

1 - ブロモブタンのラットを用いた
吸入による13週間毒性試験報告書

試験番号 : 0503

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 OF 1-BROMOBUTANE

APPENDIX A 1

IDENTITY OF 1-BROMOBUTANE IN THE 13-WEEK INHALATION STUDY

IDENTITY OF 1-BROMOBUTANE IN THE 13-WEEK INHALATION STUDY

Test Substance : 1-Bromobutane (Wako Pure Chemical Industries, Ltd.)

Lot No. : ASQ0017

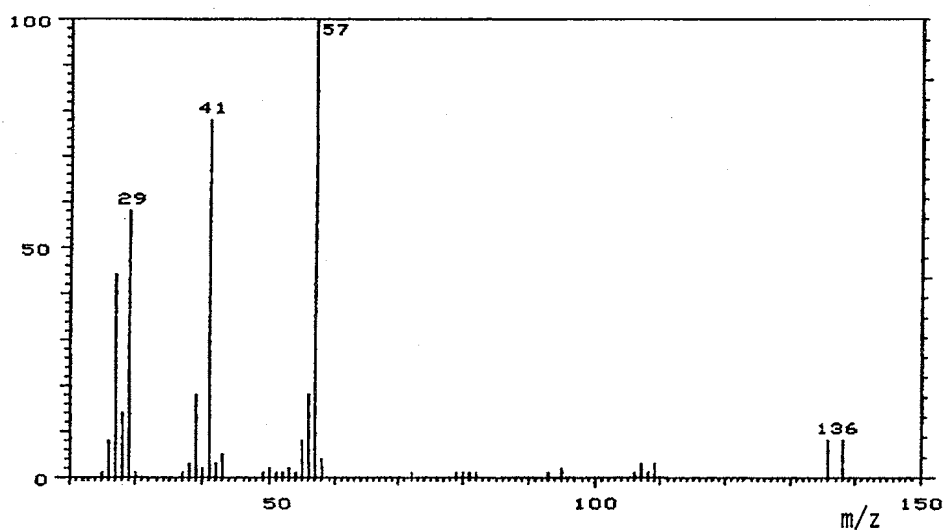
1. Spectral Data

Mass Spectrometry

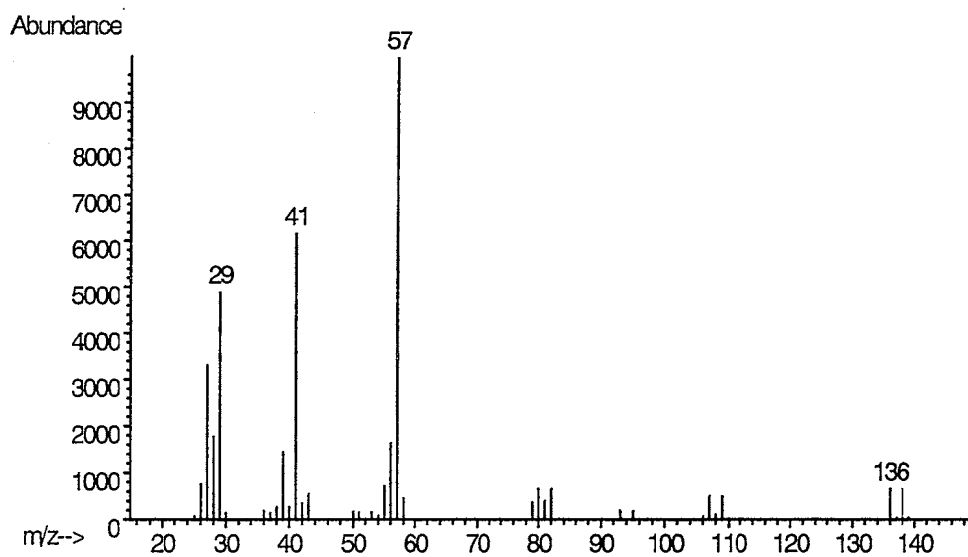
Instrument : Hitachi M-80B Mass Spectrometer

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.

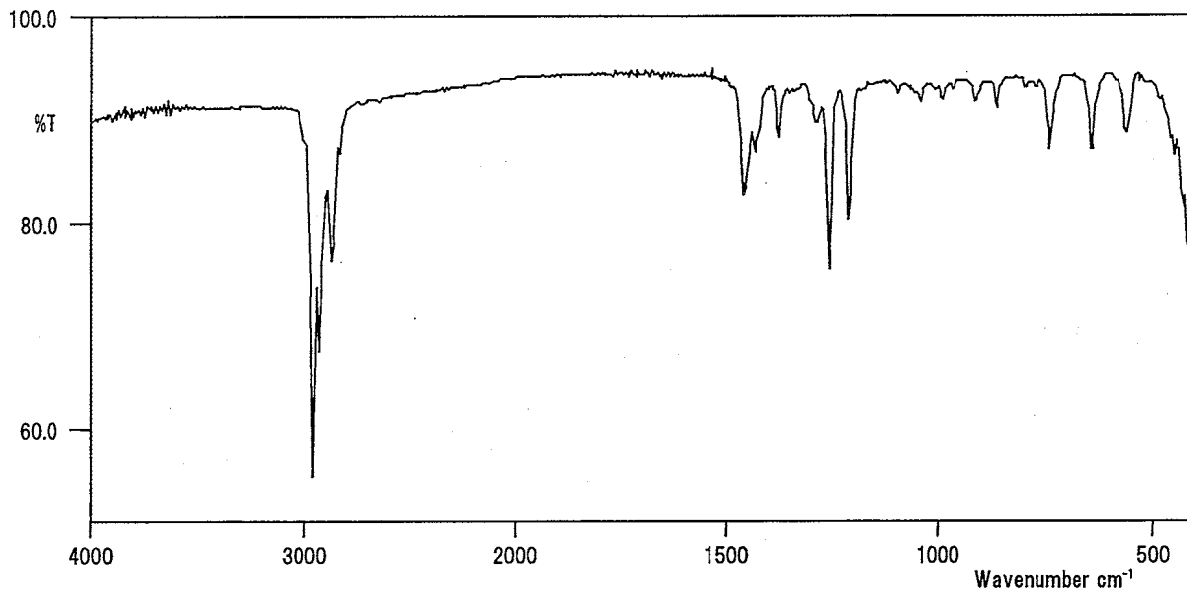
(*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed. New York, NY:John Wiley and Sons.)

Infrared Spectrometry

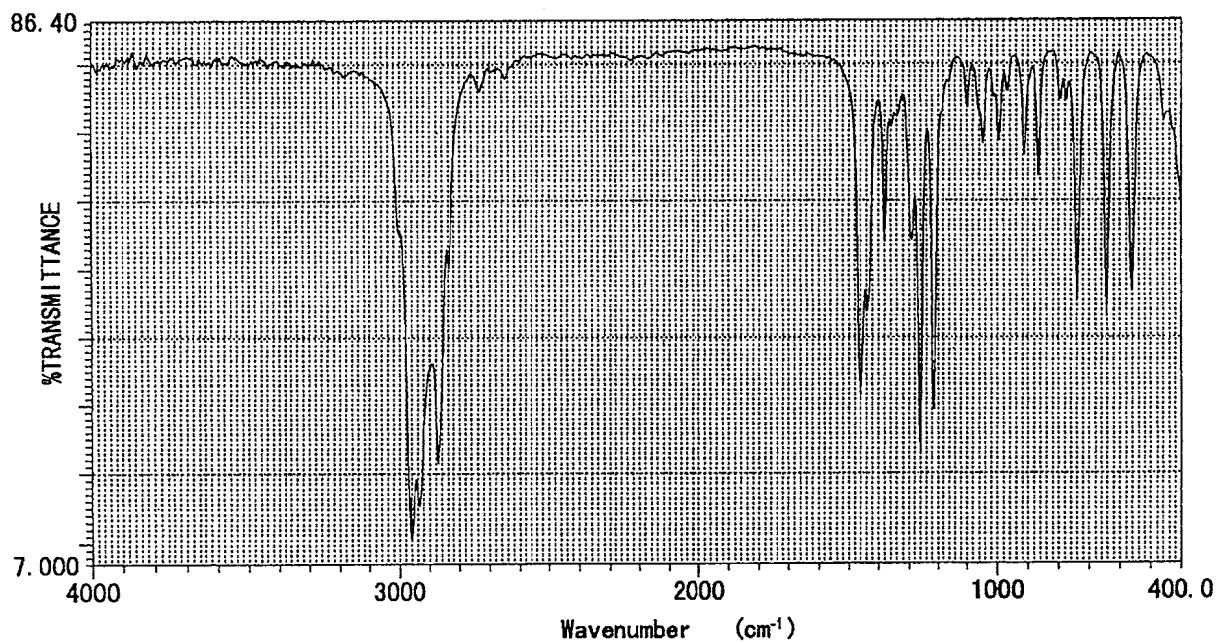
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

