1,4 - ジクロロ - 2 - 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：０３０１

APPENDIX

APPENDIXES

APPENDIXES (CONTINUED)

APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0301
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
PILOERECTION	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	0	0	0	0	0	0	1	2	1	1	1
YELLOW 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	10	10	10	10	10	10	10	10	10	10	10

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0301
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
PILOERECTION	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	0	0	0	0	0	0	0	0	0	1	0
EYE OPACITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	1481 ppm	0	0	0	0	0	1	1	1	1	1	1	1	1
	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	0	0	0	0	0	0	0	0	0	0	0
CORNEAL OPACITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	1481 ppm	0	0	0	0	0	1	1	1	1	1	1	1	1
	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	0	0	0	0	0	0	0	0	0	0	0
YELLOW URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	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	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. : 0301
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	120± 4	148± 5	181± 7	201± 10	221± 9	238± 11	250± 12
1481 ppm	120± 4	148± 5	179± 8	198± 8	218± 7	234± 7	244± 6
2222 ppm	120± 4	145± 4	175± 5	193± 7	210± 9*	224± 12*	235± 11*
3333 ppm	120± 4	144± 5	172± 9*	185± 9**	198± 10**	210± 10**	219± 11**
5000 ppm	120± 4	133± 5**	153± 9**	164± 11**	175± 11**	183± 14**	189± 16**
7500 ppm	120± 4	115± 4**	113± 5**	120± 6**	126± 7**	128± 9**	133± 9**

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

STUDY NO. : 0301
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	262± 11	269± 13	283± 12	290± 14	297± 13	304± 14	308± 16
1481 ppm	256± 7	265± 7	276± 6	282± 6	292± 8	298± 8	304± 9
2222 ppm	242± 12**	250± 12**	261± 13**	269± 13**	277± 12**	283± 10**	289± 12**
3333 ppm	226± 10**	234± 11**	244± 10**	250± 10**	257± 9**	265± 9**	272± 9**
5000 ppm	194± 16**	200± 15**	207± 14**	211± 15**	217± 16**	225± 15**	232± 13**
7500 ppm	140± 9**	141± 11**	142± 12**	144± 13**	147± 12**	153± 16**	156± 16**

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. : 0301
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	97± 3	112± 4	126± 4	133± 5	141± 6	149± 6	154± 6
1481 ppm	97± 2	112± 4	126± 6	131± 7	139± 8	145± 11	148± 10
2222 ppm	97± 3	109± 3	123± 4	128± 5	135± 7	140± 9	141± 9**
3333 ppm	97± 3	106± 4**	118± 5**	122± 4**	126± 6**	132± 7**	133± 8**
5000 ppm	97± 3	104± 4**	115± 5**	118± 5**	123± 5**	129± 6**	131± 8**
7500 ppm	97± 3	93± 3**	96± 4**	99± 5**	103± 6**	108± 7**	110± 8**

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

STUDY NO. : 0301
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± 7	159± 7	163± 7	165± 8	168± 8	171± 9	172± 10
1481 ppm	149± 12	152± 11	156± 13	155± 13	160± 14	161± 15	163± 13
2222 ppm	141± 9**	141± 10**	145± 9**	146± 11**	147± 9**	149± 12**	150± 11**
3333 ppm	135± 7**	137± 7**	138± 8**	139± 8**	141± 9**	144± 7**	144± 8**
5000 ppm	132± 8**	132± 7**	135± 8**	135± 8**	137± 9**	139± 8**	140± 8**
7500 ppm	112± 8**	113± 9**	118± 9**	118± 11**	121± 11**	123± 9**	123± 9**

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

(HAN260)

APPENDIX C 1

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0301
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	13.5± 0.5	14.3± 0.9	15.1± 0.9	14.8± 0.7	15.4± 0.6	14.8± 0.7	15.1± 0.8
1481 ppm	13.0± 0.5	14.4± 0.8	14.7± 1.0	14.5± 0.7	15.2± 0.8	14.8± 0.9	15.0± 1.0
2222 ppm	12.4± 0.4*	13.7± 0.7	14.1± 0.9	13.6± 0.9**	14.1± 1.1*	13.7± 0.7	13.8± 0.8*
3333 ppm	12.2± 0.7*	13.7± 0.9	13.5± 0.9**	12.9± 0.8**	13.5± 1.0**	13.5± 1.2*	13.7± 1.4*
5000 ppm	11.5± 1.0**	12.6± 1.7*	11.4± 1.3**	11.2± 0.5**	11.6± 0.8**	11.5± 1.2**	12.0± 0.9**
7500 ppm	9.6± 1.5**	9.5± 4.1**	7.4± 0.6**	7.8± 1.4**	8.3± 1.4**	8.3± 1.1**	8.6± 1.0**

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

STUDY NO. : 0301
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	14.6± 0.9	15.3± 0.8	15.1± 1.2	15.1± 1.1	14.9± 1.0	15.2± 1.2
1481 ppm	14.9± 1.0	15.3± 1.0	15.3± 1.2	15.6± 1.3	15.3± 1.2	15.6± 1.1
2222 ppm	13.6± 0.9	14.0± 0.9**	14.0± 0.9	14.3± 0.7	14.1± 0.7	14.6± 0.7
3333 ppm	13.4± 1.1*	13.5± 0.8**	13.3± 0.8**	13.4± 0.8**	13.4± 0.5**	13.6± 0.6**
5000 ppm	11.7± 0.9**	11.8± 0.9**	11.5± 0.9**	11.8± 0.8**	11.9± 0.9**	12.5± 0.8**
7500 ppm	8.9± 1.4**	7.8± 0.4**	8.5± 1.2**	8.2± 0.6**	9.0± 1.1**	9.3± 1.2**

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. : 0301
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	10.8± 0.6	10.7± 0.8	10.7± 0.8	10.7± 0.9	11.0± 1.0	10.9± 1.0	11.1± 1.1
1481 ppm	10.1± 0.5*	10.4± 0.8	10.3± 0.8	10.0± 0.5	10.7± 0.8	10.2± 0.9	10.6± 1.0
2222 ppm	9.8± 0.4**	10.2± 0.6	9.8± 0.5*	9.9± 0.9	10.7± 1.2	10.0± 1.1	9.8± 0.9
3333 ppm	9.4± 0.5**	9.7± 0.6**	9.5± 0.6**	9.2± 0.6**	9.5± 0.6	9.3± 0.5*	9.4± 0.5
5000 ppm	8.8± 0.7**	9.2± 0.6**	8.3± 0.8**	8.3± 0.8**	9.1± 1.2*	9.0± 1.4*	9.0± 1.6**
7500 ppm	7.5± 0.8**	6.8± 0.6**	6.1± 0.3**	6.4± 0.4**	6.6± 0.5**	6.4± 0.5**	6.5± 0.4**

