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 2 週間毒性試験(混水試験)報告書

試験番号：０３１４

APPENDIX

APPENDIXES

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 1-1	1-3	1-7	2-3	2-7
DEATH	Control	0	0	0	0	0
	512 ppm	0	0	0	0	0
	1280 ppm	0	0	0	0	0
	3200 ppm	0	0	0	0	0
	8000 ppm	0	0	0	0	1
	20000 ppm	0	0	1	1	10
HUNCHBACK POSITION	Control	0	0	0	0	0
	512 ppm	0	0	0	0	0
	1280 ppm	0	0	0	0	0
	3200 ppm	0	0	0	0	0
	8000 ppm	0	0	0	0	8
	20000 ppm	0	0	0	0	-
PILOERECTION	Control	0	0	0	0	0
	512 ppm	0	0	0	0	0
	1280 ppm	0	0	0	0	0
	3200 ppm	0	0	0	0	0
	8000 ppm	0	0	0	0	9
	20000 ppm	0	0	0	0	-
NOSE HEMORRHAGIC DISCHA	Control	0	0	0	0	0
	512 ppm	0	0	0	0	0
	1280 ppm	0	0	0	0	0
	3200 ppm	0	0	0	0	0
	8000 ppm	0	0	0	0	1
	20000 ppm	0	0	0	0	-
SMALL STOOL	Control	0	0	0	0	0
	512 ppm	0	0	0	0	0
	1280 ppm	0	0	0	0	0
	3200 ppm	0	0	0	1	1
	8000 ppm	0	10	10	10	9
	20000 ppm	0	10	9	9	-
OLIGO-STOOL	Control	0	0	0	0	0
	512 ppm	0	0	0	0	0
	1280 ppm	0	0	0	0	0
	3200 ppm	0	0	0	0	0
	8000 ppm	0	0	10	10	9
	20000 ppm	0	5	9	9	-

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day 1-1	1-3	1-7	2-3	2-7
DEATH	Control	0	0	0	0	0
	512 ppm	0	0	0	0	0
	1280 ppm	0	0	0	0	0
	3200 ppm	0	0	0	0	0
	8000 ppm	0	0	0	0	6
	20000 ppm	0	0	2	9	10
HUNCHBACK POSITION	Control	0	0	0	0	0
	512 ppm	0	0	0	0	0
	1280 ppm	0	0	0	0	0
	3200 ppm	0	0	0	0	0
	8000 ppm	0	0	0	7	4
	20000 ppm	0	0	0	1	-
SOILED	Control	0	0	0	0	0
	512 ppm	0	0	0	0	0
	1280 ppm	0	0	0	0	0
	3200 ppm	0	0	0	0	0
	8000 ppm	0	0	0	0	2
	20000 ppm	0	4	2	0	-
PILOERECTION	Control	0	0	0	0	0
	512 ppm	0	0	0	0	0
	1280 ppm	0	0	0	0	0
	3200 ppm	0	0	0	0	0
	8000 ppm	0	0	0	0	4
	20000 ppm	0	0	0	0	-
SOILED PERI GENITALIA	Control	0	0	0	0	0
	512 ppm	0	0	0	0	0
	1280 ppm	0	0	0	0	0
	3200 ppm	0	0	0	0	0
	8000 ppm	0	0	0	1	0
	20000 ppm	0	0	0	0	-
SMALL STOOL	Control	0	0	0	0	0
	512 ppm	0	0	0	0	0
	1280 ppm	0	0	0	0	0
	3200 ppm	0	0	0	0	0
	8000 ppm	0	10	10	10	4
	20000 ppm	0	10	8	1	-

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day 1-1	1-3	1-7	2-3	2-7
OLIGO-STOOL	Control	0	0	0	0	0
	512 ppm	0	0	0	0	0
	1280 ppm	0	0	0	0	0
	3200 ppm	0	0	0	0	0
	8000 ppm	0	1	8	10	4
	20000 ppm	0	10	8	1	-

APPENDIX B 1

BODY WEIGHT CHANGES :SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-3	1-7	2-3	2-7
Control	125± 5	137± 6	155± 6	166± 7	183± 7
512 ppm	125± 5	136± 6	152± 7	163± 7	180± 8
1280 ppm	125± 5	133± 7	149± 8	159± 8	174± 9*
3200 ppm	125± 5	117± 5**	124± 6**	133± 6**	147± 6**
8000 ppm	125± 5	105± 4**	90± 5**	81± 5**	71± 6**
20000 ppm	125± 5	102± 5**	82± 4**	69± 4**	-

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

APPENDIX B 2

BODY WEIGHT CHANGES : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-3(3)	1-7(4)	2-3(3)	2-7(4)
Control	17.0± 1.4	17.0± 1.2	17.6± 1.4	17.7± 1.2
512 ppm	15.1± 1.0	14.3± 0.8	14.1± 0.8	14.3± 0.9
1280 ppm	12.9± 0.8	12.2± 0.5*	12.5± 0.6	12.4± 0.6**
3200 ppm	6.3± 0.6**	8.0± 0.7**	9.0± 0.7**	9.3± 0.4**
8000 ppm	1.9± 0.2**	1.9± 0.4**	2.0± 0.6**	1.6± 1.0**
20000 ppm	1.2± 0.2**	0.8± 0.1**	0.7± 0.2**	-

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

APPENDIX C 1

WATER CONSUMPTION CHANGES : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-3	1-7	2-3	2-7
Control	101± 4	107± 4	114± 5	119± 5	127± 4
512 ppm	101± 4	107± 4	114± 4	120± 4	126± 5
1280 ppm	101± 4	105± 4	112± 4	117± 4	125± 5
3200 ppm	100± 4	94± 4**	99± 5**	105± 6**	112± 6**
8000 ppm	101± 4	81± 3**	69± 5**	62± 5**	58± 4**
20000 ppm	101± 4	79± 3**	62± 4**	57± 2**	-

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

APPENDIX C 2

WATER CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-3(3)	1-7(4)	2-3(3)	2-7(4)
Control	15.0± 1.1	14.4± 1.3	14.6± 1.3	16.0± 2.2
512 ppm	13.4± 1.0	13.3± 4.0	12.4± 2.2	15.1± 8.3
1280 ppm	11.0± 0.7	9.9± 0.6	9.7± 0.6*	10.0± 0.8**
3200 ppm	6.0± 1.0**	7.7± 0.8**	7.8± 0.8**	7.9± 0.7**
8000 ppm	1.6± 0.3**	2.2± 0.7**	2.0± 0.7**	1.8± 0.3**
20000 ppm	1.1± 0.3**	0.8± 0.4**	1.1± 0.0 ?	-

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

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

APPENDIX D 1

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-3(3)	1-7(4)	2-3(3)	2-7(4)
Control	13.8± 0.9	14.2± 1.1	14.9± 1.3	15.1± 1.0
512 ppm	13.3± 0.8	13.4± 0.7	14.2± 0.8	14.5± 0.8
1280 ppm	12.7± 0.9**	12.8± 0.8	14.1± 0.7	13.7± 0.8**
3200 ppm	9.2± 0.6**	9.4± 0.8**	11.2± 0.9*	11.7± 0.6**
8000 ppm	6.3± 0.5**	3.8± 0.5**	4.8± 0.5**	4.3± 0.7**
20000 ppm	5.4± 0.5**	2.4± 0.4**	3.9± 0.3**	-

