o－クロロ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：　０４３９

APPENDICES

APPENDICES

APPENDICES (CONTINUED)

APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0439
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
	63 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	250 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
	4000 ppm	0	0	0	0	1	2	2	2	2	3	3	3	3
YELLOW URINE	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	63 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000 ppm	0	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
	4000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
NON REMARKABLE	Control	10	10	10	10	10	10	10	10	10	10	10	10	10
	63 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	250 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	1000 ppm	10	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
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0439
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
	63 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000 ppm	0	0	1	1	2	2	2	2	3	5	5	5	5
	2000 ppm	3	5	4	4	4	5	5	5	5	5	5	5	5
	4000 ppm	5	5	5	5	6	6	6	6	7	8	8	8	8
SOILED PERI GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	63 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	250 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	1	0	0	0	0	0
	4000 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
	63 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	250 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000 ppm	0	0	2	2	10	10	10	10	10	10	10	10	10
	2000 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
NON REMARKABLE	Control	10	10	10	10	10	10	10	10	10	10	10	10	10
	63 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	250 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	1000 ppm	10	10	8	8	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0

APPENDIX B 1

BODY WEIGHT CHANGES : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0439
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	127± 4	154± 6	180± 7	202± 10	219± 11	230± 12	242± 11
63 ppm	127± 4	156± 4	182± 6	207± 7	225± 8	236± 10	248± 10
250 ppm	127± 4	156± 5	182± 7	202± 8	219± 8	231± 8	243± 7
1000 ppm	127± 4	154± 6	181± 8	204± 6	221± 7	234± 8	245± 8
2000 ppm	127± 4	148± 4*	173± 6	194± 6	213± 7	225± 7	237± 7
4000 ppm	127± 4	133± 5**	154± 7**	172± 9**	187± 10**	199± 8**	207± 8**

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

STUDY NO. : 0439
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-7
Control	254± 12	265± 12	272± 13	281± 14	289± 16	295± 17	298± 17
63 ppm	261± 12	273± 12	283± 13	290± 13	297± 14	304± 14	307± 14
250 ppm	257± 8	268± 11	276± 13	284± 14	291± 13	297± 13	300± 14
1000 ppm	259± 10	272± 11	280± 12	288± 13	294± 13	300± 13	301± 15
2000 ppm	249± 8	260± 9	269± 9	277± 10	282± 11	289± 10	289± 10
4000 ppm	217± 8**	228± 9**	236± 8**	242± 7**	247± 8**	250± 8**	248± 9**

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. : 0439
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-7	2-7	3-7	4-7	5-7	6-7
Control	99± 3	112± 3	122± 2	132± 4	139± 4	145± 5	149± 5
63 ppm	99± 3	113± 2	123± 4	132± 5	140± 7	145± 6	149± 6
250 ppm	99± 2	113± 3	124± 4	132± 4	139± 5	146± 5	149± 5
1000 ppm	99± 3	111± 7	121± 7	128± 8	135± 7	139± 8	144± 7
2000 ppm	99± 3	108± 4	119± 7	127± 8	132± 10	137± 10	141± 10
4000 ppm	99± 3	99± 3**	110± 5**	118± 8**	123± 7**	128± 9**	131± 8**

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

STUDY NO. : 0439
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 7-7	8-7	9-7	10-7	11-7	12-7	13-7
Control	152± 7	156± 6	160± 7	165± 7	167± 7	169± 7	169± 7
63 ppm	153± 7	158± 7	162± 7	166± 8	167± 7	168± 7	168± 6
250 ppm	154± 7	157± 8	163± 8	165± 8	168± 9	170± 9	170± 7
1000 ppm	148± 10	150± 10	154± 10	158± 11	160± 10	163± 11	162± 12
2000 ppm	146± 9	148± 11	152± 12	155± 10	157± 11	159± 11	160± 11
4000 ppm	136± 11**	137± 11**	141± 12**	144± 10**	145± 11**	147± 11**	147± 10**

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. : 0439
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	12.4± 0.5	13.1± 0.4	13.7± 0.7	13.9± 0.6	13.6± 0.6	13.4± 0.7	13.7± 0.8
63 ppm	12.6± 0.4	13.5± 0.6	14.3± 0.6	14.5± 0.7	14.1± 0.7	13.8± 0.7	14.2± 0.9
250 ppm	12.6± 0.6	13.5± 0.8	14.0± 0.9	14.5± 0.7	14.0± 0.6	13.6± 0.7	14.1± 0.9
1000 ppm	12.3± 0.7	13.6± 0.7	14.4± 0.6	14.5± 0.6	14.0± 0.5	14.0± 0.5	14.5± 1.0
2000 ppm	11.2± 0.5**	13.4± 0.7	14.0± 0.7	14.0± 0.7	14.0± 0.6	13.9± 0.6	14.2± 0.6
4000 ppm	8.4± 0.7**	11.8± 0.7**	12.2± 0.8**	12.4± 0.8**	12.5± 0.7**	12.4± 0.6**	12.5± 0.7**

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

STUDY NO. : 0439
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	13.3± 0.8	13.4± 0.9	13.8± 0.9	13.9± 1.0	13.6± 1.0	13.6± 1.0
63 ppm	13.8± 0.8	13.8± 0.9	13.9± 0.8	14.0± 1.1	14.0± 1.1	13.8± 1.3
250 ppm	13.9± 1.1	13.9± 0.9	13.9± 1.2	13.7± 0.9	13.6± 0.9	13.3± 0.8
1000 ppm	14.5± 1.1*	14.0± 0.8	14.2± 1.1	13.9± 1.0	13.9± 0.9	13.6± 0.9
2000 ppm	13.9± 0.7	14.0± 0.5	14.1± 0.6	13.8± 0.8	13.9± 0.6	13.6± 0.8
4000 ppm	12.6± 0.5	12.4± 0.5*	12.8± 0.5	12.6± 0.6**	12.2± 0.6**	11.9± 0.7**

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. : 0439
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	9.5± 0.3	10.0± 0.7	10.0± 0.3	10.2± 1.0	9.8± 0.6	9.6± 0.8	9.4± 0.8
63 ppm	9.4± 0.2	10.5± 2.5	10.0± 0.6	10.0± 0.6	9.8± 0.5	10.0± 1.6	9.6± 0.5
250 ppm	9.2± 0.4	9.6± 0.4	10.0± 0.4	10.1± 0.2	9.9± 0.4	9.4± 0.4	9.6± 0.4
1000 ppm	8.8± 0.6**	9.5± 0.6	9.5± 0.6	9.7± 0.5	9.4± 0.5	9.3± 0.5	9.4± 0.7
2000 ppm	8.0± 0.3**	9.5± 0.6	9.5± 0.8	9.4± 0.8	9.3± 0.8	9.7± 2.3	9.5± 0.9
4000 ppm	6.3± 0.4**	8.7± 0.4**	8.6± 0.6**	8.7± 0.7**	8.6± 0.9**	8.2± 0.5**	8.5± 1.0*