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

STUDY NO. : 0301
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	10.9± 1.0	10.9± 0.8	10.3± 0.7	10.8± 1.2	10.5± 0.9	10.6± 0.9
1481 ppm	10.7± 1.0	10.6± 1.4	9.8± 1.1	10.4± 1.2	10.1± 0.9	10.1± 0.9
2222 ppm	9.6± 1.1*	9.9± 0.9	9.8± 1.2	10.4± 1.7	9.9± 1.4	10.0± 1.9
3333 ppm	9.4± 0.6**	9.3± 0.8*	9.0± 0.8*	9.4± 0.9*	9.3± 0.5*	9.2± 0.5
5000 ppm	8.6± 1.2**	9.0± 1.6*	8.2± 0.9**	8.9± 1.5**	8.7± 0.9**	8.9± 1.3*
7500 ppm	6.8± 0.7**	6.8± 0.6**	6.5± 0.7**	7.0± 0.6**	6.8± 0.6**	6.7± 0.7**

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. : 0301
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
1481 ppm	0.130± 0.003	0.119± 0.004	0.110± 0.006	0.099± 0.005	0.096± 0.005	0.090± 0.006	0.087± 0.005
2222 ppm	0.190± 0.003	0.174± 0.006	0.162± 0.006	0.143± 0.004	0.140± 0.006	0.130± 0.003	0.126± 0.003
3333 ppm	0.282± 0.010	0.267± 0.007	0.243± 0.010	0.218± 0.008	0.214± 0.010	0.206± 0.019	0.201± 0.023
5000 ppm	0.432± 0.037	0.411± 0.045	0.347± 0.030	0.321± 0.010	0.318± 0.013	0.305± 0.017	0.309± 0.014
7500 ppm	0.628± 0.095	0.627± 0.282	0.456± 0.039	0.466± 0.108	0.474± 0.094	0.460± 0.081	0.459± 0.060

STUDY NO. : 0301
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
1481 ppm	0.083± 0.006	0.082± 0.006	0.080± 0.007	0.079± 0.007	0.076± 0.006	0.076± 0.007
2222 ppm	0.121± 0.004	0.119± 0.003	0.116± 0.005	0.114± 0.005	0.110± 0.004	0.112± 0.003
3333 ppm	0.191± 0.017	0.185± 0.011	0.177± 0.007	0.173± 0.010	0.168± 0.006	0.167± 0.007
5000 ppm	0.294± 0.016	0.286± 0.014	0.273± 0.010	0.272± 0.008	0.266± 0.013	0.269± 0.009
7500 ppm	0.470± 0.088	0.404± 0.016	0.431± 0.070	0.405± 0.029	0.443± 0.055	0.442± 0.055

APPENDIX D 2

CHEMICAL INTAKE CHANGES : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0301
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
1481 ppm	0.133± 0.006	0.123± 0.005	0.116± 0.005	0.107± 0.004	0.110± 0.010	0.102± 0.009	0.106± 0.009
2222 ppm	0.200± 0.009	0.184± 0.009	0.170± 0.008	0.163± 0.012	0.170± 0.020	0.158± 0.018	0.155± 0.013
3333 ppm	0.295± 0.013	0.274± 0.012	0.258± 0.010	0.243± 0.011	0.242± 0.009	0.234± 0.012	0.233± 0.010
5000 ppm	0.420± 0.024	0.399± 0.016	0.351± 0.025	0.336± 0.026	0.354± 0.031	0.341± 0.039	0.338± 0.041
7500 ppm	0.606± 0.076	0.533± 0.038	0.465± 0.022	0.467± 0.029	0.457± 0.018	0.440± 0.022	0.433± 0.025

STUDY NO. : 0301
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
1481 ppm	0.104± 0.009	0.100± 0.013	0.093± 0.008	0.097± 0.009	0.094± 0.006	0.091± 0.004
2222 ppm	0.151± 0.017	0.151± 0.013	0.149± 0.018	0.158± 0.026	0.149± 0.028	0.148± 0.028
3333 ppm	0.229± 0.007	0.223± 0.014	0.217± 0.013	0.221± 0.014	0.216± 0.009	0.212± 0.008
5000 ppm	0.325± 0.031	0.331± 0.044	0.302± 0.023	0.323± 0.039	0.310± 0.020	0.316± 0.033
7500 ppm	0.449± 0.028	0.430± 0.020	0.414± 0.027	0.436± 0.033	0.416± 0.028	0.406± 0.024

APPENDIX E 1

HEMATOLOGY : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0301
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 f ℓ		MCH p g		MCHC g/dℓ		PLATELET $10^3/\mu\ell$	
Control	10	9.76±	0.22	16.7±	0.4	48.7±	1.4	49.9±	0.7	17.1±	0.3	34.3±	0.5	667±	33
1481 ppm	10	9.82±	0.33	16.3±	0.5	47.9±	1.7	48.8±	0.4**	16.6±	0.2	34.0±	0.5	694±	30
2222 ppm	10	9.34±	0.54	15.8±	0.4**	46.1±	2.3*	49.4±	0.6	17.0±	0.9	34.4±	1.5	674±	33
3333 ppm	10	9.17±	0.44**	15.5±	0.4**	45.6±	2.5**	49.7±	0.6	16.9±	0.9	34.1±	1.9	641±	49
5000 ppm	9	9.01±	0.36**	15.6±	0.2**	46.3±	1.7	51.4±	0.6**	17.3±	0.7	33.7±	1.2	608±	34*
7500 ppm	9	8.01±	0.39**	15.0±	0.5**	45.1±	2.3**	56.3±	0.9**	18.7±	0.7	33.3±	1.4**	484±	56**

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

STUDY NO. : 0301
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	25±	6	0.2±	0.1	13.7±	1.1	23.8±	2.1
1481 ppm	10	26±	7	0.2±	0.1	14.0±	2.8	22.7±	3.5
2222 ppm	10	28±	4	0.2±	0.1	13.0±	1.6	21.6±	1.7
3333 ppm	10	33±	8	0.3±	0.1	12.3±	0.9	20.1±	2.0**
5000 ppm	9	36±	8**	0.3±	0.1	12.3±	0.8	21.5±	2.1
7500 ppm	9	57±	8**	0.4±	0.2**	13.0±	0.9	18.2±	2.8**

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

STUDY NO. : 0301
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	OTHERS
Control	10	5.70± 0.98	0± 0	25± 4	1± 1	0± 0	4± 2	70± 5	0± 1
1481 ppm	10	6.02± 1.67	0± 0	22± 6	2± 1	0± 0	4± 1	72± 6	0± 1
2222 ppm	10	6.83± 2.44	0± 0	22± 5	1± 1	0± 0	4± 2	73± 7	0± 1
3333 ppm	10	6.17± 1.77	0± 1	22± 4	1± 1	0± 0	3± 2	73± 5	0± 0
5000 ppm	9	5.25± 1.63	0± 0	25± 5	1± 1	0± 0	3± 1	71± 5	0± 0
7500 ppm	9	3.88± 1.29	0± 0	23± 6	1± 0	0± 0	3± 2	73± 6	0± 0

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

APPENDIX E 2

HEMATOLOGY : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0301
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	8.98± 0.22	16.4± 0.3	46.9± 0.9	52.3± 0.5	18.2± 0.3	34.9± 0.3	672± 33
1481 ppm	9	8.70± 0.35	15.6± 0.6**	44.9± 2.1	51.6± 0.9	17.9± 0.2	34.7± 0.5	662± 50
2222 ppm	10	8.63± 0.28	15.4± 0.4**	44.8± 1.2	51.9± 0.7	17.8± 0.4	34.3± 0.4	638± 51
3333 ppm	9	8.10± 0.50**	15.0± 0.6**	42.4± 2.5**	52.3± 0.6	18.6± 1.4	35.6± 2.5	588± 37*
5000 ppm	9	8.15± 0.51**	14.8± 0.6**	43.3± 3.1**	53.1± 0.8	18.2± 0.8	34.4± 1.9	567± 82**
7500 ppm	9	7.91± 0.27**	14.6± 0.4**	44.0± 1.6**	55.6± 1.1**	18.5± 0.8	33.2± 1.2**	485± 99**