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

APPENDIX D 2

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-3(3)	1-7(4)	2-3(3)	2-7(4)
Control	11.0± 0.7	10.9± 0.6	10.8± 0.6	11.3± 0.5
512 ppm	10.7± 0.7	10.7± 0.5	10.5± 0.7	10.9± 0.8
1280 ppm	9.6± 0.7**	9.7± 1.0**	10.3± 0.5	10.4± 0.5*
3200 ppm	7.1± 0.7**	8.7± 0.8**	9.5± 0.5**	9.6± 0.7**
8000 ppm	3.9± 0.3**	3.2± 0.8**	4.0± 0.5**	4.2± 0.4**
20000 ppm	3.5± 0.5**	2.6± 0.5**	2.3± 0.0 ?	-

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

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

APPENDIX E 1

CHEMICAL INTAKE CHANGES : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0314
ANIMAL : RAT F344
SEX : MALE
UNIT : g/kg/day

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration Week−Day	1-4	1-7	2-4	2-7
Control		0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000
512 ppm		0.057 ± 0.003	0.048 ± 0.002	0.044 ± 0.002	0.041 ± 0.002
1280 ppm		0.124 ± 0.005	0.105 ± 0.004	0.100 ± 0.004	0.091 ± 0.003
3200 ppm		0.172 ± 0.010	0.205 ± 0.016	0.216 ± 0.013	0.203 ± 0.012
8000 ppm		0.148 ± 0.009	0.168 ± 0.027	0.194 ± 0.048	0.180 ± 0.099
20000 ppm		0.229 ± 0.050	0.188 ± 0.027	0.201 ± 0.056	−

APPENDIX E 2

CHEMICAL INTAKE CHANGES : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0314
ANIMAL : RAT F344
SEX : FEMALE
UNIT : g/kg/day

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration Week−Day	1-4	1-7	2-4	2-7
Control		0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000	0.000 ± 0.000
512 ppm		0.064 ± 0.004	0.060 ± 0.017	0.053 ± 0.009	0.061 ± 0.032
1280 ppm		0.134 ± 0.006	0.113 ± 0.005	0.106 ± 0.006	0.102 ± 0.006
3200 ppm		0.205 ± 0.031	0.248 ± 0.021	0.239 ± 0.014	0.226 ± 0.010
8000 ppm		0.161 ± 0.069	0.247 ± 0.067	0.258 ± 0.070	0.254 ± 0.040
20000 ppm		0.282 ± 0.073	0.252 ± 0.132	0.373 ± 0.000	−

APPENDIX F 1

HEMATOLOGY : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

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	5	7.89± 0.23	14.6± 0.4	43.7± 1.2	55.4± 0.7	18.6± 0.2	33.5± 0.3	864± 60
512 ppm	5	8.03± 0.21	14.9± 0.3	44.3± 1.0	55.1± 0.4	18.5± 0.2	33.6± 0.2	804± 35
1280 ppm	5	7.95± 0.17	14.7± 0.3	43.9± 0.9	55.2± 0.5	18.6± 0.5	33.6± 0.7	799± 26
3200 ppm	5	8.17± 0.07	15.0± 0.2	44.9± 0.4	55.0± 0.4	18.4± 0.3	33.4± 0.7	690± 44**
8000 ppm	8	11.00± 0.99**	20.7± 1.4**	63.5± 7.2**	57.7± 1.6	18.9± 0.6	32.8± 1.7	201± 98**
20000 ppm	0	-	-	-	-	-	-	-

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

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	RETICULOCYTE ‰		PROTHROMBIN TIME sec		APTT sec	
Control	5	45±	12	12.2±	0.3	18.7±	0.6
512 ppm	5	36±	8	12.3±	0.4	17.6±	1.8
1280 ppm	5	36±	7	12.1±	0.1	19.1±	1.0
3200 ppm	5	33±	4	12.6±	0.3	19.9±	2.3
8000 ppm	8	2±	1**	16.9±	3.7*	33.4±	24.0
20000 ppm	0	-		-		-	

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

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
Control	5	6.34± 1.31	1± 1	14± 4	1± 1	0± 0	3± 1	81± 4	0± 0
512 ppm	5	6.09± 1.13	0± 0	19± 5	1± 0	0± 0	4± 1	76± 6	0± 0
1280 ppm	5	5.78± 1.12	0± 0	15± 2	1± 1	0± 0	5± 1	79± 2	0± 0
3200 ppm	5	5.30± 0.45	0± 0	16± 4	1± 1	0± 0	3± 2	80± 4	0± 0
8000 ppm	8	2.52± 1.10**	0± 1	33± 10**	0± 1	0± 0	3± 1	63± 11**	0± 0
20000 ppm	0	-	-	-	-	-	-	-	-

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

APPENDIX F 2

HEMATOLOGY : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

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	5	8.19± 0.42	15.6± 0.3	44.6± 2.4	54.5± 0.4	19.1± 0.8	35.0± 1.5	732± 24
512 ppm	5	8.18± 0.27	15.5± 0.4	45.0± 1.4	54.9± 0.5	18.9± 0.2	34.4± 0.5	739± 45
1280 ppm	5	8.04± 0.64	15.7± 0.3	43.7± 3.6	54.3± 0.6	19.6± 1.9	36.1± 3.6	703± 48
3200 ppm	5	8.39± 0.23	15.7± 0.3	45.5± 1.3	54.3± 0.6	18.8± 0.2	34.6± 0.5	647± 41
8000 ppm	3	11.17± 0.27**	20.9± 0.7**	64.0± 3.3**	57.3± 1.6**	18.7± 0.2	32.6± 0.6	305± 117**
20000 ppm	0	-	-	-	-	-	-	-

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

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	RETICULOCYTE ‰	PROTHROMBIN TIME sec	APTT sec
Control	5	22± 5	12.4± 0.2	18.2± 0.3
512 ppm	5	20± 4	12.3± 0.2	18.2± 1.0
1280 ppm	5	21± 3	12.4± 0.2	18.6± 0.9
3200 ppm	5	23± 2	12.2± 0.4	17.4± 1.5
8000 ppm	3	3± 2**	19.9± 6.5 ?	42.4± 32.5 ?
20000 ppm	0	-	-	-

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

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

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
Control	5	5.49± 1.04	1± 1	14± 5	0± 1	0± 0	4± 1	81± 6	0± 0
512 ppm	5	5.37± 1.52	0± 0	17± 4	1± 1	0± 0	4± 3	77± 5	0± 0
1280 ppm	5	5.11± 1.01	0± 0	11± 3	1± 1	0± 0	2± 0	86± 2	0± 0
3200 ppm	5	6.04± 0.71	0± 0	12± 3	1± 1	0± 0	2± 1	84± 3	0± 0
8000 ppm	3	5.73± 1.91	0± 1	75± 7**	0± 0	0± 0	3± 3	22± 6**	0± 0
20000 ppm	0	-	-	-	-	-	-	-	-

