.6 ± 0.2 0.27 ± 0.12 $194\pm$ 20 $252\pm$ 19** $27\pm$ 5 Significant difference; $*: P \leq 0.05$ **: $P \leq 0.01$ Test of Dunnett BAIS 3

(HCL074)

ANIMAL : MOUSE Crj:BDF1

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (14W)

MEASURE. TIME : 1

SEX : FEMALE

REPORT TYPE : A1

PAGE: 5

roup Name	NO. of Animals	PHOSPHO mg/dl	LIPID	GOT IU/A	?	GPT IU/A	2	LDH IU/	2	ALP IU/A		G-GTP IU/A		CPK IU/A	!
Control	10	135±	10	54±	7	22±	4	353±	75	256±	28	1±	1	71±	42
1481 ppm	10	214±	16	61±	9	50±	12	368±	131	$245\pm$	25	1±	1	72±	45
2222 ppm	10	248±	24*	73±	15*	67±	28*	391±	76	249±	30	2±	2	78±	29
3333 ppm	10	277±	18**	71±	11*	86±	21**	356±	106	236±	23	2±	1	58±	19
5000 ppm	10	315±	19**	107±	37**	144±	43**	397±	129	258±	29	4 ±	1**	71±	22
7500 ppm	6	420±	36**	96±	33**	164±	50**	492±	67	403±	20**	46±	10**	100±	43

(HCL074) BAIS 3

ANIMAL : MOUSE Crj:BDF1

BIOCHEMISTRY (SUMMARY) ALL ANIMALS (14W)

MEASURE. TIME: 1

SEX : FEMALE

REPORT TYPE : A1

PAGE: 6

oup Name	NO. of Animals	UREA NI mg/dl	TROGEN	SODIUM m Eq / l		POTASS1 m Eq/		CHLORIDE m Eq / l		calciuw mg/dl		INORGAN mg/dl	VIC PHOSPHORUS
Control	10	19.1±	2. 6	153±	1	5.0±	0.5	124±	1	8.5±	0.4	6.5±	0.9
1481 ppm	10	20.8±	2.5	$152\pm$	2	4.4±	0.4**	124±	2	8.8±	0.3	6.1±	0.6
2222 ppm	10	20.9±	2.4	153±	3	4.6±	0.7	123±	3	8.9±	0.3	6.7±	1. 3
3333 ppm	10	19.9±	1.3	152±	2	4.1±	0.3**	122±	2*	9.0±	0.1*	6.0±	0.6
5000 ppm	10	23.0±	3, 0**	151±	1	4.1±	0.3**	121±	2**	9.1±	0.2**	5.8±	0.7
7500 ppm	6	29.3±	4.1**	150±	2*	4.4±	0.5*	116±	2**	9.3±	0.3**	6.0±	2. 0

(HCL074)

APPENDIX G 1

URINALYSIS: SUMMARY, MOUSE: MALE

URINALYSIS

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : A1

Group Name NO. of pH_ Protein_ Glucose___ Ketone body Occult blood Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI $-\pm +2+3+4+$ CHI $-\pm + 2+ 3+ 4+$ CHI $-\pm + 2 + 3 + 4 + CHI$ - \pm + 2+ 3+ CHI Control 10 2 0 0 7 3 0 0 10 0 0 0 0 0 6 4 0 0 0 0 10 0 0 0 0 1481 ppm 9 0 0 9 0 0 0 4 5 0 * 9 0 0 0 0 0 6 3 0 0 0 0 9 0 0 0 0 2222 ppm 10 3 5 0 0 9 1 0 0 10 0 0 0 0 0 6 4 0 0 0 0 10 0 0 0 0 3333 ppm 9 1 8 0 0 0 0 * 0 2 7 0 0 0 9 0 0 0 0 0 9 0 0 0 0 5000 ppm 10 1 6 3 0 1 9 0 0 0 10 0 0 0 0 0 5 5 0 0 0 0 10 0 0 0 0 7500 ppm 6 0 2 2 1 1 0 0 3 3 0 0 0 * 6 0 0 0 0 0 5 1 0 0 0 0 6 0 0 0 0 Significant difference ; $*: P \le 0.05$ ** : $P \leq 0.01$ Test of CHI SQUARE

(HCL101) BAIS 3

URINALYSIS

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1

SEX : MALE

REPORT TYPE : A1

PAGE: 2 NO. of Group Name Urobilinogen \pm + 2+ 3+ 4+ CHI Animals Control 10 10 0 0 0 0 1481 ppm 9 9 0 0 0 0 2222 ppm 10 10 0 0 0 0 3333 ppm 9 9 0 0 0 0 5000 ppm 10 10 0 0 0 0 7500 ppm 6 6 0 0 0 0 Significant difference ; $*: P \leq 0.05$ **: $P \leq 0.01$ Test of CHI SQUARE

(HCL101)

APPENDIX G 2

URINALYSIS: SUMMARY, MOUSE: FEMALE

URINALYSIS ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1

SEX : FEMALE

REPORT TYPE : A1

Group Name NO. of Protein_ Glucose_ Ketone body Occult blood Animals 5.0 6.0 6.5 7.0 7.5 8.0 8.5 CHI $-\pm + 2+ 3+ 4+$ CHI $-\pm +2+3+4+$ CHI $-\pm + 2 + 3 + 4 + CHI$ $- \pm + 2 + 3 +$ CHI Control 10 5 0 1 9 0 0 0 10 0 0 0 0 0 1 9 0 0 0 0 10 0 0 0 0 1481 ppm 10 0 1 1 6 2 0 5 5 0 0 0 10 0 0 0 0 0 5 5 0 0 0 0 10 0 0 0 0 2222 ppm 10 1 5 0 4 6 0 0 0 10 0 0 0 0 0 4 6 0 0 0 0 10 0 0 0 0 3333 ppm 10 3 3 0 6 4 0 0 0 * 10 0 0 0 0 0 3 7 0 0 0 0 10 0 0 0 0 5000 ppm 10 5 5 0 0 5 5 0 0 0 10 0 0 0 0 0 4 6 0 0 0 0 10 0 0 0 0 7500 ppm 6 . 0 1 1 3 1 0 4 2 0 0 0 * 6 0 0 0 0 0 1 5 0 0 0 0 6 0 0 0 0

PAGE: 3

Significant difference : $*: P \leq 0.05$ ** : $P \leq 0.01$ Test of CHI SQUARE

(HCL101) BAIS 3

URINALYSIS

ANIMAL : MOUSE Crj:BDF1

MEASURE. TIME: 1

SEX : FEMALE

REPORT TYPE : A1

PAGE: 4 Group Name NO. of Urobilinogen Animals \pm + 2+ 3+ 4+ CHI Control 10 10 0 0 0 0 1481 ppm 10 10 0 0 0 0 2222 ppm 10 10 0 0 0 0 3333 ppm 10 10 0 0 0 0 5000 ppm 10 10 0 0 0 0 7500 ppm 6 6 0 0 0 0 Significant difference ; $*: P \le 0.05$ **: $P \leq 0.01$ Test of CHI SQUARE (HCL101)

APPENDIX H 1

GROSS FINDINGS: SUMMARY, MOUSE: MALE ALL ANIMALS

ANIMAL : MOUSE Crj:BDF1

GROSS FINDINGS (SUMMARY) ALL ANIMALS (0- 14W)

REPORT TYPE : A1

SEX : MALE

PAGE: 1

Organ	Findings	Group Name Control NO. of Animals 10 (%)	1481 ppm 9 (%)	2222 ppm 10 (%)	3333 ppm 10 (%)
thymus	atrophic	0 (0)	0 (0)	0 (0)	1 (10)
spleen	black zone	2 (20)	1 (11)	0 (0)	0 (0)
liver	white zone	2 (20)	1 (11)	3 (30)	3 (30)
	nodule	0 (0)	0 (0)	0 (0)	1 (10)
kidney	hydronephrosis	1 (10)	1 (11)	0 (0)	0 (0)
kidney	hydronephrosis	1 (10)	1 (11)	0 (0)	0
					TAC

(HPT080)

ANIMAL : MOUSE Crj:BDF1

GROSS FINDINGS (SUMMARY)

ALL ANIMALS (0- 14W)

REPORT TYPE : A1

SEX : MALE

Organ	Findings	Group Name 5000 ppm NO. of Animals 10 (%)	7500 ppm 10 (%)	
thymus	atrophic	0 (0)	3 (30)	
spleen	black zone	0 (0)	0 (0)	
liver	white zone	6 (60)	3 (30)	
	nodule	0 (0)	0 (0)	
kidney	hydronephrosis	1 (10)	0 (0)	
(HPT080)				RAIS 3

(HPT080)

BAIS 3

APPENDIX H 2

GROSS FINDINGS: SUMMARY, MOUSE: FEMALE ALL ANIMALS

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1

GROSS FINDINGS (SUMMARY) ALL ANIMALS (0- 14W)

SEX : FEMALE

Organ	Findings	Group Name Control NO. of Animals 10 (%)	1481 ppm 10 (%)	2222 ppm 10 (%)	3333 ppm 10 (%)
thymus	atrophic	0 (0)	0 (0)	0 (0)	0 (0)
stomach	ulcer	0 (0)	0 (0)	0 (0)	0 (0)
(HPT080)		``			BAI

ANIMAL : MOUSE Crj:BDF1

GROSS FINDINGS (SUMMARY) ALL ANIMALS (0- 14W)

REPORT TYPE : A1

SEX : FEMALE

Organ	Findings	Group Name NO. of Animals	5000 ppm 10 (%)	7500 ppm 10 (%)	
thymus	atrophic		0 (0)	3 (30)	
stomach	ulcər		0 (0)	1 (10)	
(HPT080)					BAIS 3

APPENDIX H 3

GROSS FINDINGS: SUMMARY, MOUSE: MALE

DEAD AND MORIBUND ANIMALS

ANIMAL : MOUSE Crj:BDF1

GROSS FINDINGS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 14W)

REPORT TYPE : A1

SEX : MALE

Organ	Findings	Group Name NO. of Animals	Control 0 (%)	1481 ppm 0 (%)	2222 ppm 0 (%)	3333 ppm 1 (%)
thymus	atrophic		- (-)	- (-)	- (-)	1 (100)
(HPT080)						BAI

GROSS FINDINGS (SUMMARY)

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : MALE DEAD AND MORIBUND ANIMALS (0- 14W)

