

プロピオノニトリルのラットを用いた
吸入による2週間毒性試験報告書

試験番号：0446

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APPENDIX A 1

CLINICAL OBSERVATION : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0446
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

PAGE : 1

Clinical sign	Group Name	Administration Week-day				
		1-2	1-4	1-7	2-3	2-7
		1	1	1	1	1
<hr/>						
SALIVATION	Control	0	0	0	0	0
	25ppm	0	0	0	0	0
	50ppm	0	0	0	0	0
	100ppm	1	0	0	0	0
	200ppm	0	-	-	-	-
	400ppm	0	-	-	-	-

(HAN190)

BAS 4

APPENDIX A 2

CLINICAL OBSERVATION : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0446
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 2

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

PAGE : 2

Clinical sign	Group Name	Administration Week-day				
		1-2	1-4	1-7	2-3	2-7
		1	1	1	1	1
WASTING	Control	0	0	0	0	0
	25ppm	0	0	0	0	0
	50ppm	0	0	0	0	0
	100ppm	0	0	0	0	0
	200ppm	0	0	0	0	0
	400ppm	0	1	1	0	0
PILOBRECTION	Control	0	0	0	0	0
	25ppm	0	0	0	0	0
	50ppm	0	0	0	0	0
	100ppm	0	0	0	0	0
	200ppm	0	0	0	0	0
	400ppm	0	1	1	0	0

(HAN190)

BATS 4

APPENDIX B 1

BODY WEIGHT CHANGES : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0446
 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	1-2	1-4	1-7	2-3	2-7
Control	119± 4	128± 3	132± 3	142± 4	151± 6	167± 9
25ppm	119± 3	128± 5	132± 6	141± 6	148± 8	162± 11
50ppm	119± 3	129± 3	134± 3	143± 3	153± 2	167± 3
100ppm	120± 3	120± 11	122± 7*	133± 9	139± 7*	154± 9
200ppm	120± 4	-	-	-	-	-
400ppm	119± 4	-	-	-	-	-

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

APPENDIX B 2

BODY WEIGHT CHANGES : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0446
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 2
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

Group Name	Administration		week-day		1-2		1-4		1-7		2-3		2-7	
	0-0													
Control	95±	3	100±	3	102±	5	107±	5	112±	5	118±	4		
25ppm	95±	3	101±	3	101±	3	108±	4	109±	3	116±	3		
50ppm	95±	3	100±	4	101±	4	107±	4	110±	4	115±	4		
100ppm	95±	3	97±	4	98±	4	103±	3	107±	3	114±	3		
200ppm	94±	4	96±	4	97±	2	104±	4	107±	4	116±	5		
400ppm	95±	3	84±	4**	84±	9**	84±	18*	98	?	111	?		

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

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

APPENDIX C 1

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0446
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 2
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective)	
	1-7(6)	2-7(7)
Control	14.4± 0.7	14.1± 0.8
25ppm	14.3± 0.9	14.0± 0.9
50ppm	14.9± 0.2	14.1± 0.3
100ppm	11.3± 1.6*	12.9± 0.5*
200ppm	-	-
400ppm	-	-

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

APPENDIX C 2

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0446
ANIMAL : RAT F344/DuCrj
UNIT : g
REPORT TYPE : A1 2
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

PAGE : 2

Group Name	Administration week-day(effective)	
	1-7(6)	2-7(7)
Control	11.2± 0.3	10.4± 0.4
25ppm	11.3± 0.6	10.2± 0.4
50ppm	11.4± 0.4	10.2± 0.6
100ppm	9.5± 0.7	10.1± 0.3
200ppm	9.4± 0.8	9.9± 0.6
400ppm	5.7± 2.5*	9.5 ?

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

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

APPENDIX D 1

HEMATOLOGY : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0446
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : MALE

HEMATOLOGY (SUMMARY)
 ALL ANIMALS (3W)

REPORT TYPE : A1

PAGE : 1

Group Name	NO. of Animals	RED BLOOD CELL 10 ⁶ /μℓ		HEMOGLOBIN g/dℓ		HEMATOCRIT %		MCV fℓ		MCH p g		MCHC g/dℓ		PLATELET 10 ³ /μℓ	
Control	5	8.45±	0.30	16.2±	0.4	43.8±	1.1	51.9±	0.7	19.1±	0.3	36.9±	0.3	927±	62
25ppm	5	8.64±	0.13	16.3±	0.2	44.7±	0.4	51.8±	0.6	18.8±	0.2*	36.4±	0.2	906±	52
50ppm	5	8.53±	0.05	16.1±	0.1	44.3±	0.6	51.9±	0.8	18.9±	0.1	36.5±	0.6	958±	60
100ppm	5	8.48±	0.19	15.8±	0.4	43.2±	0.8	50.9±	0.4	18.7±	0.2**	36.6±	0.1	981±	44
200ppm	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-
400ppm	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01

Test of Dunnett

STUDY NO. : 0446
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : MALE

HEMATOLOGY (SUMMARY)
 ALL ANIMALS (3W)

REPORT TYPE : A1

Group Name	NO. of Animals	RETICULOCYTE %		PROTHROMBIN TIME s e c		APTT s e c	
Control	5	2.5±	0.8	15.0±	0.7	21.7±	3.0
25ppm	5	2.2±	0.3	15.0±	0.3	22.7±	1.5
50ppm	5	2.3±	0.2	16.7±	3.2	24.0±	3.2
100ppm	5	3.3±	0.3	15.3±	1.1	19.2±	1.4
200ppm	0	-	-	-	-	-	-
400ppm	0	-	-	-	-	-	-

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

STUDY NO. : 0446
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : MALE

HEMATOLOGY (SUMMARY)
 ALL ANIMALS (3W)

