2,4-ジクロロ-1-ニトロベンゼンのラットを用いた
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：０４０９

APPENDIXES

APPENDIXES

APPENDIXES (CONTINUED)

APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7
COLORED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	3000 ppm	0	0	0	0	10	10	10	10	10	10	10	10	10
	4000 ppm	0	1	10	10	10	10	10	10	10	10	10	10	10
YELLOW URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	2000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	3000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	4000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day 1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7
COLORED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000 ppm	0	0	0	0	0	2	3	3	3	3	3	3	3
	2000 ppm	3	4	5	5	5	6	7	8	8	8	8	8	8
	3000 ppm	5	6	9	9	9	9	9	9	9	9	9	9	9
	4000 ppm	5	5	9	9	10	10	10	10	10	10	10	10	10
YELLOW URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	2000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	3000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	4000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10

APPENDIX B 1

BODY WEIGHT CHANGES :SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 0	1	2	3	4	5	6
Control	119± 4	151± 5	179± 5	203± 8	222± 9	238± 10	251± 12
500 ppm	119± 4	149± 5	175± 9	195± 19	217± 11	233± 10	245± 10
1000 ppm	119± 4	149± 5	176± 5	200± 4	219± 4	234± 4	245± 6
2000 ppm	119± 4	146± 4	171± 5*	193± 6	212± 7*	228± 9	240± 10
3000 ppm	119± 4	141± 5**	162± 6**	183± 7**	203± 7**	217± 9**	230± 8**
4000 ppm	119± 4	133± 6**	151± 8**	171± 9**	188± 8**	197± 8**	210± 9**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
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	266± 14	277± 14	288± 16	297± 16	306± 19	313± 20	319± 20
500 ppm	259± 10	271± 10	279± 12	287± 13	297± 13	303± 12	308± 12
1000 ppm	258± 7	269± 7	279± 9	288± 10	295± 10	300± 11	306± 10
2000 ppm	253± 11*	266± 11	275± 10	284± 11	291± 11	297± 13*	302± 11*
3000 ppm	244± 10**	253± 11**	262± 13**	271± 14**	279± 14**	287± 14**	293± 14**
4000 ppm	222± 11**	228± 9**	234± 12**	244± 14**	252± 15**	260± 14**	263± 13**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX B 2

BODY WEIGHT CHANGES : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 0	1	2	3	4	5	6
Control	96± 3	111± 4	122± 4	131± 5	138± 6	145± 6	149± 6
500 ppm	96± 3	110± 4	120± 4	129± 5	136± 5	144± 7	148± 8
1000 ppm	96± 3	110± 3	118± 6	127± 6	133± 8	139± 9	143± 9
2000 ppm	96± 3	108± 4	118± 4	125± 5	130± 5*	135± 8*	140± 8*
3000 ppm	96± 3	105± 4**	113± 6**	120± 5**	127± 5**	132± 6**	136± 5**
4000 ppm	96± 3	104± 3**	114± 4**	121± 5**	126± 5**	131± 6**	136± 8**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 7	8	9	10	11	12	13
Control	154± 8	160± 7	161± 8	165± 8	167± 8	168± 9	170± 9
500 ppm	151± 6	155± 8	158± 7	162± 9	165± 8	167± 9	169± 8
1000 ppm	147± 11	150± 10	152± 11	157± 11	160± 10	163± 11	163± 12
2000 ppm	143± 9*	147± 9**	150± 10*	153± 10*	156± 9	158± 9	160± 8
3000 ppm	140± 7**	143± 6**	146± 7**	149± 9**	151± 8**	154± 8**	155± 9**
4000 ppm	140± 8**	142± 8**	145± 10**	147± 8**	150± 10**	153± 10**	155± 9**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX C 1

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group 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	12.6± 0.5	13.8± 0.7	14.1± 1.0	14.5± 1.3	14.5± 1.0	14.8± 0.9	15.1± 0.8
500 ppm	12.1± 0.7	13.5± 0.5	13.0± 2.8	14.2± 0.8	14.2± 0.6	14.2± 0.6	14.7± 0.6
1000 ppm	12.1± 0.4	13.5± 0.4	14.0± 0.3	14.3± 0.4	14.3± 0.5	14.4± 0.6	14.8± 0.7
2000 ppm	11.6± 0.5**	13.2± 0.8	13.7± 0.7	14.0± 0.7	14.2± 0.9	14.2± 0.8	14.7± 1.0
3000 ppm	11.4± 0.4**	13.4± 0.5	13.9± 0.9	14.3± 1.3	14.3± 1.3	14.1± 1.1	14.4± 1.1
4000 ppm	10.4± 0.6**	12.5± 1.0**	13.2± 0.9	13.5± 0.9	14.0± 1.4	13.8± 1.3	14.0± 1.4

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)
Control	14.9± 0.8	14.9± 1.4	15.4± 1.4	15.4± 1.4	15.4± 1.2	15.2± 1.5
500 ppm	14.7± 0.7	14.6± 0.9	15.1± 0.9	15.3± 0.7	15.1± 0.9	14.6± 0.7
1000 ppm	14.8± 0.9	14.8± 1.1	15.5± 1.4	15.3± 1.5	15.2± 1.4	15.0± 1.3
2000 ppm	14.5± 0.9	14.3± 0.8	14.5± 0.9	14.6± 0.7	14.5± 0.9	14.3± 1.0
3000 ppm	14.4± 1.2	14.3± 1.5	14.6± 1.8	14.8± 1.6	14.8± 1.3	14.7± 1.5
4000 ppm	14.1± 1.5	13.8± 1.5	13.8± 1.4*	13.9± 1.4	14.3± 1.5	14.0± 1.3

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX C 2

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group 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	9.8± 0.5	9.8± 0.4	10.3± 0.6	10.2± 0.6	10.3± 0.5	9.8± 0.7	10.2± 0.7
500 ppm	9.6± 0.4	9.6± 0.5	10.1± 0.6	10.2± 0.7	10.5± 0.8	10.0± 0.7	10.2± 0.6
1000 ppm	9.4± 0.5	9.7± 0.5	9.9± 0.6	9.8± 0.7	9.8± 0.8	9.8± 0.9	9.8± 0.9
2000 ppm	9.0± 0.4**	9.4± 0.6	9.5± 0.5*	9.3± 0.6	9.2± 0.7*	9.5± 0.8	9.4± 0.7
3000 ppm	8.2± 0.3**	8.9± 0.6**	8.8± 0.7**	9.9± 2.8*	9.3± 1.3	9.2± 0.7	9.9± 2.4
4000 ppm	7.9± 0.4**	9.4± 0.6	9.0± 0.5**	8.8± 0.6**	9.1± 0.8*	9.2± 0.8	9.4± 0.7

