アクリル酸=2 - ヒドロキシエチルのラットを用いた
経口投与による 13 週間毒性試験(混水試験)報告書

試験番号：０３２３

APPENDIX

APPENDIXES

APPENDIXES (CONTINUED)

APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, RAT : MALE

(13 - WEEK STUDY)

STUDY NO. : 0323
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
SOILED	Control	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
	500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	1	1	0	0	0	0	0	0	0	0	0	0
PILOERECTION	Control	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
	500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	1	1	0	0	0	0	0	0	0	0	0	0

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

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
SOILED	Control	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
	500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	2	0	0	0	0	0	0	0	0	0	0	0
PILOERECTION	Control	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
	500 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	2000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	4	5	5	3	0	0	0	0	0	0	0	0
OLIGO-STOOL	Control	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
	500 ppm	0	0	0	0	1	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	0	0	0	0	0	0	0	0	0

APPENDIX B 1

BODY WEIGHT CHANGES :SUMMARY, RAT : MALE

(13 - WEEK STUDY)

STUDY NO. : 0323
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	124± 4	154± 6	188± 7	212± 7	230± 7	244± 9	255± 9
250 ppm	124± 4	154± 7	186± 10	208± 12	226± 13	240± 12	252± 13
500 ppm	124± 4	153± 6	184± 7	206± 7	224± 8	239± 8	251± 9
1000 ppm	124± 4	150± 7	181± 7	204± 7	221± 6	235± 6	248± 7
2000 ppm	124± 4	144± 6**	170± 7**	192± 6**	207± 7**	221± 7**	231± 7**
4000 ppm	124± 4	112± 5**	131± 7**	156± 8**	171± 7**	182± 9**	189± 10**

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

STUDY NO. : 0323
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	268± 11	278± 12	287± 13	296± 13	302± 14	308± 14	312± 17
250 ppm	262± 13	272± 12	279± 13	286± 13	293± 12	300± 13	303± 13
500 ppm	261± 9	271± 9	278± 8	286± 7	293± 7	299± 7	303± 7
1000 ppm	257± 6	266± 6	274± 7*	281± 8*	288± 7*	294± 8*	298± 8
2000 ppm	240± 8**	247± 11**	252± 10**	258± 10**	266± 11**	271± 11**	276± 12**
4000 ppm	196± 11**	202± 12**	211± 13**	217± 13**	226± 13**	230± 13**	235± 13**

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

APPENDIX B 2

BODY WEIGHT CHANGES : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0323
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	98± 3	113± 4	129± 5	135± 6	144± 5	151± 6	154± 10
250 ppm	98± 3	111± 4	126± 5	134± 6	141± 6	146± 7	150± 11
500 ppm	98± 3	111± 4	125± 4	127± 6**	141± 6	144± 8*	150± 6
1000 ppm	98± 3	110± 4	124± 4	128± 4*	139± 4	145± 5	148± 5
2000 ppm	98± 3	105± 3**	119± 4**	128± 4**	134± 4**	139± 4**	144± 5*
4000 ppm	98± 3	85± 5**	99± 5**	111± 4**	119± 4**	123± 4**	127± 5**

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

STUDY NO. : 0323
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	161± 7	165± 7	169± 8	173± 8	177± 6	180± 8	182± 8
250 ppm	154± 8*	157± 9*	160± 9	164± 9*	167± 10*	171± 10*	171± 10**
500 ppm	156± 7	158± 8	162± 8	166± 7	168± 7*	171± 7*	173± 7*
1000 ppm	152± 5**	155± 4**	158± 4	162± 5**	166± 4**	168± 6**	168± 6**
2000 ppm	148± 3**	150± 4**	153± 3**	157± 5**	161± 5**	164± 7**	165± 6**
4000 ppm	131± 5**	132± 6**	134± 6**	137± 6**	141± 6**	143± 5**	145± 7**

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

APPENDIX C 1

WATER CONSUMPTION CHANGES : SUMMARY, RAT : MALE

(13 - WEEK STUDY)

STUDY NO. : 0323
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 1	2	3	4	5	6	7
Control	16.7± 1.1	18.3± 1.1	18.6± 1.0	19.0± 1.3	18.7± 1.1	18.6± 1.5	18.7± 1.6
250 ppm	15.1± 1.0**	16.3± 1.6**	16.4± 1.3**	16.3± 1.1**	16.5± 0.9	16.5± 0.9**	16.7± 1.2**
500 ppm	14.4± 0.5**	14.8± 0.7**	15.2± 1.0**	15.5± 0.8**	15.6± 1.8	15.2± 1.2**	16.2± 1.9**
1000 ppm	13.3± 0.9**	13.8± 1.0**	14.0± 0.9**	13.9± 0.8**	13.8± 0.5**	14.1± 0.8**	14.1± 0.9**
2000 ppm	11.6± 0.8**	11.7± 1.0**	12.0± 0.7**	11.5± 0.8**	11.9± 0.8**	12.0± 0.7**	11.9± 0.9**
4000 ppm	5.8± 0.9**	8.4± 0.6**	9.1± 0.5**	8.7± 0.4**	8.8± 0.7**	8.7± 0.7**	9.3± 0.9**

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

STUDY NO. : 0323
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 8	9	10	11	12	13
Control	17.8± 1.0	18.3± 1.3	18.5± 1.7	17.7± 1.3	17.1± 1.4	17.5± 1.2
250 ppm	16.2± 1.1**	16.2± 0.8**	15.7± 0.7	15.3± 0.9**	15.1± 0.9**	15.2± 0.7**
500 ppm	14.9± 0.9**	15.2± 0.5**	14.9± 0.7	14.8± 0.6**	14.3± 0.8**	14.4± 0.7**
1000 ppm	14.0± 1.0**	13.7± 0.9**	13.6± 0.9**	13.5± 1.2**	13.3± 1.1**	13.3± 1.1**
2000 ppm	12.0± 0.9**	12.3± 1.0**	11.7± 1.0**	12.0± 1.1**	11.4± 1.0**	11.5± 0.9**
4000 ppm	8.9± 0.9**	9.3± 0.8**	9.0± 0.4**	9.6± 0.6**	9.1± 0.6**	9.3± 0.5**

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

APPENDIX C 2

WATER CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0323
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 1	2	3	4	5	6	7
Control	14.1± 1.2	15.2± 2.0	18.9± 9.7	17.0± 5.5	16.9± 4.7	16.9± 4.1	20.7± 9.3
250 ppm	12.6± 1.1**	13.3± 1.4	12.7± 1.4	12.6± 1.2	13.1± 1.7	17.5± 10.8	16.8± 11.5
500 ppm	12.1± 1.1**	13.4± 4.4	12.6± 3.0	14.4± 8.1	11.8± 0.8	12.1± 1.6	16.6± 8.9
1000 ppm	10.5± 0.6**	10.5± 0.8**	10.7± 1.1**	10.1± 0.6**	10.6± 0.5**	10.2± 0.6**	11.0± 1.9**
2000 ppm	9.1± 0.8**	9.8± 1.1**	9.5± 1.1**	9.3± 1.8**	9.8± 1.4**	9.7± 1.9**	10.5± 2.3**
4000 ppm	5.6± 0.8**	7.5± 0.5**	7.2± 0.5**	7.0± 0.6**	7.1± 0.6**	7.2± 0.5**	7.4± 0.7**