REPORT TYPE : A1

Group Name	NO. of Animals	WBC		Differential		WBC (%)		EOSINO	BASO	MONO	LYMPHO	OTHER					
		10 ⁹ /μl		N-BAND		N-SEG											
Control	5	6.44±	1.74	1±	2	18±	4	1±	1	0±	0	3±	1	77±	6	0±	0
25ppm	5	5.93±	0.42	1±	1	16±	4	1±	1	0±	0	2±	1	79±	4	0±	0
50ppm	5	6.24±	2.30	1±	1	16±	5	0±	1	0±	0	2±	1	80±	6	0±	0
100ppm	5	5.96±	2.02	1±	1	21±	4	1±	1	0±	0	2±	1	75±	4	0±	0
200ppm	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
400ppm	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01

Test of Dunnett

APPENDIX D 2

HEMATOLOGY : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0446
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : FEMALE

HEMATOLOGY (SUMMARY)
 ALL ANIMALS (3W)

REPORT TYPE : A1

PAGE : 4

Group Name	NO. of Animals	RED BLOOD CELL 10 ⁶ /μℓ	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	MCH p g	MCHC g/dℓ	PLATELET 10 ³ /μℓ
Control	4	8.67± 0.08	16.7± 0.2	44.4± 0.5	51.1± 0.2	19.2± 0.1	37.7± 0.1	859± 70
25ppm	5	8.89± 0.12	17.1± 0.3	45.5± 0.8	51.2± 0.5	19.3± 0.2	37.6± 0.1	808± 41
50ppm	5	8.87± 0.30	17.0± 0.5	45.4± 1.5	51.2± 0.4	19.1± 0.1	37.3± 0.3	809± 55
100ppm	5	8.64± 0.24	16.3± 0.4	43.4± 0.9	50.3± 0.8	18.9± 0.2*	37.6± 0.3	908± 85
200ppm	5	8.47± 0.23	16.2± 0.3	43.0± 0.6	50.8± 0.8	19.1± 0.2	37.6± 0.3	984± 52*
400ppm	2	7.33 ?	14.0 ?	38.4 ?	52.5 ?	19.0 ?	36.3 ?	1021 ?

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. : 0446
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : FEMALE

HEMATOLOGY (SUMMARY)
ALL ANIMALS (3W)

REPORT TYPE : A1

Group Name	NO. of Animals	RETICULOCYTE %		PROTHROMBIN TIME s e c		APTT s e c	
Control	4	1.4±	0.2	14.3±	1.0	17.8±	1.9
25ppm	5	1.2±	0.1	14.1±	0.6	18.0±	0.7
50ppm	5	1.3±	0.1	14.7±	0.8	18.7±	0.9
100ppm	5	2.1±	0.2**	14.8±	1.1	18.7±	1.0
200ppm	5	2.7±	0.3**	14.5±	0.4	17.3±	2.1
400ppm	2	6.2	?	16.9	?	21.7	?

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

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

STUDY NO. : 0446
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : FEMALE

HEMATOLOGY (SUMMARY)
 ALL ANIMALS (3W)

REPORT TYPE : A1

PAGE : 6

Group Name	NO. of Animals	WBC		Differential		WBC (%)		EOSINO	BASO	MONO	LYMPHO	OTHER					
		10 ⁹ /μℓ		N-BAND	N-SEG												
Control	4	5.64±	1.94	1±	1	17±	2	1±	1	0±	0	2±	1	79±	2	0±	0
25ppm	5	4.78±	1.19	1±	2	12±	1	1±	1	0±	0	3±	1	83±	3	0±	0
50ppm	5	4.14±	1.43	1±	1	15±	5	1±	1	0±	0	2±	1	81±	6	0±	0
100ppm	5	5.18±	2.05	2±	1	16±	3	1±	1	0±	0	2±	1	80±	4	0±	0
200ppm	5	5.47±	1.10	1±	1	17±	2	1±	0	0±	0	3±	1	78±	3	0±	0
400ppm	2	3.22	?	3	?	34	?	2	?	0	?	3	?	59	?	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

BIOCHEMISTRY : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0446
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : MALE

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (3W)

REPORT TYPE : A1

Group Name	NO. of Animals	TOTAL PROTEIN g/dl		ALBUMIN g/dl		A/G- RATIO		T-BILIRUBIN mg/dl		GLUCOSE mg/dl		T-CHOLESTEROL mg/dl		TRIGLYCERIDE mg/dl	
Control	5	5.7±	0.0	3.7±	0.0	1.9±	0.0	0.11±	0.00	139±	11	52±	5	39±	8
25ppm	5	5.6±	0.1	3.7±	0.0	2.0±	0.1	0.11±	0.01	135±	9	48±	3	27±	5
50ppm	5	5.7±	0.1	3.7±	0.1	1.9±	0.0	0.11±	0.01	140±	6	47±	2	30±	7
100ppm	5	5.8±	0.1	3.8±	0.1	1.9±	0.1	0.12±	0.01	134±	36	53±	4	27±	8
200ppm	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-
400ppm	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Significant difference : * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

STUDY NO. : 0446
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : MALE

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (3W)

REPORT TYPE : A1

PAGE : 2

Group Name	NO. of Animals	PHOSPHOLIPID mg/dl		GOT IU/l		GPT IU/l		LDH IU/l		ALP IU/l		G-GTP IU/l		CPK IU/l	
Control	5	105±	9	53±	8	32±	1	316±	119	673±	62	1±	1	245±	39
25ppm	5	96±	3	61±	2	33±	2	243±	73	665±	44	2±	1	201±	26
50ppm	5	95±	3	58±	4	32±	1	260±	62	692±	32	2±	1	214±	16
100ppm	5	100±	6	63±	9	31±	2	321±	157	599±	52	1±	1	223±	36
200ppm	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-
400ppm	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

STUDY NO. : 0446
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : MALE

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (3W)

