2-アミノ-4-クロロフェノールのラットを用いた
経口投与による 13 週間毒性試験（混餌試験）報告書

試験番号：0549

APPENDICES

APPENDICES

APPENDICES (CONTINUED)

APPENDIX A 1

IDENTITY OF 2-AMINO-4-CHLOROPHENOL

IN THE 13-WEEK FEED STUDY

IDENTITY OF 2-AMINO-4-CHLOROPHENOL IN THE 13-WEEK FEED STUDY

Test Substance : 2-Amino-4-chlorophenol (Wako Pure Chemical Industries, Ltd.)

Lot No. : CEQ0194

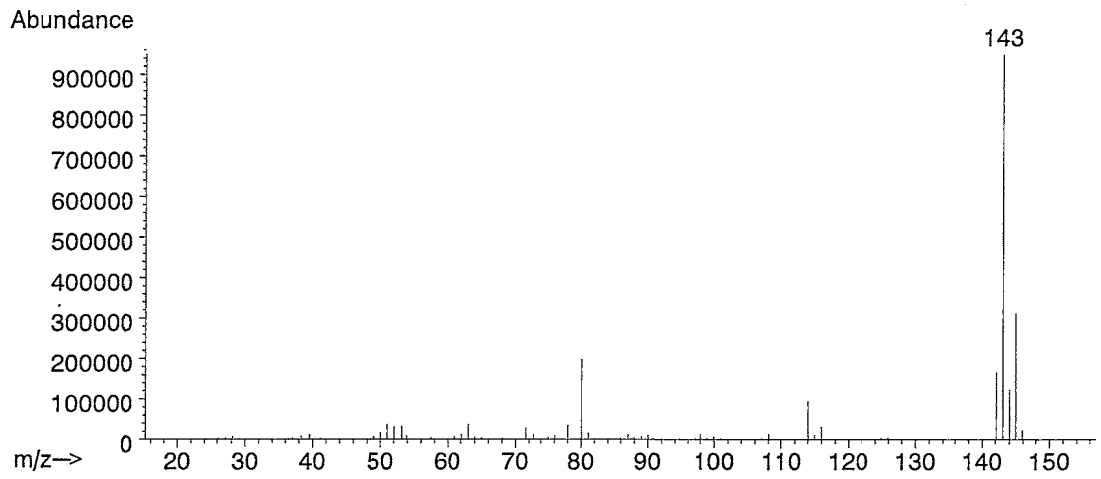
1. Spectral data

Mass Spectrometry

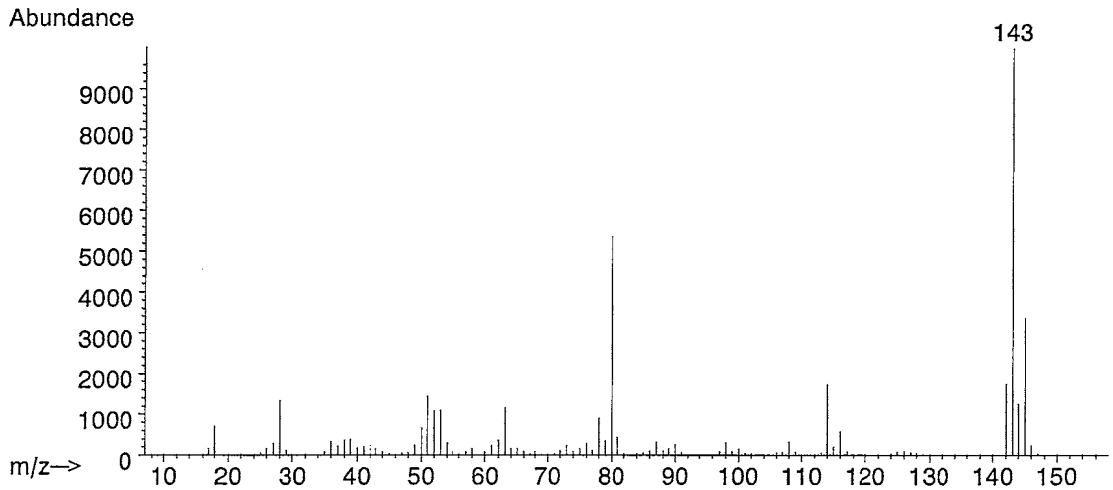
Instrument : Hewlett Packard 5989B Mass Spectrometer

Ionization : EI (Electron Ionization)

Ionization Voltage : 70eV



Mass Spectrum of Test Substance



Mass Spectrum of Literature Data*

Result: The mass spectrum was consistent with literature spectrum.

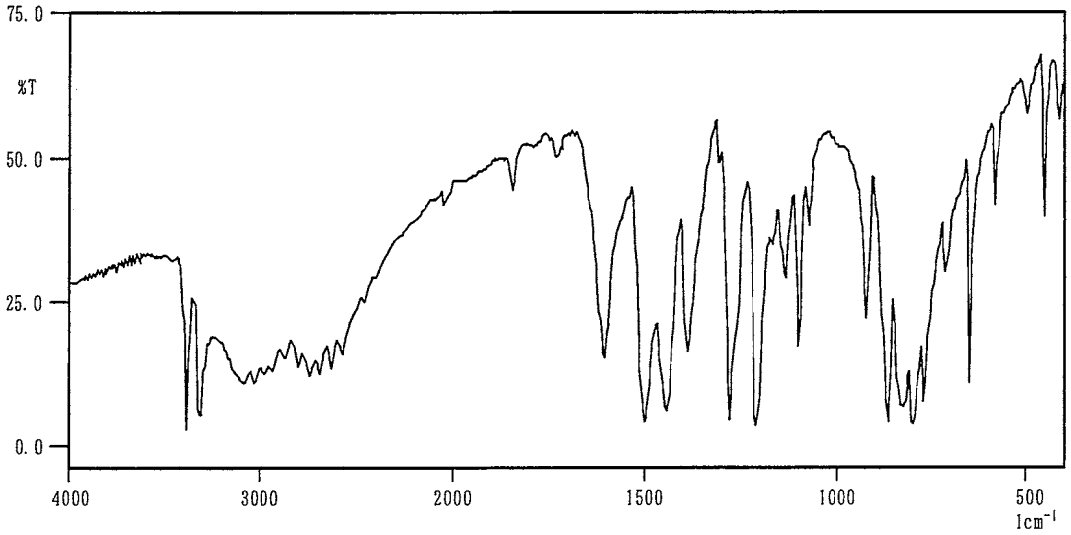
(*McLafferty FW, ed. 1994. Wiley Registry of Mass Spectral Data. 6th ed. New York, NY : John Wiley and Sons.)

Infrared Spectrometry

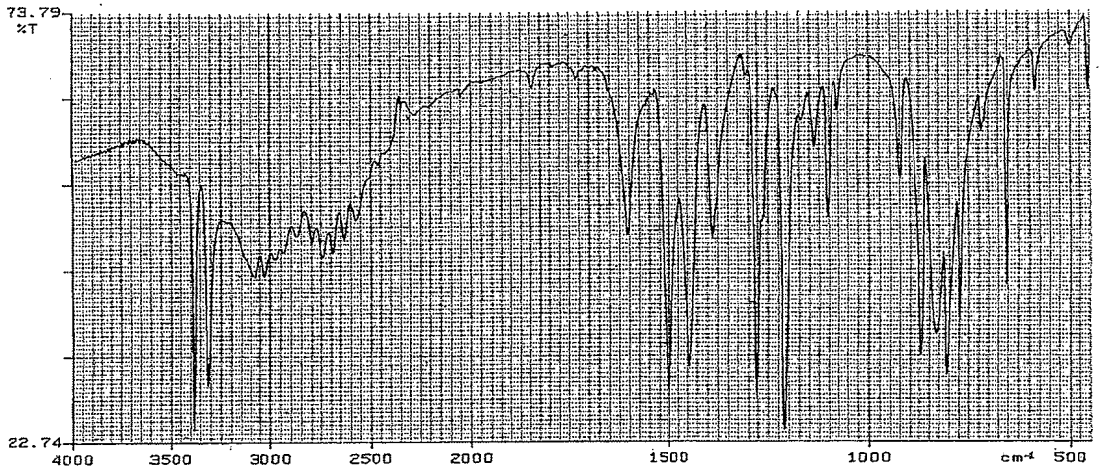
Instrument : Shimadzu FTIR-8200PC Infrared Spectrometer

Cell : KBr Liquid Cell

Resolution : 2.0 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 2-amino-4-chlorophenol by mass spectrum and infrared spectrum.