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

STUDY NO. : 0323
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 8	9	10	11	12	13
Control	19.3± 9.5	19.1± 6.9	16.6± 2.9	18.1± 7.2	16.0± 4.7	18.1± 8.6
250 ppm	14.1± 3.7	13.2± 2.6	14.7± 4.4	12.6± 1.3	12.9± 2.3	16.1± 5.1
500 ppm	17.1± 8.9	15.9± 7.0	16.1± 6.2	15.8± 7.4	14.7± 5.0	14.5± 5.9
1000 ppm	10.5± 1.0**	10.4± 0.7**	10.7± 0.7*	11.2± 1.6*	11.0± 1.8*	9.9± 1.1*
2000 ppm	9.8± 1.9**	9.9± 1.4**	9.4± 1.1**	9.4± 0.9**	9.1± 1.0**	9.2± 1.5**
4000 ppm	7.0± 0.4**	6.9± 0.7**	7.0± 0.5**	7.5± 0.4**	6.9± 0.4**	7.1± 0.5**

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

APPENDIX D 1

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : MALE

(13 - WEEK STUDY)

STUDY NO. : 0323
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 1	2	3	4	5	6	7
Control	14.3± 0.7	16.1± 0.7	16.4± 0.7	16.2± 0.5	15.8± 0.9	15.6± 0.5	15.6± 0.8
250 ppm	13.5± 1.4	15.5± 1.3	15.8± 1.2	15.3± 0.8*	15.3± 0.9	14.9± 1.0	14.7± 1.0
500 ppm	14.1± 0.4	15.3± 0.8	15.6± 0.9	15.5± 0.7	15.6± 0.8	15.0± 0.9	14.9± 0.8
1000 ppm	13.5± 0.7	14.9± 0.7**	15.7± 1.1	15.5± 0.9	15.2± 0.4	15.3± 0.5	14.6± 0.6*
2000 ppm	12.2± 0.6**	13.9± 0.6**	14.4± 0.5**	14.2± 0.6**	14.2± 0.4**	13.9± 0.6**	13.7± 0.8**
4000 ppm	7.7± 1.0**	10.1± 0.8**	12.3± 0.6**	12.2± 0.5**	12.2± 0.9**	11.4± 0.8**	11.3± 0.9**

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

STUDY NO. : 0323
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 8	9	10	11	12	13
Control	15.5± 0.9	15.7± 1.1	15.3± 0.9	15.5± 0.8	15.4± 0.8	15.2± 0.9
250 ppm	14.6± 0.9	14.8± 0.9	14.3± 0.7*	14.5± 0.9*	14.2± 0.7**	14.6± 0.6
500 ppm	14.6± 0.6	14.8± 0.7	14.6± 0.6	14.8± 0.5	14.4± 0.7*	14.8± 0.6
1000 ppm	14.5± 0.7*	14.7± 0.7*	14.3± 0.7*	14.7± 0.5	14.6± 0.7	14.7± 0.7
2000 ppm	13.3± 0.7**	13.4± 0.7**	13.3± 0.8**	13.9± 0.8**	13.6± 0.7**	13.7± 0.8**
4000 ppm	11.6± 0.9**	11.8± 0.9**	11.9± 1.0**	12.7± 1.0**	12.3± 1.0**	12.8± 0.8**

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

APPENDIX D 2

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0323
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 1	2	3	4	5	6	7
Control	10.9± 0.4	11.2± 0.4	10.9± 0.6	11.0± 0.6	11.0± 0.8	10.9± 1.0	11.1± 0.8
250 ppm	10.5± 0.6	10.7± 0.5	10.7± 0.7	10.4± 0.7	10.4± 0.7	10.0± 1.0	10.1± 0.7**
500 ppm	10.5± 0.5	10.7± 0.5	10.7± 0.7	10.6± 0.5	10.3± 0.6*	10.3± 0.6	10.4± 0.7
1000 ppm	10.1± 0.4**	10.3± 0.4**	10.3± 0.4	10.2± 0.5**	10.3± 0.4*	9.8± 0.6*	9.7± 0.3**
2000 ppm	9.1± 0.3**	10.1± 0.5**	10.2± 0.5	9.9± 0.4**	10.1± 0.3**	9.8± 0.5**	9.7± 0.4**
4000 ppm	6.0± 0.6**	8.6± 0.5**	9.3± 0.5**	9.0± 0.4**	8.9± 0.4**	8.7± 0.5**	8.4± 0.5**

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

STUDY NO. : 0323
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 8	9	10	11	12	13
Control	11.0± 0.8	11.1± 0.8	10.7± 0.7	11.1± 0.7	10.9± 0.5	11.1± 0.8
250 ppm	10.3± 0.9	10.1± 0.8**	10.0± 0.6*	10.3± 0.8*	10.4± 0.8	10.3± 0.7**
500 ppm	10.1± 0.4	10.3± 0.4*	10.1± 0.6	10.4± 0.4*	10.2± 0.5	10.3± 0.4**
1000 ppm	9.7± 0.3*	9.5± 0.5**	9.6± 0.4**	9.8± 0.5**	9.6± 0.5**	9.7± 0.5**
2000 ppm	9.4± 0.5**	9.5± 0.6**	9.3± 0.6**	9.7± 0.6**	9.5± 0.5**	9.8± 0.5**
4000 ppm	8.3± 0.4**	8.4± 0.5**	8.5± 0.5**	8.7± 0.4**	8.7± 0.5**	8.9± 0.4**

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

APPENDIX E 1

CHEMICAL INTAKE CHANGES : SUMMARY, RAT : MALE

(13 - WEEK STUDY)

STUDY NO. : 0323
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
250 ppm	0.024± 0.001	0.022± 0.002	0.020± 0.001	0.018± 0.001	0.017± 0.001	0.016± 0.001	0.016± 0.001
500 ppm	0.047± 0.001	0.040± 0.002	0.037± 0.002	0.035± 0.002	0.033± 0.003	0.030± 0.002	0.031± 0.004
1000 ppm	0.089± 0.003	0.076± 0.003	0.069± 0.002	0.063± 0.003	0.059± 0.002	0.057± 0.003	0.055± 0.003
2000 ppm	0.162± 0.011	0.138± 0.009	0.126± 0.006	0.111± 0.007	0.108± 0.006	0.104± 0.006	0.100± 0.006
4000 ppm	0.208± 0.024	0.256± 0.015	0.234± 0.011	0.203± 0.010	0.193± 0.011	0.184± 0.011	0.189± 0.012

STUDY NO. : 0323
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
250 ppm	0.015± 0.001	0.014± 0.001	0.014± 0.001	0.013± 0.001	0.013± 0.001	0.013± 0.001
500 ppm	0.028± 0.001	0.027± 0.001	0.026± 0.001	0.025± 0.001	0.024± 0.001	0.024± 0.001
1000 ppm	0.053± 0.003	0.050± 0.003	0.048± 0.003	0.047± 0.003	0.045± 0.003	0.045± 0.003
2000 ppm	0.097± 0.007	0.098± 0.007	0.091± 0.007	0.090± 0.006	0.084± 0.006	0.084± 0.005
4000 ppm	0.176± 0.008	0.176± 0.010	0.166± 0.005	0.169± 0.006	0.158± 0.008	0.158± 0.006