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

APPENDIX G 1

BIOCHEMISTRY : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

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	PHOSPHOLIPID mg/dl
Control	5	5.7± 0.1	3.6± 0.1	1.7± 0.1	0.14± 0.02	189± 9	66± 3	126± 3
512 ppm	5	5.7± 0.1	3.6± 0.1	1.8± 0.1	0.13± 0.01	187± 5	65± 4	127± 6
1280 ppm	5	5.7± 0.1	3.6± 0.1	1.8± 0.1	0.14± 0.01	183± 12	64± 5	131± 9
3200 ppm	5	5.5± 0.2	3.5± 0.1	1.8± 0.0	0.14± 0.01	177± 11	71± 4	138± 3
8000 ppm	8	5.3± 0.3*	3.4± 0.2	1.8± 0.2**	0.21± 0.04*	96± 15**	88± 12*	143± 17
20000 ppm	0	-	-	-	-	-	-	-

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

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	GOT IU/ℓ		GPT IU/ℓ		LDH IU/ℓ		G-GTP IU/ℓ		CPK IU/ℓ		UREA NITROGEN mg/dℓ		CREATININE mg/dℓ	
Control	5	55±	3	32±	4	162±	93	1±	1	161±	37	14.2±	1.5	0.4±	0.0
512 ppm	5	52±	2	29±	2	178±	62	1±	0	155±	24	16.3±	1.9	0.4±	0.0
1280 ppm	5	52±	2	27±	1	147±	34	1±	1	151±	11	17.9±	1.1	0.4±	0.0
3200 ppm	5	55±	2	28±	2	179±	46	1±	1	158±	24	21.3±	1.3*	0.4±	0.1
8000 ppm	8	347±	189	201±	96	341±	204*	4±	1**	255±	90	55.3±	20.8**	0.5±	0.1
20000 ppm	0	-		-		-		-		-		-		-	

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

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	SODIUM mEq／ℓ		POTASSIUM mEq／ℓ		CHLORIDE mEq／ℓ		CALCIUM mg／dℓ		INORGANIC PHOSPHORUS mg／dℓ	
Control	5	140±	1	4.0±	0.2	100±	0	11.2±	0.2	8.2±	0.5
512 ppm	5	139±	1	3.9±	0.2	100±	2	11.2±	0.2	7.0±	0.3
1280 ppm	5	138±	1	4.1±	0.2	101±	1	11.2±	0.2	7.1±	0.7
3200 ppm	5	139±	1	3.9±	0.4	103±	1	11.1±	0.2	6.3±	0.4**
8000 ppm	8	180±	18	3.5±	0.5	141±	18**	10.2±	0.3**	7.7±	1.2
20000 ppm	0	-		-		-		-		-	

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

APPENDIX G 2

BIOCHEMISTRY : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

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	PHOSPHOLIPID mg/dl
Control	5	5.7± 0.2	3.7± 0.1	1.8± 0.1	0.14± 0.00	192± 10	73± 2	128± 5
512 ppm	5	5.7± 0.1	3.7± 0.1	1.9± 0.1	0.15± 0.01	185± 6	72± 4	128± 7
1280 ppm	5	5.6± 0.1	3.7± 0.1	1.9± 0.1	0.14± 0.01	183± 8	68± 8	130± 10
3200 ppm	5	5.5± 0.1	3.6± 0.1	1.9± 0.1	0.15± 0.01	175± 13	74± 6	134± 10
8000 ppm	2	5.2± 0.6 ?	3.3± 0.4 ?	1.7± 0.0 ?	0.19± 0.01 ?	92± 8 ?	70± 11 ?	121± 13 ?
20000 ppm	0	-	-	-	-	-	-	-

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

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

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	GOT IU/ℓ	GPT IU/ℓ	LDH IU/ℓ	G-GTP IU/ℓ	CPK IU/ℓ	UREA NITROGEN mg/dℓ	CREATININE mg/dℓ
Control	5	58± 3	30± 2	205± 100	2± 1	180± 94	16.6± 2.0	0.5± 0.1
512 ppm	5	54± 2	25± 3	237± 101	2± 1	158± 28	19.3± 1.9	0.4± 0.1
1280 ppm	5	55± 4	26± 3	189± 62	3± 1	139± 20	19.1± 1.2	0.4± 0.0
3200 ppm	5	56± 6	26± 3	207± 78	2± 1	147± 30	24.1± 2.9**	0.4± 0.1
8000 ppm	2	257± 48 ?	144± 6 ?	267± 47 ?	8± 4 ?	239± 66 ?	61.3± 14.8 ?	0.6± 0.1 ?
20000 ppm	0	-	-	-	-	-	-	-

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

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

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (2W)

Group Name	NO. of Animals	SODIUM mEq／ℓ	POTASSIUM mEq／ℓ	CHLORIDE mEq／ℓ	CALCIUM mg／dℓ	INORGANIC PHOSPHORUS mg／dℓ
Control	5	139± 0	3.4± 0.3	103± 1	10.6± 0.1	6.7± 0.7
512 ppm	5	135± 5*	3.6± 0.3	101± 4	10.8± 0.1	6.8± 0.2
1280 ppm	5	137± 1	3.7± 0.4	103± 2	10.7± 0.1	6.5± 0.7
3200 ppm	5	137± 1	3.6± 0.3	104± 2	10.8± 0.1	6.4± 0.9
8000 ppm	2	185± 10 ?	3.5± 0.4 ?	144± 8 ?	10.3± 0.2 ?	8.5± 0.6 ?
20000 ppm	0	-	-	-	-	-

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

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

APPENDIX H 1

GROSS FINDINGS : SUMMARY, RAT : MALE ALL ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
ALL ANIMALS (0- 2W)

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	512 ppm 10 (%)	1280 ppm 10 (%)	3200 ppm 10 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
gl stomach	red		0 (0)	0 (0)	0 (0)	0 (0)
stomach	fluid:brown		0 (0)	0 (0)	0 (0)	0 (0)
	fluid:transparent		0 (0)	0 (0)	0 (0)	0 (0)
liver	herniation		1 (10)	0 (0)	1 (10)	1 (10)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
ALL ANIMALS (0- 2W)

Organ	Findings	Group Name NO. of Animals	8000 ppm 10 (%)	20000 ppm 10 (%)
thymus	atrophic		10 (100)	9 (90)
gl stomach	red		6 (60)	0 (0)
stomach	fluid:brown		0 (0)	1 (10)
	fluid:transparent		0 (0)	1 (10)
liver	herniation		1 (10)	0 (0)

APPENDIX H 2

GROSS FINDINGS : SUMMARY, RAT : FEMALE ALL ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
ALL ANIMALS (0- 2W)

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	512 ppm 10 (%)	1280 ppm 10 (%)	3200 ppm 10 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
gl stomach	red		0 (0)	0 (0)	0 (0)	0 (0)
stomach	fluid:brown		0 (0)	0 (0)	0 (0)	0 (0)
	fluid:transparent		0 (0)	0 (0)	0 (0)	0 (0)
liver	herniation		0 (0)	0 (0)	0 (0)	2 (20)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
ALL ANIMALS (0- 2W)