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 1-bromobutane by mass spectrum and infrared spectrum.

APPENDIX A 2

STABILITY OF 1-BROMOBUTANE IN THE 13-WEEK INHALATION STUDY

STABILITY OF 1-BROMOBUTANE IN THE 13-WEEK INHALATION STUDY

Test Substance : 1-Bromobutane (Wako Pure Chemical Industries, Ltd.)
Lot No. : ASQ0017
1. Sample : This lot was used from 2003.9.16 to 2003.12.15. 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 : 100° C
Flow Rate : 15 mL/min
Detector : FID (Flame Ionization Detector)
Injection Volume : 1 μ L

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
2003.09.11	1	4.096	100
2003.12.26	1	4.096	100

Result: Gas chromatography indicated one major peak (peak No. 1) analyzed on 2003.9.11 and one major peak (peak No. 1) analyzed on 2003.12.26. No new trace impurity peak in the test substance analyzed on 2003.12.26 was detected.

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

APPENDIX B 1

CONCENTRATION OF 1-BROMOBUTANE IN THE INHALATION CHAMBER OF THE 13-WEEK INHALATION STUDY

CONCENTRATION OF 1-BROMOBUTANE IN THE INHALATION
CHAMBER OF THE 13-WEEK INHALATION STUDY

Group Name	Concentration(ppm)
	Mean \pm S.D.
Control	0.0 \pm 0.0
63ppm	63.3 \pm 0.3
125ppm	125.4 \pm 0.6
250ppm	251.0 \pm 1.5
500ppm	501.2 \pm 2.4
1000ppm	1001.4 \pm 3.9

APPENDIX B 2

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 13-WEEK INHALATION STUDY OF 1-BROMOBUTANE

ENVIRONMENTAL CONDITIONS OF INHALATION CHAMBER IN THE 13-WEEK
INHALATION STUDY OF 1-BROMOBUTANE

Group Name	Temperature (°C) Mean ± S.D.	Humidity (%) Mean ± S.D.	Ventilation Rate (L/min) Mean ± S.D.	Air Change (time/h) Mean
Control	22.8 ± 0.2	55.4 ± 0.8	212.0 ± 1.1	12.0
63ppm	22.8 ± 0.2	58.3 ± 1.1	212.4 ± 1.0	12.0
125ppm	22.6 ± 0.2	56.9 ± 0.7	212.4 ± 0.9	12.0
250ppm	22.5 ± 0.2	56.7 ± 0.9	212.2 ± 1.0	12.0
500ppm	22.7 ± 0.3	56.1 ± 1.2	212.1 ± 0.9	12.0
1000ppm	22.9 ± 0.3	54.5 ± 1.5	212.0 ± 1.0	12.0

APPENDIX C

CLINICAL OBSERVATION : SUMMARY,
RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0503
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

PAGE : 1

Clinical sign	Group Name	Administration Week-day												
		1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7
		1	1	1	1	1	1	1	1	1	1	1	1	1
WASTING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	63ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	125ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	250ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	500ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000ppm	0	0	0	0	0	0	0	0	0	0	0	0	1
PILORECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	63ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	125ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	250ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	500ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000ppm	0	0	0	0	0	0	0	0	0	0	0	0	1
SOILED PERI-GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	63ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	125ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	250ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	500ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1000ppm	0	0	0	0	0	0	0	0	0	0	0	0	1

(HAN190)

BAIS 4

APPENDIX D 1

BODY WEIGHT CHANGES : SUMMARY,
RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 13
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 1

Group Name	Administration		week-day									
	0-0		1-7		2-7		3-7		4-7		5-7	
Control	123±	4	149±	4	177±	5	200±	6	220±	5	236±	7
63ppm	123±	4	149±	5	180±	7	203±	7	222±	7	238±	8
125ppm	123±	4	148±	6	178±	8	201±	8	221±	9	236±	10
250ppm	123±	3	146±	5	174±	5	197±	5	215±	5	233±	5
500ppm	123±	4	141±	4**	166±	5**	185±	5**	201±	6**	217±	6**
1000ppm	123±	4	136±	8**	159±	10**	174±	11**	185±	10**	198±	11**
Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett												
(HAN260)											BAIS 4	

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 13
 SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 2

Group Name	Administration week-day		7-7		8-7		9-7		10-7		11-7		12-7		13-7	
Control	263±	7	272±	9	283±	9	292±	10	300±	10	304±	12	309±	12		
63ppm	265±	11	278±	13	287±	13	296±	15	302±	15	308±	15	312±	15		
125ppm	263±	12	274±	12	283±	12	292±	13	298±	13	303±	14	308±	14		
250ppm	259±	5	271±	6	280±	6	287±	7	293±	8	299±	8	303±	8		
500ppm	240±	8**	249±	8**	258±	8**	264±	9**	269±	8**	274±	9**	277±	8**		
1000ppm	211±	11**	220±	12**	223±	12**	223±	13**	228±	12**	230±	12**	229±	13**		
Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Dunnett																
(HAN250)															BAIS 4	

APPENDIX D 2

BODY WEIGHT CHANGES : SUMMARY,
RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 13
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 3

Group Name	Administration		week-day									
	0-0		1-7		2-7		3-7		4-7		5-7	
Control	95±	3	106±	4	118±	5	127±	6	134±	6	142±	7
63ppm	95±	2	106±	2	120±	3	129±	3	136±	3	143±	5
125ppm	95±	2	107±	6	120±	6	129±	6	137±	7	144±	8
250ppm	95±	2	106±	3	119±	4	128±	4	135±	4	141±	5
500ppm	95±	2	105±	3	116±	4	125±	4	131±	4	136±	4
1000ppm	95±	3	103±	4	116±	5	122±	5	127±	4**	132±	5**

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

Test of Dunnett

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 13
 SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 4

Group Name	Administration week-day		7-7		8-7		9-7		10-7		11-7		12-7		13-7	
Control	151±	8	153±	9	158±	8	162±	11	166±	11	169±	11	171±	11		
63ppm	153±	5	159±	8	161±	4	166±	7	169±	6	172±	7	175±	8		
125ppm	154±	7	156±	9	162±	10	169±	11	170±	10	174±	9	176±	11		
250ppm	153±	5	157±	4	161±	5	165±	5	168±	3	171±	5	173±	5		
500ppm	146±	4	151±	4	155±	4	156±	5	162±	6	162±	5	165±	5		
1000ppm	138±	4**	141±	5*	144±	4**	147±	5**	148±	5**	148±	6**	145±	10**		