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

STUDY NO. : 0301
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	24±	5	0.2±	0.1	11.6±	0.3	18.5±	2.5
1481 ppm	9	28±	8	0.2±	0.1	11.3±	0.2	16.9±	1.0
2222 ppm	10	27±	7	0.2±	0.1	11.6±	0.5	17.3±	3.3
3333 ppm	9	32±	6	0.2±	0.1	11.7±	0.6	17.1±	1.8
5000 ppm	9	37±	9**	0.4±	0.1**	11.9±	0.4	16.2±	2.0
7500 ppm	9	50±	10**	0.3±	0.1	12.9±	0.5**	17.0±	1.8

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

STUDY NO. : 0301
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		OTHERS	
Control	10	3.59±	0.92	0±	0	24±	7	1±	1	0±	0	4±	2	71±	7	0±	0
1481 ppm	9	3.92±	1.48	0±	0	21±	4	1±	1	0±	0	5±	1	73±	5	0±	0
2222 ppm	10	2.97±	0.80	0±	0	20±	5	1±	1	0±	0	4±	2	74±	5	0±	0
3333 ppm	9	2.49±	0.91	0±	0	22±	5	1±	1	0±	0	3±	1	74±	5	0±	0
5000 ppm	9	2.65±	0.66	0±	0	22±	5	0±	1	0±	0	3±	2	74±	5	0±	0
7500 ppm	9	2.06±	1.25**	0±	0	22±	8	0±	1	0±	0	3±	1	74±	9	0±	1

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

APPENDIX F 1

BIOCHEMISTRY : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0301
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	6.3±	0.1	3.9±	0.0	1.7±	0.1	0.14±	0.01	178±	10	67±	10	52±	11
1481 ppm	10	7.1±	0.1**	4.5±	0.1*	1.7±	0.1	0.15±	0.01	183±	21	118±	14**	63±	27
2222 ppm	10	7.2±	0.2**	4.6±	0.1**	1.7±	0.1	0.15±	0.01	185±	31	126±	11**	67±	16
3333 ppm	10	7.2±	0.2**	4.6±	0.1**	1.8±	0.1	0.16±	0.01*	183±	17	140±	14**	65±	14
5000 ppm	9	7.3±	0.3**	4.7±	0.1**	1.8±	0.1	0.17±	0.01**	174±	10	143±	10**	51±	14
7500 ppm	9	6.5±	0.2	4.2±	0.2	1.9±	0.1**	0.19±	0.02**	149±	5**	126±	11**	25±	11**

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

STUDY NO. : 0301
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	114± 12	76± 12	45± 6	182± 65	266± 29	2± 1	105± 17
1481 ppm	10	186± 15**	77± 16	56± 22	182± 36	231± 32	2± 1	102± 13
2222 ppm	10	206± 13**	71± 12	42± 7	187± 43	245± 32	2± 1	97± 12
3333 ppm	10	231± 19**	62± 7*	42± 5	184± 50	234± 21	3± 1	93± 16
5000 ppm	9	246± 19**	84± 58	74± 64	216± 86	247± 22	6± 1**	104± 23
7500 ppm	9	220± 20**	84± 14	78± 17**	290± 116	300± 42	26± 4**	116± 26

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

STUDY NO. : 0301
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	19.1± 1.8	0.5± 0.0	141± 1	3.8± 0.4	106± 1	10.2± 0.1	5.6± 0.5
1481 ppm	10	21.4± 1.2*	0.6± 0.1	141± 1	3.9± 0.3	104± 2*	10.6± 0.3*	5.5± 0.4
2222 ppm	10	22.1± 2.3**	0.6± 0.1	140± 1	3.9± 0.4	105± 1	10.7± 0.3**	5.6± 0.6
3333 ppm	10	22.3± 1.3**	0.5± 0.1	140± 1	4.1± 0.2	104± 1*	10.8± 0.1**	5.7± 0.7
5000 ppm	9	19.2± 1.6	0.5± 0.1	139± 1**	4.0± 0.2	104± 1**	10.7± 0.3**	5.7± 0.4
7500 ppm	9	20.8± 2.4	0.4± 0.0**	138± 1**	4.1± 0.3	105± 2	10.1± 0.3	6.3± 0.5*

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

APPENDIX F 2

BIOCHEMISTRY : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0301
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	1.7±	0.1	0.16±	0.01	139±	16	73±	5	18±	6
1481 ppm	9	6.8±	0.2**	4.2±	0.1**	1.7±	0.1	0.17±	0.01	146±	10	136±	14**	22±	7
2222 ppm	10	6.7±	0.2**	4.2±	0.2**	1.7±	0.1	0.16±	0.01	154±	9*	136±	10**	20±	4
3333 ppm	9	6.8±	0.2**	4.3±	0.1**	1.7±	0.1	0.16±	0.02	151±	14	148±	11**	20±	5
5000 ppm	9	6.9±	0.2**	4.3±	0.2**	1.7±	0.2	0.18±	0.01*	156±	9*	154±	12**	23±	4
7500 ppm	9	6.5±	0.2	4.2±	0.2**	1.9±	0.3	0.19±	0.02**	156±	15*	142±	13**	19±	3

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

STUDY NO. : 0301
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	135±	10	74±	9	37±	4	290±	151	195±	22	2±	1	139±	45
1481 ppm	9	220±	20**	66±	9	36±	9	245±	92	166±	17	3±	1	114±	28
2222 ppm	10	221±	19**	66±	6	37±	6	258±	96	167±	25	4±	1	114±	26
3333 ppm	9	241±	19**	69±	5	47±	16	258±	88	161±	21*	6±	2**	115±	22
5000 ppm	9	255±	21**	68±	7	39±	6	309±	136	168±	27	18±	7**	119±	33
7500 ppm	9	244±	16**	69±	7	38±	4	402±	191	232±	34*	49±	6**	146±	47

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

STUDY NO. : 0301
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	18.3± 1.5	0.5± 0.1	140± 1	3.7± 0.2	107± 2	9.9± 0.1	5.4± 1.0
1481 ppm	9	18.7± 1.1	0.5± 0.0	140± 1	3.8± 0.2	107± 1	10.2± 0.2	5.0± 0.7
2222 ppm	10	20.1± 2.2	0.5± 0.0**	140± 1	3.8± 0.3	108± 2	10.2± 0.3*	5.3± 1.0
3333 ppm	9	20.2± 2.1	0.5± 0.1**	139± 1	3.7± 0.3	108± 2	10.2± 0.2	5.1± 0.9
5000 ppm	9	20.7± 3.3	0.5± 0.1**	139± 1*	3.9± 0.2	107± 1	10.3± 0.3**	5.2± 0.4
7500 ppm	9	22.6± 2.8**	0.4± 0.0**	138± 2**	4.1± 0.3**	108± 2	10.0± 0.2	5.6± 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. : 0301 URINALYSIS
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