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)
Control	10.4± 1.2	9.5± 0.7	9.8± 0.9	9.7± 0.8	9.9± 0.9	9.9± 1.1
500 ppm	10.2± 0.9	9.7± 0.8	10.1± 0.8	10.0± 0.8	10.0± 0.8	10.0± 0.9
1000 ppm	9.8± 0.8	9.3± 0.9	9.9± 0.8	9.8± 0.6	10.0± 0.8	9.6± 0.9
2000 ppm	9.4± 0.9	9.2± 1.0	9.6± 0.9	9.8± 0.8	9.8± 0.7	9.8± 0.6
3000 ppm	9.0± 0.5**	8.8± 0.4	9.2± 0.6	9.2± 0.5	9.3± 0.4	9.3± 0.8
4000 ppm	8.9± 0.6**	8.8± 0.7	8.9± 0.6	9.3± 0.6	9.3± 0.5	9.1± 0.4

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX D 1

CHEMICAL INTAKE CHANGES : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
UNIT : g／kg／d a y
REPORT TYPE : A1 13
SEX : MALE

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
500 ppm	0.041± 0.001	0.039± 0.001	0.033± 0.005	0.033± 0.003	0.030± 0.002	0.029± 0.001	0.028± 0.001
1000 ppm	0.081± 0.002	0.077± 0.002	0.070± 0.002	0.065± 0.001	0.061± 0.002	0.059± 0.002	0.057± 0.002
2000 ppm	0.159± 0.004	0.154± 0.006	0.142± 0.004	0.132± 0.003	0.124± 0.004	0.118± 0.003	0.116± 0.004
3000 ppm	0.243± 0.008	0.248± 0.008	0.228± 0.010	0.211± 0.015	0.198± 0.013	0.183± 0.010	0.177± 0.009
4000 ppm	0.312± 0.007	0.331± 0.010	0.308± 0.011	0.286± 0.014	0.284± 0.026	0.263± 0.020	0.252± 0.020

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
UNIT : g／kg／d a y
REPORT TYPE : A1 13
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

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
500 ppm	0.027± 0.001	0.026± 0.001	0.027± 0.001	0.026± 0.001	0.025± 0.001	0.024± 0.001
1000 ppm	0.055± 0.002	0.053± 0.003	0.054± 0.003	0.052± 0.004	0.051± 0.004	0.049± 0.003
2000 ppm	0.109± 0.004	0.104± 0.004	0.102± 0.004	0.100± 0.003	0.098± 0.004	0.095± 0.004
3000 ppm	0.171± 0.009	0.164± 0.012	0.161± 0.015	0.158± 0.014	0.154± 0.010	0.151± 0.011
4000 ppm	0.247± 0.023	0.235± 0.020	0.226± 0.018	0.220± 0.018	0.221± 0.022	0.213± 0.020

APPENDIX D 2

CHEMICAL INTAKE CHANGES : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
UNIT : g／kg／d a y
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
500 ppm	0.044± 0.002	0.040± 0.002	0.039± 0.002	0.037± 0.002	0.037± 0.003	0.034± 0.002	0.034± 0.002
1000 ppm	0.086± 0.003	0.082± 0.003	0.078± 0.003	0.073± 0.002	0.070± 0.003	0.069± 0.003	0.067± 0.003
2000 ppm	0.166± 0.007	0.159± 0.007	0.152± 0.003	0.143± 0.005	0.136± 0.004	0.135± 0.006	0.131± 0.008
3000 ppm	0.236± 0.009	0.236± 0.012	0.220± 0.013	0.234± 0.072	0.212± 0.034	0.204± 0.017	0.213± 0.055
4000 ppm	0.306± 0.014	0.328± 0.012	0.300± 0.009	0.280± 0.012	0.279± 0.016	0.270± 0.012	0.268± 0.009

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
UNIT : g／kg／d a y
REPORT TYPE : A1 13
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

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
500 ppm	0.033± 0.002	0.031± 0.002	0.031± 0.002	0.030± 0.003	0.030± 0.002	0.030± 0.003
1000 ppm	0.065± 0.003	0.061± 0.003	0.063± 0.002	0.062± 0.002	0.061± 0.002	0.059± 0.002
2000 ppm	0.128± 0.007	0.124± 0.009	0.126± 0.006	0.125± 0.006	0.124± 0.006	0.122± 0.005
3000 ppm	0.189± 0.010	0.182± 0.009	0.185± 0.009	0.183± 0.009	0.181± 0.008	0.179± 0.013
4000 ppm	0.250± 0.010	0.242± 0.010	0.242± 0.008	0.247± 0.006	0.243± 0.005	0.236± 0.009

APPENDIX E 1

HEMATOLOGY : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$		HEMOGLOBIN g/dℓ		HEMATOCRIT %		MCV fℓ		MCH pg		MCHC g/dℓ		PLATELET $10^3/\mu\ell$	
Control	10	9.76±	0.30	16.5±	0.4	47.9±	1.4	49.1±	0.3	17.0±	0.3	34.5±	0.5	719±	43
500 ppm	10	9.73±	0.36	16.3±	0.4	47.3±	1.3	48.7±	1.1	16.8±	0.5	34.5±	0.5	728±	74
1000 ppm	10	9.75±	0.21	15.9±	0.4**	46.4±	1.2	47.5±	0.3**	16.3±	0.1**	34.3±	0.1	752±	56
2000 ppm	10	9.65±	0.21	15.5±	0.3**	45.6±	0.9**	47.3±	0.9**	16.0±	0.4**	33.9±	0.5	796±	39*
3000 ppm	10	9.39±	0.15*	15.2±	0.2**	45.4±	0.4**	48.3±	0.6	16.2±	0.3**	33.6±	0.4**	850±	29**
4000 ppm	10	9.31±	0.24**	15.1±	0.4**	45.2±	1.4**	48.6±	0.8	16.3±	0.3**	33.5±	0.5**	818±	22**

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

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RETICULOCYTE ‰	METHEMOGLOBIN %	PROTHROMBIN TIME sec	APTT sec
Control	10	18± 3	0.4± 0.1	17.0± 1.6	26.8± 1.6
500 ppm	10	18± 5	0.4± 0.2	16.0± 1.9	25.2± 3.1
1000 ppm	10	17± 5	0.4± 0.2	16.0± 2.2	26.9± 2.5
2000 ppm	10	24± 5*	0.4± 0.2	17.0± 3.2	27.2± 5.1
3000 ppm	10	26± 9*	0.5± 0.2	15.4± 2.1	26.8± 2.6
4000 ppm	10	23± 6	0.5± 0.2	15.3± 2.4	26.0± 3.5

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHER
Control	10	5.49± 1.25	0± 0	23± 2	1± 1	0± 0	3± 1	74± 3	0± 0
500 ppm	10	5.63± 1.28	0± 0	22± 4	1± 1	0± 0	3± 1	75± 4	0± 0
1000 ppm	10	6.53± 1.51	0± 1	21± 5	1± 1	0± 0	3± 1	76± 6	0± 0
2000 ppm	10	6.75± 1.16	0± 1	23± 6	1± 1	0± 0	3± 2	73± 6	0± 0
3000 ppm	10	6.96± 1.51	0± 0	21± 6	1± 1	0± 0	3± 1	75± 5	0± 0
4000 ppm	10	5.55± 1.30	0± 0	23± 4	1± 1	0± 0	3± 1	73± 4	0± 0