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

STUDY NO. : 0439
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	9.0± 0.7	9.0± 0.7	9.3± 0.6	9.6± 0.7	9.3± 0.7	9.4± 0.7
63 ppm	9.7± 1.7	9.1± 0.4	9.4± 1.0	9.6± 1.5	9.0± 0.8	9.0± 0.9
250 ppm	9.2± 0.6	9.4± 0.7	9.5± 0.8	9.6± 0.8	9.1± 0.7	9.1± 0.6
1000 ppm	8.8± 0.8	9.0± 0.7	9.2± 0.8	9.1± 0.7	8.9± 0.7	8.8± 0.7
2000 ppm	8.9± 0.9	9.5± 2.9	9.3± 1.5	9.2± 1.4	9.1± 1.6	9.3± 2.5
4000 ppm	8.0± 1.0	8.0± 1.0*	8.1± 0.9*	8.2± 0.9*	7.9± 0.8**	8.1± 0.8**

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. : 0439
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
63 ppm	0.005± 0.000	0.005± 0.000	0.004± 0.000	0.004± 0.000	0.004± 0.000	0.004± 0.001	0.003± 0.000
250 ppm	0.020± 0.001	0.019± 0.000	0.018± 0.001	0.017± 0.001	0.015± 0.001	0.014± 0.001	0.014± 0.001
1000 ppm	0.080± 0.002	0.075± 0.002	0.071± 0.002	0.066± 0.002	0.060± 0.002	0.057± 0.002	0.056± 0.003
2000 ppm	0.151± 0.003	0.154± 0.005	0.144± 0.005	0.132± 0.005	0.124± 0.005	0.118± 0.005	0.114± 0.006
4000 ppm	0.252± 0.015	0.306± 0.006	0.283± 0.008	0.266± 0.007	0.251± 0.007	0.239± 0.007	0.230± 0.006

STUDY NO. : 0439
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
63 ppm	0.003± 0.000	0.003± 0.000	0.003± 0.000	0.003± 0.000	0.003± 0.000	0.003± 0.000
250 ppm	0.013± 0.001	0.012± 0.001	0.012± 0.001	0.012± 0.001	0.011± 0.001	0.011± 0.001
1000 ppm	0.053± 0.004	0.050± 0.003	0.049± 0.003	0.047± 0.003	0.046± 0.003	0.045± 0.003
2000 ppm	0.107± 0.007	0.104± 0.005	0.102± 0.005	0.098± 0.007	0.097± 0.005	0.094± 0.007
4000 ppm	0.220± 0.003	0.211± 0.006	0.212± 0.004	0.203± 0.005	0.194± 0.005	0.192± 0.005

APPENDIX D 2

CHEMICAL INTAKE CHANGES : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0439
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
63 ppm	0.005± 0.000	0.005± 0.001	0.005± 0.000	0.005± 0.001	0.004± 0.000	0.004± 0.001	0.004± 0.000
250 ppm	0.020± 0.000	0.019± 0.000	0.019± 0.001	0.018± 0.001	0.017± 0.000	0.016± 0.000	0.016± 0.001
1000 ppm	0.080± 0.003	0.079± 0.002	0.074± 0.003	0.072± 0.003	0.068± 0.003	0.064± 0.002	0.063± 0.002
2000 ppm	0.148± 0.005	0.161± 0.004	0.150± 0.004	0.143± 0.007	0.135± 0.006	0.138± 0.031	0.130± 0.010
4000 ppm	0.256± 0.016	0.315± 0.013	0.292± 0.013	0.282± 0.017	0.269± 0.013	0.252± 0.011	0.249± 0.013

STUDY NO. : 0439
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
63 ppm	0.004± 0.001	0.004± 0.000	0.004± 0.001	0.003± 0.001	0.003± 0.000	0.003± 0.000
250 ppm	0.015± 0.001	0.014± 0.001	0.014± 0.001	0.014± 0.001	0.013± 0.001	0.013± 0.000
1000 ppm	0.059± 0.003	0.058± 0.003	0.058± 0.002	0.057± 0.002	0.055± 0.002	0.055± 0.002
2000 ppm	0.120± 0.008	0.125± 0.033	0.119± 0.015	0.118± 0.015	0.115± 0.018	0.116± 0.028
4000 ppm	0.232± 0.015	0.228± 0.013	0.226± 0.016	0.224± 0.012	0.214± 0.012	0.219± 0.012

APPENDIX E 1

HEMATOLOGY : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0439
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	9.49±	0.19	16.0±	0.4	46.1±	0.8	48.6±	0.3	16.9±	0.2	34.8±	0.5	786±	34
63 ppm	10	9.44±	0.17	15.8±	0.3	45.8±	0.9	48.5±	0.3	16.8±	0.2	34.6±	0.4	816±	36
250 ppm	10	9.35±	0.20	15.5±	0.4**	45.1±	0.8	48.3±	0.4	16.5±	0.2**	34.2±	0.3*	844±	32*
1000 ppm	10	8.78±	0.11**	14.4±	0.2**	43.4±	0.5**	49.4±	0.5	16.4±	0.2**	33.2±	0.3**	830±	58
2000 ppm	10	8.42±	0.20**	13.9±	0.3**	41.9±	0.8**	49.8±	0.5*	16.5±	0.2**	33.2±	0.3**	788±	63
4000 ppm	9	7.83±	0.33**	14.0±	0.5**	42.6±	1.1**	54.5±	1.3**	17.9±	0.3**	32.9±	0.4**	654±	48**

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

STUDY NO. : 0439
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	1.8±	0.2	0.3±	0.0	17.3±	2.0	26.9±	3.5
63 ppm	10	2.0±	0.2	0.3±	0.1	17.0±	2.2	26.7±	3.4
250 ppm	10	2.3±	0.2	0.3±	0.1	17.4±	2.7	27.8±	5.6
1000 ppm	10	3.6±	0.3**	0.4±	0.2	15.8±	1.3	22.1±	2.6*
2000 ppm	10	4.8±	0.6**	0.9±	0.4**	16.5±	1.3	22.3±	5.4
4000 ppm	9	8.5±	1.1**	1.4±	0.5**	18.0±	2.0	25.5±	3.0