REPORT TYPE : A1

PAGE : 3

Group Name	NO. of Animals	UREA NITROGEN mg/dℓ		CREATININE mg/dℓ		SODIUM mEq/ℓ		POTASSIUM mEq/ℓ		CHLORIDE mEq/ℓ		CALCIUM mg/dℓ		INORGANIC PHOSPHORUS mg/dℓ	
Control	5	17.9±	1.6	0.4±	0.1	140±	1	4.1±	0.4	103±	1	10.1±	0.2	8.2±	0.7
25ppm	5	17.7±	2.4	0.4±	0.1	140±	1	3.8±	0.2	104±	2	10.0±	0.2	7.6±	0.6
50ppm	5	17.2±	1.2	0.5±	0.1	140±	1	3.8±	0.4	104±	2	10.1±	0.2	7.7±	0.4
100ppm	5	15.3±	2.1	0.4±	0.0	140±	1	4.1±	0.2	103±	1	10.3±	0.1	8.1±	0.3
200ppm	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-
400ppm	0	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Significant difference : * : P ≤ 0.05 ** : P ≤ 0.01

Test of Dunnett

APPENDIX E 2

BIOCHEMISTRY : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0446
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (3W)

REPORT TYPE : A1

PAGE : 4

Group Name	NO. of Animals	TOTAL PROTEIN g/dl		ALBUMIN g/dl		A/G RATIO		T-BILIRUBIN mg/dl		GLUCOSE mg/dl		T-CHOLESTEROL mg/dl		TRIGLYCERIDE mg/dl	
Control	4	5.7±	0.1	3.7±	0.1	1.9±	0.1	0.13±	0.01	128±	7	63±	4	19±	3
25ppm	5	5.6±	0.1	3.7±	0.1	1.9±	0.1	0.13±	0.01	131±	7	66±	12	16±	4
50ppm	5	5.6±	0.2	3.6±	0.1	1.9±	0.1	0.13±	0.02	120±	12	62±	7	16±	4
100ppm	5	5.5±	0.0	3.5±	0.1	1.8±	0.1	0.14±	0.02	121±	16	68±	6	19±	6
200ppm	5	5.6±	0.0	3.6±	0.0	1.8±	0.1	0.13±	0.01	126±	12	69±	9	18±	2
400ppm	2	5.8	?	3.8	?	1.9	?	0.13	?	158	?	58	?	29	?

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

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

STUDY NO. : 0446
 ANIMAL : RAT F344/DuCrj
 MEASURE, TIME : 1
 SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (3W)

REPORT TYPE : A1

PAGE : 5

Group Name	NO. of Animals	PHOSPHOLIPID mg/dl		GOT IU/l		GPT IU/l		LDH IU/l		ALP IU/l		G-GTP IU/l		CPK IU/l	
Control	4	122±	7	63±	2	29±	2	318±	74	566±	46	2±	1	204±	30
25ppm	5	124±	18	66±	5	28±	3	386±	126	562±	16	3±	1	205±	32
50ppm	5	121±	9	68±	5	29±	1	454±	159	578±	10	2±	1	237±	44
100ppm	5	127±	8	65±	5	29±	4	444±	181	489±	43	2±	1	231±	27
200ppm	5	126±	11	63±	2	29±	3	356±	93	484±	45*	2±	1	193±	11
400ppm	2	127	?	70	?	34	?	363	?	583	?	3	?	200	?

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

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

STUDY NO. : 0446
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (3W)

REPORT TYPE : A1

PAGE : 6

Group Name	NO. of Animals	UREA NITROGEN mg/dl		CREATININE mg/dl		SODIUM mEq/l		POTASSIUM mEq/l		CHLORIDE mEq/l		CALCIUM mg/dl		INORGANIC PHOSPHORUS mg/dl	
Control	4	17.7±	1.0	0.5±	0.0	138±	1	3.7±	0.3	103±	2	10.0±	0.2	7.5±	1.1
25ppm	5	18.4±	0.7	0.5±	0.1	139±	1	3.8±	0.2	105±	2	9.8±	0.2	6.7±	1.0
50ppm	5	17.2±	1.2	0.5±	0.0	139±	2	3.8±	0.3	105±	3	9.9±	0.2	7.0±	0.7
100ppm	5	15.6±	0.7*	0.5±	0.1	137±	1	4.2±	0.3	104±	1	9.8±	0.2	7.1±	1.0
200ppm	5	16.1±	1.5	0.5±	0.0	138±	1	4.0±	0.3	105±	2	9.9±	0.1	7.2±	1.1
400ppm	2	15.2	?	0.5	?	136	?	3.8	?	105	?	9.8	?	6.7	?

Significant difference : * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

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

APPENDIX F 1

GROSS FINDINGS : SUMMARY, RAT : MALE : DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0446
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 3W)

PAGE : 1

Organ	Findings	Group Name NO. of Animals	Control 0 (%)	25ppm 0 (%)	50ppm 0 (%)	100ppm 0 (%)
stomach	gas		- (-)	- (-)	- (-)	- (-)
thoracic ca	pleural fluid		- (-)	- (-)	- (-)	- (-)

(HPT080)

BAIS 4

STUDY NO. : 0446
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 3W)

Organ	Findings	Group Name NO. of Animals	200ppm		400ppm	
			5	(%)	5	(%)
stomach	gas		4	(80)	5	(100)
thoracic ca	pleural fluid		1	(20)	1	(20)

(HPT080)

APPENDIX F 2

GROSS FINDINGS : SUMMARY, RAT : FEMALE : DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0446
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 3W)

PAGE : 3

Organ	Findings	Group Name NO. of Animals	Control			
			0 (%)	25ppm 0 (%)	50ppm 0 (%)	100ppm 0 (%)
thymus	atrophic		- (-)	- (-)	- (-)	- (-)
stomach	gas		- (-)	- (-)	- (-)	- (-)

(HPT080)

BAIS 4

STUDY NO. : 0446
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 3W)

Organ	Findings	Group Name NO. of Animals	200ppm		400ppm	
			0	(%)	3	(%)
thymus	atrophic		-	(-)	1	(33)
stomach	gas		-	(-)	2	(67)

APPENDIX F 3

GROSS FINDINGS : SUMMARY, RAT : FEMALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0446
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (3W)