Organ	Findings	Group Name NO. of Animals	8000 ppm 10 (%)	20000 ppm 10 (%)
thymus	atrophic		10 (100)	8 (80)
gl stomach	red		2 (20)	0 (0)
stomach	fluid:brown		0 (0)	1 (10)
	fluid:transparent		0 (0)	1 (10)
liver	herniation		0 (0)	0 (0)

APPENDIX H 3

GROSS FINDINGS : SUMMARY, RAT : MALE

DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name NO. of Animals	Control 0 (%)	512 ppm 0 (%)	1280 ppm 0 (%)	3200 ppm 0 (%)
thymus	atrophic		- (-)	- (-)	- (-)	- (-)
gl stomach	red		- (-)	- (-)	- (-)	- (-)
stomach	fluid:brown		- (-)	- (-)	- (-)	- (-)
	fluid:transparent		- (-)	- (-)	- (-)	- (-)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name NO. of Animals	8000 ppm 1 (%)	20000 ppm 10 (%)
thymus	atrophic		1 (100)	9 (90)
gl stomach	red		1 (100)	0 (0)
stomach	fluid:brown		0 (0)	1 (10)
	fluid:transparent		0 (0)	1 (10)

APPENDIX H 4

GROSS FINDINGS : SUMMARY, RAT : FEMALE

DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name NO. of Animals	Control 0 (%)	512 ppm 0 (%)	1280 ppm 0 (%)	3200 ppm 0 (%)
thymus	atrophic		- (-)	- (-)	- (-)	- (-)
stomach	fluid:brown		- (-)	- (-)	- (-)	- (-)
	fluid:transparent		- (-)	- (-)	- (-)	- (-)

(HPT080)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name / NO. of Animals	8000 ppm 6 (%)	20000 ppm 10 (%)
thymus	atrophic		6 (100)	8 (80)
stomach	fluid:brown		0 (0)	1 (10)
	fluid:transparent		0 (0)	1 (10)

(HPT080)

APPENDIX H 5

GROSS FINDINGS : SUMMARY, RAT : MALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	512 ppm 10 (%)	1280 ppm 10 (%)	3200 ppm 10 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
gl stomach	red		0 (0)	0 (0)	0 (0)	0 (0)
liver	herniation		1 (10)	0 (0)	1 (10)	1 (10)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name NO. of Animals	8000 ppm 9 (%)	20000 ppm 0 (%)
thymus	atrophic		9 (100)	- (-)
gl stomach	red		5 (56)	- (-)
liver	herniation		1 (11)	- (-)

APPENDIX H 6

GROSS FINDINGS : SUMMARY, RAT : FEMALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	512 ppm 10 (%)	1280 ppm 10 (%)	3200 ppm 10 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
gl stomach	red		0 (0)	0 (0)	0 (0)	0 (0)
liver	herniation		0 (0)	0 (0)	0 (0)	2 (20)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name NO. of Animals	8000 ppm 4 (%)	20000 ppm 0 (%)
thymus	atrophic		4 (100)	- (-)
gl stomach	red		2 (50)	- (-)
liver	herniation		0 (0)	- (-)

APPENDIX I 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	5	183± 7	0.377± 0.032	0.047± 0.009	2.216± 0.078	0.664± 0.041	0.837± 0.030
512 ppm	5	176± 8	0.360± 0.016	0.045± 0.005	2.312± 0.182	0.617± 0.037	0.787± 0.043
1280 ppm	5	176± 7	0.347± 0.039	0.046± 0.010	2.412± 0.088	0.645± 0.038	0.833± 0.035
3200 ppm	5	145± 6**	0.303± 0.028**	0.042± 0.003	2.141± 0.145	0.522± 0.049**	0.726± 0.047**
8000 ppm	5	70± 7**	0.038± 0.020**	0.030± 0.002**	1.067± 0.398	0.308± 0.021**	0.519± 0.018**
20000 ppm	0	-	-	-	-	-	-

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

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	1.362± 0.064	0.469± 0.011	7.182± 0.604	1.690± 0.056
512 ppm	5	1.408± 0.083	0.436± 0.026	6.746± 0.353	1.726± 0.022
1280 ppm	5	1.480± 0.052*	0.472± 0.036	7.087± 0.277	1.667± 0.083
3200 ppm	5	1.281± 0.064	0.367± 0.024**	5.564± 0.382**	1.649± 0.033
8000 ppm	5	0.876± 0.065**	0.124± 0.041**	2.213± 0.417**	1.556± 0.041**
20000 ppm	0	-	-	-	-

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

(HCL040)

APPENDIX I 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	5	126± 3	0.303± 0.030	0.049± 0.006	0.083± 0.008	0.506± 0.048	0.683± 0.021
512 ppm	5	125± 5	0.292± 0.014	0.052± 0.004	0.084± 0.021	0.496± 0.032	0.681± 0.046
1280 ppm	5	125± 6	0.303± 0.013	0.043± 0.007	0.077± 0.017	0.496± 0.047	0.687± 0.068
3200 ppm	5	113± 5**	0.283± 0.024	0.047± 0.004	0.077± 0.017	0.454± 0.035	0.620± 0.034
8000 ppm	4	58± 4**	0.019± 0.005**	0.039± 0.003*	0.043± 0.004**	0.267± 0.024**	0.499± 0.024**
20000 ppm	0	-	-	-	-	-	-

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

(HCL040)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	1.020± 0.055	0.359± 0.023	4.563± 0.109	1.590± 0.015
512 ppm	5	1.081± 0.062	0.337± 0.013	4.703± 0.270	1.601± 0.030
1280 ppm	5	1.113± 0.066	0.341± 0.026	4.691± 0.535	1.602± 0.061
3200 ppm	5	1.096± 0.052	0.315± 0.031*	4.393± 0.292	1.562± 0.048
8000 ppm	4	0.757± 0.049**	0.083± 0.034**	2.198± 0.124*	1.506± 0.077
20000 ppm	0	-	-	-	-

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

APPENDIX J 1

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	5	183± 7	0.207± 0.020	0.026± 0.005	1.214± 0.032	0.364± 0.025	0.458± 0.018
512 ppm	5	176± 8	0.205± 0.016	0.026± 0.004	1.316± 0.066	0.351± 0.007	0.448± 0.021
1280 ppm	5	176± 7	0.197± 0.019	0.026± 0.005	1.369± 0.042	0.366± 0.020	0.474± 0.023
3200 ppm	5	145± 6**	0.208± 0.017	0.029± 0.003	1.473± 0.079**	0.359± 0.024	0.500± 0.030
8000 ppm	5	70± 7**	0.052± 0.023**	0.043± 0.003**	1.499± 0.464	0.439± 0.013**	0.743± 0.063**
20000 ppm	0	-	-	-	-	-	-