SEX	: MALE				PAGE : 2
Organ	Findings	Group Name NO. of Animals	5000 ppm 0 (%)	7500 ppm 4 (%)	
thymus	atrophic		- (-)	3 (75)	
(HPT080)					BAIS 3

APPENDIX H 4

GROSS FINDINGS: SUMMARY, MOUSE: FEMALE

DEAD AND MORIBUND ANIMALS

ANIMAL : MOUSE Crj:BDF1

GROSS FINDINGS (SUMMARY)

REPORT TYPE : A1 SEX : FEMALE DEAD AND MORIBUND ANIMALS (0- 14W)

rgan	Findings	Group Name NO. of Animals	Control 0 (%)	1481 ppm 0 (%)	2222 ppm 0 (%)	3333 ppm 0 (%)
ymus	atrophic		- (-)	- (-)	- (-)	- (-)
tomach	ulcer		- (-)	- (-)	- (-)	- (-)

ANIMAL : MOUSE Crj:BDF1

GROSS FINDINGS (SUMMARY)

REPORT TYPE : A1

SEX : FEMALE

DEAD AND MORIBUND ANIMALS (0- 14W)

Organ	Findings	Group Name NO. of Animals	5000 ppm 0 (%)	7500 ppm 4 (%)	
thymus	atrophic		- (-)	3 (75)	
stomach	ulcer		- (-)	1 (25)	
(HPT080)					BAIS 3

APPENDIX H 5

GROSS FINDINGS: SUMMARY, MOUSE: MALE

SACRIFICED ANIMALS

ANIMAL : MOUSE Crj:BDF1

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (14W)

REPORT TYPE : A1

SEX : MALE

PAGE: 1

Group Name Control NO. of Animals 10 (%)	1481 ppm 9 (%)	2222 ppm 10 (%)	3333 ppm 9 (%)
2 (20)	1 (11)	0 (0)	0 (0)
2 (20)	1 (11)	3 (30)	3 (33)
0 (0)	0 (0)	0 (0)	1 (11)
1 (10)	1 (11)	0 (0)	0 (0)
1 (10)	1 (11)	0 (0)	0
	NO. of Animals 10 (%) 2 (20) 2 (20) 0 (0)	NO. of Animals 10 (%) 9 (%) 2 (20) 1 (11) 2 (20) 1 (11) 0 (0) 0 (0)	NO. of Animals 10 (%) 9 (%) 10 (%) 2 (20) 1 (11) 0 (0) 2 (20) 1 (11) 3 (30) 0 (0) 0 (0) 0 (0)

(HPT080)

: MOUSE Crj:BDF1 ANIMAL

GROSS FINDINGS (SUMMARY) SACRIFICED ANIMALS (14W)

REPORT TYPE : A1 SEX : MALE

5000 ppm 7500 ppm Group Name 10 (%) 6 (%) Organ___ Findings_ NO. of Animals 0 (0) 0 (0) spleen black zone 6 (60) liver white zone 3 (50) nodule 0 (0) 0 (0) kidney hydronephrosis 1 (10) 0 (0) (HPT080) BAIS 3

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 (14W)

PAGE: 1

												
10	27.4±	1. 3	0.039±	0.006	0.005±	0.002	0.007±	0.002	0.012±	0.003	0.108±	0.007
9	27.1±	1.9	0.037±	0.006	0.005±	0.002	0.006±	0.003	0.012±	0.005	0.109±	0.014
10	27.1±	1.7	0.035±	0.008	0.006±	0.003	0.006±	0.002	0.012±	0.004	0.109±	0.011
9	26.9±	1.6	0.040±	0.005	0.006±	0.003	0.006±	0.001	0.012±	0.004	0.115±	0,006
10	25.9±	1.2	0.035±	0.006	0.006±	0.002	0.005±	0.002	0.011±	0.003	0.103±	0.011
6	17.9±	2. 2**	0.031±	0.014	0.005±	0.001	0.005±	0.002	0.010±	0.003	0.056±	0.011**
_	9 10 9 10	9 27. $1\pm$ 10 27. $1\pm$ 9 26. $9\pm$ 10 25. $9\pm$	9 27.1± 1.9 10 27.1± 1.7 9 26.9± 1.6 10 25.9± 1.2	9 27.1± 1.9 0.037± 10 27.1± 1.7 0.035± 9 26.9± 1.6 0.040± 10 25.9± 1.2 0.035±	9 27.1 \pm 1.9 0.037 \pm 0.006 10 27.1 \pm 1.7 0.035 \pm 0.008 9 26.9 \pm 1.6 0.040 \pm 0.005 10 25.9 \pm 1.2 0.035 \pm 0.006	9 27.1± 1.9 0.037± 0.006 0.005± 10 27.1± 1.7 0.035± 0.008 0.006± 9 26.9± 1.6 0.040± 0.005 0.006± 10 25.9± 1.2 0.035± 0.006 0.006±	9 27.1 \pm 1.9 0.037 \pm 0.006 0.005 \pm 0.002 10 27.1 \pm 1.7 0.035 \pm 0.008 0.006 \pm 0.003 9 26.9 \pm 1.6 0.040 \pm 0.005 0.006 \pm 0.003 10 25.9 \pm 1.2 0.035 \pm 0.006 0.006 \pm 0.002	9 27.1± 1.9 0.037± 0.006 0.005± 0.002 0.006± 10 27.1± 1.7 0.035± 0.008 0.006± 0.003 0.006± 9 26.9± 1.6 0.040± 0.005 0.006± 0.003 0.006± 10 25.9± 1.2 0.035± 0.006 0.006± 0.002 0.005±	9 27.1± 1.9 0.037± 0.006 0.005± 0.002 0.006± 0.003 10 27.1± 1.7 0.035± 0.008 0.006± 0.003 0.006± 0.002 9 26.9± 1.6 0.040± 0.005 0.006± 0.003 0.006± 0.001 10 25.9± 1.2 0.035± 0.006 0.006± 0.002 0.005± 0.002	9 27.1± 1.9 0.037± 0.006 0.005± 0.002 0.006± 0.003 0.012± 10 27.1± 1.7 0.035± 0.008 0.006± 0.003 0.006± 0.002 0.012± 9 26.9± 1.6 0.040± 0.005 0.006± 0.003 0.006± 0.001 0.012± 10 25.9± 1.2 0.035± 0.006 0.006± 0.002 0.005± 0.002 0.011±	9 27.1± 1.9 0.037± 0.006 0.005± 0.002 0.006± 0.003 0.012± 0.005 10 27.1± 1.7 0.035± 0.008 0.006± 0.003 0.006± 0.002 0.012± 0.004 9 26.9± 1.6 0.040± 0.005 0.006± 0.003 0.006± 0.001 0.012± 0.004 10 25.9± 1.2 0.035± 0.006 0.006± 0.002 0.005± 0.002 0.011± 0.003	9 27.1± 1.9 0.037± 0.006 0.005± 0.002 0.006± 0.003 0.012± 0.005 0.109± 10 27.1± 1.7 0.035± 0.008 0.006± 0.003 0.006± 0.002 0.012± 0.004 0.109± 9 26.9± 1.6 0.040± 0.005 0.006± 0.003 0.006± 0.001 0.012± 0.004 0.115± 10 25.9± 1.2 0.035± 0.006 0.006± 0.002 0.005± 0.002 0.011± 0.003 0.103±

(HCL040)

STUDY NO. : 0302

ANIMAL : MOUSE Crj:BDF1

ORGAN WEIGHT: ABSOLUTE (SUMMARY)

SURVIVAL ANIMALS (14W)

REPORT TYPE : A1

SEX : MALE UNIT: g PAGE : 2

roup Name	NO. of Animals	TES	ris L	TES'	res	HEA	RT	LUN	G R	LUN	G L	LUN	GS
Control	10	0.113±	0.009	0.221±	0.016	0.147±	0.016	0.100±	0.006	0.051±	0.004	0.151±	0.009
1481 ppm	9	0.111±	0.011	0.220±	0. 025	0.148±	0.011	0.105±	0.008	0.053±	0.004	0.158±	0.010
2222 ppm	10	0.112±	0.010	0.221±	0.020	0.152±	0.008	0.108±	0.005	0.054±	0.006	0.162±	0.009
3333 ppm	9	0.113±	0.008	0.228±	0.014	0.144±	0.010	0.103±	0.010	0.054±	0.004	0.156±	0.012
5000 ppm	10	0.104±	0. 011	0.207±	0.022	0.143±	0.009	0.104±	0.009	0.052±	0.006	0.156±	0.014
7500 ppm	6	0.055±	0.009**	0.110±	0.019**	0.105±	0.012**	0.085±	0.005**	0.044±	0.005*	0.130±	0.006**

(HCL040) BAIS 3

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : MALE UNIT: g ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (14W)

PAGE: 3

roup Name	NO. of Animals	KID	NEY R	KIDI	NEY L	KID	NEYS	SPL	EEN	LIV	ER	BRA	IN
Control	10	0.251±	0. 128	0.211±	0. 025	0.462±	0. 148	0.047±	0.006	1.054±	0. 066	0.434±	0.016
1481 ppm	9	0.326±	0.308	0.231±	0.044	0.557±	0. 350	0.052±	0.009	1.359±	0.099**	0.442±	0.014
2222 ppm	10	0.228±	0.019	0.222±	0.016	0.449±	0.035	0.056±	0.006	1.459 \pm	0.132**	0.447±	0.013
3333 ppm	9	0.226±	0.013	0.224±	0.009	0.450±	0. 017	0.065±	0.017**	1.704±	0.145**	0.429±	0.016
5000 ppm	10	0.232±	0.020	0.271±	0. 153	0.503±	0. 172	0.072±	0.017**	1.880±	0.120**	0.428±	0. 024
7500 ppm	6	0.159±	0.024	0.158±	0.026	0.317±	0.050	0.050±	0.017	1.587±	0. 195**	0.380±	0.012**

(HCL040)

APPENDIX I 2

ORGAN WEIGHT, ABSOLUTE: SUMMARY, MOUSE: FEMALE

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : FEMALE UNIT: g ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (14W)

