N,N-ジメチルホルムアミドのラット及びマウスを用いた
吸 入 に よ る が ん 原 性 予 備 試 験 報 告 書

APPENDIX

(A1-1～A12)
2 週間試験：ラット/0263；マウス/0264

APPENDIXES

APPENDIXES (CONTINUED)

APPENDIXES (CONTINUED)

APPENDIX A 1-1

CLINICAL OBSERVATION (TWO-WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0263
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 0-0 1	1-1 1	1-2 1	1-3 1	1-4 1	1-5 1	1-6 1	1-7 1	2-1 1	2-2 1	2-3 1	2-4 1	2-5 1	2-6 1
LOCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	100 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	200 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	400 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	800 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	3	1	0	0	0	0	0	0	1	1	0
HUNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	100 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	200 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	400 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	800 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	1	1	0
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	100 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	200 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	400 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	800 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	2	2	0

Clinical sign	Group Name	Administration Week-day 2-7 1
LOCOMOTOR MOVEMENT DECR	Control	0
	100 ppm	0
	200 ppm	0
	400 ppm	0
	800 ppm	0
	1600 ppm	0
HUNCHBACK POSITION	Control	0
	100 ppm	0
	200 ppm	0
	400 ppm	0
	800 ppm	0
	1600 ppm	0
PILOERECTION	Control	0
	100 ppm	0
	200 ppm	0
	400 ppm	0
	800 ppm	0
	1600 ppm	0

APPENDIX A 1-2

CLINICAL OBSERVATION (TWO-WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO. : 0263
ANIMAL : RAT F344
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

Clinical sign	Group Name	Administration Week-day 0-0 1	1-1 1	1-2 1	1-3 1	1-4 1	1-5 1	1-6 1	1-7 1	2-1 1	2-2 1	2-3 1	2-4 1	2-5 1	2-6 1
LOCOMOTOR MOVEMENT DECR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	100 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	200 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	400 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	800 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	3	0	0	0	0	0	0	0	0	0	0

APPENDIX A 2-1

BODY WEIGHT CHANGES (TWO-WEEK STUDY:SUMMARY)

RAT : MALE

STUDY NO. : 0263
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-1	1-7	2-7
Control	122± 3	124± 3	144± 5	168± 9
100 ppm	122± 4	125± 5	146± 8	175± 15
200 ppm	123± 3	125± 3	149± 6	176± 13
400 ppm	122± 4	122± 4	142± 6	165± 8
800 ppm	122± 4	121± 4	130± 7**	147± 10**
1600 ppm	122± 3	121± 3	109± 7**	109± 13**

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

APPENDIX A 2-2

BODY WEIGHT CHANGES (TWO-WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO. : 0263
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0		1-1		1-7		2-7	
Control	101±	4	102±	4	112±	5	125±	6
100 ppm	100±	4	102±	3	114±	4	127±	4
200 ppm	100±	3	101±	3	111±	3	123±	3
400 ppm	100±	2	98±	3	107±	4*	116±	4**
800 ppm	100±	4	98±	3	103±	4**	110±	6**
1600 ppm	99±	3	97±	4*	89±	5**	94±	3**

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

APPENDIX A 2-3

BODY WEIGHT CHANGES(TWO-WEEK STUDY:SUMMARY)

MOSUE : MALE

STUDY NO. : 0264
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-1	1-7	2-7
Control	22.9± 1.0	22.8± 0.9	24.0± 1.0	25.1± 1.3
100 ppm	22.8± 0.9	22.4± 1.0	23.4± 0.9	24.6± 1.2
200 ppm	22.3± 1.0	22.2± 0.7	23.4± 1.1	24.7± 1.1
400 ppm	22.4± 1.0	22.2± 0.9	23.6± 1.1	25.1± 1.1
800 ppm	22.5± 0.8	21.6± 0.8*	22.9± 1.1	24.0± 1.1
1600 ppm	22.9± 1.0	21.6± 0.9*	22.6± 0.9*	23.3± 1.0**

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

APPENDIX A 2-4

BODY WEIGHT CHANGES (TWO-WEEK STUDY: SUMMARY)

MOSUE: FEMALE

STUDY NO. : 0264
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day 0-0	1-1	1-7	2-7
Control	17.9± 0.7	18.0± 1.0	18.7± 1.1	20.4± 1.0
100 ppm	17.7± 1.1	17.8± 0.8	18.6± 1.0	20.0± 0.6
200 ppm	17.8± 0.5	17.7± 0.4	18.5± 0.5	20.2± 0.7
400 ppm	17.8± 0.8	17.8± 0.8	19.0± 0.8	20.6± 1.3
800 ppm	18.1± 0.8	17.6± 1.0	17.9± 0.7	19.4± 0.9
1600 ppm	18.0± 0.9	16.6± 1.0**	18.2± 1.1	18.8± 0.9**

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

APPENDIX A 3-1

FOOD CONSUMPTION CHANGES (TWO-WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0263
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(7)	2-7(7)
Control	14.6± 0.6	14.8± 0.7
100 ppm	14.4± 1.0	16.2± 1.8
200 ppm	15.0± 1.0	16.1± 2.0
400 ppm	13.1± 0.7**	14.2± 0.7
800 ppm	11.8± 0.5**	12.5± 0.8*
1600 ppm	6.7± 1.1**	7.2± 2.3**

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

APPENDIX A 3-2

FOOD CONSUMPTION CHANGES (TWO-WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO. : 0263
ANIMAL : RAT F344
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration 1-7(7)	week-day(effective) 2-7(7)
Control	12.0± 0.9	11.6± 0.8
100 ppm	11.8± 0.3	11.8± 0.5
200 ppm	11.5± 0.5	11.9± 0.5
400 ppm	10.4± 0.7*	9.9± 0.6**
800 ppm	9.4± 0.7**	9.3± 0.7**
1600 ppm	5.8± 1.1**	7.5± 0.9**

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

APPENDIX A 3-3

FOOD CONSUMPTION CHANGES (TWO-WEEK STUDY: SUMMARY)

MOSUE : MALE

STUDY NO. : 0264
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(7)	2-7(7)
Control	4.2± 0.3	4.2± 0.3
100 ppm	4.1± 0.3	4.4± 0.4
200 ppm	4.1± 0.3	4.4± 0.2
400 ppm	3.9± 0.3	4.3± 0.5
800 ppm	3.6± 0.3**	3.6± 0.2**
1600 ppm	3.5± 0.2**	4.0± 0.4

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

APPENDIX A 3-4

FOOD CONSUMPTION CHANGES(TWO-WEEK STUDY: SUMMARY)

MOSUE : FEMALE

STUDY NO. : 0264
ANIMAL : MOUSE BDF1
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective) 1-7(7)	2-7(7)
Control	3.5± 0.4	3.8± 0.2
100 ppm	3.4± 0.2	3.7± 0.2
200 ppm	3.4± 0.2	3.8± 0.2
400 ppm	3.4± 0.2	3.6± 0.4
800 ppm	3.1± 0.2**	3.4± 0.2**
1600 ppm	2.9± 0.3**	3.6± 0.3

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

APPENDIX A 4-1

HEMATOLOGY (TWO-WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0263
ANIMAL : RAT F344
SAMPLING DATE : 002-7
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
SURVIVAL ANIMALS (2)

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	7.68± 0.33	14.1± 0.6	41.6± 1.7	54.2± 0.5	18.4± 0.1	33.9± 0.1	779± 78
100 ppm	5	7.70± 0.38	13.9± 0.6	41.6± 1.6	54.0± 0.7	18.1± 0.2	33.5± 0.2	946± 69
200 ppm	5	7.63± 0.33	13.8± 0.6	40.9± 1.4	53.6± 0.5	18.1± 0.2	33.8± 0.5	933± 100
400 ppm	5	7.76± 0.34	14.1± 0.5	41.5± 1.7	53.6± 0.6	18.2± 0.3	33.9± 0.6	821± 85
800 ppm	5	8.24± 0.38	14.9± 0.4	43.3± 1.6	52.6± 0.6*	18.1± 0.3	34.4± 0.5	883± 54
1600 ppm	5	7.28± 0.94	13.1± 1.5	39.5± 3.9	54.5± 2.1	18.1± 0.4	33.2± 0.8	682± 652

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

STUDY NO. : 0263
ANIMAL : RAT F344
SAMPLING DATE : 002-7
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	RETICULOCYTE ‰		PROTHROMBIN TIME sec		APTT sec	
Control	5	56±	15	12.3±	0.2	18.1±	0.4
100 ppm	5	63±	9	11.9±	0.2	18.1±	0.9
200 ppm	5	59±	13	11.9±	0.2	18.8±	0.3
400 ppm	5	54±	8	12.3±	0.3	19.1±	0.5
800 ppm	5	47±	10	14.3±	0.7	19.4±	2.9
1600 ppm	5	83±	19*	12.7±	1.1	17.2±	2.6