PAGE : 1

Organ	Findings	Group Name NO. of Animals	Control					
			5	(%)	5	(%)		
					25ppm			
					50ppm			
					100ppm			
			5	(%)	5	(%)	5	(%)

liver	adhesion		0	(0)	0	(0)	0	(0)
	herniation		0	(0)	0	(0)	0	(0)

(HPT080)

BAIS 4

STUDY NO. : 0446
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (3W)

PAGE : 2

Organ	Findings	Group Name NO. of Animals	200ppm		400ppm	
			5	(%)	2	(%)
liver	adhesion		0	(0)	1	(50)
	herniation		1	(20)	1	(50)

(HPT080)

BAIS 4

APPENDIX G 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0446
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE
 UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
 SURVIVAL ANIMALS (3W)

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	5	148± 8	0.277± 0.027	0.038± 0.004	2.280± 0.167	0.612± 0.036	0.707± 0.035
25ppm	5	145± 9	0.285± 0.029	0.037± 0.004	2.310± 0.135	0.605± 0.043	0.693± 0.038
50ppm	5	149± 3	0.274± 0.022	0.035± 0.005	2.331± 0.039	0.641± 0.024	0.691± 0.026
100ppm	5	138± 8	0.233± 0.022*	0.039± 0.002	2.075± 0.279	0.617± 0.035	0.682± 0.031
200ppm	0	-	-	-	-	-	-
400ppm	0	-	-	-	-	-	-

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

STUDY NO. : 0446
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE
 UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
 SURVIVAL ANIMALS (3W)

PAGE : 2

Group Name	NO. of Animals	KIDNEYS		SPLEEN		LIVER		BRAIN	
Control	5	1.257±	0.080	0.362±	0.014	4.623±	0.348	1.735±	0.033
25ppm	5	1.200±	0.082	0.331±	0.033	4.439±	0.401	1.724±	0.030
50ppm	5	1.218±	0.037	0.343±	0.014	4.625±	0.094	1.727±	0.015
100ppm	5	1.206±	0.069	0.318±	0.021*	4.672±	0.488	1.706±	0.030
200ppm	0	-	-	-	-	-	-	-	-
400ppm	0	-	-	-	-	-	-	-	-

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$

Test of Dunnett

APPENDIX G 2

ORGAN WEIGHT, ABSOLUTE: SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0446
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE
 UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
 SURVIVAL ANIMALS (3W)

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	5	105± 3	0.229± 0.015	0.042± 0.005	0.065± 0.012	0.466± 0.039	0.583± 0.021
25ppm	5	103± 3	0.241± 0.015	0.041± 0.003	0.060± 0.011	0.461± 0.031	0.569± 0.043
50ppm	5	103± 4	0.237± 0.011	0.042± 0.001	0.068± 0.014	0.457± 0.023	0.570± 0.045
100ppm	5	103± 3	0.221± 0.012	0.042± 0.005	0.068± 0.009	0.498± 0.051	0.563± 0.045
200ppm	5	103± 3	0.211± 0.010	0.046± 0.002	0.070± 0.009	0.523± 0.035	0.581± 0.067
400ppm	2	94 ?	0.113 ?	0.048 ?	0.054 ?	0.536 ?	0.549 ?

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

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

STUDY NO. : 0446
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE
 UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
 SURVIVAL ANIMALS (3W)

Group Name	NO. of Animals	KIDNEYS		SPLEEN		LIVER		BRAIN	
Control	5	0.988±	0.037	0.263±	0.014	3.546±	0.262	1.654±	0.018
25ppm	5	0.927±	0.042	0.240±	0.014	3.158±	0.105*	1.620±	0.013
50ppm	5	0.932±	0.047	0.257±	0.032	3.236±	0.225	1.591±	0.009**
100ppm	5	0.921±	0.038	0.245±	0.018	3.343±	0.208	1.617±	0.023
200ppm	5	0.948±	0.036	0.251±	0.022	3.568±	0.219	1.609±	0.037*
400ppm	2	0.934	?	0.216	?	4.128	?	1.602	?

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

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

APPENDIX H 1

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : MALE

(2-WEEK STUDY)

STUDY NO. : 0446
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE
 UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
 SURVIVAL ANIMALS (3W)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	5	148± 8	0.187± 0.010	0.026± 0.004	1.546± 0.133	0.415± 0.029	0.478± 0.011
25ppm	5	145± 9	0.196± 0.015	0.025± 0.002	1.593± 0.079	0.417± 0.014	0.478± 0.012
50ppm	5	149± 3	0.185± 0.017	0.023± 0.003	1.569± 0.024	0.431± 0.024	0.465± 0.018
100ppm	5	138± 8	0.169± 0.016	0.028± 0.002	1.499± 0.143	0.447± 0.016	0.495± 0.022
200ppm	0	-	-	-	-	-	-
400ppm	0	-	-	-	-	-	-

Significant difference : * : P ≤ 0.05 ** : P ≤ 0.01

Test of Dunnett

STUDY NO. : 0446
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE
 UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
 SURVIVAL ANIMALS (3W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.850 ± 0.015	0.245 ± 0.007	3.126 ± 0.099	1.176 ± 0.043
25ppm	5	0.826 ± 0.018	0.227 ± 0.011*	3.053 ± 0.099	1.190 ± 0.053
50ppm	5	0.820 ± 0.031	0.231 ± 0.010	3.113 ± 0.035	1.162 ± 0.027
100ppm	5	0.874 ± 0.020	0.231 ± 0.010	3.379 ± 0.188	1.239 ± 0.057
200ppm	0	-	-	-	-
400ppm	0	-	-	-	-

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

APPENDIX H 2

ORGAN WEIGHT, RELATIVE : SUMMARY, RAT : FEMALE

(2-WEEK STUDY)

STUDY NO. : 0446
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE
 UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
 SURVIVAL ANIMALS (3W)

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	5	105± 3	0.218± 0.013	0.040± 0.005	0.062± 0.010	0.442± 0.030	0.555± 0.029
25ppm	5	103± 3	0.234± 0.015	0.040± 0.003	0.058± 0.011	0.447± 0.032	0.552± 0.035
50ppm	5	103± 4	0.230± 0.009	0.040± 0.001	0.066± 0.011	0.444± 0.024	0.554± 0.035
100ppm	5	103± 3	0.215± 0.007	0.041± 0.004	0.067± 0.011	0.485± 0.042	0.548± 0.033
200ppm	5	103± 3	0.204± 0.012	0.045± 0.002	0.068± 0.009	0.505± 0.025*	0.561± 0.054
400ppm	2	94 ?	0.121 ?	0.051 ?	0.058 ?	0.573 ?	0.587 ?