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

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.746± 0.015	0.257± 0.011	3.928± 0.188	0.927± 0.042
512 ppm	5	0.802± 0.018**	0.248± 0.005	3.844± 0.176	0.984± 0.038
1280 ppm	5	0.840± 0.019**	0.268± 0.024	4.023± 0.103	0.947± 0.053
3200 ppm	5	0.881± 0.014**	0.252± 0.010	3.824± 0.132	1.137± 0.069**
8000 ppm	5	1.251± 0.059**	0.174± 0.043**	3.135± 0.308**	2.230± 0.180**
20000 ppm	0	-	-	-	-

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

APPENDIX J 2

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	5	126± 3	0.241± 0.026	0.039± 0.006	0.066± 0.006	0.402± 0.030	0.543± 0.012
512 ppm	5	125± 5	0.235± 0.018	0.042± 0.003	0.067± 0.016	0.398± 0.016	0.547± 0.046
1280 ppm	5	125± 6	0.243± 0.016	0.034± 0.006	0.062± 0.012	0.398± 0.043	0.550± 0.040
3200 ppm	5	113± 5**	0.251± 0.018	0.042± 0.002	0.068± 0.013	0.403± 0.024	0.550± 0.020
8000 ppm	4	58± 4**	0.032± 0.007**	0.069± 0.010**	0.074± 0.005	0.465± 0.058	0.869± 0.054**
20000 ppm	0	-	-	-	-	-	-

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

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (2W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.811± 0.041	0.286± 0.016	3.628± 0.091	1.265± 0.036
512 ppm	5	0.867± 0.018	0.270± 0.004	3.778± 0.237	1.286± 0.033
1280 ppm	5	0.892± 0.023**	0.273± 0.014	3.750± 0.261	1.285± 0.026
3200 ppm	5	0.972± 0.028**	0.279± 0.021	3.892± 0.112	1.386± 0.056**
8000 ppm	4	1.317± 0.065**	0.142± 0.050**	3.830± 0.251	2.625± 0.191**
20000 ppm	0	-	-	-	-

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

APPENDIX K 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : ALL ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
ALL ANIMALS (0- 2W)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 2				512 ppm 2				1280 ppm 2				3200 ppm 2			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Hematopoietic system}																		
bone marrow			< 2>				< 2>				< 2>				< 2>			
	congestion		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)
	decreased hematopoiesis		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)
thymus			< 2>				< 2>				< 2>				< 2>			
	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)
	karyorrhexis		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			< 2>				< 2>				< 2>				< 2>			
	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)
{Digestive system}																		
stomach			< 2>				< 2>				< 2>				< 2>			
	hemorrhage:glandular stomach		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

Organ	Findings	Group Name	8000 ppm				20000 ppm			
		No. of Animals on Study	2				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
bone marrow			< 2>				< 2>			
	congestion		0	2	0	0	0	2	0	0
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
	decreased hematopoiesis		0	2	0	0	0	2	0	0
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
thymus			< 2>				< 2>			
	atrophy		0	0	2	0	0	0	1	0
			(0)	(0)	(100)	(0)	(0)	(0)	(50)	(0)
	karyorrhexis		0	0	0	0	0	0	1	0
			(0)	(0)	(0)	(0)	(0)	(0)	(50)	(0)
spleen			< 2>				< 2>			
	atrophy		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
{Digestive system}										
stomach			< 2>				< 2>			
	hemorrhage:glandular stomach		1	0	0	0	1	0	0	0
			(50)	(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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 2 1 (%)	Control 2 2 (%)	Control 2 3 (%)	Control 2 4 (%)	512 ppm 2 1 (%)	512 ppm 2 2 (%)	512 ppm 2 3 (%)	512 ppm 2 4 (%)	1280 ppm 2 1 (%)	1280 ppm 2 2 (%)	1280 ppm 2 3 (%)	1280 ppm 2 4 (%)	3200 ppm 2 1 (%)	3200 ppm 2 2 (%)	3200 ppm 2 3 (%)	3200 ppm 2 4 (%)
{Digestive system}																		
liver		< a >	< 2>				< 2>				< 2>				< 2>			
	increase in mitosis	b	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
		(c)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Reproductive system}																		
testis		< a >	< 2>				< 2>				< 2>				< 2>			
	germ cell necrosis	b	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(c)	(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

Organ	Findings	Group Name	8000 ppm				20000 ppm			
		No. of Animals on Study	2				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
liver			< 2>				< 2>			
	increase in mitosis		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Reproductive system}										
testis			< 2>				< 2>			
	germ cell necrosis		2	0	0	0	1	0	0	0
			(100)	(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

APPENDIX K 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE: ALL ANIMALS

(2-WEEK STUDY)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 2 1 (%)	Control 2 2 (%)	Control 2 3 (%)	Control 2 4 (%)	512 ppm 2 1 (%)	512 ppm 2 2 (%)	512 ppm 2 3 (%)	512 ppm 2 4 (%)	1280 ppm 2 1 (%)	1280 ppm 2 2 (%)	1280 ppm 2 3 (%)	1280 ppm 2 4 (%)	3200 ppm 2 1 (%)	3200 ppm 2 2 (%)	3200 ppm 2 3 (%)	3200 ppm 2 4 (%)
{Hematopoietic system}																		
bone marrow		< a >	< 2>				< 2>				< 2>				< 2>			
	congestion	b	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(c)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	decreased hematopoiesis	b	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(c)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thymus		< a >	< 2>				< 2>				< 2>				< 2>			
	atrophy	b	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(c)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	karyorrhexis	b	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(c)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen		< a >	< 2>				< 2>				< 2>				< 2>			
	atrophy	b	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(c)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}																		
stomach		< a >	< 2>				< 2>				< 2>				< 2>			
	hemorrhage:glandular stomach	b	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(c)	(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

Organ	Findings	Group Name	8000 ppm				20000 ppm			
		No. of Animals on Study	3				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
bone marrow			< 3>				< 2>			
	congestion		0	3	0	0	0	2	0	0
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
	decreased hematopoiesis		0	3	0	0	0	2	0	0
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
thymus			< 3>				< 2>			
	atrophy		0	0	3	0	0	0	1	0
			(0)	(0)	(100)	(0)	(0)	(0)	(50)	(0)
	karyorrhexis		0	0	0	0	0	0	1	0
			(0)	(0)	(0)	(0)	(0)	(0)	(50)	(0)
spleen			< 3>				< 2>			
	atrophy		2	0	0	0	2	0	0	0
			(67)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Digestive system}										
stomach			< 3>				< 2>			
	hemorrhage:glandular stomach		2	0	0	0	0	0	0	0
			(67)	(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

Organ	Findings	Group Name	Control				512 ppm				1280 ppm				3200 ppm			
		No. of Animals on Study	2				2				2				2			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
stomach			< 2>				< 2>				< 2>				< 2>			
	degeneration:glandular stomach		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			< 2>				< 2>				< 2>				< 2>			
	increase in mitosis		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)	(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

Organ	Findings	Group Name	8000 ppm				20000 ppm			
		No. of Animals on Study	3				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
stomach			< 3>				< 2>			
	degeneration:glandular stomach		1	0	0	0	0	0	0	0
			(33)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
liver			< 3>				< 2>			
	increase in mitosis		0	1	0	0	0	0	0	0
			(0)	(33)	(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

APPENDIX K 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 2W)