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

STUDY NO. : 0263
ANIMAL : RAT F344
SAMPLING DATE : 002-7
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
Control	5	2.47± 0.86	0± 1	24± 11	1± 1	0± 0	4± 2	70± 10	1± 1
100 ppm	5	2.14± 0.79	0± 0	24± 12	1± 1	0± 0	4± 1	70± 11	1± 1
200 ppm	5	2.26± 0.70	0± 0	21± 5	0± 1	0± 0	3± 2	75± 6	1± 1
400 ppm	5	1.94± 0.30	0± 0	19± 4	0± 0	0± 0	3± 1	77± 5	1± 2
800 ppm	5	2.35± 1.18	1± 1	31± 5	1± 1	0± 0	3± 2	64± 6	0± 0
1600 ppm	5	2.49± 0.80	0± 0	32± 8	0± 0	0± 0	4± 2	62± 7	2± 1

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

APPENDIX A 4-2

HEMATOLOGY (TWO-WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO. : 0263
ANIMAL : RAT F344
SAMPLING DATE : 002-7
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
SURVIVAL ANIMALS (2)

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	8.05± 0.19	15.1± 0.7	43.5± 1.0	54.0± 0.4	18.7± 0.4	34.7± 0.8	641± 77
100 ppm	5	8.06± 0.17	15.0± 0.3	43.4± 1.2	53.8± 0.6	18.6± 0.2	34.5± 0.3	749± 140
200 ppm	5	8.13± 0.07	15.0± 0.1	43.8± 0.2	53.8± 0.3	18.5± 0.1	34.4± 0.1	749± 48
400 ppm	5	8.30± 0.24	15.1± 0.5	44.0± 1.3	53.0± 0.3*	18.2± 0.2	34.4± 0.4	707± 114
800 ppm	5	8.49± 0.18	15.7± 0.6	45.0± 1.1	53.0± 0.2*	18.5± 0.4	34.9± 0.6	705± 61
1600 ppm	3	7.60± 1.20	14.1± 2.0	43.0± 5.4	56.8± 4.1	18.5± 0.5	32.7± 1.4	714± 569

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

STUDY NO. : 0263
ANIMAL : RAT F344
SAMPLING DATE : 002-7
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	RETICULOCYTE ‰		PROTHROMBIN TIME sec		APTT sec	
Control	5	28±	6	12.1±	0.3	16.9±	0.7
100 ppm	5	34±	9	12.1±	0.2	17.6±	0.2
200 ppm	5	41±	10	12.0±	0.1	17.5±	0.7
400 ppm	5	27±	3	12.5±	0.1	18.1±	0.4*
800 ppm	5	27±	2	14.0±	1.0*	19.2±	0.9**
1600 ppm	3	144±	146*	12.0±	0.3	16.4±	1.0

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

STUDY NO. : 0263
ANIMAL : RAT F344
SAMPLING DATE : 002-7
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
Control	5	2.40± 1.11	0± 0	21± 3	2± 1	0± 0	3± 1	73± 3	1± 1
100 ppm	5	3.25± 1.49	0± 0	22± 6	1± 1	0± 0	4± 3	71± 2	1± 2
200 ppm	5	2.41± 0.67	0± 0	22± 4	1± 1	0± 0	3± 2	73± 3	0± 1
400 ppm	5	1.55± 0.52	0± 0	23± 9	1± 1	0± 0	3± 1	72± 8	1± 1
800 ppm	5	1.17± 0.16	0± 1	30± 5	1± 1	0± 0	4± 3	64± 6	1± 1
1600 ppm	3	2.16± 0.99	0± 0	36± 18	1± 1	0± 0	6± 2	51± 13*	6± 4

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

APPENDIX A 4-3

HEMATOLOGY (TWO-WEEK STUDY: SUMMARY)

MOSUE : MALE

STUDY NO. : 0264
ANIMAL : MOUSE BDF1
SAMPLING DATE : 002-7
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
SURVIVAL ANIMALS (2)

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	10.79± 0.39	16.3± 0.4	51.5± 2.4	47.7± 0.7	15.1± 0.2	31.6± 0.7	1193± 79
100 ppm	5	10.47± 0.31	15.7± 0.5	49.5± 1.5	47.3± 0.5	15.1± 0.2	31.8± 0.5	1298± 106
200 ppm	5	10.47± 0.32	15.8± 0.3	49.3± 2.2	47.1± 1.0	15.0± 0.2	32.0± 0.9	1324± 99
400 ppm	5	10.54± 0.32	15.8± 0.6	49.5± 2.0	46.9± 0.7	15.0± 0.1	32.0± 0.3	1431± 119**
800 ppm	5	11.04± 0.54	16.7± 0.8	52.3± 3.2	47.4± 0.6	15.1± 0.0	31.9± 0.5	1271± 84
1600 ppm	5	11.30± 0.37	17.2± 0.6	52.4± 2.0	46.4± 0.6	15.2± 0.2	32.8± 0.3	1375± 69*

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

STUDY NO. : 0264
ANIMAL : MOUSE BDF1
SAMPLING DATE : 002-7
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHERS
Control	5	2.19± 0.92	0± 1	10± 1	1± 1	0± 0	2± 1	87± 1	0± 0
100 ppm	5	2.93± 1.48	0± 1	9± 2	1± 1	0± 0	2± 1	87± 2	0± 0
200 ppm	5	2.46± 1.01	0± 0	12± 2	0± 1	0± 0	2± 1	86± 2	0± 0
400 ppm	5	3.21± 1.45	0± 1	15± 5	2± 1	0± 0	3± 2	79± 6*	1± 1
800 ppm	5	3.37± 1.71	0± 0	10± 2	1± 1	0± 0	1± 1	86± 2	0± 0
1600 ppm	5	3.94± 1.19	0± 0	21± 19	1± 1	0± 0	3± 1	74± 18	0± 0

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

APPENDIX A 4-4

HEMATOLOGY (TWO-WEEK STUDY: SUMMARY)

MOSUE : FEMALE

STUDY NO. : 0264
ANIMAL : MOUSE BDF1
SAMPLING DATE : 002-7
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
SURVIVAL ANIMALS (2)

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	10.13± 0.57	15.6± 0.5	47.9± 3.0	47.3± 1.1	15.4± 0.9	32.7± 1.8	932± 61
100 ppm	5	10.52± 0.26	15.8± 0.7	49.4± 2.1	46.9± 0.9	15.0± 0.3	32.0± 0.3	1174± 74**
200 ppm	5	10.28± 0.28	15.9± 0.6	48.1± 1.1	46.8± 0.5	15.4± 0.8	33.0± 1.4	1254± 95**
400 ppm	5	10.25± 0.37	15.4± 0.6	47.7± 1.8	46.5± 0.3	15.1± 0.1	32.4± 0.2	1283± 65**
800 ppm	5	10.75± 0.42	16.3± 0.6	50.2± 2.0	46.7± 0.2	15.2± 0.1	32.5± 0.3	1202± 81**
1600 ppm	5	10.86± 0.37*	16.8± 0.9*	50.1± 1.8	46.2± 1.0	15.5± 0.5	33.5± 1.4	1265± 113**

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

STUDY NO. : 0264
ANIMAL : MOUSE BDF1
SAMPLING DATE : 002-7
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$		Differential WBC (%) N-BAND		N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHERS	
Control	5	2.13±	0.78	0±	1	9±	2	1±	1	0±	0	3±	1	86±	2	0±	0
100 ppm	5	3.17±	1.63	1±	1	10±	2	0±	1	0±	0	2±	0	87±	2	0±	0
200 ppm	5	2.42±	1.24	0±	0	10±	1	2±	1	0±	0	2±	1	86±	2	0±	0
400 ppm	5	3.06±	1.45	1±	2	10±	1	2±	2	0±	0	2±	1	85±	4	0±	0
800 ppm	5	4.10±	1.59	0±	0	11±	3	2±	1	0±	0	2±	1	85±	3	0±	0
1600 ppm	5	3.28±	0.32	1±	1	27±	11**	2±	2	0±	0	3±	1	66±	12*	1±	1

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

APPENDIX A 5-1

BIOCHEMISTRY (TWO-WEEK STUDY: SUMMARY)

RAT : MALE

STUDY NO. : 0263
ANIMAL : RAT F344
SAMPLING DATE : 003-1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