APPENDIX E 2

CHEMICAL INTAKE CHANGES : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0323
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
250 ppm	0.029± 0.002	0.026± 0.003	0.024± 0.002	0.023± 0.002	0.022± 0.002	0.030± 0.021	0.027± 0.017
500 ppm	0.054± 0.005	0.053± 0.017	0.050± 0.012	0.051± 0.029	0.041± 0.003	0.041± 0.007	0.054± 0.031
1000 ppm	0.095± 0.004	0.085± 0.006	0.083± 0.007	0.073± 0.004	0.073± 0.002	0.069± 0.004	0.072± 0.014
2000 ppm	0.174± 0.016	0.164± 0.018	0.150± 0.016	0.139± 0.025	0.141± 0.020	0.134± 0.023	0.142± 0.030
4000 ppm	0.264± 0.027	0.302± 0.019	0.259± 0.011	0.234± 0.015	0.230± 0.018	0.226± 0.011	0.227± 0.017

STUDY NO. : 0323
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
250 ppm	0.022± 0.005	0.021± 0.005	0.022± 0.007	0.019± 0.002	0.019± 0.003	0.024± 0.008
500 ppm	0.055± 0.030	0.050± 0.022	0.049± 0.021	0.048± 0.023	0.044± 0.017	0.042± 0.017
1000 ppm	0.068± 0.008	0.066± 0.004	0.066± 0.005	0.068± 0.011	0.066± 0.013	0.059± 0.007
2000 ppm	0.130± 0.024	0.129± 0.018	0.119± 0.013	0.117± 0.009	0.112± 0.010	0.112± 0.017
4000 ppm	0.213± 0.010	0.207± 0.019	0.203± 0.014	0.213± 0.007	0.193± 0.012	0.195± 0.012

APPENDIX F 1

HEMATOLOGY : SUMMARY, RAT : MALE

(13 - WEEK STUDY)

STUDY NO. : 0323
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV fℓ	MCH pg	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	10	8.98± 0.18	15.7± 0.3	44.2± 0.9	49.2± 0.3	17.5± 0.2	35.6± 0.5	664± 36
250 ppm	10	8.92± 0.20	15.8± 0.3	44.2± 1.3	49.6± 0.7	17.7± 0.5	35.8± 1.0	647± 58
500 ppm	10	8.75± 0.40	15.5± 0.3	43.6± 2.1	49.8± 1.0	17.8± 0.8	35.6± 1.4	643± 50
1000 ppm	10	8.77± 0.21	15.6± 0.3	43.9± 1.3	50.0± 0.8	17.8± 0.5	35.6± 1.1	645± 30
2000 ppm	10	8.49± 0.30**	15.2± 0.4**	42.9± 1.6	50.6± 0.7**	17.9± 0.3*	35.3± 0.7	672± 62
4000 ppm	10	8.58± 0.25**	15.5± 0.2	43.8± 1.6	51.1± 0.8**	18.1± 0.4**	35.3± 1.0	692± 51

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

STUDY NO. : 0323
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RETICULOCYTE ‰	PROTHROMBIN TIME sec	APTT sec
Control	10	31± 6	15.0± 3.2	26.0± 4.1
250 ppm	10	27± 8	15.6± 1.5	28.1± 7.7
500 ppm	10	25± 5	13.8± 0.8	23.7± 1.7
1000 ppm	10	30± 8	13.0± 1.0	26.6± 8.0
2000 ppm	10	29± 6	12.9± 1.2	23.6± 4.8
4000 ppm	10	35± 6	12.5± 0.3*	24.7± 5.7

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

STUDY NO. : 0323
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	3.68± 0.86	0± 0	28± 4	1± 1	0± 0	4± 1	67± 5	0± 0
250 ppm	10	3.83± 1.02	0± 0	32± 7	1± 1	0± 0	4± 2	63± 7	0± 0
500 ppm	10	3.39± 0.98	0± 0	26± 4	1± 1	0± 0	4± 1	69± 5	0± 0
1000 ppm	10	3.66± 1.07	0± 0	28± 5	1± 1	0± 0	4± 1	67± 4	0± 0
2000 ppm	10	3.42± 1.11	0± 0	28± 8	1± 1	0± 0	4± 2	67± 8	0± 0
4000 ppm	10	3.51± 0.70	0± 0	30± 6	2± 1	0± 0	4± 1	64± 6	0± 0

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

APPENDIX F 2

HEMATOLOGY : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0323
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 fℓ	MCH pg	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	10	8.02± 0.41	15.4± 0.4	41.9± 2.2	52.2± 0.8	19.3± 1.0	36.9± 1.7	681± 80
250 ppm	10	8.26± 0.26	15.6± 0.5	43.3± 1.9	52.5± 1.0	18.9± 0.2	36.1± 0.8	710± 55
500 ppm	10	8.10± 0.30	15.5± 0.5	42.7± 1.7	52.8± 0.6	19.1± 0.4	36.2± 0.6	671± 73
1000 ppm	10	8.04± 0.40	15.6± 0.3	42.6± 2.1	53.0± 0.6	19.5± 0.9	36.7± 1.7	697± 46
2000 ppm	10	7.78± 0.30	15.4± 0.3	41.9± 1.8	53.8± 0.9**	19.8± 0.7*	36.7± 1.3	678± 68
4000 ppm	9	8.06± 0.27	15.5± 0.4	43.1± 2.1	53.3± 1.0*	19.3± 0.3	36.1± 1.1	728± 82

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

STUDY NO. : 0323
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RETICULOCYTE ‰		PROTHROMBIN TIME sec		APTT sec	
Control	10	26±	5	12.1±	0.5	19.3±	1.4
250 ppm	10	23±	5	12.2±	0.6	24.3±	9.7
500 ppm	10	27±	5	12.0±	0.4	23.2±	6.8
1000 ppm	10	23±	4	12.2±	0.3	18.6±	1.1
2000 ppm	10	31±	3	12.1±	0.3	18.4±	2.4
4000 ppm	9	34±	9**	12.0±	0.5	20.4±	4.0

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

STUDY NO. : 0323
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	1.93± 0.57	0± 0	28± 5	2± 1	0± 0	4± 2	66± 6	0± 0
250 ppm	10	1.89± 0.61	0± 0	28± 5	1± 1	0± 0	4± 2	66± 5	0± 0
500 ppm	10	2.07± 1.01	0± 0	25± 4	1± 1	0± 0	4± 2	70± 5	0± 0
1000 ppm	10	2.07± 0.56	0± 0	24± 3	1± 1	0± 0	4± 2	70± 4	0± 0
2000 ppm	10	2.24± 0.71	0± 0	25± 6	1± 1	0± 0	4± 2	70± 7	0± 0
4000 ppm	9	2.87± 1.11	0± 0	27± 12	2± 1	0± 0	4± 1	67± 12	0± 0

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

APPENDIX G 1

BIOCHEMISTRY : SUMMARY, RAT : MALE

(13 - WEEK STUDY)

STUDY NO. : 0323
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± 0.1	1.6± 0.1	0.13± 0.01	188± 10	61± 7	56± 19
250 ppm	10	6.3± 0.1	3.9± 0.1	1.6± 0.1	0.14± 0.01	184± 6	62± 4	59± 16
500 ppm	10	6.3± 0.2	3.9± 0.1	1.6± 0.1	0.14± 0.01	179± 10	67± 4	54± 23
1000 ppm	10	6.4± 0.1	4.0± 0.1	1.7± 0.1	0.14± 0.01	180± 15	70± 5*	59± 16
2000 ppm	10	6.2± 0.2	3.9± 0.1	1.7± 0.1**	0.14± 0.01	172± 9**	72± 3**	43± 14
4000 ppm	10	6.0± 0.2**	3.8± 0.1	1.7± 0.1**	0.16± 0.01**	172± 11**	79± 8**	64± 10

