

1,4-ジオキサンのラット及びマウスを用いた
経口(混水)投与によるがん原性予備試験
(急性・2週間・13週間) 報告書

APPENDIX

(C1-1~C4)

13Week STUDY NO. 0053 ; 0054

APPENDIX C 1

CHEMICAL INTAKE CHANGES (THIRTEEN-WEEK STUDIES:SUMMARY)

RAT:MALE

STUDY NO. : 0053
ANIMAL : RAT F344
UNIT : mg/kg/day
REPORT TYPE : A1 13
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

PAGE : 1

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
640 ppm	66.107± 22.823	68.485± 4.044	63.140± 3.584	56.856± 3.004	57.494± 7.351	52.470± 7.391	50.903± 11.827
1600 ppm	185.306± 6.903	173.990± 14.709	165.981± 28.281	149.400± 28.971	148.498± 42.552	129.103± 16.320	120.452± 17.200
4000 ppm	440.795± 14.462	392.927± 16.667	354.657± 16.956	322.676± 19.602	298.449± 14.230	285.080± 19.459	264.801± 14.222
10000 ppm	1006.081± 50.123	909.327± 39.687	829.962± 48.588	759.279± 29.515	716.795± 48.328	680.693± 40.623	770.113±223.122
25000 ppm	2644.971±175.595	2282.790±183.817	2004.045±235.960	1737.345±148.437	1718.880±164.640	1597.856±148.498	1565.649±109.871

(HAN300)

BAIS 2

STUDY NO. : 0053
 ANIMAL : RAT F344
 UNIT : mg/kg/d a y
 REPORT TYPE : A1 13
 SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 2

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
640 ppm	49.157± 10.853	49.224± 13.368	49.607± 14.176	46.642± 12.657	46.414± 12.989	43.717± 11.463
1600 ppm	115.497± 20.511	107.596± 22.798	111.958± 24.175	106.787± 18.530	105.967± 22.990	101.871± 19.192
4000 ppm	254.545± 10.890	245.480± 12.603	244.809± 10.096	228.609± 12.839	218.787± 9.402	215.084± 8.924
10000 ppm	597.791± 25.169	568.227± 27.666	581.222± 15.163	534.436± 19.351	513.845± 32.328	515.075± 20.598
25000 ppm	1547.043±118.252	1402.541± 79.919	1462.559± 99.329	1317.607± 56.937	1154.345± 49.622	1214.489± 71.222

(HAN300)

BAIS2

APPENDIX C 2

CHEMICAL INTAKE CHANGES (THIRTEEN-WEEK STUDIES:SUMMARY)

RAT:FEMALE

STUDY NO. : 0053
ANIMAL : RAT F344
UNIT : mg/kg/day
REPORT TYPE : A1 13
SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

PAGE : 3

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
640	ppm	100.174±	16.262	116.811±	68.715	99.044±	36.124	99.650±	54.631	89.400±	38.327	87.635±	37.134	78.259±	28.508
1600	ppm	225.518±	16.025	225.320±	39.663	208.842±	48.520	204.416±	58.920	197.182±	44.850	216.037±	88.538	183.539±	43.316
4000	ppm	519.039±	27.769	474.953±	25.876	442.738±	23.823	504.148±	326.432	505.282±	392.143	490.989±	332.135	485.496±	347.743
10000	ppm	1113.952±	65.775	991.841±	89.098	896.597±	94.283	845.541±	122.063	799.546±	65.095	737.795±	58.789	726.470±	62.997
25000	ppm	2698.463±	237.433	2209.615±	204.372	1904.874±	146.499	1835.438±	219.190	1768.655±	172.791	1570.985±	122.660	1571.212±	219.271

(HAN300)

BAIS2

STUDY NO. : 0053
 ANIMAL : RAT F344
 UNIT : mg/kg/day
 REPORT TYPE : A1 13
 SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 4

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
640 ppm	75.772± 24.704	84.932± 36.935	82.812± 27.732	84.028± 38.425	68.591± 20.551	68.898± 20.447
1600 ppm	169.744± 38.733	185.256± 65.665	185.217± 64.677	166.239± 59.917	174.672± 67.901	167.639± 52.100
4000 ppm	400.878±202.471	448.704±269.389	363.369± 95.240	372.730±214.369	334.921± 98.139	325.325± 73.478
10000 ppm	702.722± 70.531	668.487± 58.251	698.861± 37.950	666.622± 72.694	651.520± 54.608	618.888± 59.406
25000 ppm	1528.379±113.411	1389.080± 99.939	1552.107± 86.432	1399.400±119.151	1344.325±150.202	1384.920±148.162

(HAN300)

BAIS 2

APPENDIX C 3

CHEMICAL INTAKE CHANGES (THIRTEEN-WEEK STUDIES:SUMMARY)

MOUSE:MALE

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 UNIT : mg/kg/day
 REPORT TYPE : A1 13
 SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 1

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
640 ppm	122.614± 17.447	109.531± 16.339	102.151± 11.748	97.628± 12.073	89.641± 10.446	88.767± 20.081	90.710± 25.567
1600 ppm	318.981± 77.426	288.817± 68.422	258.625± 58.374	278.818±132.892	239.122± 58.600	243.137± 89.269	228.356± 80.337
4000 ppm	724.859± 82.439	792.678±405.704	758.418±397.007	679.111±355.340	586.094±104.340	578.319±204.689	646.292±350.064
10000 ppm	1156.518±215.851	1045.717±165.134	1071.160±192.907	1011.069±186.952	965.229±138.469	922.560±203.983	908.092±133.244
25000 ppm	1802.926±622.095	2299.568±579.960	1940.100±200.509	1782.229±240.545	1652.994±177.578	1567.601±223.135	1681.619±188.357

(HAN300)

BAIS 2

STUDY NO. : 0054
ANIMAL : MOUSE BDF1
UNIT : mg/kg/day
REPORT TYPE : A1 13
SEX : MALE

CHEMICAL INTAKE CHANGES (SUMMARY)
ALL ANIMALS

PAGE : 2

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
640 ppm	82.314± 21.883	78.620± 19.329	74.244± 18.064	67.667± 15.285	69.855± 27.885	69.694± 23.568
1600 ppm	235.342±121.480	214.097± 75.075	189.566± 46.871	190.835± 56.615	189.597± 69.889	189.193± 61.526
4000 ppm	530.074±189.470	595.103±307.920	471.841±188.040	434.336± 92.309	364.005±183.639	497.895±267.999
10000 ppm	832.121±114.985	804.274±178.734	750.531±117.366	727.184±111.487	667.924±219.132	735.107±146.681
25000 ppm	1680.116±225.274	1454.967±194.914	1401.523±225.585	1537.277±195.328	1350.574±295.357	1548.749±382.668

(HAN300)

BAIS2

APPENDIX C 4

CHEMICAL INTAKE CHANGES (THIRTEEN-WEEK STUDIES:SUMMARY)

MOUSE:FEMALE

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 UNIT : mg/kg/d a y
 REPORT TYPE : A1 13
 SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 3

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
640 ppm	151.336± 18.213	149.642± 24.585	175.412± 55.617	192.558± 64.561	180.644± 65.947	190.736± 96.261	182.929± 98.835
1600 ppm	412.088± 61.878	505.452±134.071	461.660±144.503	473.188±140.441	373.037± 74.500	432.211±254.003	412.227±195.128
4000 ppm	913.144± 98.250	988.628±252.627	1024.205±335.221	1054.281±360.395	947.137±335.406	973.196±462.218	875.143±251.366
10000 ppm	1628.620±196.041	1709.360±193.406	1711.962±222.541	1968.744±362.192	1795.113±207.443	1696.613±270.706	1726.812±458.366
25000 ppm	2983.661±443.718	2751.614±327.561	2926.582±478.947	2985.594±647.029	2786.741±353.161	2718.226±614.064	2792.352±481.569

(HAN300)

BAIS2

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 UNIT : mg/kg/d a y
 REPORT TYPE : A1 13
 SEX : FEMALE

CHEMICAL INTAKE CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 4

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
640 ppm	156.198± 50.922	164.414± 64.864	176.358± 76.643	176.271± 76.348	156.143± 75.367	153.328± 52.841
1600 ppm	364.612±101.120	338.583± 65.067	318.058± 48.180	336.149± 81.468	299.483± 48.254	342.573± 85.216
4000 ppm	833.369±158.877	944.540±377.845	848.787±218.060	857.893±261.097	792.084±315.560	791.680±245.675
10000 ppm	1580.423±287.329	1509.303±168.635	1487.121±195.790	1465.195±182.768	1439.941±132.091	1464.115±205.607
25000 ppm	2873.526±660.119	2736.046±481.589	2738.233±424.394	2617.839±367.972	2409.937±275.827	2634.824±360.279

(HAN300)

BAIS2

1,4-ジオキサンのラット及びマウスを用いた
経口(混水)投与によるがん原性予備試験
(急性・2週間・13週間) 報告書

APPENDIX

(D1~D4)

13Week STUDY NO. 0053 ; 0054

APPENDIX D 1

CLINICAL OBSERVATION (THIRTEEN-WEEK STUDIES:SUMMARY)

RAT:MALE

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

PAGE : 1

Clinical sign	Group Name	Administration Week-day													
		0-0	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	1
SOILED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	640 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	25000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	1	1
COLORED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	640 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	25000 ppm	0	0	0	0	0	0	0	6	6	6	6	6	5	5
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	640 ppm	0	1	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	25000 ppm	0	2	1	0	4	4	5	2	6	7	6	7	7	9
LOSS OF HAIR	Control	0	0	0	0	0	0	0	1	1	1	0	0	0	0
	640 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	25000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
TRAUMA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	640 ppm	0	0	0	0	0	0	1	0	0	0	0	0	1	0
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	25000 ppm	0	0	0	0	0	0	0	0	0	1	0	0	0	0

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

PAGE : 2

Clinical sign	Group Name	Administration Week-day													
		0-0	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	1
SOILED PERI GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	640 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	25000 ppm	0	0	0	0	0	0	1	1	2	1	1	1	1	1
GUM	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	640 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	0	0	0	1	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	25000 ppm	0	0	0	0	0	0	0	0	0	0	0	2	0	0
EYE OPACITY	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	640 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	25000 ppm	0	0	0	0	0	0	0	1	1	1	1	1	1	1
SORE OF SOLE	Control	0	0	0	0	0	0	0	0	0	1	3	6	7	9
	640 ppm	0	0	0	0	0	0	0	0	1	5	6	8	8	10
	1600 ppm	0	0	0	0	0	0	0	0	2	3	6	6	8	8
	4000 ppm	0	0	0	0	0	0	0	0	0	1	2	5	6	9
	10000 ppm	0	0	0	0	0	0	0	0	1	1	1	2	4	4
	25000 ppm	0	0	0	0	0	0	0	0	0	0	1	2	4	6
NOSE HEMORRHAGIC DISCHA	Control	0	0	0	0	0	0	0	1	3	1	1	1	2	2
	640 ppm	0	0	0	0	1	0	2	0	1	4	1	3	4	1
	1600 ppm	0	0	0	1	1	0	3	0	2	3	1	2	2	4
	4000 ppm	0	0	0	0	1	0	1	0	0	1	2	2	0	5
	10000 ppm	0	0	0	0	0	0	3	1	0	4	1	1	1	2
	25000 ppm	0	2	0	1	3	1	6	4	3	5	7	6	2	4

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

PAGE : 3

Clinical sign	Group Name	Administration Week-day													
		0-0	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	1
DIARRHEA	Control	0	0	0	1	1	0	0	0	0	0	0	0	0	0
	640 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	1	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	25000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
LOOSE STOOL	Control	0	2	0	0	0	0	0	0	0	0	0	0	0	0
	640 ppm	0	0	0	1	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	1	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	25000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SALIVATION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	640 ppm	0	0	0	0	0	0	0	1	0	0	0	0	0	0
	1600 ppm	0	0	0	0	0	0	0	1	0	0	0	0	0	0
	4000 ppm	0	0	2	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	25000 ppm	0	0	0	0	0	0	0	0	0	0	1	0	0	0

(HAN190)

BAIS2

APPENDIX D 2

CLINICAL OBSERVATION (THIRTEEN-WEEK STUDIES:SUMMARY)

RAT:FEMALE

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

PAGE : 4

Clinical sign	Group Name	Administration Week-day													
		0-0	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	1
DEATH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	640 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	25000 ppm	0	0	1	1	1	1	1	1	1	1	1	1	1	1
HUNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	640 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	25000 ppm	0	1	0	0	1	0	1	0	0	1	1	1	1	1
SOILED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	640 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	25000 ppm	0	1	0	0	0	0	0	0	0	0	0	0	0	0
COLORED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	640 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	25000 ppm	0	2	0	0	0	0	0	0	2	4	3	3	3	2
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	640 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	25000 ppm	0	3	1	0	3	1	6	0	1	1	4	3	3	3

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

PAGE : 5

Clinical sign	Group Name	Administration Week-day													
		0-0	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	1
LOSS OF HAIR	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	640 ppm	0	0	0	0	0	0	0	0	0	0	0	0	1	1
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	25000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SOILED PERI GENITALIA	Control	0	0	0	0	0	0	0	0	0	0	2	2	0	0
	640 ppm	0	0	0	0	0	0	0	0	0	1	4	1	3	1
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	1	1	1	1
	10000 ppm	0	0	0	0	4	0	3	1	2	1	2	0	1	2
	25000 ppm	0	1	0	0	1	1	1	0	0	0	1	1	1	1
GUM	Control	0	0	0	0	0	0	0	0	0	1	1	1	1	1
	640 ppm	0	0	0	0	0	0	1	0	0	0	0	1	1	1
	1600 ppm	0	0	0	0	0	0	0	0	0	0	1	0	0	1
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	1	0	0
	25000 ppm	0	0	0	0	1	0	0	0	0	0	0	0	0	0
EYE HEMORRHAGIC DISCHA	Control	0	0	0	0	0	0	1	0	0	0	0	0	1	2
	640 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	2	1	1	1	0	0
	25000 ppm	0	0	0	0	0	0	0	0	0	1	4	2	2	1
SORE OF SOLE	Control	0	0	0	0	0	0	0	0	0	0	2	2	3	5
	640 ppm	0	0	0	0	0	0	0	0	0	0	1	2	3	3
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	0	2	2
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	25000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

PAGE : 6

Clinical sign	Group Name	Administration Week-day													
		0-0	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	1
NOSE HEMORRHAGIC DISCHA	Control	0	0	0	0	0	0	0	0	1	3	1	1	1	1
	640 ppm	0	0	0	1	1	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	0	1	0	0	0	2	0	4	0	1	1
	4000 ppm	0	0	0	0	0	0	1	1	0	0	3	2	0	2
	10000 ppm	0	0	0	0	2	0	2	0	2	0	1	0	3	1
	25000 ppm	0	1	0	0	4	0	0	0	1	1	4	2	1	3
LOOSE STOOL	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	640 ppm	0	0	0	0	0	0	0	0	0	1	0	0	0	0
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	25000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
SALIVATION	Control	0	0	0	2	0	0	0	0	1	0	0	1	0	0
	640 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	0	0	0	0	0	1	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	1	0	0	0	0	0	0	0
	25000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0

(HAN190)

BAIS2

APPENDIX D 3

CLINICAL OBSERVATION (THIRTEEN-WEEK STUDIES:SUMMARY)

MOUSE:MALE

STUDY NO. : 0054
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : MALE

PAGE : 1

Clinical sign	Group Name	Administration Week-day													
		0-0	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	1
DEATH	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	640 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	25000 ppm	0	0	1	1	1	1	1	1	1	1	1	1	1	1
HUNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	640 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	25000 ppm	0	3	0	0	0	0	0	0	0	0	0	0	0	0
WASTING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	640 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	25000 ppm	0	1	0	0	0	0	0	0	0	0	0	0	0	0
SOILED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	640 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	25000 ppm	0	5	4	0	0	0	0	0	1	0	0	0	0	1
PILOERECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	640 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	1
	1600 ppm	0	0	0	0	0	0	0	0	1	0	0	0	0	2
	4000 ppm	0	1	1	0	1	1	1	1	1	1	1	1	2	1
	10000 ppm	0	2	2	0	0	2	1	1	0	2	2	2	3	2
	25000 ppm	0	10	8	1	1	0	7	4	5	5	4	6	8	9

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
 ALL ANIMALS

SEX : MALE

PAGE : 2

Clinical sign	Group Name	Administration Week-day													
		0-0	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	1
LOSS OF HAIR	Control	0	0	0	1	1	1	2	2	2	1	2	3	3	3
	640 ppm	0	0	0	0	1	2	5	5	5	5	4	5	5	6
	1600 ppm	0	0	1	2	3	3	4	4	4	4	4	5	5	5
	4000 ppm	0	0	1	1	3	3	3	4	4	6	7	7	7	8
	10000 ppm	0	1	1	2	3	3	4	4	4	4	5	5	5	5
	25000 ppm	0	0	0	1	1	2	2	2	2	1	1	1	1	2
SOILED PERI GENITALIA	Control	0	0	0	0	0	0	0	0	1	0	0	0	0	0
	640 ppm	0	0	0	0	0	1	0	0	2	2	1	1	2	2
	1600 ppm	0	0	0	0	0	0	0	0	2	0	0	0	0	0
	4000 ppm	0	0	0	0	0	1	0	0	2	1	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	25000 ppm	0	1	0	0	0	0	0	0	0	0	0	0	0	0

(HAN190)

BAIS 2

APPENDIX D. 4

CLINICAL OBSERVATION (THIRTEEN-WEEK STUDIES:SUMMARY)

MOUSE:FEMALE

STUDY NO. : 0054
ANIMAL : MOUSE BDF1
REPORT TYPE : A1 13

CLINICAL OBSERVATION (SUMMARY)
ALL ANIMALS

SEX : FEMALE

PAGE : 3

Clinical sign	Group Name	Administration Week-day													
		0-0	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	1
HUNCHBACK POSITION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	640 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	25000 ppm	0	1	1	0	0	0	0	0	0	0	0	0	0	1
WASTING	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	640 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	25000 ppm	0	0	0	0	0	0	0	0	0	1	1	1	1	1
SOILED	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	640 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	25000 ppm	0	1	2	0	0	0	1	1	1	1	1	1	1	1
PILORECTION	Control	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	640 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	1600 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	4000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	10000 ppm	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	25000 ppm	0	8	4	3	0	1	2	1	1	1	1	2	2	2
LOSS OF HAIR	Control	0	0	1	2	2	2	3	3	3	3	3	3	3	5
	640 ppm	0	0	0	0	3	3	4	4	4	4	5	5	6	6
	1600 ppm	0	0	0	0	3	3	5	5	5	5	5	5	5	6
	4000 ppm	0	0	1	1	1	2	4	6	6	6	8	8	8	8
	10000 ppm	0	0	0	0	0	3	5	5	5	4	5	6	6	6
	25000 ppm	0	0	1	0	0	1	2	1	1	3	3	3	3	3

1,4-ジオキサンのラット及びマウスを用いた
経口(混水)投与によるがん原性予備試験
(急性・2週間・13週間) 報告書

APPENDIX

(E1～E4)

13Week STUDY NO. 0053 ; 0054

APPENDIX E 1

BODY WEIGHT CHANGES (THIRTEEN-WEEK STUDIES:SUMMARY)

RAT:MALE

STUDY NO. : 0053
 ANIMAL : RAT F344
 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	130±	4	162±	7	195±	9	224±	9	246±	9	265±	8
640 ppm	130±	4	158±	17	194±	11	225±	8	250±	7	268±	8
1600 ppm	130±	4	165±	5	201±	5	231±	5	255±	5	272±	5
4000 ppm	130±	4	162±	7	197±	8	224±	9	247±	10	264±	10
10000 ppm	130±	4	158±	4	193±	5	219±	6	240±	6	255±	6
25000 ppm	130±	4	137±	6**	165±	8**	191±	10**	210±	12**	222±	14**