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 0 1 (%)	Control 0 2 (%)	Control 0 3 (%)	Control 0 4 (%)	512 ppm 0 1 (%)	512 ppm 0 2 (%)	512 ppm 0 3 (%)	512 ppm 0 4 (%)	1280 ppm 0 1 (%)	1280 ppm 0 2 (%)	1280 ppm 0 3 (%)	1280 ppm 0 4 (%)	3200 ppm 0 1 (%)	3200 ppm 0 2 (%)	3200 ppm 0 3 (%)	3200 ppm 0 4 (%)
{Hematopoietic system}																		
bone marrow	congestion	< a >	< 0>				< 0>				< 0>				< 0>			
		b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	decreased hematopoiesis	< a >																
		b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
thymus	atrophy	< a >	< 0>				< 0>				< 0>				< 0>			
		b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	karyorrhexis	< a >																
		b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
spleen	atrophy	< a >	< 0>				< 0>				< 0>				< 0>			
		b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
{Digestive system}																		
stomach	hemorrhage:glandular stomach	< a >	< 0>				< 0>				< 0>				< 0>			
		b	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
		(c)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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

Organ	Findings	Group Name	8000 ppm				20000 ppm			
		No. of Animals on Study	0				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
bone marrow			< 0>				< 2>			
	congestion		-	-	-	-	0	2	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
	decreased hematopoiesis		-	-	-	-	0	2	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
thymus			< 0>				< 2>			
	atrophy		-	-	-	-	0	0	1	0
			(-)	(-)	(-)	(-)	(0)	(0)	(50)	(0)
	karyorrhexis		-	-	-	-	0	0	1	0
			(-)	(-)	(-)	(-)	(0)	(0)	(50)	(0)
spleen			< 0>				< 2>			
	atrophy		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(50)	(0)	(0)	(0)
{Digestive system}										
stomach			< 0>				< 2>			
	hemorrhage:glandular stomach		-	-	-	-	1	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

Organ	Findings	Group Name	Control				512 ppm				1280 ppm				3200 ppm			
		No. of Animals on Study	0				0				0				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Reproductive system}																		
testis			< 0>				< 0>				< 0>				< 0>			
	germ cell necrosis		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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

Organ	Findings	Group Name	8000 ppm				20000 ppm			
		No. of Animals on Study	0				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Reproductive system}										
testis			< 0>				< 2>			
	germ cell necrosis		-	-	-	-	1	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

APPENDIX K 4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

Organ	Findings	Group Name	Control	512 ppm	1280 ppm	3200 ppm
		No. of Animals on Study	0	0	0	0
		Grade	1 2 3 4	1 2 3 4	1 2 3 4	1 2 3 4
			(%) (%) (%) (%)	(%) (%) (%) (%)	(%) (%) (%) (%)	(%) (%) (%) (%)
{Hematopoietic system}						
bone marrow	congestion		< 0>	< 0>	< 0>	< 0>
			(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
	decreased hematopoiesis		(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
thymus	atrophy		< 0>	< 0>	< 0>	< 0>
			(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
	karyorrhexis		(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
spleen	atrophy		< 0>	< 0>	< 0>	< 0>
			(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)	(-) (-) (-) (-)
{Digestive system}						
stomach	hemorrhage:glandular stomach		< 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

Organ	Findings	Group Name	8000 ppm				20000 ppm			
		No. of Animals on Study	1				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
bone marrow			< 1>				< 2>			
	congestion		0	1	0	0	0	2	0	0
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
	decreased hematopoiesis		0	1	0	0	0	2	0	0
			(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
thymus			< 1>				< 2>			
	atrophy		0	0	1	0	0	0	1	0
			(0)	(0)	(100)	(0)	(0)	(0)	(50)	(0)
	karyorrhexis		0	0	0	0	0	0	1	0
			(0)	(0)	(0)	(0)	(0)	(0)	(50)	(0)
spleen			< 1>				< 2>			
	atrophy		1	0	0	0	2	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Digestive system}										
stomach			< 1>				< 2>			
	hemorrhage:glandular stomach		1	0	0	0	0	0	0	0
			(100)	(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

Organ	Findings	Group Name	Control				512 ppm				1280 ppm				3200 ppm			
		No. of Animals on Study	0				0				0				0			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
liver				< 0>				< 0>				< 0>				< 0>		
	increase in mitosis		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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

Organ	Findings	Group Name	8000 ppm				20000 ppm			
		No. of Animals on Study	1				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
liver			< 1>				< 2>			
	increase in mitosis		0	1	0	0	0	0	0	0
			(0)	(100)	(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

APPENDIX K 5

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : MALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name	Control				512 ppm				1280 ppm				3200 ppm			
		No. of Animals on Study	2				2				2				2			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}																		
bone marrow			< 2>				< 2>				< 2>				< 2>			
	congestion		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)
	decreased hematopoiesis		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)
thymus			< 2>				< 2>				< 2>				< 2>			
	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)
{Digestive system}																		
stomach			< 2>				< 2>				< 2>				< 2>			
	hemorrhage:glandular stomach		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			< 2>				< 2>				< 2>				< 2>			
	increase in mitosis		0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Reproductive system}																		
testis			< 2>				< 2>				< 2>				< 2>			
	germ cell necrosis		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(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

Organ	Findings	Group Name	8000 ppm				20000 ppm			
		No. of Animals on Study	2				0			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
bone marrow			< 2>				< 0>			
	congestion		0	2	0	0	-	-	-	-
			(0)	(100)	(0)	(0)	(-)	(-)	(-)	(-)
	decreased hematopoiesis		0	2	0	0	-	-	-	-
			(0)	(100)	(0)	(0)	(-)	(-)	(-)	(-)
thymus			< 2>				< 0>			
	atrophy		0	0	2	0	-	-	-	-
			(0)	(0)	(100)	(0)	(-)	(-)	(-)	(-)
{Digestive system}										
stomach			< 2>				< 0>			
	hemorrhage:glandular stomach		1	0	0	0	-	-	-	-
			(50)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
liver			< 2>				< 0>			
	increase in mitosis		0	0	0	0	-	-	-	-
			(0)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
{Reproductive system}										
testis			< 2>				< 0>			
	germ cell necrosis		2	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

APPENDIX K 6

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY

RAT : FEMALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

Organ	Findings	Group Name	Control				512 ppm				1280 ppm				3200 ppm			
		No. of Animals on Study	2				2				2				2			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}																		
bone marrow			< 2>				< 2>				< 2>				< 2>			
	congestion		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)
	decreased hematopoiesis		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)
thymus			< 2>				< 2>				< 2>				< 2>			
	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)
spleen			< 2>				< 2>				< 2>				< 2>			
	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)
{Digestive system}																		
stomach			< 2>				< 2>				< 2>				< 2>			
	hemorrhage:glandular stomach		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)
	degeneration:glandular stomach		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