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

STUDY NO. : 0323
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± 10	94± 18	53± 9	203± 36	268± 15	3± 5	110± 10
250 ppm	10	115± 4	100± 26	53± 9	218± 70	267± 16	2± 1	111± 23
500 ppm	10	119± 7	119± 37	62± 16	256± 78	259± 19	1± 1	101± 11
1000 ppm	10	125± 9*	101± 44	54± 18	231± 85	260± 16	2± 1	100± 11
2000 ppm	10	126± 7**	99± 26	54± 13	233± 46	253± 23	6± 15	116± 61
4000 ppm	10	145± 16**	103± 32	62± 21	222± 42	263± 24	3± 2	118± 20

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

STUDY NO. : 0323
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	0.6±	0.1	141±	1	3.8±	0.3	106±	1	10.2±	0.1	6.1±	0.8
250 ppm	10	18.6±	0.6	0.5±	0.0	141±	1	3.8±	0.4	106±	1	10.3±	0.1	6.0±	0.7
500 ppm	10	19.7±	1.2	0.5±	0.1	140±	1	3.9±	0.3	105±	1	10.3±	0.2	6.0±	0.7
1000 ppm	10	19.9±	1.5	0.5±	0.1	140±	1	3.9±	0.4	105±	1	10.4±	0.2	6.0±	0.5
2000 ppm	10	26.1±	15.9*	0.8±	0.8	139±	2**	4.9±	2.1**	105±	2	10.2±	0.1	7.3±	3.1
4000 ppm	10	22.8±	3.1**	0.5±	0.1	140±	1	4.3±	0.3*	105±	1	10.2±	0.2	6.5±	0.5

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

APPENDIX G 2

BIOCHEMISTRY : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0323
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± 0.01	146± 9	70± 5	15± 1
250 ppm	10	6.2± 0.2	3.9± 0.1	1.6± 0.1	0.15± 0.01	146± 12	73± 9	16± 3
500 ppm	10	6.2± 0.2	3.9± 0.1	1.7± 0.1	0.15± 0.01	150± 10	76± 6	19± 5
1000 ppm	10	6.1± 0.2	3.9± 0.1	1.7± 0.1**	0.15± 0.01	150± 9	77± 5	19± 3*
2000 ppm	10	6.1± 0.1	3.9± 0.1	1.7± 0.0*	0.16± 0.01	151± 12	84± 8**	20± 5*
4000 ppm	9	5.7± 0.2**	3.6± 0.1*	1.7± 0.2**	0.17± 0.07	149± 12	92± 62	35± 45**

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

STUDY NO. : 0323
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	127± 10	77± 15	40± 10	270± 82	188± 9	2± 1	140± 33
250 ppm	10	133± 17	81± 18	43± 22	280± 55	180± 26	3± 1	131± 27
500 ppm	10	137± 12	73± 14	37± 12	264± 44	174± 15	2± 1	117± 17
1000 ppm	10	139± 8	77± 17	38± 9	263± 86	182± 18	2± 1	128± 39
2000 ppm	10	148± 12**	79± 13	39± 7	307± 111	181± 13	3± 1	137± 51
4000 ppm	9	164± 104	93± 54	47± 30	273± 54	258± 141	20± 47**	129± 26

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

STUDY NO. : 0323
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	19.5± 2.2	0.5± 0.0	141± 1	3.8± 0.4	108± 2	9.9± 0.2	5.1± 1.3
250 ppm	10	18.8± 1.8	0.5± 0.0	140± 1	3.8± 0.3	107± 2	9.9± 0.2	5.3± 1.2
500 ppm	10	18.6± 2.0	0.5± 0.0	140± 1	3.9± 0.4	108± 2	9.9± 0.2	5.5± 1.1
1000 ppm	10	20.4± 0.8	0.5± 0.0	139± 1*	4.1± 0.5	106± 2	10.0± 0.1	5.3± 1.0
2000 ppm	10	20.7± 1.7	0.5± 0.0	138± 1**	4.1± 0.5	106± 1	9.9± 0.2	5.6± 0.9
4000 ppm	9	24.4± 3.4**	0.4± 0.1**	138± 1**	4.1± 0.4	106± 1	9.7± 0.3	5.9± 0.5

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

APPENDIX H 1

URINALYSIS : SUMMARY, RAT : MALE

(13 - WEEK STUDY)

STUDY NO. : 0323
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

URINALYSIS

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

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

STUDY NO. : 0323 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	
250 ppm	10	10	0	0	0	0		10	0	0	0	0	
500 ppm	10	10	0	0	0	0		10	0	0	0	0	
1000 ppm	10	10	0	0	0	0		10	0	0	0	0	
2000 ppm	10	10	0	0	0	0		10	0	0	0	0	
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 2

URINALYSIS : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0323
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

URINALYSIS

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

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

STUDY NO. : 0323 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	
250 ppm	10	10	0	0	0	0		10	0	0	0	0	
500 ppm	10	10	0	0	0	0		10	0	0	0	0	
1000 ppm	10	10	0	0	0	0		10	0	0	0	0	
2000 ppm	10	10	0	0	0	0		10	0	0	0	0	
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 I 1

GROSS FINDINGS : SUMMARY, RAT : MALE ALL ANIMALS

(13 - WEEK STUDY)

STUDY NO. : 0323
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 (%)	250 ppm 10 (%)	500 ppm 10 (%)	1000 ppm 10 (%)
liver	herniation		0 (0)	0 (0)	0 (0)	1 (10)

Organ	Findings	Group Name	2000 ppm	4000 ppm
		NO. of Animals	10 (%)	10 (%)
liver	herniation		0 (0)	1 (10)

APPENDIX I 2

GROSS FINDINGS : SUMMARY, RAT : FEMALE ALL ANIMALS

(13 - WEEK STUDY)

STUDY NO. : 0323
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 (%)	250 ppm 10 (%)	500 ppm 10 (%)	1000 ppm 10 (%)
liver	herniation		0 (0)	3 (30)	2 (20)	0 (0)

Organ	Findings	Group Name	2000 ppm	4000 ppm
		NO. of Animals	10 (%)	10 (%)
liver	herniation		0 (0)	0 (0)

APPENDIX J 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE

(13 - WEEK STUDY)

STUDY NO. : 0323
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	290± 15	0.218± 0.019	0.053± 0.008	3.010± 0.148	0.906± 0.050	1.011± 0.045
250 ppm	10	284± 13	0.213± 0.022	0.053± 0.008	3.049± 0.117	0.903± 0.059	1.005± 0.064
500 ppm	10	284± 8	0.216± 0.022	0.048± 0.005	3.000± 0.085	0.900± 0.053	0.984± 0.034
1000 ppm	10	281± 8	0.218± 0.019	0.049± 0.004	3.027± 0.110	0.883± 0.053	0.999± 0.054
2000 ppm	10	259± 11**	0.177± 0.024**	0.050± 0.002	2.969± 0.072	0.847± 0.047	0.950± 0.037*
4000 ppm	10	222± 12**	0.162± 0.028**	0.044± 0.004**	2.888± 0.090	0.776± 0.063**	0.864± 0.049**