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. : 0446
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE
 UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
 SURVIVAL ANIMALS (3W)

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	5	0.939 ± 0.028	0.251 ± 0.011	3.379 ± 0.352	1.574 ± 0.052
25ppm	5	0.901 ± 0.038	0.233 ± 0.014	3.066 ± 0.040	1.574 ± 0.039
50ppm	5	0.904 ± 0.027	0.249 ± 0.027	3.140 ± 0.136	1.546 ± 0.055
100ppm	5	0.898 ± 0.018	0.239 ± 0.011	3.257 ± 0.126	1.577 ± 0.028
200ppm	5	0.916 ± 0.010	0.243 ± 0.016	3.449 ± 0.116	1.557 ± 0.063
400ppm	2	0.999 ?	0.231 ?	4.414 ?	1.714 ?

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

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

APPENDIX I 1

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY,
RAT : MALE : DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0446
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 3W)

Organ	Findings	Control				25ppm				50ppm				100ppm				
		No. of Animals on Study				0				0				0				
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	
{Respiratory system}																		
nasal cavit	congestion	< 0>				< 0>				< 0>				< 0>				
		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	
lung	congestion	< 0>				< 0>				< 0>				< 0>				
		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	
	hemorrhage	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
		(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	

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

STUDY NO. : 0446
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0- 3W)

Organ	Findings	200ppm				400ppm			
		No. of Animals on Study				No. of Animals on Study			
		5				5			
Grade		1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}									
nasal cavit	congestion	< 5>				< 5>			
		5	0	0	0	5	0	0	0
		(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
lung	congestion	< 5>				< 5>			
		3	0	0	0	3	0	0	0
		(60)	(0)	(0)	(0)	(60)	(0)	(0)	(0)
	hemorrhage	1	0	0	0	3	0	0	0
		(20)	(0)	(0)	(0)	(60)	(0)	(0)	(0)

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

APPENDIX I 2

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY,
RAT : MALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0446
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 SACRIFICED ANIMALS (3W)

Organ	Findings	Control				25ppm				50ppm				100ppm			
		No. of Animals on Study				No. of Animals on Study				No. of Animals on Study				No. of Animals on Study			
		Grade				Grade				Grade				Grade			
		1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}																	
kidney	eosinophilic body	< 5>				< 5>				< 5>				< 5>			
		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Endocrine system}																	
pituitary	Rathke pouch	< 5>				< 5>				< 5>				< 5>			
		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Reproductive system}																	
prostate	lymphocytic infiltration	< 5>				< 5>				< 5>				< 5>			
		0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
		(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)

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

STUDY NO. : 0446
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 SACRIFICED ANIMALS (3W)

Organ	Findings	200ppm				400ppm				
		No. of Animals on Study		0		0		0		
		Grade	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	
(Urinary system)										
kidney	eosinophilic body		< 0>				< 0>			
		(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
(Endocrine system)										
pituitary	Rathke pouch		< 0>				< 0>			
		(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
(Reproductive system)										
prostate	lymphocytic infiltration		< 0>				< 0>			
		(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

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

APPENDIX I 3

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY,
RAT : FEMALE : DEAD AND MORIBUND ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0446
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0- 3W)

Organ	Findings	Group Name No. of Animals on Study Grade	Control 0				25ppm 0				50ppm 0				100ppm 0				
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	
{Respiratory system}																			
nasal cavit	congestion		< 0>				< 0>					< 0>					< 0>		
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	
lung	congestion		< 0>				< 0>					< 0>					< 0>		
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	
{Hematopoietic system}																			
thymus	atrophy		< 0>				< 0>					< 0>					< 0>		
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	
{Endocrine system}																			
pituitary	cyst		< 0>				< 0>					< 0>					< 0>		
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	
adrenal	hemorrhage		< 0>				< 0>					< 0>					< 0>		
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	

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

STUDY NO. : 0446
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0- 3W)

Organ	Findings	Group Name No. of Animals on Study Grade	200ppm				400ppm			
			0				3			
			1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	
{Respiratory system}										
nasal cavit	congestion		< 0>				< 3>			
			-	-	-	-	2	0	0	0
			(-)	(-)	(-)	(-)	(67)	(0)	(0)	(0)
lung	congestion		< 0>				< 3>			
			-	-	-	-	3	0	0	0
			(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)
{Hematopoietic system}										
thymus	atrophy		< 0>				< 3>			
			-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(33)	(0)	(0)	(0)
{Endocrine system}										
pituitary	cyst		< 0>				< 3>			
			-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(33)	(0)	(0)	(0)
adrenal	hemorrhage		< 0>				< 3>			
			-	-	-	-	1	0	0	0
			(-)	(-)	(-)	(-)	(33)	(0)	(0)	(0)

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

APPENDIX I 4

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS : SUMMARY,
RAT : FEMALE : SACRIFICED ANIMALS

(2-WEEK STUDY)

STUDY NO. : 0446
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 SACRIFICED ANIMALS (3W)

Organ	Findings	Group Name No. of Animals on Study Grade	Control 5				25ppm 5				50ppm 5				100ppm 5				
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4	
				(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}																			
lung	hemorrhage		< 5>				< 5>				< 5>				< 5>				
			1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	
	osseous metaplasia		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)	(20)	(0)	(0)	(0)	
{Circulatory system}																			
heart	granulation		< 5>				< 5>				< 5>				< 5>				
			0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	
{Digestive system}																			
liver	herniation		< 5>				< 5>				< 5>				< 5>				
			0	0	0	0	0	0	0	0	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		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
			(20)	(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 : Number of animals with lesion
 (c) c : b / a * 100