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX E 2

HEMATOLOGY : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$		HEMOGLOBIN g/dℓ		HEMATOCRIT %		MCV f ℓ		MCH p g		MCHC g/dℓ		PLATELET $10^3/\mu\ell$	
Control	10	8.93±	0.19	16.4±	0.4	46.2±	1.2	51.7±	0.7	18.4±	0.2	35.5±	0.7	794±	44
500 ppm	10	8.87±	0.17	16.0±	0.3	45.3±	1.1	51.1±	1.0	18.0±	0.3	35.3±	0.4	790±	48
1000 ppm	10	8.77±	0.24	15.9±	0.4	45.1±	1.1	51.4±	0.6	18.1±	0.2	35.3±	0.6	823±	37
2000 ppm	10	8.72±	0.20	15.7±	0.4**	45.0±	0.9	51.6±	1.2	18.0±	0.4*	34.9±	0.2	844±	32*
3000 ppm	9	8.50±	0.28**	15.3±	0.5**	43.9±	1.4**	51.7±	0.6	18.0±	0.2	34.9±	0.4	856±	49**
4000 ppm	10	8.56±	0.29**	15.3±	0.5**	44.3±	1.6**	51.7±	0.3	17.9±	0.2**	34.5±	0.4**	848±	39*

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RETICULOCYTE ‰		METHEMOGLOBIN %		PROTHROMBIN TIME sec		APTT sec	
Control	10	15±	4	0.3±	0.1	14.2±	0.5	18.6±	1.1
500 ppm	10	19±	4	0.3±	0.1	14.2±	0.8	19.6±	1.2
1000 ppm	10	19±	5	0.4±	0.1	14.4±	1.0	19.6±	2.0
2000 ppm	10	22±	9	0.4±	0.1	14.2±	0.9	19.4±	1.9
3000 ppm	9	25±	7**	0.3±	0.1	14.4±	0.5	20.0±	1.3
4000 ppm	10	28±	3**	0.5±	0.2*	14.4±	1.0	19.0±	1.6

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHER
Control	10	2.63± 1.00	0± 0	24± 9	1± 1	0± 0	3± 2	71± 11	0± 0
500 ppm	10	2.89± 0.66	0± 0	22± 4	1± 1	0± 0	2± 1	74± 4	0± 0
1000 ppm	10	3.16± 0.86	0± 0	26± 6	1± 1	0± 0	2± 0	70± 6	0± 0
2000 ppm	10	3.33± 0.77	0± 0	26± 6	1± 1	0± 0	2± 1	72± 6	0± 0
3000 ppm	9	2.81± 0.97	0± 0	23± 5	2± 1	0± 0	2± 1	73± 5	0± 0
4000 ppm	10	3.12± 0.79	0± 0	22± 6	1± 1	0± 0	2± 1	74± 7	0± 0

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

APPENDIX F 1

BIOCHEMISTRY : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	TOTAL PROTEIN g／dℓ		ALBUMIN g／dℓ		A/G RATIO		T-BILIRUBIN mg／dℓ		GLUCOSE mg／dℓ		T-CHOLESTEROL mg／dℓ		TRIGLYCERIDE mg／dℓ	
Control	10	6.4±	0.2	3.9±	0.1	1.6±	0.1	0.12±	0.01	202±	19	57±	4	49±	12
500 ppm	10	6.6±	0.1*	4.1±	0.1**	1.7±	0.1	0.13±	0.01	206±	23	65±	5*	50±	15
1000 ppm	10	6.7±	0.1**	4.2±	0.1**	1.7±	0.1	0.13±	0.01	208±	15	66±	5**	51±	14
2000 ppm	10	6.9±	0.2**	4.3±	0.1**	1.7±	0.1	0.13±	0.01	215±	9	71±	9**	55±	7
3000 ppm	10	7.0±	0.2**	4.4±	0.1**	1.7±	0.1	0.13±	0.01	223±	18	58±	4	45±	12
4000 ppm	10	6.7±	0.2**	4.2±	0.1**	1.7±	0.1	0.13±	0.01	207±	16	49±	6*	38±	15

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dℓ		GOT IU/ℓ		GPT IU/ℓ		LDH IU/ℓ		ALP IU/ℓ		G-GTP IU/ℓ		CPK IU/ℓ	
Control	10	115±	7	86±	34	49±	13	251±	69	252±	17	3±	1	119±	14
500 ppm	10	127±	6	76±	25	43±	9	260±	52	224±	18**	2±	1	117±	16
1000 ppm	10	132±	12**	76±	22	43±	10	254±	72	199±	13**	3±	1	112±	20
2000 ppm	10	144±	14**	77±	27	44±	13	255±	67	195±	23**	4±	3	105±	9
3000 ppm	10	120±	10	50±	12**	30±	4**	208±	40	182±	11**	3±	1	101±	15
4000 ppm	10	104±	10	60±	19	34±	5*	263±	103	188±	16**	2±	1	107±	17

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	UREA NITROGEN mg/dl	CREATININE mg/dl	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dl	INORGANIC PHOSPHORUS mg/dl
Control	10	18.4± 1.3	0.5± 0.1	141± 1	3.4± 0.2	105± 1	10.1± 0.2	5.6± 0.7
500 ppm	10	19.5± 1.1	0.5± 0.1	141± 2	3.5± 0.3	103± 1	10.3± 0.1	5.7± 0.3
1000 ppm	10	20.1± 1.9	0.5± 0.0	141± 1	3.6± 0.2	103± 1	10.3± 0.2**	5.5± 0.4
2000 ppm	10	20.4± 1.4	0.5± 0.0	141± 1	3.5± 0.2	103± 1*	10.5± 0.2**	5.5± 0.5
3000 ppm	10	19.8± 1.7	0.5± 0.0	141± 1	3.5± 0.2	102± 2**	10.5± 0.1**	5.6± 0.6
4000 ppm	10	19.1± 1.7	0.5± 0.1	141± 1	3.8± 0.2**	104± 1	10.3± 0.1	5.6± 0.6

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX F 2

BIOCHEMISTRY : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	TOTAL PROTEIN g/dl		ALBUMIN g/dl		A/G RATIO		T-BILIRUBIN mg/dl		GLUCOSE mg/dl		T-CHOLESTEROL mg/dl		TRIGLYCERIDE mg/dl	
Control	10	6.3±	0.2	3.9±	0.1	1.6±	0.1	0.16±	0.01	151±	12	64±	8	13±	3
500 ppm	10	6.4±	0.2	4.0±	0.1	1.6±	0.1	0.16±	0.02	162±	17	76±	7**	14±	2
1000 ppm	10	6.5±	0.2	4.0±	0.1	1.6±	0.1	0.16±	0.01	163±	18	82±	8**	15±	5
2000 ppm	9	6.5±	0.2	4.0±	0.1	1.6±	0.1	0.15±	0.01	165±	10	85±	6**	15±	2*
3000 ppm	10	6.5±	0.2	4.0±	0.1	1.6±	0.1	0.17±	0.03	172±	11**	88±	6**	15±	2
4000 ppm	10	6.6±	0.2**	4.1±	0.1**	1.7±	0.1	0.15±	0.01	163±	11	94±	6**	16±	2*