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	5.9±	0.1	3.6±	0.1	1.5±	0.0	0.23±	0.02	190±	8	58±	3	120±	3
100 ppm	5	6.1±	0.1	3.7±	0.1	1.5±	0.0	0.25±	0.02	190±	7	72±	4	145±	8
200 ppm	5	6.1±	0.1	3.7±	0.1	1.5±	0.0	0.27±	0.04	186±	7	75±	3	148±	11
400 ppm	5	6.0±	0.2	3.6±	0.2	1.5±	0.1	0.28±	0.03	178±	5*	82±	4*	152±	6*
800 ppm	5	6.1±	0.1	3.7±	0.1	1.5±	0.1	0.34±	0.08	162±	5**	92±	4**	147±	3
1600 ppm	5	6.1±	0.9	3.7±	0.5	1.5±	0.0	0.68±	0.39**	156±	6**	129±	21**	255±	16**

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

STUDY NO. : 0263
ANIMAL : RAT F344
SAMPLING DATE : 003-1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

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	59±	4	21±	2	177±	29	0±	1	154±	27	14.2±	2.3	0.4±	0.1
100 ppm	5	66±	10	25±	5	172±	14	1±	1	139±	7	14.8±	2.9	0.3±	0.1
200 ppm	5	62±	10	26±	5	168±	32	0±	1	128±	15	13.4±	0.9	0.4±	0.1
400 ppm	5	64±	8	26±	4	176±	34	1±	1	134±	17	14.0±	3.6	0.4±	0.0
800 ppm	5	188±	83*	170±	107**	266±	73	1±	0	152±	32	19.3±	2.9	0.3±	0.1
1600 ppm	5	452±	290**	232±	131**	469±	605	16±	10**	150±	38	15.7±	4.1	0.3±	0.1

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

STUDY NO. : 0263
ANIMAL : RAT F344
SAMPLING DATE : 003-1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	SODIUM mEq／ℓ		POTASSIUM mEq／ℓ		CHLORIDE mEq／ℓ		CALCIUM mg／dℓ		INORGANIC PHOSPHORUS mg／dℓ	
Control	5	141±	1	4.1±	0.3	105±	1	10.8±	0.3	7.5±	1.6
100 ppm	5	142±	1	4.3±	0.2	105±	2	10.7±	0.5	7.5±	1.4
200 ppm	5	142±	2	4.2±	0.2	106±	1	10.7±	0.5	7.9±	1.3
400 ppm	5	141±	1	4.4±	0.1	106±	1	10.9±	0.3	7.1±	1.2
800 ppm	5	140±	1	4.6±	0.2*	106±	2	10.4±	0.4	8.1±	1.4
1600 ppm	5	143±	1*	4.6±	0.2*	107±	3	11.1±	0.4	6.5±	1.4

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

APPENDIX A 5-2

BIOCHEMISTRY (TWO-WEEK STUDY: SUMMARY)

RAT : FEMALE

STUDY NO. : 0263
ANIMAL : RAT F344
SAMPLING DATE : 003-1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

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	5.8± 0.1	3.5± 0.1	1.6± 0.1	0.36± 0.05	192± 7	71± 4	137± 8
100 ppm	5	5.8± 0.1	3.5± 0.1	1.5± 0.1	0.36± 0.09	188± 6	93± 3	168± 7**
200 ppm	5	5.9± 0.1	3.6± 0.1	1.6± 0.1	0.37± 0.11	184± 10	98± 8	171± 12**
400 ppm	5	5.7± 0.1	3.4± 0.1	1.5± 0.1	0.60± 0.17	165± 14**	100± 7	165± 13**
800 ppm	5	5.9± 0.2	3.6± 0.1	1.6± 0.1	0.52± 0.37	171± 7**	120± 3**	187± 7**
1600 ppm	3	6.1± 0.7	3.7± 0.5	1.5± 0.1	0.58± 0.13	153± 3**	128± 15**	248± 23**

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

STUDY NO. : 0263
ANIMAL : RAT F344
SAMPLING DATE : 003-1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

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	60±	3	20±	2	227±	42	1±	0	139±	22	15.8±	3.4	0.4±	0.0
100 ppm	5	59±	4	21±	2	225±	29	1±	1	142±	9	15.9±	2.2	0.3±	0.0
200 ppm	5	62±	4	24±	2	248±	59	1±	1	141±	16	14.9±	2.8	0.4±	0.0
400 ppm	5	65±	5	25±	3	261±	68	1±	1	143±	27	14.6±	4.4	0.4±	0.1
800 ppm	5	135±	95**	101±	98**	309±	89	2±	1	144±	17	19.5±	5.8	0.4±	0.0
1600 ppm	3	157±	140*	79±	72*	233±	77	14±	9*	144±	28	15.6±	4.3	0.4±	0.1

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

STUDY NO. : 0263
ANIMAL : RAT F344
SAMPLING DATE : 003-1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	SODIUM mEq／ℓ	POTASSIUM mEq／ℓ	CHLORIDE mEq／ℓ	CALCIUM mg／dℓ	INORGANIC PHOSPHORUS mg／dℓ
Control	5	141± 1	3.9± 0.3	108± 1	10.5± 0.4	6.1± 1.1
100 ppm	5	142± 2	4.0± 0.3	109± 1	10.5± 0.4	6.8± 1.1
200 ppm	5	142± 1	3.7± 0.4	109± 1	10.6± 0.4	6.5± 1.0
400 ppm	5	141± 1	4.1± 0.2	108± 1	10.2± 0.2	6.6± 1.4
800 ppm	5	142± 2	4.0± 0.2	108± 1	10.4± 0.3	7.4± 1.0
1600 ppm	3	141± 1	4.3± 0.3	108± 4	11.5± 0.7**	6.2± 0.2

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

APPENDIX A 5-3

BIOCHEMISTRY (TWO-WEEK STUDY: SUMMARY)

MOUSE: MALE

STUDY NO. : 0264
ANIMAL : MOUSE BDF1
SAMPLING DATE : 003-1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

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		GOT IU／ℓ	
Control	5	5.3±	0.2	2.9±	0.2	1.2±	0.1	0.31±	0.04	311±	26	88±	10	35±	3
100 ppm	5	5.1±	0.3	2.8±	0.2	1.3±	0.1	0.28±	0.09	306±	9	85±	13	36±	3
200 ppm	5	5.0±	0.2	2.9±	0.1	1.4±	0.1*	0.31±	0.05	309±	18	89±	6	33±	2
400 ppm	5	5.4±	0.3	3.0±	0.1	1.3±	0.0	0.34±	0.09	277±	17	103±	8	39±	6
800 ppm	5	5.3±	0.3	3.0±	0.2	1.3±	0.0	0.40±	0.17	303±	22	89±	10	42±	10
1600 ppm	5	5.4±	0.2	3.2±	0.1*	1.5±	0.1**	0.42±	0.16	291±	15	108±	6**	246±	348*

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

STUDY NO. : 0264
ANIMAL : MOUSE BDF1
SAMPLING DATE : 003-1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	GPT IU/ℓ		LDH IU/ℓ		CPK IU/ℓ		UREA NITROGEN mg/dℓ		SODIUM mEq/ℓ		POTASSIUM mEq/ℓ		CHLORIDE mEq/ℓ	
Control	5	16±	2	236±	50	150±	133	20.6±	4.2	151±	2	4.8±	0.7	119±	5
100 ppm	5	20±	4	230±	52	126±	81	23.2±	4.9	150±	1	4.5±	0.7	119±	3
200 ppm	5	19±	2	197±	19	86±	23	20.7±	3.2	150±	2	4.4±	0.4	121±	1
400 ppm	5	26±	5	280±	148	71±	24	23.0±	2.8	152±	1	4.8±	0.5	121±	1
800 ppm	5	23±	5	381±	270	202±	219	21.5±	4.5	150±	2	5.6±	1.0	116±	5
1600 ppm	5	367±	585**	1479±	2493	114±	102	19.1±	3.3	150±	1	5.0±	0.6	117±	5

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

STUDY NO. : 0264
ANIMAL : MOUSE BDF1
SAMPLING DATE : 003-1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	CALCIUM mg/dℓ		INORGANIC PHOSPHORUS mg/dℓ	
Control	5	9.4±	0.5	8.7±	1.1
100 ppm	5	9.2±	0.2	8.1±	1.0
200 ppm	5	9.6±	0.5	6.8±	2.1
400 ppm	5	10.2±	0.5*	7.2±	1.4
800 ppm	5	9.8±	0.2	7.8±	2.0
1600 ppm	5	10.0±	0.3	8.7±	0.7

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

APPENDIX A 5-4

BIOCHEMISTRY (TWO-WEEK STUDY: SUMMARY)

MOUSE: FEMALE

STUDY NO. : 0264
ANIMAL : MOUSE BDF1
SAMPLING DATE : 003-1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