STUDY NO. : 0446
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 SACRIFICED ANIMALS (3W)

Organ	Findings	Group Name		200ppm				400ppm			
		No. of Animals on Study		5				2			
		Grade		1	2	3	4	1	2	3	4
				(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}											
lung	hemorrhage	< 5>				< 2>					
		0	0	0	0	0	0	0	0		
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)		
	osseous metaplasia	0	0	0	0	0	0	0	0		
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)		
{Circulatory system}											
heart	granulation	< 5>				< 2>					
		0	0	0	0	0	0	0	0		
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)		
{Digestive system}											
liver	herniation	< 5>				< 2>					
		1	0	0	0	1	0	0	0		
		(20)	(0)	(0)	(0)	(50)	(0)	(0)	(0)		
	granulation	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 : Number of animals with lesion
 (c) c : b / a * 100

STUDY NO. : 0446
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 SACRIFICED ANIMALS (3W)

Organ	Findings	Control				25ppm				50ppm				100ppm				
		No. of Animals on Study				5				5				5				
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	
(Urinary system)																		
kidney	mineralization:cortico-medullary junction	< 5>				< 5>				< 5>				< 5>				
		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
(Endocrine system)																		
pituitary	Rathke pouch	< 5>				< 5>				< 5>				< 5>				
		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
		(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thyroid	ultimibranchial body remanet	< 5>				< 5>				< 5>				< 5>				
		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)	(0)	(20)	(0)	(0)	(0)	(0)

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

STUDY NO. : 0446
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS (SUMMARY)
 SACRIFICED ANIMALS (3W)

Organ	Findings	Group Name		200ppm				400ppm			
		No. of Animals on Study		5				2			
		Grade		1	2	3	4	1	2	3	4
				(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Urinary system)											
Kidney	mineralization:cortico-medullary junction	< 5>				< 2>					
		1	0	0	0	0	0	0	0	0	0
		(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
(Endocrine system)											
Pituitary	Rathke pouch	< 5>				< 2>					
		0	0	0	0	0	0	0	0	0	0
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
Thyroid	ultimibranchial body remanet	< 5>				< 2>					
		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										

APPENDIX J 1

IDENTITY OF PROPIONONITRILE IN THE 2-WEEK INHALATION STUDY

IDENTITY OF PROPIONONITRILE IN THE 2-WEEK INHALATION STUDY

Test Substance : Propiononitrile (Wako Pure Chemical Industries, Ltd.)

Lot No. : WAR4790

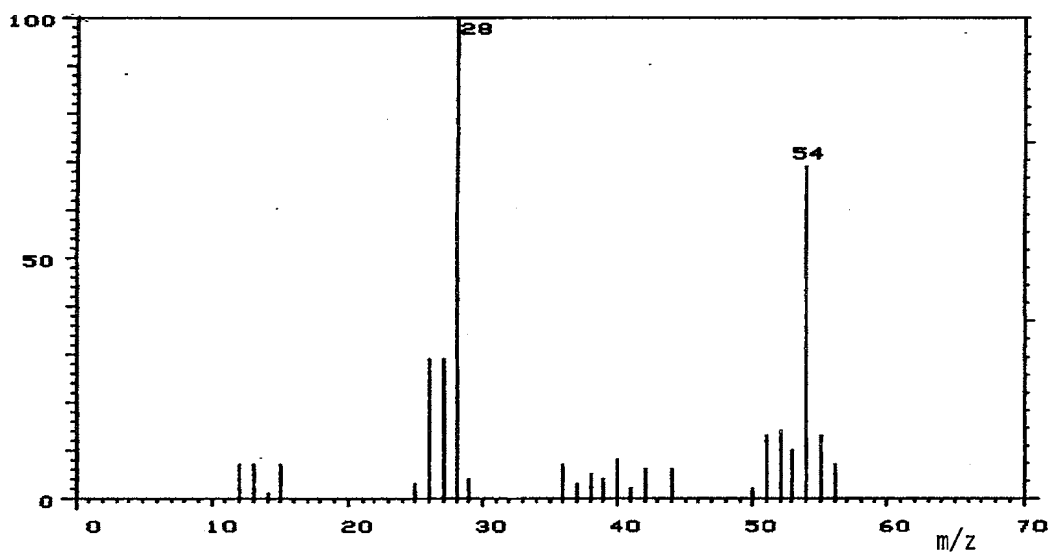
1. Spectral Data

Mass Spectrometry

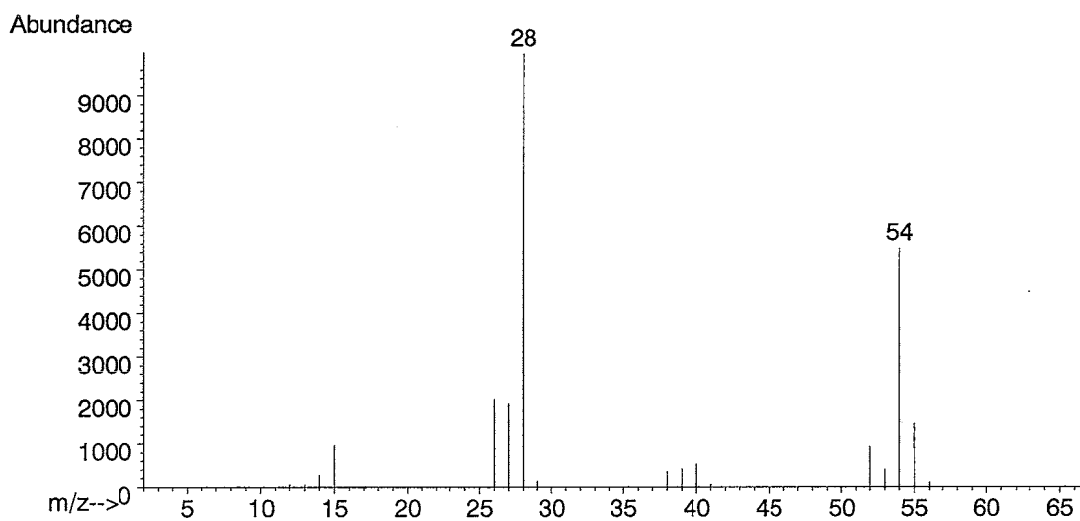
Instrument : Hitachi M-80B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance