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dℓ	GOT IU/ℓ	GPT IU/ℓ	LDH IU/ℓ	ALP IU/ℓ	G-GTP IU/ℓ	CPK IU/ℓ
Control	10	134± 18	88± 23	40± 14	466± 188	181± 18	3± 1	165± 50
500 ppm	10	149± 13*	84± 11	38± 7	435± 123	180± 18	3± 1	159± 31
1000 ppm	10	157± 12**	66± 6	29± 4	373± 107	173± 18	3± 1	139± 27
2000 ppm	9	161± 8**	66± 7	30± 4	375± 90	151± 13**	3± 1	151± 21
3000 ppm	10	162± 8**	64± 6*	29± 3	482± 300	146± 10**	2± 1	167± 74
4000 ppm	10	173± 10**	59± 4**	28± 3	373± 103	146± 15**	3± 1	136± 33

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	UREA NITROGEN mg/dl	CREATININE mg/dl	SODIUM mEq/l	POTASSIUM mEq/l	CHLORIDE mEq/l	CALCIUM mg/dl	INORGANIC PHOSPHORUS mg/dl
Control	10	18.4± 1.3	0.5± 0.1	141± 1	3.6± 0.2	106± 2	9.9± 0.3	4.7± 0.8
500 ppm	10	17.7± 2.1	0.5± 0.0	140± 1	3.7± 0.2	106± 2	9.9± 0.1	4.9± 0.8
1000 ppm	10	19.0± 1.1	0.5± 0.1*	140± 1	3.6± 0.3	105± 2	9.8± 0.2	4.7± 1.0
2000 ppm	9	19.6± 1.8	0.5± 0.0	140± 1	3.8± 0.3	105± 1	10.0± 0.1	5.0± 1.0
3000 ppm	10	20.2± 1.7	0.5± 0.0	140± 1	3.9± 0.3	105± 1	9.9± 0.2	5.1± 0.8
4000 ppm	10	18.7± 1.6	0.5± 0.0	140± 1	3.9± 0.4	103± 2**	10.1± 0.1	5.3± 0.3

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX G 1

URINALYSIS : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Bilirubin −	+	2+	3+	CHI
Control	10	0	0	0	0	0	6	4		0	0	1	8	1	0		10	0	0	0	0	0		1	7	2	0	0	0		10	0	0	0	
500 ppm	10	0	0	0	0	0	4	6		0	0	4	6	0	0		10	0	0	0	0	0		3	7	0	0	0	0		10	0	0	0	
1000 ppm	10	0	0	0	0	0	6	4		0	0	4	6	0	0		10	0	0	0	0	0		3	7	0	0	0	0		10	0	0	0	
2000 ppm	10	0	0	0	0	0	3	7		0	0	3	7	0	0		10	0	0	0	0	0		5	5	0	0	0	0		10	0	0	0	
3000 ppm	10	0	0	0	0	1	4	5		0	0	2	8	0	0		10	0	0	0	0	0		6	4	0	0	0	0	*	10	0	0	0	
4000 ppm	10	0	0	0	0	3	7	0	*	0	0	1	9	0	0		10	0	0	0	0	0		1	9	0	0	0	0		10	0	0	0	

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	Occult blood −	±	+	2+	3+	CHI	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0		10	0	0	0	0	
500 ppm	10	10	0	0	0	0		10	0	0	0	0	
1000 ppm	10	10	0	0	0	0		10	0	0	0	0	
2000 ppm	10	10	0	0	0	0		10	0	0	0	0	
3000 ppm	10	10	0	0	0	0		10	0	0	0	0	
4000 ppm	10	10	0	0	0	0		10	0	0	0	0	

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

APPENDIX G 2

URINALYSIS : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Bilirubin −	+	2+	3+	CHI
Control	10	0	0	0	0	0	7	3		0	2	8	0	0	0		10	0	0	0	0	0		8	2	0	0	0	0		10	0	0	0	
500 ppm	10	0	0	0	0	1	6	3		0	3	5	2	0	0		10	0	0	0	0	0		9	1	0	0	0	0		10	0	0	0	
1000 ppm	10	0	0	0	0	0	8	2		0	5	5	0	0	0		10	0	0	0	0	0		9	1	0	0	0	0		10	0	0	0	
2000 ppm	10	0	0	0	0	1	6	3		0	4	6	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
3000 ppm	10	0	0	0	0	0	4	6		0	3	6	1	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
4000 ppm	10	0	0	0	0	0	7	3		0	1	9	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	Occult blood −	±	+	2+	3+	CHI	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0		10	0	0	0	0	
500 ppm	10	10	0	0	0	0		10	0	0	0	0	
1000 ppm	10	10	0	0	0	0		10	0	0	0	0	
2000 ppm	10	10	0	0	0	0		10	0	0	0	0	
3000 ppm	10	10	0	0	0	0		10	0	0	0	0	
4000 ppm	10	10	0	0	0	0		10	0	0	0	0	

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of CHI SQUARE

APPENDIX H 1

GROSS FINDINGS : SUMMARY, RAT : MALE ALL ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	500 ppm 10 (%)	1000 ppm 10 (%)	2000 ppm 10 (%)
liver	herniation		1 (10)	1 (10)	0 (0)	1 (10)

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	3000 ppm	4000 ppm
		NO. of Animals	10 (%)	10 (%)
liver	herniation		1 (10)	2 (20)

APPENDIX H 2

GROSS FINDINGS : SUMMARY, RAT : FEMALE ALL ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name	Control	500 ppm	1000 ppm	2000 ppm
		NO. of Animals	10 (%)	10 (%)	10 (%)	10 (%)
liver	herniation		2 (20)	3 (30)	2 (20)	2 (20)

Organ	Findings	Group Name	3000 ppm	4000 ppm
		NO. of Animals	10 (%)	10 (%)
liver	herniation		0 (0)	1 (10)