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

STUDY NO. : 0439
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	6.93± 1.43	1± 1	19± 4	1± 1	0± 0	2± 1	76± 4	0± 0
63 ppm	10	6.15± 1.10	2± 1	16± 2	1± 0	0± 0	2± 1	79± 2	0± 0
250 ppm	10	6.58± 1.35	1± 1	17± 2	1± 1	0± 0	2± 1	79± 3	0± 0
1000 ppm	10	7.25± 1.01	1± 1	14± 3**	1± 1	0± 0	3± 1	81± 5	0± 0
2000 ppm	10	7.24± 1.15	2± 1	17± 3	1± 1	0± 0	3± 1	78± 4	0± 0
4000 ppm	9	6.42± 1.27	1± 1	15± 3**	1± 1	0± 0	2± 2	80± 4	1± 1

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. : 0439
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	8.84± 0.22	16.1± 0.4	44.6± 1.3	50.4± 0.5	18.2± 0.1	36.1± 0.5	859± 57
63 ppm	10	8.54± 0.16**	15.5± 0.3**	43.4± 0.8	50.9± 0.5	18.1± 0.1	35.6± 0.4	893± 59
250 ppm	10	8.48± 0.14**	15.3± 0.3**	43.7± 0.8	51.5± 0.4	18.0± 0.1	35.0± 0.3**	896± 52
1000 ppm	10	8.03± 0.21**	14.3± 0.4**	41.8± 1.2**	52.0± 0.4**	17.9± 0.2**	34.3± 0.4**	836± 70
2000 ppm	10	7.67± 0.23**	13.7± 0.4**	40.4± 1.0**	52.7± 1.0**	17.9± 0.3*	33.9± 0.4**	742± 30**
4000 ppm	10	7.20± 0.18**	13.4± 0.4**	40.2± 1.1**	55.8± 0.4**	18.6± 0.2	33.3± 0.4**	598± 42**

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

STUDY NO. : 0439
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	1.8±	0.2	0.3±	0.1	14.8±	1.0	17.1±	1.9
63 ppm	10	2.1±	0.3	0.3±	0.1	15.4±	0.8	18.2±	1.3
250 ppm	10	2.4±	0.3	0.4±	0.1	15.3±	0.8	17.0±	1.3
1000 ppm	10	3.7±	0.6**	0.5±	0.2	15.5±	0.9	17.9±	3.9
2000 ppm	10	4.9±	0.6**	1.1±	0.3**	16.2±	1.4*	16.7±	3.1
4000 ppm	10	7.9±	0.9**	1.5±	0.7**	17.9±	1.2**	17.5±	2.8

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

STUDY NO. : 0439
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	4.19± 0.87	1± 1	16± 3	1± 1	0± 0	2± 1	80± 3	0± 0
63 ppm	10	4.37± 0.52	2± 1	16± 4	1± 0	0± 0	2± 1	80± 4	0± 0
250 ppm	10	4.14± 0.84	1± 1	16± 4	1± 1	0± 0	2± 1	80± 4	0± 0
1000 ppm	10	4.37± 1.46	1± 1	14± 3	1± 1	0± 0	1± 1	82± 4	0± 0
2000 ppm	10	4.40± 1.35	1± 1	16± 3	1± 1	0± 0	2± 1	80± 4	0± 0
4000 ppm	10	4.83± 1.12	1± 1	14± 3	1± 0	0± 0	2± 1	81± 4	0± 1

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. : 0439
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	6.1±	0.2	3.8±	0.1	1.7±	0.1	0.11±	0.01	174±	10	60±	4	44±	13
63 ppm	10	6.4±	0.1**	4.0±	0.1**	1.7±	0.1	0.12±	0.01	175±	10	72±	8	47±	17
250 ppm	10	6.6±	0.2**	4.2±	0.1**	1.8±	0.1**	0.12±	0.01	176±	13	85±	6	55±	8
1000 ppm	10	7.1±	0.1**	4.6±	0.1**	1.8±	0.1**	0.16±	0.01*	175±	28	132±	6**	68±	16
2000 ppm	10	7.3±	0.2**	4.6±	0.1**	1.8±	0.1**	0.30±	0.08**	162±	8	181±	17**	101±	8**
4000 ppm	9	7.1±	0.2**	4.4±	0.1**	1.6±	0.1	0.69±	0.13**	150±	6**	240±	22**	168±	29**

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

STUDY NO. : 0439
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	110±	7	60±	5	40±	4	160±	22	248±	17	2±	1	103±	23
63 ppm	10	125±	13	73±	24	45±	9	183±	43	235±	16	1±	1	94±	8
250 ppm	10	145±	8	74±	23	45±	9	192±	45	207±	10*	2±	1	93±	12
1000 ppm	10	221±	14**	67±	13	59±	12*	151±	10	208±	13*	5±	2	82±	6**
2000 ppm	10	316±	28**	139±	53**	205±	77**	182±	40	298±	12	56±	17**	78±	5**
4000 ppm	9	433±	27**	223±	32**	448±	71**	219±	27**	482±	39*	398±	64**	100±	15

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

STUDY NO. : 0439
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	19.8± 1.7	0.5± 0.0	142± 1	4.0± 0.2	107± 1	10.1± 0.2	5.8± 0.7
63 ppm	10	20.0± 1.6	0.5± 0.1	142± 1	4.0± 0.2	106± 1	10.2± 0.2	5.7± 0.7
250 ppm	10	19.7± 1.7	0.5± 0.0	142± 2	4.0± 0.2	106± 1	10.3± 0.1**	5.8± 0.6
1000 ppm	10	20.8± 2.2	0.5± 0.1	142± 1	3.8± 0.2	105± 1**	10.7± 0.1**	5.8± 0.7
2000 ppm	10	21.0± 1.4	0.5± 0.0	141± 1	3.9± 0.2	104± 2**	10.9± 0.2**	5.8± 0.4
4000 ppm	9	21.9± 1.3*	0.4± 0.1	140± 1**	3.9± 0.1	104± 1**	10.8± 0.1**	6.0± 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. : 0439
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	6.2±	0.1	3.8±	0.1	1.6±	0.1	0.15±	0.02	135±	13	73±	7	17±	5
63 ppm	10	6.3±	0.2	3.9±	0.1	1.6±	0.1	0.14±	0.02	145±	15	82±	11	19±	7
250 ppm	10	6.5±	0.2**	4.1±	0.2**	1.7±	0.1*	0.14±	0.01	154±	15**	101±	9	19±	6
1000 ppm	10	6.9±	0.2**	4.4±	0.1**	1.8±	0.1**	0.17±	0.01	144±	10	135±	15**	27±	10
2000 ppm	10	7.1±	0.2**	4.5±	0.1**	1.7±	0.1**	0.21±	0.03*	149±	8	161±	21**	41±	17**
4000 ppm	10	7.1±	0.2**	4.5±	0.1**	1.7±	0.1*	0.41±	0.04**	144±	10	187±	22**	77±	31**