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

STUDY NO. : 0323
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	1.801± 0.067	0.539± 0.032	7.195± 0.571	1.870± 0.037
250 ppm	10	1.823± 0.094	0.527± 0.033	7.102± 0.472	1.898± 0.040
500 ppm	10	1.873± 0.107	0.533± 0.022	7.150± 0.393	1.884± 0.030
1000 ppm	10	1.883± 0.080	0.525± 0.023	7.316± 0.257	1.876± 0.036
2000 ppm	10	1.861± 0.104	0.507± 0.044	7.062± 0.356	1.844± 0.040
4000 ppm	10	1.750± 0.096	0.462± 0.025**	6.479± 0.577**	1.812± 0.041**

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

APPENDIX J 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0323
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	168± 8	0.196± 0.033	0.056± 0.005	0.115± 0.012	0.617± 0.050	0.755± 0.029
250 ppm	10	160± 9*	0.171± 0.021*	0.056± 0.005	0.105± 0.009	0.602± 0.054	0.737± 0.037
500 ppm	10	161± 7	0.181± 0.017	0.052± 0.005	0.105± 0.011	0.599± 0.037	0.726± 0.040
1000 ppm	10	158± 6**	0.178± 0.014	0.055± 0.006	0.102± 0.010	0.591± 0.047	0.726± 0.036
2000 ppm	10	155± 6**	0.169± 0.017*	0.050± 0.004	0.107± 0.007	0.590± 0.026	0.720± 0.034
4000 ppm	10	136± 6**	0.158± 0.021**	0.050± 0.007	0.102± 0.016	0.530± 0.024**	0.655± 0.018**

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

STUDY NO. : 0323
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	1.155± 0.034	0.385± 0.022	3.979± 0.168	1.739± 0.056
250 ppm	10	1.163± 0.068	0.359± 0.029	3.890± 0.178	1.747± 0.036
500 ppm	10	1.181± 0.075	0.356± 0.025	3.964± 0.207	1.725± 0.060
1000 ppm	10	1.238± 0.045**	0.370± 0.029	3.970± 0.163	1.738± 0.024
2000 ppm	10	1.307± 0.054**	0.380± 0.028	4.210± 0.199	1.734± 0.040
4000 ppm	10	1.259± 0.045**	0.349± 0.025*	4.088± 0.418	1.674± 0.036**

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

APPENDIX K 1

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : MALE

(13 - WEEK STUDY)

STUDY NO. : 0323
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	290± 15	0.075± 0.006	0.018± 0.003	1.040± 0.031	0.313± 0.009	0.350± 0.008
250 ppm	10	284± 13	0.075± 0.007	0.019± 0.003	1.077± 0.054	0.318± 0.015	0.355± 0.016
500 ppm	10	284± 8	0.076± 0.008	0.017± 0.002	1.058± 0.028	0.318± 0.017	0.347± 0.012
1000 ppm	10	281± 8	0.078± 0.006	0.018± 0.001	1.079± 0.029*	0.314± 0.017	0.356± 0.013
2000 ppm	10	259± 11**	0.068± 0.009	0.019± 0.001	1.146± 0.050**	0.327± 0.015	0.366± 0.009**
4000 ppm	10	222± 12**	0.073± 0.011	0.020± 0.001	1.307± 0.076**	0.350± 0.022**	0.391± 0.024**

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

STUDY NO. : 0323
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	0.623± 0.015	0.186± 0.004	2.483± 0.095	0.647± 0.028
250 ppm	10	0.643± 0.022	0.186± 0.006	2.503± 0.073	0.670± 0.025
500 ppm	10	0.660± 0.023**	0.188± 0.005	2.520± 0.088	0.665± 0.018
1000 ppm	10	0.671± 0.020**	0.187± 0.005	2.607± 0.082*	0.669± 0.018
2000 ppm	10	0.717± 0.026**	0.195± 0.014	2.723± 0.088**	0.712± 0.033**
4000 ppm	10	0.791± 0.029**	0.209± 0.006**	2.921± 0.136**	0.820± 0.040**

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

APPENDIX K 2

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : FEMALE

(13 - WEEK STUDY)

STUDY NO. : 0323
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	168± 8	0.116± 0.017	0.033± 0.003	0.068± 0.006	0.367± 0.021	0.449± 0.020
250 ppm	10	160± 9*	0.107± 0.011	0.035± 0.004	0.066± 0.009	0.377± 0.024	0.463± 0.031
500 ppm	10	161± 7	0.112± 0.009	0.032± 0.003	0.066± 0.006	0.373± 0.018	0.452± 0.022
1000 ppm	10	158± 6**	0.112± 0.007	0.035± 0.003	0.064± 0.006	0.374± 0.025	0.459± 0.020
2000 ppm	10	155± 6**	0.109± 0.009	0.033± 0.002	0.069± 0.004	0.381± 0.018	0.465± 0.019
4000 ppm	10	136± 6**	0.116± 0.012	0.036± 0.006	0.075± 0.011	0.389± 0.018	0.481± 0.022*

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

STUDY NO. : 0323
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	0.687± 0.025	0.229± 0.015	2.366± 0.100	1.035± 0.058
250 ppm	10	0.729± 0.025**	0.225± 0.013	2.440± 0.081	1.098± 0.061*
500 ppm	10	0.735± 0.040**	0.222± 0.012	2.468± 0.087*	1.075± 0.039
1000 ppm	10	0.782± 0.016**	0.234± 0.013	2.510± 0.070**	1.100± 0.040*
2000 ppm	10	0.844± 0.024**	0.245± 0.015*	2.718± 0.079**	1.121± 0.041**
4000 ppm	10	0.924± 0.034**	0.256± 0.013**	2.997± 0.271**	1.229± 0.049**

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

APPENDIX L 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : ALL ANIMALS

(13 - WEEK STUDY)

STUDY NO. : 0323
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control				250 ppm				500 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}																		
nasal cavit			<10>				<10>				<10>				<10>			
	inflammation:foreign body		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)
	respiratory metaplasia:gland		2	0	0	0	2	0	0	0	3	0	0	0	2	0	0	0
			(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
{Digestive system}																		
salivary gl			<10>				<10>				<10>				<10>			
	atrophy		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)
stomach			<10>				<10>				<10>				<10>			
	hyperplasia:forestomach		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)
liver			<10>				<10>				<10>				<10>			
	herniation		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)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	basophilic change		2	0	0	0	1	0	0	0	2	0	0	0	2	0	0	0
			(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(20)	(0)	(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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			<10>				<10>			
	inflammation:foreign body		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	respiratory metaplasia:gland		5	0	0	0	2	0	0	0
			(50)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
{Digestive system}										
salivary gl			<10>				<10>			
	atrophy		0	0	0	0	5	0	0	0 *
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
stomach			<10>				<10>			
	hyperplasia:forestomach		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
liver			<10>				<10>			
	herniation		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Urinary system}										
kidney			<10>				<10>			
	basophilic change		1	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100
Significant difference ; * : P ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name	Control				250 ppm				500 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>			
	eosinophilic body		0	10	0	0	1	9	0	0	0	10	0	0	0	10	0	0
			(0)	(100)	(0)	(0)	(10)	(90)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(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)
{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)
	Rathke pouch		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)
{Special sense organs/appendage}																		
Harder gl			<10>				<10>				<10>				<10>			
	lymphocytic infiltration		1	0	0	0	1	1	0	0	1	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(10)	(10)	(0)	(0)	(10)	(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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}										
kidney			<10>				<10>			
	eosinophilic body		2	8	0	0	0	10	0	0
			(20)	(80)	(0)	(0)	(0)	(100)	(0)	(0)
	hyaline cast		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Endocrine system}										
pituitary			<10>				<10>			
	cyst		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	Rathke pouch		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		2	0	0	0	0	0	0	0
			(20)	(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 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE: ALL ANIMALS