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

Test of Dunnett

(HAN260)

BAIS 4

APPENDIX E 1

FOOD CONSUMPTION CHANGES : SUMMARY,
RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 13
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 1

Group Name	Administration 1-7 (6)	week-day(effective) 2-7 (7)	3-7 (7)	4-7 (7)	5-7 (7)	6-7 (7)	7-7 (7)
Control	14.5± 0.9	15.2± 0.9	16.2± 1.2	16.1± 1.0	16.3± 0.9	15.8± 0.9	15.5± 0.8
63ppm	13.7± 0.6	15.9± 0.9	16.6± 1.1	16.9± 1.0	17.2± 0.8	16.6± 0.8	16.3± 0.6
125ppm	13.5± 0.6*	15.4± 0.7	16.2± 0.7	16.9± 1.1	16.5± 0.9	15.9± 1.0	16.1± 1.1
250ppm	13.2± 0.5**	15.2± 0.3	16.3± 0.5	16.9± 0.8	17.6± 1.1	16.9± 0.8	17.1± 0.6**
500ppm	11.9± 0.8**	14.6± 1.1	15.8± 1.1	16.5± 1.3	17.3± 1.8	16.9± 1.7	17.1± 1.2**
1000ppm	11.6± 1.1**	14.1± 1.2	15.5± 1.3	15.7± 1.3	16.3± 1.2	16.6± 1.0	16.5± 1.1

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

Test of Dunnett

(HAN260)

BAIS 4

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 13
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 2

Group Name	Administration 8-7(7)	week-day(effective) 9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)
Control	16.0± 0.8	16.0± 0.9	15.8± 0.8	15.6± 1.1	15.5± 1.0	15.3± 0.8
63ppm	16.7± 0.9	17.0± 1.1	16.9± 0.9	16.1± 0.9	16.6± 0.9	16.3± 0.8
125ppm	16.6± 1.3	16.7± 1.3	16.4± 1.1	16.0± 0.8	16.1± 0.9	15.7± 0.8
250ppm	17.2± 0.8*	17.7± 0.9**	17.0± 0.7	16.6± 0.7*	16.5± 0.7	16.5± 0.7
500ppm	17.2± 1.5	17.4± 1.2*	16.7± 1.1	16.8± 0.8*	16.7± 1.1*	16.7± 1.3*
1000ppm	15.9± 0.7	16.8± 1.2	16.5± 1.5	16.1± 1.1	17.3± 1.3**	16.9± 1.7**

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

Test of Dunnett

(HAN260)

BAIS 4

APPENDIX E 2

FOOD CONSUMPTION CHANGES : SUMMARY, RAT : FEMALE

(13-WEEK STUDY)

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week-day(effective)													
	1-7 (6)		2-7 (7)		3-7 (7)		4-7 (7)		5-7 (7)		6-7 (7)		7-7 (7)	
Control	10.2±	0.4	10.3±	0.7	10.5±	0.7	10.2±	0.7	10.6±	0.8	10.0±	0.6	9.8±	0.7
63ppm	10.0±	0.3	10.8±	0.4	10.6±	0.5	10.6±	0.5	10.7±	0.4	10.5±	0.4	10.4±	0.5
125ppm	10.1±	0.7	10.7±	1.1	11.1±	0.7	11.4±	0.9**	10.9±	0.6	10.7±	1.0	10.4±	0.9
250ppm	9.5±	0.5*	10.9±	0.4	11.1±	0.5	11.4±	0.5**	11.5±	0.5*	11.5±	0.6**	11.7±	0.7**
500ppm	9.5±	0.4*	11.2±	0.6	11.4±	0.9	11.8±	0.9**	12.0±	0.8**	11.5±	0.8**	11.8±	0.8**
1000ppm	9.4±	1.0*	11.0±	0.9	11.3±	1.0	11.6±	0.8**	11.9±	0.9**	12.4±	1.0**	12.5±	1.1**

Test of Dunnett

BAIS 4

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 UNIT : g
 REPORT TYPE : A1 13
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 4

Group Name	Administration 8-7(7)	week-day(effective) 9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)
Control	9.7± 0.8	10.4± 0.8	9.7± 0.9	10.2± 0.8	10.1± 0.9	9.8± 0.7
63ppm	10.5± 0.5	10.4± 0.8	10.5± 0.7	10.5± 0.6	10.6± 0.6	10.6± 0.4
125ppm	10.4± 1.0	10.8± 1.0	10.9± 1.5*	10.3± 1.0	11.1± 1.5	10.5± 0.7
250ppm	11.5± 0.6**	11.9± 0.5**	11.5± 0.6**	11.7± 0.4**	11.8± 0.5**	11.7± 0.6**
500ppm	11.7± 0.9**	11.9± 0.7**	11.6± 0.9**	11.8± 0.9**	11.8± 0.8**	12.1± 0.6**
1000ppm	12.4± 0.8**	12.8± 0.9**	12.7± 0.9**	12.2± 0.7**	13.0± 1.3**	12.5± 1.3**

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

Test of Dunnett

APPENDIX F 1

URINALYSIS : SUMMARY,
RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 MEASURE TIME : 1
 SEX : MALE

URINALYSIS

REPORT TYPE : A1

PAGE : 1

Group Name	NO. of Animals	pH							CHI	Protein						CHI	Glucose						CHI	Ketone body						CHI	Bilirubin				CHI
		5.0	6.0	6.5	7.0	7.5	8.0	8.5		-	±	+	2+	3+	4+		-	±	+	2+	3+	4+		-	±	+	2+	3+	4+		-	+	2+	3+	
Control	10	0	0	0	0	0	8	2		0	3	7	0	0	0		10	0	0	0	0	0		1	6	3	0	0	0		10	0	0	0	
63ppm	10	0	0	0	0	3	5	2		2	6	2	0	0	0		10	0	0	0	0	0		4	6	0	0	0	0		10	0	0	0	
125ppm	10	0	0	0	0	0	8	2		0	5	4	1	0	0		10	0	0	0	0	0		4	5	1	0	0	0		10	0	0	0	
250ppm	10	0	0	0	0	3	4	3		0	6	4	0	0	0		10	0	0	0	0	0		6	3	1	0	0	0		10	0	0	0	
500ppm	10	0	0	0	1	2	7	0		0	6	4	0	0	0		10	0	0	0	0	0		6	4	0	0	0	0	*	10	0	0	0	
1000ppm	10	0	0	0	0	1	9	0		0	4	5	1	0	0		10	0	0	0	0	0		0	10	0	0	0	0		10	0	0	0	

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

Test of CHI SQUARE

(HCL101)

BAIS 4

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : MALE

URINALYSIS

REPORT TYPE : A1

PAGE : 2

Group Name	NO. of Animals	Occult blood					CHI	Urobilinogen					CHI
		-	±	+	2+	3+		±	+	2+	3+	4+	
Control	10	10	0	0	0	0	0	10	0	0	0	0	0
63ppm	10	10	0	0	0	0	0	10	0	0	0	0	0
125ppm	10	10	0	0	0	0	0	10	0	0	0	0	0
250ppm	10	10	0	0	0	0	0	10	0	0	0	0	0
500ppm	10	10	0	0	0	0	0	10	0	0	0	0	0
1000ppm	10	10	0	0	0	0	0	10	0	0	0	0	0

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

Test of CHI SQUARE

APPENDIX F 2

URINALYSIS : SUMMARY,
RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : FEMALE