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

STUDY NO. : 0439
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	141± 11	69± 14	36± 9	377± 159	178± 20	1± 1	152± 41
63 ppm	10	153± 19	65± 8	33± 4	338± 67	164± 18	2± 1	141± 22
250 ppm	10	176± 15	66± 12	37± 9	304± 110	153± 29	2± 1	124± 25
1000 ppm	10	227± 25**	68± 6	40± 7	311± 91	153± 21	7± 2*	135± 35
2000 ppm	10	275± 35**	77± 10	60± 16**	294± 93	189± 21	46± 22**	118± 24
4000 ppm	10	351± 33**	132± 34**	144± 37**	281± 49	322± 28**	263± 48**	119± 21

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

STUDY NO. : 0439
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	18.7± 2.2	0.5± 0.0	140± 2	3.7± 0.3	107± 1	9.9± 0.2	4.9± 0.8
63 ppm	10	18.0± 1.0	0.5± 0.1	140± 1	3.8± 0.2	107± 1	10.0± 0.2	5.1± 1.0
250 ppm	10	18.8± 1.7	0.5± 0.1	141± 2	3.8± 0.2	107± 1	10.1± 0.3	5.1± 1.0
1000 ppm	10	20.1± 1.5	0.5± 0.1	140± 1	3.8± 0.2	106± 1	10.3± 0.2**	5.0± 0.9
2000 ppm	10	20.4± 0.8	0.5± 0.0	140± 2	3.9± 0.2	106± 1	10.5± 0.3**	4.7± 0.8
4000 ppm	10	22.4± 3.4**	0.4± 0.0	139± 1	3.9± 0.2	105± 1**	10.6± 0.2**	5.3± 0.6

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

APPENDIX G 1

URINALYSIS : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0439 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	5	5		0	0	5	5	0	0		10	0	0	0	0	0		0	5	5	0	0	0		10	0	0	0	
63 ppm	10	0	0	0	0	0	4	6		0	0	7	3	0	0		10	0	0	0	0	0		0	7	3	0	0	0		10	0	0	0	
250 ppm	10	0	0	0	0	1	4	5		0	0	3	7	0	0		10	0	0	0	0	0		0	8	2	0	0	0		10	0	0	0	
1000 ppm	10	0	0	0	0	2	7	1		0	0	5	5	0	0		10	0	0	0	0	0		0	5	5	0	0	0		10	0	0	0	
2000 ppm	10	0	0	0	0	3	7	0	*	0	0	1	7	2	0		10	0	0	0	0	0		0	3	7	0	0	0		10	0	0	0	
4000 ppm	10	0	0	0	2	7	1	0	**	0	0	1	9	0	0		10	0	0	0	0	0		0	7	3	0	0	0		10	0	0	0	

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

STUDY NO. : 0439 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	
63 ppm	10	10	0	0	0	0		10	0	0	0	0	
250 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	9	1	0	0	0		10	0	0	0	0	
4000 ppm	10	10	0	0	0	0		10	0	0	0	0	

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

APPENDIX G 2

URINALYSIS : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0439 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	7	3		0	3	6	1	0	0		10	0	0	0	0	0		9	1	0	0	0	0		10	0	0	0	
63 ppm	10	0	0	0	0	1	4	5		0	2	7	1	0	0		10	0	0	0	0	0		7	3	0	0	0	0		10	0	0	0	
250 ppm	10	0	0	0	0	0	2	8	*	0	2	7	1	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
1000 ppm	10	0	0	0	0	0	4	6		0	1	8	1	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	9	0		0	1	9	0	0	0		10	0	0	0	0	0		9	1	0	0	0	0		10	0	0	0	
4000 ppm	10	0	0	0	0	1	7	2		0	1	8	1	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. : 0439 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	
63 ppm	10	10 0 0 0 0		10 0 0 0 0	
250 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	
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. : 0439
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 (%)	63 ppm 10 (%)	250 ppm 10 (%)	1000 ppm 10 (%)
spleen	dark		0 (0)	0 (0)	0 (0)	0 (0)
	rough		0 (0)	0 (0)	0 (0)	0 (0)
liver	dark		0 (0)	0 (0)	0 (0)	0 (0)
	herniation		2 (20)	0 (0)	2 (20)	1 (10)

Organ	Findings	Group Name / NO. of Animals	2000 ppm 10 (%)	4000 ppm 10 (%)
spleen	dark		10 (100)	10 (100)
	rough		10 (100)	10 (100)
liver	dark		10 (100)	10 (100)
	herniation		1 (10)	0 (0)

APPENDIX H 2

GROSS FINDINGS : SUMMARY, RAT : FEMALE : ALL ANIMALS

(13-WEEK STUDY)

STUDY NO. : 0439
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	63 ppm 10 (%)	250 ppm 10 (%)	1000 ppm 10 (%)
spleen	dark		0 (0)	0 (0)	0 (0)	0 (0)
	rough		0 (0)	0 (0)	0 (0)	0 (0)
liver	dark		0 (0)	0 (0)	0 (0)	0 (0)
	herniation		0 (0)	1 (10)	0 (0)	1 (10)

STUDY NO. : 0439
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name NO. of Animals	2000 ppm 10 (%)	4000 ppm 10 (%)
spleen	dark		0 (0)	10 (100)
	rough		0 (0)	10 (100)
liver	dark		0 (0)	10 (100)
	herniation		2 (20)	1 (10)

APPENDIX I 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0439
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	281± 16	0.196± 0.022	0.045± 0.006	2.912± 0.107	0.874± 0.051	0.975± 0.051
63 ppm	10	290± 14	0.214± 0.017	0.046± 0.006	3.034± 0.100	0.908± 0.045	0.987± 0.040
250 ppm	10	281± 14	0.189± 0.022	0.045± 0.004	3.036± 0.099	0.905± 0.025	0.968± 0.047
1000 ppm	10	282± 14	0.199± 0.022	0.045± 0.005	3.069± 0.199	0.913± 0.041	0.985± 0.039
2000 ppm	10	269± 11	0.191± 0.020	0.044± 0.006	3.107± 0.128*	0.897± 0.044	0.972± 0.044
4000 ppm	10	229± 9**	0.170± 0.015*	0.042± 0.003	1.457± 0.194**	0.804± 0.037**	0.949± 0.047