APPENDIX A 2

STABILITY OF 2-AMINO-4-CHLOROPHENOL IN THE 13-WEEK FEED STUDY

STABILITY OF 2-AMINO-4-CHLOROPHENOL IN THE 13-WEEK FEED STUDY

Test Substance : 2-Amino-4-chlorophenol (Wako Pure Chemical Industries, Ltd.)

Lot No. : CEQ0194

1. Sample : This lot was used from 2004.9.24 to 2004.12.27. Test substance was stored in cold storage in a dark place.

2. Gas Chromatography

Instrument : Hewlett Packard 5890A Gas Chromatograph

Column : DB-1 (0.25 mmϕ × 60 m)

Column Temperature : 100 °C → (10 °C/min) → 250 °C (5 min)

Flow Rate : 1 mL/min

Detector : FID (Flame Ionization Detector)

Injection Volume : 1 μL

Date (date analyzed)	Peak No.	Retention Time (min)	Area (%)
2004.07.27	1	12.373	100
2005.01.11	1	12.374	100

Result: Gas chromatography indicated one major peak (peak No.1) analyzed on 2004.7.27 and one major peak (peak No.1) analyzed on 2005.1.11. No new trace impurity peak in the test substance analyzed on 2005.1.11 was detected.

3. Conclusion: The test substance was stable for about 6 months in cold storage in a dark place.

APPENDIX A 3

CONCENTRATION OF 2-AMINO-4-CHLOROPHENOL IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

CONCENTRATION OF 2-AMINO-4-CHLOROPHENOL IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

	Target Concentration				
Date Analyzed	512[a]	1280	3200	8000	20000
2004.09.23	498 (97.3)[b]	1250 (97.7)	3350 (105)	8080 (101)	20600 (103)

[a] ppm
[b] %

Analytical method : The samples were analyzed by high performance liquid chromatography.

Instrument : Shimadzu LC-10 High Performance Liquid Chromatograph
Column : TSK GEL ODS-80TM (4.6 mmϕ × 15 cm)
Column Temperature : 40 ℃
Flow Rate : 0.8 mL/min
Mobile Phase : Methanol : Acetonitrile : Phosphoric Acid
(5 mM Octanesulfonic Acid Sodium Salt Monohydrate pH2.4) = 1 : 1 : 3
Detector : UV (284 nm)
Injection Volume : 10 μL

APPENDIX A 4

HOMOGENEITY OF 2-AMINO-4-CHLOROPHENOL IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

HOMOGENEITY OF 2-AMINO-4-CHLOROPHENOL IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

	Target Concentration				
	512[a]	1280	3200	8000	20000
Coefficient Variation	1.62[b]	2.85	1.62	2.16	3.77

[a] ppm
[b] % (n=7)

Analytical method : The samples were analyzed by high performance liquid chromatography.

Instrument : Shimadzu LC-10 High Performance Liquid Chromatograph
Column : TSK GEL ODS-80TM (4.6 mmϕ × 15 cm)
Column Temperature : 40 ℃
Flow Rate : 0.8 mL/min
Mobile Phase : Methanol : Acetonitrile : Phosphoric Acid
(5 mM Octanesulfonic Acid Sodium Salt Monohydrate pH2.4) = 1 : 1 : 3
Detector : UV (284 nm)
Injection Volume : 10 μL

APPENDIX A 5

STABILITY OF 2-AMINO-4-CHLOROPHENOL IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

STABILITY OF 2-AMINO-4-CHLOROPHENOL IN FORMULATED DIETS IN THE 13-WEEK FEED STUDY

		Target Concentration	
Date Prepared	Date Analyzed	512[a]	20000
2004.06.11	2004.06.11	484 (100)[b]	19900 (100)
	2004.06.16[c]	437 (90.3)	19600 (98.5)
	2004.06.25[d]	477 (98.6)	19400 (97.5)

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

Analytical method : The samples were analyzed by high performance liquid chromatography.

Instrument : Shimadzu LC-10 High Performance Liquid Chromatograph
Column : TSK GEL ODS-80TM (4.6 mmϕ × 15 cm)
Column Temperature : 40 ℃
Flow Rate : 0.8 mL/min
Mobile Phase : Methanol : Acetonitrile : Phosphoric Acid
(5 mM Octanesulfonic Acid Sodium Salt Monohydrate pH2.4) = 1 : 1 : 3
Detector : UV (284 nm)
Injection Volume : 10 μL

APPENDIX B 1

CLINICAL OBSERVATION : MALE

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

Clinical sign	Group Name	Administration Week-day 1-7	2-7	3-7	4-7	5-7	6-7	7-7	8-7	9-7	10-7	11-7	12-7	13-7
COLORED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	512 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1280 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	3200 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	8000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	10	10	2	4	4	4	4	4	4	6	6	6
NON REMARKABLE	Control	10	10	10	10	10	10	10	10	10	10	10	10	10
	512 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	1280 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	3200 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	8000 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	20000 ppm	10	0	0	8	6	6	6	6	6	6	4	4	4

APPENDIX B 2

CLINICAL OBSERVATION : FEMALE

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
COLORED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	512 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1280 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	3200 ppm	0	2	2	2	2	2	2	2	2	2	2	2	2
	8000 ppm	0	0	0	2	2	2	2	2	2	2	2	2	2
	20000 ppm	2	6	6	7	7	7	7	7	7	7	7	7	7
SOILED PERI-GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	512 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1280 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	3200 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	8000 ppm	0	1	2	3	3	3	3	3	3	3	3	3	3
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
CORNEAL OPACITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0
	512 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	1280 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	3200 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	8000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0
	20000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	1
NON REMARKABLE	Control	10	10	10	10	10	10	10	10	10	10	10	10	10
	512 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	1280 ppm	10	10	10	10	10	10	10	10	10	10	10	10	10
	3200 ppm	10	8	8	8	8	8	8	8	8	8	8	8	8
	8000 ppm	10	9	8	5	5	5	5	5	5	5	5	5	5
	20000 ppm	8	4	4	3	3	3	3	3	3	3	3	3	3

APPENDIX C 1

BODY WEIGHT CHANGES : MALE

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 0	1	2	3	4	5	6
Control	123± 4	153± 6	188± 9	210± 9	229± 11	245± 12	260± 13
512 ppm	123± 4	152± 5	198± 44	205± 7	220± 9	238± 8	252± 10
1280 ppm	123± 4	152± 4	185± 6	209± 6	226± 7	242± 9	257± 8
3200 ppm	123± 4	151± 4	186± 5	206± 5	221± 5	237± 7	253± 6
8000 ppm	123± 4	150± 5	181± 5	200± 4**	212± 7**	223± 10**	240± 12**
20000 ppm	123± 4	132± 5**	161± 6**	181± 6**	192± 8**	202± 10**	216± 11**

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

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 7	8	9	10	11	12	13
Control	273± 14	286± 15	296± 14	307± 15	314± 15	323± 17	330± 16
512 ppm	267± 10	281± 10	292± 11	301± 11	309± 11	317± 11	325± 13
1280 ppm	274± 9	289± 9	300± 9	309± 10	318± 11	327± 11	334± 11
3200 ppm	269± 8	283± 8	296± 10	306± 10	316± 11	325± 11	332± 9
8000 ppm	255± 12**	270± 12**	280± 15*	290± 14**	298± 14*	307± 14*	312± 17*
20000 ppm	230± 11**	241± 10**	253± 10**	262± 10**	271± 10**	278± 11**	285± 10**