URINALYSIS

REPORT TYPE : A1

PAGE : 3

Group Name	NO. of Animals	pH							CHI	Protein						CHI	Glucose						CHI	Ketone body						CHI	Bilirubin				CHI
		5.0	6.0	6.5	7.0	7.5	8.0	8.5		-	±	+	2+	3+	4+		-	±	+	2+	3+	4+		-	±	+	2+	3+	4+		-	+	2+	3+	
Control	10	0	0	0	0	0	8	2		5	4	1	0	0	0		10	0	0	0	0	0		9	1	0	0	0	0		10	0	0	0	
63ppm	10	0	0	0	0	0	10	0		8	2	0	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
125ppm	10	0	0	0	0	1	9	0		6	4	0	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
250ppm	10	0	0	0	0	0	9	1		5	4	1	0	0	0		10	0	0	0	0	0		9	1	0	0	0	0		10	0	0	0	
500ppm	10	0	0	0	0	3	6	1		7	3	0	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0		10	0	0	0	
1000ppm	10	0	0	0	1	3	5	1		4	6	0	0	0	0		10	0	0	0	0	0		9	1	0	0	0	0		10	0	0	0	

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

Test of CHI SQUARE

STUDY NO. : 0503

URINALYSIS

ANIMAL : RAT F344/DuCrj

MEASURE. TIME : 1

SEX : FEMALE

REPORT TYPE : A1

PAGE : 4

Group Name	NO. of Animals	Occult blood					Urobilinogen				
		-	±	+	2+	3+	±	+	2+	3+	4+
Control	10	10	0	0	0	0	10	0	0	0	0
63ppm	10	10	0	0	0	0	10	0	0	0	0
125ppm	10	10	0	0	0	0	10	0	0	0	0
250ppm	10	10	0	0	0	0	10	0	0	0	0
500ppm	10	10	0	0	0	0	10	0	0	0	0
1000ppm	10	10	0	0	0	0	10	0	0	0	0

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of CHI SQUARE

(HCL101)

BAIS 4

APPENDIX G 1

HEMATOLOGY : SUMMARY,
RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : MALE

HEMATOLOGY (SUMMARY)
 ALL ANIMALS (14W)

REPORT TYPE : A1

PAGE : 1

Group Name	NO. of Animals	RED BLOOD CELL 10 ⁶ /μl		HEMOGLOBIN g/dl		HEMATOCRIT %		MCV fl		MCH pg		MCHC g/dl		PLATELET 10 ³ /μl	
Control	10	9.47±	0.22	16.0±	0.2	45.2±	1.1	47.7±	0.4	16.9±	0.3	35.4±	0.5	714±	77
63ppm	10	9.51±	0.29	15.8±	0.3	44.9±	1.2	47.2±	0.2*	16.7±	0.3	35.3±	0.5	747±	71
125ppm	10	9.56±	0.26	16.0±	0.4	45.2±	1.1	47.3±	0.4	16.8±	0.2	35.4±	0.3	750±	58
250ppm	10	9.52±	0.15	15.9±	0.3	45.0±	0.6	47.3±	0.4	16.7±	0.3	35.3±	0.6	782±	42*
500ppm	10	9.47±	0.21	16.0±	0.3	45.2±	0.9	47.8±	0.4	16.9±	0.3	35.4±	0.4	825±	48**
1000ppm	10	9.04±	0.24**	15.5±	0.3**	44.8±	1.0	49.5±	0.6**	17.2±	0.2*	34.7±	0.4**	884±	27**

Significant difference : * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 4

STUDY NO. : 0503
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

REPORT TYPE : A1

PAGE : 2

Group Name	NO. of Animals	RETICULOCYTE %		PROTHROMBIN TIME s e c		APTT s e c	
Control	10	1.8±	0.2	13.9±	0.7	23.6±	1.4
63ppm	10	1.9±	0.2	14.2±	2.2	23.8±	1.7
125ppm	10	1.9±	0.2	14.4±	2.2	23.3±	1.4
250ppm	10	2.1±	0.2*	13.5±	1.4	22.1±	3.5
500ppm	10	2.2±	0.3**	12.6±	0.3**	21.9±	2.0
1000ppm	10	3.2±	0.2**	12.5±	0.5**	21.0±	1.3*

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

Test of Dunnett

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : MALE

HEMATOLOGY (SUMMARY)
 ALL ANIMALS (14W)

REPORT TYPE : A1

PAGE : 3

Group Name	NO. of Animals	WBC 10 ³ /μl		Differential N-BAND		WBC (%) N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHER	
Control	10	5.77±	1.32	0±	0	23±	5	1±	0	0±	0	3±	1	73±	5	0±	0
63ppm	10	5.44±	1.32	0±	0	23±	4	1±	1	0±	0	3±	2	73±	4	0±	0
125ppm	10	5.14±	1.07	0±	0	20±	4	2±	1	0±	0	4±	1	75±	4	0±	0
250ppm	10	5.52±	1.21	0±	0	22±	4	1±	1	0±	0	4±	1	74±	5	0±	0
500ppm	10	5.88±	1.47	0±	0	22±	4	1±	1	0±	0	3±	1	73±	4	0±	0
1000ppm	10	6.16±	1.16	0±	0	20±	5	1±	1	0±	0	4±	1	75±	5	0±	0

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 4

APPENDIX G 2

HEMATOLOGY : SUMMARY,
RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : FEMALE

HEMATOLOGY (SUMMARY)
 ALL ANIMALS (14W)

REPORT TYPE : A1

PAGE : 4

Group Name	NO. of Animals	RED BLOOD CELL 10 ⁶ /μl		HEMOGLOBIN g/dl		HEMATOCRIT %		MCV fl		MCH pg		MCHC g/dl		PLATELET 10 ³ /μl	
Control	10	8.80±	0.19	16.1±	0.3	44.4±	1.0	50.4±	0.3	18.3±	0.2	36.3±	0.4	778±	51
63ppm	10	8.85±	0.31	16.1±	0.4	44.5±	1.5	50.3±	0.3	18.2±	0.3	36.2±	0.6	760±	42
125ppm	10	8.87±	0.21	16.1±	0.4	44.6±	0.8	50.3±	0.5	18.2±	0.3	36.2±	0.6	802±	44
250ppm	10	8.95±	0.16	16.3±	0.2	45.1±	0.9	50.4±	0.3	18.2±	0.2	36.0±	0.4	820±	38
500ppm	10	8.80±	0.19	16.2±	0.3	44.7±	0.9	50.8±	0.3*	18.4±	0.3	36.2±	0.4	868±	45**
1000ppm	10	8.50±	0.19*	15.6±	0.5*	44.3±	0.9	52.2±	0.3**	18.4±	0.3	35.2±	0.6**	867±	36**

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 4

STUDY NO. : 0503

ANIMAL : RAT F344/DuCrj

MEASURE. TIME : 1

SEX : FEMALE

REPORT TYPE : A1

HEMATOLOGY (SUMMARY)

ALL ANIMALS (14W)

PAGE : 5

Group Name	NO. of Animals	RETICULOCYTE %		PROTHROMBIN TIME s e c		APTT s e c	
Control	10	1.8±	0.2	12.2±	0.5	19.0±	1.2
63ppm	10	1.8±	0.2	11.9±	0.7	18.5±	0.9
125ppm	10	1.9±	0.3	12.4±	0.4	18.6±	1.8
250ppm	10	2.2±	0.2	12.6±	0.8	18.2±	0.9
500ppm	10	2.8±	0.2**	12.8±	0.4	18.3±	1.8
1000ppm	10	3.1±	0.5**	13.2±	0.9*	19.3±	2.8

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 4

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : FEMALE

HEMATOLOGY (SUMMARY)
 ALL ANIMALS (14W)