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

STUDY NO. : 0439
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	1.777± 0.082	0.517± 0.033	6.823± 0.524	1.877± 0.046
63 ppm	10	1.829± 0.068	0.552± 0.032	7.762± 0.492**	1.879± 0.048
250 ppm	10	1.849± 0.091	0.560± 0.028	8.646± 0.460**	1.866± 0.036
1000 ppm	10	1.986± 0.108**	0.679± 0.038**	10.997± 0.721**	1.882± 0.037
2000 ppm	10	2.045± 0.093**	1.010± 0.076**	13.502± 0.477**	1.847± 0.042
4000 ppm	10	2.231± 0.125**	1.579± 0.163**	15.148± 0.822**	1.806± 0.062**

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. : 0439
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± 6	0.182± 0.019	0.049± 0.003	0.108± 0.015	0.580± 0.022	0.722± 0.038
63 ppm	10	158± 7	0.174± 0.013	0.050± 0.005	0.110± 0.018	0.584± 0.039	0.712± 0.035
250 ppm	10	158± 7	0.174± 0.013	0.049± 0.005	0.106± 0.010	0.595± 0.036	0.715± 0.025
1000 ppm	10	152± 11	0.166± 0.012	0.049± 0.004	0.107± 0.011	0.579± 0.032	0.709± 0.033
2000 ppm	10	147± 10*	0.165± 0.010	0.047± 0.005	0.105± 0.009	0.593± 0.043	0.695± 0.046
4000 ppm	10	135± 9**	0.153± 0.018**	0.040± 0.007**	0.096± 0.016	0.550± 0.039	0.657± 0.042**

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

STUDY NO. : 0439
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	1.074± 0.054	0.365± 0.033	3.779± 0.180	1.740± 0.061
63 ppm	10	1.080± 0.062	0.350± 0.027	4.038± 0.163	1.709± 0.066
250 ppm	10	1.113± 0.071	0.374± 0.027	4.544± 0.240	1.711± 0.033
1000 ppm	10	1.196± 0.062**	0.448± 0.031	5.700± 0.536**	1.738± 0.051
2000 ppm	10	1.244± 0.078**	0.593± 0.057**	6.948± 0.625**	1.735± 0.045
4000 ppm	10	1.313± 0.085**	0.898± 0.122**	8.636± 0.754**	1.681± 0.041

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. : 0439
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	281± 16	0.070± 0.008	0.016± 0.002	1.041± 0.069	0.312± 0.015	0.347± 0.008
63 ppm	10	290± 14	0.074± 0.006	0.016± 0.002	1.048± 0.045	0.313± 0.012	0.341± 0.009
250 ppm	10	281± 14	0.067± 0.009	0.016± 0.001	1.084± 0.049	0.323± 0.015	0.345± 0.010
1000 ppm	10	282± 14	0.071± 0.006	0.016± 0.002	1.091± 0.077	0.324± 0.008	0.350± 0.013
2000 ppm	10	269± 11	0.071± 0.006	0.017± 0.002	1.155± 0.033**	0.334± 0.015**	0.362± 0.012*
4000 ppm	10	229± 9**	0.074± 0.006	0.018± 0.001	0.635± 0.084**	0.350± 0.012**	0.414± 0.012**

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

STUDY NO. : 0439
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	0.634± 0.021	0.184± 0.008	2.430± 0.075	0.670± 0.037
63 ppm	10	0.632± 0.028	0.191± 0.009	2.677± 0.073	0.649± 0.030
250 ppm	10	0.660± 0.028	0.200± 0.010	3.083± 0.085*	0.666± 0.032
1000 ppm	10	0.705± 0.022*	0.241± 0.011**	3.900± 0.098**	0.669± 0.031
2000 ppm	10	0.760± 0.019**	0.376± 0.025**	5.023± 0.211**	0.687± 0.021
4000 ppm	10	0.973± 0.048**	0.687± 0.050**	6.603± 0.226**	0.788± 0.027**

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. : 0439
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± 6	0.115± 0.010	0.031± 0.002	0.069± 0.010	0.369± 0.015	0.459± 0.017
63 ppm	10	158± 7	0.110± 0.008	0.031± 0.003	0.069± 0.011	0.370± 0.022	0.452± 0.026
250 ppm	10	158± 7	0.110± 0.009	0.031± 0.003	0.067± 0.007	0.376± 0.022	0.452± 0.018
1000 ppm	10	152± 11	0.110± 0.007	0.032± 0.003	0.071± 0.009	0.383± 0.016	0.469± 0.022
2000 ppm	10	147± 10*	0.112± 0.009	0.032± 0.003	0.071± 0.003	0.404± 0.026**	0.473± 0.016
4000 ppm	10	135± 9**	0.114± 0.012	0.030± 0.004	0.071± 0.011	0.409± 0.019**	0.489± 0.021**

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

STUDY NO. : 0439
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	0.683± 0.019	0.232± 0.016	2.402± 0.060	1.108± 0.058
63 ppm	10	0.685± 0.034	0.222± 0.014	2.562± 0.065	1.085± 0.051
250 ppm	10	0.703± 0.027	0.236± 0.013	2.870± 0.041*	1.083± 0.049
1000 ppm	10	0.791± 0.036**	0.296± 0.012*	3.758± 0.099**	1.152± 0.074
2000 ppm	10	0.846± 0.022**	0.402± 0.021**	4.718± 0.240**	1.183± 0.079
4000 ppm	10	0.977± 0.050**	0.666± 0.061**	6.417± 0.287**	1.255± 0.083**

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)