(13 - WEEK STUDY)

Organ	Findings	Group Name	Control				250 ppm				500 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}																		
nasal cavit			<10>				<10>				<10>				<10>			
	respiratory metaplasia:gland		5	0	0	0	5	0	0	0	4	0	0	0	0	0	0	0 *
			(50)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	(40)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lung			<10>				<10>				<10>				<10>			
	osseous metaplasia		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)
{Hematopoietic system}																		
bone marrow			<10>				<10>				<10>				<10>			
	granulation		2	2	0	0	1	2	0	0	1	4	0	0	1	1	0	0
			(20)	(20)	(0)	(0)	(10)	(20)	(0)	(0)	(10)	(40)	(0)	(0)	(10)	(10)	(0)	(0)
{Digestive system}																		
salivary gl			<10>				<10>				<10>				<10>			
	atrophy		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)
liver			<10>				<10>				<10>				<10>			
	herniation		0	0	0	0	3	0	0	0	2	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(30)	(0)	(0)	(0)	(20)	(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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			<10>				<10>			
	respiratory metaplasia:gland		5	0	0	0	3	0	0	0
			(50)	(0)	(0)	(0)	(30)	(0)	(0)	(0)
lung			<10>				<10>			
	osseous metaplasia		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}										
bone marrow			<10>				<10>			
	granulation		2	1	1	0	2	0	0	0
			(20)	(10)	(10)	(0)	(20)	(0)	(0)	(0)
{Digestive system}										
salivary gl			<10>				<10>			
	atrophy		0	0	0	0	7	0	0	0 **
			(0)	(0)	(0)	(0)	(70)	(0)	(0)	(0)
liver			<10>				<10>			
	herniation		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				250 ppm				500 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>			
	granulation		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)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	basophilic change		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)
	mineralization:cortico-medullary junction		1	0	0	0	1	0	0	0	2	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	eosinophilic droplet:proximal tubule		0	0	0	0	0	0	0	0	4	0	0	0	8	0	0	0 **
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(40)	(0)	(0)	(0)	(80)	(0)	(0)	(0)
{Endocrine system}																		
pituitary			<10>				<10>				<10>				<10>			
	Rathke pouch		1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)

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	granulation		<10>				<10>			
			0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Urinary system}										
kidney	basophilic change		<10>				<10>			
			0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:cortico-medullary junction		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	eosinophilic droplet:proximal tubule		10	0	0	0 **	10	0	0	0 **
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Endocrine system}										
pituitary	Rathke pouch		<10>				<10>			
			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

STUDY NO. : 0323
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name	Control				250 ppm				500 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}																		
Harder gl			<10>				<10>				<10>				<10>			
	lymphocytic infiltration		2	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
			(20)	(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	2000 ppm				4000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Special sense organs/appendage}										
Harder gl			<10>				<10>			
	lymphocytic infiltration		2	0	0	0	0	0	0	0
			(20)	(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 M 1

IDENTITY AND IMPURITY OF 2 - HYDROXYETHYL ACRYLATE

IN THE 13 - WEEK DRINKING WATER STUDY

IDENTITY AND IMPURITY OF 2-HYDROXYETHYL ACRYLATE IN THE 13-WEEK DRINKING WATER STUDY

Test Substance : 2-Hydroxyethyl Acrylate (Wako Pure Chemical Industries, Ltd.)

Lot No. : LEM4569

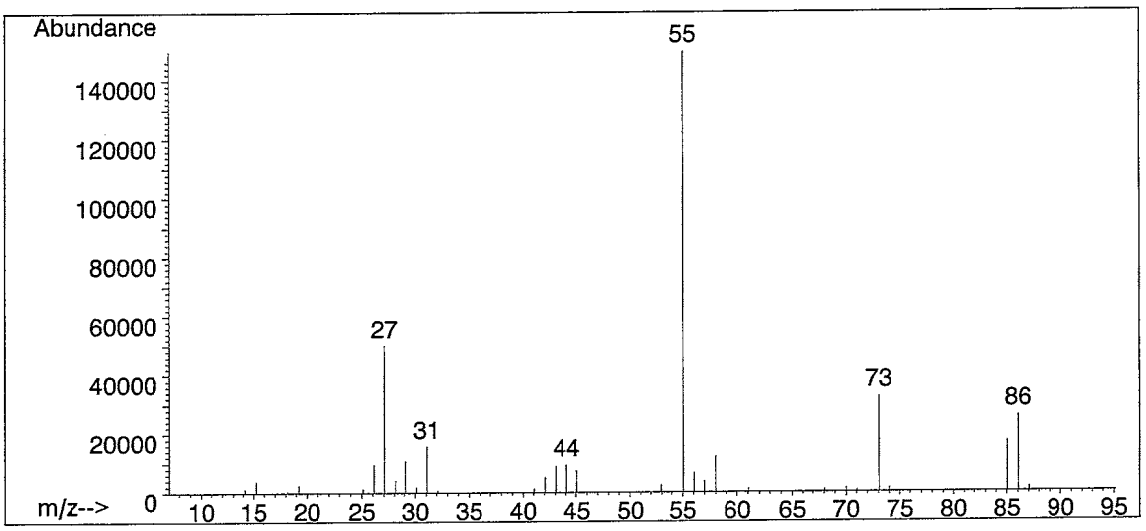
1. Spectral Data

Mass Spectrometry

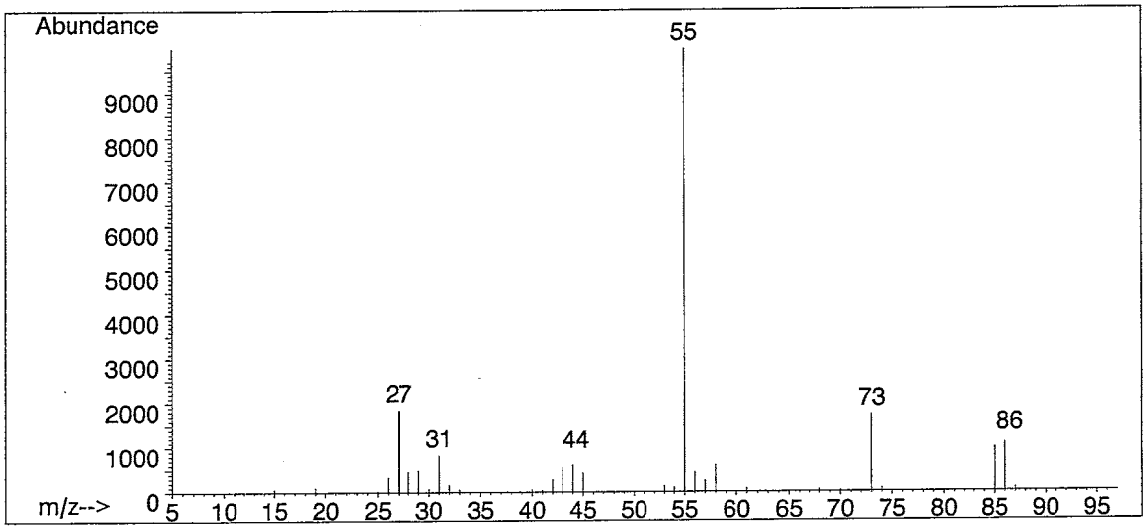
Instrument : Hewlett Packard 5989B Mass Spectrometer

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.