REPORT TYPE : A1

PAGE : 6

Group Name	NO. of Animals	WBC 10 ³ /μl		Differential N-BAND		WBC (%) N-SEG		EOSINO		BASO		MONO		LYMPHO		OTHER	
Control	10	4.05±	1.07	0±	0	20±	3	1±	1	0±	0	3±	1	75±	3	0±	0
63ppm	10	4.38±	1.43	0±	0	22±	3	2±	1	0±	0	5±	1	72±	3	0±	0
125ppm	10	3.91±	0.71	0±	0	20±	4	1±	1	0±	0	4±	1	75±	3	0±	0
250ppm	10	4.48±	1.08	0±	0	22±	4	2±	1	0±	0	3±	2	73±	5	0±	0
500ppm	10	4.14±	0.91	0±	0	20±	5	1±	1	0±	0	3±	2	76±	6	0±	0
1000ppm	10	5.17±	1.42	0±	0	19±	2	1±	1	0±	0	4±	2	76±	3	0±	0

Significant difference : * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 4

APPENDIX H 1

BIOCHEMISTRY : SUMMARY,
RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0503
ANIMAL : RAT F344/DuCrj
MEASURE. TIME : 1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

REPORT TYPE : A1

PAGE : 1

Group Name	NO. of Animals	TOTAL PROTEIN g/dl		ALBUMIN g/dl		A/G RATIO		T-BILIRUBIN mg/dl		GLUCOSE mg/dl		T-CHOLESTEROL mg/dl		TRIGLYCERIDE mg/dl	
Control	10	6.5±	0.1	3.5±	0.1	1.2±	0.1	0.11±	0.01	186±	14	63±	6	58±	16
63ppm	10	6.6±	0.1	3.5±	0.1	1.2±	0.1	0.11±	0.01	185±	13	61±	5	42±	12
125ppm	10	6.7±	0.1*	3.6±	0.1	1.2±	0.1	0.11±	0.01	189±	12	66±	8	54±	21
250ppm	10	6.9±	0.2**	3.6±	0.1	1.1±	0.0**	0.11±	0.01	189±	12	65±	4	42±	14*
500ppm	10	6.9±	0.1**	3.7±	0.1**	1.2±	0.0	0.11±	0.01	183±	11	60±	5	41±	8*
1000ppm	10	7.3±	0.2**	4.0±	0.1**	1.2±	0.1	0.12±	0.01*	172±	17	65±	9	29±	10**

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 4

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : MALE

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (14W)

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	10	121±	7	89±	34	58±	12	208±	69	248±	19	1±	1	115±	17
63ppm	10	113±	6	89±	38	57±	14	191±	71	244±	22	1±	1	115±	20
125ppm	10	122±	11	102±	38	65±	18	220±	73	236±	26	1±	1	112±	17
250ppm	10	117±	7	69±	18	46±	9	161±	40	212±	15**	1±	1	110±	23
500ppm	10	112±	8	51±	8**	36±	4**	135±	33*	204±	20**	1±	1	85±	7**
1000ppm	10	120±	11	50±	4**	34±	2**	136±	36*	189±	28**	1±	0	66±	7**

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

Test of Dunnett

(HCL074)

BAIS 4

STUDY NO. : 0503

ANIMAL : RAT F344/DuCrj

MEASURE. TIME : 1

SEX : MALE

REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)

ALL ANIMALS (14W)

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	10	18.3±	1.6	0.5±	0.0	142±	1	3.5±	0.2	103±	1	10.4±	0.2	5.9±	0.8
63ppm	10	17.3±	2.0	0.5±	0.0	142±	1	3.4±	0.1	104±	1	10.3±	0.3	5.6±	1.0
125ppm	10	17.6±	1.0	0.5±	0.0	142±	1	3.5±	0.2	105±	1	10.4±	0.1	5.7±	0.8
250ppm	10	17.7±	1.2	0.5±	0.1	142±	1	3.5±	0.3	105±	2	10.5±	0.2	5.9±	0.8
500ppm	10	16.9±	1.1	0.5±	0.1	140±	1**	3.7±	0.3	105±	1	10.6±	0.2**	6.1±	0.7
1000ppm	10	15.1±	0.8**	0.5±	0.1	139±	1**	3.9±	0.4	106±	1**	10.9±	0.2**	6.5±	0.3

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

Test of Dunnett

(HCL074)

BAIS 4

APPENDIX H 2

BIOCHEMISTRY : SUMMARY,
RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (14W)

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	10	6.1±	0.2	3.4±	0.1	1.2±	0.1	0.12±	0.01	147±	14	70±	7	13±	2
63ppm	10	6.1±	0.2	3.3±	0.1	1.2±	0.1	0.13±	0.01	142±	13	69±	5	12±	3
125ppm	10	6.1±	0.2	3.3±	0.1	1.1±	0.1	0.14±	0.02**	145±	12	66±	10	12±	3
250ppm	10	6.2±	0.2	3.3±	0.1	1.2±	0.1	0.13±	0.01	142±	11	65±	5	13±	2
500ppm	10	6.3±	0.2	3.4±	0.1	1.1±	0.1	0.13±	0.01	139±	17	71±	8	18±	4*
1000ppm	10	6.8±	0.1**	3.7±	0.1**	1.2±	0.0	0.14±	0.02**	142±	24	64±	15	16±	1

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 4

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (14W)

REPORT TYPE : A1

PAGE : 5

Group Name	NO. of Animals	PHOSPHOLIPID mg/dl		GOT I U / l		GPT I U / l		LDH I U / l		ALP I U / l		G-GTP I U / l		CPK I U / l	
Control	10	136±	11	75±	15	46±	14	242±	131	206±	23	1±	1	145±	63
63ppm	10	132±	6	79±	9	46±	9	248±	106	220±	24	2±	0	167±	43
125ppm	10	128±	16	74±	9	41±	8	262±	80	204±	22	2±	1	151±	37
250ppm	10	127±	9	70±	6	37±	5	334±	84	181±	18	2±	1	176±	33
500ppm	10	137±	11	62±	5	34±	5*	312±	103	178±	20*	2±	1	137±	49
1000ppm	10	127±	16	68±	21	35±	6*	258±	81	194±	29	4±	1**	92±	18

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

Test of Dunnett

(HCL074)

BAIS 4

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 MEASURE. TIME : 1
 SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
 ALL ANIMALS (14W)

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	10	19.4±	1.6	0.5±	0.0	140±	1	3.6±	0.3	105±	2	9.8±	0.2	5.2±	0.8
63ppm	10	18.6±	2.7	0.5±	0.1	140±	1	3.5±	0.2	105±	1	9.8±	0.2	5.8±	0.6
125ppm	10	17.4±	2.9	0.5±	0.1	140±	1	3.6±	0.2	106±	1	9.9±	0.2	5.5±	0.8
250ppm	10	17.6±	1.7	0.5±	0.0	140±	1	3.6±	0.3	107±	2*	10.0±	0.1	5.6±	0.8
500ppm	10	17.3±	2.3	0.5±	0.0	139±	1**	3.8±	0.2	106±	1	10.2±	0.2**	6.0±	0.9
1000ppm	10	13.1±	1.9**	0.5±	0.1*	137±	1**	3.8±	0.2	108±	2**	10.4±	0.2**	6.1±	0.7

Significant difference : * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 4

APPENDIX I 1

GROSS FINDINGS : SUMMARY,
RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0503
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 1

Organ_____	Findings_____	Group Name		Control		63ppm		125ppm		250ppm	
		NO. of Animals		10	(%)	10	(%)	10	(%)	10	(%)
liver	herniation			3	(30)	0	(0)	2	(20)	0	(0)

(HPT080)

BAIS 4

STUDY NO. : 0503
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 2

Organ_____	Findings_____	Group Name	500ppm		1000ppm	
		NO. of Animals	10	(%)	10	(%)
<hr/>						
liver	herniation		0	(0)	1	(10)