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

APPENDIX C 2

BODY WEIGHT CHANGES : FEMALE

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 0	1	2	3	4	5	6
Control	99± 3	113± 4	127± 4	135± 4	141± 5	149± 6	152± 5
512 ppm	99± 3	115± 5	129± 6	137± 7	144± 7	152± 8	157± 9
1280 ppm	99± 3	112± 3	127± 4	135± 6	142± 5	148± 8	153± 8
3200 ppm	99± 3	113± 4	125± 5	134± 6	141± 5	147± 6	151± 7
8000 ppm	99± 3	111± 4	123± 6	129± 6	134± 6	141± 8	145± 9
20000 ppm	99± 3	104± 4**	118± 5**	125± 5**	129± 5**	135± 7**	140± 7**

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

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

BODY WEIGHT CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 7	8	9	10	11	12	13
Control	155± 6	158± 6	162± 7	167± 7	169± 7	172± 8	174± 8
512 ppm	160± 11	162± 12	166± 14	170± 14	174± 15	176± 15	178± 15
1280 ppm	156± 8	158± 10	164± 10	167± 10	171± 11	172± 9	175± 12
3200 ppm	156± 7	159± 8	162± 8	166± 7	168± 9	170± 7	172± 7
8000 ppm	149± 9	153± 9	156± 9	159± 10	162± 11	164± 11	167± 11
20000 ppm	143± 7**	147± 8*	149± 7*	151± 8**	156± 8*	158± 8*	161± 9*

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

APPENDIX D 1

FOOD CONSUMPTION CHANGES : MALE

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 1	2	3	4	5	6	7
Control	13.5± 0.7	14.1± 0.8	13.9± 0.7	14.4± 0.8	14.4± 0.9	14.4± 1.0	14.5± 1.0
512 ppm	13.2± 0.7	13.2± 0.7*	13.7± 0.7	13.8± 0.8	14.0± 0.7	14.2± 0.7	14.3± 0.9
1280 ppm	13.4± 0.8	13.8± 0.7	13.7± 0.8	14.1± 0.6	14.1± 0.7	14.5± 0.9	14.7± 0.6
3200 ppm	13.4± 0.5	14.1± 0.7	14.0± 0.7	14.1± 0.7	13.8± 0.5	14.3± 0.4	14.5± 0.8
8000 ppm	13.0± 0.5	13.6± 0.5	13.5± 0.4	13.7± 0.6	13.1± 0.9**	13.5± 0.9	13.8± 0.9
20000 ppm	11.1± 0.6**	12.4± 0.6**	12.9± 0.7**	12.8± 0.6**	12.3± 0.7**	12.7± 0.8**	13.0± 0.7**

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

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 13
SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 8	9	10	11	12	13
Control	14.4± 0.8	14.2± 0.7	14.3± 0.7	14.2± 0.9	14.4± 1.0	14.4± 0.9
512 ppm	14.0± 0.9	14.1± 0.8	14.1± 0.6	13.9± 0.8	14.3± 0.9	14.1± 0.8
1280 ppm	14.3± 0.7	14.3± 0.7	14.3± 0.6	14.5± 0.7	14.2± 0.6	14.2± 0.7
3200 ppm	14.4± 0.7	14.5± 0.8	14.6± 0.5	14.6± 0.6	14.9± 0.5	14.7± 0.8
8000 ppm	14.1± 0.8	13.6± 0.9	13.7± 0.9	13.8± 0.7	13.8± 0.9	13.6± 1.7
20000 ppm	12.9± 0.8**	13.2± 0.6*	13.1± 0.8**	13.2± 0.6**	13.1± 0.8**	13.2± 0.6*

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

APPENDIX D 2

FOOD CONSUMPTION CHANGES : FEMALE

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 1	2	3	4	5	6	7
Control	9.7± 0.5	9.9± 0.4	9.9± 0.6	9.9± 0.8	10.3± 0.8	9.9± 0.6	9.7± 0.8
512 ppm	9.9± 0.5	9.9± 0.8	10.1± 0.9	10.3± 0.8	10.3± 0.9	9.8± 0.9	9.9± 0.8
1280 ppm	9.4± 0.6	9.7± 0.7	10.0± 0.6	10.2± 1.0	10.4± 1.1	10.1± 0.8	9.7± 1.1
3200 ppm	9.9± 0.4	9.4± 0.5	9.7± 0.7	10.2± 0.5	9.9± 0.7	9.8± 0.6	9.8± 0.8
8000 ppm	9.3± 0.5	9.4± 0.6	9.2± 0.8	9.6± 0.8	9.7± 0.8	9.1± 0.9	9.1± 0.7
20000 ppm	9.4± 0.7	9.2± 0.7	9.5± 0.4	9.0± 0.7	9.3± 0.7*	9.0± 0.9	8.8± 0.7

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

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g
REPORT TYPE : A1 13
SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration week 8	9	10	11	12	13
Control	9.5± 0.5	9.5± 0.5	9.4± 0.6	9.3± 0.5	9.3± 0.6	9.2± 0.5
512 ppm	9.0± 1.1	9.2± 1.1	9.4± 0.9	9.5± 1.1	9.6± 0.8	9.2± 0.9
1280 ppm	9.3± 1.1	9.7± 1.2	9.7± 1.1	9.6± 1.1	9.3± 1.0	9.4± 1.1
3200 ppm	9.2± 0.6	9.3± 0.6	9.3± 0.5	8.9± 0.4	9.2± 0.6	8.9± 0.5
8000 ppm	9.0± 0.6	9.1± 0.5	9.0± 0.7	9.0± 0.8	9.0± 0.7	8.9± 0.9
20000 ppm	9.0± 0.5	8.7± 0.7	8.6± 0.6	9.0± 0.6	9.0± 0.6	8.9± 0.8

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

APPENDIX E 1

CHEMICAL INTAKE CHANGES : MALE

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g／kg／d a y
REPORT TYPE : A1 13
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2	3	4	5	6	7
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
512 ppm	0.044± 0.002	0.035± 0.005	0.034± 0.001	0.032± 0.001	0.030± 0.001	0.029± 0.001	0.027± 0.001
1280 ppm	0.113± 0.005	0.095± 0.003	0.084± 0.003	0.080± 0.002	0.075± 0.001	0.072± 0.002	0.069± 0.001
3200 ppm	0.284± 0.011	0.242± 0.008	0.218± 0.009	0.204± 0.008	0.186± 0.005	0.181± 0.004	0.172± 0.008
8000 ppm	0.694± 0.018	0.600± 0.012	0.540± 0.019	0.520± 0.022	0.469± 0.014	0.451± 0.014	0.433± 0.018
20000 ppm	1.681± 0.065	1.540± 0.048	1.425± 0.064	1.333± 0.077	1.216± 0.024	1.174± 0.042	1.127± 0.037

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g／kg／d a y
REPORT TYPE : A1 13
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8	9	10	11	12	13
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
512 ppm	0.026± 0.001	0.025± 0.001	0.024± 0.001	0.023± 0.001	0.023± 0.001	0.022± 0.001
1280 ppm	0.064± 0.002	0.061± 0.002	0.059± 0.001	0.058± 0.001	0.056± 0.002	0.054± 0.002
3200 ppm	0.163± 0.006	0.156± 0.005	0.153± 0.003	0.149± 0.005	0.146± 0.004	0.142± 0.007
8000 ppm	0.417± 0.021	0.389± 0.014	0.380± 0.016	0.372± 0.014	0.361± 0.013	0.348± 0.033
20000 ppm	1.070± 0.067	1.043± 0.049	0.997± 0.056	0.972± 0.036	0.940± 0.050	0.925± 0.044