PAGE: 4

NO. of Animals	Body Weight	THYMUS	ADRENL R	ADRENL L	ADRENALS	OVARY R	
10	20.8± 0.8	0.047± 0.005	0.006± 0.001	0.007± 0.001	0.013± 0.002	0.014± 0.003	
10	21.5± 1.0	0.043± 0.007	0.007± 0.001	0.007± 0.001	0.014± 0.002	0.013± 0.002	
10	21.9± 0.7	0.046± 0.006	0.007± 0.001	0.007± 0.001	0.014± 0.002	0.013± 0.002	
10	22.3± 1.4**	0.046± 0.004	0.007± 0.001	0.008± 0.002	0.015± 0.003	0.013± 0.001	
10	21.6± 0.7	0.046± 0.006	0.006± 0.002	0.007± 0.002	0.014± 0.004	0.013± 0.002	
6	17.2± 1.5**	0.044± 0.017	0.005± 0.003	0.005± 0.002	0.011± 0.004	0.010± 0.003	
	10 10 10 10 10 10	10 20.8± 0.8 10 21.5± 1.0 10 21.9± 0.7 10 22.3± 1.4** 10 21.6± 0.7	Animals 10	Animals 10	Animals 10	10 20.8± 0.8 0.047± 0.005 0.006± 0.001 0.007± 0.001 0.013± 0.002 10 21.5± 1.0 0.043± 0.007 0.007± 0.001 0.007± 0.001 0.014± 0.002 10 21.9± 0.7 0.046± 0.006 0.007± 0.001 0.007± 0.001 0.014± 0.002 10 22.3± 1.4** 0.046± 0.004 0.007± 0.001 0.008± 0.002 0.015± 0.003 10 21.6± 0.7 0.046± 0.006 0.006± 0.002 0.007± 0.002 0.014± 0.004	10

(HCL040)

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : FEMALE UNIT: g ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (14W)

PAGE: 5

Group Name	NO. of Animals	OVA	RY L	OVAI	RIES	HEA	RT	LUN	G R	LUNG	3 L	LUN	GS
Control	10	0.015±	0.003	0.029±	0.005	0.121±	0.006	0.096±	0.006	0.049±	0.003	0.145±	0.007
1481 ppm	10	0.015±	0.001	0.028±	0.003	0.125±	0.008	0.097±	0.006	0.050±	0.003	0.147±	0. 007
2222 ppm	10	0.013±	0.002	0.026±	0.003	0.129±	0.009	0.100±	0.007	0.051±	0.004	0.151±	0.007
3333 ppm	10	0.015±	0.002	0.028±	0.003	0.124±	0.007	0.107±	0.009**	0.049±	0.003	0.155±	0.010*
5000 ppm	10	0.014±	0.002	0.027±	0.003	0.129±	0.007	0.097±	0.006	0.049±	0.003	0.146±	0.008
7500 ppm	6	0.009±	0.003**	0.019±	0.006**	0.096±	0.007**	0.083±	0.007**	0.044±	0.005*	0.127±	0.010**

(HCL040)

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : FEMALE UNIT: g ORGAN WEIGHT: ABSOLUTE (SUMMARY) SURVIVAL ANIMALS (14W)

PAGE: 6

oup Name	up Name NO. of Animals		KIDNEY R		KIDNEY L		KIDNEYS		SPLEEN		LIVER		IN
Control	10	0.148±	0.009	0. 143±	0.008	0.291±	0.013	0.050±	0,003	0.858±	0.044	0.452±	0.024
1481 ppm	10	0.157±	0.008	0.154±	0.005**	0.311±	0.009*	0.057±	0. 005	1.093±	0.048	0.442±	0.014
2222 ppm	10	0.165±	0.011**	0.156±	0.006**	0.321±	0.015**	0.063±	0.005*	1.231±	0.057*	0.442±	0.015
3333 ppm	10	0.166±	0.012**	0.163±	0.006**	0.329±	0. 016**	0.068±	0.004**	1.415±	0.107**	0.437±	0. 023
5000 ppm	10	0.167±	0.011**	0.163±	0.006**	0.329±	0.016**	0.077±	0.007**	1.600±	0.108**	0.434±	0. 017
7500 ppm	6	0.132±	0.012*	0.127±	0.013**	0.259±	0.024**	0.054±	0.014	1.573±	0.108**	0.386±	0.009**

(HCL040)

APPENDIX J 1

ORGAN WEIGHT, RELATIVE: SUMMARY, MOUSE: MALE

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : MALE UNIT: % ORGAN WEIGHT: RELATIVE (SUMMARY) SURVIVAL ANIMALS (14W)

PAGE: 1

0.143± 0.019 0.138± 0.020		0.024± 0.006	0.042± 0.010	0.395± 0.022	
0.138± 0.020	0.020± 0.008	0.000 0.010			
		0.022± 0.010	0.043± 0.018	0.403± 0.048	
0.130± 0.029	0.023± 0.009	0.020± 0.007	0.043± 0.014	0.403± 0.034	
0.149± 0.020	0.022± 0.009	0.021± 0.004	0.043± 0.012	0.429± 0.037	
0.136± 0.020	0.022± 0.008	0.020± 0.007	0.042± 0.013	0.400± 0.052	
3** 0.167± 0.062	0.027± 0.005	0.026± 0.010	0.053± 0.009	0.308± 0.042**	

(HCL042)

ANIMAL : MOUSE Crj:BDF1 REPORT TYPE : A1

SEX : MALE UNIT: %

ORGAN WEIGHT: RELATIVE (SUMMARY) SURVIVAL ANIMALS (14W)

PAGE: 2

Group Name	NO. of Animals	TESTIS L	TESTES	HEART	LUNG R	LUNG L	LUNGS
Control	10	0.412± 0.030	0.807± 0.049	0.536± 0.050	0.366± 0.021	0.186± 0.012	0.552± 0.028
1481 ppm	9	0.409± 0.042	0.813± 0.090	0.546± 0.038	0.389± 0.023	0.196± 0.019	0.585± 0.037
2222 ppm	10	0.413± 0.035	0.816± 0.067	0.561± 0.030	0.401± 0.028*	0.200± 0.027	0.602± 0.050
3333 ppm	9	0.422± 0.042	0.851± 0.078	0.536± 0.042	0.383± 0.045	0.200± 0.021	0.583± 0.060
5000 ppm	10	0.404± 0.046	0.804± 0.098	0.554± 0.036	0.404± 0.037*	0.200± 0.020	0.604± 0.052
7500 ppm	6	0.304± 0.025**	0.612± 0.066**	0.586± 0.031	0.482± 0.066**	0.248± 0.027**	0.730± 0.080**
Significant	t difference ;	*: P ≤ 0.05 **:	P ≤ 0.01	Tes	st of Dunnett		

(HCL042)

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : MALE UNIT: % ORGAN WEIGHT: RELATIVE (SUMMARY) SURVIVAL ANIMALS (14W)

PAGE: 3

oup Name	NO. of Animals	KIDNEY R	KIDNEY L	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.916± 0.479	0.770± 0.087	1.685± 0.554	0.171± 0.024	3.843± 0.201	1.583± 0.078
1481 ppm	9	1.215± 1.176	0.854± 0.165	2.069± 1.340	0.193± 0.027	5.021± 0.194**	1.640± 0.122
2222 ppm	10	0.841 ± 0.050	0.821± 0.048	1.662± 0.094	0.206± 0.019*	5.394± 0.365**	1.657± 0.102
3333 ppm	9	0.842± 0.030	0.838± 0.060	1.680± 0.077*	0.243± 0.068**	6.342± 0.311**	1.603± 0.127
5000 ppm	10	0.901± 0.116**	1.070± 0.691**	1.971± 0.803**	0.279± 0.080**	7.275± 0.360**	1.658± 0.111
7500 ppm	6	0.886± 0.043**	0.876± 0.063**	1.762± 0.097**	0.270± 0.065**	8.849± 0.246**	2.137± 0.209**

(HCL042)

APPENDIX J 2

ORGAN WEIGHT, RELATIVE: SUMMARY, MOUSE: FEMALE

(13-WEEK STUDY)

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : FEMALE UNIT: %

ORGAN WEIGHT: RELATIVE (SUMMARY) SURVIVAL ANIMALS (14W)

PAG

GΕ	
UC	

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENL R	ADRENL L	ADRENALS	OVARY R	
Control	10	20.8± 0.8	0.224± 0.020	0.030± 0.007	0.032± 0.006	0.062± 0.009	0.066± 0.015	
1481 ppm	10	21.5± 1.0	0.202± 0.034	0.031± 0.007	0.035± 0.006	0.065± 0.010	0.062± 0.008	
2222 ppm	10	21.9± 0.7	0.212± 0.023	0.031± 0.006	0.031± 0.005	0.062± 0.008	0.060± 0.011	
3333 ppm	10	22.3± 1.4**	0.207± 0.020	0.031± 0.005	0.036± 0.009	0.067± 0.012	0.060± 0.008	
5000 ppm	10	21.6± 0.7	0.213± 0.026	0.029± 0.007	0.034± 0.010	0.063± 0.016	0.062± 0.010	
7500 ppm	6	17.2± 1.5**	0.251 ± 0.084	0.030± 0.014	0.031± 0.010	0.060± 0.019	0.057± 0.012	
Significant	difference;	*: P ≤ 0.05 **	: P ≤ 0.01	Tes	st of Dunnett			

(HCL042)

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : FEMALE UNIT: % ORGAN WEIGHT: RELATIVE (SUMMARY) SURVIVAL ANIMALS (14W)

PAGE: 5

oup Name	NO. of Animals	OVARY L	OVARIES	HEART	LUNG R	LUNG L	LUNGS
Control	10	0.072± 0.012	0.137± 0.019	0.584± 0.036	0.463± 0.031	0.235± 0.017	0.698± 0.044
1481 ppm	10	0.068± 0.007	0.131± 0.013	0.582± 0.042	0.451± 0.038	0.232± 0.016	0.683± 0.049
2222 ppm	10	0.059± 0.010	0.119± 0.015	0,589± 0.049	0.458± 0.038	0.234± 0.020	0.693± 0.043
3333 ppm	10	0.068± 0.012	0.128± 0.016	0.558± 0.036	0.481± 0.052	0.219± 0.016	0.699± 0.064
5000 ppm	10	0.063± 0.010	0.125± 0.013	0.596± 0.042	0.449± 0.029	0.229± 0.015	0.678± 0.038
7500 ppm	6	0.051± 0.017**	0.108± 0.027**	0.561± 0.035	0.485± 0.032	0.254± 0.031	0.739± 0.054

(HCL042)