(HPT080)

BAIS 4

APPENDIX I 2

GROSS FINDINGS : SUMMARY,
RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0503
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 3

Organ	Findings	Group Name NO. of Animals	Control		63ppm		125ppm		250ppm	
			10	(%)	10	(%)	10	(%)	10	(%)
thymus	atrophic		0	(0)	0	(0)	0	(0)	0	(0)
liver	herniation		4	(40)	1	(10)	2	(20)	1	(10)
ovary	cyst		0	(0)	1	(10)	1	(10)	0	(0)

(HPT080)

BAIS 4

STUDY NO. : 0503
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE

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

PAGE : 4

Organ	Findings	Group Name NO. of Animals	500ppm		1000ppm	
			10	(%)	10	(%)
thymus	atrophic		0	(0)	1	(10)
liver	herniation		3	(30)	1	(10)
ovary	cyst		0	(0)	0	(0)

(HPT080)

BAIS 4

APPENDIX J 1

ORGAN WEIGHT, ABSOLUTE : SUMMARY,
RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE
 UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
 SURVIVAL ANIMALS (14W)

PAGE : 1

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	288± 13	0.255± 0.037	0.053± 0.004	3.044± 0.137	0.929± 0.064	0.946± 0.036
63ppm	10	291± 14	0.264± 0.031	0.052± 0.005	3.109± 0.246	0.961± 0.031	0.969± 0.040
125ppm	10	287± 14	0.262± 0.020	0.052± 0.005	3.067± 0.081	0.946± 0.051	0.972± 0.022
250ppm	10	280± 7	0.265± 0.030	0.049± 0.003	3.031± 0.122	0.943± 0.036	0.986± 0.050
500ppm	10	255± 8**	0.229± 0.027	0.048± 0.003	3.030± 0.113	0.894± 0.051	0.959± 0.033
1000ppm	10	209± 10**	0.180± 0.023**	0.049± 0.006	2.694± 0.106**	0.841± 0.058**	0.893± 0.047*

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

Test of Dunnett

(HCL040)

BATS 4

STUDY NO. : 0503
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (14W)

PAGE : 2

Group Name	NO. of Animals	KIDNEYS		SPLEEN		LIVER		BRAIN	
Control	10	1.783±	0.103	0.534±	0.040	7.185±	0.339	1.861±	0.035
63ppm	10	1.843±	0.105	0.537±	0.035	7.671±	0.491*	1.902±	0.043
125ppm	10	1.853±	0.079	0.538±	0.035	7.798±	0.436**	1.879±	0.056
250ppm	10	1.869±	0.072	0.534±	0.028	7.904±	0.290**	1.879±	0.038
500ppm	10	1.867±	0.074	0.510±	0.023	7.938±	0.276**	1.841±	0.049
1000ppm	10	1.755±	0.089	0.431±	0.033**	7.605±	0.475	1.692±	0.033**

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

Test of Dunnett

(HCL040)

BATS 4

APPENDIX J 2

ORGAN WEIGHT, ABSOLUTE : SUMMARY,
RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0503
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (14W)

PAGE : 3

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	157± 10	0.212± 0.025	0.053± 0.003	0.091± 0.007	0.596± 0.048	0.694± 0.039
63ppm	10	160± 7	0.210± 0.021	0.058± 0.006	0.100± 0.012	0.605± 0.041	0.738± 0.054
125ppm	10	161± 9	0.214± 0.023	0.058± 0.005	0.103± 0.020	0.620± 0.036	0.712± 0.042
250ppm	10	157± 6	0.198± 0.036	0.058± 0.005	0.099± 0.012	0.630± 0.029	0.730± 0.028
500ppm	10	151± 5	0.188± 0.013	0.058± 0.005	0.101± 0.007	0.635± 0.033	0.716± 0.033
1000ppm	10	132± 8**	0.156± 0.033**	0.064± 0.011	0.078± 0.020	0.638± 0.040	0.686± 0.024

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

Test of Dunnett

(HCL040)

BAIS 4

STUDY NO. : 0503
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (14W)

PAGE : 4

Group Name	NO. of Animals	KIDNEYS		SPLEEN		LIVER		BRAIN	
Control	10	1.090±	0.071	0.348±	0.021	3.794±	0.266	1.747±	0.034
63ppm	10	1.106±	0.058	0.354±	0.021	4.018±	0.277	1.732±	0.034
125ppm	10	1.112±	0.051	0.371±	0.023	4.027±	0.284	1.721±	0.041
250ppm	10	1.144±	0.049	0.370±	0.022	4.193±	0.176**	1.713±	0.040
500ppm	10	1.166±	0.036*	0.369±	0.023	4.468±	0.165**	1.690±	0.040**
1000ppm	10	1.205±	0.058**	0.310±	0.032**	4.878±	0.322**	1.550±	0.039**

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

Test of Dunnett

(HCL040)

BAIS 4

APPENDIX K 1

ORGAN WEIGHT, RELATIVE : SUMMARY,
RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0503
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (14W)

PAGE : 1

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	288± 13	0.089± 0.012	0.019± 0.002	1.059± 0.032	0.323± 0.017	0.329± 0.011
63ppm	10	291± 14	0.091± 0.011	0.018± 0.002	1.069± 0.066	0.331± 0.010	0.333± 0.011
125ppm	10	287± 14	0.091± 0.007	0.018± 0.001	1.071± 0.048	0.330± 0.018	0.340± 0.014
250ppm	10	280± 7	0.095± 0.011	0.017± 0.001	1.082± 0.040	0.337± 0.011	0.352± 0.015**
500ppm	10	255± 8**	0.090± 0.011	0.019± 0.001	1.187± 0.043**	0.350± 0.017**	0.376± 0.010**
1000ppm	10	209± 10**	0.086± 0.009	0.023± 0.003**	1.289± 0.059**	0.402± 0.016**	0.427± 0.019**

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

Test of Dunnett

(HCL042)

BAIS 4

STUDY NO. : 0503
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (14W)

PAGE : 2

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.620± 0.017	0.186± 0.010	2.498± 0.048	0.648± 0.024
63ppm	10	0.634± 0.012	0.184± 0.008	2.635± 0.057	0.655± 0.024
125ppm	10	0.647± 0.029*	0.188± 0.008	2.720± 0.073	0.656± 0.028
250ppm	10	0.667± 0.019**	0.191± 0.011	2.819± 0.057**	0.671± 0.019
500ppm	10	0.731± 0.016**	0.200± 0.006**	3.109± 0.094**	0.721± 0.021**
1000ppm	10	0.839± 0.020**	0.206± 0.007**	3.633± 0.126**	0.810± 0.035**

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

Test of Dunnett

(HCL042)

BAIS 4

APPENDIX K 2

ORGAN WEIGHT, RELATIVE : SUMMARY,
RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE
 UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
 SURVIVAL ANIMALS (14W)

PAGE : 3

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	157± 10	0.135± 0.013	0.034± 0.002	0.058± 0.005	0.378± 0.019	0.442± 0.018
63ppm	10	160± 7	0.131± 0.011	0.036± 0.004	0.063± 0.007	0.379± 0.019	0.462± 0.027
125ppm	10	161± 9	0.133± 0.015	0.036± 0.004	0.065± 0.012	0.387± 0.020	0.444± 0.018
250ppm	10	157± 6	0.126± 0.020	0.037± 0.003	0.063± 0.006	0.401± 0.009	0.465± 0.016
500ppm	10	151± 5	0.125± 0.012	0.038± 0.003*	0.067± 0.006	0.421± 0.022**	0.474± 0.016**
1000ppm	10	132± 8**	0.118± 0.022	0.049± 0.009**	0.059± 0.013	0.486± 0.025**	0.522± 0.024**