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

Test of Dunnett

(HAN260)

BAIS 2

STUDY NO. : 0053
 ANIMAL : RAT F344
 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	293±	10	308±	11	319±	11	328±	13	336±	13	345±	15	355±	15		
640 ppm	296±	7	310±	8	322±	8	331±	8	340±	8	351±	8	359±	9		
1600 ppm	301±	5	315±	6	327±	5	334±	6	343±	6	352±	6	360±	6		
4000 ppm	289±	11	300±	12	313±	13	319±	14	326±	14	334±	14	343±	14		
10000 ppm	280±	6	290±	5*	302±	5*	309±	7*	315±	6*	322±	7*	329±	7*		
25000 ppm	238±	15**	246±	17**	255±	17**	264±	19**	269±	20**	273±	22**	279±	23**		

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

Test of Dunnett

(HAN260)

BAIS 2

APPENDIX E 2

BODY WEIGHT CHANGES (THIRTEEN-WEEK STUDIES:SUMMARY)

RAT:FEMALE

STUDY NO. : 0053
 ANIMAL : RAT F344
 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		6-7			
Control	102±	3	119±	3	135±	4	147±	3	158±	5	167±	5	175±	6		
640 ppm	102±	3	121±	4	138±	6	150±	7	161±	5	170±	8	178±	7		
1600 ppm	102±	3	119±	4	136±	5	147±	6	158±	7	166±	6	173±	6		
4000 ppm	102±	3	118±	5	134±	5	146±	6	155±	6	165±	7	171±	7		
10000 ppm	102±	3	116±	4	131±	6	141±	6	149±	6	156±	7*	161±	7**		
25000 ppm	102±	3	104±	10**	121±	5**	131±	5**	138±	7**	142±	10**	148±	10**		

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

Test of Dunnett

(HAN260)

BAIS 2

STUDY NO. : 0053
 ANIMAL : RAT F344
 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	184±	7	188±	7	196±	8	198±	8	203±	8	206±	6	210±	7		
640 ppm	186±	7	190±	7	198±	6	200±	6	206±	6	209±	7	213±	8		
1600 ppm	179±	8	185±	8	190±	7	193±	8	198±	9	201±	9	204±	9		
4000 ppm	177±	7	181±	6	186±	8	189±	9	193±	8	196±	9	198±	8		
10000 ppm	166±	8**	169±	8**	173±	8**	176±	8**	180±	10**	182±	9**	184±	9**		
25000 ppm	152±	8**	154±	7**	157±	7**	160±	8**	162±	8**	163±	8**	165±	9**		

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

Test of Dunnett

(HAN260)

BAIS 2

APPENDIX E 3

BODY WEIGHT CHANGES (THIRTEEN-WEEK STUDIES:SUMMARY)

MOUSE:MALE

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 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	6-7
Control	23.5± 0.9	24.7± 0.9	25.6± 1.4	26.6± 1.3	27.3± 1.6	28.3± 1.7	29.5± 2.1
640 ppm	23.5± 0.9	24.9± 0.9	26.1± 1.1	27.4± 1.2	28.3± 1.3	29.1± 1.8	30.2± 1.9
1600 ppm	23.5± 0.9	24.8± 1.3	26.2± 1.6	27.4± 1.8	28.1± 2.0	28.9± 2.1	29.9± 2.4
4000 ppm	23.5± 0.9	24.6± 1.2	25.7± 1.3	26.6± 1.7	27.8± 2.0	28.4± 2.3	29.2± 2.5
10000 ppm	23.5± 0.9	24.1± 0.8	25.4± 0.9	26.5± 0.8	27.7± 0.9	28.0± 1.2	28.9± 1.5
25000 ppm	23.5± 0.9	19.3± 2.5**	22.9± 0.8**	23.9± 0.9**	24.2± 0.7**	24.4± 1.0**	24.7± 1.2**

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS2

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 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	29.9± 2.3	30.9± 2.3	31.6± 2.2	32.8± 2.3	33.5± 2.5	34.4± 2.4	34.5± 2.6
640 ppm	31.3± 2.1	32.0± 2.4	32.9± 2.3	34.0± 2.4	34.7± 2.6	35.7± 2.9	36.1± 3.0
1600 ppm	30.9± 2.8	31.7± 2.8	32.2± 2.7	33.1± 3.0	33.9± 2.9	34.7± 3.3	35.2± 3.4
4000 ppm	30.0± 2.9	31.1± 3.2	31.6± 3.3	32.6± 3.4	33.7± 3.6	33.1± 4.6	34.6± 4.0
10000 ppm	29.9± 1.5	30.7± 1.4	31.4± 1.7	32.1± 1.9	32.4± 2.3	32.7± 2.9	32.5± 2.9
25000 ppm	25.2± 1.2**	25.7± 1.0**	25.8± 1.2**	25.8± 1.2**	25.9± 1.4**	25.3± 1.8**	24.6± 2.2**

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

Test of Dunnett

(HAN260)

BAIS2

APPENDIX E 4

BODY WEIGHT CHANGES (THIRTEEN-WEEK STUDIES:SUMMARY)

MOUSE:FEMALE

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 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	6-7
Control	18.9± 0.6	19.3± 0.5	19.4± 1.0	20.9± 0.8	20.8± 0.8	21.2± 0.8	21.4± 0.6
640 ppm	18.9± 0.6	19.4± 0.7	20.3± 0.6	20.7± 0.7	20.9± 0.5	21.3± 0.5	21.8± 0.5
1600 ppm	18.9± 0.6	19.2± 0.8	19.7± 0.9	20.9± 0.8	20.9± 0.8	21.7± 0.9	21.9± 1.0
4000 ppm	18.9± 0.6	19.3± 1.1	20.4± 1.5	21.0± 1.4	21.4± 2.4	21.9± 2.2	22.0± 1.5
10000 ppm	18.9± 0.6	19.4± 0.8	20.4± 0.7	21.1± 0.6	21.3± 0.9	21.9± 0.8	22.2± 1.0
25000 ppm	18.9± 0.6	18.7± 0.9	19.7± 0.7	20.3± 0.6	20.9± 0.7	21.2± 0.9	21.0± 1.5

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

Test of Dunnett

(HAN260)

BAIS 2

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 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	22.7± 0.9	22.4± 1.0	22.8± 1.0	23.3± 1.3	24.2± 1.8	23.8± 1.1	23.8± 1.1
640 ppm	22.3± 0.5	22.5± 1.0	23.1± 0.8	23.3± 0.8	24.2± 0.9	24.4± 1.1	24.2± 0.9
1600 ppm	22.3± 0.9	22.7± 1.2	23.7± 1.3	24.4± 1.5	24.6± 1.1	24.5± 1.5	24.2± 1.3
4000 ppm	22.7± 2.0	23.2± 1.9	24.3± 2.0	24.1± 2.3	24.8± 2.0	24.2± 1.4	24.5± 1.7
10000 ppm	22.4± 0.8	23.2± 0.8	24.1± 1.2	23.7± 1.1	24.5± 0.8	24.3± 1.1	24.5± 0.9
25000 ppm	22.1± 0.8	21.7± 1.3	22.3± 1.3	22.0± 1.2	22.1± 1.4**	22.4± 1.6	22.9± 1.6

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

Test of Dunnett

(HAN260)

BAIS 2

1,4-ジオキサンのラット及びマウスを用いた
経口(混水)投与によるがん原性予備試験
(急性・2週間・13週間) 報告書

APPENDIX

(F1～F4)

13Week STUDY NO. 0053 ; 0054

APPENDIX F 1

FOOD CONSUMPTION CHANGES (THIRTEEN-WEEK STUDIES:SUMMARY)

RAT:MALE

STUDY NO. : 0053
 ANIMAL : RAT F344
 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	130±	4	162±	7	195±	9	224±	9	246±	9	265±	8
640 ppm	130±	4	158±	17	194±	11	225±	8	250±	7	268±	8
1600 ppm	130±	4	165±	5	201±	5	231±	5	255±	5	272±	5
4000 ppm	130±	4	162±	7	197±	8	224±	9	247±	10	264±	10
10000 ppm	130±	4	158±	4	193±	5	219±	6	240±	6	255±	6
25000 ppm	130±	4	137±	6**	165±	8**	191±	10**	210±	12**	222±	14**

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

Test of Dunnett

(HAN260)

BAIS 2

STUDY NO. : 0053
 ANIMAL : RAT F344
 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	293±	10	308±	11	319±	11	328±	13	336±	13	345±	15	355±	15		
640 ppm	296±	7	310±	8	322±	8	331±	8	340±	8	351±	8	359±	9		
1600 ppm	301±	5	315±	6	327±	5	334±	6	343±	6	352±	6	360±	6		
4000 ppm	289±	11	300±	12	313±	13	319±	14	326±	14	334±	14	343±	14		
10000 ppm	280±	6	290±	5*	302±	5*	309±	7*	315±	6*	322±	7*	329±	7*		
25000 ppm	238±	15**	246±	17**	255±	17**	264±	19**	269±	20**	273±	22**	279±	23**		

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

Test of Dunnett

(HAN260)

BAIS 2

APPENDIX F 2

FOOD CONSUMPTION CHANGES (THIRTEEN-WEEK STUDIES:SUMMARY)

RAT:FEMALE

STUDY NO. : 0053
 ANIMAL : RAT F344
 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	102±	3	119±	3	135±	4	147±	3	158±	5	167±	5
640 ppm	102±	3	121±	4	138±	6	150±	7	161±	5	170±	8
1600 ppm	102±	3	119±	4	136±	5	147±	6	158±	7	166±	6
4000 ppm	102±	3	118±	5	134±	5	146±	6	155±	6	165±	7
10000 ppm	102±	3	116±	4	131±	6	141±	6	149±	6	156±	7*
25000 ppm	102±	3	104±	10**	121±	5**	131±	5**	138±	7**	142±	10**

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

Test of Dunnett

(HAN260)

BAIS 2

STUDY NO. : 0053
 ANIMAL : RAT F344
 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	184±	7	188±	7	196±	8	198±	8	203±	8	206±	6	210±	7		
640 ppm	186±	7	190±	7	198±	6	200±	6	206±	6	209±	7	213±	8		
1600 ppm	179±	8	185±	8	190±	7	193±	8	198±	9	201±	9	204±	9		
4000 ppm	177±	7	181±	6	186±	8	189±	9	193±	8	196±	9	198±	8		
10000 ppm	166±	8**	169±	8**	173±	8**	176±	8**	180±	10**	182±	9**	184±	9**		
25000 ppm	152±	8**	154±	7**	157±	7**	160±	8**	162±	8**	163±	8**	165±	9**		

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

Test of Dunnett

(HAN260)

BAIS 2

APPENDIX F 3

FOOD CONSUMPTION CHANGES (THIRTEEN-WEEK STUDIES:SUMMARY)

MOUSE:MALE

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 UNIT : g
 REPORT TYPE : A1 13
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 1

Group Name	Administration week-day(effective)						
	1-7(7)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	3.8± 0.2	3.7± 0.3	3.8± 0.2	4.0± 0.3	4.1± 0.3	4.4± 0.3	4.1± 0.3
640 ppm	3.8± 0.2	3.8± 0.2	3.9± 0.1	4.1± 0.2	4.1± 0.3	4.3± 0.3	4.1± 0.3
1600 ppm	3.8± 0.3	3.9± 0.2	4.0± 0.3	4.1± 0.2	4.2± 0.3	4.4± 0.2	4.2± 0.2
4000 ppm	3.8± 0.2	3.8± 0.2	3.9± 0.3	4.0± 0.2	4.1± 0.2	4.3± 0.3	4.1± 0.2
10000 ppm	3.5± 0.1	3.7± 0.2	3.8± 0.2	4.0± 0.2	4.0± 0.2	4.2± 0.2	4.1± 0.2
25000 ppm	2.5± 0.5**	4.0± 0.4	3.5± 0.2*	3.7± 0.3	3.8± 0.3	3.9± 0.3**	3.8± 0.3

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

Test of Dunnett

(HAN260)

BAIS2

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 UNIT : g
 REPORT TYPE : A1 13
 SEX : MALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 2

Group Name	Administration week-day(effective)					
	8-7(7)	9-7(7)	10-7(7)	11-7(7)	12-7(7)	13-7(7)
Control	4.2± 0.3	4.3± 0.3	4.6± 0.4	4.2± 0.3	4.3± 0.4	3.8± 0.3
640 ppm	4.1± 0.3	4.3± 0.2	4.6± 0.2	4.2± 0.1	4.3± 0.2	3.8± 0.1
1600 ppm	4.2± 0.2	4.3± 0.3	4.4± 0.4	4.2± 0.2	4.3± 0.3	3.9± 0.2
4000 ppm	4.1± 0.3	4.3± 0.2	4.5± 0.2	4.3± 0.2	4.0± 0.7	3.9± 0.2
10000 ppm	4.0± 0.2	4.2± 0.3	4.3± 0.3	4.0± 0.3	3.9± 0.5	3.6± 0.3
25000 ppm	3.9± 0.3	3.9± 0.3**	4.0± 0.3**	3.7± 0.4**	3.5± 0.4**	3.3± 0.5

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

Test of Dunnett

(HAN260)

BAIS 2

APPENDIX F 4

FOOD CONSUMPTION CHANGES (THIRTEEN-WEEK STUDIES:SUMMARY)

MOUSE:FEMALE

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 UNIT : g
 REPORT TYPE : A1 13
 SEX : FEMALE

FOOD CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 3

Group Name	Administration week-day(effective)						
	1-7(7)	2-7(7)	3-7(7)	4-7(7)	5-7(7)	6-7(7)	7-7(7)
Control	3.2± 0.2	3.3± 0.3	3.6± 0.3	4.0± 0.3	4.0± 0.4	4.3± 0.4	4.3± 0.3
640 ppm	3.2± 0.2	3.4± 0.1	3.5± 0.2	3.9± 0.2	4.0± 0.2	4.2± 0.2	4.1± 0.3
1600 ppm	3.2± 0.3	3.5± 0.3	3.6± 0.3	4.0± 0.2	4.0± 0.3	4.2± 0.3	4.1± 0.4
4000 ppm	3.3± 0.3	3.5± 0.2	3.6± 0.2	4.1± 0.4	4.0± 0.2	4.2± 0.3	4.3± 0.2
10000 ppm	3.2± 0.2	3.4± 0.2	3.6± 0.2	4.0± 0.1	4.0± 0.2	4.2± 0.2	4.1± 0.2
25000 ppm	3.0± 0.3	3.3± 0.2	3.5± 0.3	3.9± 0.3	3.9± 0.3	4.0± 0.3	4.1± 0.2

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS 2

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 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	4.2± 0.4	4.5± 0.4	4.7± 0.4	4.5± 0.4	4.3± 0.3	3.9± 0.3
640 ppm	4.1± 0.3	4.5± 0.2	4.4± 0.3	4.3± 0.4	4.4± 0.3	3.8± 0.4
1600 ppm	4.1± 0.3	4.4± 0.3	4.6± 0.4	4.4± 0.4	4.6± 0.6	3.8± 0.3
4000 ppm	4.2± 0.2	4.5± 0.3	4.6± 0.3	4.4± 0.3	4.2± 0.3	3.8± 0.2
10000 ppm	4.1± 0.2	4.4± 0.3	4.4± 0.3	4.2± 0.2	4.2± 0.2	3.8± 0.3
25000 ppm	3.8± 0.4*	4.2± 0.5	4.2± 0.4*	4.0± 0.3*	4.1± 0.3	3.8± 0.3

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS 2

1,4-ジオキサンのラット及びマウスを用いた
経口(混水)投与によるがん原性予備試験
(急性・2週間・13週間) 報告書

APPENDIX

(G1~G4)

13Week STUDY NO. 0053 ; 0054

APPENDIX G 1

WATER CONSUMPTION CHANGES (THIRTEEN-WEEK STUDIES:SUMMARY)

RAT:MALE

STUDY NO. : 0053
 ANIMAL : RAT F344
 UNIT : g
 REPORT TYPE : A1 13
 SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 1

Group Name	Administration week-day(effective)						
	1-3(3)	1-7(4)	2-3(3)	2-7(4)	3-3(3)	3-7(4)	4-3(3)
Control	19.8± 3.8	20.3± 3.9	20.5± 2.6	21.4± 3.8	28.7± 9.4	29.8± 10.2	25.6± 6.5
640 ppm	18.1± 1.0	16.8± 5.9	20.4± 2.4	20.7± 1.3	21.3± 1.4	22.2± 1.6	22.4± 1.8
1600 ppm	18.2± 0.8	19.1± 0.8	20.5± 0.7	21.8± 1.9	22.7± 2.6	24.0± 4.2	23.5± 3.4
4000 ppm	17.2± 0.9	17.8± 0.9	18.7± 1.2	19.3± 0.9	19.0± 1.1*	19.9± 1.2*	19.7± 1.1*
10000 ppm	16.1± 0.8**	15.9± 0.8**	17.0± 0.9**	17.6± 0.9**	17.2± 1.0**	18.2± 1.0**	18.1± 1.4**
25000 ppm	10.8± 0.6**	14.5± 1.1**	15.2± 0.9**	15.1± 1.5**	14.6± 1.6**	15.3± 1.6**	15.1± 1.4**

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

Test of Dunnett

(HAN260)

BAIS2

STUDY NO. : 0053
 ANIMAL : RAT F344
 UNIT : g
 REPORT TYPE : A1 13
 SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 2

Group Name	Administration		week-day(effective)					
	4-7(4)		5-3(3)		5-7(4)		6-3(3)	
Control	27.9±	9.1	27.3±	9.6	28.8±	10.6	27.6±	10.2
640 ppm	22.2±	1.4	22.8±	1.6	24.0±	2.8	24.0±	4.9
1600 ppm	23.9±	4.9	25.4±	7.2	25.3±	7.5	23.1±	3.0
4000 ppm	19.9±	1.6	19.6±	1.3	19.7±	1.3	19.7±	1.5*
10000 ppm	18.2±	0.9**	18.3±	1.1**	18.3±	1.2**	17.6±	1.5**
25000 ppm	14.6±	1.4**	14.8±	1.5**	15.2±	1.3**	14.5±	1.1**

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

Test of Dunnett

(HAN260)

BAIS 2

STUDY NO. : 0053
 ANIMAL : RAT F344
 UNIT : g
 REPORT TYPE : A1 13
 SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 3

Group Name	Administration 8-3(3)	week-day(effective) 8-7(4)	9-3(3)	9-7(4)	10-3(3)	10-7(4)	11-3(3)
Control	28.7± 9.6	29.0± 9.8	26.4± 7.2	28.6± 10.3	26.6± 8.4	30.4± 9.0	27.5± 10.7
640 ppm	23.6± 4.5	23.7± 4.9	24.9± 7.0	24.7± 6.5	24.6± 6.8	25.6± 6.8	25.5± 6.7
1600 ppm	21.7± 3.7	22.7± 3.7	21.7± 3.7	21.9± 4.3	21.9± 4.8	23.3± 4.8	23.5± 4.8
4000 ppm	18.5± 1.3*	19.1± 1.2*	19.4± 2.1	19.2± 1.3	18.0± 1.1*	19.5± 1.0*	18.5± 0.9
10000 ppm	16.7± 1.2**	17.3± 0.6**	16.7± 1.0**	17.2± 0.8**	15.7± 0.9**	18.0± 0.7**	17.0± 1.0**
25000 ppm	12.9± 1.6**	15.2± 1.3**	13.3± 1.3**	14.3± 1.3**	13.6± 1.7**	15.4± 0.9**	14.0± 0.6**

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

Test of Dunnett

(HAN260)

BAIS2

STUDY NO. : 0053
 ANIMAL : RAT F344
 UNIT : g
 REPORT TYPE : A1 13
 SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 4