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1 SEX : FEMALE UNIT: % ORGAN WEIGHT: RELATIVE (SUMMARY)

SURVIVAL ANIMALS (14W)

roup Name	NO. of Animals	KIDNEY R	KIDNEY L	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.711± 0.051	0.689± 0.049	1.399± 0.087	0.240± 0.009	4.125± 0.143	2. 175± 0. 132
1481 ppm	10	0.729± 0.046	0.718± 0.039	1.446± 0.074	0.265± 0.021	5.083± 0.226**	2.056± 0.118
2222 ppm	10	0.755± 0.047	0.714± 0.040	1.469± 0.076	0.285± 0.017**	5.623± 0.198**	2.022± 0.078*
3333 ppm	10	0.743± 0.028	0.733± 0.043	1.476± 0.054	0.305± 0.024**	6.350± 0.307**	1.967± 0.151**
5000 ppm	10	0.771± 0.052*	0.754± 0.027**	1.526± 0.075**	0.358± 0.033**	7.403± 0.396**	2.010± 0.099*
7500 ppm	6	0.769± 0.042	0.736± 0.054	1.506± 0.091*	0.307± 0.060**	9.153± 0.495**	2.251± 0.170

(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)

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1

ALL ANIMALS (0- 14W)

SEX : MALE

Organ	No.	oup Name Control of Animals on Study 10 ade 1/2 3 4 (%) (%) (%) (%)	1481 ppm 9 1 2 3 4 (%) (%) (%) (%)	2222 ppm 10 1 2 3 4 (%) (%) (%) (%)	3333 ppm 10 1 2 3 4 (%) (%) (%) (%)
{Respiratory	system)				
nasal cavit	atrophy:olfactory epithelium	<10> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<pre></pre>	<10> 0 0 0 0 (0) (0) (0) (0)	(10) 0 0 0 0 (0) (0) (0) (0)
{Hematopoieti	ic system}				
thymus	atrophy	<10> 0 0 0 0 0 0 0 0 0 0 0	<pre></pre>	<pre></pre>	<pre></pre>
spleen	atrophy	<10> 0 0 0 0 (0) (0) (0) (0)	(0) (0) (0) (0) (0) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	<pre></pre>
	deposit of hemosiderin	1 1 0 0 (10) (10) (0) (0)	5 1 0 0 (56) (11) (0) (0)	10 0 0 0 *** (100) (0) (0) (0)	9 0 0 0 ***
	increased extramedullary hematopoiesis	0 0 0 0 0 (0) (0)	1 0 0 0 (11) (0) (0) (0)	5 0 0 0 * (50) (0) (0) (0)	7 2 0 0 ***
{Circulatory	system)				
heart	hemorrhage	(10) 0 0 0 0 (0) (0) (0) (0)	<pre></pre>	1 0 0 0 (10) (0) (0) (0)	(10) 0 0 0 0 (0) (0) (0) (0)
Grade <a> b (c) Significant	1: Slight 2: Moderate 3: 1 a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 difference; *: P ≤ 0.05 **: P ≤ 0	Marked 4: Severe			

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0- 14W)

ANIMAL : MOUSE Crj:BDF1 REPORT TYPE : A1

SEX : MALE

Organ	No	roup Name 5000 ppm 2 of Animals on Study 10 2 ade 1 2 3 4 3 (%) (%) (%) (%)	7500 ppm 10 1 2 3 4 (%) (%) (%) (%)	
{Respiratory	system)			
nasal cavit	atrophy:olfactory epithelium	<10> 0 0 0 0 0 0 0 0 0 0 0	6 0 0 0 * (60) (0) (0) (0)	
{Hematopoieti	c system)			
thymus	atrophy	<10> 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<pre></pre>	
spleen	atrophy	(0) (0) (0) (0)	<10> 4 0 0 0 (40) (0) (0) (0)	
	deposit of hemosiderin	10 0 0 0 ** (100) (0) (0) (0)	3 4 0 0 (30) (40) (0) (0)	
	increased extramedullary hematopoiesis	3 7 0 0 *** (30) (70) (0) (0)	2 · 4 0 0 * (20) (40) (0) (0)	
{Circulatory	system}			
heart	hemorrhage	(0) (0) (0) (0)	<10> 0 0 0 0 (0) (0) (0) (0)	
Grade <a> b (c) Significant d	a: Number of animals examined at the siteb: Number of animals with lesionc: b / a * 100			D. Z.O.

(HPT150)

BAIS3

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0- 14W)

ANIMAL : MOUSE Crj:BDF1

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

REPORT TYPE : A1 SEX : MALE

Organ	Findings	Group Name No. of Animals on Study Grade 1 (%)	Control 10 2 3 (%) (%)	4	148 1 2 (%) (%)	31 ppm 9 3 (%)	<u>4</u> (%)	1 (%)	2222 10 2 (%)	3 4 (%) (%)		1 (%)	3333 1 10 2 (%)	3	<u>4</u> (%)
{Digestive s	system)														
stomach	ulcer:forestomach	0 (0)	<10> 0 0 (0) (0)	0 (0)	0 0 (0)		0 (0)	0 (0)	<10) 0 (0) (0 0 0) (0)	(0 (<10> 0 0) (0	0
liver	necrosis:focal	1 (10)	<10> 0 0 (0) (0)	0 (0)	1 0 (11) (0)	9> 0 (0)	0 (0)	2 (20)	<10) 0 (0) (0 0 0) (0)	(:	3 30) (<10> 0 0) (0	0
	necrosis:single coll	1 (10)	0 0	0 (0)	1 0 (11) (0)	0 (0)	0 (0)	3 (30)	0 (0) (0 0	()	8 80) (0 (0 (0 ** 0)
	deposit of crystal	0 (0)	0 0	0 (0)	0 0	0 (0)	0 (0)	5 (50)	0 (0) (0 0	*	9 90) (0 (0 (0 ***
	cytomegaly of hepatocyte:central	0 (0)	0 0	0 (0)	0 9 (0) (100)	0 (0)	0 **	0 (0)	10 (100) (0 0	**	0 (1 10) (:	8 80) (0 ** 0)
	vacuolic change:central	0 (0)	0 0	0 (0)	0 0	0 (0)	0 (0)	0 (0)	0 (0) (0 0	(0 (0	0 (0 0)
{Urinary sys	stem)														
kidney	inflammatory polyp	0 (0)	<10> 1 0 (10) (0)	0 (0)	0 1 (0) (11)		0 (0)	0 (0)	<103 0 (0) (0 0		0 (<10> 0 0) (0	0

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0- 14W)

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1

SEX : MALE

: MALE

0rgan	Findings_	Group Name 5000 ppm No. of Animals on Study 10 Grade 1 2 3 4 (%) (%) (%) (%)	7500 ppm 10 1 2 3 4 (%) (%) (%) (%)	
	1 Indings	\(\(\lambda\)\(\lambda\)\(\lambda\)\(\lambda\)\(\lambda\)		
{Digestive s	system}			
stomach	ulcer:forestomach	<10> 1 0 0 0 (10) (0) (0) (0)	0 0 0 0 (0) (0) (0) (0)	
liver	necrosis:focal	<10> 4 1 0 0 (40) (10) (0) (0)	1 0 0 0 (10) (0) (0) (0)	
	necrosis:single cell	10 0 0 0 *** (100) (0) (0) (0)	10 0 0 0 *** (100) (0) (0) (0)	
	deposit of crystal	10 0 0 0 *** (100) (0) (0) (0)	9 0 0 0 *** (90) (0) (0) (0)	
	cytomegaly of hepatocyte:central	0 1 9 0 ** (0) (10) (90) (0)	1 2 7 0 ** (10) (20) (70) (0)	
	vacuolic change:central	0 0 0 0 0 (0) (0)	0 0 1 0 (0) (10) (0)	
{Urinary sys	stem}			
kidney	inflammatory polyp	<10> 0 1 0 0 0 1 0 0 0 1 0 0 0 10) (0) (0)	(10) 0 0 0 0 (0) (0) (0) (0)	
Grade <a>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)				 DATO

(HPT150)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1

ALL ANIMALS (0- 14W)

PAGE: 5 : MALE Group Name Control 1481 ppm 2222 ppm 3333 ppm 10 No. of Animals on Study 10 9 10 Grade (%) (%) (%) (%) (%) Findings_ (%) (%) (%) {Urinary system} kidnev <10> < 9> <10> <10> 0 0 0 1 0 1 0 0 0 0 0 hydronephrosis 0 (0)(10)(0)(0) (0)(11)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) {Endocrine system} <10> < 9> <10> pituitary <10> 0 0 0 0 0 0 cyst (0)(0)(0)(0) (11) (0) (0) (0) (0)(0)(0)(0) (0)(0)(0)(0) {Reproductive system} testis <10> < 9> <10> <10> germ cell necrosis 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) < 9> epididymis <10> <10> <10> debris of spermatic elements 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) disappear:sperma 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) a : Number of animals examined at the site 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

ANIMAL

: MOUSE Crj:BDF1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0- 14W)

REPORT TYPE : A1

SEA	· MALE				P
		Group Name	5000 ppm	7500 ppm	

	No. of Animals on	Study	1	0				0	
	Grade	_1	2	3	4_	_1_	2	3	4
Organ Findings		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

{Urinary system}

{Endocrine system}

{Reproductive system}

epididymis <10> <10> debris of spermatic elements 0 0 6 4 0 0 ** (0)(0)(0)(0) (60) (40) (0) (0)

> disappear:sperma 1 0 0 0 0 0 6 0* (0)(0)(60)(0) (10) (0) (0) (0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

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

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

(HPT150)

BAIS3

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- 14W)