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		GOT IU／ℓ	
Control	5	5.1±	0.2	3.2±	0.2	1.6±	0.1	0.32±	0.04	284±	19	78±	7	46±	3
100 ppm	5	5.1±	0.3	3.1±	0.2	1.5±	0.0	0.41±	0.15	293±	20	96±	8**	45±	4
200 ppm	5	5.3±	0.3	3.2±	0.2	1.6±	0.1	0.37±	0.07	291±	15	97±	6**	45±	5
400 ppm	5	5.2±	0.2	3.1±	0.1	1.5±	0.1	0.34±	0.03	264±	13	94±	7**	42±	5
800 ppm	5	5.1±	0.1	3.2±	0.0	1.6±	0.1	0.27±	0.11	287±	30	85±	6	48±	5
1600 ppm	5	5.5±	0.3	3.5±	0.2*	1.7±	0.1	0.52±	0.26	231±	28**	128±	9**	3452±	3478

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

STUDY NO. : 0264
ANIMAL : MOUSE BDF1
SAMPLING DATE : 003-1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	GPT IU/ℓ		LDH IU/ℓ		CPK IU/ℓ		UREA NITROGEN mg/dℓ		SODIUM mEq/ℓ		POTASSIUM mEq/ℓ		CHLORIDE mEq/ℓ	
Control	5	22±	4	277±	33	94±	32	18.2±	1.5	149±	1	5.0±	0.6	117±	3
100 ppm	5	22±	3	281±	80	89±	28	18.3±	1.1	150±	2	4.8±	0.8	121±	5
200 ppm	5	25±	3	242±	45	83±	40	19.0±	0.9	149±	2	4.8±	0.7	120±	1
400 ppm	5	26±	6	197±	20	61±	15	19.8±	3.9	150±	2	4.8±	0.4	122±	3
800 ppm	5	33±	7*	273±	41	122±	71	16.4±	2.6	150±	2	5.0±	0.5	119±	2
1600 ppm	5	4627±	4361**	15692±	17575	142±	49	20.0±	3.9	149±	1	5.2±	0.8	113±	5

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

STUDY NO. : 0264
ANIMAL : MOUSE BDF1
SAMPLING DATE : 003-1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (2)

Group Name	NO. of Animals	CALCIUM mg/dℓ		INORGANIC PHOSPHORUS mg/dℓ	
Control	5	9.2±	0.3	7.6±	1.7
100 ppm	5	9.7±	0.5	8.2±	2.0
200 ppm	5	9.8±	0.4	6.4±	1.3
400 ppm	5	10.0±	0.5	6.7±	1.2
800 ppm	5	9.4±	0.3	6.8±	1.9
1600 ppm	5	9.6±	0.5	9.1±	1.2

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

APPENDIX A 6-1

GROSS FINDINGS (TWO-WEEK STUDY: SUMMARY)

RAT : MALE : SACRIFICED ANIMALS

STUDY NO. : 0263
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	100 ppm 10 (%)	200 ppm 10 (%)	400 ppm 10 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
liver	red zone		0 (0)	0 (0)	0 (0)	0 (0)
	herniation		1 (10)	0 (0)	0 (0)	0 (0)
	accentuation of lobular structure		0 (0)	0 (0)	0 (0)	0 (0)

STUDY NO. : 0263
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name	800 ppm	1600 ppm
		NO. of Animals	10 (%)	7 (%)
thymus	atrophic		0 (0)	6 (86)
liver	red zone		0 (0)	3 (43)
	herniation		0 (0)	0 (0)
	accentuation of lobular structure		0 (0)	6 (86)

APPENDIX A 6-2

GROSS FINDINGS (TWO-WEEK STUDY: SUMMARY)

RAT : FEMALE : SACRIFICED ANIMALS

STUDY NO. : 0263
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	100 ppm 10 (%)	200 ppm 10 (%)	400 ppm 10 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
liver	red zone		0 (0)	0 (0)	0 (0)	0 (0)
	herniation		0 (0)	0 (0)	1 (10)	1 (10)
	accentuation of lobular structure		0 (0)	0 (0)	0 (0)	0 (0)

STUDY NO. : 0263
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name	800 ppm	1600 ppm
		NO. of Animals	10 (%)	3 (%)
thymus	atrophic		0 (0)	3 (100)
liver	red zone		0 (0)	2 (67)
	herniation		0 (0)	0 (0)
	accentuation of lobular structure		0 (0)	3 (100)

APPENDIX A 6-3

GROSS FINDINGS (TWO-WEEK STUDY: SUMMARY)

RAT: MALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0263
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name NO. of Animals	Control 0 (%)	100 ppm 0 (%)	200 ppm 0 (%)	400 ppm 0 (%)
liver	red zone		- (-)	- (-)	- (-)	- (-)
	accentuation of lobular structure		- (-)	- (-)	- (-)	- (-)
testis	red		- (-)	- (-)	- (-)	- (-)

STUDY NO. : 0263
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name NO. of Animals	800 ppm 0 (%)	1600 ppm 3 (%)
liver	red zone		- (-)	3 (100)
	accentuation of lobular structure		- (-)	3 (100)
testis	red		- (-)	2 (67)

APPENDIX A 6-4

GROSS FINDINGS (TWO-WEEK STUDY: SUMMARY)

RAT: FEMALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0263
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name / NO. of Animals	Control 0 (%)	100 ppm 0 (%)	200 ppm 0 (%)	400 ppm 0 (%)
lung	red zone		- (-)	- (-)	- (-)	- (-)
liver	red zone		- (-)	- (-)	- (-)	- (-)
	accentuation of lobular structure		- (-)	- (-)	- (-)	- (-)
abdominal c	hemorrhage		- (-)	- (-)	- (-)	- (-)
	ascites		- (-)	- (-)	- (-)	- (-)
thoracic ca	pleural fluid		- (-)	- (-)	- (-)	- (-)

STUDY NO. : 0263
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name NO. of Animals	800 ppm 0 (%)	1600 ppm 7 (%)
lung	red zone		- (-)	3 (43)
liver	red zone		- (-)	6 (86)
	accentuation of lobular structure		- (-)	5 (71)
abdominal c	hemorrhage		- (-)	2 (29)
	ascites		- (-)	2 (29)
thoracic ca	pleural fluid		- (-)	3 (43)

APPENDIX A 6-5

GROSS FINDINGS (TWO-WEEK STUDY: SUMMARY)

MOUSE: MALE : SACRIFICED ANIMALS

STUDY NO. : 0264
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name / NO. of Animals	Control 10 (%)	100 ppm 10 (%)	200 ppm 10 (%)	400 ppm 10 (%)
spleen	black zone		0 (0)	0 (0)	1 (10)	0 (0)
kidney	hydronephrosis		0 (0)	0 (0)	0 (0)	2 (20)

STUDY NO. : 0264
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (2W)

Organ	Findings	Group Name	800 ppm	1600 ppm
		NO. of Animals	10 (%)	10 (%)
spleen	black zone		1 (10)	1 (10)
kidney	hydronephrosis		0 (0)	0 (0)

APPENDIX A 7-1

ORGAN WEIGHT (TWO-WEEK STUDY: SUMMARY),ABSOLUTE

RAT : MALE

STUDY NO. : 0263
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	5	173± 9	0.319± 0.046	0.034± 0.005	2.007± 0.215	0.646± 0.036	0.736± 0.041
100 ppm	5	177± 13	0.309± 0.042	0.033± 0.004	2.138± 0.213	0.649± 0.036	0.763± 0.038
200 ppm	5	174± 14	0.314± 0.033	0.031± 0.005	2.028± 0.304	0.636± 0.047	0.732± 0.064
400 ppm	5	168± 7	0.284± 0.029	0.040± 0.009	2.148± 0.211	0.630± 0.010	0.748± 0.054
800 ppm	5	149± 11*	0.234± 0.040*	0.036± 0.005	1.953± 0.199	0.561± 0.043**	0.699± 0.065
1600 ppm	5	110± 13**	0.064± 0.059**	0.037± 0.010	1.438± 0.377**	0.475± 0.020**	0.637± 0.044*

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

STUDY NO. : 0263
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	1.247± 0.075	0.376± 0.049	6.788± 0.748	1.645± 0.076
100 ppm	5	1.311± 0.095	0.380± 0.042	7.842± 0.801	1.672± 0.039
200 ppm	5	1.306± 0.035	0.393± 0.049	7.777± 0.936	1.595± 0.093
400 ppm	5	1.335± 0.079	0.371± 0.022	7.363± 0.637	1.640± 0.112
800 ppm	5	1.237± 0.115	0.343± 0.038	6.354± 0.659	1.619± 0.070
1600 ppm	5	1.242± 0.085	0.289± 0.027**	7.842± 0.483	1.547± 0.043