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	9	1		0	0	9	1	0	0		10	0	0	0	0	0		0	5	5	0	0	0		10	0	0	0	
1481 ppm	10	0	0	0	0	1	9	0		0	0	10	0	0	0		10	0	0	0	0	0		2	8	0	0	0	0	*	10	0	0	0	
2222 ppm	10	0	0	0	0	0	9	1		0	0	9	1	0	0		10	0	0	0	0	0		3	7	0	0	0	0	*	10	0	0	0	
3333 ppm	10	0	0	0	0	1	9	0		0	0	8	2	0	0		10	0	0	0	0	0		6	4	0	0	0	0	**	10	0	0	0	
5000 ppm	10	0	0	0	0	3	6	1		0	0	8	2	0	0		10	0	0	0	0	0		4	6	0	0	0	0	*	10	0	0	0	
7500 ppm	10	0	0	0	2	1	7	0		0	1	9	0	0	0		10	0	0	0	0	0		4	6	0	0	0	0	*	10	0	0	0	

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

STUDY NO. : 0301 URINALYSIS
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

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	
1481 ppm	10	10	0	0	0	0		10	0	0	0	0	
2222 ppm	10	10	0	0	0	0		10	0	0	0	0	
3333 ppm	10	10	0	0	0	0		10	0	0	0	0	
5000 ppm	10	10	0	0	0	0		10	0	0	0	0	
7500 ppm	10	9	0	0	1	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. : 0301 URINALYSIS
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

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	10	0		0	5	5	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
1481 ppm	10	0	0	0	0	2	8	0		0	5	5	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
2222 ppm	10	0	0	0	0	3	6	1		0	2	8	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
3333 ppm	10	0	0	0	0	2	8	0		0	4	6	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
5000 ppm	10	0	0	0	1	1	8	0		0	3	7	0	0	0		10	0	0	0	0	0		9	1	0	0	0	0		10	0	0	0	
7500 ppm	10	0	0	0	1	2	7	0		0	3	7	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. : 0301 URINALYSIS
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

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	
1481 ppm	10	10	0	0	0	0		10	0	0	0	0	
2222 ppm	10	10	0	0	0	0		10	0	0	0	0	
3333 ppm	10	10	0	0	0	0		10	0	0	0	0	
5000 ppm	10	10	0	0	0	0		10	0	0	0	0	
7500 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. : 0301
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 (%)	1481 ppm 10 (%)	2222 ppm 10 (%)	3333 ppm 10 (%)
liver	herniation		0 (0)	1 (10)	1 (10)	0 (0)
	accentuation of lobular structure		0 (0)	0 (0)	0 (0)	0 (0)

Organ	Findings	Group Name	5000 ppm	7500 ppm
		NO. of Animals	10 (%)	10 (%)
liver	herniation		2 (20)	0 (0)
	accentuation of lobular structure		3 (30)	10 (100)

APPENDIX H 2

GROSS FINDINGS : SUMMARY, RAT : FEMALE ALL ANIMALS

(13-WEEK STUDY)

Organ	Findings	Group Name	Control	1481 ppm	2222 ppm	3333 ppm
		NO. of Animals	10 (%)	10 (%)	10 (%)	10 (%)
liver	herniation		0 (0)	0 (0)	0 (0)	0 (0)

STUDY NO. : 0301
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name	5000 ppm	7500 ppm
		NO. of Animals	10 (%)	10 (%)
liver	herniation		1 (10)	1 (10)

APPENDIX I 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0301
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	ADRENL R	ADRENL L	ADRENALS	TESTIS R
Control	10	282± 15	0.204± 0.020	0.031± 0.007	0.031± 0.007	0.061± 0.013	1.486± 0.064
1481 ppm	10	273± 11	0.182± 0.024	0.031± 0.005	0.033± 0.007	0.064± 0.011	1.498± 0.033
2222 ppm	10	264± 12**	0.184± 0.030	0.028± 0.004	0.031± 0.007	0.059± 0.010	1.286± 0.062
3333 ppm	10	247± 8**	0.185± 0.022	0.030± 0.005	0.032± 0.004	0.062± 0.009	0.809± 0.076**
5000 ppm	10	210± 13**	0.161± 0.027**	0.026± 0.002	0.032± 0.006	0.058± 0.007	0.542± 0.038**
7500 ppm	10	144± 15**	0.104± 0.022**	0.022± 0.004**	0.027± 0.004	0.049± 0.008*	0.401± 0.030**

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

STUDY NO. : 0301
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	TESTIS L	TESTES	HEART	LUNG R	LUNG L	LUNGS
Control	10	1.502± 0.067	2.988± 0.125	0.928± 0.050	0.659± 0.040	0.354± 0.020	1.013± 0.054
1481 ppm	10	1.542± 0.057	3.041± 0.079	0.905± 0.056	0.647± 0.028	0.357± 0.020	1.004± 0.035
2222 ppm	10	1.334± 0.085**	2.619± 0.139**	0.871± 0.072	0.632± 0.042	0.343± 0.016	0.975± 0.044
3333 ppm	10	0.812± 0.067**	1.621± 0.106**	0.863± 0.059	0.623± 0.041	0.341± 0.019	0.964± 0.054
5000 ppm	10	0.596± 0.076**	1.138± 0.082**	0.757± 0.039**	0.557± 0.035**	0.305± 0.025**	0.862± 0.052**
7500 ppm	10	0.456± 0.072**	0.857± 0.097**	0.525± 0.058**	0.449± 0.037**	0.243± 0.020**	0.692± 0.055**

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

STUDY NO. : 0301
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	KIDNEY R	KIDNEY L	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.902± 0.060	0.907± 0.037	1.809± 0.086	0.533± 0.021	7.042± 0.323	1.879± 0.044
1481 ppm	10	1.021± 0.063**	1.041± 0.069**	2.063± 0.128**	0.520± 0.042	9.681± 0.740**	1.865± 0.043
2222 ppm	10	1.049± 0.073**	1.027± 0.070**	2.076± 0.133**	0.542± 0.042	9.946± 0.686**	1.859± 0.048
3333 ppm	10	1.032± 0.039**	1.038± 0.047**	2.070± 0.084**	0.549± 0.120	9.976± 0.490**	1.848± 0.040
5000 ppm	10	0.896± 0.051	0.917± 0.055	1.813± 0.100	0.465± 0.030**	9.163± 0.646**	1.793± 0.041**
7500 ppm	10	0.681± 0.038**	0.708± 0.032**	1.389± 0.069**	0.377± 0.046**	6.352± 0.802	1.665± 0.040**

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. : 0301
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	ADRENL R	ADRENL L	ADRENALS	OVARY R
Control	10	159± 9	0.168± 0.023	0.030± 0.005	0.032± 0.005	0.062± 0.008	0.052± 0.006
1481 ppm	10	149± 12	0.166± 0.019	0.029± 0.004	0.031± 0.003	0.060± 0.004	0.045± 0.007
2222 ppm	10	138± 12**	0.152± 0.025	0.026± 0.003	0.031± 0.004	0.058± 0.006	0.048± 0.006
3333 ppm	10	133± 8**	0.147± 0.024	0.025± 0.003*	0.030± 0.004	0.055± 0.007	0.045± 0.006
5000 ppm	10	129± 7**	0.140± 0.019*	0.024± 0.003**	0.027± 0.003*	0.051± 0.005**	0.043± 0.006*
7500 ppm	10	113± 9**	0.124± 0.026**	0.022± 0.003**	0.025± 0.005**	0.047± 0.007**	0.029± 0.005**