APPENDIX E 2

CHEMICAL INTAKE CHANGES : FEMALE

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g／kg／d a y
REPORT TYPE : A1 13
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2	3	4	5	6	7
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
512 ppm	0.044± 0.003	0.039± 0.002	0.038± 0.003	0.037± 0.002	0.035± 0.002	0.032± 0.002	0.032± 0.002
1280 ppm	0.107± 0.005	0.098± 0.007	0.095± 0.003	0.092± 0.007	0.090± 0.006	0.085± 0.004	0.080± 0.006
3200 ppm	0.280± 0.007	0.241± 0.008	0.232± 0.010	0.232± 0.009	0.217± 0.009	0.207± 0.009	0.202± 0.011
8000 ppm	0.674± 0.029	0.614± 0.031	0.567± 0.031	0.569± 0.030	0.548± 0.022	0.502± 0.033	0.491± 0.022
20000 ppm	1.807± 0.089	1.566± 0.108	1.519± 0.075	1.398± 0.069	1.367± 0.064	1.283± 0.076	1.230± 0.064

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
UNIT : g／kg／d a y
REPORT TYPE : A1 13
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8	9	10	11	12	13
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
512 ppm	0.028± 0.002	0.029± 0.001	0.029± 0.001	0.028± 0.001	0.028± 0.001	0.026± 0.001
1280 ppm	0.075± 0.005	0.076± 0.006	0.075± 0.006	0.072± 0.005	0.069± 0.005	0.069± 0.005
3200 ppm	0.187± 0.010	0.184± 0.009	0.179± 0.007	0.171± 0.010	0.174± 0.011	0.165± 0.009
8000 ppm	0.470± 0.012	0.467± 0.019	0.455± 0.021	0.445± 0.017	0.439± 0.020	0.424± 0.028
20000 ppm	1.234± 0.044	1.165± 0.059	1.142± 0.058	1.152± 0.038	1.136± 0.029	1.111± 0.039

APPENDIX F 1

HEMATOLOGY : MALE

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RED BLOOD CELL $10^5/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	10	9.34± 0.17	16.3± 0.3	45.6± 0.6	48.8± 0.6	17.5± 0.4	35.8± 0.6	687± 53
512 ppm	10	9.40± 0.19	16.4± 0.3	45.9± 1.0	48.9± 0.6	17.4± 0.2	35.6± 0.4	680± 29
1280 ppm	10	9.32± 0.17	16.2± 0.2	45.5± 0.8	48.9± 0.6	17.4± 0.2	35.6± 0.6	711± 40
3200 ppm	10	8.97± 0.13**	15.6± 0.3**	44.5± 0.9*	49.6± 0.5*	17.4± 0.3	35.1± 0.5**	745± 64*
8000 ppm	10	8.56± 0.17**	15.3± 0.3**	44.0± 0.6**	51.4± 0.7**	17.8± 0.2**	34.7± 0.3**	796± 60**
20000 ppm	10	7.82± 0.15**	14.6± 0.2**	42.3± 0.8**	54.0± 0.6**	18.7± 0.2**	34.5± 0.3**	748± 42*

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

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RETICULOCYTE %	METHEMOGLOBIN %
Control	10	1.8± 0.1	0.3± 0.1
512 ppm	10	1.8± 0.2	0.3± 0.1
1280 ppm	10	2.0± 0.2*	0.3± 0.1
3200 ppm	10	2.6± 0.2**	0.5± 0.1
8000 ppm	10	3.8± 0.3**	0.8± 0.3**
20000 ppm	10	5.6± 0.2**	1.0± 0.2**

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

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHER
Control	10	4.54± 1.14	0± 0	19± 3	1± 1	0± 0	3± 2	77± 4	0± 0
512 ppm	10	4.81± 0.87	0± 0	17± 3	1± 1	0± 0	3± 1	78± 4	0± 0
1280 ppm	10	5.11± 0.93	0± 0	18± 3	1± 1	0± 0	3± 2	78± 4	0± 0
3200 ppm	10	4.82± 1.04	0± 0	20± 3	1± 1	0± 0	3± 2	76± 4	0± 0
8000 ppm	10	5.03± 0.85	0± 0	17± 4	1± 1	0± 0	3± 1	79± 4	0± 0
20000 ppm	10	4.94± 0.98	0± 1	16± 4	1± 1	0± 0	3± 2	80± 4	0± 0

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

APPENDIX F 2

HEMATOLOGY : FEMALE

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RED BLOOD CELL $10^6/\mu\ell$	HEMOGLOBIN g/dℓ	HEMATOCRIT %	MCV f ℓ	MCH p g	MCHC g/dℓ	PLATELET $10^3/\mu\ell$
Control	10	8.76± 0.23	16.3± 0.5	44.5± 1.1	50.9± 0.5	18.6± 0.1	36.5± 0.5	740± 33
512 ppm	10	8.60± 0.21	16.0± 0.4	43.8± 1.0	50.9± 0.6	18.6± 0.1	36.6± 0.3	724± 60
1280 ppm	10	8.50± 0.16*	15.9± 0.3	43.8± 0.6	51.6± 0.6*	18.7± 0.2	36.3± 0.4	776± 53
3200 ppm	10	8.20± 0.22**	15.6± 0.4**	43.6± 1.3	53.2± 0.6**	19.0± 0.2**	35.8± 0.4**	763± 61
8000 ppm	10	7.75± 0.25**	15.0± 0.4**	41.9± 1.2**	54.1± 0.4**	19.4± 0.3**	35.8± 0.4**	869± 85**
20000 ppm	10	7.14± 0.16**	14.1± 0.3**	40.0± 0.8**	56.1± 0.5**	19.8± 0.3**	35.4± 0.5**	848± 65**

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

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	RETICULOCYTE %	METHEMOGLOBIN %
Control	10	1.7± 0.2	0.3± 0.1
512 ppm	10	1.7± 0.2	0.3± 0.1
1280 ppm	10	2.1± 0.2	0.3± 0.0
3200 ppm	10	2.5± 0.4**	0.3± 0.1
8000 ppm	10	3.7± 0.7**	0.7± 0.3
20000 ppm	10	5.7± 0.7**	1.0± 0.3**

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

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

HEMATOLOGY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	WBC $10^3/\mu\ell$	Differential WBC (%) N-BAND	N-SEG	EOSINO	BASO	MONO	LYMPHO	OTHER
Control	10	2.45± 0.70	0± 0	17± 4	1± 1	0± 0	4± 2	78± 5	0± 0
512 ppm	10	2.66± 1.20	0± 0	18± 4	1± 1	0± 0	3± 2	77± 5	0± 0
1280 ppm	10	2.52± 0.78	0± 0	17± 3	2± 1	0± 0	4± 2	78± 3	0± 0
3200 ppm	10	2.49± 0.47	0± 0	18± 3	1± 1	0± 0	4± 2	78± 4	0± 0
8000 ppm	10	2.86± 0.82	0± 0	17± 4	1± 1	0± 0	3± 2	79± 4	0± 0
20000 ppm	10	3.22± 1.25	0± 0	18± 4	1± 1	0± 0	4± 2	78± 5	0± 0

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

APPENDIX G 1

BIOCHEMISTRY : MALE

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	TOTAL PROTEIN g/dl	ALBUMIN g/dl	A/G RATIO	T-BILIRUBIN mg/dl	GLUCOSE mg/dl	T-CHOLESTEROL mg/dl	TRIGLYCERIDE mg/dl
Control	10	6.3± 0.2	3.5± 0.1	1.3± 0.1	0.11± 0.01	210± 22	65± 4	60± 15
512 ppm	10	6.4± 0.2	3.5± 0.1	1.3± 0.1	0.12± 0.01	214± 18	63± 4	68± 16
1280 ppm	10	6.4± 0.1	3.5± 0.1	1.2± 0.1	0.12± 0.01	213± 15	62± 5	63± 20
3200 ppm	10	6.5± 0.1	3.6± 0.1	1.2± 0.0	0.12± 0.01	221± 19	63± 5	66± 16
8000 ppm	10	6.4± 0.1	3.5± 0.1	1.3± 0.1	0.12± 0.01	206± 12	62± 4	56± 23
20000 ppm	10	6.5± 0.2	3.6± 0.1	1.2± 0.1	0.16± 0.02**	201± 12	73± 6**	54± 16