Organ	Findings	Group Name	8000 ppm				20000 ppm			
		No. of Animals on Study	2				0			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
bone marrow	congestion		< 2>				< 0>			
			0	2	0	0	-	-	-	-
			(0)	(100)	(0)	(0)	(-)	(-)	(-)	(-)
	decreased hematopoiesis		0	2	0	0	-	-	-	-
			(0)	(100)	(0)	(0)	(-)	(-)	(-)	(-)
thymus	atrophy		< 2>				< 0>			
			0	0	2	0	-	-	-	-
			(0)	(0)	(100)	(0)	(-)	(-)	(-)	(-)
spleen	atrophy		< 2>				< 0>			
			1	0	0	0	-	-	-	-
			(50)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
{Digestive system}										
stomach	hemorrhage:glandular stomach		< 2>				< 0>			
			1	0	0	0	-	-	-	-
			(50)	(0)	(0)	(0)	(-)	(-)	(-)	(-)
	degeneration:glandular stomach		1	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

STUDY NO. : 0314
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name	Control				512 ppm				1280 ppm				3200 ppm			
		No. of Animals on Study	2				2				2				2			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
liver			< 2>				< 2>				< 2>				< 2>			
	increase in mitosis		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)	(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

(HPT150)

Organ	Findings	Group Name	8000 ppm				20000 ppm			
		No. of Animals on Study	2				0			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
liver			< 2>				< 0>			
	increase in mitosis		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

APPENDIX L 1

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

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

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

Lot No. : SKR5565

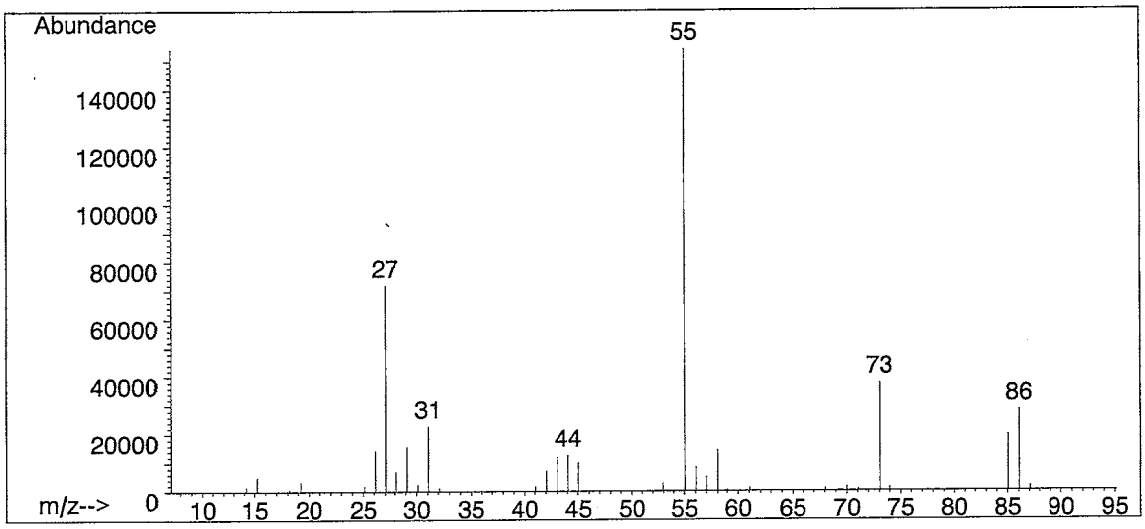
1. Spectral Data

Mass Spectrometry

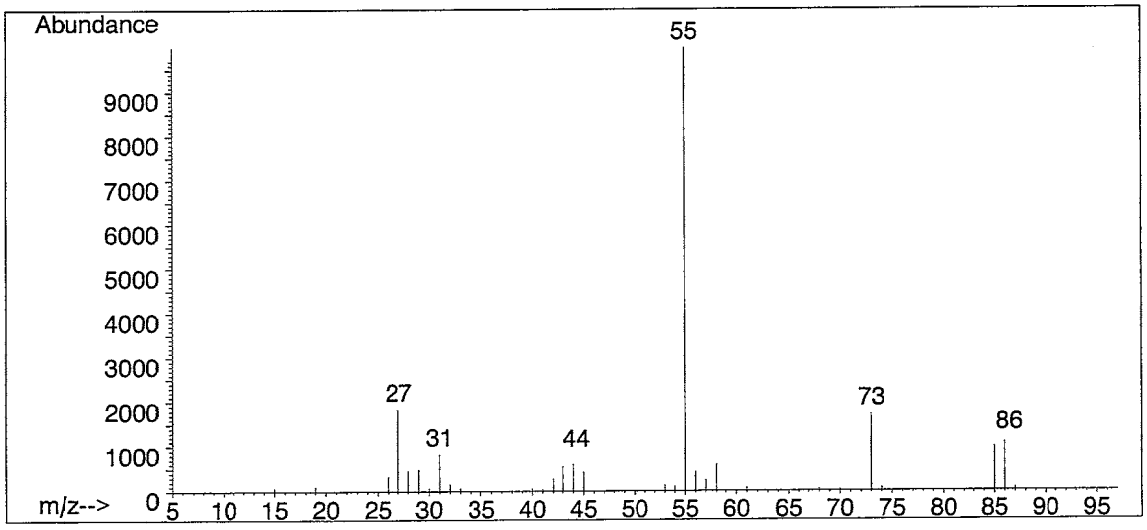
Instrument : Hewlett Packard 5989B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance



Mass Spectrum of Literature Data*

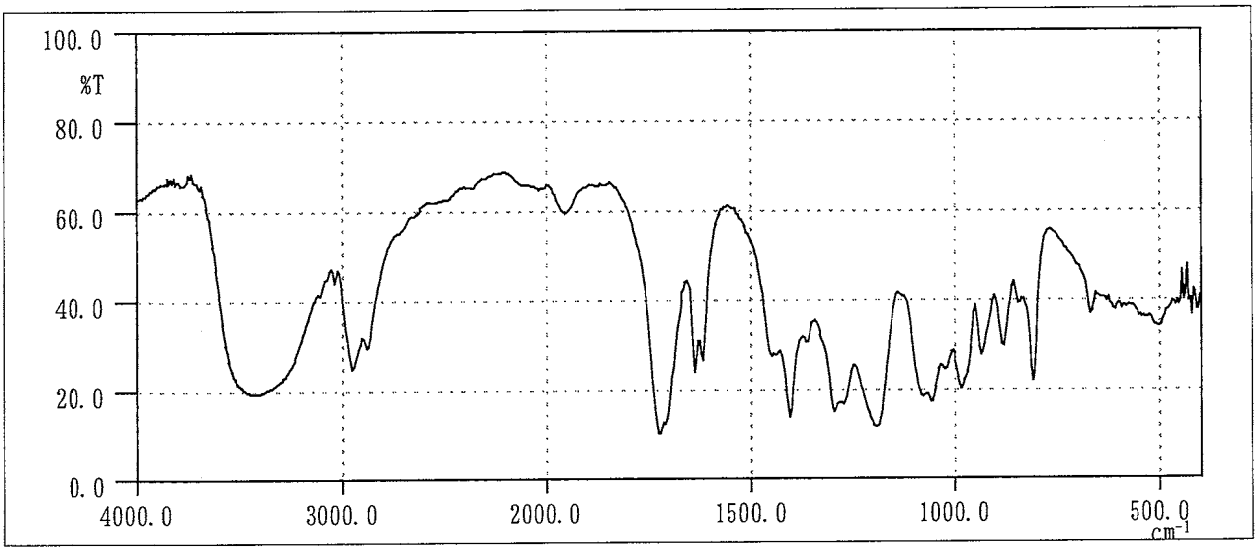
Results: The mass spectrum was consistent with literature spectrum.
(*Fred W. McLafferty (1994) Wiley Registry of Mass Spectral Data, 6th edition. John Wiley and Sons, Inc. (U.S.), Entry Number 12762)

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	0.843	Acrylic Acid
	2	96.338	2-Hydroxyethyl Acrylate
	3	2.766	Material which cannot be identified
	4	0.054	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 0.843%, 2.766% and 0.054%.