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

APPENDIX A 7-2

ORGAN WEIGHT (TWO-WEEK STUDY: SUMMARY),ABSOLUTE

RAT : FEMALE

STUDY NO. : 0263
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	5	124± 3	0.267± 0.042	0.041± 0.008	0.058± 0.009	0.481± 0.025	0.595± 0.046
100 ppm	5	129± 4	0.279± 0.022	0.044± 0.005	0.061± 0.010	0.515± 0.012	0.621± 0.034
200 ppm	5	123± 4	0.256± 0.024	0.041± 0.006	0.062± 0.010	0.505± 0.032	0.594± 0.049
400 ppm	5	114± 4**	0.235± 0.017	0.039± 0.010	0.058± 0.009	0.460± 0.025	0.551± 0.051
800 ppm	5	113± 6**	0.212± 0.028*	0.038± 0.005	0.047± 0.009	0.464± 0.040	0.568± 0.036
1600 ppm	3	94± 3**	0.044± 0.010**	0.035± 0.003	0.048± 0.003	0.418± 0.025*	0.621± 0.034

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

STUDY NO. : 0263
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.932± 0.038	0.267± 0.015	4.453± 0.427	1.527± 0.088
100 ppm	5	1.019± 0.029*	0.282± 0.011	5.122± 0.159	1.557± 0.046
200 ppm	5	0.986± 0.051	0.279± 0.016	4.810± 0.225	1.551± 0.069
400 ppm	5	0.945± 0.062	0.265± 0.019	4.266± 0.339	1.543± 0.072
800 ppm	5	0.950± 0.039	0.258± 0.009	4.483± 0.265	1.537± 0.034
1600 ppm	3	1.007± 0.013	0.230± 0.027*	5.947± 1.338	1.471± 0.105

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

APPENDIX A 7-3

ORGAN WEIGHT (TWO-WEEK STUDY: SUMMARY),ABSOLUTE

MOUSE: MALE

STUDY NO. : 0264
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	5	24.3± 1.3	0.051± 0.010	0.011± 0.001	0.177± 0.018	0.115± 0.012	0.138± 0.010
100 ppm	5	24.9± 1.3	0.043± 0.011	0.009± 0.002	0.171± 0.023	0.125± 0.021	0.142± 0.007
200 ppm	5	24.7± 1.1	0.044± 0.006	0.009± 0.002	0.177± 0.011	0.116± 0.007	0.138± 0.010
400 ppm	5	24.8± 0.7	0.039± 0.008	0.010± 0.002	0.167± 0.035	0.119± 0.014	0.136± 0.014
800 ppm	5	23.7± 0.7	0.039± 0.007	0.008± 0.002	0.175± 0.018	0.111± 0.015	0.140± 0.020
1600 ppm	5	23.0± 0.7	0.026± 0.009**	0.008± 0.002	0.158± 0.013	0.108± 0.005	0.155± 0.009

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

STUDY NO. : 0264
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.362± 0.027	0.047± 0.006	1.278± 0.057	0.424± 0.008
100 ppm	5	0.399± 0.041	0.043± 0.006	1.422± 0.159	0.419± 0.013
200 ppm	5	0.390± 0.035	0.045± 0.007	1.470± 0.149	0.438± 0.008
400 ppm	5	0.398± 0.047	0.048± 0.007	1.628± 0.160**	0.426± 0.015
800 ppm	5	0.383± 0.028	0.046± 0.009	1.375± 0.121	0.420± 0.017
1600 ppm	5	0.374± 0.018	0.039± 0.008	1.478± 0.062	0.416± 0.011

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

APPENDIX A 7-4

ORGAN WEIGHT (TWO-WEEK STUDY: SUMMARY),ABSOLUTE

MOUSE: FEMALE

STUDY NO. : 0264
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	5	20.0± 0.9	0.064± 0.006	0.010± 0.003	0.017± 0.004	0.093± 0.008	0.125± 0.008
100 ppm	5	19.7± 0.5	0.063± 0.011	0.009± 0.002	0.013± 0.005	0.093± 0.004	0.128± 0.009
200 ppm	5	20.0± 0.8	0.055± 0.007	0.011± 0.003	0.015± 0.004	0.094± 0.004	0.122± 0.008
400 ppm	5	20.8± 1.0	0.059± 0.005	0.010± 0.002	0.014± 0.003	0.101± 0.006	0.133± 0.014
800 ppm	5	19.6± 0.6	0.057± 0.007	0.009± 0.002	0.014± 0.001	0.096± 0.007	0.133± 0.020
1600 ppm	5	18.7± 0.9*	0.030± 0.004**	0.009± 0.003	0.014± 0.004	0.091± 0.010	0.146± 0.013

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

STUDY NO. : 0264
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.254± 0.008	0.051± 0.004	1.011± 0.105	0.413± 0.023
100 ppm	5	0.248± 0.012	0.049± 0.005	1.067± 0.055	0.405± 0.020
200 ppm	5	0.246± 0.014	0.047± 0.007	1.166± 0.112	0.408± 0.016
400 ppm	5	0.271± 0.012	0.053± 0.005	1.273± 0.095**	0.414± 0.014
800 ppm	5	0.261± 0.021	0.050± 0.006	1.146± 0.109	0.436± 0.021
1600 ppm	5	0.264± 0.019	0.053± 0.013	1.282± 0.141**	0.399± 0.015

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

APPENDIX A 8-1

ORGAN WEIGHT (TWO-WEEK STUDY: SUMMARY),RELATIVE

RAT: MALE

STUDY NO. : 0263
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	5	173± 9	0.184± 0.024	0.020± 0.002	1.160± 0.096	0.374± 0.016	0.427± 0.021
100 ppm	5	177± 13	0.174± 0.016	0.019± 0.002	1.209± 0.109	0.367± 0.014	0.432± 0.015
200 ppm	5	174± 14	0.181± 0.018	0.018± 0.003	1.159± 0.100	0.365± 0.013	0.420± 0.023
400 ppm	5	168± 7	0.170± 0.021	0.024± 0.005	1.280± 0.088	0.377± 0.010	0.446± 0.029
800 ppm	5	149± 11*	0.156± 0.019	0.024± 0.002	1.305± 0.053	0.376± 0.018	0.467± 0.010
1600 ppm	5	110± 13**	0.054± 0.043**	0.035± 0.013	1.297± 0.220	0.437± 0.052	0.585± 0.042**

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

STUDY NO. : 0263
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.721± 0.013	0.217± 0.018	3.919± 0.241	0.953± 0.039
100 ppm	5	0.741± 0.026	0.214± 0.008	4.424± 0.161	0.948± 0.064
200 ppm	5	0.753± 0.045	0.225± 0.013	4.452± 0.199*	0.921± 0.098
400 ppm	5	0.797± 0.042	0.221± 0.008	4.387± 0.206	0.979± 0.068
800 ppm	5	0.827± 0.023*	0.229± 0.011	4.245± 0.145	1.087± 0.063
1600 ppm	5	1.152± 0.201**	0.264± 0.019**	7.262± 1.194**	1.428± 0.181**

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

APPENDIX A 8-2

ORGAN WEIGHT (TWO-WEEK STUDY: SUMMARY),RELATIVE

RAT: FEMALE

STUDY NO. : 0263
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	5	124± 3	0.216± 0.032	0.033± 0.006	0.047± 0.006	0.389± 0.023	0.481± 0.036
100 ppm	5	129± 4	0.217± 0.018	0.034± 0.005	0.048± 0.007	0.401± 0.011	0.483± 0.025
200 ppm	5	123± 4	0.209± 0.019	0.034± 0.005	0.051± 0.009	0.412± 0.028	0.484± 0.026
400 ppm	5	114± 4**	0.207± 0.017	0.034± 0.008	0.051± 0.010	0.404± 0.022	0.484± 0.042
800 ppm	5	113± 6**	0.188± 0.019	0.034± 0.006	0.041± 0.006	0.412± 0.026	0.505± 0.029
1600 ppm	3	94± 3**	0.047± 0.011**	0.038± 0.004	0.052± 0.005	0.445± 0.027	0.661± 0.057**

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

STUDY NO. : 0263
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.754± 0.013	0.216± 0.008	3.597± 0.267	1.236± 0.076
100 ppm	5	0.793± 0.033	0.219± 0.004	3.984± 0.096	1.213± 0.074
200 ppm	5	0.804± 0.033	0.228± 0.008	3.926± 0.196	1.265± 0.035
400 ppm	5	0.831± 0.043**	0.233± 0.013	3.744± 0.184	1.356± 0.031
800 ppm	5	0.844± 0.021**	0.229± 0.008	3.981± 0.098	1.368± 0.088*
1600 ppm	3	1.072± 0.026**	0.246± 0.036	6.318± 1.319**	1.567± 0.149**