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

STUDY NO. : 0301
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	OVARY L	OVARIES	HEART	LUNG R	LUNG L	LUNGS
Control	10	0.054± 0.009	0.105± 0.010	0.619± 0.029	0.483± 0.036	0.265± 0.017	0.748± 0.049
1481 ppm	10	0.052± 0.007	0.097± 0.012	0.592± 0.045	0.473± 0.043	0.263± 0.010	0.736± 0.045
2222 ppm	10	0.054± 0.011	0.101± 0.013	0.557± 0.029	0.450± 0.033	0.251± 0.015	0.701± 0.044
3333 ppm	10	0.049± 0.005	0.094± 0.009	0.547± 0.067*	0.446± 0.018	0.245± 0.016*	0.691± 0.022*
5000 ppm	10	0.045± 0.011	0.088± 0.014**	0.522± 0.026**	0.423± 0.028**	0.243± 0.018**	0.667± 0.042**
7500 ppm	10	0.034± 0.005**	0.063± 0.009**	0.435± 0.052**	0.377± 0.032**	0.210± 0.013**	0.587± 0.041**

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

STUDY NO. : 0301
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	KIDNEY R	KIDNEY L	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.555± 0.033	0.571± 0.041	1.126± 0.069	0.376± 0.026	3.828± 0.268	1.736± 0.027
1481 ppm	10	0.600± 0.036*	0.615± 0.033*	1.215± 0.066*	0.357± 0.030	4.871± 0.387**	1.738± 0.047
2222 ppm	10	0.580± 0.050	0.598± 0.055	1.178± 0.102	0.333± 0.029**	4.855± 0.356**	1.721± 0.045
3333 ppm	10	0.585± 0.032	0.608± 0.021	1.193± 0.048	0.332± 0.025**	5.149± 0.314**	1.714± 0.032
5000 ppm	10	0.579± 0.037	0.602± 0.025	1.181± 0.059	0.341± 0.027*	5.444± 0.346**	1.687± 0.060*
7500 ppm	10	0.523± 0.021	0.539± 0.033	1.062± 0.047	0.299± 0.037**	5.126± 0.569**	1.625± 0.034**

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. : 0301
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	ADRENL R	ADRENL L	ADRENALS	TESTIS R
Control	10	282± 15	0.072± 0.006	0.011± 0.003	0.011± 0.003	0.022± 0.005	0.528± 0.025
1481 ppm	10	273± 11	0.067± 0.009	0.011± 0.002	0.012± 0.002	0.024± 0.004	0.548± 0.020
2222 ppm	10	264± 12**	0.070± 0.011	0.011± 0.001	0.012± 0.003	0.022± 0.004	0.489± 0.033**
3333 ppm	10	247± 8**	0.075± 0.008	0.012± 0.002	0.013± 0.002	0.025± 0.003	0.328± 0.035**
5000 ppm	10	210± 13**	0.077± 0.013	0.012± 0.001	0.015± 0.003**	0.028± 0.003**	0.259± 0.021**
7500 ppm	10	144± 15**	0.071± 0.010	0.015± 0.002**	0.019± 0.003**	0.034± 0.004**	0.280± 0.023**

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

STUDY NO. : 0301
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	TESTIS L	TESTES	HEART	LUNG R	LUNG L	LUNGS
Control	10	0.533± 0.016	1.061± 0.040	0.330± 0.017	0.234± 0.014	0.126± 0.004	0.360± 0.016
1481 ppm	10	0.565± 0.025	1.113± 0.041	0.331± 0.018	0.237± 0.012	0.131± 0.006	0.368± 0.015
2222 ppm	10	0.507± 0.040	0.996± 0.070*	0.330± 0.021	0.240± 0.012	0.130± 0.007	0.370± 0.012
3333 ppm	10	0.329± 0.028**	0.657± 0.050**	0.350± 0.023	0.253± 0.019*	0.138± 0.010**	0.391± 0.026**
5000 ppm	10	0.284± 0.033**	0.542± 0.037**	0.360± 0.010**	0.265± 0.007**	0.145± 0.009**	0.410± 0.012**
7500 ppm	10	0.316± 0.025**	0.596± 0.037**	0.365± 0.022**	0.313± 0.019**	0.170± 0.011**	0.483± 0.029**

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

STUDY NO. : 0301
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEY R	KIDNEY L	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.320± 0.020	0.322± 0.009	0.643± 0.026	0.190± 0.007	2.499± 0.039	0.668± 0.035
1481 ppm	10	0.373± 0.017**	0.381± 0.023**	0.755± 0.038**	0.190± 0.011	3.539± 0.195**	0.683± 0.022
2222 ppm	10	0.398± 0.019**	0.390± 0.017**	0.787± 0.029**	0.206± 0.016**	3.772± 0.124**	0.706± 0.027**
3333 ppm	10	0.418± 0.018**	0.420± 0.018**	0.839± 0.035**	0.223± 0.053**	4.040± 0.144**	0.749± 0.028**
5000 ppm	10	0.427± 0.022**	0.437± 0.024**	0.864± 0.043**	0.221± 0.008**	4.361± 0.167**	0.856± 0.048**
7500 ppm	10	0.476± 0.032**	0.496± 0.037**	0.971± 0.068**	0.262± 0.015**	4.412± 0.253**	1.168± 0.110**

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. : 0301
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	ADRENL R	ADRENL L	ADRENALS	OVARY R
Control	10	159± 9	0.106± 0.014	0.019± 0.003	0.020± 0.003	0.039± 0.005	0.033± 0.003
1481 ppm	10	149± 12	0.112± 0.010	0.019± 0.004	0.021± 0.002	0.040± 0.005	0.031± 0.005
2222 ppm	10	138± 12**	0.110± 0.013	0.019± 0.002	0.023± 0.004	0.042± 0.005	0.035± 0.003
3333 ppm	10	133± 8**	0.110± 0.017	0.019± 0.002	0.023± 0.003	0.042± 0.004	0.034± 0.005
5000 ppm	10	129± 7**	0.109± 0.016	0.019± 0.003	0.021± 0.002	0.040± 0.004	0.034± 0.003
7500 ppm	10	113± 9**	0.109± 0.017	0.020± 0.003	0.022± 0.004	0.042± 0.006	0.025± 0.003**

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

STUDY NO. : 0301
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	OVARY L	OVARIES	HEART	LUNG R	LUNG L	LUNGS
Control	10	0.034± 0.007	0.066± 0.007	0.391± 0.021	0.304± 0.018	0.168± 0.007	0.472± 0.022
1481 ppm	10	0.035± 0.006	0.065± 0.010	0.398± 0.018	0.318± 0.024	0.177± 0.012	0.495± 0.027
2222 ppm	10	0.039± 0.009	0.074± 0.010	0.405± 0.019	0.327± 0.015	0.182± 0.007**	0.509± 0.018**
3333 ppm	10	0.037± 0.003	0.071± 0.008	0.410± 0.034	0.337± 0.019**	0.185± 0.012**	0.521± 0.024**
5000 ppm	10	0.035± 0.009	0.068± 0.010	0.407± 0.019	0.329± 0.013*	0.189± 0.010**	0.518± 0.016**
7500 ppm	10	0.030± 0.004	0.055± 0.007*	0.385± 0.024	0.335± 0.027**	0.187± 0.008**	0.522± 0.031**