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 0.843%, 2.766% and 0.054%.

APPENDIX L 2

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

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

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

Lot No. : SKR5565

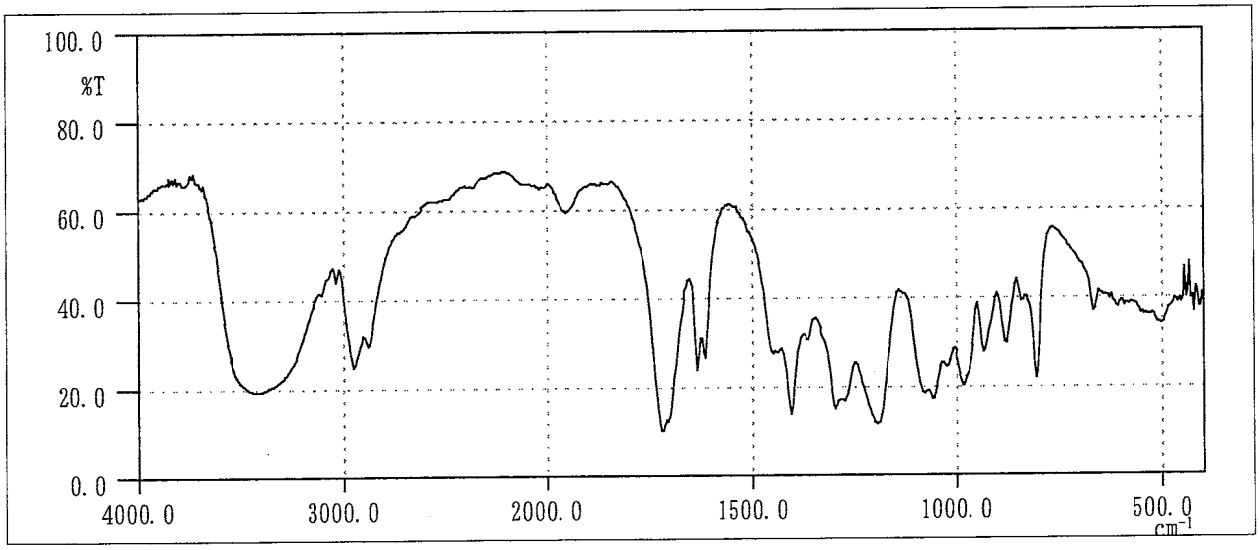
1. Sample : This lot was used from 1996.7.16 to 1996.7.30. Test substance was stored at room temperature.

2. Infrared Spectrometry

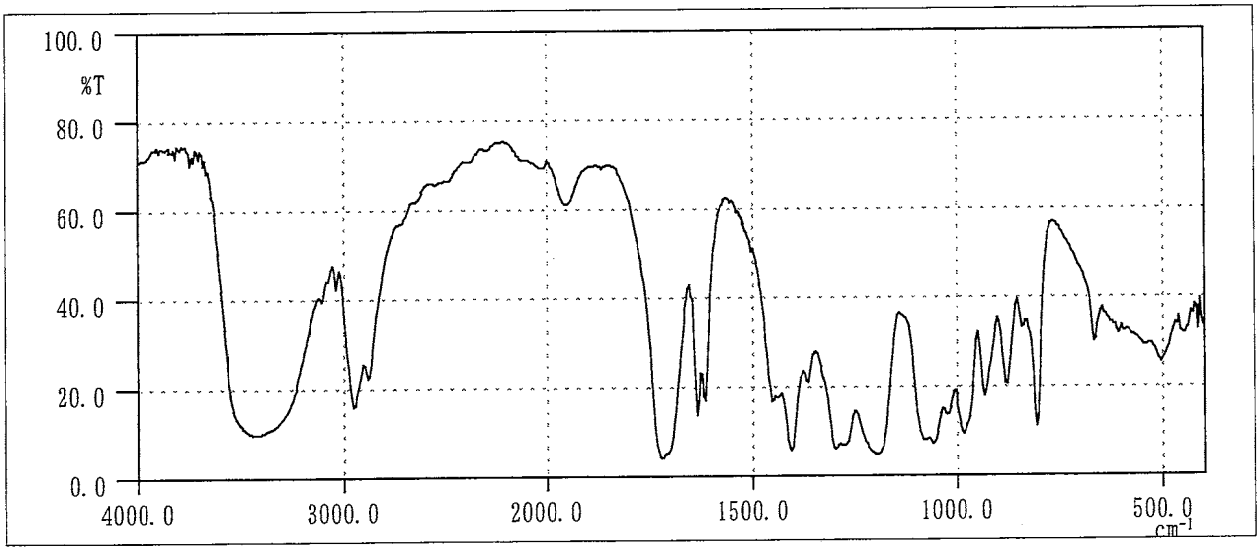
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 2 cm^{-1}



Infrared Spectrum of Test Substance (date analyzed : 1996.07.09)



Infrared Spectrum of Test Substance (date analyzed : 1996.08.13)

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 (%)
1996.07.05	1	2.750	0.843
	2	3.477	96.338
	3	7.748	2.766
	4	20.975	0.054
1996.08.13	1	2.726	0.841
	2	3.449	96.315
	3	7.687	2.793
	4	20.824	0.051

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 1996.7.5 and one major peak (peak No.2) and three impurities (peaks No.1, No.3 and No.4 < 4% of total area) analyzed on 1996.8.13. No new trace impurity peak in the test substance analyzed on 1996.8.13 was detected.

4. Conclusions: The test substance was stable for about 1 month at room temperature.

APPENDIX L 3

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

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

	Target Concentration				
Date Analyzed	512[a]	1280	3200	8000	20000
1996.07.16	517 (101)[b]	1300 (102)	3240 (101)	7950 (99.4)	20500 (103)

[a] ppm
[b] %

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 L 4

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

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

		Target Concentration	
Date Prepared	Date Analyzed	512[a]	20000
1996.07.05	1996.07.05	519 (100)[b]	20000 (100)
	1996.07.12[c]	488 (94.0)	18800 (94.0)

[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 M 1

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

METHODS FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-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]
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]
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]

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.)

APPENDIX M 2

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

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-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
Phospholipid	mg/dL	0
Glutamic oxaloacetic transaminase (GOT)	IU/L	0
Glutamic pyruvic transaminase (GPT)	IU/L	0
Lactate dehydrogenase (LDH)	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