STUDY NO. : 0302 ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1

: FEMALE

PAGE: 7

		roup Name o. of Animals on Study		ontrol			1481 10	ppm			2	222 p	pm				333 1	3 ppr	1	
Organ		rade(9	. 2	(%)	(%)	(%)	(%)	(%)	<u>4</u> (%)	<u>1</u> (%)	(%		3 %)	(%)	-	<u>1</u> (%)	(%)	(%)	(<u>4</u> (%)
{Respiratory	system}																			
nasal cavit	eosinophilic change:respiratory epithel	ium (0 (0)	0 (0)	0 (0)	<10 0 (0) ()> 0 (0)	0 (0)	0 (0)	0	<10>	0 0) (0 0)	(0 0) (0	0 (0)		0 0)
	atrophy:olfactory epithelium		0 0	0 (0)	0 (0)	0 (0)	0 (0) (0 (0)	0 (0)	0 (0)	0) (0 0) (0		0 0) (0	0 (0)		0 0)
lung	congestion			0 (0)	0 (0)	0 (0)	<10 0 (0) (0	0 (0)	0 (0)	0	<10>	0 0) (0 0)	(0 0) (0	(0) (0)		0 0)
	bronchiolar—alveolar cell hyperplasia		0 0	0 (0)	0 (0)	0 (0)	0 (0) (0 (0)	0 (0)	0 (0)	0)) (0 0) (0	(0 0)	(0)		0
(Hematopoleti	c system}																			
thymus	atrophy		(;) 0)) (0)		0 (0)	0 (0)	<10 0 (0) (Ω	0 (0)	0 (0)	0	<10>	0 0) (0	(0 0) (0	.0> 0 (0)		0 0)
spleen	atrophy		(1 (0) (0)		0 (0)	0 (0)	<10 0 (0)	0	0 (0)	0 (0)	0	<10>	0 0) (0 0)		0 0) (0	(0)		0 0)
Grade <a>> b <c) c)="" d<="" significant="" td=""><td>a: Number of animals examined at the sitb: Number of animals with lesionc: b / a * 100</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></c)>	a: Number of animals examined at the sitb: Number of animals with lesionc: b / a * 100																			

(HPT150)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0- 14W)

ANIMAL : MOUSE Crj:BDF1 REPORT TYPE : A1

SEX : FEMALE PAGE: 8

Organ		Group Name No. of Animals on Study Grade	5000 ppm 10 2 3 (%) (%)	<u>4</u> (%)	7500 pp. 10 1 2 3 (%) (%) (%	3 4	
{Respiratory	system}						
nasal cavit	eosinophilic change:respiratory epithe		<10> 0 0 0) (0) (0 (0)	1 0 0 (10) (0) (0		
	atrophy:olfactory epithelium	(0) (0 0	0 (0)	2 0 0 (20) (0) (0)		
lung	congestion	(0) (<10> 0 0 0) (0) (3 0 0 (30) (0) (0		
	bronchiolar-alveolar cell hyperplasia	2 (20) (0 0 0 0 0	0 (0)	0 0 0 0 (0) (0)	0 0 0) (0)	
{Hematopoiet	cic system}						
thymus	atrophy	0 (0) (<10> 0 0 0) (0) (0 (0)	7> 1 0 0 (14) (0) (0		
spleen	atrophy	0 (0) (<10> 0 0 0) (0) (0 (0)	<10> 2 2 0 (20) (20) (0		
Grade <a>a> b (c) Significant	1: Slight 2: Modorate 3 a: Number of animals examined at the si b: Number of animals with lesion c: b / a * 100 difference; *: P ≤ 0.05 **: P ≤						
(HPT150)							BAIS3

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0- 14\)

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1

SEX : FEMALE

	Ne	roup Name Control o. of Animals on Study 10	1481 ppm 10	2222 ppm 10	3333 ppm 10
Organ	Gi Findings	rade <u>1 2 3 4</u> (%) (%) (%) (9)		1 2 3 4 (%) (%) (%) (%)	1 2 3 4 (%) (%) (%) (%)
{Hematopoie	etic system)				
spleen	congestion	<10> 0 0 0 0 ((0) (0) (0) ((<10> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	(10) 0 0 0 0 (0) (0) (0) (0)
	deposit of hemosiderin	0 0 0 0 (7 0 0 0 *** (70) (0) (0) (0)	10 0 0 0 *** (100) (0) (0) (0)
	increased extramedullary hematopoiesis	0 0 0 0 (4 0 0 0 0 (40) (0) (0)	10 0 0 0 ***
{Digestive	system)				
stomach	ulcer:forestomach	<10> 0 0 0 0 (0) (0) (0) (0		<10> 0 0 0 0 0 0 0 0 0 0 0 0 0	(10) 0 0 0 0 (0) (0) (0) (0)
liver	necrosis:single cell	(0) (0) (0) (0		4 0 0 0 (40) (0) (0) (0)	(10) (0) (0) (0) (0)
	deposit of crystal	0 0 0 0 (10 0 0 0 ** (100) (0) (0) (0)	10 0 0 0 *** (100) (0) (0) (0)
Grade <a>> b (c) Significant	1: Slight 2: Moderate 3: 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				

(HPT150)

BAIS3

0302

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0- 14W)

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1

: FEMALE

PAGE: 10

Organ	Group No. oi Grade Findings	Name 5000 ppm F Animals on Study 10 1 2 3 4 (%) (%) (%) (%)	7500 ppm 10 1 2 3 4 (%) (%) (%)	
{Hematopoie	etic system}			
spleen	congestion	0 0 0 0 (0) (0) (0) (0)	1 0 0 0 (10) (0) (0) (0)	
	deposit of hemosiderin	10 0 0 0 *** (100) (0) (0) (0)	8 0 0 0 ** (80) (0) (0) (0)	
	increased extramedullary hematopoiesis	8 2 0 0 *** (80) (20) (0) (0)	1 4 0 0 * (10) (40) (0) (0)	
{Digestive	system)			
stomach	ulcer:forestomach	<10> 0 0 0 0 0 0 0 0 0 0 0	1 0 0 0 (10) (0) (0) (0)	
liver	necrosis:single cell	<10> 10 0 0 0 *** (100) (0) (0) (0)	<10> 6 0 0 0 * (60) (0) (0) (0)	
	deposit of crystal	10 0 0 0 *** (100) (0) (0) (0)	9 0 0 0 ** (90) (0) (0) (0)	
Grade (a) b (c) Significant	1: Slight 2: Moderate 3: Mark a: Number of animals examined at the site b: Number of animals with lesion c: b / a * 100 c difference; *: P ≤ 0.05 **: P ≤ 0.01	Ked 4: Severe Test of Chi Square		

(HPT150)

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0- 14W)

ANIMAL : MOUSE Crj:BDF1 REPORT TYPE : A1

SEX : FEMALE

PAGE: 11

Organ	Findings	Group Name No. of Animals on Study Grade 1 (%)	Control 10 2 3 (%) (%)	<u>4</u> (%)	1 (%)		3	<u>4</u> %)	<u>1</u> (%)	2222 10 2 (%)	2 ppm) 3 (%)	<u>4</u> (%)		1 (%)		33 ppm 10 3 (%)	<u>4</u> (%)
{Digestive	system)																
liver	cytomegaly of hepatocyte:central	0 (0) (<10> 0 0 0) (0) (0	10 (100) (0 ** 0)	5 (50)	<10 5 (50)	0	0 ** (0)	(0	4	10> 6 (60)	0 **
	vacuolic change:central	0 (0) (0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	0 0)	0 (0) (0 (0 0) (0 0)	0 (0)	0	0	0 (0)	(0	0	0 (0)	0 (0)
{Nervous s	vstem)																
brain	hemorrhage	0 (0) (<10> 0 0 0) (0) (0	0 (0) (<10> 0 0) (0 0) (0 0)	0 (0)	<10 0 (0)	0	0	(0	0	10> 0 (0)	0 (0)
Grade <a>b (c) Significan	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															
(HPT150)		-			·										—		BA

ANIMAL : MOUSE Crj:BDF1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ALL ANIMALS (0- 14W)

REPORT TYPE : A1

SEX : FEMALE PAGE: 12

Organ	Findings	Group Name 5000 ppm No. of Animals on Study 10 Grade 1 2 3 4 (%) (%) (%) (%)	7500 ppm 10 1 2 3 4 (%) (%) (%) (%)	
{Digestive s	system)			
liver	cytomegaly of hepatocyte:central	<10> 0 0 10 0 ** (0) (0) (100) (0)	<10> 1 2 7 0 *** (10) (20) (70) (0)	
	vacuolic change:central	0 0 0 0 0 (0) (0)	1 0 0 0 (10) (0) (0) (0)	
{Nervous sys	etem)			
brain	hemorrhage	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 b: Number of animals with lesion c: b / a * 100 difference; *: P ≤ 0.05 **: P			

(HPT150)

APPENDIX K 3

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY

MOUSE: MALE: DEAD AND MORIBUND ANIMALS

(13-WEEK STUDY)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1

DEAD AND MORIBUND ANIMALS (0- 14W)

: MALE				PAGE :
	No. of Animals on Study 0	1481 ppm 0 1 2 3 4 (%) (%) (%) (%)	2222 ppm 0 1 2 3 4 (%) (%) (%) (%)	3333 ppm 1 2 3 4 (%) (%) (%) (%)
system}				
atrophy:olfactory epithelium	< 0> (-) (-) (-) (-)	< 0> (-) (-) (-) (-)	(-) (-) (-)	0 0 0 0 0 (0) (0)
ic system}				
atrophy	< 0> (-) (-) (-) (-)	< 0> (-) (-) (-) (-)	< 0> (-) (-) (-) (-)	<pre></pre>
atrophy	(-) (-) (-) (-)	< 0> (-) (-) (-) (-)	< 0> (-) (-) (-) (-)	0 0 0 0 (0) (0) (0) (0)
deposit of hemosiderin	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	0 0 0 0 0 (0)
ystem}				
necrosis:single cell	<pre></pre>	< 0> (-) (-) (-) (-)	(-) (-) (-) (-)	0 0 0 0 (0) (0) (0) (0)
	system) atrophy:olfactory epithelium ic system) atrophy atrophy deposit of hemosiderin ystem) necrosis:single cell 1: Slight 2: Moderate 3 a: Number of animals examined at the sib: Number of animals with lesion	Group Name No. of Animals on Study O 1 2 3 4 4 (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (Group Name No. of Animals on Study O O O	Control Cont

(HPT150)

SEX

ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1

: MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 14W)