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

STUDY NO. : 0301
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEY R	KIDNEY L	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.351± 0.018	0.361± 0.029	0.711± 0.045	0.238± 0.021	2.414± 0.091	1.098± 0.065
1481 ppm	10	0.404± 0.029**	0.414± 0.028**	0.818± 0.054**	0.239± 0.010	3.270± 0.122**	1.172± 0.096
2222 ppm	10	0.421± 0.022**	0.434± 0.031**	0.855± 0.050**	0.241± 0.007	3.525± 0.119**	1.255± 0.100**
3333 ppm	10	0.442± 0.036**	0.459± 0.031**	0.900± 0.064**	0.250± 0.012	3.876± 0.145**	1.294± 0.077**
5000 ppm	10	0.450± 0.015**	0.469± 0.022**	0.919± 0.033**	0.265± 0.016**	4.233± 0.150**	1.314± 0.061**
7500 ppm	10	0.466± 0.027**	0.479± 0.023**	0.945± 0.045**	0.264± 0.016**	4.538± 0.229**	1.447± 0.095**

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. : 0301
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control				1481 ppm				2222 ppm				3333 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}																		
spleen			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		0	0	0	0	1	0	0	0	10	0	0	0 **	10	0	0	0 **
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	increased extramedullary hematopoiesis		0	0	0	0	0	0	0	0	1	0	0	0	4	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(40)	(0)	(0)	(0)
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	herniation		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)
	hemorrhage		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:focal		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:single cell		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)
	swelling:central		0	0	0	0	6	0	0	0 *	10	0	0	0 **	10	0	0	0 **
			(0)	(0)	(0)	(0)	(60)	(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	5000 ppm				7500 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
spleen			<10>				<10>			
	deposit of hemosiderin		10	0	0	0 **	10	0	0	0 **
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	increased extramedullary hematopoiesis		9	0	0	0 **	10	0	0	0 **
			(90)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Digestive system}										
liver			<10>				<10>			
	herniation		2	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hemorrhage		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	necrosis:focal		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:single cell		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	swelling:central		9	0	0	0 **	8	0	0	0 **
			(90)	(0)	(0)	(0)	(80)	(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				1481 ppm				2222 ppm				3333 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	vacuolic change:central		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)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	basophilic change		0	0	0	0	10	0	0	0 **	10	0	0	0 **	10	0	0	0 **
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	eosinophilic body		0	8	2	0	0	0	10	0 **	0	0	10	0 **	0	0	10	0 **
			(0)	(80)	(20)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)
	desquamation:tubular epithelium		0	0	0	0	4	6	0	0 **	3	7	0	0 **	2	8	0	0 **
			(0)	(0)	(0)	(0)	(40)	(60)	(0)	(0)	(30)	(70)	(0)	(0)	(20)	(80)	(0)	(0)
{Reproductive system}																		
testis			<10>				<10>				<10>				<10>			
	germ cell necrosis		0	0	0	0	0	0	0	0	6	0	0	0 *	0	9	1	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(60)	(0)	(0)	(0)	(0)	(90)	(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	5000 ppm				7500 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
liver			<10>				<10>			
	vacuolic change:central		7	3	0	0 **	2	8	0	0 **
			(70)	(30)	(0)	(0)	(20)	(80)	(0)	(0)
{Urinary system}										
kidney			<10>				<10>			
	basophilic change		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	eosinophilic body		0	0	10	0 **	5	4	0	0 *
			(0)	(0)	(100)	(0)	(50)	(40)	(0)	(0)
	desquamation:tubular epithelium		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Reproductive system}										
testis			<10>				<10>			
	germ cell necrosis		0	0	10	0 **	0	0	10	0 **
			(0)	(0)	(100)	(0)	(0)	(0)	(100)	(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				1481 ppm				2222 ppm				3333 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Reproductive system}																		
epididymis			<10>				<10>				<10>				<10>			
	debris of spermatic elements		0	0	0	0	0	0	0	0	6	0	0	0 *	10	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(60)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	disappear:sperma		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)	(100)	(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	5000 ppm				7500 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Reproductive system)										
epididymis			<10>				<10>			
	debris of spermatic elements		10	0	0	0 **	10	0	0	0 **
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	disappear:sperma		0	0	10	0 **	0	0	10	0 **
			(0)	(0)	(100)	(0)	(0)	(0)	(100)	(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				1481 ppm				2222 ppm				3333 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}																		
bone marrow			<10>				<10>				<10>				<10>			
	granulation		3	2	0	0	1	1	0	0	1	0	0	0	0	0	0	0 *
			(30)	(20)	(0)	(0)	(10)	(10)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		0	0	0	0	8	0	0	0 **	10	0	0	0 **	10	0	0	0 **
			(0)	(0)	(0)	(0)	(80)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	increased extramedullary hematopoiesis		0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	herniation		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:single cell		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)
	swelling:central		0	0	0	0	10	0	0	0 **	10	0	0	0 **	10	0	0	0 **
			(0)	(0)	(0)	(0)	(100)	(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	5000 ppm				7500 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{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		10	0	0	0 **	9	0	0	0 **
			(100)	(0)	(0)	(0)	(90)	(0)	(0)	(0)
	increased extramedullary hematopoiesis		8	0	0	0 **	9	0	0	0 **
			(80)	(0)	(0)	(0)	(90)	(0)	(0)	(0)
{Digestive system}										
liver			<10>				<10>			
	herniation		1	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	necrosis:single cell		2	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	swelling:central		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				1481 ppm				2222 ppm				3333 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	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)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	eosinophilic droplet:proximal tubule		0	0	0	0	2	8	0	0 **	3	7	0	0 **	0	10	0	0 **
			(0)	(0)	(0)	(0)	(20)	(80)	(0)	(0)	(30)	(70)	(0)	(0)	(0)	(100)	(0)	(0)
{Endocrine system}																		
pituitary			<10>				<10>				<10>				<10>			
	cyst		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)
{Special sense organs/appendage}																		
Harder gl			<10>				<10>				<10>				<10>			
	lymphocytic infiltration		0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(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	5000 ppm				7500 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
liver			<10>				<10>			
	vacuolic change:central		0	0	0	0	8	0	0	0 **
			(0)	(0)	(0)	(0)	(80)	(0)	(0)	(0)
{Urinary system}										
kidney			<10>				<10>			
	eosinophilic droplet:proximal tubule		2	8	0	0 **	3	1	0	0
			(20)	(80)	(0)	(0)	(30)	(10)	(0)	(0)
{Endocrine system}										
pituitary			<10>				<10>			
	cyst		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Special sense organs/appendage}										
Harder gl			<10>				<10>			
	lymphocytic infiltration		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 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