Organ	Findings	Group Name	Control				63 ppm				250 ppm				1000 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>			
	erythropoiesis:increased		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		0	0	0	0	0	0	0	0	10	0	0	0 **	10	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(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	10	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	engorgement of erythrocyte		0	0	0	0	0	0	0	0	10	0	0	0 **	10	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	capsule hyperplasia		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	herniation		2	0	0	0	0	0	0	0	2	0	0	0	1	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(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	2000 ppm				4000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
bone marrow			<10>				<10>			
	erythropoiesis:increased		10	0	0	0 **	10	0	0	0 **
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
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		10	0	0	0 **	10	0	0	0 **
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	engorgement of erythrocyte		0	10	0	0 **	0	0	10	0 **
			(0)	(100)	(0)	(0)	(0)	(0)	(100)	(0)
	capsule hyperplasia		9	1	0	0 **	0	10	0	0 **
			(90)	(10)	(0)	(0)	(0)	(100)	(0)	(0)
{Digestive system}										
liver			<10>				<10>			
	herniation		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				63 ppm				250 ppm				1000 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>			
	necrosis:single cell		0	0	0	0	0	0	0	0	0	0	0	0	8	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(80)	(0)	(0)	(0)
	deposit of hemosiderin		0	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0 *
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
	hydropic change:central		0	0	0	0	0	0	0	0	0	0	0	0	7	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(70)	(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)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	basophilic change		5	0	0	0	4	0	0	0	5	0	0	0	3	0	0	0
			(50)	(0)	(0)	(0)	(40)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	(30)	(0)	(0)	(0)
	eosinophilic body		4	6	0	0	2	8	0	0	6	4	0	0	4	6	0	0
			(40)	(60)	(0)	(0)	(20)	(80)	(0)	(0)	(60)	(40)	(0)	(0)	(40)	(60)	(0)	(0)
	hyaline cast		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	2000 ppm				4000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
liver			<10>				<10>			
	necrosis:single cell		10	0	0	0 **	10	0	0	0 **
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	deposit of hemosiderin		10	0	0	0 **	10	0	0	0 **
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	hydropic change:central		0	10	0	0 **	0	6	4	0 **
			(0)	(100)	(0)	(0)	(0)	(60)	(40)	(0)
	hepatocellular hypertrophy:central		10	0	0	0 **	0	10	0	0 **
			(100)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
{Urinary system}										
kidney			<10>				<10>			
	basophilic change		5	0	0	0	5	0	0	0
			(50)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
	eosinophilic body		0	0	0	0 **	0	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyaline cast		8	0	0	0 **	5	0	0	0 *
			(80)	(0)	(0)	(0)	(50)	(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				63 ppm				250 ppm				1000 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>			
	deposit of brown pigment:proximal tubule		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)
{Endocrine system}																		
pituitary			<10>				<10>				<10>				<10>			
	Rathke pouch		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)	(0)	(0)	(0)	(0)
thyroid			<10>				<10>				<10>				<10>			
	ultimibranchial body remanet		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)
{Reproductive system}																		
testis			<10>				<10>				<10>				<10>			
	germ cell necrosis		2	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)
epididymis			<10>				<10>				<10>				<10>			
	decreased:sperma		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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	2000 ppm				4000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}										
kidney			<10>				<10>			
	deposit of brown pigment:proximal tubule		0	10	0	0 **	0	0	10	0 **
			(0)	(100)	(0)	(0)	(0)	(0)	(100)	(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}										
testis			<10>				<10>			
	germ cell necrosis		0	0	0	0	4	5	1	0 **
			(0)	(0)	(0)	(0)	(40)	(50)	(10)	(0)
epididymis			<10>				<10>			
	decreased:sperma		0	0	0	0	0	0	10	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	Control				63 ppm				250 ppm				1000 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	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Special sense organs/appendage}																		
eye			<10>				<10>				<10>				<10>			
	retinal atrophy		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)
Harder gl			<10>				<10>				<10>				<10>			
	lymphocytic infiltration		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)

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	2000 ppm				4000 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		0	0	0	0	8	1	0	0 **
			(0)	(0)	(0)	(0)	(80)	(10)	(0)	(0)
{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>			
	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 K 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : ALL ANIMALS

(13-WEEK STUDY)

Organ	Findings	Group Name	Control				63 ppm				250 ppm				1000 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)																		
lung			<10>				<10>				<10>				<10>			
	accumulation of foamy cells		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)	(0)	(0)	(0)	(0)
(Hematopoietic system)																		
bone marrow			<10>				<10>				<10>				<10>			
	granulation		2	0	0	0	1	2	0	0	0	0	0	0	2	0	0	0
			(20)	(0)	(0)	(0)	(10)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	erythropoiesis:increased		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		0	0	0	0	0	0	0	0	10	0	0	0 **	10	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(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	10	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	engorgement of erythrocyte		0	0	0	0	0	0	0	0	9	0	0	0 **	10	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(90)	(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	2000 ppm				4000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
lung			<10>				<10>			
	accumulation of foamy cells		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}										
bone marrow			<10>				<10>			
	granulation		2	1	0	0	2	0	0	0
			(20)	(10)	(0)	(0)	(20)	(0)	(0)	(0)
	erythropoiesis:increased		10	0	0	0 **	10	0	0	0 **
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
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		10	0	0	0 **	10	0	0	0 **
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	engorgement of erythrocyte		0	10	0	0 **	0	0	10	0 **
			(0)	(100)	(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	Control				63 ppm				250 ppm				1000 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>			
	capsule hyperplasia		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}																		
stomach			<10>				<10>				<10>				<10>			
	hyperplasia:forestomach		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)	(0)	(0)	(0)
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)
	necrosis:single cell		0	0	0	0	0	0	0	0	0	0	0	0	8	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(80)	(0)	(0)	(0)
	deposit of hemosiderin		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)
	hydropic change:central		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	2000 ppm				4000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Hematopoietic system)										
spleen			<10>				<10>			
	capsule hyperplasia		6	0	0	0 *	6	4	0	0 **
			(60)	(0)	(0)	(0)	(60)	(40)	(0)	(0)
(Digestive system)										
stomach			<10>				<10>			
	hyperplasia:forestomach		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
liver			<10>				<10>			
	herniation		2	0	0	0	1	0	0	0
			(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	necrosis:single cell		9	0	0	0 **	10	0	0	0 **
			(90)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	deposit of hemosiderin		10	0	0	0 **	10	0	0	0 **
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	hydropic change:central		7	3	0	0 **	0	5	5	0 **
			(70)	(30)	(0)	(0)	(0)	(50)	(50)	(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				63 ppm				250 ppm				1000 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>			
	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)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	basophilic 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)
	mineralization:cortico-medullary junction		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)
	deposit of brown pigment:proximal tubule		0	0	0	0	0	0	0	0	10	0	0	0 **	10	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Endocrine system}																		
thyroid			<10>				<10>				<10>				<10>			
	ultimibranchial body remanet		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	2000 ppm				4000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
liver			<10>				<10>			
	hepatocellular hypertrophy:central		2	0	0	0	10	0	0	0 **
			(20)	(0)	(0)	(0)	(100)	(0)	(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)
	mineralization:cortico-medullary junction		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	deposit of brown pigment:proximal tubule		0	10	0	0 **	0	0	10	0 **
			(0)	(100)	(0)	(0)	(0)	(0)	(100)	(0)
{Endocrine system}										
thyroid			<10>				<10>			
	ultimibranchial body remanet		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				63 ppm				250 ppm				1000 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	0	1	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
Harder gl			<10>				<10>				<10>				<10>			
	lymphocytic infiltration		3	1	0	0	2	0	0	0	1	1	0	0	2	0	0	0
			(30)	(10)	(0)	(0)	(20)	(0)	(0)	(0)	(10)	(10)	(0)	(0)	(20)	(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	2000 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	1	0	0	0	0	0	0
			(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)
Harder gl			<10>				<10>			
	lymphocytic infiltration		1	0	0	0	3	0	0	0
			(10)	(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 OF *o*-CHLORONITROBENZENE IN THE 13-WEEK FEED STUDY

IDENTITY OF *o*-CHLORONITROBENZENE IN THE 13-WEEK FEED STUDY

Test Substance : *o*-Chloronitrobenzene (Wako Pure Chemical Industries, Ltd.)