PAGE: 2

Organ	Ī	Group Name 5000 ppm No. of Animals on Study 0 Grade 1 2 3 4 (%) (%) (%) (%)	7500 ppm 4 1 2 3 4 (%) (%) (%) (%)	
{Respiratory	r system}			
nasal cavit	atrophy:olfactory epithelium	< 0> (-) (-) (-) (-)	2 0 0 0 (50) (0) (0) (0)	
{Hematopoiet	ic system)			
thymus	atrophy	(-) (-) (-)	<pre></pre>	
spleen	atrophy	< 0> (-) (-) (-) (-)	4 0 0 0 (100) (0) (0) (0)	
	deposit of hemosiderin	(-) (-) (-) (-)	0 1 0 0 (0) (25) (0) (0)	
{Digestive s	system}			
liver	necrosis:single cell	< 0> (-) (-) (-) (-)	4 0 0 0 (100) (0) (0) (0)	
Grade < a > b (c)	1: Slight 2: Moderate 3 a: Number of animals examined at the sib: Number of animals with lesion c: b/a * 100	: Marked 4 : Severe te		
(HPT150)				DATO

(HPT150)

: MOUSE Crj:BDF1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

ANIMAL REPORT TYPE : A1

: MALE

DEAD AND MORIBUND ANIMALS (0- 14W)

PAGE: 3 2222 ppm 3333 ppm Group Name Control 1481 ppm No. of Animals on Study 0 0 1 Grade Findings_ {Digestive system} liver < 1> deposit of crystal 0 0 0 0 (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (0)(0)(0)(0) cytomegaly of hepatocyte:central (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (0)(0)(0)(0) vacuolic change:central (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (0)(0)(0)(0) {Reproductive system} < 0> testis < 0> < 1> germ cell necrosis 0 0 0 0 (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (0)(0)(0)(0) epididymis < 0> < 0> < 0> < 1> debris of spermatic elements 0 0 0 0 (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (0)(0)(0)(0) disappear:sperma 0 0 0 0 (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (-) (0)(0)(0)(0) Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe (a) a : Number of animals examined at the site b b: Number of animals with lesion (c) c:b/a * 100

(HPT150)

ANIMAL : MOUSE Crj:BDF1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

REPORT TYPE : A1

SEX : MALE

DEAD AND MORIBUND ANIMALS (0- 14W)

Organ	Findings	Group Name 5000 ppm No. of Animals on Study 0 Grade 1 2 3 4 (%) (%) (%) (%)	7500 ppm 4 1 2 3 4 (%) (%) (%) (%)	
{Digestive s	ystem)			
liver	deposit of crystal	< 0> (-) (-) (-) (-)	3 0 0 0 (75) (0) (0) (0)	
	cytomegaly of hepatocyte:central	(-) (-) (-) (-)	0 2 2 0 (0) (50) (50) (0)	
	vacuolic change∶central	(-) (-) (-)	0 0 1 0 (0) (25) (0)	
Reproductiv	e system}			
estis	germ cell necrosis	< 0> 	<pre></pre>	
pididymis	debris of spermatic elements	(-) (-) (-) (-)	<pre></pre>	
	disappear:sperma	(-) (-) (-) (-)	0 0 1 0 (0) (25) (0)	
rade a > b	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		

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- 14W)

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1

SEX : FEMALE

Organ	No	oup Name	1481 ppm C 1 2 3 4 (%) (%) (%) (%)	2222 ppm 0 1 2 3 4 (%) (%) (%) (%)	3333 ppm 0 1 2 3 4 (%) (%) (%) (%)
{Respiratory	system)				
nasal cavit		< 0>	< 0>	< 0>	< 0>
	atrophy:olfactory epithelium	(-) (-) (-) (-)	(-) (-) (-) (-)	·	(-) (-) (-) (-)
lung		⟨ 0>	< 0>	< 0>	< 0>
	congestion	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
{Hematopoieti	c system)				
thymus	atrophy	< 0>		< 0>	< 0>
	autopiij	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
spleen		< 0>	< 0>	< 0>	< 0>
	atrophy	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
	deposit of hemosiderin		(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
{Digestive sy	rstem)				
stomach		⟨ 0>	< 0>	< 0>	< 0>
	ulcer:forestomach	(-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
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)

DEAD AND MORIBUND ANIMALS (0- 14W)

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1

SEX : FEMALE

Organ	Findings	Group Name 5000 ppm No. of Animals on Study 0 Grade 1 2 3 4 (%) (%) (%) (%)	7500 ppm 4 1 2 3 4 (%) (%) (%) (%)	
{Respiratory	system}			
nasal cavit	atrophy:olfactory epithelium	< 0> (-) (-) (-) (-)	<pre></pre>	
lung	congestion	(-) (-) (-) (-)	3 0 0 0 (75) (0) (0) (0)	
{Hematopoieti	c system}			
thymus	atrophy	< 0> (-) (-) (-) (-)	<pre></pre>	
spleen	atrophy	< 0> (-) (-) (-) (-)	<pre></pre>	
	deposit of hemosiderin	(-) (-) (-)	2 0 0 0 (50) (0) (0) (0)	
{Digestive sy	stem)			
stomach	ulcer:forestomach	(-) (-) (-) (-)	<pre></pre>	

(c) (HPT150)

b

b : Number of animals with lesion

c:b/a*100

BAIS3

SEX : FEMALE

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 14W)

PAGE: 7

Organ	Findings	Group Name Cont	3 4 1 (%) (%) (%)	1481 ppm 0 . 2 3 4 5) (%) (%) (%)	2222 ppm 0 1 2 3 4 (%) (%) (%) (%)	3333 ppm 0 1 2 3 4 (%) (%) (%) (%)
{Digestive s	system)					
liver	necrosis:single cell	(-) (-) (< 0> -) (-) (-) (-)	< 0> (-) (-) (-) (-)	(-) (-) (-)
	deposit of crystal	(-) (-) ((-) (-) (-)	(-) (-) (-)
	cytomegaly of hepatocyte:central	(-) (-) (-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
	vacuolic change:central	(-) (-) ((-) (-) (-) (-)	(-) (-) (-) (-)
{Nervous sys	stem}					
brain	hemorrhage	(-) (-) (< 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				

(HPT150)

ANIMAL

: MOUSE Crj:BDF1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

DEAD AND MORIBUND ANIMALS (0- 14W)

REPORT TYPE : A1 SEX : FEMALE

Group Name 5000 ppm 7500 ppm No. of Animals on Study 4 Grade (%) (%) (%) (%) Findings_ (Digestive system) liver < 0> < 4> necrosis:single cell 1 0 0 0 (-) (-) (-) (25) (0) (0) (0) deposit of crystal 3 0 (-) (-) (-) (-) (75) (0) (0) (0) cytomegaly of hepatocyte:central 1 2 1 0 (-) (-) (-) (-) (25) (50) (25) (0) vacuolic change:central 0 0 0 (-) (-) (-) (-) (25) (0) (0) (0) {Nervous system} brain < 0> < 4> 1 0 0 0 hemorrhage (-) (-) (-) (-) (25) (0) (0) (0) Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe < a > a : Number of animals examined at the site b b: Number of animals with lesion (c) c:b/u*100

(HPT150)

BAIS3

APPENDIX K 5

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY

MOUSE: MALE: SACRIFICED ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0302 REPORT TYPE: A1

ANIMAL : MOUSE Crj:BDF1 : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (14W)

PAGE: 1 3333 ppm Group Name Control 1481 ppm 2222 ppm No. of Animals on Study 10 10 Grade Organ Findings_ {Respiratory system} nasal cavit <10> < 9> <10> < 9> atrophy:olfactory epithelium 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) {Hematopoietic system} spleen <10> < 9> <10> < 9> deposit of hemosiderin 1 0 1 0 0 0 0 0 ** 0 10 0 0 0 *** (10) (10) (0) (0) (56) (11) (0) (0) (100) (0) (0) (0) (100) (0) (0) (0) increased extramedullary hematopoiesis 0 0 (0)(0)(0)(0) (11) (0) (0) (0) (50) (0) (0) (0) (78) (22) (0) (0) {Circulatory system} heart <10> < 9> <10> 0 0 hemorrhage 0 0 0 0 1 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (10) (0) (0) (0) (0)(0)(0)(0) (Digestive system) stomach <10> < 9> <10> < 9> ulcer:forestomach 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 > a : Number of animals examined at the site b : Number of animals with lesion b (c) c:b/a * 100 Significant difference ; * : $P \le 0.05$ ** : $P \le 0.01$ Test of Chi Square

(HPT150)

: MOUSE Crj:BDF1

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (14W)

REPORT TYPE : A1 SEX : MALE

ANIMAL

Group Name 5000 ppm 7500 ppm No. of Animals on Study 10 6 Organ_ Findings_ (%) (%) (%) (%) (%) {Respiratory system} nasal cavit <10> < 6> atrophy:olfactory epithelium 0 0 4 0 0 0 * (0)(0)(0)(0) (67) (0) (0) (0) {Hematopoietic system} spleen <10> < 6> deposit of hemosiderin 0 0 0 ** 3 3 0 0 *** (100) (0) (0) (0) (50) (50) (0) (0) increased extramedullary hematopoiesis 0 ** 2 4 0 (30) (70) (0) (0) (33) (67) (0) (0) {Circulatory system} heart <10> < 6> hemorrhage 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) {Digestive system} stomach <10> < 6> ulcer: forestomach 0 0 0 (10) (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 Significant difference; $*: P \le 0.05$ **: $P \le 0.01$ Test of Chi Square

(HPT150)

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (14W)

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 (%) (%) (%)	1481 ppm 9 1 2 3 4 (%) (%) (%) (%)	2222 ppm 10 1 2 3 4 (%) (%) (%)	3333 ppm 9 1 2 3 4 (%) (%) (%)
{Digestive s	ystem)				
liver	necrosis:focal	(10) 1 0 0 0 (10) (0) (0) (0)	<pre></pre>	<10> 2 0 0 0 (20) (0) (0) (0)	3 0 0 0 (33) (0) (0) (0)
	necrosis:single cell	1 0 0 0 0 (10) (10) (10)	1 0 0 0 (11) (0) (0) (0)	3 0 0 0 0 (30) (0) (0)	8 0 0 0 **
	deposit of crystal	0 0 0 0 0 (0) (0)	0 0 0 0 0 (0) (0)	5 0 0 0 *	9 0 0 0 ***
	cytomegaly of hepatocyte:central	0 0 0 0 0 (0) (0) (0)	0 9 0 0 ***	0 10 0 0 ***	0 1 8 0 ** (0) (11) (89) (0)
{Urinary sys	tem)				
kidney	inflammatory polyp	(10) 0 1 0 0 (0) (10) (0) (0)	0 1 0 0 (0) (11) (0) (0)	0 0 0 0 (0) (0) (0) (0)	(0) (0) (0) (0)
	hydronephrosis	0 1 0 0 (0) (10) (0)	0 1 0 0 (0) (11) (0) (0)	0 0 0 0 0 (0) (0) (0)	0 0 0 0 0 (0) (0)
{Endocrine s	ystem}				
pituitary	cyst	<10> 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	<pre></pre>	0 0 0 0 (0) (0) (0) (0)	(0) (0) (0) (0)
Grade <a>a> b (c) Significant	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				