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

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dl	AST IU/l	ALT IU/l	LDH IU/l	ALP IU/l	G-GTP IU/l	CK IU/l
Control	10	115± 7	109± 45	56± 16	215± 74	242± 15	1± 1	112± 11
512 ppm	10	115± 6	122± 34	59± 13	227± 48	248± 15	1± 1	109± 11
1280 ppm	10	116± 9	110± 37	53± 12	205± 67	252± 10	1± 0	108± 14
3200 ppm	10	118± 8	131± 68	59± 20	257± 134	250± 22	2± 1	118± 21
8000 ppm	10	115± 7	99± 28	45± 10	177± 46	242± 25	2± 1	100± 11
20000 ppm	10	130± 7**	84± 10	35± 3**	160± 45	225± 27	4± 1**	94± 14*

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

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	UREA NITOROGEN mg/dl	CREATININE mg/dl	SODIUM mEq/ℓ	POTASSIUM mEq/ℓ	CHLORIDE mEq/ℓ	CALCIUM mg/dl	INORGANIC PHOSPHORUS mg/dl
Control	10	18.4± 1.2	0.5± 0.1	141± 1	3.4± 0.2	104± 1	10.2± 0.2	5.3± 0.6
512 ppm	10	18.5± 1.0	0.5± 0.1	141± 1	3.3± 0.2	104± 2	10.2± 0.2	5.5± 0.5
1280 ppm	10	18.5± 1.8	0.5± 0.1	142± 1	3.4± 0.2	104± 1	10.3± 0.2	5.4± 0.5
3200 ppm	10	18.9± 1.3	0.6± 0.1	142± 1	3.4± 0.2	104± 1	10.3± 0.2	5.5± 0.5
8000 ppm	10	18.4± 2.0	0.5± 0.1	141± 1	3.5± 0.2	104± 1	10.2± 0.3	5.5± 0.6
20000 ppm	10	18.9± 1.9	0.5± 0.1	141± 1	3.8± 0.2**	103± 1	10.4± 0.2	5.7± 0.5

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

APPENDIX G 2

BIOCHEMISTRY : FEMALE

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	TOTAL PROTEIN g/dl	ALBUMIN g/dl	A/G RATIO	T-BILIRUBIN mg/dl	GLUCOSE mg/dl	T-CHOLESTEROL mg/dl	TRIGLYCERIDE mg/dl
Control	10	6.3± 0.2	3.5± 0.1	1.2± 0.1	0.14± 0.02	151± 16	75± 6	14± 4
512 ppm	10	6.2± 0.2	3.5± 0.1	1.3± 0.1	0.14± 0.02	152± 11	74± 5	14± 4
1280 ppm	10	6.3± 0.2	3.5± 0.1	1.3± 0.1	0.14± 0.03	151± 16	79± 3	16± 7
3200 ppm	10	6.2± 0.2	3.4± 0.1	1.3± 0.1	0.19± 0.14	143± 17	75± 4	14± 4
8000 ppm	10	6.3± 0.2	3.6± 0.1	1.4± 0.1**	0.15± 0.02	162± 10	82± 6**	14± 7
20000 ppm	10	6.3± 0.2	3.5± 0.1	1.3± 0.1	0.17± 0.02*	180± 20**	93± 6**	16± 5

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

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	PHOSPHOLIPID mg/dℓ	AST IU/ℓ	ALT IU/ℓ	LDH IU/ℓ	ALP IU/ℓ	G-GTP IU/ℓ	CK IU/ℓ
Control	10	140± 11	87± 12	40± 5	261± 84	179± 21	2± 1	127± 23
512 ppm	10	139± 9	80± 10	37± 3	266± 190	188± 26	2± 1	134± 50
1280 ppm	10	150± 8	78± 9	37± 6	252± 154	174± 24	1± 1	126± 46
3200 ppm	10	141± 6	81± 18	34± 6*	427± 605	187± 18	2± 1	179± 120
8000 ppm	10	150± 11	90± 33	37± 13*	268± 110	186± 17	3± 1**	125± 29
20000 ppm	10	158± 8**	86± 11	34± 5	294± 155	191± 19	7± 2**	126± 41

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

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

BIOCHEMISTRY (SUMMARY)
ALL ANIMALS (14W)

Group Name	NO. of Animals	UREA NITOROGEN mg/dl	CREATININE mg/dl	SODIUM mEq/l	POTASSIUM mEq/l	CHLORIDE mEq/l	CALCIUM mg/dl	INORGANIC PHOSPHORUS mg/dl
Control	10	19.0± 1.0	0.5± 0.1	141± 1	3.5± 0.3	105± 2	9.8± 0.3	5.2± 1.0
512 ppm	10	19.0± 1.6	0.5± 0.1	141± 1	3.6± 0.2	105± 2	9.9± 0.3	5.2± 0.8
1280 ppm	10	18.0± 2.4	0.6± 0.1	141± 2	3.5± 0.3	105± 2	9.7± 0.3	5.0± 0.8
3200 ppm	10	17.7± 2.0	0.6± 0.1	140± 2	3.8± 0.5	106± 2	9.7± 0.3	5.6± 0.7
8000 ppm	10	19.1± 1.3	0.6± 0.1	141± 1	3.6± 0.3	105± 1	9.7± 0.4	5.1± 0.8
20000 ppm	10	20.6± 1.3	0.5± 0.0	140± 1	3.7± 0.3	105± 1	9.8± 0.3	5.2± 0.7

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

APPENDIX H 1

URINALYSIS : MALE

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

URINALYSIS

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Bilirubin −	+	2+	3+	CHI
Control	10	0	0	0	0	0	4	6		0	0	6	4	0	0		10	0	0	0	0	0		0	3	7	0	0	0		10	0	0	0	
512 ppm	10	0	0	0	0	0	3	7		0	0	8	2	0	0		10	0	0	0	0	0		0	6	4	0	0	0		10	0	0	0	
1280 ppm	10	0	0	0	0	0	4	6		0	1	7	2	0	0		10	0	0	0	0	0		2	4	4	0	0	0		10	0	0	0	
3200 ppm	10	0	0	0	0	0	2	8		0	0	10	0	0	0	*	10	0	0	0	0	0		0	8	2	0	0	0	*	10	0	0	0	
8000 ppm	10	0	0	0	0	2	4	4		0	3	7	0	0	0	*	10	0	0	0	0	0		2	6	2	0	0	0		10	0	0	0	
20000 ppm	10	0	0	0	1	6	2	1	*	0	10	0	0	0	0	**	10	0	0	0	0	0		7	2	1	0	0	0	**	0	10	0	0	**

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

STUDY NO. : 0549 URINALYSIS
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : MALE REPORT TYPE : A1

Group Name	NO. of Animals	Occult blood −	±	+	2+	3+	CHI	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	9	1	0	0	0		10	0	0	0	0	
512 ppm	10	10	0	0	0	0		10	0	0	0	0	
1280 ppm	10	10	0	0	0	0		10	0	0	0	0	
3200 ppm	10	9	0	1	0	0		10	0	0	0	0	
8000 ppm	10	10	0	0	0	0		10	0	0	0	0	
20000 ppm	10	10	0	0	0	0		10	0	0	0	0	