Group Name	Administration week-day(effective)				
	11-7(4)	12-3(3)	12-7(4)	13-3(3)	13-7(4)
Control	28.6± 9.1	27.6± 8.8	29.6± 9.1	29.0± 8.1	27.7± 7.9
640 ppm	24.8± 6.6	24.8± 6.9	25.4± 6.8	24.6± 6.9	24.5± 6.4
1600 ppm	22.9± 3.8	22.7± 4.4	23.3± 4.8	24.2± 6.1	22.9± 4.2
4000 ppm	18.7± 1.3*	18.7± 0.9*	18.3± 1.0*	18.4± 1.3*	18.4± 0.8*
10000 ppm	16.8± 0.7**	17.5± 0.7**	16.5± 1.1**	16.4± 1.1**	16.9± 0.8**
25000 ppm	14.2± 1.1**	14.2± 0.9**	12.6± 0.9**	13.2± 0.9**	13.5± 1.2**

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

Test of Dunnett

(IIAN260)

BAIS2

APPENDIX G 2

WATER CONSUMPTION CHANGES (THIRTEEN-WEEK STUDIES:SUMMARY)

RAT:FEMALE

STUDY NO. : 0053
 ANIMAL : RAT F344
 UNIT : g
 REPORT TYPE : A1 13
 SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 5

Group Name	Administration week-day(effective)						
	1-3(3)	1-7(4)	2-3(3)	2-7(4)	3-3(3)	3-7(4)	4-3(3)
Control	16.6± 2.4	19.2± 3.8	17.8± 2.8	18.7± 2.6	18.7± 3.2	20.2± 3.8	19.6± 4.4
640 ppm	16.8± 1.0	18.9± 2.9	19.7± 3.6	25.1± 14.4	24.5± 13.0	23.0± 7.5	23.8± 10.4
1600 ppm	15.8± 1.2	16.8± 1.5	17.3± 3.1	19.2± 4.1	18.5± 4.0	19.2± 4.9	19.5± 5.2
4000 ppm	14.8± 1.1	15.3± 1.0*	15.2± 1.0	15.9± 1.1	15.7± 1.0	16.2± 1.1	16.2± 1.5
10000 ppm	12.5± 0.6**	12.9± 0.9**	12.7± 1.1**	13.0± 1.3**	12.2± 1.4**	12.7± 1.5**	12.6± 1.8**
25000 ppm	7.9± 0.8**	11.2± 1.0**	10.3± 2.7**	10.7± 1.1**	10.3± 2.1**	10.0± 0.6**	8.7± 0.5**

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS2

STUDY NO. : 0053
 ANIMAL : RAT F344
 UNIT : g
 REPORT TYPE : A1 13
 SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 6

Group Name	Administration 4-7(4)	week-day(effective) 5-3(3)	5-7(4)	6-3(3)	6-7(4)	7-3(3)	7-7(4)
Control	20.4± 5.6	21.4± 6.1	21.9± 5.4	21.1± 5.6	24.9± 8.8	23.5± 8.1	24.3± 8.7
640 ppm	24.9± 13.5	23.6± 12.2	23.5± 9.3	24.2± 8.8	24.4± 10.0	23.0± 5.9	22.7± 8.2
1600 ppm	20.2± 6.3	19.1± 5.5	20.6± 5.1	21.2± 6.9	23.4± 9.6	19.1± 4.9	20.6± 5.2
4000 ppm	19.6± 12.9	20.6± 16.5	21.0± 16.7	17.9± 5.7	21.2± 14.7	22.5± 19.5	21.6± 15.9
10000 ppm	12.6± 2.0*	12.1± 2.0**	12.5± 1.3**	12.2± 1.5**	11.9± 1.3**	11.8± 1.0**	12.1± 1.3**
25000 ppm	10.1± 0.9**	8.9± 0.8**	10.0± 0.4**	9.2± 1.1**	9.3± 0.5**	8.6± 1.0**	9.5± 1.2**

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

Test of Dunnett

(HAN260)

BAIS 2

STUDY NO. : 0053
 ANIMAL : RAT F344
 UNIT : g
 REPORT TYPE : A1 13
 SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 7

Group Name	Administration 8-3(3)	week-day(effective) 8-7(4)	9-3(3)	9-7(4)	10-3(3)	10-7(4)	11-3(3)
Control	22.5± 6.4	23.1± 7.6	23.1± 6.9	27.3± 10.9	21.8± 7.3	30.0± 13.9	23.5± 7.2
640 ppm	21.2± 4.6	22.4± 7.2	22.0± 5.2	26.2± 11.2	22.5± 5.4	25.9± 8.3	22.9± 8.2
1600 ppm	19.7± 5.4	19.7± 5.3	23.9± 15.0	22.1± 8.4	18.8± 4.4	22.5± 8.3	19.0± 4.7
4000 ppm	20.2± 12.5	18.1± 9.1	22.3± 19.6	20.9± 12.8	17.7± 8.8	17.2± 4.7	17.5± 6.3
10000 ppm	11.5± 1.0**	11.9± 1.5**	11.5± 1.4**	11.6± 1.3**	11.6± 1.2**	12.3± 1.0**	12.2± 1.4**
25000 ppm	8.2± 1.0**	9.4± 0.6**	9.1± 1.0**	8.7± 0.5**	8.7± 0.9**	9.9± 0.6**	8.9± 0.9**

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

Test of Dunnett

(HAN260)

BAIS2

STUDY NO. : 0053
 ANIMAL : RAT F344
 UNIT : g
 REPORT TYPE : A1 13
 SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 8

Group Name	Administration week-day(effective)				
	11-7(4)	12-3(3)	12-7(4)	13-3(3)	13-7(4)
Control	25.9± 8.8	25.9± 11.0	25.2± 11.2	26.3± 12.6	25.1± 12.6
640 ppm	26.9± 11.8	21.8± 4.7	22.4± 6.8	21.9± 6.3	22.9± 6.6
1600 ppm	20.8± 8.1	20.1± 6.9	22.1± 9.2	19.4± 4.5	21.5± 7.0
4000 ppm	18.1± 10.6	17.3± 5.5	16.4± 4.9	16.4± 5.7	16.1± 3.8
10000 ppm	12.0± 1.6**	12.1± 1.2**	11.9± 1.2**	11.6± 1.2**	11.4± 1.3*
25000 ppm	9.1± 0.7**	9.4± 0.5**	8.7± 0.7**	8.6± 0.9**	9.2± 1.2**

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

Test of Dunnett

(HAN260)

BAIS2

APPENDIX G 3

WATER CONSUMPTION CHANGES (THIRTEEN-WEEK STUDIES:SUMMARY)

MOUSE:MALE

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 UNIT : g
 REPORT TYPE : A1 13
 SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 1

Group Name	Administration week-day(effective)						
	1-3(3)	1-7(4)	2-3(3)	2-7(4)	3-3(3)	3-7(4)	4-3(3)
Control	4.6± 0.6	5.0± 0.5	4.8± 1.0	5.1± 1.1	6.1± 2.6	5.8± 2.2	6.6± 3.6
640 ppm	4.4± 0.5	4.8± 0.6	4.3± 0.6	4.4± 0.5	4.6± 0.5	4.4± 0.4	4.5± 0.5
1600 ppm	4.6± 0.9	4.9± 1.1	4.8± 1.8	4.7± 1.0	4.4± 0.9	4.4± 0.9	4.5± 0.9
4000 ppm	4.2± 0.5	4.5± 0.4	4.3± 0.9	5.0± 2.2	4.7± 2.4	5.0± 2.2	5.3± 3.7
10000 ppm	2.3± 0.6**	2.8± 0.5**	2.5± 0.4**	2.7± 0.4**	2.6± 0.4**	2.8± 0.5**	2.9± 0.9**
25000 ppm	0.3± 0.1**	1.4± 0.6**	2.3± 0.3**	2.1± 0.5**	1.5± 0.3**	1.9± 0.2**	1.7± 0.1**

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS 2

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 UNIT : g
 REPORT TYPE : A1 13
 SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 2

Group Name	Administration week-day(effective)						
	4-7(4)	5-3(3)	5-7(4)	6-3(3)	6-7(4)	7-3(3)	7-7(4)
Control	5.8± 2.1	5.6± 2.8	4.8± 1.0	5.2± 1.7	5.8± 2.6	5.4± 2.6	5.4± 2.5
640 ppm	4.3± 0.4	4.0± 0.4	4.1± 0.3	4.0± 0.6	4.2± 0.8	4.2± 1.0	4.4± 1.0
1600 ppm	4.8± 2.2	4.1± 0.8	4.3± 0.9	4.2± 1.3	4.5± 1.5	4.2± 1.1	4.3± 1.3
4000 ppm	4.6± 2.0	5.1± 4.2	4.1± 0.5	4.4± 2.2	4.1± 1.1	4.5± 2.2	4.7± 2.0
10000 ppm	2.8± 0.5**	2.6± 0.4**	2.7± 0.3**	2.8± 0.8**	2.7± 0.5**	2.7± 0.3**	2.7± 0.4**
25000 ppm	1.7± 0.2**	1.6± 0.2**	1.6± 0.2**	1.3± 0.2**	1.5± 0.2**	1.6± 0.3**	1.7± 0.2**

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

(HAN260)

BAIS2

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 UNIT : g
 REPORT TYPE : A1 13
 SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 3

Group Name	Administration 8-3(3)	week-day(effective) 8-7(4)	9-3(3)	9-7(4)	10-3(3)	10-7(4)	11-3(3)
Control	5.4± 2.8	5.1± 2.3	5.0± 1.6	4.6± 1.3	4.5± 1.0	4.3± 0.9	4.4± 1.3
640 ppm	4.0± 0.9	4.1± 0.8	4.2± 0.9	4.0± 0.7	4.1± 0.6	3.9± 0.7	3.7± 0.5
1600 ppm	4.5± 1.8	4.6± 2.2	4.3± 1.5	4.2± 1.2	4.3± 1.1	3.9± 0.8	4.0± 0.9
4000 ppm	4.3± 2.0	4.0± 1.1	4.0± 2.0	4.5± 1.9	4.1± 0.9	3.8± 1.1	3.8± 0.8
10000 ppm	2.5± 0.4**	2.6± 0.3**	2.6± 0.6**	2.5± 0.6**	2.7± 0.4**	2.4± 0.4**	2.5± 0.3**
25000 ppm	1.5± 0.2**	1.7± 0.2**	1.4± 0.2**	1.5± 0.2**	1.7± 0.2**	1.4± 0.2**	1.0± 0.4**

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS 2

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 UNIT : g
 REPORT TYPE : A1 13
 SEX : MALE

WATER CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 4

Group Name	Administration week-day(effective)				
	11-7(4)	12-3(3)	12-7(4)	13-3(3)	13-7(4)
Control	4.1± 0.9	4.4± 1.2	4.2± 1.2	4.1± 1.1	4.1± 1.1
640 ppm	3.6± 0.5	3.8± 0.6	3.8± 1.0	3.8± 0.9	3.8± 0.8
1600 ppm	4.0± 0.9	4.2± 1.1	4.0± 1.1	4.2± 1.2	4.1± 1.0
4000 ppm	3.6± 0.5	3.6± 0.5	3.0± 1.5	4.0± 0.5	4.2± 1.7
10000 ppm	2.4± 0.4**	2.5± 0.3**	2.2± 0.7**	2.6± 0.4**	2.4± 0.4**
25000 ppm	1.6± 0.2**	1.0± 0.4**	1.4± 0.3**	1.3± 0.5**	1.5± 0.4**

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS 2

APPENDIX G 4

WATER CONSUMPTION CHANGES (THIRTEEN-WEEK STUDIES:SUMMARY)

MOUSE:FEMALE

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 UNIT : g
 REPORT TYPE : A1 13
 SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 5

Group Name	Administration		week-day(effective)		2-3(3)	2-7(4)	3-3(3)	3-7(4)	4-3(3)
	1-3(3)		1-7(4)						
Control	4.1± 0.8		5.0± 1.6		4.7± 1.0	4.8± 1.9	5.3± 1.9	5.6± 1.7	5.8± 2.0
640 ppm	4.0± 0.2		4.6± 0.5		4.6± 0.8	4.8± 0.8	4.7± 1.0	5.7± 1.8	6.0± 2.6
1600 ppm	4.8± 1.2		5.0± 0.8		5.3± 1.3	6.2± 1.7	5.6± 1.7	6.0± 1.8	5.9± 1.1
4000 ppm	3.8± 0.3		4.4± 0.4		4.6± 0.8	5.0± 1.1	4.7± 1.2	5.3± 1.6	5.2± 1.0
10000 ppm	2.9± 0.4*		3.2± 0.3**		3.3± 0.3*	3.5± 0.3	3.5± 0.5	3.6± 0.5*	3.9± 0.5*
25000 ppm	1.0± 0.2**		2.2± 0.4**		2.2± 0.4**	2.2± 0.2**	2.2± 0.4**	2.4± 0.4**	2.5± 0.9**

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS2

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 UNIT : g
 REPORT TYPE : A1 13
 SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 6

Group Name	Administration week-day(effective)						
	4-7(4)	5-3(3)	5-7(4)	6-3(3)	6-7(4)	7-3(3)	7-7(4)
Control	6.1± 2.8	5.5± 1.6	5.5± 2.1	5.6± 1.5	5.5± 1.7	5.7± 1.5	5.5± 1.7
640 ppm	6.3± 2.2	6.0± 2.1	6.0± 2.2	6.1± 2.8	6.5± 3.3	6.1± 2.5	6.3± 3.3
1600 ppm	6.2± 1.9	5.4± 1.7	5.0± 0.8	5.3± 1.4	5.8± 2.9	6.0± 2.2	5.7± 2.5
4000 ppm	5.5± 1.6	5.3± 1.6	5.1± 1.6	4.6± 1.0	5.3± 2.5	5.7± 2.1	4.9± 1.3
10000 ppm	4.2± 0.9	3.9± 0.7*	3.9± 0.5	3.7± 0.5*	3.8± 0.7*	3.9± 1.0*	3.9± 1.1*
25000 ppm	2.5± 0.6**	2.1± 0.4**	2.4± 0.3**	2.1± 0.4**	2.3± 0.5**	2.4± 0.7**	2.5± 0.4**

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

Test of Dunnett

(HAN260)

BAIS2

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 UNIT : g
 REPORT TYPE : A1 13
 SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 7

Group Name		Administration		week-day(effective)											
		8-3(3)		8-7(4)		9-3(3)		9-7(4)		10-3(3)		10-7(4)		11-3(3)	
Control		5.3±	1.3	5.0±	1.3	6.2±	3.4	5.8±	3.5	5.3±	1.4	5.4±	1.8	5.6±	2.1
640	ppm	6.1±	2.4	5.5±	1.6	6.7±	3.6	5.9±	2.3	6.7±	2.8	6.4±	2.7	6.0±	2.2
1600	ppm	5.9±	2.2	5.1±	1.3	5.1±	0.9	5.0±	0.9	5.7±	1.5	4.8±	0.6	4.8±	0.6
4000	ppm	5.1±	1.1	4.9±	1.1	5.4±	1.5	5.7±	2.1	5.1±	1.3	5.1±	1.2	5.3±	1.6
10000	ppm	3.8±	0.8*	3.7±	0.7	3.8±	0.5**	3.6±	0.4*	3.7±	0.5*	3.5±	0.5*	3.7±	0.5*
25000	ppm	2.2±	0.4**	2.5±	0.7**	2.5±	0.6**	2.4±	0.5**	2.4±	0.3**	2.4±	0.4**	2.3±	0.4**

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

Test of Dunnett

(HAN260)

BAIS2

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 UNIT : g
 REPORT TYPE : A1 13
 SEX : FEMALE

WATER CONSUMPTION CHANGES (SUMMARY)
 ALL ANIMALS

PAGE : 8

Group Name	Administration week-day(effective)				
	11-7(4)	12-3(3)	12-7(4)	13-3(3)	13-7(4)
Control	5.6± 3.0	5.5± 2.5	4.9± 2.0	5.7± 3.7	5.7± 3.0
640 ppm	6.6± 2.7	7.3± 3.5	5.9± 2.6	6.4± 3.2	5.8± 2.0
1600 ppm	5.1± 1.2	5.2± 1.3	4.6± 0.7	5.2± 1.4	5.1± 1.1
4000 ppm	5.3± 1.5	5.1± 1.3	4.8± 1.9	4.7± 0.8	4.8± 1.4
10000 ppm	3.6± 0.4*	3.7± 0.6	3.5± 0.4*	3.6± 0.5	3.6± 0.5*
25000 ppm	2.3± 0.3**	2.3± 0.3**	2.2± 0.2**	2.2± 0.3**	2.4± 0.3**

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HAN260)

BAIS 2

1,4-ジオキサンのラット及びマウスを用いた
経口(混水)投与によるがん原性予備試験
(急性・2週間・13週間) 報告書

APPENDIX

(H1~H4)

13Week STUDY NO. 0053 ; 0054

APPENDIX H 1

HEMATOLOGY (THIRTEEN-WEEK STUDIES:SUMMARY)

RAT:MALE

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HEMATOLOGY(1) (SUMMARY)
SURVIVAL ANIMALS (13)

PAGE : 1

Group Name	NO. of Animals	RED BLOOD CELL 10 ⁶ /μl		HEMOGLOBIN g/dl		HEMATOCRIT %		MCV fl		PLATELET 10 ³ /μl	
Control	10	9.61±	0.24	16.2±	0.2	43.4±	1.3	45.1±	0.6	782±	38
640 ppm	10	9.66±	0.25	16.1±	0.3	43.4±	1.2	44.8±	0.4	779±	54
1600 ppm	10	9.70±	0.21	16.1±	0.3	43.3±	0.9	44.6±	0.4	771±	49
4000 ppm	10	9.59±	0.29	16.0±	0.3	43.0±	1.5	44.8±	0.5	771±	23
10000 ppm	10	9.72±	0.24	16.4±	0.4	43.9±	1.2	45.2±	0.4	784±	32
25000 ppm	10	9.96±	0.28*	16.6±	0.3*	45.0±	1.7*	45.2±	0.6	760±	55

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS2

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HEMATOLOGY(2) (SUMMARY)
SURVIVAL ANIMALS (13)

PAGE : 1

Group Name		NO. of Animals	WBC 1 O ³ /μℓ		Differential N-BAND		WBC (%) N-SEG	EOSINO		BASO		MONO		LYMPHO		OTHER		
Control		10	3.62±	0.58	0±	0	20±	3	1±	1	0±	0	3±	2	76±	4	0±	0
640	ppm	10	3.60±	0.98	0±	0	20±	4	1±	1	0±	0	3±	2	75±	5	0±	0
1600	ppm	10	3.76±	0.51	0±	0	21±	4	1±	1	0±	0	3±	2	76±	5	0±	0
4000	ppm	10	3.70±	1.02	0±	0	19±	4	1±	1	0±	0	4±	1	77±	5	0±	0
10000	ppm	10	3.92±	0.81	0±	0	22±	5	1±	1	0±	0	4±	2	73±	6	0±	0
25000	ppm	10	3.60±	1.06	0±	0	26±	4**	1±	1	0±	0	5±	2	67±	5**	0±	0

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

Test of Dunnett

(JCL71A)

BAIS 2

APPENDIX H 2

HEMATOLOGY (THIRTEEN-WEEK STUDIES:SUMMARY)

RAT:FEMALE

STUDY NO. : 0053
 ANIMAL : RAT F344
 REPORT TYPE : A1
 SEX : FEMALE

HEMATOLOGY(1) (SUMMARY)
 SURVIVAL ANIMALS (13)