(חשרובת)

DATCO

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (14W)

ANIMAL : MOUSE Crj:BDF1
REPORT TYPE : A1

SEX : MALE

		Group Name 5000 ppm No. of Animals on Study 10 Grade 1 2 3 4	7500 ppm 6 1 2 3 4 (%) (%) (%) (%)	
Organ	Findings	(%) (%) (%) (%)	(%) (%) (%)	
{Digestive sy	vstem}			
liver	necrosis:focal	<10> 4 1 0 0 (40) (10) (0) (0)	<pre></pre>	
	necrosis:single cell	10 0 0 0 *** (100) (0) (0) (0)	6 0 0 0 *** (100) (0) (0) (0)	
	deposit of crystal	10 0 0 0 ******************************	6 0 0 0 *** (100) (0) (0) (0)	•
	cytomegaly of hepatocyte:central	0 1 9 0 ** (0) (10) (90) (0)	1 0 5 0 ** (17) (0) (83) (0)	
{Urinary syst	tem)			
kidney	inflammatory polyp	0 1 0 0 (0) (10) (0) (0)	<pre></pre>	
	hydronephrosis	0 1 0 0 (0) (10) (0)	0 0 0 0 0 0 (0) (0)	
{Endocrine sy	ystem}			
pituitary	cyst	<10> 0 0 0 0 (0) (0) (0) (0)	<pre></pre>	
Grade <a>a><a>b (c) Significant of	a: Number of animals examined at the sib: Number of animals with lesionc: b/a * 100			· · · · · · · · · · · · · · · · · · ·

(UDT1 EA)

DATCO

STUDY NO. : 0302

ANIMAL : MOUSE Crj:BDF1 HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (14W)

REPORT TYPE : A1 SEX : MALE

3333 ppm Group Name Control 1481 ppm 2222 ppm No. of Animals on Study 10 10 9 Grade Organ_ Findings {Reproductive system} testis <10> < 9> <10> < 9> germ cell necrosis 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) epididymis <10> < 9> <10> < 9> debris of spermatic elements 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) disappear:sperma 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) (0)(0)(0)(0) 1 : Slight 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 Significant difference; $*: P \leq 0.05$ **: $P \leq 0.01$ Test of Chi Square

(HPT150)

BAIS3

PAGE: 5

STUDY NO. : 0302

ANIMAL : MOUSE Crj:BDF1 REPORT TYPE : A1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (14W)

SEX : MALE

Group Name 5000 ppm 7500 ppm No. of Animals on Study 10 Grade Findings_ {Reproductive system} testis <10> < 6> germ cell necrosis 0 0 0 0 6 0 0 ** (0)(0)(0)(0) (0) (100) (0) (0) epididymis <10≻ < 6> 0 0 0 0 3 3 0 0 ** debris of spermatic elements (0) (0) (0) (0) (50) (50) (0) (0) disappear:sperma 1 0 0 0 0 0 5 0 ** (10) (0) (0) (0) (0)(0)(83)(0) 1 : Slight 4 : Severe Grade 2 : Moderate 3 : Marked (a) a : Number of animals examined at the site b 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

PAGE: 6

APPENDIX K 6

HISTOLOGICAL FINDINGS: NON-NEOPLASTIC LESIONS: SUMMARY

MOUSE: FEMALE: SACRIFICED ANIMALS

(13-WEEK STUDY)

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (14W)

STUDY NO. : 0302 ANIMAL : MOUSE Crj:BDF1

REPORT TYPE : A1

SEX : FEMALE PAGE: 7

Organ	Group Name No. of Ani Grade Findings	Control 10 1 2 3 4 (%) (%) (%) (%)	1481 ppm 10 1 2 3 4 (%) (%) (%) (%)	2222 ppm 10 10 (%) (%) (%) (%)	3333 ppm 10 1 2 3 4 (%) (%) (%) (%)
{Respiratory	system)				
nasal cavit	eosinophilic change:respiratory epithelium	<10> 0 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 0 0 0 0 0 0	<10> 0 0 0 0 0 0 0 0 0 0 0	<10> 0 0 0 0 0 0 0 0 0 0 0
lung	bronchiolar-alveolar cell hyperplasia	<10> 0 0 0 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 0 0	<10> 0 0 0 0 (0) (0) (0) (0)
{Hematopoiet:	ic system)				
spleen	congestion	<10> 0 0 0 0 0 0 0 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)
	deposit of hemosiderin	0 0 0 0 0 (0) (0)	10 0 0 0 ** (100) (0) (0) (0)	7 0 0 0 ** (70) (0) (0) (0)	10 0 0 0 ** (100) (0) (0) (0)
	increased extramedullary hematopoiesis	0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0	2 0 0 0 0 (20) (0) (0)	4 0 0 0 (40) (0) (0) (0)	10 0 0 0 *** (100) (0) (0)
{Digestive s	ystem)				
liver	necrosis:single cell	(0) (0) (0) (0)	2 0 0 0 (20) (0) (0) (0)	<10> 4 0 0 0 (40) (0) (0) (0)	10 0 0 0 *** (100) (0) (0) (0)
Grade <a>> b (c) Significant	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; *: $P \le 0.05$ **: $P \le 0.01$ T	4 : Severe			

(HPT150)

BAIS3

STUDY NO. : 0302

ANIMAL : MOUSE Crj:BDF1

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (14W)

REPORT TYPE : A1

SEX : FEMALE

		Group Name No. of Animals on Study Grade 1	5000 ppm 10 2 3		1	7500 r 6 2	opm 3	4.		
Organ	Findings	(%)	(%) (%)	(%)	(%)	(%)	(%)	(%)		
{Respiratory	system}									
nasal cavit	eosinophilic change:respiratory epithe		<10> 0 0 (0) (0)		1 (17)	< 6> 0 (0) (0	0 0)		
lung	bronchiolar-alveolar cell hyperplasia	2 (20)	<10> 0 0 (0) (0)		0 (0)	< 6> 0 (0) (0	0 0)		
{Hematopoietic	c system}									
spleen	congestion	0 (0)	<10> 0 0 (0) (0)		1 (17)	< 6> 0 (0) (0	0 0)		
	deposit of hemosiderin	10 (100)	0 0		6 (100)	0 (0) (0 0) (0 ** 0)		
	increased extramedullary hematopoiesis		2 0 (20) (0)		1 (17)	4 (67) (0 (0 **		
{Digestive sys	stem}									
liver	necrosis:single cell	10 (100)	<10> 0 0 (0) (0)		5 (83)	< 6> 0 (0) (0	0 ** 0)		
Grade <a>> b (c) Significant d	a: Number of animals examined at the sib: Number of animals with lesion c: b / a * 100									

(HPT150)

PAGE: 8

STUDY NO. : 0302

: MOUSE Crj:BDF1

ANIMAL

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)

SACRIFICED ANIMALS (14W)

REPORT TYPE : A1 : FEMALE

Group Name Control 1481 ppm 2222 ppm 3333 ppm No. of Animals on Study 10 10 10 10 Findings_ (%) (%) (%) (%) (%) (%) (%) (%) Organ_

> 0 0

(0)(0)(0)(0)

(Digestive system)

liver

<10> <10> <10> <10> 0 0 0 0 0 0 0 0 0 0 ** deposit of crystal 10 0 0 10 (0)(0)(0)(0) (0)(0)(0)(0) (100) (0) (0) (0) (100) (0) (0) (0)

10

0 0

(100) (0) (0) (0)

5 5 0

(50) (50) (0) (0)

cytomegaly of hepatocyte:central

1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a: Number of animals examined at the site

ь b: Number of animals with lesion

c:b/a*100 (c)

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

(HPT150)

Grade

BAIS3

0

4 6

(0)(40)(60)(0)

PAGE: 9

STUDY NO. : 0302 ANIMAL : MOUSE Crj:BDF1

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY) SACRIFICED ANIMALS (14W)

REPORT TYPE : A1

(HPT150)

SEX : FEMALE PAGE: 10

BAIS3

Organ	_ Findings	Group Name 5000 ppm 7500 ppm No. of Animals on Study 10 6 Grade 1 2 3 4 1 2 3 4 (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%) (%)
{Digestive	system)	
liver	deposit of crystal	(10) (0) (0) (100) (0) (0) (0) (0
	cytomegaly of hepatocyte:central	0 0 10 0 ** 0 0 6 0 ** (0) (0) (100) (0) (0) (100) (0)
Grade <a> b (c) Significant	1: Slight 2: Moderate a: Number of animals examined at the b: Number of animals with lesion c: b / a * 100 t difference; *: P ≤ 0.05 **: P	3 : Marked 4 : Severe site ≤ 0.01 Test of Chi Square

APPENDIX L 1

IDENTITY OF 1,4-DICHLORO-2-NITROBENZENE
IN THE 13-WEEK FEED STUDY

IDENTITY OF 1,4-DICHLORO-2-NITROBENZENE IN THE 13-WEEK FEED STUDY

Test Substance

: 1,4-Dichloro-2-nitrobenzene (Wako Pure Chemical Industries, Ltd.)

Lot No.

: SKG1643

1. Spectral Data

Mass Spectrometry

Instrument

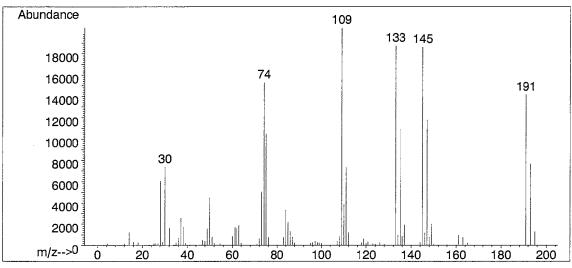
: Hewlett Packard 5989B Mass Spectrometer

Ionization

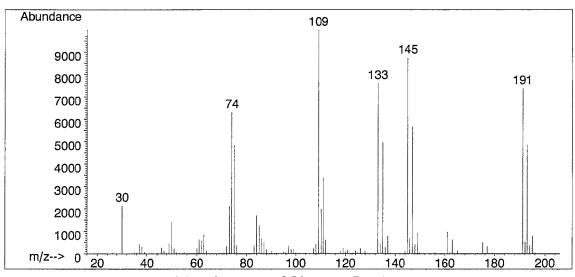
: EI (Electron Ionization)

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.