APPENDIX I 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	297± 21	0.219± 0.031	0.048± 0.007	2.974± 0.126	0.916± 0.069	0.982± 0.059
500 ppm	10	289± 12	0.190± 0.018*	0.047± 0.003	3.031± 0.119	0.895± 0.030	0.970± 0.051
1000 ppm	10	286± 10	0.196± 0.021	0.049± 0.008	3.043± 0.099	0.875± 0.059	0.960± 0.031
2000 ppm	10	281± 11	0.188± 0.033*	0.048± 0.005	3.083± 0.099	0.870± 0.047	0.964± 0.033
3000 ppm	10	272± 14**	0.181± 0.020**	0.047± 0.002	3.030± 0.139	0.887± 0.071	0.949± 0.052
4000 ppm	10	246± 15**	0.160± 0.022**	0.044± 0.003	3.080± 0.085	0.823± 0.043**	0.898± 0.050**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.774± 0.136	0.543± 0.047	7.314± 0.744	1.912± 0.040
500 ppm	10	1.859± 0.059	0.556± 0.023	8.128± 0.368**	1.895± 0.043
1000 ppm	10	1.920± 0.073**	0.553± 0.031	8.786± 0.354**	1.888± 0.029
2000 ppm	10	1.917± 0.086**	0.565± 0.035	9.740± 0.662**	1.899± 0.040
3000 ppm	10	1.904± 0.099*	0.578± 0.029	9.915± 0.642**	1.875± 0.039
4000 ppm	10	1.829± 0.103	0.512± 0.030	8.892± 0.515**	1.854± 0.035**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX I 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	157± 9	0.160± 0.022	0.053± 0.005	0.105± 0.010	0.583± 0.044	0.733± 0.053
500 ppm	10	157± 8	0.167± 0.019	0.053± 0.005	0.103± 0.013	0.595± 0.032	0.724± 0.038
1000 ppm	10	151± 11	0.151± 0.019	0.053± 0.007	0.101± 0.014	0.578± 0.037	0.709± 0.042
2000 ppm	10	148± 8	0.154± 0.021	0.055± 0.007	0.097± 0.010	0.561± 0.028	0.692± 0.043
3000 ppm	10	143± 8**	0.145± 0.021	0.051± 0.004	0.095± 0.012	0.555± 0.022	0.686± 0.018
4000 ppm	10	143± 8**	0.135± 0.014*	0.053± 0.010	0.095± 0.010	0.569± 0.044	0.692± 0.038

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.036± 0.047	0.350± 0.026	3.747± 0.332	1.757± 0.036
500 ppm	10	1.097± 0.069*	0.367± 0.036	4.128± 0.140*	1.760± 0.053
1000 ppm	10	1.100± 0.046*	0.345± 0.027	4.172± 0.336**	1.746± 0.038
2000 ppm	10	1.110± 0.050*	0.366± 0.041	4.510± 0.203**	1.725± 0.039
3000 ppm	10	1.113± 0.042**	0.365± 0.027	4.598± 0.239**	1.769± 0.043
4000 ppm	10	1.103± 0.058*	0.365± 0.025	4.808± 0.324**	1.744± 0.054

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX J 1

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	297± 21	0.074± 0.009	0.016± 0.002	1.006± 0.068	0.309± 0.016	0.332± 0.017
500 ppm	10	289± 12	0.066± 0.006	0.016± 0.001	1.050± 0.036	0.310± 0.013	0.336± 0.015
1000 ppm	10	286± 10	0.069± 0.006	0.017± 0.003	1.066± 0.044*	0.306± 0.016	0.336± 0.011
2000 ppm	10	281± 11	0.067± 0.010	0.017± 0.002	1.097± 0.045**	0.309± 0.012	0.343± 0.014
3000 ppm	10	272± 14**	0.066± 0.005	0.017± 0.001	1.114± 0.037**	0.326± 0.020	0.349± 0.020
4000 ppm	10	246± 15**	0.065± 0.009	0.018± 0.002	1.256± 0.063**	0.335± 0.012**	0.365± 0.005**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.599± 0.015	0.184± 0.011	2.462± 0.083	0.647± 0.036
500 ppm	10	0.644± 0.016**	0.192± 0.009	2.814± 0.058**	0.657± 0.023
1000 ppm	10	0.672± 0.027**	0.193± 0.008	3.073± 0.056**	0.661± 0.020
2000 ppm	10	0.681± 0.020**	0.201± 0.008**	3.459± 0.143**	0.676± 0.030
3000 ppm	10	0.700± 0.034**	0.213± 0.007**	3.640± 0.100**	0.690± 0.033*
4000 ppm	10	0.744± 0.028**	0.208± 0.008**	3.618± 0.109**	0.756± 0.042**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX J 2

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	157± 9	0.102± 0.011	0.034± 0.003	0.067± 0.005	0.371± 0.015	0.468± 0.037
500 ppm	10	157± 8	0.106± 0.010	0.034± 0.004	0.066± 0.008	0.381± 0.024	0.464± 0.035
1000 ppm	10	151± 11	0.100± 0.011	0.035± 0.004	0.067± 0.008	0.383± 0.017	0.472± 0.045
2000 ppm	10	148± 8	0.104± 0.011	0.037± 0.006	0.066± 0.007	0.381± 0.016	0.469± 0.027
3000 ppm	10	143± 8**	0.101± 0.012	0.035± 0.003	0.067± 0.009	0.390± 0.019	0.481± 0.020
4000 ppm	10	143± 8**	0.095± 0.011	0.037± 0.006	0.067± 0.006	0.398± 0.022	0.485± 0.023

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.661± 0.028	0.223± 0.009	2.384± 0.101	1.123± 0.073
500 ppm	10	0.701± 0.028	0.234± 0.015	2.642± 0.117**	1.127± 0.059
1000 ppm	10	0.731± 0.057**	0.228± 0.011	2.761± 0.077**	1.162± 0.098
2000 ppm	10	0.754± 0.047**	0.248± 0.018**	3.059± 0.060**	1.172± 0.056
3000 ppm	10	0.781± 0.035**	0.255± 0.013**	3.225± 0.126**	1.242± 0.049**
4000 ppm	10	0.774± 0.041**	0.256± 0.009**	3.368± 0.059**	1.224± 0.054**

Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Dunnett

APPENDIX K 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : ALL ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0409
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control				500 ppm				1000 ppm				2000 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}																		
nasal cavit			<10>				<10>				<10>				<10>			
	inflammation:foreign body		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lung			<10>				<10>				<10>				<10>			
	accumulation of foamy cells		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}																		
bone marrow			<10>				<10>				<10>				<10>			
	granulation		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		10	0	0	0	10	0	0	0	10	0	0	0	0	10	0	0 **
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
	engorgement of erythrocyte		0	0	0	0	0	0	0	0	0	0	0	0	10	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Circulatory system}																		
heart			<10>				<10>				<10>				<10>			
	vacuolic change		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(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 ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	3000 ppm				4000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			<10>				<10>			
	inflammation:foreign body		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lung			<10>				<10>			
	accumulation of foamy cells		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Hematopoietic system}										
bone marrow			<10>				<10>			
	granulation		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			<10>				<10>			
	deposit of hemosiderin		0	10	0	0 **	0	10	0	0 **
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
	engorgement of erythrocyte		10	0	0	0 **	10	0	0	0 **
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Circulatory system}										
heart			<10>				<10>			
	vacuolic change		0	0	0	0	4	1	0	0 *
			(0)	(0)	(0)	(0)	(40)	(10)	(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 ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				500 ppm				1000 ppm				2000 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Circulatory system}																		
heart			<10>				<10>				<10>				<10>			
	granulation		4	0	0	0	1	0	0	0	1	0	0	0	1	0	0	0
			(40)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	herniation		1	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	inflammatory cell nest		2	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	perivascular inflammation		2	0	0	0	1	0	0	0	3	0	0	0	1	0	0	0
			(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	hepatocellular hypertrophy:central		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
pancreas			<10>				<10>				<10>				<10>			
	atrophy		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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 ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	3000 ppm				4000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Circulatory system}										
heart			<10>				<10>			
	granulation		3	0	0	0	1	0	0	0
			(30)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Digestive system}										
liver			<10>				<10>			
	herniation		1	0	0	0	2	0	0	0
			(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	inflammatory cell nest		1	0	0	0	2	0	0	0
			(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	perivascular inflammation		2	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hepatocellular hypertrophy:central		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
pancreas			<10>				<10>			
	atrophy		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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				500 ppm				1000 ppm				2000 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	basophilic change		2	0	0	0	9	0	0	0 **	3	7	0	0 **	0	10	0	0 **
			(20)	(0)	(0)	(0)	(90)	(0)	(0)	(0)	(30)	(70)	(0)	(0)	(0)	(100)	(0)	(0)
	eosinophilic body		2	8	0	0	0	1	9	0 **	0	0	10	0 **	0	0	10	0 **
			(20)	(80)	(0)	(0)	(0)	(10)	(90)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)
	mineralization:papilla		2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Endocrine system}																		
pituitary			<10>				<10>				<10>				<10>			
	Rathke pouch		1	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
thyroid			<10>				<10>				<10>				<10>			
	ultimibranchial body remanet		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Reproductive system}																		
prostate			<10>				<10>				<10>				<10>			
	inflammation		0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(20)	(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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	3000 ppm				4000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}										
kidney			<10>				<10>			
	basophilic change		0	10	0	0 **	4	4	0	0 *
			(0)	(100)	(0)	(0)	(40)	(40)	(0)	(0)
	eosinophilic body		0	0	10	0 **	0	0	10	0 **
			(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)
	mineralization:papilla		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Endocrine system}										
pituitary			<10>				<10>			
	Rathke pouch		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thyroid			<10>				<10>			
	ultimibranchial body remanet		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Reproductive system}										
prostate			<10>				<10>			
	inflammation		1	0	0	0	0	0	0	0
			(10)	(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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				500 ppm				1000 ppm				2000 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Special sense organs/appendage)																		
eye			<10>				<10>				<10>				<10>			
	retinal atrophy		0	0	0	0	1	0	0	0	1	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
Harder gl			<10>				<10>				<10>				<10>			
	granulation		0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(20)	(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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	3000 ppm				4000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Special sense organs/appendage}										
eye			<10>				<10>			
	retinal atrophy		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
Harder gl			<10>				<10>			
	granulation		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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

APPENDIX K 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE: ALL ANIMALS

(13-WEEK STUDY)

Organ	Findings	Group Name	Control				500 ppm				1000 ppm				2000 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}																		
nasal cavit			<10>				<10>				<10>				<10>			
	inflammation:foreign body		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	inflammation:respiratory epithelium		0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lung			<10>				<10>				<10>				<10>			
	accumulation of foamy cells		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Hematopoietic system}																		
bone marrow			<10>				<10>				<10>				<10>			
	granulation		2	1	0	0	2	1	0	0	2	0	0	0	1	0	0	0
			(20)	(10)	(0)	(0)	(20)	(10)	(0)	(0)	(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
spleen			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		0	10	0	0	0	10	0	0	0	10	0	0	0	0	10	0 **
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(0)	(100)	(0)
	engorgement of erythrocyte		0	0	0	0	0	0	0	0	0	0	0	0	6	0	0	0 *
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(60)	(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 ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	3000 ppm				4000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			<10>				<10>			
	inflammation:foreign body		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	inflammation:respiratory epithelium		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lung			<10>				<10>			
	accumulation of foamy cells		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}										
bone marrow			<10>				<10>			
	granulation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			<10>				<10>			
	deposit of hemosiderin		0	0	10	0 **	0	0	10	0 **
			(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)
	engorgement of erythrocyte		10	0	0	0 **	10	0	0	0 **
			(100)	(0)	(0)	(0)	(100)	(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 ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				500 ppm				1000 ppm				2000 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
{Circulatory system}																		
heart			<10>				<10>				<10>				<10>			
	granulation		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	herniation		2	0	0	0	3	0	0	0	2	0	0	0	2	0	0	0
			(20)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	granulation		1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	inflammatory cell nest		2	0	0	0	2	0	0	0	1	0	0	0	1	0	0	0
			(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	perivascular inflammation		4	0	0	0	2	0	0	0	5	0	0	0	4	0	0	0
			(40)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	(40)	(0)	(0)	(0)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	basophilic change		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(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 ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	3000 ppm				4000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Circulatory system}										
heart			<10>				<10>			
	granulation		2	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}										
liver			<10>				<10>			
	herniation		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	granulation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	inflammatory cell nest		3	0	0	0	0	0	0	0
			(30)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	perivascular inflammation		5	0	0	0	3	0	0	0
			(50)	(0)	(0)	(0)	(30)	(0)	(0)	(0)
{Urinary system}										
kidney			<10>				<10>			
	basophilic change		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(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 ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				500 ppm				1000 ppm				2000 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	mineralization:cortico-medullary junction		0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:papilla		2	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	eosinophilic droplet:proximal tubule		0	0	0	0	10	0	0	0 **	0	10	0	0 **	0	10	0	0 **
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
{Endocrine system}																		
pituitary			<10>				<10>				<10>				<10>			
	Rathke pouch		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thyroid			<10>				<10>				<10>				<10>			
	ultimibranchial body remanet		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Reproductive system}																		
vagina			<10>				<10>				<10>				<10>			
	epidermal cyst		0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(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 ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	3000 ppm				4000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}										
kidney			<10>				<10>			
	mineralization:cortico-medullary junction		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:papilla		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	eosinophilic droplet:proximal tubule		0	10	0	0 **	0	10	0	0 **
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
{Endocrine system}										
pituitary			<10>				<10>			
	Rathke pouch		1	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
thyroid			<10>				<10>			
	ultimibranchial body remanet		1	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Reproductive system}										
vagina			<10>				<10>			
	epidermal cyst		0	1	0	0	0	0	0	0
			(0)	(10)	(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
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				500 ppm				1000 ppm				2000 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Special sense organs/appendage}																		
Harder gl			<10>				<10>				<10>				<10>			
	granulation		2	0	1	0	2	1	1	0	2	0	0	0	1	0	0	0
			(20)	(0)	(10)	(0)	(20)	(10)	(10)	(0)	(20)	(0)	(0)	(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 ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	3000 ppm				4000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Special sense organs/appendage}										
Harder gl			<10>				<10>			
	granulation		2	0	0	0	3	0	0	0
			(20)	(0)	(0)	(0)	(30)	(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 ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