PAGE : 2

Group Name	NO. of Animals	RED BLOOD CELL 10 ⁶ /μl	HEMOGLOBIN g/dl	HEMATOCRIT %	MCV fl	PLATELET 10 ³ /μl
Control	10	8.82± 0.32	16.3± 0.5	43.1± 1.6	48.8± 0.3	824± 43
640 ppm	10	8.86± 0.23	16.3± 0.4	43.0± 1.1	48.5± 0.3	839± 32
1600 ppm	09	8.77± 0.26	16.2± 0.4	42.8± 1.2	48.8± 0.3	818± 42
4000 ppm	10	8.82± 0.17	16.2± 0.3	43.0± 0.7	48.7± 0.5	856± 53
10000 ppm	10	8.76± 0.27	16.0± 0.5	42.2± 1.5	48.2± 0.5**	814± 26
25000 ppm	09	8.94± 0.27	16.2± 0.5	42.6± 1.4	47.6± 0.4**	739± 50**

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 2

STUDY NO. : 0053
 ANIMAL : RAT F344
 REPORT TYPE : A1
 SEX : FEMALE

HEMATOLOGY(2) (SUMMARY)
 SURVIVAL ANIMALS (13)

PAGE : 2

Group Name	NO. of Animals	WBC 10 ³ /μl		Differential N-BAND		WBC	(%) N-SEG	EOSINO		BASO		MONO		LYMPHO		OTHER	
Control	10	2.83±	0.79	0±	0	18±	4	1±	1	0±	0	3±	1	79±	5	0±	0
640 ppm	10	3.27±	1.65	0±	0	20±	6	1±	1	0±	0	4±	2	75±	7	0±	0
1600 ppm	09	2.53±	0.71	0±	0	16±	3	2±	1	0±	0	3±	2	80±	4	0±	0
4000 ppm	10	2.78±	0.86	0±	0	17±	4	1±	1	0±	0	4±	2	78±	4	0±	0
10000 ppm	10	2.84±	0.69	0±	0	19±	4	1±	1	0±	0	3±	2	77±	4	0±	1
25000 ppm	09	2.98±	1.05	0±	0	20±	7	2±	1	0±	0	4±	1	73±	8	0±	1

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

Test of Dunnett

(JCL71A)

BAIS 2

APPENDIX H 3

HEMATOLOGY (THIRTEEN-WEEK STUDIES:SUMMARY)

MOUSE:MALE

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 REPORT TYPE : A1
 SEX : MALE

HEMATOLOGY(1) (SUMMARY)
 SURVIVAL ANIMALS (13)

PAGE : 1

Group Name	NO. of Animals	RED BLOOD CELL 10 ⁶ /μl		HEMOGLOBIN g/dl		HEMATOCRIT %		MCV fl		PLATELET 10 ³ /μl	
Control	09	10.67±	0.41	14.9±	0.5	43.3±	1.8	40.5±	0.3	1232±	116
640 ppm	10	10.77±	0.34	15.0±	0.3	44.0±	1.5	40.9±	0.5	1321±	112
1600 ppm	10	10.39±	0.45	14.6±	0.4	42.6±	1.7	41.0±	0.5	1224±	104
4000 ppm	09	10.70±	0.42	15.1±	0.4	44.1±	1.7	41.2±	0.6	1392±	114**
10000 ppm	10	10.91±	0.44	15.4±	0.6	45.2±	1.9	41.4±	0.5**	1349±	68
25000 ppm	09	11.31±	0.51*	16.3±	0.6**	47.6±	1.5**	42.1±	1.3**	1176±	105

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS2

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 REPORT TYPE : A1
 SEX : MALE

HEMATOLOGY(2) (SUMMARY)
 SURVIVAL ANIMALS (13)

PAGE : 1

Group Name		NO. of Animals	WBC 1 O ³ /μℓ		Differential N-BAND		WBC (%) N-SEG	EOSINO		BASO		MONO		LYMPHO		OTHER		
Control		09	1.63±	0.60	0±	1	17±	5	1±	1	0±	0	3±	1	79±	5	0±	0
640	ppm	10	2.10±	1.41	0±	0	15±	3	1±	1	0±	0	3±	2	81±	4	0±	0
1600	ppm	10	1.59±	0.73	0±	0	16±	4	1±	1	0±	0	3±	2	80±	5	0±	0
4000	ppm	09	1.81±	0.80	0±	0	15±	2	1±	1	0±	0	3±	3	81±	4	0±	0
10000	ppm	10	1.53±	0.37	0±	0	17±	3	1±	1	0±	0	2±	1	80±	4	0±	0
25000	ppm	09	1.49±	0.66	0±	0	19±	7	2±	2	0±	0	3±	1	76±	7	0±	0

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

Test of Dunnett

(JCL71A)

BAIS 2

APPENDIX H 4

HEMATOLOGY (THIRTEEN-WEEK STUDIES:SUMMARY)

MOUSE:FEMALE

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 REPORT TYPE : A1
 SEX : FEMALE

HEMATOLOGY(1) (SUMMARY)
 SURVIVAL ANIMALS (13)

PAGE : 2

Group Name	NO. of Animals	RED BLOOD CELL 10 ⁶ /μl		HEMOGLOBIN g/dl		HEMATOCRIT %		MCV fl		PLATELET 10 ³ /μl	
Control	09	10.20±	0.37	14.6±	0.5	42.3±	1.6	41.5±	0.4	1053±	88
640 ppm	10	10.21±	0.38	14.7±	0.5	42.5±	1.7	41.6±	0.2	1086±	84
1600 ppm	10	10.47±	0.42	15.0±	0.6	43.6±	1.9	41.6±	0.4	1103±	90
4000 ppm	10	10.52±	0.34	15.1±	0.6	43.6±	1.9	41.4±	0.8	1100±	149
10000 ppm	10	10.43±	0.66	15.3±	0.9	44.1±	2.8	42.3±	0.3**	1074±	41
25000 ppm	09	10.45±	0.33	15.4±	0.4	44.7±	1.4	42.8±	0.5**	1007±	123

Significant difference : * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL070)

BAIS 2

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 REPORT TYPE : A1
 SEX : FEMALE

HEMATOLOGY(2) (SUMMARY)
 SURVIVAL ANIMALS (13)

PAGE : 2

Group Name	NO. of Animals	WBC 10 ³ /μl		Differential N-BAND		WBC	(%) N-SEG	EOSINO		BASO		MONO		LYMPHO		OTHER	
Control	09	1.16±	0.53	0±	0	19±	5	1±	1	0±	0	2±	1	78±	5	0±	0
640 ppm	10	1.49±	0.67	0±	0	16±	5	0±	1	0±	0	2±	1	81±	5	0±	0
1600 ppm	10	1.97±	1.05	0±	1	18±	5	0±	0	0±	0	2±	1	80±	5	0±	0
4000 ppm	10	2.42±	1.84	0±	0	18±	6	1±	1	0±	0	2±	1	80±	8	0±	0
10000 ppm	10	1.56±	1.07	0±	0	17±	4	1±	1	0±	0	2±	1	81±	4	0±	0
25000 ppm	09	1.47±	0.61	0±	0	18±	7	1±	1	0±	0	2±	1	79±	7	0±	0

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

Test of Dunnett

(JCL71A)

BAIS2

1,4-ジオキサンのラット及びマウスを用いた
経口(混水)投与によるがん原性予備試験
(急性・2週間・13週間) 報告書

APPENDIX

(I1~I4)

13Week STUDY NO. 0053 ; 0054

APPENDIX I 1

BIOCHEMISTRY (THIRTEEN-WEEK STUDIES:SUMMARY)

RAT:MALE

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

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	6.7±	0.2	3.8±	0.1	1.3±	0.1	0.22±	0.03	181±	23	54±	6	87±	27
640 ppm	10	6.6±	0.1	3.8±	0.1	1.4±	0.1	0.22±	0.04	179±	20	53±	2	90±	19
1600 ppm	10	6.6±	0.2	3.8±	0.1	1.3±	0.0	0.22±	0.02	177±	10	54±	4	87±	21
4000 ppm	10	6.4±	0.2**	3.7±	0.1**	1.3±	0.1	0.22±	0.03	177±	18	52±	4	84±	17
10000 ppm	10	6.3±	0.1**	3.6±	0.0**	1.3±	0.1	0.21±	0.03	164±	12	50±	4	81±	15
25000 ppm	10	5.8±	0.2**	3.4±	0.1**	1.4±	0.1**	0.21±	0.04	138±	14**	41±	6**	54±	11**

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 2

STUDY NO. : 0053
 ANIMAL : RAT F344
 REPORT TYPE : A1
 SEX : MALE

BIOCHEMISTRY (SUMMARY)
 SURVIVAL ANIMALS (13)

PAGE : 2

Group Name	NO. of Animals	GOT IU/ℓ		GPT IU/ℓ		LDH IU/ℓ		ALP IU/ℓ		LAP IU/ℓ		CPK IU/ℓ		UREA NITROGEN mg/dℓ	
Control	10	75±	16	26±	5	203±	55	242±	11	51±	2	119±	17	16.4±	1.6
640 ppm	10	79±	15	27±	4	218±	33	243±	17	52±	2	120±	17	16.3±	1.0
1600 ppm	10	80±	9	29±	3	216±	38	243±	16	52±	2	117±	18	15.9±	0.9
4000 ppm	10	78±	11	28±	3	208±	31	248±	19	54±	1	118±	19	16.5±	1.3
10000 ppm	10	83±	6	29±	2	250±	76	271±	23**	60±	2**	128±	21	17.0±	1.3
25000 ppm	10	104±	15**	43±	9**	283±	90	308±	23**	74±	2**	140±	20	18.7±	3.0

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 2

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

PAGE : 3

Group Name	NO. of Animals	CREATININE mg/dl		SODIUM mEq/l		POTASSIUM mEq/l		CHLORIDE mEq/l		CALCIUM mg/dl		INORGANIC PHOSPHORUS mg/dl	
Control	10	0.5±	0.1	142±	1	3.3±	0.3	103±	1	10.5±	0.3	5.8±	0.4
640 ppm	10	0.5±	0.1	142±	1	3.2±	0.1	102±	1	10.6±	0.2	5.9±	0.6
1600 ppm	10	0.5±	0.1	142±	2	3.2±	0.3	102±	2	10.6±	0.1	5.9±	0.8
4000 ppm	10	0.5±	0.1	140±	1	3.2±	0.2	102±	2	10.6±	0.2	5.8±	0.6
10000 ppm	10	0.5±	0.1	140±	1	3.2±	0.2	102±	1	10.5±	0.1	5.8±	0.5
25000 ppm	10	0.5±	0.1	140±	1*	3.3±	0.2	102±	1	10.5±	0.2	5.9±	0.4

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 2

APPENDIX I 2

BIOCHEMISTRY (THIRTEEN-WEEK STUDIES:SUMMARY)

RAT:FEMALE

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

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	6.6±	0.2	3.8±	0.1	1.3±	0.1	0.25±	0.05	150±	14	82±	7	47±	8
640 ppm	10	6.6±	0.2	3.7±	0.1	1.3±	0.1	0.23±	0.05	155±	11	84±	7	44±	8
1600 ppm	09	6.5±	0.2	3.7±	0.1	1.3±	0.1	0.22±	0.04	149±	8	83±	10	49±	11
4000 ppm	10	6.3±	0.2**	3.6±	0.1**	1.3±	0.1	0.23±	0.03	144±	11	79±	6	42±	6
10000 ppm	10	6.1±	0.2**	3.5±	0.1**	1.4±	0.1	0.24±	0.03	138±	11	83±	9	42±	5
25000 ppm	09	5.9±	0.2**	3.4±	0.1**	1.4±	0.1*	0.22±	0.04	124±	15**	68±	6**	39±	4

Significant difference : * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 2

STUDY NO. : 0053
 ANIMAL : RAT F344
 REPORT TYPE : A1
 SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
 SURVIVAL ANIMALS (13)

PAGE : 5

Group Name	NO. of Animals	GOT I U / ℓ		GPT I U / ℓ		LDH I U / ℓ		ALP I U / ℓ		LAP I U / ℓ		CPK I U / ℓ		UREA NITROGEN mg / dl	
Control	10	67±	9	21±	4	258±	53	166±	14	53±	3	130±	17	18.2±	1.4
640 ppm	10	65±	10	20±	3	232±	29	165±	15	53±	1	124±	27	17.5±	0.9
1600 ppm	09	67±	7	20±	3	273±	102	163±	20	53±	4	133±	31	16.8±	2.4
4000 ppm	10	69±	7	21±	3	278±	91	164±	9	55±	2	136±	21	16.8±	1.6
10000 ppm	10	68±	3	21±	1	233±	49	167±	18	57±	2*	119±	20	19.0±	2.6
25000 ppm	09	81±	6**	24±	2	301±	94	212±	21**	65±	3**	149±	27	20.8±	2.8

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 2

STUDY NO. : 0053
 ANIMAL : RAT F344
 REPORT TYPE : A1
 SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
 SURVIVAL ANIMALS (13)

PAGE : 6

Group Name	NO. of Animals	CREATININE mg/dl		SODIUM mEq/l		POTASSIUM mEq/l		CHLORIDE mEq/l		CALCIUM mg/dl		INORGANIC PHOSPHORUS mg/dl	
Control	10	0.4±	0.1	141±	2	3.2±	0.2	105±	2	10.5±	0.2	4.9±	0.6
640 ppm	10	0.5±	0.1	141±	2	3.1±	0.2	104±	1	10.5±	0.2	5.0±	1.1
1600 ppm	09	0.4±	0.1	142±	2	3.3±	0.6	104±	2	10.6±	0.4	5.4±	0.8
4000 ppm	10	0.4±	0.1	142±	1	3.1±	0.3	105±	1	10.3±	0.3	5.1±	0.9
10000 ppm	10	0.4±	0.1	141±	1	3.2±	0.2	104±	1	10.3±	0.3	5.1±	1.0
25000 ppm	09	0.4±	0.1	139±	2*	3.3±	0.3	104±	2	10.2±	0.2*	5.4±	1.1

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS2

APPENDIX I 3

BIOCHEMISTRY (THIRTEEN-WEEK STUDIES:SUMMARY)

MOUSE:MALE

STUDY NO. : 0054
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

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		GOT I U/l	
Control	09	5.0±	0.1	2.9±	0.1	1.4±	0.1	0.19±	0.05	209±	37	92±	4	48±	10
640 ppm	10	5.1±	0.1	3.0±	0.1	1.5±	0.1	0.16±	0.03	207±	35	90±	7	49±	11
1600 ppm	10	5.0±	0.2	2.9±	0.1	1.4±	0.1	0.16±	0.06	193±	31	89±	10	44±	8
4000 ppm	09	5.0±	0.1	3.0±	0.1	1.4±	0.1	0.17±	0.03	190±	31	80±	6**	43±	10
10000 ppm	10	4.9±	0.3	2.9±	0.1	1.5±	0.1	0.19±	0.04	188±	25	72±	8**	44±	6
25000 ppm	09	4.6±	0.2**	2.8±	0.1*	1.6±	0.2	0.23±	0.03	132±	11**	56±	6**	70±	12**

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 2

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 REPORT TYPE : A1
 SEX : MALE

BIOCHEMISTRY (SUMMARY)
 SURVIVAL ANIMALS (13)

PAGE : 2

Group Name	NO. of Animals	GPT I U / ℓ		LDH I U / ℓ		ALP I U / ℓ		LAP I U / ℓ		UREA NITROGEN mg / dl		SODIUM mEq / ℓ		POTASSIUM mEq / ℓ	
Control	09	11±	2	337±	99	146±	9	38±	2	25.4±	3.6	150±	1	3.8±	0.2
640 ppm	10	13±	3	375±	82	146±	7	39±	2	24.0±	2.3	150±	1	4.3±	0.3*
1600 ppm	10	10±	2	396±	103	143±	6	35±	1*	23.9±	2.7	151±	2	4.3±	0.4*
4000 ppm	09	12±	2	354±	76	158±	11*	36±	1	26.1±	2.2	150±	2	4.2±	0.5
10000 ppm	10	13±	2	365±	138	178±	13**	34±	3**	23.1±	2.3	150±	2	4.2±	0.4
25000 ppm	09	25±	9**	409±	33	207±	9**	36±	3	23.1±	2.8	151±	2	3.8±	0.3

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS2

STUDY NO. : 0054
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

PAGE : 3

Group Name	NO. of Animals	CHLORIDE mEq/l	
Control	09	121±	1
640 ppm	10	121±	1
1600 ppm	10	122±	2
4000 ppm	09	122±	2
10000 ppm	10	120±	1
25000 ppm	09	120±	2

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 2

APPENDIX I 4

BIOCHEMISTRY (THIRTEEN-WEEK STUDIES:SUMMARY)

MOUSE:FEMALE

STUDY NO. : 0054
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

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		GOT I U/l	
Control	09	5.0±	0.1	3.0±	0.1	1.5±	0.1	0.23±	0.06	151±	14	71±	5	88±	19
640 ppm	10	4.9±	0.2	3.0±	0.1	1.5±	0.1	0.24±	0.07	151±	27	70±	6	87±	30
1600 ppm	10	5.1±	0.2	3.1±	0.1	1.5±	0.1	0.20±	0.04	139±	17	74±	8	89±	18
4000 ppm	10	5.0±	0.2	3.0±	0.1	1.5±	0.1	0.23±	0.08	136±	15	70±	11	87±	29
10000 ppm	10	4.8±	0.2*	2.9±	0.2	1.5±	0.1	0.26±	0.09	130±	15*	53±	7**	93±	14
25000 ppm	09	4.5±	0.2**	2.7±	0.1**	1.5±	0.1	0.24±	0.08	123±	10**	45±	10**	139±	35**

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 2

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 REPORT TYPE : A1
 SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
 SURVIVAL ANIMALS (13)

PAGE : 5

Group Name	NO. of Animals	GPT IU/ℓ		LDH IU/ℓ		ALP IU/ℓ		LAP IU/ℓ		UREA NITROGEN mg/dℓ		SODIUM mEq/ℓ		POTASSIUM mEq/ℓ	
Control	09	17±	4	440±	66	253±	23	38±	2	25.0±	2.3	150±	2	4.3±	0.2
640 ppm	10	17±	5	449±	99	262±	21	37±	3	23.7±	2.7	149±	2	4.3±	0.3
1600 ppm	10	20±	5	515±	95	264±	22	39±	3	25.2±	3.8	150±	2	4.9±	0.8
4000 ppm	10	22±	6	477±	117	248±	22	37±	2	23.6±	2.2	149±	2	4.4±	0.4
10000 ppm	10	30±	6**	575±	157*	284±	25	35±	2	25.1±	1.9	150±	2	4.4±	0.5
25000 ppm	09	50±	8**	637±	105**	314±	41**	36±	3	25.2±	4.3	150±	3	4.2±	0.3

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS 2

STUDY NO. : 0054
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

BIOCHEMISTRY (SUMMARY)
SURVIVAL ANIMALS (13)

PAGE : 6

Group Name	NO. of Animals	CHLORIDE mEq/ℓ	
Control	09	122±	2
840 ppm	10	120±	2
1600 ppm	10	121±	2
4000 ppm	10	119±	2
10000 ppm	10	121±	2
25000 ppm	09	121±	2

Significant difference ; * : $P \leq 0.05$

** : $P \leq 0.01$

Test of Dunnett

(HCL074)

BAIS2

1,4-ジオキサンのラット及びマウスを用いた
経口(混水)投与によるがん原性予備試験
(急性・2週間・13週間) 報告書

APPENDIX

(J1~J4)

13Week STUDY NO. 0053 ; 0054

APPENDIX J 1

URINALYSIS (THIRTEEN-WEEK STUDIES:SUMMARY)