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

APPENDIX H 2

URINALYSIS : FEMALE

STUDY NO. : 0549 URINALYSIS
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
MEASURE. TIME : 1
SEX : FEMALE REPORT TYPE : A1

Group Name	NO. of Animals	pH 5.0	6.0	6.5	7.0	7.5	8.0	8.5	CHI	Protein −	±	+	2+	3+	4+	CHI	Glucose −	±	+	2+	3+	4+	CHI	Ketone body −	±	+	2+	3+	4+	CHI	Bilirubin −	+	2+	3+	CHI
Control	10	0	0	0	0	0	8	2		0	4	6	0	0	0		10	0	0	0	0	0		4	6	0	0	0	0		10	0	0	0	
512 ppm	10	0	0	0	0	0	1	9	**	0	4	6	0	0	0		10	0	0	0	0	0		6	4	0	0	0	0		10	0	0	0	
1280 ppm	10	0	0	0	0	0	2	8	**	0	4	6	0	0	0		10	0	0	0	0	0		6	4	0	0	0	0		10	0	0	0	
3200 ppm	10	0	0	0	0	0	1	9	**	0	7	3	0	0	0		10	0	0	0	0	0		6	4	0	0	0	0		10	0	0	0	
8000 ppm	10	0	0	0	0	0	3	7	*	2	6	2	0	0	0		10	0	0	0	0	0		7	3	0	0	0	0		7	3	0	0	
20000 ppm	10	0	0	0	0	0	10	0		1	7	2	0	0	0		10	0	0	0	0	0		10	0	0	0	0	0	**	2	8	0	0	**

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

Group Name	NO. of Animals	Occult blood −	±	+	2+	3+	CHI	Urobilinogen ±	+	2+	3+	4+	CHI
Control	10	10	0	0	0	0		10	0	0	0	0	
512 ppm	10	10	0	0	0	0		10	0	0	0	0	
1280 ppm	10	10	0	0	0	0		10	0	0	0	0	
3200 ppm	10	10	0	0	0	0		10	0	0	0	0	
8000 ppm	10	10	0	0	0	0		10	0	0	0	0	
20000 ppm	10	10	0	0	0	0		10	0	0	0	0	

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

APPENDIX I 1

GROSS FINDINGS : MALE

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	512 ppm 10 (%)	1280 ppm 10 (%)	3200 ppm 10 (%)
spleen	enlarged		0 (0)	0 (0)	0 (0)	0 (0)
forestomach	ulcer		0 (0)	0 (0)	0 (0)	0 (0)
	thick		0 (0)	0 (0)	0 (0)	0 (0)
liver	herniation		0 (0)	2 (20)	0 (0)	1 (10)

Organ	Findings	Group Name	8000 ppm	20000 ppm
		NO. of Animals	10 (%)	10 (%)
spleen	enlarged		0 (0)	10 (100)
forestomach	ulcer		0 (0)	1 (10)
	thick		1 (10)	10 (100)
liver	herniation		2 (20)	1 (10)

APPENDIX I 2

GROSS FINDINGS : FEMALE

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	512 ppm 10 (%)	1280 ppm 10 (%)	3200 ppm 10 (%)
spleen	enlarged		0 (0)	0 (0)	0 (0)	0 (0)
forestomach	ulcer		0 (0)	0 (0)	0 (0)	0 (0)
	thick		0 (0)	0 (0)	0 (0)	0 (0)
liver	herniation		2 (20)	4 (40)	1 (10)	1 (10)
urin bladd	white zone		0 (0)	0 (0)	1 (10)	0 (0)
eye	turbid		0 (0)	0 (0)	0 (0)	0 (0)

Organ	Findings	Group Name NO. of Animals	8000 ppm 10 (%)	20000 ppm 10 (%)
spleen	enlarged		0 (0)	10 (100)
forestomach	ulcer		0 (0)	2 (20)
	thick		0 (0)	10 (100)
liver	herniation		1 (10)	1 (10)
urin bladd	white zone		0 (0)	0 (0)
eye	turbid		0 (0)	1 (10)

APPENDIX J 1

ORGAN WEIGHT, ABSOLUTE : MALE

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	310± 16	0.224± 0.031	0.047± 0.003	3.058± 0.115	0.926± 0.034	0.964± 0.038
512 ppm	10	304± 12	0.229± 0.028	0.048± 0.004	3.069± 0.068	0.912± 0.044	0.976± 0.048
1280 ppm	10	313± 11	0.226± 0.023	0.048± 0.004	3.086± 0.065	0.932± 0.031	0.991± 0.052
3200 ppm	10	311± 9	0.218± 0.020	0.048± 0.003	3.077± 0.144	0.932± 0.035	0.975± 0.035
8000 ppm	10	291± 17**	0.203± 0.028	0.046± 0.002	3.089± 0.051	0.908± 0.045	0.968± 0.036
20000 ppm	10	266± 11**	0.190± 0.019*	0.042± 0.002*	3.057± 0.089	0.858± 0.025**	0.910± 0.040*

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

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE
UNIT: g

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.836± 0.066	0.579± 0.022	7.419± 0.467	1.959± 0.043
512 ppm	10	1.820± 0.069	0.562± 0.025	7.353± 0.488	1.960± 0.023
1280 ppm	10	1.864± 0.068	0.597± 0.029	7.523± 0.422	1.954± 0.031
3200 ppm	10	1.927± 0.080*	0.638± 0.034	7.872± 0.439	1.956± 0.033
8000 ppm	10	1.922± 0.073*	0.748± 0.058**	7.485± 0.514	1.947± 0.041
20000 ppm	10	1.871± 0.081	1.211± 0.061**	7.892± 0.263	1.899± 0.027**

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

APPENDIX J 2

ORGAN WEIGHT, ABSOLUTE : FEMALE

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	Body Weight	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	160± 8	0.178± 0.016	0.052± 0.002	0.104± 0.007	0.584± 0.014	0.710± 0.027
512 ppm	10	165± 15	0.185± 0.026	0.052± 0.004	0.104± 0.014	0.593± 0.036	0.739± 0.048
1280 ppm	10	162± 10	0.172± 0.019	0.050± 0.004	0.101± 0.009	0.592± 0.038	0.718± 0.043
3200 ppm	10	159± 6	0.175± 0.016	0.048± 0.003	0.100± 0.016	0.577± 0.035	0.708± 0.022
8000 ppm	10	154± 10	0.168± 0.011	0.049± 0.003	0.097± 0.012	0.573± 0.037	0.709± 0.033
20000 ppm	10	149± 9*	0.166± 0.026	0.047± 0.003**	0.088± 0.006**	0.579± 0.046	0.695± 0.048

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

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	1.062± 0.031	0.376± 0.026	3.739± 0.186	1.800± 0.028
512 ppm	10	1.099± 0.053	0.379± 0.032	3.813± 0.345	1.800± 0.039
1280 ppm	10	1.069± 0.080	0.381± 0.025	3.871± 0.432	1.804± 0.033
3200 ppm	10	1.055± 0.034	0.408± 0.027	3.820± 0.162	1.792± 0.033
8000 ppm	10	1.060± 0.041	0.461± 0.029**	3.880± 0.268	1.768± 0.029
20000 ppm	10	1.090± 0.063	0.740± 0.064**	4.439± 0.313**	1.765± 0.038

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

APPENDIX K 1

ORGAN WEIGHT, RELATIVE : MALE

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	TESTES	HEART	LUNGS
Control	10	310± 16	0.072± 0.008	0.015± 0.001	0.989± 0.058	0.299± 0.017	0.311± 0.016
512 ppm	10	304± 12	0.075± 0.008	0.016± 0.001	1.011± 0.045	0.300± 0.012	0.321± 0.015
1280 ppm	10	313± 11	0.072± 0.006	0.015± 0.001	0.988± 0.044	0.298± 0.010	0.317± 0.013
3200 ppm	10	311± 9	0.070± 0.006	0.015± 0.001	0.991± 0.042	0.300± 0.012	0.314± 0.009
8000 ppm	10	291± 17**	0.070± 0.007	0.016± 0.001	1.064± 0.063**	0.312± 0.007	0.333± 0.017**
20000 ppm	10	266± 11**	0.071± 0.005	0.016± 0.001	1.152± 0.055**	0.323± 0.011**	0.343± 0.017**