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

APPENDIX A 8-3

ORGAN WEIGHT (TWO-WEEK STUDY: SUMMARY),RELATIVE

MOUSE: MALE

STUDY NO. : 0264
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	5	24.3± 1.3	0.208± 0.038	0.044± 0.005	0.726± 0.043	0.472± 0.045	0.568± 0.045
100 ppm	5	24.9± 1.3	0.173± 0.043	0.037± 0.009	0.685± 0.075	0.498± 0.061	0.572± 0.038
200 ppm	5	24.7± 1.1	0.178± 0.030	0.037± 0.008	0.715± 0.044	0.468± 0.016	0.558± 0.041
400 ppm	5	24.8± 0.7	0.158± 0.028	0.040± 0.008	0.675± 0.147	0.479± 0.054	0.550± 0.048
800 ppm	5	23.7± 0.7	0.163± 0.025	0.032± 0.007	0.740± 0.071	0.468± 0.055	0.588± 0.072
1600 ppm	5	23.0± 0.7	0.114± 0.036**	0.037± 0.011	0.685± 0.064	0.469± 0.023	0.673± 0.049*

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

STUDY NO. : 0264
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	1.485± 0.064	0.194± 0.027	5.263± 0.367	1.745± 0.077
100 ppm	5	1.597± 0.093	0.173± 0.025	5.695± 0.459	1.682± 0.100
200 ppm	5	1.575± 0.084	0.183± 0.025	5.940± 0.470	1.776± 0.071
400 ppm	5	1.608± 0.193	0.196± 0.027	6.568± 0.528**	1.722± 0.055
800 ppm	5	1.616± 0.087	0.195± 0.034	5.797± 0.355	1.773± 0.079
1600 ppm	5	1.624± 0.088	0.170± 0.034	6.430± 0.459**	1.807± 0.077

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

APPENDIX A 8-4

ORGAN WEIGHT (TWO-WEEK STUDY: SUMMARY),RELATIVE

MOUSE: FEMALE

STUDY NO. : 0264
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	5	20.0± 0.9	0.322± 0.027	0.051± 0.013	0.086± 0.021	0.465± 0.032	0.622± 0.024
100 ppm	5	19.7± 0.5	0.320± 0.057	0.047± 0.010	0.066± 0.025	0.473± 0.024	0.647± 0.040
200 ppm	5	20.0± 0.8	0.276± 0.028	0.053± 0.013	0.074± 0.019	0.471± 0.017	0.611± 0.041
400 ppm	5	20.8± 1.0	0.283± 0.026	0.048± 0.011	0.068± 0.016	0.489± 0.038	0.641± 0.074
800 ppm	5	19.6± 0.6	0.291± 0.034	0.046± 0.007	0.072± 0.003	0.488± 0.025	0.678± 0.099
1600 ppm	5	18.7± 0.9*	0.159± 0.028**	0.046± 0.015	0.074± 0.022	0.487± 0.033	0.782± 0.058**

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

STUDY NO. : 0264
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	1.268± 0.056	0.253± 0.014	5.039± 0.386	2.067± 0.213
100 ppm	5	1.257± 0.074	0.248± 0.025	5.411± 0.393	2.053± 0.093
200 ppm	5	1.228± 0.039	0.235± 0.033	5.821± 0.470*	2.039± 0.072
400 ppm	5	1.306± 0.077	0.255± 0.020	6.135± 0.436**	2.001± 0.133
800 ppm	5	1.334± 0.071	0.254± 0.022	5.843± 0.384*	2.227± 0.108
1600 ppm	5	1.415± 0.071**	0.281± 0.060	6.863± 0.626**	2.142± 0.090

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

APPENDIX A 9-1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

RAT : MALE : SACRIFICED ANIMALS

STUDY NO. : 0263
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control				100 ppm				200 ppm				400 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]																		
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]																		
liver			< 2>				< 2>				< 2>				< 2>			
	herniation		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(50)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:focal		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:single cell		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	fibrosis		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Reproductive system]																		
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	800 ppm				1600 ppm			
		No. of Animals on Study	2				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
thymus			< 2>				< 2>			
	atrophy		0	0	0	0	1	0	1	0
			(0)	(0)	(0)	(0)	(50)	(0)	(50)	(0)
[Digestive system]										
liver			< 2>				< 2>			
	herniation		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:focal		0	0	0	0	0	2	0	0
			(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
	necrosis:single cell		2	0	0	0	0	0	0	0
			(100)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	fibrosis		0	0	0	0	0	2	0	0
			(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
[Reproductive system]										
testis			< 2>				< 2>			
	germ cell necrosis		0	0	0	0	1	1	0	0
			(0)	(0)	(0)	(0)	(50)	(50)	(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				100 ppm				200 ppm				400 ppm			
			2				2				2				2			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Reproductive system]																		
epididymis			< 2>				< 2>				< 2>				< 2>			
	decreased:sperma		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	debris of spermatic elements		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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	800 ppm				1600 ppm			
		No. of Animals on Study	2				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Reproductive system]										
epididymis			< 2>				< 2>			
	decreased:sperma		0	0	0	0	0	0	1	0
			(0)	(0)	(0)	(0)	(0)	(0)	(50)	(0)
	debris of spermatic elements		0	0	0	0	1	1	0	0
			(0)	(0)	(0)	(0)	(50)	(50)	(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 A 9-2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

RAT : FEMALE : SACRIFICED ANIMALS

Organ	Findings	Group Name	Control				100 ppm				200 ppm				400 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]																		
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)
[Circulatory system]																		
heart			< 2>				< 2>				< 2>				< 2>			
	necrosis:focal		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	granulation		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]																		
liver			< 2>				< 2>				< 2>				< 2>			
	increase in mitosis		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:focal		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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	800 ppm				1600 ppm			
		No. of Animals on Study	2				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Hematopoietic system]										
thymus			< 2>				< 2>			
	atrophy		0	0	0	0	0	2	0	0
			(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
[Circulatory system]										
heart			< 2>				< 2>			
	necrosis:focal		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
	granulation		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
[Digestive system]										
liver			< 2>				< 2>			
	increase in mitosis		0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(50)	(0)	(0)
	necrosis:focal		0	0	0	0	0	2	0	0
			(0)	(0)	(0)	(0)	(0)	(100)	(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				100 ppm				200 ppm				400 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>			
	necrosis:single cell		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	fibrosis		0	0	0	0	0	0	0	0	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	800 ppm				1600 ppm			
		No. of Animals on Study	2				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]										
liver			< 2>				< 2>			
	necrosis:single cell		1	1	0	0	0	0	0	0
			(50)	(50)	(0)	(0)	(0)	(0)	(0)	(0)
	fibrosis		0	0	0	0	1	1	0	0
			(0)	(0)	(0)	(0)	(50)	(50)	(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 A 9-3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

RAT : MALE : DEAD AND MORIBUND ANIMALS

STUDY NO. : 0263
ANIMAL : RAT F344
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				100 ppm 0				200 ppm 0				400 ppm 0			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]																		
bone marrow		< 0>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	congestion	(0)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	hemorrhage	(0)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
thymus		< 0>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	hemorrhage	(0)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	karyorrhexis	(0)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
spleen		< 0>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	karyorrhexis	(0)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Circulatory system]																		
heart		< 0>	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
	hemorrhage	(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	Grade	800 ppm 0				1600 ppm 1			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Hematopoietic system]										
bone marrow			< 0>				< 1>			
	congestion		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
	hemorrhage		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
thymus			< 0>				< 1>			
	hemorrhage		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
	karyorrhexis		-	-	-	-	0	0	1	0
			(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)
spleen			< 0>				< 1>			
	karyorrhexis		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
[Circulatory system]										
heart			< 0>				< 1>			
	hemorrhage		-	-	-	-	1	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

Organ	Findings	Group Name	Control				100 ppm				200 ppm				400 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>			
	necrosis:central		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Reproductive system]																		
testis			< 0>				< 0>				< 0>				< 0>			
	hemorrhage		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	germ cell necrosis		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
epididymis			< 0>				< 0>				< 0>				< 0>			
	debris of spermatic elements		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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	800 ppm				1600 ppm			
		No. of Animals on Study	0				1			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]										
liver			< 0>				< 1>			
	necrosis:central		-	-	-	-	0	0	1	0
			(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)
[Reproductive system]										
testis			< 0>				< 1>			
	hemorrhage		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
	germ cell necrosis		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
epididymis			< 0>				< 1>			
	debris of spermatic elements		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(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 A 9-4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

RAT : FEMALE : DEAD AND MORIBUND ANIMALS

Organ	Findings	Group Name	Control				100 ppm				200 ppm				400 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
lung			< 0>				< 0>				< 0>				< 0>			
	congestion		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Hematopoietic system]																		
bone marrow			< 0>				< 0>				< 0>				< 0>			
	congestion		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	hemorrhage		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
thymus			< 0>				< 0>				< 0>				< 0>			
	hemorrhage		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	karyorrhexis		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
spleen			< 0>				< 0>				< 0>				< 0>			
	karyorrhexis		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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	800 ppm				1600 ppm			
		No. of Animals on Study	0				1			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
lung			< 0>				< 1>			
	congestion		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
[Hematopoietic system]										
bone marrow			< 0>				< 1>			
	congestion		-	-	-	-	0	1	0	0
			(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)
	hemorrhage		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
thymus			< 0>				< 1>			
	hemorrhage		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
	karyorrhexis		-	-	-	-	0	0	1	0
			(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)
spleen			< 0>				< 1>			
	karyorrhexis		-	-	-	-	1	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