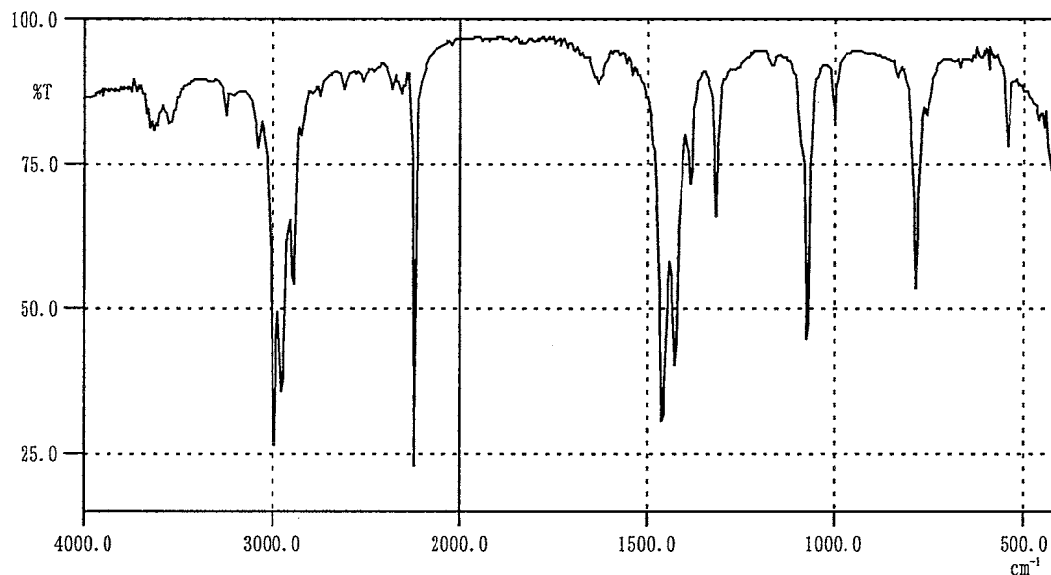
Mass Spectrum of Literature Data*

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

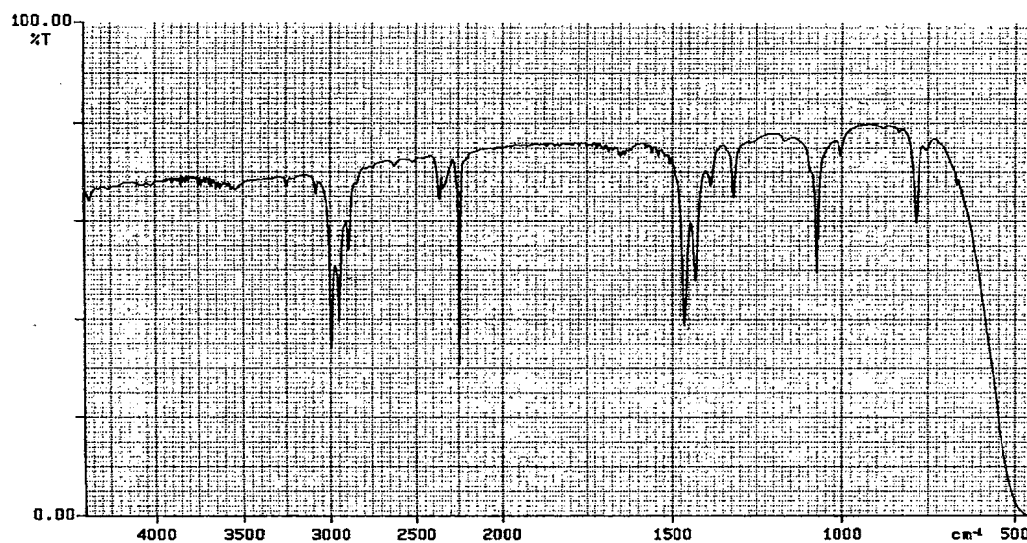
Infrared Spectrometry

Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 4 cm^{-1} 

Infrared Spectrum of Test Substance



Infrared Spectrum of Literature Data*

Result: The infrared spectrum was consistent with literature spectrum.

(*Performed by Wako Pure Chemical Industries, Ltd.)

2. Conclusion: The test substance was identified as propionitrile by mass spectrum and infrared spectrum.

APPENDIX J 2

STABILITY OF PROPIONONITRILE IN THE 2-WEEK INHALATION STUDY

STABILITY OF PROPIONONITRILE IN THE 2-WEEK INHALATION STUDY

Test Substance : Propiononitrile (Wako Pure Chemical Industries, Ltd.)

Lot No. : WAR4790

1. Sample : This lot was used from 2002.4.2 to 2002.4.15. Test substance was stored in a dark place at room temperature.

2. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : Methyl Silicone (0.53 mm ϕ \times 60 m)

Column Temperature: 80° C

Flow Rate : 10 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μ L

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
2002.03.29	1	3.597	100
2002.04.19	1	3.576	100

Result: Gas chromatography indicated one major peak (peak No.1) analyzed on 2002.3.29 and one major peak (peak No.1) analyzed on 2002.4.19. No new trace impurity peak in the test substance analyzed on 2002.4.19 was detected.