RAT:MALE

STUDY NO. : 0053
ANIMAL : RAT F344
SAMPLING DATE : 013-7
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+	—	+		2+	3+
Control		10	0	0	0	1	6	3	0		3	1	5	1	0	0		10	0	0	0	0	0		10	0	0	0		10	0	0	0	
640	ppm	10	0	0	0	2	6	2	0		3	1	6	0	0	0		10	0	0	0	0	0		10	0	0	0		10	0	0	0	
1600	ppm	10	0	0	0	2	3	5	0		2	0	8	0	0	0		10	0	0	0	0	0		10	0	0	0		10	0	0	0	
4000	ppm	10	0	0	2	7	1	0	0	**	0	4	6	0	0	0		10	0	0	0	0	0		9	1	0	0		10	0	0	0	
10000	ppm	10	0	0	7	2	1	0	0	**	1	7	2	0	0	0		10	0	0	0	0	0		9	1	0	0		10	0	0	0	
25000	ppm	10	0	3	7	0	0	0	0	**	0	1	6	3	0	0		10	0	0	0	0	0		8	2	0	0		10	0	0	0	

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

Test of CHI SQUARE

(JCL103X)

BAIS 2

STUDY NO. : 0053
ANIMAL : RAT F344
SAMPLING DATE : 013-7
SEX : MALE

URINALYSIS

REPORT TYPE : A1

PAGE : 2

Group Name		NO. of Animals	Occult blood					Urobilinogen						
			-	±	+	2+	3+	CHI	±	+	2+	3+	4+	CHI
Control		10	10	0	0	0	0	0	10	0	0	0	0	0
640	ppm	10	10	0	0	0	0	0	10	0	0	0	0	0
1600	ppm	10	9	0	0	1	0	0	10	0	0	0	0	0
4000	ppm	10	10	0	0	0	0	0	10	0	0	0	0	0
10000	ppm	10	10	0	0	0	0	0	10	0	0	0	0	0
25000	ppm	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

(JCL103X)

BAIS 2

APPENDIX J 2

URINALYSIS (THIRTEEN-WEEK STUDIES:SUMMARY)

RAT:FEMALE

STUDY NO. : 0053
 ANIMAL : RAT F344
 SAMPLING DATE : 013-7
 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+	-	+		2+	3+
Control		10	0	0	0	0	5	5	0		0	1	9	0	0	0		10	0	0	0	0	0		9	1	0	0		10	0	0	0	
640	ppm	10	0	0	0	0	8	2	0		0	3	6	1	0	0		10	0	0	0	0	0		10	0	0	0		10	0	0	0	
1600	ppm	10	0	0	0	0	5	5	0		0	1	8	1	0	0		10	0	0	0	0	0		9	1	0	0		10	0	0	0	
4000	ppm	10	0	0	3	2	3	2	0		0	0	9	1	0	0		10	0	0	0	0	0		10	0	0	0		10	0	0	0	
10000	ppm	10	0	2	8	0	0	0	0	**	0	0	6	4	0	0		10	0	0	0	0	0		9	1	0	0		10	0	0	0	
25000	ppm	9	0	2	7	0	0	0	0	**	0	0	6	3	0	0		9	0	0	0	0	0		7	2	0	0		9	0	0	0	

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

Test of CHI SQUARE

(JCL103X)

BAIS 2

STUDY NO. : 0053

ANIMAL : RAT F344

SAMPLING DATE : 013-7

SEX : FEMALE

REPORT TYPE : A1

URINALYSIS

PAGE : 4

Group Name		NO. of Animals	Occult blood					Urobilinogen						
			-	±	+	2+	3+	CHI	±	+	2+	3+	4+	CHI
Control		10	10	0	0	0	0	0	10	0	0	0	0	0
640	ppm	10	10	0	0	0	0	0	10	0	0	0	0	0
1600	ppm	10	10	0	0	0	0	0	10	0	0	0	0	0
4000	ppm	10	10	0	0	0	0	0	10	0	0	0	0	0
10000	ppm	10	10	0	0	0	0	0	10	0	0	0	0	0
25000	ppm	9	9	0	0	0	0	0	9	0	0	0	0	0

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

Test of CHI SQUARE

(JCL103X)

BAIS 2

APPENDIX J 3

URINALYSIS (THIRTEEN-WEEK STUDIES:SUMMARY)

MOUSE:MALE

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 SAMPLING DATE : 013-7
 SEX : MALE

URINALYSIS

REPORT TYPE : A1

PAGE : 1

Group Name		NO. of Animals	pH_____							CHI	Protein_____						CHI	Glucose_____						CHI	Ketone body				CHI	Occult blood					CHI
			5.0	6.0	6.5	7.0	7.5	8.0	8.5		-	±	+	2+	3+	4+		-	±	+	2+	3+	4+		-	+	2+	3+		-	±	+	2+	3+	
Control		10	0	0	0	0	4	5	1		2	4	4	0	0	0		10	0	0	0	0	0		9	1	0	0		10	0	0	0	0	
640	ppm	10	0	0	0	0	2	6	2		2	1	7	0	0	0		10	0	0	0	0	0		8	2	0	0		10	0	0	0	0	
1600	ppm	10	0	0	0	0	3	7	0		0	0	7	3	0	0	*	10	0	0	0	0	0		9	1	0	0		10	0	0	0	0	
4000	ppm	10	0	0	0	1	4	5	0		0	5	5	0	0	0		10	0	0	0	0	0		10	0	0	0		10	0	0	0	0	
10000	ppm	10	0	0	4	4	2	0	0	**	0	1	7	2	0	0		10	0	0	0	0	0		7	3	0	0		10	0	0	0	0	
25000	ppm	9	0	3	6	0	0	0	0	**	0	0	2	7	0	0	**	9	0	0	0	0	0		6	3	0	0		9	0	0	0	0	

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

Test of CHI SQUARE

(JCL104X)

BAIS 2

STUDY NO. : 0054
ANIMAL : MOUSE BDF1
SAMPLING DATE : 013-7
SEX : MALE

URINALYSIS

REPORT TYPE : A1

PAGE : 2

Group Name	NO. of Animals	Urobilinogen ± + 2+ 3+ 4+ CHI
Control	10	10 0 0 0 0
640 ppm	10	10 0 0 0 0
1600 ppm	10	10 0 0 0 0
4000 ppm	10	10 0 0 0 0
10000 ppm	10	10 0 0 0 0
25000 ppm	9	9 0 0 0 0

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

Test of CHI SQUARE

(JCL104X)

BAIS2

APPENDIX J 4

URINALYSIS (THIRTEEN-WEEK STUDIES:SUMMARY)

MOUSE:FEMALE

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 SAMPLING DATE : 013-7
 SEX : FEMALE

URINALYSIS

REPORT TYPE : A1

PAGE : 3

Group Name		NO. of Animals	pH							CHI	Protein					CHI	Glucose					CHI	Ketone body				CHI	Occult blood				CHI			
			5.0	6.0	6.5	7.0	7.5	8.0	8.5		-	±	+	2+	3+		4+	-	±	+	2+		3+	4+	-	±		+	2+	3+	-		±	+	2+
Control		10	0	0	0	1	4	5	0		0	0	3	7	0	0		10	0	0	0	0	0		6	4	0	0		10	0	0	0	0	
640	ppm	10	0	0	0	0	7	3	0		0	0	2	8	0	0		10	0	0	0	0	0		4	6	0	0		10	0	0	0	0	
1600	ppm	10	0	0	1	0	4	5	0		0	0	5	5	0	0		10	0	0	0	0	0		4	6	0	0		10	0	0	0	0	
4000	ppm	10	0	0	1	0	4	5	0		0	0	4	6	0	0		10	0	0	0	0	0		6	4	0	0		10	0	0	0	0	
10000	ppm	10	0	0	6	3	1	0	0	**	0	0	5	5	0	0		10	0	0	0	0	0		6	4	0	0		10	0	0	0	0	
25000	ppm	10	0	1	9	0	0	0	0	**	0	0	2	8	0	0		10	0	0	0	0	0		5	5	0	0		10	0	0	0	0	

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

Test of CHI SQUARE

(JCL104X)

BAIS 2

STUDY NO. : 0054
ANIMAL : MOUSE BDF1
SAMPLING DATE : 013-7
SEX : FEMALE

URINALYSIS

REPORT TYPE : A1

PAGE : 4

Group Name	NO. of Animals	Urobilinogen ± + 2+ 3+ 4+ CHI
Control	10	10 0 0 0 0
640 ppm	10	10 0 0 0 0
1600 ppm	10	10 0 0 0 0
4000 ppm	10	10 0 0 0 0
10000 ppm	10	10 0 0 0 0
25000 ppm	10	10 0 0 0 0

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

Test of CHI SQUARE

(JCL104X)

BAIS 2

1,4-ジオキサンのラット及びマウスを用いた
経口(混水)投与によるがん原性予備試験
(急性・2週間・13週間) 報告書

APPENDIX

(K1~K6)

13Week STUDY NO. 0053 ; 0054

APPENDIX K 1

GROSS FINDINGS (THIRTEEN-WEEK STUDIES:SUMMARY)

RAT:FEMALE:DEAD AND MORIBUND ANIMALS

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 13W)

PAGE : 1

Organ	Findings	Group Name NO. of Animals	Control 0 (%)	640 ppm 0 (%)	1600 ppm 0 (%)	4000 ppm 0 (%)
thymus	atrophic		- (-)	- (-)	- (-)	- (-)
spleen	atrophic		- (-)	- (-)	- (-)	- (-)
liver	accentuation of lobular structure		- (-)	- (-)	- (-)	- (-)
kidney	enlarged		- (-)	- (-)	- (-)	- (-)

(HPT080)

BAIS 2

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 13W)

PAGE : 2

Organ	Findings	Group Name	10000 ppm	25000 ppm
		NO. of Animals	0 (%)	1 (%)
thymus	atrophic		- (-)	1 (100)
spleen	atrophic		- (-)	1 (100)
liver	accentuation of lobular structure		- (-)	1 (100)
kidney	enlarged		- (-)	1 (100)

(HPT080)

BAIS 2

APPENDIX K 2

GROSS FINDINGS (THIRTEEN-WEEK STUDIES:SUMMARY)

RAT:MALE:SACRIFICED ANIMALS

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (13W)

PAGE : 1

Organ	Findings	Group Name	Control	640 ppm	1600 ppm	4000 ppm
		NO. of Animals	10 (%)	10 (%)	10 (%)	10 (%)
thymus	atrophic		0 (0)	0 (0)	0 (0)	0 (0)
Liver	enlarged		0 (0)	0 (0)	0 (0)	0 (0)
	nodule		0 (0)	0 (0)	0 (0)	0 (0)
	herniation		0 (0)	0 (0)	1 (10)	0 (0)
	accentuation of lobular structure		0 (0)	2 (20)	2 (20)	2 (20)
Kidney	white patch/zone		0 (0)	0 (0)	0 (0)	1 (10)
adipose	nodule		0 (0)	1 (10)	0 (0)	0 (0)

(HPT080)

BAIS 2

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (13W)

PAGE : 2

Organ	Findings	Group Name	10000 ppm	25000 ppm
		NO. of Animals	10 (%)	10 (%)
thymus	atrophic		0 (0)	1 (10)
Liver	enlarged		0 (0)	1 (10)
	nodule		0 (0)	1 (10)
	herniation		0 (0)	0 (0)
	accentuation of lobular structure		2 (20)	0 (0)
kidney	white patch/zone		0 (0)	0 (0)
adipose	nodule		0 (0)	0 (0)

(HPT080)

BAIS 2

APPENDIX K 3

GROSS FINDINGS (THIRTEEN-WEEK STUDIES:SUMMARY)

RAT:FEMALE:SACRIFICED ANIMALS

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (13W)

PAGE : 3

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	640 ppm 10 (%)	1600 ppm 10 (%)	4000 ppm 10 (%)
lung/branch	nodule		0 (0)	0 (0)	0 (0)	0 (0)
liver	congestion		0 (0)	0 (0)	1 (10)	0 (0)
	nodule		2 (20)	1 (10)	0 (0)	0 (0)
	accentuation of lobular structure		1 (10)	0 (0)	0 (0)	0 (0)
ovary	red patch/zone		0 (0)	1 (10)	1 (10)	0 (0)
uterus	dilated lumen		1 (10)	2 (20)	3 (30)	2 (20)

(HPT080)

BAIS 2

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (13W)

PAGE : 4

Organ	Findings	Group Name	10000. ppm	25000 ppm
		NO. of Animals	10 (%)	9 (%)
lung/branch	nodule		1 (10)	0 (0)
liver	congestion		0 (0)	0 (0)
	nodule		0 (0)	0 (0)
	accentuation of lobular structure		1 (10)	1 (11)
ovary	red patch/zone		1 (10)	0 (0)
uterus	dilated lumen		4 (40)	2 (22)

(HPT080)

BAIS 2

APPENDIX K 4

GROSS FINDINGS (THIRTEEN-WEEK STUDIES:SUMMARY)

MOUSE:MALE:DEAD AND MORIBUND ANIMALS

STUDY NO. : 0054
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 13W)

PAGE : 1

Organ	Findings	Group Name NO. of Animals	Control 0 (%)	640 ppm 0 (%)	1600 ppm 0 (%)	4000 ppm 0 (%)
thymus	atrophic		- (-)	- (-)	- (-)	- (-)
gl stomach	fluid:black		- (-)	- (-)	- (-)	- (-)
duodenum	fluid:black		- (-)	- (-)	- (-)	- (-)
whole body	wasting		- (-)	- (-)	- (-)	- (-)

(HPT080)

BAIS 2

STUDY NO. : 0054
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 13W)

PAGE : 2

Organ	Findings	Group Name	10000 ppm	25000 ppm
		NO. of Animals	0 (%)	1 (%)
thymus	atrophic		- (-)	1 (100)
gl stomach	fluid:black		- (-)	1 (100)
duodenum	fluid:black		- (-)	1 (100)
whole body	wasting		- (-)	1 (100)

(HPT080)

BAIS 2

APPENDIX K 5

GROSS FINDINGS (THIRTEEN-WEEK STUDIES:SUMMARY)

MOUSE:MALE:SACRIFICED ANIMALS

STUDY NO. : 0054
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (13W)

PAGE : 1

Organ	Findings	Group Name	Control	640 ppm	1600 ppm	4000 ppm
		NO. of Animals	10 (%)	10 (%)	10 (%)	10 (%)
Lung/branch	white patch/zone		0 (0)	0 (0)	0 (0)	0 (0)
spleen	black patch/zone		0 (0)	0 (0)	0 (0)	0 (0)
kidney	red patch/zone		0 (0)	0 (0)	1 (10)	0 (0)
	hydronephrosis		1 (10)	0 (0)	0 (0)	0 (0)

(HPT080)

BAIS 2

STUDY NO. : 0054
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (13W)

PAGE : 2

Organ	Findings	Group Name	10000 ppm	25000 ppm
		NO. of Animals	10 (%)	9 (%)
lung/branch	white patch/zone		0 (0)	1 (11)
spleen	black patch/zone		1 (10)	2 (22)
kidney	red patch/zone		0 (0)	0 (0)
	hydronephrosis		0 (0)	0 (0)

(HPT080)

BAIS 2

APPENDIX K 6

GROSS FINDINGS (THIRTEEN-WEEK STUDIES:SUMMARY)

MOUSE:FEMALE:SACRIFICED ANIMALS

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 REPORT TYPE : A1
 SEX : FEMALE

GROSS FINDINGS (SUMMARY)
 SACRIFICED ANIMALS (13W)

PAGE : 3

Organ	Findings	Group Name NO. of Animals	Control 10 (%)	640 ppm 10 (%)	1600 ppm 10 (%)	4000 ppm 10 (%)
lung/branch	white patch/zone		0 (0)	0 (0)	0 (0)	0 (0)
spleen	black patch/zone		1 (10)	0 (0)	4 (40)	0 (0)
gl stomach	hemorrhage		1 (10)	1 (10)	0 (0)	0 (0)
pancreas	hemorrhage		1 (10)	0 (0)	0 (0)	0 (0)
urin bladd	thick		0 (0)	0 (0)	0 (0)	0 (0)
ovary	enlarged		0 (0)	0 (0)	0 (0)	1 (10)
	cyst		0 (0)	1 (10)	1 (10)	1 (10)
uterus	dilated lumen		5 (50)	7 (70)	4 (40)	3 (30)
muscle	hemorrhage		0 (0)	1 (10)	1 (10)	1 (10)
other	dilated		0 (0)	0 (0)	0 (0)	0 (0)

(HPT080)

BAIS 2

STUDY NO. : 0054
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

GROSS FINDINGS (SUMMARY)
SACRIFICED ANIMALS (13W)

PAGE : 4

Organ	Findings	Group Name	10000 ppm	25000 ppm
		NO. of Animals	10 (%)	10 (%)
lung/branch	white patch/zone		2 (20)	2 (20)
spleen	black patch/zone		0 (0)	1 (10)
gl stomach	hemorrhage		3 (30)	1 (10)
pancreas	hemorrhage		0 (0)	0 (0)
urin bladd	thick		0 (0)	1 (10)
ovary	enlarged		0 (0)	0 (0)
	cyst		0 (0)	0 (0)
uterus	dilated lumen		2 (20)	4 (40)
muscle	hemorrhage		0 (0)	0 (0)
other	dilated		0 (0)	1 (10)

1,4-ジオキサンのラット及びマウスを用いた
経口(混水)投与によるがん原性予備試験
(急性・2週間・13週間) 報告書

APPENDIX

(L1~L4)

13Week STUDY NO. 0053 ; 0054

APPENDIX L 1

ORGAN WEIGHT (THIRTEEN-WEEK STUDIES:SUMMARY), ABSOLUTE

RAT:MALE

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (13)

PAGE : 1

Group Name	NO. of Animals	Body weight	THYMUS	ADRENL R	ADRENL L	TESTIS R	TESTIS L
Control	10	331± 13	0.286± 0.035	0.026± 0.002	0.026± 0.002	1.464± 0.047	1.495± 0.061
640 ppm	10	335± 9	0.292± 0.033	0.025± 0.002	0.027± 0.003	1.486± 0.057	1.546± 0.058
1600 ppm	10	337± 7	0.289± 0.031	0.025± 0.003	0.028± 0.002	1.474± 0.071	1.500± 0.077
4000 ppm	10	322± 15	0.267± 0.037	0.026± 0.003	0.026± 0.002	1.448± 0.070	1.482± 0.061
10000 ppm	10	309± 7*	0.273± 0.021	0.027± 0.002	0.028± 0.002	1.476± 0.061	1.521± 0.062
25000 ppm	10	263± 22**	0.216± 0.039**	0.027± 0.004	0.029± 0.003	1.468± 0.060	1.517± 0.033

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

Test of Dunnett

(HCL040)

BAIS2

STUDY NO. : 0053
 ANIMAL : RAT F344
 REPORT TYPE : A1
 SEX : MALE
 UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
 SURVIVAL ANIMALS (13)

PAGE : 2

Group Name	NO. of Animals	HEART		LUNG R		LUNG L		KIDNEY R		KIDNEY L		SPLEEN	
Control	10	0.944±	0.042	0.634±	0.040	0.355±	0.013	0.960±	0.026	0.980±	0.046	0.583±	0.012
640 ppm	10	0.949±	0.056	0.652±	0.062	0.365±	0.016	0.995±	0.048	0.991±	0.053	0.612±	0.028
1600 ppm	10	0.960±	0.048	0.642±	0.031	0.364±	0.023	0.995±	0.042	1.024±	0.048	0.605±	0.026
4000 ppm	10	0.922±	0.050	0.640±	0.035	0.368±	0.019	0.982±	0.037	1.003±	0.050	0.590±	0.037
10000 ppm	10	0.876±	0.030**	0.622±	0.022	0.350±	0.016	0.971±	0.038	0.964±	0.021	0.537±	0.012
25000 ppm	10	0.739±	0.034**	0.575±	0.036**	0.333±	0.029	0.904±	0.019**	0.930±	0.035	0.453±	0.030**

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

Test of Dunnett

(HCL040)

BAIS 2

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (13)