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

Test of Dunnett

(HCL042)

BAIS 4

STUDY NO. : 0503
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (14W)

PAGE : 4

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.693± 0.033	0.221± 0.008	2.410± 0.066	1.114± 0.065
63ppm	10	0.693± 0.014	0.222± 0.008	2.517± 0.115*	1.087± 0.046
125ppm	10	0.693± 0.017	0.231± 0.006	2.509± 0.090	1.075± 0.051
250ppm	10	0.728± 0.031	0.235± 0.013*	2.668± 0.070**	1.091± 0.037
500ppm	10	0.772± 0.026**	0.244± 0.016**	2.957± 0.054**	1.119± 0.031
1000ppm	10	0.917± 0.053**	0.235± 0.014	3.707± 0.123**	1.181± 0.069*

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

Test of Dunnett

(HCL042)

BAIS 4

APPENDIX L 1

HISTOPATHOLOGICAL FINDINGS :
NON-NEOPLASTIC LESIONS : SUMMARY,
RAT : MALE

(13-WEEK STUDY)

STUDY NO. : 0503
ANIMAL : RAT F344/DuCrj
REPORT TYPE : A1
SEX : MALE

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

PAGE : 1

		Group Name	Control				63ppm				125ppm				250ppm			
		No. of Animals on Study	10				10				10				10			
Organ	Findings	Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}																		
nasal cavit			<10>				<10>				<10>				<10>			
	disarrangement:olfactory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(30)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	atrophy:olfactory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lung			<10>				<10>				<10>				<10>			
	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)	(10)	(0)	(0)	(0)
{Hematopoietic system}																		
spleen			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		10	0	0	0	10	0	0	0	10	0	0	0	10	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Circulatory system}																		
heart			<10>				<10>				<10>				<10>			
	granulation		1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b b : Number of animals with lesion

(c) c : b / a * 100

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

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 2

Organ	Findings	Group Name No. of Animals on Study Grade	500ppm				1000ppm			
			10				10			
			1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			<10>				<10>			
	disarrangement:olfactory epithelium		6	0	0	0 *	6	0	0	0 *
			(60)	(0)	(0)	(0)	(60)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		2	0	0	0	3	0	0	0
			(20)	(0)	(0)	(0)	(30)	(0)	(0)	(0)
	atrophy:olfactory epithelium		0	0	0	0	5	0	0	0 *
			(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
lung			<10>				<10>			
	osseous metaplasia		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}										
spleen			<10>				< 9>			
	deposit of hemosiderin		10	0	0	0	9	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Circulatory system}										
heart			<10>				<10>			
	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
 Significant difference : * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 3

		Group Name	Control				63ppm				125ppm				250ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
Organ	Findings		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}																		
stomach			<10>				<10>				<10>				<10>			
	hyperplasia:forestomach		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
liver			<10>				<10>				<10>				<10>			
	herniation		3	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0
			(30)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:focal		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	eosinophilic body		10	0	0	0	10	0	0	0	10	0	0	0	10	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	hyaline cast		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:papilla		2	0	0	0	1	0	0	0	1	0	0	0	3	0	0	0
			(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(30)	(0)	(0)	(0)

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

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 4

Organ	Findings	500ppm				1000ppm			
		10				10			
		1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Digestive system)									
stomach		<10>				<10>			
	hyperplasia:forestomach	1 (10)	0 (0)	0 (0)	0 (0)	3 (30)	1 (10)	0 (0)	0 (0)
liver		<10>				<10>			
	herniation	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
	necrosis:focal	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
(Urinary system)									
kidney		<10>				<10>			
	eosinophilic body	10 (100)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0)
	hyaline cast	0 (0)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)
	mineralization:papilla	4 (40)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)

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

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 5

		Group Name	Control				63ppm				125ppm				250ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
Organ	Findings		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
<hr/>																		
{Endocrine system}																		
pituitary			<10>				<10>				<10>				<10>			
	cyst		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	Rathke pouch		1	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
		(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)
thyroid			<10>				<10>				<10>				<10>			
	ultimibranhial body remanet		0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
		(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)
{Reproductive system}																		
testis			<10>				<10>				<10>				<10>			
	mineralization		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	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)	(0)
{Nervous system}																		
brain			<10>				<10>				<10>				<10>			
	degeneration:granular 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)	(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
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 6

		Group Name	500ppm				1000ppm			
		No. of Animals on Study	10				10			
Organ	Findings	Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Endocrine system}										
pituitary			<10>				<10>			
	cyst		0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)
	Rathke pouch		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
thyroid			<10>				<10>			
	ultimibranhial body remanet		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Reproductive system}										
testis			<10>				<10>			
	mineralization		0	0	0	0	4	0	0	0
			(0)	(0)	(0)	(0)	(40)	(0)	(0)	(0)
	germ cell necrosis		0	0	0	0	10	0	0	0 **
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Nervous system}										
brain			<10>				<10>			
	degeneration:granular cell		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)

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

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 7

Organ	Findings	Group Name	Control				63ppm				125ppm				250ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

{Nervous system}

brain	mineralization:granular layer	<10>				<10>				<10>				<10>			
		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

{Special sense organs/appendage}

Harder gl	lymphocytic infiltration	<10>				<10>				<10>				<10>			
		0	0	0	0	2	0	0	0	0	0	0	0	1	0	0	0
		(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)

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

(HPT150)

BAIS4

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : MALE

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

PAGE : 8

		500ppm				1000ppm			
		10				10			
		Grade				Grade			
Organ_____	Findings_____	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

{Nervous system}

brain	mineralization:granular layer	<10>				<10>			
		0	0	0	0	3	0	0	0
		(0)	(0)	(0)	(0)	(30)	(0)	(0)	(0)

{Special sense organs/appendage}

Harder gl	lymphocytic infiltration	<10>				<10>			
		1	0	0	0	0	0	0	0
		(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Grade 1 : Slight 2 : Moderate 3 : Marked 4 : Severe

< a > a : Number of animals examined at the site

b b : Number of animals with lesion

(c) c : b / a * 100

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

(HPT150)

BAIS4

APPENDIX L 2

HISTOPATHOLOGICAL FINDINGS :
NON-NEOPLASTIC LESIONS : SUMMARY,
RAT : FEMALE

(13-WEEK STUDY)

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 9

		Group Name	Control				63ppm				125ppm				250ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
Organ	Findings		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}																		
nasal cavit			<10>				<10>				<10>				<10>			
	disarrangement:olfactory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	atrophy:olfactory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
lung			<10>				<10>				<10>				<10>			
	perivascular inflammation		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}																		
bone marrow			<10>				<10>				<10>				<10>			
	granulation		0	1	0	0	1	2	0	0	2	2	0	0	0	1	0	0
			(0)	(10)	(0)	(0)	(10)	(20)	(0)	(0)	(20)	(20)	(0)	(0)	(0)	(10)	(0)	(0)
lymph node			<10>				<10>				<10>				<10>			
	granulation		0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 10

		Group Name	500ppm				1000ppm			
		No. of Animals on Study	10				10			
Organ_____	Findings_____	Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
<hr/>										
{Respiratory system}										
nasal cavit			<10>				<10>			
	disarrangement:olfactory epithelium		3	0	0	0	8	0	0	0 **
			(30)	(0)	(0)	(0)	(80)	(0)	(0)	(0)
	respiratory metaplasia:olfactory epithelium		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	atrophy:olfactory epithelium		0	0	0	0	4	0	0	0
			(0)	(0)	(0)	(0)	(40)	(0)	(0)	(0)
lung			<10>				<10>			
	perivascular inflammation		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Hematopoietic system}										
bone marrow			<10>				<10>			
	granulation		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
lymph node			<10>				<10>			
	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 b : Number of animals with lesion
 (c) c : b / a * 100
 Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 11