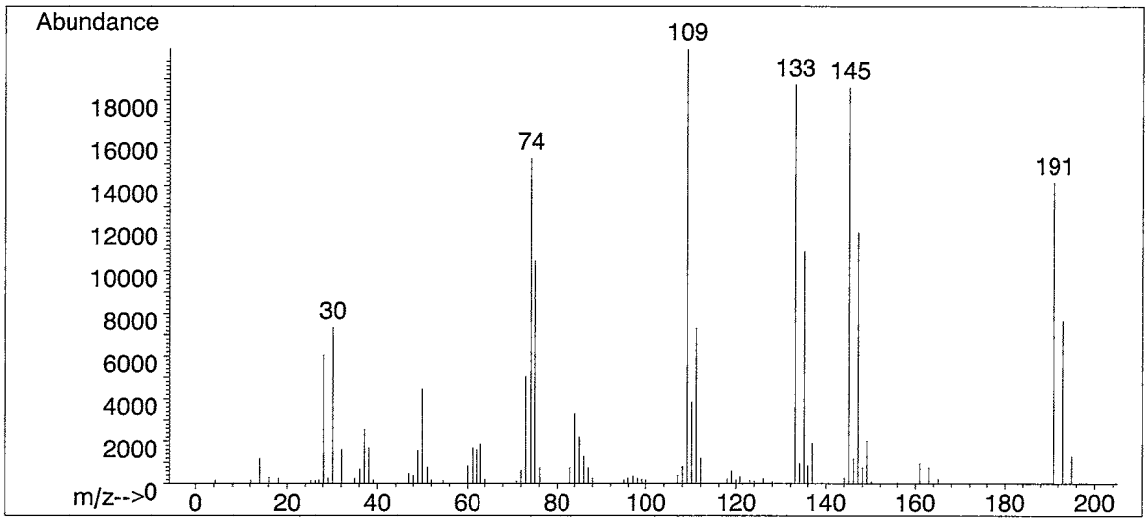
1. Spectral Data

Mass Spectrometry

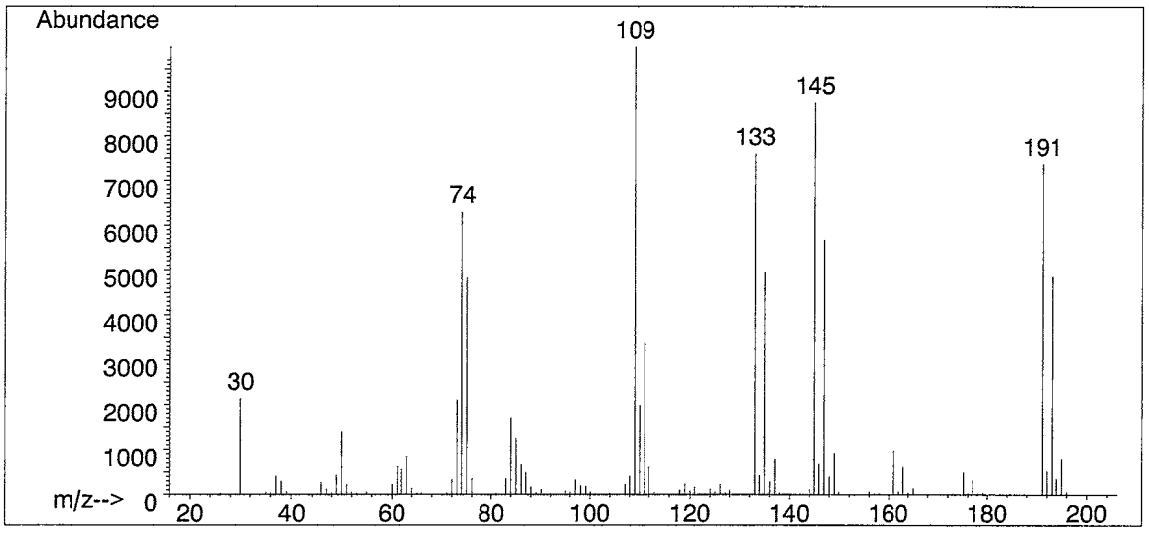
Instrument : Hewlett Packard 5989B Mass Spectrometer

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.

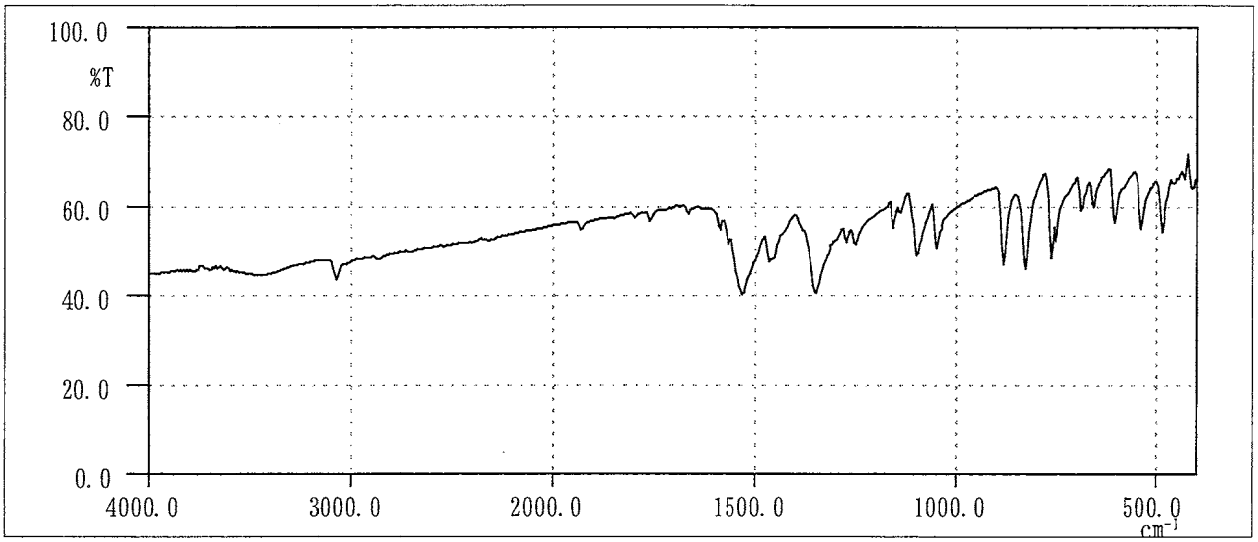
(*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition. John Wiley and Sons, Inc. (U.S.), Entry Number 74222)

Infrared Spectrometry

Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr

Resolution : 2 cm^{-1}



Infrared Spectrum of Test Substance

Determined Values Wave Number (cm^{-1})	Literature Values* Wave Number (cm^{-1})
460～ 510	460～ 510
510～ 560	510～ 560
560～ 620	560～ 620
620～ 670	620～ 670
670～ 690	670～ 690
690～ 790	690～ 790
790～ 850	790～ 850
850～ 900	850～ 900
900～1060	900～1060
1060～1120	1060～1120
1120～1170	1120～1170
1170～1180	1170～1180
1180～1260	1180～1260
1260～1280	1260～1280
1280～1400	1280～1400
1400～1470	1400～1470
1470～1580	1470～1580
1580～1600	1580～1600
1650～1690	1650～1690
1750～1780	1750～1780
1780～1810	1780～1810
1900～1950	1900～1950
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