Lot No. : SEF9795

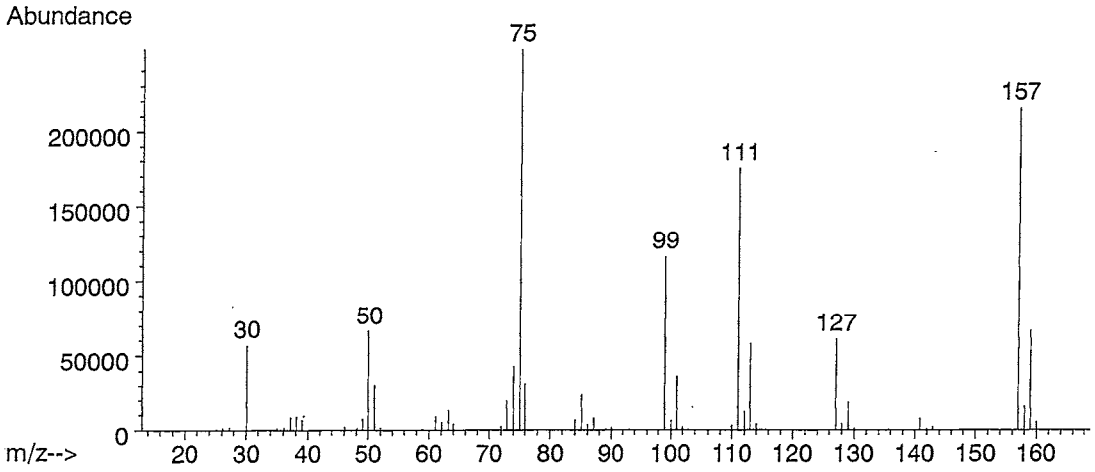
1. Spectral Data

Mass Spectrometry

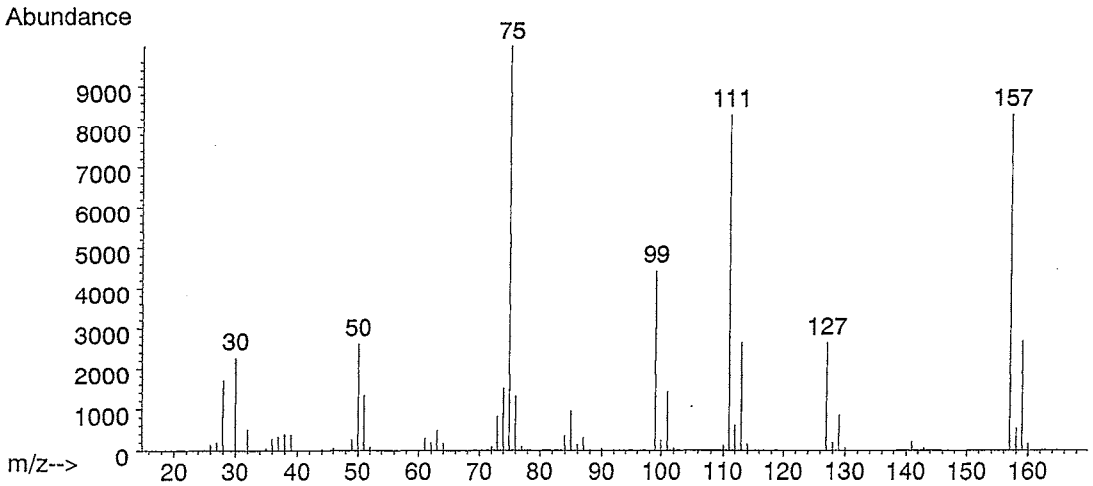
Instrument : Hewlett Packard 5989B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance



Mass Spectrum of Literature Data*

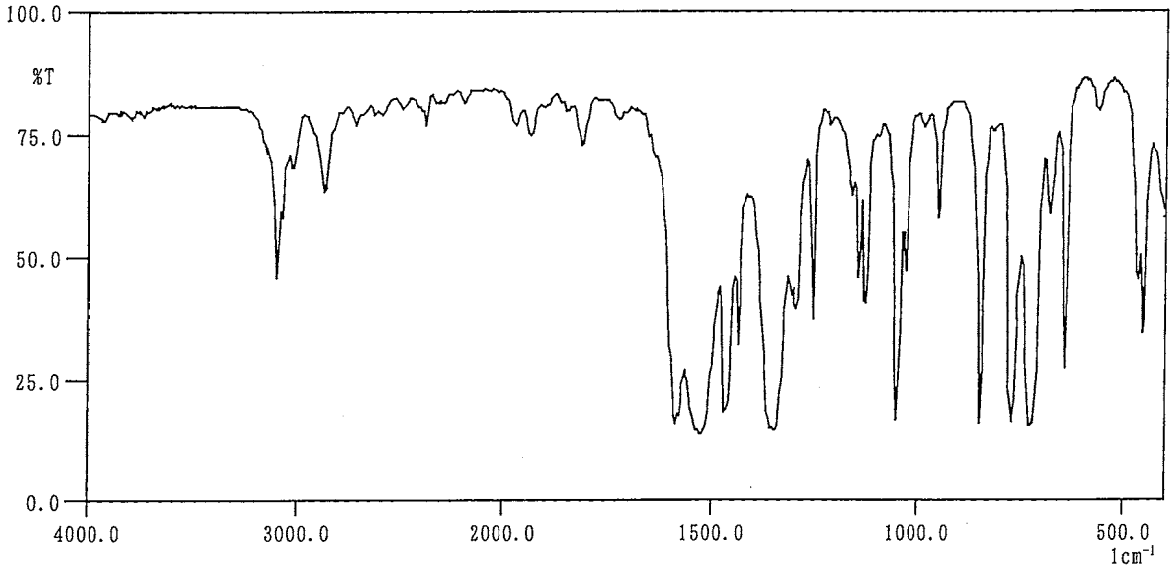
Result: The mass spectrum was consistent with literature spectrum.
(*McLafferty, FW. 1994. Wiley Registry of Mass Spectral Data, 6th ed. New York:John Wiley and Sons.)