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

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.593± 0.014	0.187± 0.006	2.394± 0.093	0.633± 0.030
512 ppm	10	0.599± 0.015	0.185± 0.006	2.418± 0.077	0.646± 0.022
1280 ppm	10	0.596± 0.018	0.191± 0.008	2.404± 0.074	0.626± 0.026
3200 ppm	10	0.620± 0.025*	0.205± 0.010	2.532± 0.083**	0.630± 0.016
8000 ppm	10	0.661± 0.027**	0.257± 0.009**	2.570± 0.077**	0.671± 0.042*
20000 ppm	10	0.704± 0.022**	0.456± 0.024**	2.972± 0.109**	0.716± 0.029**

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

APPENDIX K 2

ORGAN WEIGHT, RELATIVE : FEMALE

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	Body Weight (g)	THYMUS	ADRENALS	OVARIES	HEART	LUNGS
Control	10	160± 8	0.111± 0.010	0.032± 0.002	0.065± 0.003	0.366± 0.016	0.444± 0.023
512 ppm	10	165± 15	0.112± 0.011	0.032± 0.002	0.063± 0.008	0.361± 0.017	0.450± 0.027
1280 ppm	10	162± 10	0.106± 0.007	0.031± 0.002	0.062± 0.004	0.367± 0.018	0.445± 0.025
3200 ppm	10	159± 6	0.111± 0.011	0.030± 0.002	0.063± 0.011	0.363± 0.015	0.446± 0.025
8000 ppm	10	154± 10	0.110± 0.008	0.032± 0.003	0.063± 0.005	0.372± 0.014	0.461± 0.024
20000 ppm	10	149± 9*	0.111± 0.013	0.032± 0.003	0.060± 0.005	0.390± 0.023*	0.468± 0.023

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

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

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

Group Name	NO. of Animals	KIDNEYS	SPLEEN	LIVER	BRAIN
Control	10	0.664± 0.028	0.235± 0.012	2.335± 0.086	1.127± 0.072
512 ppm	10	0.670± 0.040	0.231± 0.009	2.315± 0.080	1.100± 0.089
1280 ppm	10	0.661± 0.026	0.236± 0.011	2.390± 0.147	1.120± 0.062
3200 ppm	10	0.665± 0.027	0.257± 0.019	2.407± 0.083	1.130± 0.051
8000 ppm	10	0.689± 0.040	0.299± 0.009**	2.517± 0.093**	1.150± 0.067
20000 ppm	10	0.734± 0.016**	0.498± 0.020**	2.990± 0.132**	1.192± 0.065

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

APPENDIX L 1

HISTOPATHOLOGICAL FINDINGS :

NON-NEOPLASTIC LESIONS : MALE

STUDY NO. : 0549
ANIMAL : RAT F344/DuCrlCrlj[F344/DuCrj]
REPORT TYPE : A1
SEX : MALE

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 10				512 ppm 10				1280 ppm 10				3200 ppm 10			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Respiratory system}																		
nasal cavit			<10>				<10>				<10>				<10>			
	inflammation:foreign body		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:gland		3 (30)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	5 (50)	0 (0)	0 (0)	0 (0)	3 (30)	0 (0)	0 (0)	0 (0)
lung			<10>				<10>				<10>				<10>			
	hemorrhage		0 (0)	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)
	accumulation of foamy cells		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)
{Hematopoietic system}																		
spleen			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0) **
	extramedullary hematopoiesis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0) **

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

Organ	Findings	Group Name	8000 ppm				20000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			<10>				<10>			
	inflammation:foreign body		2	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	respiratory metaplasia:gland		2	0	0	0	4	0	0	0
			(20)	(0)	(0)	(0)	(40)	(0)	(0)	(0)
lung			<10>				<10>			
	hemorrhage		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	accumulation of foamy cells		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Hematopoietic system}										
spleen			<10>				<10>			
	deposit of hemosiderin		10	0	0	0 **	10	0	0	0 **
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	extramedullary hematopoiesis		10	0	0	0 **	10	0	0	0 **
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 10				512 ppm 10				1280 ppm 10				3200 ppm 10			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Hematopoietic system}																		
spleen			<10>				<10>				<10>				<10>			
	engorgement of erythrocyte		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 ** (0)
{Circulatory system}																		
heart			<10>				<10>				<10>				<10>			
	inflammatory infiltration		0 (0)	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)
{Digestive system}																		
stomach			<10>				<10>				<10>				<10>			
	ulcer: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)
	hyperplasia:forestomach		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
liver			<10>				<10>				<10>				<10>			
	herniation		0 (0)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)

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

Organ	Findings	Group Name	8000 ppm				20000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
spleen			<10>				<10>			
	engorgement of erythrocyte		10	0	0	0 **	0	10	0	0 **
			(100)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
{Circulatory system}										
heart			<10>				<10>			
	inflammatory infiltration		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Digestive system}										
stomach			<10>				<10>			
	ulcer:forestomach		0	0	0	0	0	1	0	0
			(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)
	hyperplasia:forestomach		3	7	0	0 **	0	0	10	0 **
			(30)	(70)	(0)	(0)	(0)	(0)	(100)	(0)
liver			<10>				<10>			
	herniation		2	0	0	0	1	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 ≦ 0.05 ** : P ≦ 0.01 Test of Chi Square

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 10				512 ppm 10				1280 ppm 10				3200 ppm 10			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	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 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	eosinophilic body		10 (100)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0)
urin bladd			<10>				<10>				<10>				<10>			
	squamous cell metaplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	transitional cell hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	8000 ppm 10				20000 ppm 10			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
(Digestive system)										
liver			<10>				<10>			
	deposit of hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0) **
	granulation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
(Urinary system)										
kidney			<10>				<10>			
	deposit of hemosiderin		7 (70)	0 (0)	0 (0)	0 (0) **	10 (100)	0 (0)	0 (0)	0 (0) **
	eosinophilic body		10 (100)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0)
urin bladd			<10>				<10>			
	squamous cell metaplasia		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
	transitional cell hyperplasia		0 (0)	0 (0)	0 (0)	0 (0)	4 (40)	5 (50)	0 (0)	0 (0) **

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 10				512 ppm 10				1280 ppm 10				3200 ppm 10			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Urinary system}																		
urin bladd			<10>				<10>				<10>				<10>			
	swelling:transitional 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)
{Endocrine system}																		
pituitary			<10>				<10>				<10>				<10>			
	Rathke pouch		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
adrenal			<10>				<10>				<10>				<10>			
	hyperplasia:cortical cell		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)	0 (0)	0 (0)	0 (0)
{Reproductive system}																		
prostate			<10>				<10>				<10>				<10>			
	inflammatory infiltration		0 (0)	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)

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

Organ	Findings	Group Name	8000 ppm				20000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Urinary system}										
urin bladd			<10>				<10>			
	swelling:transitional epithelium		0	0	0	0	3	6	0	0 **
			(0)	(0)	(0)	(0)	(30)	(60)	(0)	(0)
{Endocrine system}										
pituitary			<10>				<10>			
	Rathke pouch		2	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
adrenal			<10>				<10>			
	hyperplasia:cortical cell		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Reproductive system}										
prostate			<10>				<10>			
	inflammatory infiltration		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

APPENDIX L 2

HISTOPATHOLOGICAL FINDINGS :