3. Conclusion: The test substance was stable for about 3 weeks in a dark place at room temperature.

APPENDIX K 1

CONCENTRATION OF PROPIONONITRILE IN THE INHALATION CHAMBER OF
THE 2-WEEK INHALATION STUDY

CONCENTRATION OF PROPIONONITRILE IN THE INHALATION CHAMBER
OF THE 2-WEEK INHALATION STUDY

Group Name	Concentration(ppm) Mean \pm S.D.
Control	0.0 \pm 0.0
25ppm	25.0 \pm 0.1
50ppm	50.1 \pm 0.2
100ppm	100.3 \pm 0.5
200ppm	200.3 \pm 0.6
400ppm	400.0 \pm 1.6

APPENDIX K 2

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 2-WEEK
INHALATION STUDY OF PROPIONONITRILE

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 2-WEEK INHALATION STUDY OF
PROPIONONITRILE

Group Name	Temperature(°C) Mean ± S.D.	Humidity(%) Mean ± S.D.	Ventilation Rate(L/min) Mean ± S.D.	Air Change(time/h) Mean
Control	22.0 ± 0.1	55.9 ± 0.4	212.3 ± 0.8	12.0
25ppm	22.1 ± 0.1	57.2 ± 0.4	212.0 ± 1.0	12.0
50ppm	22.0 ± 0.1	57.1 ± 0.3	212.2 ± 1.0	12.0
100ppm	22.1 ± 0.1	56.4 ± 0.4	212.0 ± 0.9	12.0
200ppm	21.7 ± 0.1	57.4 ± 0.5	211.7 ± 1.0	12.0
400ppm	21.8 ± 0.1	56.3 ± 1.0	212.0 ± 0.8	12.0

APPENDIX L 1

METHODS FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK INHALATION
STUDY OF PROPIONONITRILE

METHOD FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 2-WEEK
INHALATION STUDY OF PROPIONONITRILE

Item	Method
Hematology	
Red blood cell (RBC)	Light scattering method ¹⁾
Hemoglobin (Hgb)	Cyanmethemoglobin method ¹⁾
Hematocrit (Hct)	Calculated as $RBC \times MCV / 10$ ¹⁾
Mean corpuscular volume (MCV)	Light scattering method ¹⁾
Mean corpuscular hemoglobin (MCH)	Calculated as $Hgb / RBC \times 10$ ¹⁾
Mean corpuscular hemoglobin concentration (MCHC)	Calculated as $Hgb / Hct \times 100$ ¹⁾
Platelet	Light scattering method ¹⁾
Reticulocyte	Light scattering method ¹⁾
Prothrombin time	Quick one stage method ²⁾
Activated partial thromboplastin time (APTT)	Ellagic acid activaterd method ²⁾
White blood cell (WBC)	Light scattering method ¹⁾
Differential WBC	Pattern recognition method ³⁾ (Wright staining)
Biochemistry	
Total protein (TP)	Biuret method ⁴⁾
Albumin (Alb)	BCG method ⁴⁾
A/G ratio	Calculated as $Alb / (TP - Alb)$ ⁴⁾
T-bilirubin	Alkaline azobilirubin method ⁴⁾
Glucose	GlcK·G-6-PDH method ⁴⁾
T-cholesterol	CE·COD·POD method ⁴⁾
Triglyceride	LPL·GK·GPO·POD method ⁴⁾
Phospholipid	PLD·ChOD·POD method ⁴⁾
Glutamic oxaloacetic transaminase (GOT)	JSCC method ⁴⁾
Glutamic pyruvic transaminase (GPT)	JSCC method ⁴⁾
Lactate dehydrogenase (LDH)	SFBC method ⁴⁾
Alkaline phosphatase (ALP)	GSCC method ⁴⁾
γ -Glutamyl transpeptidase (γ -GTP)	L- γ -Glutamyl-p-nitroanilide method ⁴⁾
Creatine phosphokinase (CPK)	JSCC method ⁴⁾
Urea nitrogen	Urease·GLDH method ⁴⁾
Creatinine	Jaffe method ⁴⁾
Sodium	Ion selective electrode method ⁴⁾
Potassium	Ion selective electrode method ⁴⁾
Chloride	Ion selective electrode method ⁴⁾
Calcium	OCPC method ⁴⁾
Inorganic phosphorus	PNP·XOD·POD method ⁴⁾

1) Automatic blood cell analyzer (ADVIA120 : Bayer Corporation)

2) Automatic coagulometer (Sysmex CA-5000 : Sysmex Corporation)

3) Automatic blood cell differential analyzer (MICROX HEG-120NA : OMRON Corporation)

4) Automatic analyzer (Hitachi 7070 : Hitachi,Ltd.)

APPENDIX L 2

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE
2-WEEK INHALATION STUDY OF PROPIONONITRILE

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY
IN THE 2-WEEK INHALATION STUDY OF PROPIONONITRILE

Item	Unit	Decimal place
Hematology		
Red blood cell (RBC)	$\times 10^6 / \mu\text{L}$	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	$\times 10^3 / \mu\text{L}$	0
Reticulocyte	%	1
Prothrombin time	sec	1
Activated partial thromboplastin time (APTT)	sec	1
White blood cell (WBC)	$\times 10^3 / \mu\text{L}$	2
Differential WBC	%	0
Biochemistry		
Total protein	g/dL	1
Albumin	g/dL	1
A/G ratio	-	1
T-bilirubin	mg/dL	2
Glucose	mg/dL	0
T-cholesterol	mg/dL	0
Triglyceride	mg/dL	0
Phospholipid	mg/dL	0
Glutamic oxaloacetic transaminase (GOT)	IU/L	0
Glutamic pyruvic transaminase (GPT)	IU/L	0
Lactate dehydrogenase (LDH)	IU/L	0
Alkaline phosphatase (ALP)	IU/L	0
γ -Glutamyl transpeptidase (γ -GTP)	IU/L	0
Creatine phosphokinase (CPK)	IU/L	0
Urea nitrogen	mg/dL	1
Creatinine	mg/dL	1
Sodium	mEq/L	0
Potassium	mEq/L	1
Chloride	mEq/L	0
Calcium	mg/dL	1
Inorganic phosphorus	mg/dL	1