Organ	Findings	Group Name No. of Animals on Study Grade	Control				63ppm				125ppm				250ppm			
			10				10				10				10			
			1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}																		
thymus	atrophy		<10>				<10>				<10>				<10>			
			0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen	deposit of hemosiderin		<10>				<10>				<10>				<10>			
			10	0	0	0	10	0	0	0	10	0	0	0	10	0	0	0
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
{Digestive system}																		
stomach	erosion:forestomach		<10>				<10>				<10>				<10>			
			0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hyperplasia:forestomach		0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
liver	herniation		<10>				<10>				<10>				<10>			
			4	0	0	0	1	0	0	0	2	0	0	0	1	0	0	0
			(40)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	granulation		0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)

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
 Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 12

		500ppm				1000ppm			
		No. of Animals on Study				No. of Animals on Study			
		Grade				Grade			
Organ	Findings	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}									
thymus		<10>				<10>			
	atrophy	0	0	0	0	1	0	0	0
		(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
spleen		<10>				<10>			
	deposit of hemosiderin	9	1	0	0	8	2	0	0
		(90)	(10)	(0)	(0)	(80)	(20)	(0)	(0)
{Digestive system}									
stomach		<10>				<10>			
	erosion:forestomach	0	0	0	0	1	0	0	0
		(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
	hyperplasia:forestomach	0	0	0	0	2	0	0	0
		(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
liver		<10>				<10>			
	herniation	3	0	0	0	1	0	0	0
		(30)	(0)	(0)	(0)	(10)	(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
 Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 13

		Group Name	Control				63ppm				125ppm				250ppm			
		No. of Animals on Study	10				10				10				10			
Organ_____	Findings_____	Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	mineralization:cortico-medullary junction		2 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	mineralization:papilla		2 (20)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	3 (30)	0 (0)	0 (0)	0 (0)
{Endocrine system}																		
pituitary			<10>				<10>				<10>				<10>			
	cyst		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
	Rathke pouch		1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
thyroid			<10>				<10>				<10>				<10>			
	ultimibranhial body remanet		0 (0)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
{Reproductive system}																		
ovary			<10>				<10>				<10>				<10>			
	cyst		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	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

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

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 14

		500ppm				1000ppm			
		10				10			
Group Name	No. of Animals on Study								
Grade		1	2	3	4	1	2	3	4
Organ_____	Findings_____	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
<hr/>									
{Urinary system}									
kidney		<10>				<10>			
	mineralization:cortico-medullary junction	0	0	0	0	0	0	0	0
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:papilla	3	0	0	0	3	0	0	0
		(30)	(0)	(0)	(0)	(30)	(0)	(0)	(0)
{Endocrine system}									
pituitary		<10>				<10>			
	cyst	0	0	0	0	0	0	0	0
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	Rathke pouch	0	0	0	0	1	0	0	0
		(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
thyroid		<10>				<10>			
	ultimibranchial body remanet	0	0	0	0	0	0	0	0
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Reproductive system}									
ovary		<10>				<10>			
	cyst	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
 Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 15

		Group Name	Control				63ppm				125ppm				250ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
Organ_____	Findings_____		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
<hr/>																		
{Nervous system}																		
brain																		
			<10>				<10>				<10>				<10>			
	degeneration:granular 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)
	mineralization:granular layer		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Special sense organs/appendage}																		
Harder gl																		
			<10>				<10>				<10>				<10>			
	lymphocytic infiltration		3	0	0	0	0	0	0	0	2	0	0	0	1	0	0	0
			(30)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)

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

STUDY NO. : 0503
 ANIMAL : RAT F344/DuCrj
 REPORT TYPE : A1
 SEX : FEMALE

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

PAGE : 16

		500ppm				1000ppm			
		10				10			
		Grade				Grade			
Organ_____	Findings_____	1	2	3	4	1	2	3	4
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)

{Nervous system}

brain	degeneration:granular cell	<10>				<10>			
		0	0	0	0	3	2	0	0 *
		(0)	(0)	(0)	(0)	(30)	(20)	(0)	(0)
	mineralization:granular layer	<10>				<10>			
		0	0	0	0	1	0	0	0
		(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)

{Special sense organs/appendage}

Harder gl	lymphocytic infiltration	<10>				<10>			
		0	0	0	0	2	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
 Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square

(HPT150)

BAIS4

APPENDIX M

METHODS, UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK INHALATION STUDY OF 1-BROMOBUTANE

METHODS, UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY
IN THE 13-WEEK INHALATION STUDY OF 1-BROMOBUTANE

Item	Method	Unit	Decimal place
Hematology			
Red blood cell (RBC)	Light scattering method ¹⁾	$\times 10^6/\mu\text{L}$	2
Hemoglobin (Hgb)	Cyanmethemoglobin method ¹⁾	g/dL	1
Hematocrit (Hct)	Calculated as $\text{RBC} \times \text{MCV} / 10$ ¹⁾	%	1
Mean corpuscular volume (MCV)	Light scattering method ¹⁾	fL	1
Mean corpuscular hemoglobin (MCH)	Calculated as $\text{Hgb} / \text{RBC} \times 10$ ¹⁾	pg	1
Mean corpuscular hemoglobin concentration (MCHC)	Calculated as $\text{Hgb} / \text{Hct} \times 100$ ¹⁾	g/dL	1
Platelet	Light scattering method ¹⁾	$\times 10^3/\mu\text{L}$	0
Reticulocyte	Light scattering method ¹⁾	%	1
Prothrombin time	Quick one stage method ²⁾	sec	1
Activated partial thromboplastin time (APTT)	Ellagic acid activated method ²⁾	sec	1
White blood cell (WBC)	Light scattering method ¹⁾	$\times 10^3/\mu\text{L}$	2
Differential WBC	Pattern recognition method ³⁾ (Wright staining)	%	0
Biochemistry			
Total protein (TP)	Biuret method ⁴⁾	g/dL	1
Albumin (Alb)	BCG method ⁴⁾	g/dL	1
A/G ratio	Calculated as $\text{Alb} / (\text{TP} - \text{Alb})$ ⁴⁾	—	1
T-bilirubin	Alkaline azobilirubin method ⁴⁾	mg/dL	2
Glucose	GlcK·G-6-PDH method ⁴⁾	mg/dL	0
T-cholesterol	CE·COD·POD method ⁴⁾	mg/dL	0
Triglyceride	LPL·GK·GPO·POD method ⁴⁾	mg/dL	0
Phospholipid	PLD·ChOD·POD method ⁴⁾	mg/dL	0
Glutamic oxaloacetic transaminase (GOT)	JSCC method ⁴⁾	IU/L	0
Glutamic pyruvic transaminase (GPT)	JSCC method ⁴⁾	IU/L	0
Lactate dehydrogenase (LDH)	SFBC method ⁴⁾	IU/L	0
Alkaline phosphatase (ALP)	GSCC method ⁴⁾	IU/L	0
γ -Glutamyl transpeptidase (γ -GTP)	JSCC method ⁴⁾	IU/L	0
Creatine phosphokinase (CPK)	JSCC method ⁴⁾	IU/L	0
Urea nitrogen	Urease·GLDH method ⁴⁾	mg/dL	1
Creatinine	Jaffe method ⁴⁾	mg/dL	1
Sodium	Ion selective electrode method ⁴⁾	mEq/L	0
Potassium	Ion selective electrode method ⁴⁾	mEq/L	1
Chloride	Ion selective electrode method ⁴⁾	mEq/L	0
Calcium	OCPC method ⁴⁾	mg/dL	1
Inorganic phosphorus	PNP·XOD·POD method ⁴⁾	mg/dL	1

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.)