APPENDIX L 1

IDENTITY AND IMPURITY OF 2,4-DICHLORO-1-NITROBENZENE

IN THE 13-WEEK FEED STUDY

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

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

Lot No. : CKK5596

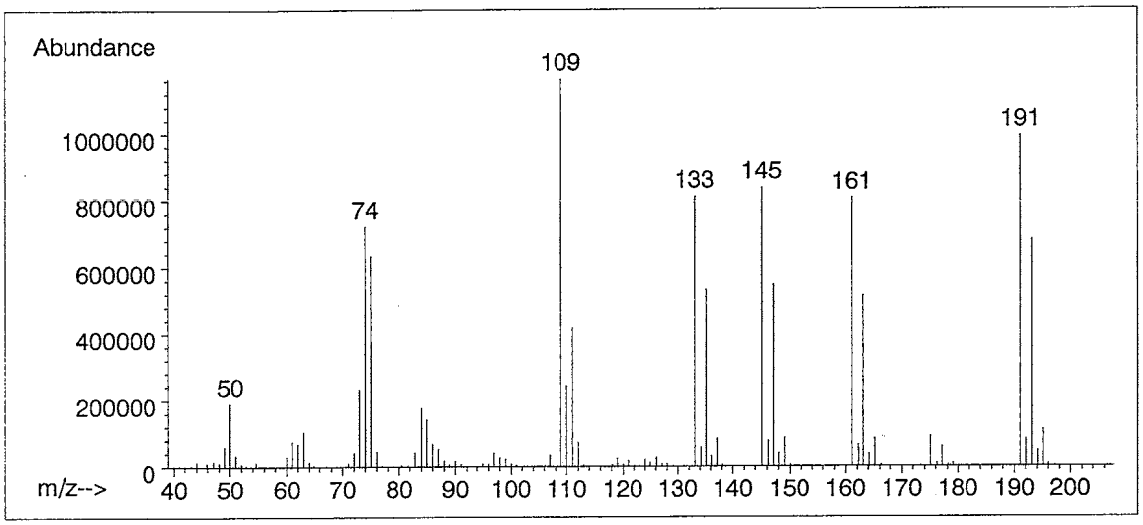
1. Spectral Data

Mass Spectrometry

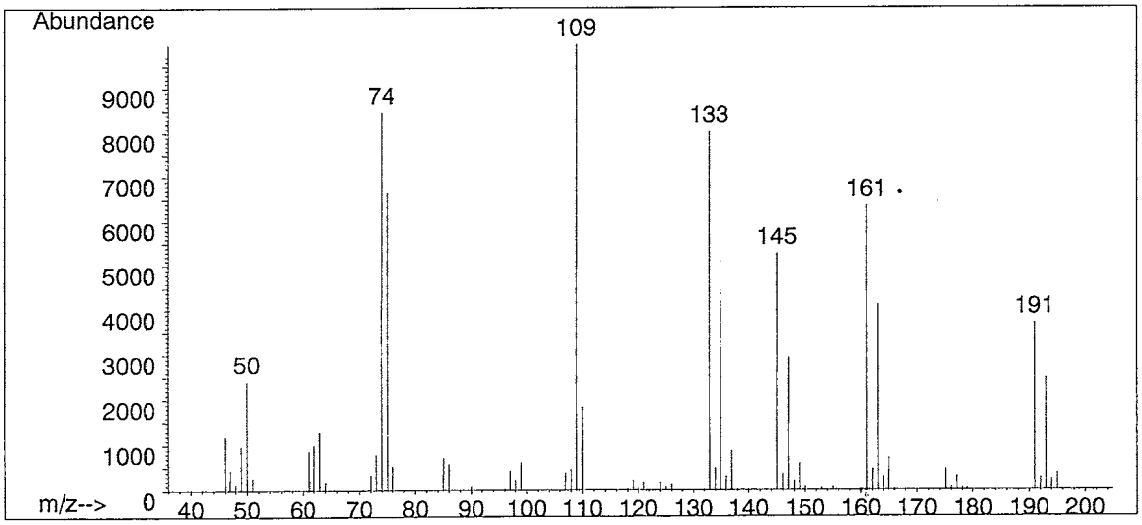
Instrument : Hewlett Packard 5989B Mass Spectrometer

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.

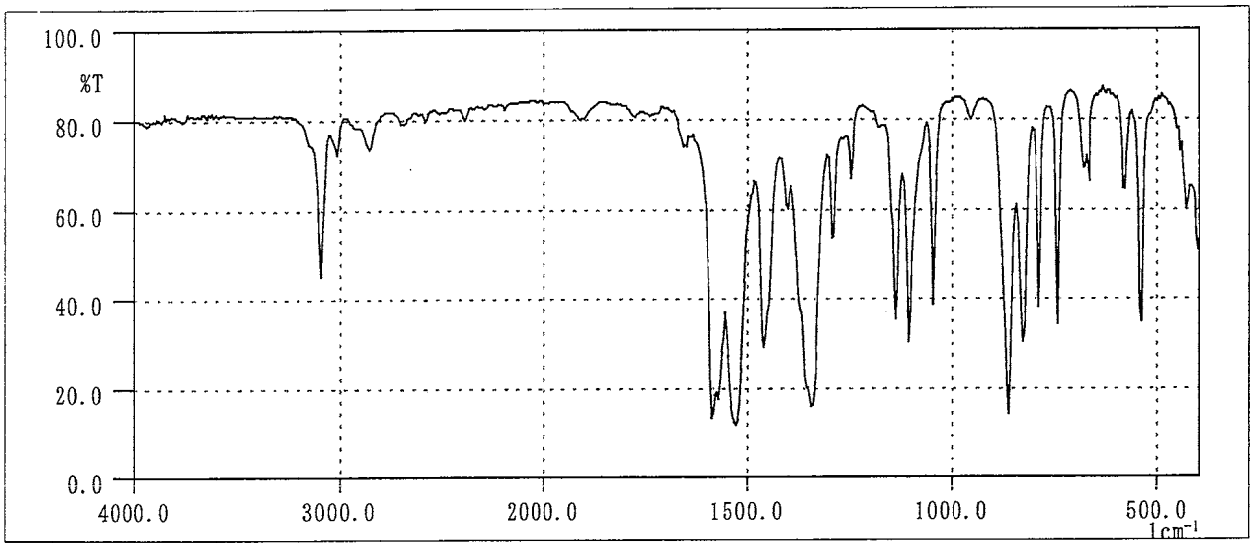
(*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition. John Wiley and Sons, Inc. (U.S.), Entry Number 74218)

Infrared Spectrometry

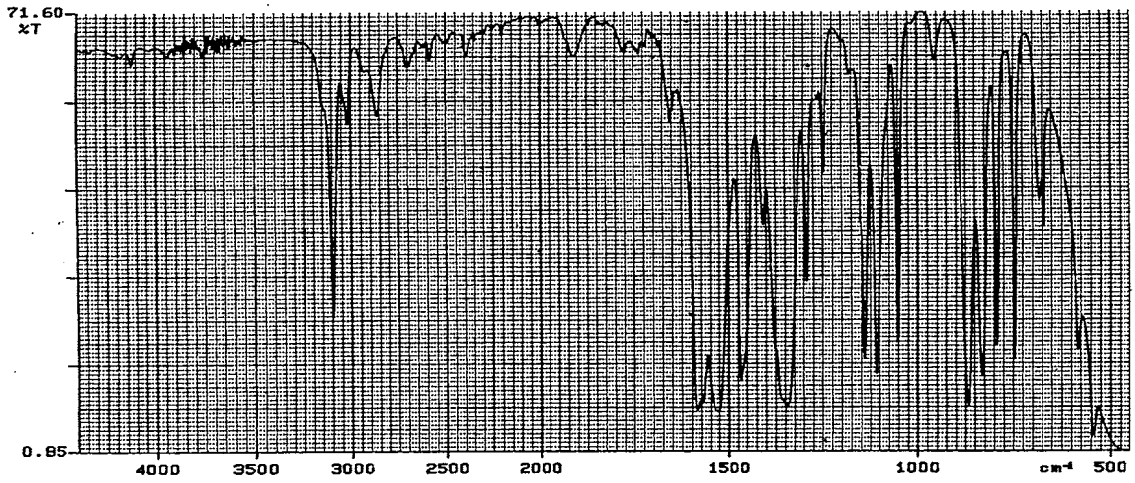
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

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.
(*Performed by Wako Pure Chemical Industries, Ltd.)