PAGE : 3

Group Name	NO. of Animals	LIVER		BRAIN	
Control	10	8.144±	0.420	1.889±	0.044
640 ppm	10	8.360±	0.387	1.895±	0.024
1600 ppm	10	8.487±	0.272	1.888±	0.031
4000 ppm	10	8.216±	0.405	1.895±	0.034
10000 ppm	10	7.948±	0.221	1.853±	0.023
25000 ppm	10	7.159±	0.506**	1.852±	0.081

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

Test of Dunnett

(HCL040)

BAIS 2

APPENDIX L 2

ORGAN WEIGHT (THIRTEEN-WEEK STUDIES:SUMMARY), ABSOLUTE

RAT:FEMALE

STUDY NO. : 0053
 ANIMAL : RAT F344
 REPORT TYPE : A1
 SEX : FEMALE
 UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
 SURVIVAL ANIMALS (13)

PAGE : 4

Group Name	NO. of Animals	Body weight	THYMUS	ADREN L R	ADREN L L	OVARY R	OVARY L
Control	10	194± 6	0.220± 0.018	0.028± 0.003	0.031± 0.004	0.056± 0.008	0.063± 0.009
840 ppm	10	197± 7	0.241± 0.032	0.030± 0.002	0.031± 0.003	0.059± 0.012	0.060± 0.006
1600 ppm	10	188± 8	0.221± 0.031	0.030± 0.004	0.030± 0.006	0.060± 0.009	0.063± 0.009
4000 ppm	10	183± 7**	0.217± 0.023	0.029± 0.004	0.031± 0.003	0.055± 0.007	0.059± 0.009
10000 ppm	10	172± 7**	0.201± 0.016	0.028± 0.002	0.029± 0.002	0.058± 0.007	0.061± 0.013
25000 ppm	09	155± 7**	0.168± 0.020**	0.026± 0.003	0.027± 0.002*	0.048± 0.006	0.058± 0.009

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

Test of Dunnett

(HCL040)

BAIS 2

STUDY NO. : 0053
 ANIMAL : RAT F344
 REPORT TYPE : A1
 SEX : FEMALE
 UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
 SURVIVAL ANIMALS (13)

PAGE : 5

Group Name	NO. of Animals	HEART		LUNG R		LUNG L		KIDNEY R		KIDNEY L		SPLEEN	
Control	10	0.619±	0.022	0.478±	0.023	0.278±	0.018	0.580±	0.022	0.586±	0.028	0.404±	0.017
640 ppm	10	0.642±	0.044	0.478±	0.030	0.272±	0.013	0.600±	0.032	0.611±	0.021	0.411±	0.024
1600 ppm	10	0.611±	0.029	0.481±	0.025	0.274±	0.015	0.618±	0.030*	0.628±	0.050*	0.416±	0.031
4000 ppm	10	0.586±	0.025	0.471±	0.022	0.273±	0.018	0.613±	0.019	0.612±	0.026	0.392±	0.018
10000 ppm	10	0.569±	0.039**	0.474±	0.027	0.265±	0.014	0.652±	0.031**	0.670±	0.033**	0.380±	0.018
25000 ppm	09	0.520±	0.028**	0.445±	0.021*	0.254±	0.010**	0.656±	0.034**	0.678±	0.022**	0.346±	0.039**

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

Test of Dunnett

(HCL040)

BAIS 2

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (13)

PAGE : 6

Group Name	NO. of Animals	LIVER		BRAIN	
Control	10	4.517±	0.174	1.753±	0.036
640 ppm	10	4.638±	0.253	1.758±	0.024
1600 ppm	10	4.819±	0.305*	1.763±	0.027
4000 ppm	10	4.485±	0.167	1.755±	0.029
10000 ppm	10	4.457±	0.175	1.744±	0.024
25000 ppm	09	4.473±	0.215	1.703±	0.047**

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

Test of Dunnett

(HCL040)

BAIS 2

APPENDIX L 3

ORGAN WEIGHT (THIRTEEN-WEEK STUDIES:SUMMARY), ABSOLUTE

MOUSE:MALE

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 REPORT TYPE : A1
 SEX : MALE
 UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
 SURVIVAL ANIMALS (13)

PAGE : 1

Group Name	NO. of Animals	Body weight	THYMUS	ADREN L R	ADREN L L	TESTIS R	TESTIS L
Control	10	30.9± 2.6	0.039± 0.009	0.005± 0.001	0.005± 0.001	0.124± 0.013	0.121± 0.011
640 ppm	10	32.3± 3.0	0.041± 0.006	0.005± 0.001	0.005± 0.001	0.127± 0.009	0.124± 0.009
1600 ppm	10	31.3± 3.3	0.041± 0.010	0.005± 0.001	0.005± 0.001	0.126± 0.011	0.121± 0.011
4000 ppm	10	30.7± 4.0	0.040± 0.009	0.005± 0.001	0.005± 0.001	0.123± 0.009	0.120± 0.012
10000 ppm	10	29.4± 2.5	0.038± 0.006	0.005± 0.001	0.005± 0.001	0.122± 0.009	0.117± 0.008
25000 ppm	09	22.2± 2.0**	0.028± 0.010*	0.005± 0.002	0.005± 0.001	0.114± 0.016	0.108± 0.014

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

Test of Dunnett

(HCL040)

BAIS 2

STUDY NO. : 0054
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (13)

PAGE : 2

Group Name	NO. of Animals	HEART		LUNG R		LUNG L		KIDNEY R		KIDNEY L		SPLEEN	
Control	10	0.145±	0.007	0.092±	0.005	0.047±	0.003	0.219±	0.020	0.213±	0.017	0.050±	0.007
640 ppm	10	0.145±	0.009	0.101±	0.014	0.049±	0.004	0.223±	0.015	0.223±	0.006	0.048±	0.005
1600 ppm	10	0.147±	0.008	0.093±	0.007	0.049±	0.004	0.221±	0.010	0.226±	0.020	0.045±	0.004
4000 ppm	10	0.140±	0.009	0.096±	0.012	0.050±	0.005	0.220±	0.013	0.219±	0.020	0.049±	0.004
10000 ppm	10	0.136±	0.007	0.098±	0.006	0.050±	0.003	0.228±	0.014	0.213±	0.010	0.046±	0.007
25000 ppm	09	0.116±	0.014**	0.112±	0.010**	0.057±	0.007**	0.201±	0.013*	0.202±	0.017	0.042±	0.012*

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

Test of Dunnett

(HCL040)

BAIS 2

STUDY NO. : 0054
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (13)

PAGE : 3

Group Name	NO. of Animals	LIVER		BRAIN	
Control	10	1.119±	0.039	0.436±	0.011
640 ppm	10	1.191±	0.083	0.436±	0.010
1600 ppm	10	1.184±	0.084	0.435±	0.011
4000 ppm	10	1.178±	0.108	0.438±	0.010
10000 ppm	10	1.104±	0.068	0.432±	0.013
25000 ppm	09	0.861±	0.120**	0.423±	0.008*

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

Test of Dunnett

(HCL040)

BAIS 2

APPENDIX L 4

ORGAN WEIGHT (THIRTEEN-WEEK STUDIES:SUMMARY), ABSOLUTE

MOUSE:FEMALE

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 REPORT TYPE : A1
 SEX : FEMALE
 UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
 SURVIVAL ANIMALS (13)

PAGE : 4

Group Name	NO. of Animals	Body weight	THYMUS	ADREN L R	ADREN L L	OVARY R	OVARY L
Control	10	20.0± 1.2	0.039± 0.008	0.007± 0.001	0.007± 0.001	0.020± 0.006	0.016± 0.003
640 ppm	10	20.5± 1.1	0.039± 0.008	0.007± 0.001	0.007± 0.000	0.017± 0.007	0.017± 0.006
1600 ppm	10	20.3± 1.1	0.037± 0.007	0.007± 0.002	0.008± 0.002	0.019± 0.005	0.019± 0.008
4000 ppm	10	21.0± 1.6	0.043± 0.008	0.007± 0.002	0.007± 0.001	0.020± 0.005	0.020± 0.004
10000 ppm	10	20.8± 1.6	0.042± 0.006	0.007± 0.001	0.007± 0.001	0.018± 0.004	0.020± 0.003
25000 ppm	10	19.5± 1.2	0.039± 0.008	0.007± 0.002	0.006± 0.002	0.015± 0.003	0.015± 0.004

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

Test of Dunnett

(HCL040)

BAIS 2

STUDY NO. : 0054
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (13)

PAGE : 5

Group Name	NO. of Animals	HEART		LUNG R		LUNG L		KIDNEY R		KIDNEY L		SPLEEN	
Control	10	0.115±	0.002	0.094±	0.007	0.049±	0.003	0.151±	0.013	0.141±	0.008	0.054±	0.009
640 ppm	10	0.116±	0.006	0.093±	0.007	0.049±	0.004	0.149±	0.008	0.143±	0.008	0.053±	0.005
1600 ppm	10	0.118±	0.007	0.095±	0.008	0.048±	0.004	0.154±	0.010	0.146±	0.011	0.055±	0.007
4000 ppm	10	0.117±	0.007	0.097±	0.005	0.050±	0.002	0.155±	0.004	0.145±	0.005	0.059±	0.012
10000 ppm	10	0.115±	0.007	0.123±	0.009**	0.064±	0.004**	0.164±	0.009*	0.158±	0.007**	0.060±	0.005
25000 ppm	10	0.113±	0.009	0.138±	0.009**	0.066±	0.006**	0.186±	0.045**	0.175±	0.012**	0.053±	0.010

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

Test of Dunnett

(HCL040)

BAIS2

STUDY NO. : 0054
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: g

ORGAN WEIGHT:ABSOLUTE (SUMMARY)
SURVIVAL ANIMALS (13)

PAGE : 6

Group Name	NO. of Animals	LIVER		BRAIN	
Control	10	0.919±	0.067	0.455±	0.009
640 ppm	10	0.899±	0.050	0.407±	0.144
1600 ppm	10	0.934±	0.082	0.457±	0.008
4000 ppm	10	0.944±	0.073	0.453±	0.008
10000 ppm	10	0.910±	0.043	0.457±	0.014
25000 ppm	10	0.839±	0.056*	0.438±	0.011*

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

Test of Dunnett

(HCL040)

BAIS 2

1,4-ジオキサンのラット及びマウスを用いた
経口(混水)投与によるがん原性予備試験
(急性・2週間・13週間) 報告書

APPENDIX

(M1~M4)

13Week STUDY NO. 0053 ; 0054

APPENDIX M 1

ORGAN WEIGHT (THIRTEEN-WEEK STUDIES:SUMMARY), RELATIVE

RAT:MALE

STUDY NO. : 0053
 ANIMAL : RAT F344
 REPORT TYPE : A1
 SEX : MALE
 UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
 SURVIVAL ANIMALS (13)

PAGE : 1

Group Name	NO. of Animals	Body weight (g)	THYMUS	ADRENL R	ADRENL L	TESTIS R	TESTIS L
Control	10	331± 13	0.086± 0.008	0.008± 0.001	0.008± 0.001	0.444± 0.025	0.453± 0.029
640 ppm	10	335± 9	0.087± 0.009	0.007± 0.001	0.008± 0.001	0.443± 0.017	0.461± 0.018
1600 ppm	10	337± 7	0.086± 0.009	0.008± 0.001	0.009± 0.001	0.438± 0.020	0.445± 0.018
4000 ppm	10	322± 15	0.083± 0.011	0.008± 0.001	0.008± 0.001	0.450± 0.022	0.460± 0.020
10000 ppm	10	309± 7*	0.088± 0.007	0.009± 0.001	0.009± 0.001*	0.478± 0.019	0.492± 0.019*
25000 ppm	10	263± 22**	0.081± 0.008	0.010± 0.001**	0.011± 0.001**	0.561± 0.045**	0.580± 0.043**

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

Test of Dunnett

(HCL042)

BAIS 2

STUDY NO. : 0053
 ANIMAL : RAT F344
 REPORT TYPE : A1
 SEX : MALE
 UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
 SURVIVAL ANIMALS (13)

PAGE : 2

Group Name	NO. of Animals	HEART	LUNG R	LUNG L	KIDNEY R	KIDNEY L	SPLEEN
Control	10	0.286± 0.018	0.192± 0.014	0.108± 0.006	0.291± 0.010	0.297± 0.009	0.177± 0.007
840 ppm	10	0.283± 0.017	0.194± 0.017	0.109± 0.004	0.297± 0.011	0.295± 0.013	0.182± 0.009
1600 ppm	10	0.285± 0.010	0.191± 0.009	0.108± 0.006	0.296± 0.011	0.304± 0.010	0.180± 0.005
4000 ppm	10	0.286± 0.011	0.199± 0.010	0.114± 0.006*	0.305± 0.011	0.311± 0.014	0.183± 0.009
10000 ppm	10	0.283± 0.008	0.202± 0.010	0.113± 0.004	0.314± 0.010**	0.312± 0.009	0.174± 0.006
25000 ppm	10	0.282± 0.013	0.219± 0.016**	0.127± 0.005**	0.345± 0.021**	0.355± 0.021**	0.173± 0.008

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

Test of Dunnett

(HCL042)

BAIS 2

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (13)

PAGE : 3

Group Name	NO. of Animals	LIVER	BRAIN
Control	10	2.464± 0.071	0.572± 0.025
640 ppm	10	2.492± 0.073	0.566± 0.016
1600 ppm	10	2.520± 0.077	0.561± 0.014
4000 ppm	10	2.550± 0.072	0.589± 0.022
10000 ppm	10	2.571± 0.040*	0.600± 0.015
25000 ppm	10	2.727± 0.118**	0.709± 0.069**

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

Test of Dunnett

(HCL042)

BAIS 2

APPENDIX M 2

ORGAN WEIGHT (THIRTEEN-WEEK STUDIES:SUMMARY), RELATIVE

RAT:FEMALE

STUDY NO. : 0053
 ANIMAL : RAT F344
 REPORT TYPE : A1
 SEX : FEMALE
 UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
 SURVIVAL ANIMALS (13)

PAGE : 4

Group Name	NO. of Animals	Body weight (g)	THYMUS	ADRENL R	ADRENL L	OVARY R	OVARY L
Control	10	194± 6	0.114± 0.009	0.015± 0.002	0.016± 0.002	0.029± 0.004	0.032± 0.004
640 ppm	10	197± 7	0.123± 0.015	0.016± 0.001	0.016± 0.001	0.030± 0.007	0.031± 0.003
1600 ppm	10	188± 8	0.118± 0.015	0.016± 0.002	0.016± 0.003	0.032± 0.005	0.034± 0.006
4000 ppm	10	183± 7**	0.119± 0.014	0.016± 0.002	0.017± 0.002	0.030± 0.004	0.032± 0.005
10000 ppm	10	172± 7**	0.117± 0.009	0.016± 0.001	0.017± 0.001	0.034± 0.005	0.036± 0.007
25000 ppm	09	155± 7**	0.108± 0.009	0.017± 0.001	0.017± 0.001	0.031± 0.003	0.037± 0.006

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

Test of Dunnett

(HCL042)

BAIS2

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (13)

PAGE : 5

Group Name	NO. of Animals	HEART	LUNG R	LUNG L	KIDNEY R	KIDNEY L	SPLEEN
Control	10	0.320± 0.016	0.247± 0.013	0.144± 0.012	0.300± 0.009	0.303± 0.018	0.209± 0.009
640 ppm	10	0.326± 0.021	0.243± 0.012	0.138± 0.005	0.305± 0.018	0.310± 0.012	0.209± 0.010
1600 ppm	10	0.326± 0.019	0.256± 0.015	0.146± 0.011	0.330± 0.018**	0.335± 0.027**	0.221± 0.010
4000 ppm	10	0.320± 0.013	0.258± 0.015	0.150± 0.011	0.336± 0.019**	0.335± 0.022**	0.214± 0.011
10000 ppm	10	0.332± 0.018	0.276± 0.013**	0.154± 0.009	0.381± 0.020**	0.391± 0.026**	0.222± 0.012*
25000 ppm	09	0.335± 0.017	0.287± 0.014**	0.164± 0.008**	0.423± 0.017**	0.437± 0.016**	0.223± 0.024

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

Test of Dunnett

(HCL042)

BAIS2

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (13)

PAGE : 6

Group Name	NO. of Animals	LIVER	BRAIN
Control	10	2.332± 0.049	0.906± 0.033
640 ppm	10	2.355± 0.084	0.894± 0.030
1600 ppm	10	2.569± 0.120**	0.941± 0.037
4000 ppm	10	2.455± 0.074*	0.961± 0.044*
10000 ppm	10	2.599± 0.076**	1.018± 0.055**
25000 ppm	09	2.886± 0.110**	1.099± 0.052**

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

Test of Dunnett

(HCL042)

BAIS 2

APPENDIX M 3

ORGAN WEIGHT (THIRTEEN-WEEK STUDIES:SUMMARY), RELATIVE

MOUSE:MALE

STUDY NO. : 0054
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (13)

PAGE : 1

Group Name	NO. of Animals	Body weight (g)	THYMUS	ADRENL R	ADRENL L	TESTIS R	TESTIS L
Control	10	30.9± 2.6	0.125± 0.022	0.015± 0.003	0.015± 0.004	0.407± 0.068	0.394± 0.057
640 ppm	10	32.3± 3.0	0.127± 0.018	0.015± 0.004	0.015± 0.003	0.396± 0.050	0.388± 0.059
1600 ppm	10	31.3± 3.3	0.131± 0.028	0.015± 0.003	0.015± 0.002	0.406± 0.063	0.392± 0.058
4000 ppm	10	30.7± 4.0	0.129± 0.020	0.017± 0.005	0.016± 0.004	0.407± 0.064	0.396± 0.056
10000 ppm	10	29.4± 2.5	0.131± 0.021	0.016± 0.003	0.018± 0.003	0.417± 0.049	0.399± 0.042
25000 ppm	09	22.2± 2.0**	0.126± 0.043	0.023± 0.009	0.024± 0.007*	0.518± 0.086**	0.492± 0.081**

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

Test of Dunnett

(HCL042)

BAIS2

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 REPORT TYPE : A1
 SEX : MALE
 UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
 SURVIVAL ANIMALS (13)

PAGE : 2

Group Name	NO. of Animals	HEART	LUNG R	LUNG L	KIDNEY R	KIDNEY L	SPLEEN
Control	10	0.472± 0.043	0.300± 0.028	0.154± 0.017	0.716± 0.107	0.691± 0.056	0.165± 0.033
640 ppm	10	0.450± 0.037	0.317± 0.079	0.152± 0.013	0.695± 0.060	0.695± 0.060	0.148± 0.020
1600 ppm	10	0.473± 0.045	0.298± 0.027	0.159± 0.022	0.711± 0.072	0.728± 0.084	0.143± 0.011
4000 ppm	10	0.461± 0.055	0.315± 0.040	0.163± 0.015	0.723± 0.076	0.718± 0.062	0.162± 0.014
10000 ppm	10	0.464± 0.037	0.334± 0.030	0.171± 0.021	0.776± 0.052	0.727± 0.047	0.157± 0.022
25000 ppm	09	0.523± 0.047	0.507± 0.071**	0.260± 0.044**	0.909± 0.042**	0.912± 0.039**	0.189± 0.048

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

Test of Dunnett

(HCL042)

BAIS 2

STUDY NO. : 0054
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (13)

PAGE : 3

Group Name	NO. of Animals	LIVER	BRAIN
Control	10	3.642± 0.261	1.420± 0.106
640 ppm	10	3.700± 0.212	1.359± 0.126
1600 ppm	10	3.794± 0.208	1.401± 0.129
4000 ppm	10	3.852± 0.231	1.444± 0.161
10000 ppm	10	3.763± 0.162	1.478± 0.150
25000 ppm	09	3.871± 0.366	1.921± 0.167**

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

Test of Dunnett

(HCL042)