Organ	Findings	Group Name	Control				100 ppm				200 ppm				400 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 (%)
[Circulatory system]																		
heart			< 0>				< 0>				< 0>				< 0>			
	hemorrhage		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Digestive system]																		
liver			< 0>				< 0>				< 0>				< 0>			
	necrosis:central		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Nervous system]																		
brain			< 0>				< 0>				< 0>				< 0>			
	hemorrhage		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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	800 ppm				1600 ppm			
		No. of Animals on Study	0				1			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Circulatory system]										
heart			< 0>				< 1>			
	hemorrhage		-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
[Digestive system]										
liver			< 0>				< 1>			
	necrosis:central		-	-	-	-	0	0	1	0
			(-)	(-)	(-)	(-)	(0)	(0)	(100)	(0)
[Nervous system]										
brain			< 0>				< 1>			
	hemorrhage		-	-	-	-	1	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 A 9-5

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

MOUSE : MALE : SACRIFICED ANIMALS

STUDY NO. : 0264
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name	Control				100 ppm				200 ppm				400 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
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
lung			< 2>				< 2>				< 2>				< 2>			
	hemorrhage		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(50)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Hematopoietic system]																		
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]																		
liver			< 2>				< 2>				< 2>				< 2>			
	necrosis:focal		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)	(0)	(0)	(0)	(0)
	necrosis:single cell		0	0	0	0	0	0	0	0	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:central		0	0	0	0	0	0	0	0	1	1	0	0	0	2	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(50)	(50)	(0)	(0)	(0)	(100)	(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	800 ppm				1600 ppm			
		No. of Animals on Study	2				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
lung			< 2>				< 2>			
	hemorrhage		1	0	0	0	0	0	0	0
			(50)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Hematopoietic system]										
thymus			< 2>				< 2>			
	atrophy		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
[Digestive system]										
liver			< 2>				< 2>			
	necrosis:focal		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:single cell		0	0	0	0	1	1	0	0
			(0)	(0)	(0)	(0)	(50)	(50)	(0)	(0)
	degeneration:central		0	2	0	0	0	1	1	0
			(0)	(100)	(0)	(0)	(0)	(50)	(50)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

Organ	Findings	Group Name	Control				100 ppm				200 ppm				400 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>			
	granulation		1 (50)	0 (0)	0 (0)	0 (0)	2 (100)	0 (0)	0 (0)	0 (0)	1 (50)	0 (0)	0 (0)	0 (0)	2 (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

Organ	Findings	Group Name	800 ppm				1600 ppm			
		No. of Animals on Study	2				2			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]										
liver			< 2>				< 2>			
	granulation		2 (100)	0 (0)	0 (0)	0 (0)	1 (50)	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 A 9-6

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS

(TWO-WEEK STUDY: SUMMARY)

MOUSE : FEMALE : SACRIFICED ANIMALS

Organ	Findings	Group Name	Control	100 ppm	200 ppm	400 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
			(%) (%) (%) (%)	(%) (%) (%) (%)	(%) (%) (%) (%)	(%) (%) (%) (%)
[Respiratory system]						
lung			< 2>	< 2>	< 2>	< 2>
	hemorrhage		1 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0
			(50) (0) (0) (0)	(0) (0) (0) (0)	(0) (0) (0) (0)	(0) (0) (0) (0)
	pleuritis		0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0
			(0) (0) (0) (0)	(0) (0) (0) (0)	(0) (0) (0) (0)	(0) (0) (0) (0)
[Hematopoietic system]						
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)
[Circulatory system]						
heart			< 2>	< 2>	< 2>	< 2>
	inflammation		0 0 0 0	0 0 0 0	0 0 0 0	0 0 0 0
			(0) (0) (0) (0)	(0) (0) (0) (0)	(0) (0) (0) (0)	(0) (0) (0) (0)
[Digestive system]						
liver			< 2>	< 2>	< 2>	< 2>
	necrosis:single cell		0 0 0 0	0 0 0 0	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	800 ppm				1600 ppm			
		No. of Animals on Study	2				2			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]										
lung			< 2>				< 2>			
	hemorrhage		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	pleuritis		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
[Hematopoietic system]										
thymus			< 2>				< 2>			
	atrophy		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
[Circulatory system]										
heart			< 2>				< 2>			
	inflammation		1	0	0	0	0	0	0	0
			(50)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]										
liver			< 2>				< 2>			
	necrosis:single cell		0	0	0	0	0	1	1	0
			(0)	(0)	(0)	(0)	(0)	(50)	(50)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe
< a > a : Number of animals examined at the site
b b : Number of animals with lesion
(c) c : b / a * 100

STUDY NO. : 0264
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

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

Organ	Findings	Group Name	Control				100 ppm				200 ppm				400 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>			
	degeneration:central		0	0	0	0	0	0	0	0	2	0	0	0	0	2	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
	granulation		2	0	0	0	2	0	0	0	2	0	0	0	1	0	0	0
			(100)	(0)	(0)	(0)	(100)	(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

Organ	Findings	Group Name	800 ppm				1600 ppm			
		No. of Animals on Study	2				2			
		Grade	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
[Digestive system]										
liver			< 2>				< 2>			
	degeneration:central		2 (100)	0 (0)	0 (0)	0 (0)	1 (50)	1 (50)	0 (0)	0 (0)
	granulation		2 (100)	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

APPENDIX A 10-1

IDENTITY OF *N,N*-DIMETHYLFORMAMIDE (TWO-WEEK STUDY)

IDENTITY OF *N,N*-DIMETHYLFORMAMIDE(TWO-WEEK STUDIES)

Lot no. PTE4986

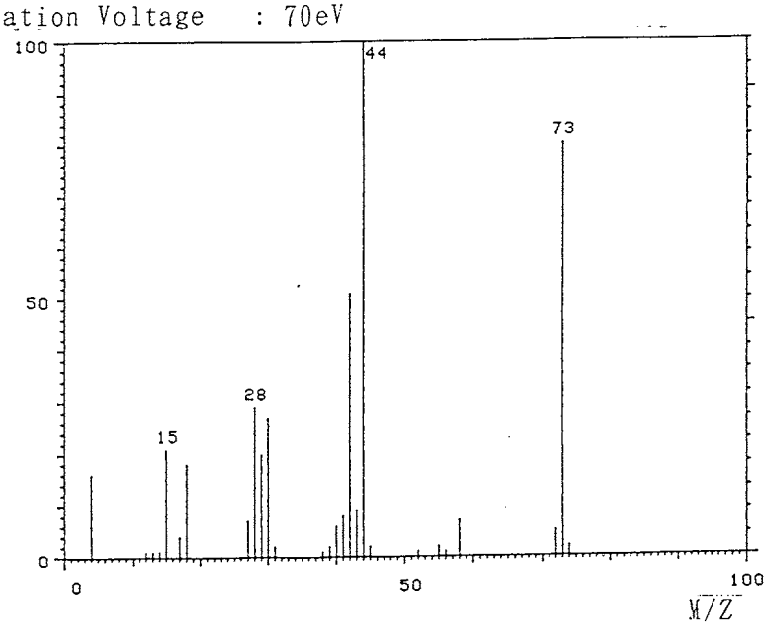
1. Spectral data

Mass Spectrometry

Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance

Results: The mass spectrum was consistent with literature spectrum.