NON-NEOPLASTIC LESIONS : FEMALE

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 10				512 ppm 10				1280 ppm 10				3200 ppm 10			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Respiratory system}																		
nasal cavit			<10>				<10>				<10>				<10>			
	inflammatory infiltration		1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
	respiratory metaplasia:gland		4 (40)	0 (0)	0 (0)	0 (0)	4 (40)	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>			
	inflammatory infiltration		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
{Hematopoietic system}																		
bone marrow			<10>				<10>				<10>				<10>			
	granulation		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)	1 (10)	0 (0)	0 (0)
spleen			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0) **
	extramedullary hematopoiesis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

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

Organ	Findings	Group Name	8000 ppm				20000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Respiratory system}										
nasal cavit			<10>				<10>			
	inflammatory infiltration		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	respiratory metaplasia:gland		2	0	0	0	2	0	0	0
			(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
lung			<10>				<10>			
	inflammatory infiltration		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
{Hematopoietic system}										
bone marrow			<10>				<10>			
	granulation		2	0	0	0	1	0	0	0
			(20)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
spleen			<10>				<10>			
	deposit of hemosiderin		10	0	0	0 **	10	0	0	0 **
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	extramedullary hematopoiesis		10	0	0	0 **	10	0	0	0 **
			(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)

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

Organ	Findings	Group Name / No. of Animals on Study / Grade	Control 10				512 ppm 10				1280 ppm 10				3200 ppm 10			
			1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)	1 (%)	2 (%)	3 (%)	4 (%)
{Hematopoietic system}																		
spleen			<10>				<10>				<10>				<10>			
	engorgement of erythrocyte		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 ** (0)
{Digestive system}																		
stomach			<10>				<10>				<10>				<10>			
	erosion: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)
	ulcer: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)
	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)
large intes			<10>				<10>				<10>				<10>			
	mineralization		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)
liver			<10>				<10>				<10>				<10>			
	herniation		2 (20)	0 (0)	0 (0)	0 (0)	4 (40)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)

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

Organ	Findings	Group Name	8000 ppm				20000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Hematopoietic system}										
spleen			<10>				<10>			
	engorgement of erythrocyte		10	0	0	0 **	0	10	0	0 **
			(100)	(0)	(0)	(0)	(0)	(100)	(0)	(0)
{Digestive system}										
stomach			<10>				<10>			
	erosion:forestomach		0	0	0	0	2	0	0	0
			(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
	ulcer:forestomach		0	0	0	0	1	1	0	0
			(0)	(0)	(0)	(0)	(10)	(10)	(0)	(0)
	hyperplasia:forestomach		3	7	0	0 **	0	0	10	0 **
			(30)	(70)	(0)	(0)	(0)	(0)	(100)	(0)
large intes			<10>				<10>			
	mineralization		0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
liver			<10>				<10>			
	herniation		1	0	0	0	1	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)

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

Organ	Findings	Group Name	Control				512 ppm				1280 ppm				3200 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
{Digestive system}																		
liver			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		0	0	0	0	0	0	0	0	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	1	0	0	0	1	0	0	0	2	0	0	0
			(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
{Urinary system}																		
kidney			<10>				<10>				<10>				<10>			
	deposit of hemosiderin		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(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:cortico-medullary junction		2	0	0	0	0	0	0	0	1	0	0	0	2	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)
urin bladd			<10>				<10>				<10>				<10>			
	swelling:transitional 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)

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

Organ	Findings	Group Name	8000 ppm				20000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Digestive system}										
liver			<10>				<10>			
	deposit of hemosiderin		0	0	0	0	10	0	0	0 **
			(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	granulation		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
{Urinary system}										
kidney			<10>				<10>			
	deposit of hemosiderin		9	0	0	0 **	10	0	0	0 **
			(90)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
	hyaline cast		1	0	0	0	0	0	0	0
			(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineralization:cortico-medullary junction		2	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
urin bladd			<10>				<10>			
	swelling:transitional epithelium		0	0	0	0	4	1	0	0 *
			(0)	(0)	(0)	(0)	(40)	(10)	(0)	(0)

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

Organ	Findings	Group Name	Control				512 ppm				1280 ppm				3200 ppm			
		No. of Animals on Study	10				10				10				10			
		Grade	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
(Special sense organs/appendage)																		
eye			<10>				<10>				<10>				<10>			
	degeneration:cornea		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
Harder gl			<10>				<10>				<10>				<10>			
	granulation		0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(10)	(0)	(0)	(0)

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

Organ	Findings	Group Name	8000 ppm				20000 ppm			
		No. of Animals on Study	10				10			
		Grade	1	2	3	4	1	2	3	4
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
{Special sense organs/appendage}										
eye			<10>				<10>			
	degeneration:cornea		0	0	0	0	1	0	0	0
			(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
Harder gl			<10>				<10>			
	granulation		2	0	0	0	0	0	0	0
			(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

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

APPENDIX M

METHODS, UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13-WEEK FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

METHODS, UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY IN THE 13- WEEK FEED STUDY OF 2-AMINO-4-CHLOROPHENOL

Item	Method	Unit	Decimal place
Hematology			
Red blood cell (RBC)	Light scattering method[1)]	$\times 10^6/\mu L$	2
Hemoglobin(Hgb)	Cyanmethemoglobin method[1)]	g/dL	1
Methemoglobin	Multiple-wavelength Spectrophotometric method[4)]	%	1
Hematocrit(Hct)	Calculated as RBC×MCV/10[1)]	%	1
Mean corpuscular volume(MCV)	Light scattering method[1)]	fL	1
Mean corpuscular hemoglobin(MCH)	Calculated as Hgb/RBC×10[1)]	pg	1
Mean corpuscular hemoglobin concentration (MCHC)	Calculated as Hgb/Hct×100[1)]	g/dL	1
Platelet	Light scattering method[1)]	$\times 10^3/\mu L$	0
Reticulocyte	Light scattering method[1)]	%	1
White blood cell(WBC)	Light scattering method[1)]	$\times 10^3/\mu L$	2
Differential WBC	Pattern recognition method[2)] (Wright staining)	%	0
Biochemistry			
Total protein(TP)	Biuret method[3)]	g/dL	1
Albumin (Alb)	BCG method[3)]	g/dL	1
A/G ratio	Calculated as Alb/(TP−Alb)[3)]	−	1
T-bilirubin	Alkaline azobilirubin method[3)]	mg/dL	2
Glucose	GlcK·G-6-PDH method[3)]	mg/dL	0
T-cholesterol	CE·COD·POD method[3)]	mg/dL	0
Triglyceride	LPL·GK·GPO·POD method[3)]	mg/dL	0
Phospholipid	PLD·ChOD·POD method[3)]	mg/dL	0
Aspartate aminotransferase (AST)	JSCC method[3)]	IU/L	0
Alanine aminotransferase (ALT)	JSCC method[3)]	IU/L	0
Lactate dehydrogenase (LDH)	SFBC method[3)]	IU/L	0
Alkaline phosphatase (ALP)	GSCC method[3)]	IU/L	0
γ-Glutamyl transpeptidase (γ-GTP)	JSCC method[3)]	IU/L	0
Creatine kinase (CK)	JSCC method[3)]	IU/L	0
Urea nitrogen	Urease·GLDH method[3)]	mg/dL	1
Creatinine	Jaffe method[3)]	mg/dL	1
Sodium	Ion selective electrode method[3)]	mEq/L	0
Potassium	Ion selective electrode method[3)]	mEq/L	1
Chloride	Ion selective electrode method[3)]	mEq/L	0
Calcium	OCPC method[3)]	mg/dL	1
Inorganic phosphorus	PNP·XOD·POD method[3)]	mg/dL	1

1) Automatic blood cell analyzer (ADVIA120 : Bayer Corporation)
2) Automatic blood cell differential analyzer (MICROX HEG-120NA : OMRON Corporation)
3) Automatic analyzer (Hitachi 7080 : Hitachi,Ltd.)
4) CO-oximeter (CIBA·CORNING 270 : Bayer Corporation)