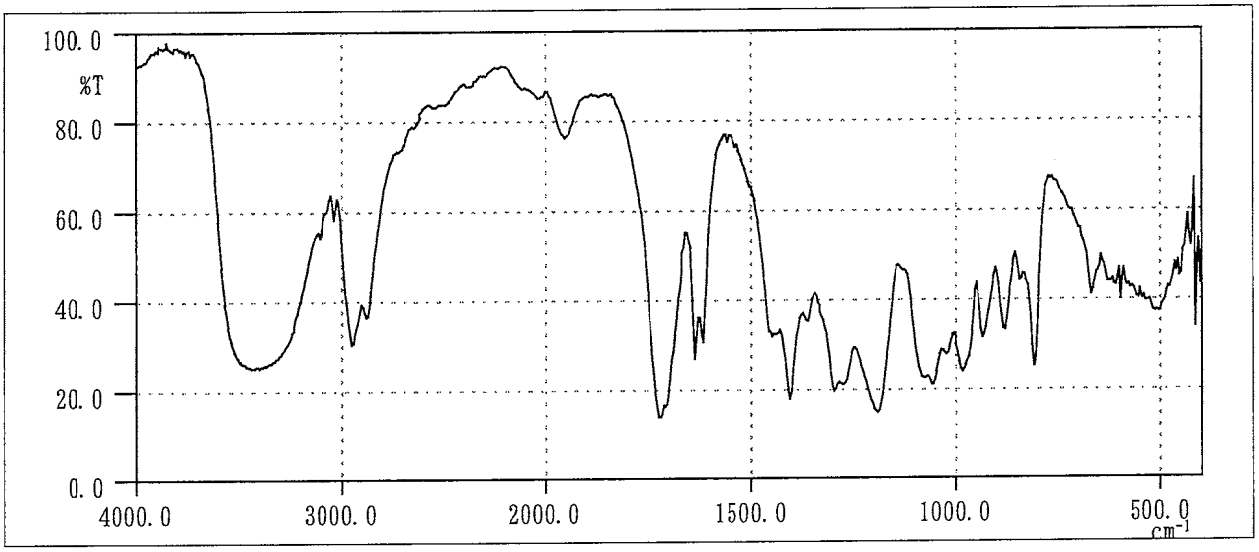
(*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition. John Wiley and Sons, Inc. (U.S.), Entry Number 12762)

Infrared Spectrometry

Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 2 cm^{-1}



Infrared Spectrum of Test Substance

Determined Values	Literature Values*
Wave Number (cm^{-1})	Wave Number (cm^{-1})
650～ 680	650～ 680
770～ 850	770～ 850
850～ 910	850～ 910
910～ 950	910～ 950
950～1010	950～1010
1010～1140	1010～1140
1140～1250	1140～1250
1250～1350	1250～1350
1350～1550	1350～1550
1580～1660	1580～1660
1660～1850	1660～1850
1920～2000	1920～2000
2750～3020	2750～3020
3060～3700	3060～3700

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

2. Impurity

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : FFAP (0.53 mmϕ × 30 m)

Column Temperature : 180 °C

Flow Rate : 3 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μL

Sample Name	Peak No.	Area (%)	Peak Name
Test Substance	1	1.125	Acrylic Acid
	2	96.190	2-Hydroxyethyl Acrylate
	3	2.632	Material which cannot be identified
	4	0.053	p-Methoxyphenol

Results: Gas chromatography indicated one major peak (peak No.2) and three impurities. It was identified only by comparing gas chromatograph with that of acrylic acid (peak No.1), material which cannot be identified (peak No.3) and p-methoxyphenol (peak No.4) in the 2-hydroxyethyl acrylate, the amount in the test substance were 1.125%, 2.632% and 0.053%.

3. Conclusions: The test substance was identified as 2-hydroxyethyl acrylate by the mass spectrum and the infrared spectrum. Gas chromatography indicated one major peak (peak No.2) and three impurities. It was identified only by comparing gas chromatograph with that of acrylic acid, material which cannot be identified and p-methoxyphenol, the amount in the test substance were 1.125%, 2.632% and 0.053%.

APPENDIX M 2

STABILITY OF 2 - HYDROXYETHYL ACRYLATE IN THE 13 - WEEK DRINKING WATER STUDY

STABILITY OF 2-HYDROXYETHYL ACRYLATE IN THE 13-WEEK DRINKING WATER STUDY

Test Substance : 2-Hydroxyethyl Acrylate (Wako Pure Chemical Industries, Ltd.)

Lot No. : LEM4569

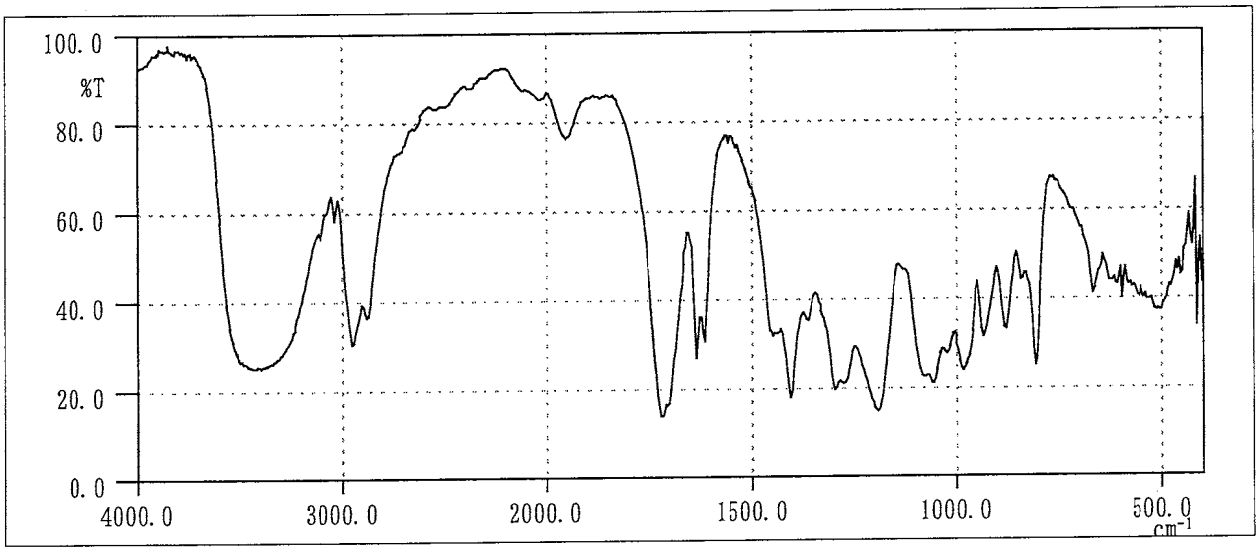
1. Sample : This lot was used from 1996.11.19 to 1997.2.20. Test substance was stored at room temperature.