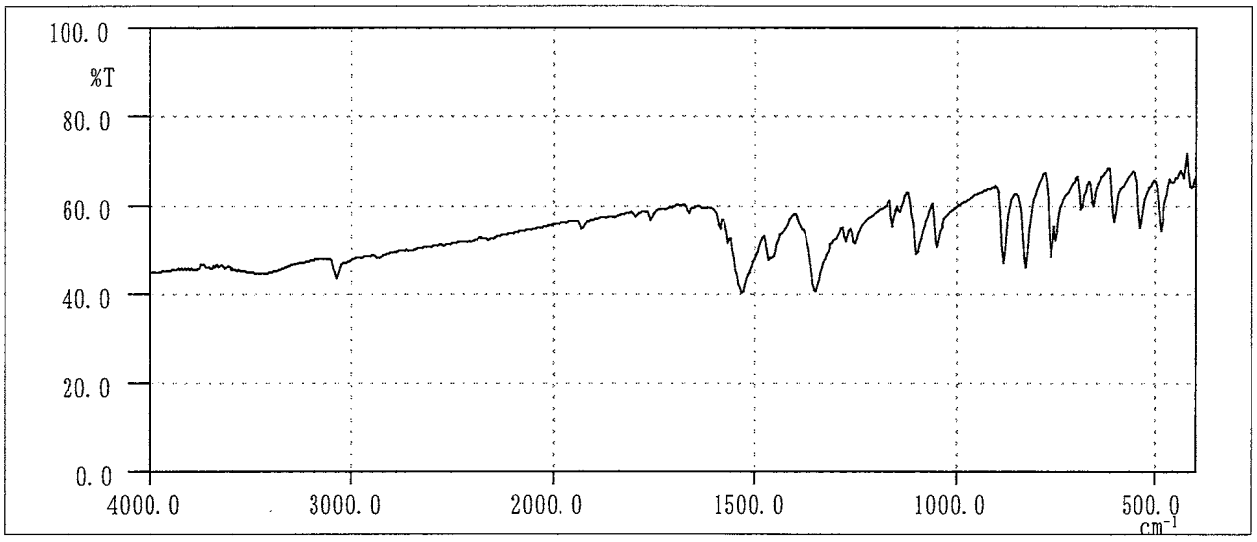
1. Sample : This lot was used from 1996.2.8 to 1996.5.12. Test substance was stored in a dark place at room temperature.

2. Infrared Spectrometry

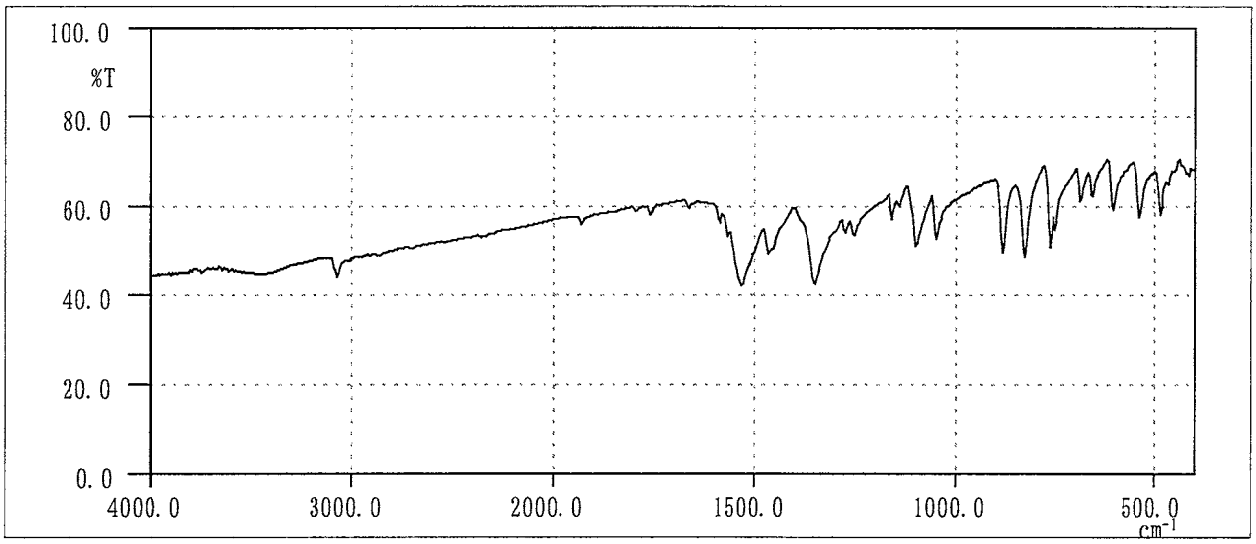
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

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 mmϕ × 50m)

Column Temperature : 180 °C → (10 °C/min) → 215 °C → (20 °C/min) → 250 °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

CONCENTRATION 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 ϕ ×50m)
Column Temperature : 180℃→(10℃/min)→215℃→(20℃/min)→250℃(2min)
Flow Rate : 1mL/min
Detector : FID(Flame Ionization Detector)
Injection Volume : 1 μ 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[c]	581.4 (96.7)	9183.9 (94.9)
	1996.01.29[d]	580.7 (96.5)	8638.9 (89.3)

[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 5890A Gas Chromatograph
Column : Methyl Silicone (0.2 mmϕ $\times$ 50m)
Column Temperature : 180 °C $\rightarrow$ (10 °C/min) $\rightarrow$ 215 °C $\rightarrow$ (20 °C/min) $\rightarrow$ 250 °C (2 min)
Flow Rate : 1 mL/min
Detector : FID (Flame Ionization Detector)
Injection Volume : 1 µL

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 [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] (May-Grunwald-Giemsa 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	Enzymatic method (GLK・G-6-PDH) [4]
T-cholesterol	Enzymatic method (CE・COD・POD) [4]
Triglyceride	Enzymatic method (LPL・GK・GPO・POD) [4]
Phospholipid	Enzymatic method (PLD・COD・POD) [4]
Glutamic oxaloacetic transaminase (GOT)	IFCC method [4]
Glutamic pyruvic transaminase (GPT)	IFCC method [4]
Lactate dehydrogenase (LDH)	Wroblewski-LaDue method [4]
Alkaline phosphatase (ALP)	GSCC method [4]
γ-Glutamyl transpeptidase (γ-GTP)	L-γ-Glutamyl-p-nitroanilide method [4]
Creatine phosphokinase (CPK)	GSCC method [4]
Urea nitrogen	Enzymatic method (Urease・GLDH) [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	Enzymatic method (PNP・XOD・POD) [4]
Urinalysis	
pH,Protein,Glucose,Ketone body,Bilirubin,Occult Blood, Urobilinogen	Urinalysis reagent paper method [6]

1) Automatic blood cell analyzer (Technicon H・1 : Technicon Instruments Corporation)
2) Automatic coagulometer (Sysmex CA-5000 : Toa Medical Electronics Co.,Ltd.)
3) Automatic blood cell differential analyzer (Hitachi 8200 : Hitachi,Ltd.)
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-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
Reticulocyte	‰	0
Prothrombin time	sec	1
Activated partial thromboplastin time (APTT)	sec	1
White blood cell (WBC)	$\times 10^3/\mu L$	2
Differential WBC	%	0
Biochemistry		
Total protein	g/dL	1
Albumin	g/dL	1
A/G ratio	–	1
T-bilirubin	mg/dL	2
Glucose	mg/dL	0
T-cholesterol	mg/dL	0
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