BAIS2

APPENDIX M 4

ORGAN WEIGHT (THIRTEEN-WEEK STUDIES:SUMMARY), RELATIVE

MOUSE:FEMALE

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 REPORT TYPE : A1
 SEX : FEMALE
 UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
 SURVIVAL ANIMALS (13)

PAGE : 4

Group Name	NO. of Animals	Body weight (g)	THYMUS	ADREN L R	ADREN L L	OVARY R	OVARY L
Control	10	20.0± 1.2	0.193± 0.040	0.035± 0.008	0.036± 0.009	0.101± 0.029	0.081± 0.016
640 ppm	10	20.5± 1.1	0.191± 0.037	0.033± 0.006	0.034± 0.003	0.082± 0.028	0.084± 0.028
1600 ppm	10	20.3± 1.1	0.180± 0.031	0.032± 0.008	0.037± 0.009	0.091± 0.019	0.093± 0.034
4000 ppm	10	21.0± 1.6	0.206± 0.037	0.034± 0.009	0.034± 0.007	1.293± 3.800	0.094± 0.022
10000 ppm	10	20.8± 1.6	0.204± 0.036	0.036± 0.007	0.034± 0.008	0.087± 0.023	0.097± 0.018
25000 ppm	10	19.5± 1.2	0.199± 0.036	0.033± 0.009	0.033± 0.010	0.075± 0.016	0.079± 0.018

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

Test of Dunnett

(HCL042)

BAIS 2

STUDY NO. : 0054
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (13)

PAGE : 5

Group Name	NO. of Animals	HEART	LUNG R	LUNG L	KIDNEY R	KIDNEY L	SPLEEN
Control	10	0.578± 0.027	0.470± 0.050	0.243± 0.023	0.753± 0.073	0.703± 0.051	0.270± 0.035
640 ppm	10	0.567± 0.045	0.457± 0.046	0.241± 0.028	0.727± 0.054	0.703± 0.067	0.259± 0.019
1600 ppm	10	0.579± 0.034	0.466± 0.043	0.238± 0.019	0.756± 0.041	0.717± 0.033	0.269± 0.026
4000 ppm	10	0.559± 0.030	0.462± 0.027	0.240± 0.018	0.741± 0.050	0.696± 0.052	0.281± 0.036
10000 ppm	10	0.555± 0.043	0.592± 0.053**	0.308± 0.026**	0.788± 0.055	0.761± 0.055	0.288± 0.031
25000 ppm	10	0.580± 0.043	0.711± 0.054**	0.338± 0.033**	0.968± 0.310**	0.905± 0.115**	0.271± 0.040

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

Test of Dunnett

(HCL042)

BAIS 2

STUDY NO. : 0054
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE
UNIT: %

ORGAN WEIGHT:RELATIVE (SUMMARY)
SURVIVAL ANIMALS (13)

PAGE : 6

Group Name	NO. of Animals	LIVER	BRAIN
Control	10	4.587± 0.265	2.280± 0.137
640 ppm	10	4.392± 0.186	1.993± 0.719
1600 ppm	10	4.593± 0.277	2.251± 0.108
4000 ppm	10	4.509± 0.190	2.171± 0.161
10000 ppm	10	4.386± 0.341	2.206± 0.197
25000 ppm	10	4.312± 0.105*	2.259± 0.097

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

Test of Dunnett

(HCL042)

BAIS2

1,4-ジオキサンのラット及びマウスを用いた
経口(混水)投与によるがん原性予備試験
(急性・2週間・13週間) 報告書

APPENDIX

(N1~N6)

13Week STUDY NO. 0053 ; 0054

APPENDIX N 1

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS

(THIRTEEN-WEEK STUDIES:SUMMARY)

RAT:FEMALE:DEAD AND MORIBUND ANIMALS

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
DEAD AND MORIBUND ANIMALS (0- 13W)

PAGE : 1

		Group Name	Control				640				1600				4000			
		No. of Animals	0				ppm				ppm				ppm			
			<1>	<2>	<3>	<4>	<1>	<2>	<3>	<4>	<1>	<2>	<3>	<4>	<1>	<2>	<3>	<4>
Organ	Findings		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
nasal cavit	nuclear enlargement:olfactory epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	nuclear enlargement:respiratory epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
trachea	nuclear enlargement:epithelium		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Digestive system]																		
liver	vacuolic change:central		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Urinary system]																		
kidney	mineraization:cortex		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
	hydropic change:proximal tubule		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)
[Nervous system]																		
brain	vacuolic change		-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
			(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)	(-)

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

STUDY NO. : 0053
 ANIMAL : RAT F344
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0- 13W)

PAGE : 2

Organ	Findings	Group Name No. of Animals				10000 ppm 0				25000 ppm 1			
		<1>	<2>	<3>	<4>	<1>	<2>	<3>	<4>	<1>	<2>	<3>	<4>
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]													
nasal cavit	nuclear enlargement:olfactory epithelium	-	-	-	-	0	1	0	0	0	1	0	0
		(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
	nuclear enlargement:respiratory epithelium	-	-	-	-	0	1	0	0	0	1	0	0
		(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
trachea	nuclear enlargement:epithelium	-	-	-	-	1	0	0	0	1	0	0	0
		(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
[Digestive system]													
liver	vacuolic change:central	-	-	-	-	0	0	0	1	0	0	0	1
		(-)	(-)	(-)	(-)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(100)
[Urinary system]													
kidney	mineraization:cortex	-	-	-	-	0	1	0	0	0	1	0	0
		(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)	(0)	(100)	(0)	(0)
	hydropic change:proximal tubule	-	-	-	-	0	0	0	1	0	0	0	1
		(-)	(-)	(-)	(-)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(100)
[Nervous system]													
brain	vacuolic change	-	-	-	-	1	0	0	0	1	0	0	0
		(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)	(100)	(0)	(0)	(0)

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

(HPT150)

BAIS2

APPENDIX N 2

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS

(THIRTEEN-WEEK STUDIES:SUMMARY)

RAT:MALE:SACRIFICED ANIMALS

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (13W)

PAGE : 1

		Group Name	Control				640 ppm				1600 ppm				4000 ppm			
		No. of Animals	10				10				10				10			
Organ	Findings		<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Respiratory system]																		
nasal cavit	inflammation		1 (10)	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)
	nuclear enlargement: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)	10 (100)	0 (0)	0 (0)	0 ** (0)
	nuclear enlargement:respiratory epithelium		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	9 (90)	0 (0)	0 (0)	0 ** (0)	0 (0)	10 (100)	0 (0)	0 ** (0)
trachea	nuclear enlargement: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)	10 (100)	0 (0)	0 (0)	0 ** (0)
lung/branch	osseous 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)
	nuclear enlargement:bronchial 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)
[Hematopoietic system]																		
bone marrow	granulation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Circulatory system]																		
heart	myocardial fibrosis		3 (30)	0 (0)	0 (0)	0 (0)	4 (40)	0 (0)	0 (0)	0 (0)	4 (40)	0 (0)	0 (0)	0 (0)	3 (30)	0 (0)	0 (0)	0 (0)
[Digestive system]																		
stomach	hyperplasia:glandular stomach		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (13W)

PAGE : 2

		Group Name	10000 ppm				25000 ppm			
		No. of Animals	10				10			
Organ_____	Findings_____	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	
[Respiratory system]										
nasal cavit	inflammation	1 (10)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	
	nuclear enlargement:olfactory epithelium	9 (90)	0 (0)	0 (0)	0 ** (0)	0 (0)	10 (100)	0 (0)	0 ** (0)	
	nuclear enlargement:respiratory epithelium	0 (0)	9 (90)	0 (0)	0 ** (0)	0 (0)	10 (100)	0 (0)	0 ** (0)	
trachea	nuclear enlargement:epithelium	10 (100)	0 (0)	0 (0)	0 ** (0)	1 (10)	0 (0)	9 (90)	0 ** (0)	
lung/branch	ossecus metaplasia	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	
	nuclear enlargement:bronchial epithelium	1 (10)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	
[Hematopoietic system]										
bone marrow	granulation	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
[Circulatory system]										
heart	myocardial fibrosis	0 (0)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	
[Digestive system]										
stomach	hyperplasia:glandular stomach	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	

Significant difference : * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (13W)

PAGE : 3

		Group Name	Control				640 ppm				1600 ppm				4000 ppm			
		No. of Animals	10				10				10				10			
Organ	Findings		<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Digestive system]																		
liver	granulation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	5 (50)	0 (0)	0 (0)	0 * (0)
	swelling:central		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	9 (90)	0 (0)	0 (0)	0 ** (0)	9 (90)	1 (10)	0 (0)	0 ** (0)
	vacuolic change:central		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)
[Urinary system]																		
kidney	eosinophilic body		0 (0)	9 (90)	1 (10)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	0 (0)	9 (90)	1 (10)	0 (0)	6 (60)	4 (40)	0 (0)	0 * (0)
	hydropic change:proximal tubule		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	regeneration proximal tubule		4 (40)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	3 (30)	0 (0)	0 (0)	0 (0)
	nuclear enlargement:proximal tubule		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)
[Endocrine system]																		
pituitary	cyst		0 (0)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	Rathke pouch		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)	0 (0)
thyroid	ultimobranchial body remnant		2 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (13W)

PAGE : 4

		Group Name				25000			
		No. of Animals				ppm			
		10				10			
Organ_____	Findings_____	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Digestive system]									
liver	granulation	2 (20)	0 (0)	0 (0)	0 (0)	9 (90)	1 (10)	0 (0)	0 ** (0)
	swelling:central	0 (0)	10 (100)	0 (0)	0 ** (0)	0 (0)	1 (10)	9 (90)	0 ** (0)
	vacuolic change:central	5 (50)	5 (50)	0 (0)	0 ** (0)	0 (0)	0 (0)	10 (100)	0 ** (0)
[Urinary system]									
kidney	eosinophilic body	10 (100)	0 (0)	0 (0)	0 ** (0)	7 (70)	3 (30)	0 (0)	0 ** (0)
	hydropic change:proximal tubule	0 (0)	0 (0)	0 (0)	0 (0)	7 (70)	0 (0)	0 (0)	0 ** (0)
	regeneration proximal tubule	1 (10)	0 (0)	0 (0)	0 (0)	3 (30)	0 (0)	0 (0)	0 (0)
	nuclear enlargement:proximal tubule	5 (50)	0 (0)	0 (0)	0 * (0)	9 (90)	0 (0)	0 (0)	0 ** (0)
[Endocrine system]									
pituitary	cyst	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	Rathke pouch	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
thyroid	ultimobranchial body remant	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (13W)

PAGE : 5

		Group Name No. of Animals	Control: 10				640 ppm 10				1600 ppm 10				4000 ppm 10			
Organ_____	Findings_____		<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Reproductive system]																		
prostate	inflammation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
[Nervous system]																		
brain	vacuolic change		0 (0)	0 (0)	0 (0)	0 (0)	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/appandage]																		
eye	iritis		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	degeneration: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	inflammation		2 (20)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)
[Body cavities]																		
adipose	granulation		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)	0 (0)

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

(HPT150)

BAIS2

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (13W)

PAGE : 6

		Group Name	10000 ppm				25000 ppm			
		No. of Animals	10				10			
Organ_____	Findings_____		<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Reproductive system]										
prostate	inflammation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Nervous system]										
brain	vacuolic change		0 (0)	0 (0)	0 (0)	0 (0)	9 (90)	0 (0)	1 (10)	0 ** (0)
[Special sense organs/appandage]										
eye	iritis		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
	degeneration:cornea		0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)
Harder gl	inflammation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Body cavities]										
adipose	granulation		0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

Significant difference : * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

(HPT150)

BAIS2

APPENDIX N 3

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS

(THIRTEEN-WEEK STUDIES:SUMMARY)

RAT:FEMALE:SACRIFICED ANIMALS

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (13W)

PAGE : 7

Organ	Findings	Group Name Control				640 ppm				1600 ppm				4000 ppm			
		No. of Animals 10				10				10				10			
		<1>	<2>	<3>	<4>	<1>	<2>	<3>	<4>	<1>	<2>	<3>	<4>	<1>	<2>	<3>	<4>
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																	
nasal cavit	inflammation	1	0	0	0	2	0	0	0	2	0	0	0	0	0	0	0
		(10)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	nuclear enlargement:olfactory epithelium	0	0	0	0	0	0	0	0	0	0	0	0	9	0	0	0 **
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(90)	(0)	(0)	(0)
	nuclear enlargement:respiratory epithelium	0	0	0	0	0	0	0	0	5	0	0	0 *	10	0	0	0 **
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)	(100)	(0)	(0)	(0)
trachea	nuclear enlargement:epithelium	0	0	0	0	0	0	0	0	0	0	0	0	9	0	0	0 **
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(90)	(0)	(0)	(0)
lung/branch	osseous 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)
	nuclear enlargement:bronchial epithelium	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]																	
bone marrow	granulation	5	0	1	0	0	0	0	0 *	2	0	0	0	0	0	0	0 *
		(50)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen	extramedullary hematopoiesis	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0
		(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Digestive system]																	
liver	granulation	2	0	0	0	0	0	0	0	1	0	0	0	5	0	0	0
		(20)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
	swelling:central	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)	(0)	(0)	(0)	(0)

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (13W)

PAGE : 8

		Group Name No. of Animals				10000 ppm 10				25000 ppm 9			
Organ_____	Findings_____	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)				
[Respiratory system]													
nasal cavit	inflammation	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)				
	nuclear enlargement:olfactory epithelium	10 (100)	0 (0)	0 (0)	0 ** (0)	8 (89)	0 (0)	0 (0)	0 ** (0)				
	nuclear enlargement:respiratory epithelium	10 (100)	0 (0)	0 (0)	0 ** (0)	8 (89)	0 (0)	0 (0)	0 ** (0)				
trachea	nuclear enlargement:epithelium	10 (100)	0 (0)	0 (0)	0 ** (0)	4 (44)	0 (0)	5 (56)	0 ** (0)				
lung/branch	ossecus metaplasia	0 (0)	0 (0)	0 (0)	0 (0)	1 (11)	0 (0)	0 (0)	0 (0)				
	nuclear enlargement:bronchial epithelium	1 (10)	0 (0)	0 (0)	0 (0)	6 (67)	0 (0)	0 (0)	0 ** (0)				
[Hematopoietic system]													
bone marrow	granulation	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 * (0)				
spleen	extramedullary hematopoiesis	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)				
[Digestive system]													
liver	granulation	4 (40)	1 (10)	0 (0)	0 (0)	6 (67)	0 (0)	2 (22)	0 ** (0)				
	swelling:centeral	9 (90)	0 (0)	0 (0)	0 ** (0)	6 (67)	0 (0)	3 (33)	0 ** (0)				

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (13W)

PAGE : 9

Organ	Findings	Group Name	Control				640 ppm				1600 ppm				4000 ppm			
		No. of Animals	10				10				10				10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Digestive system]																		
liver	vacuolic change:central		0	0	0	0	0	0	0	0	0	0	0	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	mineralization:papilla		0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	mineraization:cortex		2	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
		(20)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	hydropic change:proximal tubule		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	nuclear enlargement:proximal tubule		0	0	0	0	0	0	0	0	0	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]																		
adrenal	accessory cortical nodule		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Reproductive system]																		
uterus	dilatation		0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0
		(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)	(0)	(0)
[Nervous system]																		
brain	vacuolic change		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

STUDY NO. : 0053
ANIMAL : RAT F344
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (13W)

PAGE : 10

		Group Name				25000			
		No. of Animals				ppm			
		10				9			
Organ	Findings	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Digestive system]									
Liver	vacuolic change:centeral	0 (0)	0 (0)	0 (0)	0 (0)	3 (33)	1 (11)	5 (56)	0 ** (0)
[Urinary system]									
kidney	mineralization:papilla	0 (0)	0 (0)	0 (0)	0 (0)	3 (33)	0 (0)	0 (0)	0 (0)
	mineraization:cortex	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
	hydropic change:proximal tubule	0 (0)	0 (0)	0 (0)	0 (0)	2 (22)	3 (33)	0 (0)	0 * (0)
	nuclear enlargement:proximal tubule	8 (80)	0 (0)	0 (0)	0 ** (0)	9 (100)	0 (0)	0 (0)	0 ** (0)
[Endocrine system]									
adrenal	accessory cortical nodule	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Reproductive system]									
uterus	dilatation	4 (40)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
[Nervous system]									
brain	vacuolic change	0 (0)	0 (0)	0 (0)	0 (0)	9 (100)	0 (0)	0 (0)	0 ** (0)

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

STUDY NO. : 0053
 ANIMAL : RAT F344
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
 SACRIFICED ANIMALS (13W)

PAGE : 11

Organ	Findings	Group Name Control				640 ppm				1600 ppm				4000 ppm			
		No. of Animals 10				10				10				10			
		<1>	<2>	<3>	<4>	<1>	<2>	<3>	<4>	<1>	<2>	<3>	<4>	<1>	<2>	<3>	<4>
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Special sense organs/appandage]																	
Harder gl	inflammation	6	0	0	0	4	1	0	0	5	1	0	0	3	1	0	0
		(60)	(0)	(0)	(0)	(40)	(10)	(0)	(0)	(50)	(10)	(0)	(0)	(30)	(10)	(0)	(0)
Significant difference ;		* : $P \leq 0.05$		** : $P \leq 0.01$		Test of Chi Square		<1>:Slight		<2>:Moderate		<3>:Marked		<4>:Severe			

(HPT150)

BAIS2

STUDY NO. : 0053
 ANIMAL : RAT F344
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
 SACRIFICED ANIMALS (13W)

PAGE : 12

Organ	Findings	Group Name 10000 ppm No. of Animals 10				25000 ppm 9			
		<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)

[Special sense organs/appandage]

Harder gl	inflammation	3 (30)	1 (10)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 * (0)
-----------	--------------	------------	------------	-----------	-----------	-----------	-----------	-----------	-------------

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

(HPT150)

BAIS2

APPENDIX N 4

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS

(THIRTEEN-WEEK STUDIES:SUMMARY)

MOUSE:MALE:DEAD AND MORIBUND ANIMALS

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0- 13W)

PAGE : 1

Organ	Findings	Group Name No. of Animals	Control 0				640 ppm 0				1600 ppm 0				4000 ppm 0			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Respiratory system]																		
nasal cavit	nuclear enlargement:respiratory epithelium		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
lung/branch	emphysema		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
[Hematopoietic system]																		
bone marrow	congestion		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
thymus	atrophy		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
spleen	atrophy		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
[Digestive system]																		
stomach	erosion:glandular stomach		- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)	- (-)
Significant difference ; * : P ≤ 0.05 ** : P ≤ 0.01 Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe																		
(HPT150)																		

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
 DEAD AND MORIBUND ANIMALS (0- 13W)

PAGE : 2

		Group Name				10000 ppm				25000 ppm			
		No. of Animals				0				1			
Organ	Findings	<1>	<2>	<3>	<4>	<1>	<2>	<3>	<4>	<1>	<2>	<3>	<4>
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]													
nasal cavity	nuclear enlargement:respiratory epithelium	-	-	-	-	1	0	0	0				
		(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)				
lung/branch	emphysema	-	-	-	-	0	1	0	0				
		(-)	(-)	(-)	(-)	(0)	(100)	(0)	(0)				
[Hematopoietic system]													
bone marrow	congestion	-	-	-	-	1	0	0	0				
		(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)				
thymus	atrophy	-	-	-	-	1	0	0	0				
		(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)				
spleen	atrophy	-	-	-	-	1	0	0	0				
		(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)				
[Digestive system]													
stomach	erosion:glandular stomach	-	-	-	-	1	0	0	0				
		(-)	(-)	(-)	(-)	(100)	(0)	(0)	(0)				

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

(HPT150)

BAIS2

APPENDIX N 5

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS

(THIRTEEN-WEEK STUDIES:SUMMARY)