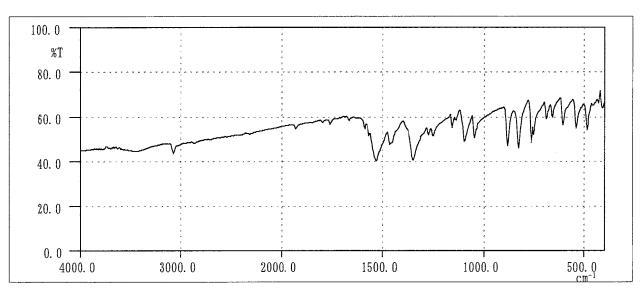
John Wiley and Sons, Inc. (U.S.), Entry Number 74222)

Infrared Spectrometry

Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr

Resolution : 2 cm⁻¹



Infrared Spectrum of Test Substance

Determined Values	Literature Values*
Wave Number (cm ⁻¹)	Wave Number (cm ⁻¹)
460~ 510	460~ 510
510~ 560	510~ 560
560~ 620	$560\sim 620$
620~ 670	620~ 670
670~ 690	670~ 690
690~ 790	690~ 790
790~ 850	790~ 850
850~ 900	850~ 900
$900 \sim 1060$	900~1060
1060~1120	$1060 \sim 1120$
$1120 \sim 1170$	$1120 \sim 1170$
$1170 \sim 1180$	$1170 \sim 1180$
$1180 \sim 1260$	$1180 \sim 1260$
$1260 \sim 1280$	$1260 \sim 1280$
$1280 \sim 1400$	$1280 \sim 1400$
$1400 \sim 1470$	$1400 \sim 1470$
$1470 \sim 1580$	$1470 \sim 1580$
$1580 \sim 1600$	$1580 \sim 1600$
$1650 \sim 1690$	$1650 \sim 1690$
$1750 \sim 1780$	$1750 \sim 1780$
$1780 \sim 1810$	$1780 \sim 1810$
$1900 \sim 1950$	$1900 \sim 1950$
3000~3100	3000~3100

Results: The infrared spectrum was consistent with literature spectrum. (*Performed by Wako Pure Chemical Industries, Ltd.)

2. Conclusions: The test substance was identified as 1,4-dichloro-2-nitrobenzene by the mass spectrum and the infrared spectrum.

APPENDIX L 2

STABILITY OF 1,4-DICHLORO-2-NITROBENZENE
IN THE 13-WEEK FEED STUDY

STABILITY OF 1,4-DICHLORO-2-NITROBENZENE IN THE 13-WEEK FEED STUDY

Test Substance : 1,4-Dichloro-2-nitrobenzene (Wako Pure Chemical Industries, Ltd.)

Lot No. : SKG1643

1. Sample : This lot was used from 1996.2.15 to 1996.5.19. Test substance was stored

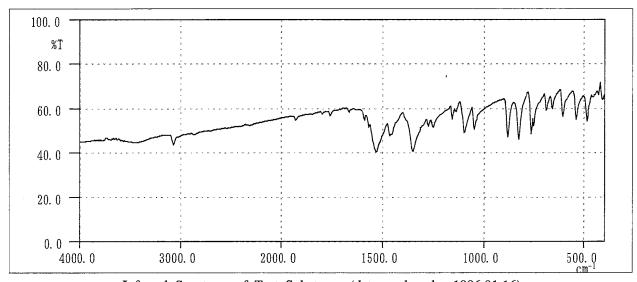
in a dark place at room temperature.

2. Infrared Spectrometry

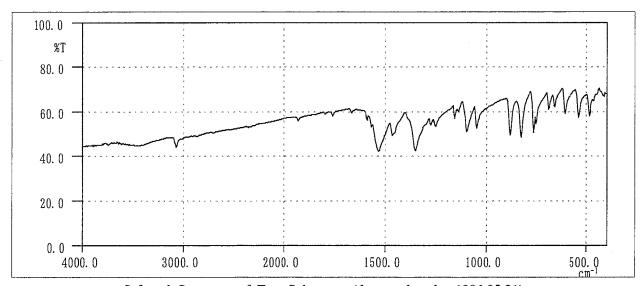
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr

Resolution : 2 cm⁻¹



Infrared Spectrum of Test Substance (date analyzed: 1996.01.16)



Infrared Spectrum of Test Substance (date analyzed: 1996.05.31)

Results: The results of infrared spectrum did not change before and after the study.

3. Gas Chromatography

)

Instrument : Hewlett Packard 5890A Gas Chromatograph

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

Column Temperature : 180 $^{\circ}$ C \rightarrow (10 $^{\circ}$ C/min) \rightarrow 215 $^{\circ}$ C \rightarrow (20 $^{\circ}$ C/min) \rightarrow 250 $^{\circ}$ C (2 min)

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μL

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
1996.01.16	1	3.635	100
1996.05.31	1	3.635	. 100

Results: Gas chromatography indicated one major peak (peak No.1) analyzed on 1996.1.16 and one major peak (peak No.1) analyzed on 1996.5.31. No new trace impurity peak in the test substance analyzed on 1996.5.31 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 1,4-DICHLORO-2-NITROBENZENE
IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

CONCENTRATION OF 1,4-DICHLORO-2-NITROBENZENE IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

Date Prepared 1996. 02. 07 Date Analyzed 1996. 02. 07

Target Concentration(A)	Number of Samples	Determined Concentration(B) Mean Value	Coefficient Variation (%)	B/A×100 (%)
1481ppm	7	1471.1ppm	1.26	99.3
2222ppm	7	2243.6ppm	2.22	101.0
3333ppm	7	3323.3ppm	3.12	99.7
5000ppm	7	5042.3ppm	3.39	100.8
7500ppm	7	7329.3ppm	1.63	97.7

Analytical Method

: The samples were analyzed by the gas Chromatography.

Instrument

: Hewlett Packard 5890A Gas Chromatograph

Column

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

Column Temperature

 $: 180^{\circ}\text{C} \rightarrow (10^{\circ}\text{C/min}) \rightarrow 215^{\circ}\text{C} \rightarrow (20^{\circ}\text{C/min}) \rightarrow 250^{\circ}\text{C} (2\text{min})$

Flow Rate

: 1mL/min

Detector

: FID(Flame Ionization Detector)

Injection Volume

 $: 1\,\mu \, \mathrm{L}$

APPENDIX L 4

STABILITY OF 1,4-DICHLORO-2-NITROBENZENE
IN FORMULATED DIETSIN THE 13-WEEK FEED STUDY

STABILITY OF 1,4-DICHLORO-2-NITROBENZENE IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

		Target Concentration				
Date Prepared	Date Analyzed	625 ^a	10000			
1995.10.25	1995.10.26	601.5 (100) ^b	9673.7 (100)			
	1995.11.02°	542.6 (90.2)	9220.0 (95.3)			
	1996.01.29 ^d	580.7 (96.5)	8638.9 (89.3)			

^a ppm

Analytical Method : The samples were analyzed by gas chromatography.

Instrument : Hewlett Packard 5890A Gas Chromatograph

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

Column Temperature : 180 $^{\circ}$ C \rightarrow (10 $^{\circ}$ C/min) \rightarrow 215 $^{\circ}$ C \rightarrow (20 $^{\circ}$ C/min) \rightarrow 250 $^{\circ}$ C (2 min)

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

d Cold storage samples

APPENDIX M 1

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALISYS IN THE 13-WEEK FEED STUDY OF 1,4-DICHLORO-2-NITROBENZENE

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS IN THE 13-WEEK FEED STUDY OF 1,4-DICHLORO-2-NITROBENZENE

Item	Method
Hematology	
Red blood cell (RBC)	Light scattering method 1)
Hemoglobin (Hgb)	Cyanmethemoglobin method 1)
Methemoglobin	Multiple-wavelength Spectrophotometric method 4)
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 11
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)
	(May-Grunwald-Giemsa 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	Enzymatic method (GLK·G-6-PDH) 3)
T-cholesterol	Enzymatic method (CE·COD·POD) 3)
Triglyceride	Enzymatic method (LPL·GK·GPO·POD) 3)
Phospholipid	Enzymatic method (PLD·COD·POD) 3)
Glutamic oxaloacetic transaminase (GOT)	IFCC method 3)
Glutamic pyruvic transaminase (GPT)	IFCC method 3)
Lactate dehydrogenase (LDH)	Wroblewski-LaDue method 3)
Alkaline phosphatase (ALP)	GSCC method ³⁾
γ -Glutamyl transpeptidase (γ -GTP)	L- γ -Glutamyl-p-nitroanilide method ³⁾
Creatine phosphokinase (CPK)	GSCC method 3)
Urea nitrogen	Enzymatic method (Urease · GLDH) 3)
Sodium	Ion selective electrode method 3)
Potassium	Ion selective electrode method 30
Chloride	Ion selective electrode method 37
Calcium	OCPC method 3)
Inorganic phosphorus	Enzymatic method (PNP·XOD·POD) 3)
Urinalysis	
pH,Protein,Glucose,Ketone body,Occult Blood, Urobilinogen	Urinalysis reagent paper method 5)

- 1) Automatic blood cell analyzer (Technicon H·1: Technicon Instruments Corporation)
- 2) Automatic blood cell differential analyzer (Hitachi 8200 : Hitachi,Ltd.)
- 3) Automatic analyzer (Hitachi 7070: Hitachi, Ltd.)
- 4) CO-oximeter (CIBA · CORNING 270 : Ciba Corning Diagnostics Corp)
- 5) Ames reagent strips for urinalysis (Uro-Labstix: Bayer-Sankyo Co.,Ltd.)

APPENDIX N 1

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK FEED STUDY OF 1,4-DICHLORO-2-NITROBENZENE

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK FEED STUDY OF 1,4-DICHLORO-2-NITROBENZENE

Item	Unit	Decimal place
Hematology		
Red blood cell (RBC)	$\times 10^6/\mu$ L	2
Hemoglobin	g/dL	1
Methemoglobin	%	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)	$\times 10^3/\mu \mathrm{L}$	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 transaminase (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