2. Impurity

Instrument : Hewlett Packard 6890 Gas Chromatograph

Column : Ultra1 (0.2 mmϕ × 50 m)

Column Temperature : 160 °C (5 min) → (20 °C/min) → 260 °C (5 min)

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μL

Sample Name	Peak No.	Area (%)	Peak Name
Test Substance	1	99.92	2,4-Dichloro-1-nitrobenzene
	2	0.03	1,5-Dichloro-2,3-dinitrobenzene
	3	0.05	1,2-Dichloro-4,5-dinitrobenzene

Results: Gas chromatography indicated one major peak (peak No.1) and two impurities. It was identified only by comparing its gas chromatograph with that of 1,5-dichloro-2,3-dinitrobenzene (peak No.2) and 1,2-dichloro-4,5-dinitrobenzene (peak No.3) in the 2,4-dichloro-1-nitrobenzene, the amount in the test substance were 0.03% and 0.05%.

3. Conclusions: The test substance was identified as 2,4-dichloro-1-nitrobenzene by the mass spectrum and the infrared spectrum. Gas chromatography indicated one major peak (peak No.1) and two impurities. It was identified only by comparing its gas chromatograph with that of 1,5-dichloro-2,3-dinitrobenzene and 1,2-dichloro-4,5-dinitrobenzene, the amount in the test substance were 0.03% and 0.05%.

APPENDIX L 2

STABILITY OF 2,4-DICHLORO-1-NITROBENZENE

IN THE 13-WEEK FEED STUDY

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

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

Lot No. : CKK5596

1. Sample : This lot was used from 2000.4.5 to 2000.7.6. Test substance was stored in a dark place at room temperature.

2. Gas Chromatography

Instrument : Hewlett Packard 6890 Gas Chromatograph

Column : Ultra1 (0.2 mmϕ × 50 m)

Column Temperature : 160 °C (5 min) → (20 °C/min) → 260 °C (5 min)

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μL

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
2000.03.27	1	5.097	99.92
	2	7.549	0.03
	3	7.719	0.05
2000.07.17	1	5.103	99.92
	2	7.559	0.03
	3	7.729	0.05

Results: Gas chromatography indicated one major peak (peak No.1) and two impurities (peak No. 2, 3 < 0.1% of total area) analyzed on 2000.3.27 and one major peak (peak No.1) and two impurities (peak No.2, 3 < 0.1% of total area) analyzed on 2000.7.17. No new trace impurity peak in the test substance analyzed on 2000.7.17 was detected.

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

APPENDIX L 3

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

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

	Target Concentration				
Date Analyzed	500[a]	1000	2000	3000	4000
2000.04.04	484 (96.7)[b]	959 (95.9)	1960 (97.8)	2860 (95.4)	4020 (101)

[a] ppm
[b] %

Analytical method : The samples were analyzed by gas chromatography.

Instrument : Hewlett Packard 6890 Gas Chromatograph
Column : Ultra 1 (0.2 mmϕ × 50 m)
Column Temperature : 160 °C → (5 min) → (20 °C/min) → 260 °C (5 min)
Flow Rate : 1 mL/min
Detector : FID (Flame Ionization Detector)
Injection Volume : 1 μL

APPENDIX L 4

HOMOGENEITY OF 2,4-DICHLORO-1-NITROBENZENE

IN FORMULATED DIETSIN IN THE 13-WEEK FEED STUDY

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

	Target Concentration				
	500[a]	1000	2000	3000	4000
Coefficient Variation	1.84[b]	0.63	1.17	0.74	1.11

[a] ppm
[b] % (n=7)

Analytical method : The samples were analyzed by gas chromatography.

Instrument : Hewlett Packard 6890 Gas Chromatograph
Column : Ultra 1 (0.2 mmϕ × 50 m)
Column Temperature : 160 °C → (5 min) → (20 °C/min) → 260 °C (5 min)
Flow Rate : 1 mL/min
Detector : FID (Flame Ionization Detector)
Injection Volume : 1 μL

APPENDIX L 5

STABILITY OF 2,4-DICHLORO-1-NITROBENZENE IN FORMULATED DIETS

STABILITY OF 2,4-DICHLORO-1-NITROBENZENE IN FORMULATED DIETS

Date Prepared	Date Analyzed	Target Concentration	
		200[a]	10000
1999.06.09	1999.06.09	210 (100)[b]	9900 (100)
	1999.06.18[c]	184 (87.6)	8730 (88.2)
	1999.06.24[d]	219 (104)	9010 (91.0)
	1999.07.07[d]	214 (102)	9080 (91.7)

[a] ppm
[b] % (Percentage was based on the concentration on date of preparation.)
[c] Animal room samples
[d] Cold storage samples

Analytical method : The samples were analyzed by gas chromatography.

Instrument : Hewlett Packard 6890 Gas Chromatograph
Column : Ultra 1 (0.2 mmϕ × 50 m)
Column Temperature : 160 °C → (5 min) → (20 °C/min) → 260 °C (5 min)
Flow Rate : 1 mL/min
Detector : FID (Flame Ionization Detector)
Injection Volume : 1 µL

APPENDIX M 1

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

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

Item	Method
Hematology	
Red blood cell (RBC)	Light scattering method [1]
Hemoglobin (Hgb)	Cyanmethemoglobin method [1]
Methemoglobin	Multiple-wavelength Spectrophotometric method [5]
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]
Triglyceride	LPL·GK·GPO·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]
Alkaline phosphatase (ALP)	GSCC 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]
Urinalysis	
pH,Protein,Glucose,Ketone body,Bilirubin,Occult Blood, Urobilinogen	Urinalysis reagent paper method [6]

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.)
5) CO-oximeter (CIBA·CORNING 270 : Ciba Corning Diagnostics Corp)
6) Ames reagent strips for urinalysis (Multistix : Bayer Corporation)

APPENDIX N 1

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

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK FEED STUDY OF 2,4-DICHLORO-1-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	0
Platelet	$\times 10^3/\mu L$	0
Reticulocyte	‰	1
Prothrombin time	sec	1
Activated partial thromboplastin time (APTT)	sec	2
White blood cell (WBC)	$\times 10^3/\mu L$	0
Differential WBC	%	
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
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