Infrared Spectrometry

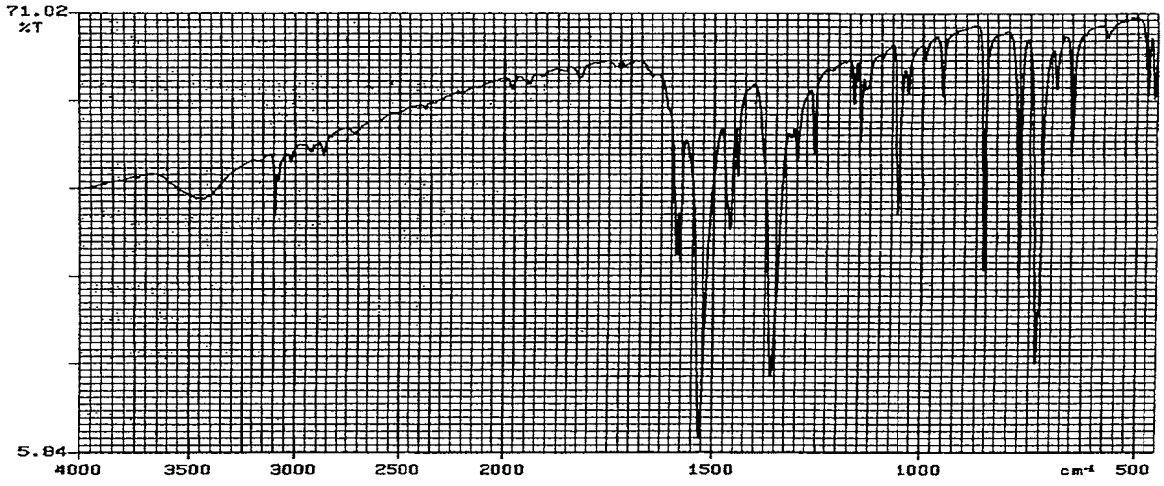
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr

Resolution : 2 cm^{-1}



Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data*

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

2. Conclusion: The test substance was identified as *o*-chloronitrobenzene by mass spectrum and infrared spectrum.

APPENDIX L 2

STABILITY OF *o*-CHLORONITROBENZENE IN THE 13-WEEK FEED STUDY

STABILITY OF *o*-CHLORONITROBENZENE IN THE 13-WEEK FEED STUDY

Test Substance : *o*-Chloronitrobenzene (Wako Pure Chemical Industries, Ltd.)

Lot No. : SEF9795

1. Sample : This lot was used from 2001.12.7 to 2002.3.11. Test substance was stored in cold storage in a dark place.

2. High Performance Liquid Chromatography

Instrument : Hewlett Packard 1090 High Performance Liquid Chromatograph

Column : TSK GEL ODS-80TM (4.6 mmϕ $\times$ 15 cm)

Column Temperature : Room Temperature

Mobile Phase : Acetonitrile : Distilled Water = 1 : 1

Flow Rate : 1 mL/min

Detector : UV (254 nm)

Injection Volume : 20 μL

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
2001.12.03	1	7.064	100
2002.03.26	1	7.022	100

Result: Gas chromatography indicated one major peak (peak No.1) analyzed on 2001.12.3 and one major peak (peak No.1) analyzed on 2002.3.26. No new trace impurity peak in the test substance analyzed on 2002.3.26 was detected.

3. Conclusion: The test substance was stable for about 4 months in cold storage in a dark place.

APPENDIX L 3

CONCENTRATION OF *o*-CHLORONITROBENZENE IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

CONCENTRATION OF *o*-CHLORONITROBENZENE IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

	Target Concentration				
Date Analyzed	63[a]	250	1000	2000	4000
2001.12.06	61.1 (97.0)[b]	240 (96.0)	988 (98.8)	2020 (101)	3980 (99.5)

[a] ppm
[b] %

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

Instrument : Hewlett Packard 1090 High Performance Liquid Chromatograph
Column : TSK GEL ODS-80TM (4.6 mmϕ × 15 cm)
Column Temperature : Room Temperature
Mobile Phase : Acetonitrile : Distilled Water = 1 : 1
Flow Rate : 1 mL/min
Detector : UV (254 nm)
Injection Volume : 20 µL

APPENDIX L 4

HOMOGENITY OF *o*-CHLORONITROBENZENE IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

HOMOGENEITY OF *o*-CHLORONITROBENZENE IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

	Target Concentration				
	63[a]	250	1000	2000	4000
Coefficient Variation	1.24[b]	1.06	1.72	1.21	0.35

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

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

Instrument : Hewlett Packard 1090 High Performance Liquid Chromatograph
Column : TSK GEL ODS-80TM (4.6 mmϕ × 15 cm)
Column Temperature : Room Temperature
Mobile Phase : Acetonitrile : Distilled Water = 1 : 1
Flow Rate : 1 mL/min
Detector : UV (254 nm)
Injection Volume : 20 µL

APPENDIX L 5

STABILITY OF *o*-CHLORONITROBENZENE IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

STABILITY OF *o*-CHLORONITROBENZENE IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

		Target Concentration	
Date Prepared	Date Analyzed	50[a]	5000
2001.10.11	2001.10.11	50.3 (100)[b]	4840 (100)
	2001.10.19[c]	44.7 (88.9)	3890 (80.4)
	2001.11.30[d]	52.2 (104)	4810 (99.4)

[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 high performance liquid chromatography.

Instrument : Hewlett Packard 1090 High Performance Liquid Chromatograph
Column : TSK GEL ODS-80TM (4.6 mmϕ × 15 cm)
Column Temperature : Room Temperature
Mobile Phase : Acetonitrile : Distilled Water = 1 : 1
Flow Rate : 1 mL/min
Detector : UV (254 nm)
Injection Volume : 20 µL

APPENDIX M 1

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS IN THE 13-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

METHOD FOR HEMATOLOGY,BIOCHEMISTRY AND URINALYSIS IN THE 13-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

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	Light scattering method [1]
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 (ADVIA120 : 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 : Bayer Corporation)
6) Ames reagent strips for urinalysis (Mult istix : Bayer Corporation)

APPENDIX N 1

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK FEED STUDY OF *o*-CHLORONITROBENZENE

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