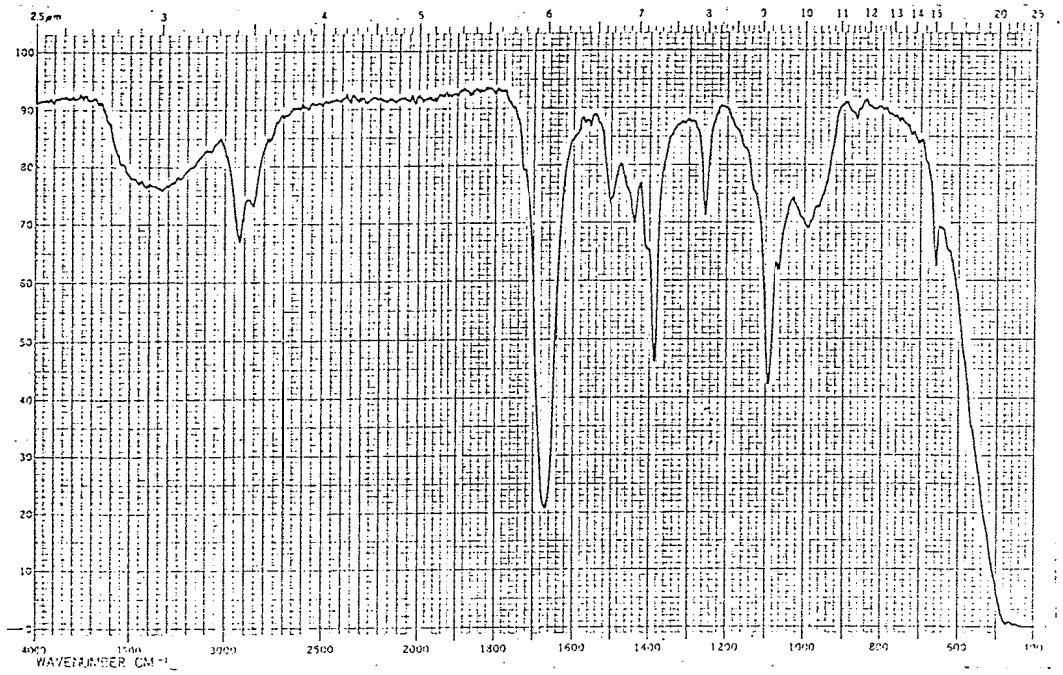
Determined Values Fragment Peak(M/Z)	Literature Values* Fragment Peak(M/Z)
15	15
28	28
44(Base Peak)	44(Base Peak)
73	73
	(*EPA/NIH Mass Spectral Data Base (1978) Vol. 1, p. 20.)

Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium



Infrared Spectrum of Test Substance

Results: The infrared spectrum was consistent with literature spectrum.

Determined Values Wave Number(cm^{-1})	Literature Values* Wave Number(cm^{-1})
650～ 680	650～ 680
850～ 890	850～ 890
920～1030	
1030～1150	1030～1150
1220～1280	1220～1280
1350～1430	1350～1430
1430～1480	1430～1480
1480～1540	1480～1540
1600～1760	1600～1760
2800～3000	2800～3000
3100～3650	3100～3700

(*Performed by the WAKO PURE CHEMICAL INDUSTRIES, LTD.)

2. Conclusions: The test substance was identified as *N,N*-Dimethylformamide, by the mass spectrum and the infrared spectrum.

APPENDIX A 10-2

STABILITY OF *N,N*-DIMETHYLFORMAMIDE (TWO-WEEK STUDY)

STABILITY OF *N,N*-DIMETHYLFORMAMIDE(TWO-WEEK STUDIES)

Lot no. PTE4986

1. Sample: This lot was used from 1994.3.22 to 1994.4.12. Test substance was stored at room temperature .

2. Infrared Spectrometry

Instrument : Hitachi 270-30 Infrared Spectrometer

Cell : KBr

Slit : Medium

Results: The result of infrared spectrum did not change when before and after studies.

1994.03.09(date analyzed)	1994.04.13(date analyzed)
Wave Number(cm^{-1})	Wave Number(cm^{-1})
650～ 680	650～ 680
850～ 890	850～ 890
920～1030	920～1030
1030～1150	1030～1150
1220～1280	1220～1280
1350～1430	1350～1430
1430～1480	1430～1480
1480～1540	1480～1540
1600～1760	1600～1760
2800～3000	2800～3000
3100～3650	3100～3650

3. Gas Chromatography

Instrument: Hewlett Packard 5890A Gas Chromatograph

Column: INNOWax(0.2mmϕ × 50m)

Column Temperature: 150°C

Flow Rate: 1 ml/min

Detector: FID(Flame Ionization Detector)

Injection Volume: 1 μl

Results: Gas chromatography indicated one major peak(peak No.1) analyzed at 1994.3.9 and one major peak(peak No.1) analyzed at 1994.4.13. No new treace impurity peak in the test substance analyzed at 1994.4.13 was detected.

Date	Peak No.	Retention Time(min)	Area Count
1994.03.09 (date analyzed)	1	6.012	28976
1994.04.13 (date analyzed)	1	6.012	29129

4. Conclusions: The test substance was stable for about 1 months in the dark at room temperature.

APPENDIX A 11-1

STABILITY OF BIPHENYL AT THE JAPAN BIOASSAY LABORATORY

(TWO-WEEK STUDY)

CONCENTRATION OF *N,N*-DIMETHYLFORMAMIDE
IN INHALTION CHAMBER
(RAT : TWO-WEEK STUDY)

Group Name	Concentration (ppm) Mean ± S.D.
Control	0.0 ± 0.0
100ppm	96.5 ± 3.1
200ppm	197.6 ± 4.6
400ppm	392.2 ± 10.2
800ppm	779.1 ± 18.7
1600ppm	1554.4 ± 40.4

CONCENTRATION OF *N,N*-DIMETHYLFORMAMIDE
IN INHALTION CHAMBER
(MOUSE : TWO-WEEK STUDY)

Group Name	Concentration (ppm) Mean ± S.D.
Control	0.0 ± 0.0
100ppm	101.1 ± 1.8
200ppm	203.6 ± 5.0
400ppm	407.9 ± 6.1
800ppm	806.6 ± 9.8
1600ppm	1623.8 ± 17.7

APPENDIX A 11-2

ENVIRONMENT OF INHALATION CHAMBER

(TWO-WEEK STUDY)

ENVIRONMENT OF INHALATION CHAMBER (RAT : TWO-WEEK STUDY)

Group Name	Temperature(℃) Mean ± S.D.	Humidity(%) Mean ± S.D.	Ventilation Rate(L/min) Mean ± S.D.	Room Air Change(time/h) Mean
Control	23.0 ± 0.1	54.6 ± 1.1	211.7 ± 0.7	12.0
100ppm	22.4 ± 0.3	53.7 ± 2.1	211.8 ± 0.9	12.0
200ppm	22.7 ± 0.2	53.3 ± 2.6	210.8 ± 0.9	11.9
400ppm	22.7 ± 0.2	48.7 ± 2.4	212.5 ± 0.7	12.0
800ppm	23.3 ± 0.3	48.0 ± 3.2	211.9 ± 1.1	12.0
1600ppm	22.4 ± 0.1	49.1 ± 3.4	212.8 ± 1.5	12.0

ENVIRONMENT OF INHALATION CHAMBER (MOUSE : TWO-WEEK STUDY)

Group Name	Temperature(℃) Mean ± S.D.	Humidity(%) Mean ± S.D.	Ventilation Rate(L/min) Mean ± S.D.	Room Air Change(time/h) Mean
Control	21.9 ± 0.2	53.5 ± 1.2	104.8 ± 0.5	12.1
100ppm	21.9 ± 0.2	50.9 ± 1.9	104.7 ± 1.1	12.1
200ppm	22.1 ± 0.1	50.2 ± 1.8	105.1 ± 1.4	12.1
400ppm	22.4 ± 0.1	48.8 ± 2.0	104.5 ± 0.6	12.1
800ppm	23.1 ± 0.1	46.8 ± 1.9	104.3 ± 1.1	12.0
1600ppm	22.7 ± 0.1	43.7 ± 1.7	104.0 ± 1.5	12.0

APPENDIX A 12

METHODS FOR HEMATOLOGY AND BIOCHEMISTRY

METHODS FOR HEMATOLOGY AND BIOCHEMISTRY (TWO-WEEK STUDIES)

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 activated 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	Michaelson method [4]
Glucose	Enzymatic method (HK·G-6-PDH) [4]
T-cholesterol	Enzymatic method (CEH·COD·POD) [4]
Triglyceride	Enzymatic method (GK·GPO·POD) [4]
Phospholipid	Enzymatic method (PLD·COD·POD) [4]
Glutamic oxaloacetic transaminase (GOT)	Karmen method [4]
Glutamic pyruvic transaminase (GPT)	Karmen method [4]
Lactate dehydrogenase (LDH)	Wroblewski-LaDue method [4]
Alkaline phosphatase (ALP)	GSCC method [4]
γ-Glutamyl transpeptidase (G-GTP)	L-γ-Glutamyl-p-nitroanilide substrate method [4]
Creatine phosphokinase (CPK)	GSCC method [4]
Urea nitrogen	Enzymatic method (Urease·GLDH) [4]
Creatinine	Jaffe metod [4]
Sodium	Flame photometry [5]
Potassium	Flame photometry [5]
Chloride	Coulometric titration [5]
Calcium	OCPC method [4]
Inorganic phosphorus	Enzymatic method (SPL·PGM·G-6-PDH) [4]

1) Automatic blood cell analyzer (Technicon H·1 : Technicon Instruments Corporation,USA)
2) Automatic coagulometer (Sysmex CA-5000 : Toa Medical Electronics Co.,Ltd.,Japan)
3) Automatic blood cell differential analyzer (Hitachi 8200 : Hitachi,Ltd.,Japan)
4) Automatic analyzer (Hitachi 705 : Hitachi,Ltd.,Japan)
5) Flame photometer (Hitachi 750 : Hitachi,Ltd.,Japan)