2. Infrared Spectrometry

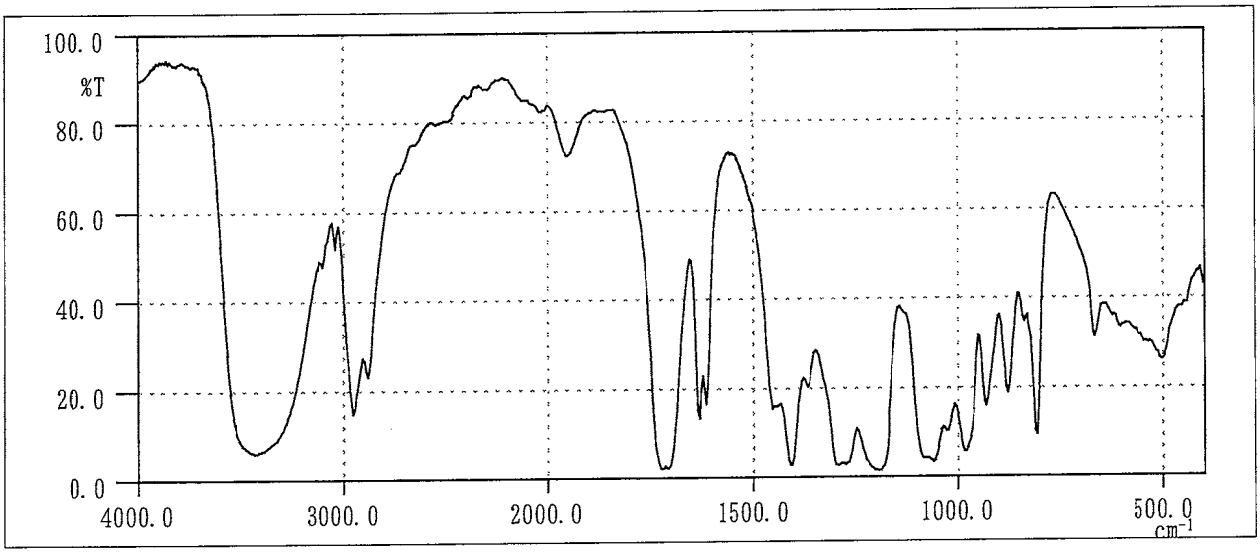
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 2 cm^{-1}



Infrared Spectrum of Test Substance (date analyzed : 1996.11.07)



Infrared Spectrum of Test Substance (date analyzed : 1997.03.10)

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

3. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : FFAP (0.53 mmϕ × 30 m)

Column Temperature : 180 °C

Flow Rate : 3 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μL

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
1996.11.07	1	2.657	1.125
	2	3.369	96.190
	3	7.527	2.632
	4	20.362	0.053
1997.03.10	1	2.439	0.857
	2	3.007	96.308
	3	6.858	2.782
	4	18.570	0.053

Results: Gas chromatography indicated one major peak (peak No.2) and three impurities (peaks No.1, No.3 and No.4 < 4% of total area) analyzed on 1996.11.7 and one major peak (peak No.2) and three impurities (peaks No.1, No.3 and No.4 < 4% of total area) analyzed on 1997.3.10. No new trace impurity peak in the test substance analyzed on 1997.3.10 was detected.

4. Conclusions: The test substance was stable for about 4 months at room temperature.

APPENDIX M 3

CONCENTRATION OF 2 - HYDROXYETHYL ACRYLATE IN FORMULATED WATER IN THE 13 - WEEK DRINKING WATER STUDY

CONCENTRATION OF 2-HYDROXYETHYL ACRYLATE IN FORMULATED WATER IN THE 13-WEEK DRINKING WATER STUDY

	Target Concentration				
Date Analyzed	250[a]	500	1000	2000	4000
1996.11.19	256 (102)[b]	512 (102)	1030 (103)	2120 (106)	4150 (104)

[a] ppm
[b] %

Analytical Method : The samples were analyzed by gas chromatography.

Instrument : Hewlett Packard 5890A Gas Chromatograph
Column : FFAP (0.53 mmϕ × 30 m)
Column Temperature : 180 °C
Flow Rate : 3 mL/min
Detector : FID (Flame Ionization Detector)
Injection Volume : 1 µL

APPENDIX M 4

STABILITY OF 2 - HYDROXYETHYL ACRYLATE IN FORMULATED WATER IN THE 13 - WEEK DRINKING WATER STUDY

STABILITY OF 2-HYDROXYETHYL ACRYLATE IN FORMULATED WATER IN THE 13-WEEK DRINKING WATER STUDY

		Target Concentration	
Date Prepared	Date Analyzed	250[a]	4000
1996.11.07	1996.11.07	238 (100)[b]	3770 (100)
	1996.11.14[c]	228 (95.8)	3670 (97.3)

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

Analytical Method : The samples were analyzed by gas chromatography.

Instrument : Hewlett Packard 5890A Gas Chromatograph
Column : FFAP (0.53 mmϕ $\times$ 30 m)
Column Temperature : 180 °C
Flow Rate : 3 mL/min
Detector : FID (Flame Ionization Detector)
Injection Volume : 1 µL

APPENDIX N 1

METHODS FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13 - WEEK DRINKING WATER STUDY OF 2 - HYDROXYETHYL ACRYLATE

METHOD FOR HEMATOLOGY,BIOCHEMISTRY AND URINALYSIS IN THE 13-WEEK DRINKING WATER STUDY OF 2-HYDROXYETHYL ACRYLATE

Item	Method
Hematology	
Red blood cell (RBC)	Light scattering method [1]
Hemoglobin (Hgb)	Cyanmethemoglobin method [1]
Hematocrit (Hct)	Calculated as RBC×MCV/10 [1]
Mean corpuscular volume (MCV)	Light scattering method [1]
Mean corpuscular hemoglobin (MCH)	Calculated as Hgb/RBC×10 [1]
Mean corpuscular hemoglobin concentration (MCHC)	Calculated as Hgb/Hct×100 [1]
Platelet	Light scattering method [1]
Reticulocyte	Pattern recognition method [3] (New methyleneblue staining)
Prothrombin time	Quick one stage method [2]
Activated partial thromboplastin time (APTT)	Ellagic acid activaterd method [2]
White blood cell (WBC)	Light scattering method [1]
Differential WBC	Pattern recognition method [3] (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)	p-Nitrophenylphosphate 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 [5]

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) Ames reagent strips for urinalysis (Multistix : Bayer-Sankyo Co.,Ltd.)

APPENDIX N 2

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13 - WEEK DRINKING WATER STUDY OF 2 - HYDROXYETHYL ACRYLATE

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK DRINKING WATER STUDY OF 2-HYDROXYETHYL ACRYLATE

Item	Unit	Decimal place
Hematology		
Red blood cell (RBC)	$\times 10^6/\mu L$	2
Hemoglobin	g/dL	1
Hematocrit	%	1
Mean corpuscular volume (MCV)	fL	1
Mean corpuscular hemoglobin (MCH)	pg	1
Mean corpuscular hemoglobin concentration (MCHC)	g/dL	1
Platelet	$\times 10^3/\mu L$	0
Reticulocyte	‰	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