MOUSE:MALE:SACRIFICED ANIMALS

STUDY NO. : 0054
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (13W)

PAGE : 1

Organ	Findings	Group Name	Control				640 ppm				1600 ppm				4000 ppm			
		No. of Animals	10				10				10				10			
			<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Respiratory system]																		
nasal cavit	eosinophilic change: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)	
	eosinophilic change:respiratory 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)	
	nuclear enlargement: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)	9 (90)	0 (0)	0 (0)	0 (0) **	
	nuclear enlargement:respiratory 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)	2 (20)	0 (0)	0 (0)	0 (0)	
	vacuolic change:olfactory nerve	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
trachea	nuclear enlargement: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)	7 (70)	0 (0)	0 (0)	0 (0) **	
lung/branch	accumulation of foamy cells	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
	nuclear enlargement:bronchial 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)	9 (90)	0 (0)	0 (0)	0 (0) **	
	degeneration:bronchial 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)	
[Hematopoietic system]																		
thymus	atrophy	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	
spleen	melanin	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

STUDY NO. : 0054
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (13W)

PAGE : 2

		Group Name				25000			
		No. of Animals				ppm			
		10				9			
Organ_____	Findings_____	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)
[Respiratory system]									
nasal cavit	eosinophilic change:olfactory epithelium	0 (0)	0 (0)	0 (0)	0 (0)	6 (67)	0 (0)	0 (0)	0 ** (0)
	eosinophilic change:respiratory epithelium	0 (0)	0 (0)	0 (0)	0 (0)	5 (56)	0 (0)	0 (0)	0 * (0)
	nuclear enlargement:olfactory epithelium	9 (90)	1 (10)	0 (0)	0 ** (0)	9 (100)	0 (0)	0 (0)	0 ** (0)
	nuclear enlargement:respiratory epithelium	5 (50)	0 (0)	0 (0)	0 * (0)	0 (0)	0 (0)	0 (0)	0 (0)
	vacuolic change:olfactory nerve	0 (0)	0 (0)	0 (0)	0 (0)	8 (89)	1 (11)	0 (0)	0 ** (0)
trachea	nuclear enlargement:epithelium	9 (90)	0 (0)	0 (0)	0 ** (0)	8 (89)	1 (11)	0 (0)	0 ** (0)
lung/branch	accumulation of foamy cells	0 (0)	0 (0)	0 (0)	0 (0)	6 (67)	0 (0)	0 (0)	0 ** (0)
	nuclear enlargement:bronchial epithelium	9 (90)	0 (0)	0 (0)	0 ** (0)	5 (56)	4 (44)	0 (0)	0 ** (0)
	degeneration:bronchial epithelium	0 (0)	0 (0)	0 (0)	0 (0)	7 (78)	1 (11)	0 (0)	0 ** (0)
[Hematopoietic system]									
thymus	atrophy	0 (0)	0 (0)	0 (0)	0 (0)	1 (11)	0 (0)	0 (0)	0 (0)
spleen	melanin	1 (10)	0 (0)	0 (0)	0 (0)	1 (11)	0 (0)	0 (0)	0 (0)

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

STUDY NO. : 0054
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (13W)

PAGE : 3

Organ	Findings	Group Name Control				640 ppm				1600 ppm				4000 ppm			
		No. of Animals 10				10				10				10			
		<1>	<2>	<3>	<4>	<1>	<2>	<3>	<4>	<1>	<2>	<3>	<4>	<1>	<2>	<3>	<4>
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																	
liver	necrosis:single cell	0	0	0	0	0	0	0	0	0	0	0	0	5	0	0	0 *
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
	swelling:central	0	0	0	0	0	0	0	0	0	0	0	0	9	1	0	0 **
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(90)	(10)	(0)	(0)
[Urinary system]																	
kidney	vacuolization of proximal tube	10	0	0	0	7	0	0	0	6	0	0	0	5	0	0	0 *
		(100)	(0)	(0)	(0)	(70)	(0)	(0)	(0)	(60)	(0)	(0)	(0)	(50)	(0)	(0)	(0)
	hydronephrosis	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)	(0)
[Reproductive system]																	
epididymis	spermatogenic granuloma	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)

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

(HPT150)

BAIS2

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 REPORT TYPE : A1
 SEX : MALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
 SACRIFICED ANIMALS (13W)

PAGE : 4

		Group Name No. of Animals				10000 ppm 10				25000 ppm 9			
Organ	Findings	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)				
[Digestive system]													
liver	necrosis:single cell	10 (100)	0 (0)	0 (0)	0 ** (0)	9 (100)	0 (0)	0 (0)	0 ** (0)				
	swelling:central	10 (100)	0 (0)	0 (0)	0 ** (0)	0 (0)	9 (100)	0 (0)	0 ** (0)				
[Urinary system]													
kidney	vacuolization of proximal tube	0 (0)	0 (0)	0 (0)	0 ** (0)	0 (0)	0 (0)	0 (0)	0 ** (0)				
	hydronephrosis	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)				
[Reproductive system]													
epididymis	spermatogenic granuloma	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)				

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

(HPT150)

BAIS2

APPENDIX N 6

HISTOLOGICAL FINDINGS :NON-NEOPLASTIC LESIONS

(THIRTEEN-WEEK STUDIES:SUMMARY)

MOUSE:FEMALE:SACRIFICED ANIMALS

STUDY NO. : 0054
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (13W)

PAGE : 5

Organ	Findings	Group Name	Control				640 ppm				1600 ppm				4000 ppm			
		No. of Animals	10				10				10				10			
			<1>	<2>	<3>	<4>	<1>	<2>	<3>	<4>	<1>	<2>	<3>	<4>	<1>	<2>	<3>	<4>
			(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Respiratory system]																		
nasal cavit	eosinophilic change:olfactory epithelium		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)
	eosinophilic change:respiratory epithelium		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)
	nuclear enlargement:olfactory epithelium		0	0	0	0	0	0	0	0	0	0	0	0	6	0	0	0 *
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(60)	(0)	(0)	(0)	
	nuclear enlargement:respiratory epithelium		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)	
	vacuolic change:olfactory nerve		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
trachea	nuclear enlargement:epithelium		0	0	0	0	0	0	0	2	0	0	0	9	0	0	0 **	
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(20)	(0)	(0)	(0)	(90)	(0)	(0)	(0)	
lung/branch	accumulation of foamy cells		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	nuclear enlargement:bronchial epithelium		0	0	0	0	0	0	0	10	0	0	0 **	9	1	0	0 **	
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(100)	(0)	(0)	(0)	(90)	(10)	(0)	(0)	
	degeneration:bronchial 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)	(0)
[Hematopoietic system]																		
bone marrow	congestion		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
spleen	melanin		1	0	0	0	0	0	0	4	0	0	0	0	0	0	0	0
		(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(40)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

STUDY NO. : 0054
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (13W)

PAGE : 6

		Group Name	10000	ppm		25000	ppm			
		No. of Animals	10				10			
Organ_____	Findings_____	<1> (%)	<2> (%)	<3> (%)	<4> (%)	<1> (%)	<2> (%)	<3> (%)	<4> (%)	
[Respiratory system]										
nasal cavit	eosinophilic change:olfactory epithelium	3 (30)	3 (30)	0 (0)	0 * (0)	2 (20)	4 (40)	0 (0)	0 * (0)	
	eosinophilic change:respiratory epithelium	4 (40)	1 (10)	0 (0)	0 * (0)	6 (60)	3 (30)	0 (0)	0 ** (0)	
	nuclear enlargement:olfactory epithelium	5 (50)	5 (50)	0 (0)	0 ** (0)	0 (0)	10 (100)	0 (0)	0 ** (0)	
	nuclear enlargement:respiratory epithelium	3 (30)	0 (0)	0 (0)	0 (0)	6 (60)	1 (10)	0 (0)	0 ** (0)	
	vacuolic change:olfactory nerve	2 (20)	0 (0)	0 (0)	0 (0)	6 (60)	2 (20)	0 (0)	0 ** (0)	
trachea	nuclear enlargement:epithelium	10 (100)	0 (0)	0 (0)	0 ** (0)	7 (70)	3 (30)	0 (0)	0 ** (0)	
lung/branch	accumulation of foamy cells	10 (100)	0 (0)	0 (0)	0 ** (0)	10 (100)	0 (0)	0 (0)	0 ** (0)	
	nuclear enlargement:bronchial epithelium	0 (0)	9 (90)	1 (10)	0 ** (0)	0 (0)	0 (0)	10 (100)	0 ** (0)	
	degeneration:bronchial epithelium	7 (70)	0 (0)	0 (0)	0 ** (0)	9 (90)	1 (10)	0 (0)	0 ** (0)	
[Hematopoietic system]										
bone marrow	congestion	0 (0)	0 (0)	0 (0)	0 (0)	2 (20)	0 (0)	0 (0)	0 (0)	
spleen	melanin	0 (0)	0 (0)	0 (0)	0 (0)	1 (10)	0 (0)	0 (0)	0 (0)	

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

STUDY NO. : 0054
ANIMAL : MOUSE BDF1
REPORT TYPE : A1
SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
SACRIFICED ANIMALS (13W)

PAGE : 7

Organ	Findings	Group Name Control				640 ppm				1600 ppm				4000 ppm			
		No. of Animals 10				10				10				10			
		<1>	<2>	<3>	<4>	<1>	<2>	<3>	<4>	<1>	<2>	<3>	<4>	<1>	<2>	<3>	<4>
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]																	
liver	necrosis:focal	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)	(0)	(0)	(0)	(0)
	necrosis:single cell	0	0	0	0	0	0	0	0	0	0	0	0	7	0	0	0 **
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(70)	(0)	(0)	(0)
	granulation	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)
	swelling:central	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)	(100)	(0)	(0)	(0)
[Urinary system]																	
kidney	hydronephrosis	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
urin bladd	edema	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
[Reproductive system]																	
ovary	cyst	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)

Significant difference ; * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

(HPT150)

BAIS2

STUDY NO. : 0054
 ANIMAL : MOUSE BDF1
 REPORT TYPE : A1
 SEX : FEMALE

HISTOLOGICAL FINDINGS : NON-NEOPLASTIC LESIONS (SUMMARY)
 SACRIFICED ANIMALS (13W)

PAGE : 8

		Group Name				25000			
		10000				ppm			
		No. of Animals				10			
		10				10			
Organ	Findings	<1>	<2>	<3>	<4>	<1>	<2>	<3>	<4>
		(%)	(%)	(%)	(%)	(%)	(%)	(%)	(%)
[Digestive system]									
liver	necrosis:focal	0	0	0	0	0	0	0	0
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
	necrosis:single cell	10	0	0	0 **	9	0	0	0 **
		(100)	(0)	(0)	(0)	(90)	(0)	(0)	(0)
granulation		0	0	0	0	0	0	0	0
		(0)	(0)	(0)	(0)	(0)	(0)	(0)	(0)
swelling:central		10	0	0	0 **	0	9	0	0 **
		(100)	(0)	(0)	(0)	(0)	(90)	(0)	(0)
[Urinary system]									
kidney	hydronephrosis	0	0	0	0	0	0	1	0
		(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)
urin bladd	edema	0	0	0	0	0	0	1	0
		(0)	(0)	(0)	(0)	(0)	(0)	(10)	(0)
[Reproductive system]									
ovary	cyst	1	0	0	0	0	0	0	0
		(10)	(0)	(0)	(0)	(0)	(0)	(0)	(0)

Significant difference : * : $P \leq 0.05$ ** : $P \leq 0.01$ Test of Chi Square <1>:Slight <2>:Moderate <3>:Marked <4>:Severe

(HPT150)

BAIS2

1,4-ジオキサンのラット及びマウスを用いた
経口(混水)投与によるがん原性予備試験
(急性・2週間・13週間) 報告書

APPENDIX

(01~04)

13Week STUDY NO. 0053 ; 0054

APPENDIX 0 1

IDENTITY AND PURITY IN THE THIRTEEN-WEEK STUDIES OF 1,4-DIOXANE
PERFORMED AT THE JAPAN BIOASSAY LABORATORY

IDENTITY AND PURITY IN THE THIRTEEN-WEEK STUDIES OF 1,4-DIOXANE PERFORMED AT
THE JAPAN BIOASSAY LABORATORY

Lot no. CDP4224

1. Physical properties	<u>Determined</u>	<u>Literature Values</u>
------------------------	-------------------	--------------------------

Appearance:	Clear, colorless liquid	Clear, colorless liquid
-------------	-------------------------	-------------------------

Boiling point:	101°C	101°C
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(ENCYCLOPAEDIA
Published by Kyooritsu
CO..LTD.)

2. Spectral data

Infrared

Instrument: Hitachi 270-30

Cell: Fixed thickness Cell (NaCl)

Slit: Medium

Results: Wave Number
(CM⁻¹)

610	610
860~900	860~900
1050~1140	1050~1140
1260	1260
1295	1290
1370	1365
1460	1455
1700~1740	1700~1740
2700~3000	2690~3000

(Sadtler handbook
by Sadtler Research
Laboratories, Inc.)

3. Gas Chromatography

Instrument: Shimazu GC-9A

Column: SBS-1

Column Temperature: 80°C

Flow Rate: 20ml/min

Detector: Hydrogen flame ionization (FID)

Injection Volume: 1 µl

Results: Only one major peak

Peak No.	Retention Time(min)	Retention Time Relative to Major Peak	Area (percent of Major peak)
1	3.823	1.00	100

C. Conclusions: The results of the boiling point agreed with the literature values. Impurity was not detected in test substance by Gas chromatography. The infrared spectra agreed with the literature values.

APPENDIX 0 2

STABILITY IN THE THIRTEEN-WEEK STUDIES OF 1,4-DIOXANE

AT THE JAPAN BIOASSAY LABORATORY

STABILITY IN THE THIRTEEN-WEEK STUDIES OF 1,4-DIOXANE AT THE JAPAN BIOASSAY LABORATORY

Lot no. CDP4224

1. Sample storage: 1,4-Dioxane were stored for about 1 year at 5°C.

2. Physical properties	<u>Previous determined of test</u>	<u>After determined of test</u>

(07/16/84)

(10/25/84)

Appearance:	Clear, colorless liquid	Clear, colorless liquid
-------------	-------------------------	-------------------------

Boiling point:	101°C	101°C
----------------	-------	-------

3. Spectral data

Infrared

Instrument: Hitachi 270-30

Fixed thickness Cell(NaCl)

Medium

Results: Wave Number
(CM^{-1})

610 610

860~900 006~098

1050~1140 1050~1140

1260	1260
------	------

1295	1295
------	------

1370	1370
------	------

1460	1460
------	------

1700~1740 1700~1740

2700~3000 2700~3000

4. Gas Chromatography

Instrument: Shimadzu GC-9A

Column: SBS-1

Column Temperature: 80°C

Flow Rate: 20ml/min

Hydrogen flame ionization(FID)

Injection Volume: 1 μ l

Results: Only one major peak

Date	Retention Time(min)	Retention Time Relative to Major Peak	Area (percent of Major peak)
07/16/84	3.823	1.00	100
10/25/84	3.832	1.00	100

C. Conclusions: The results of the Boiling point agreed with the previous determine of test Values. Impurity was not detected in test substance by Gas chromatography. The infrared spectra agreed with the previous determine of test Values.

Consequently, 1,4-dioxane was stable as the chemical when stored for about 1 year at temperatures to 5°C.

APPENDIX 0 3

RESULTS OF ANALYSIS OF FORMULATED DRINKING WATER
IN THE THIRTEEN-WEEK STUDIES OF 1,4-DIOXANE

RESULTS OF ANALYSIS OF FORMULATED DRINKING WATER IN THE THIRTEEN-WEEK STUDIES OF 1,4-DIOXANE

(Rat, Mouse)

Date Mixed	Concentration of 1,4-Dioxane in drinking water for Taget Concentration(ppm)				
	25000 (a)	10000 (a)	4000 (a)	1600 (a)	640 (a)
07/26/83	24565 (98.3)	10285 (102.9)	3894 (102.9)	1562 (97.6)	605.5 (94.6)

(a) Determined as a percent of taget

APPENDIX O 4

RESULTS OF STABILITY OF FORMULATED DRINKING WATER
IN THE THIRTEEN-WEEK STUDIES OF 1,4-DIOXANE

RESULTS OF STABILITY OF FORMULATED DRINKING WATER IN THE THIRTEEN-WEEK STUDIES OF 1,4-DIOXANE

(Rat)

Date Mixed	Concentration of 1,4-Dioxane in drinking water for Taget Concentration(ppm)				
	25000 (a)	10000 (a)	4000 (a)	1600 (a)	640 (a)
07/26/84	24565 (98.3)	10285 (102.9)	3894 (102.9)	1562 (97.6)	605.5 (94.6)
07/30/84	25273 (101.1)	9422 (94.2)	4013 (100.3)	1610 (100.6)	635.5 (99.3)

(a) Determined as a percent of taget

(Mouse)

Date Mixed	Concentration of 1,4-Dioxane in drinking water for Taget Concentration(ppm)				
	25000 (a)	10000 (a)	4000 (a)	1600 (a)	640 (a)
07/26/84	24565 (98.3)	10285 (102.9)	3894 (102.9)	1562 (97.6)	605.5 (94.6)
07/30/84	24094 (96.4)	9362 (92.8)	3713 (92.8)	1543 (96.4)	604.2 (94.4)

(a) Determined as a percent of taget

1,4-ジオキサンのラット及びマウスを用いた
経口(混水)投与によるがん原性予備試験
(急性・2週間・13週間) 報告書

APPENDIX

(P1~P2)

13Week STUDY NO. 0053 ; 0054

APPENDIX P 1

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS

METHODS FOR HEMATOLOGY, BIOCHEMISTRY AND URINALYSIS

Item	Method	Unit
Hematology		
Red blood cell (RBC)	Aperture impedance method ¹⁾	$\times 10^6 / \mu l$
Hemoglobin	Cyanmethemoglobin method ¹⁾	g/dl
Hematocrit	Calculated as $RBC \times MCV / 10$ ¹⁾	%
Mean corpuscular volume (MCV)	Aperture impedance method ¹⁾	f l
Platelet	Aperture impedance method ¹⁾	$\times 10^3 / \mu l$
White blood cell (WBC)	Aperture impedance method ¹⁾	$\times 10^3 / \mu l$
Differential WBC	Pattern recognition method ²⁾ (Wright staining)	%
Biochemistry		
Total protein (TP)	Biuret method ³⁾	g/dl
Albumin (Alb)	BCG method ³⁾	g/dl
A/G ratio	Calculated as $Alb / (TP - Alb)$ ³⁾	
T-bilirubin	Michaelson method ³⁾	mg/dl
Glucose	Enzymatic method (HK-G-6-PDH) ³⁾	mg/dl
T-cholesterol	Enzymatic method (CEH-COD-PDD) ³⁾	mg/dl
Triglyceride	Enzymatic method (GK-GPO-PDD) ³⁾	mg/dl
Glutamic oxaloacetic transaminase (GOT)	Karmen method ³⁾	IU/l
Glutamic pyruvic transaminase (GPT)	Karmen method ³⁾	IU/l
Lactate dehydrogenase (LDH)	Wroblewski-Ladue method ³⁾	IU/l
Alkaline phosphatase (ALP)	GSCC method ³⁾	IU/l
Leucine aminopeptidase (LAP)	L-Leucyl-p-nitroanilide substrate method ³⁾	IU/l
Creatine phosphokinase (CPK)	GSCC method ³⁾	mg/dl
Urea nitrogen	Enzymatic method (Urease-GLDH) ³⁾	mg/dl
Creatinine	Jaffe method ³⁾	mg/dl
Sodium	Flame photometry ⁴⁾	mEq/l
Potassium	Flame photometry ⁴⁾	mEq/l
Chloride	Coulometric titration ⁴⁾	mEq/l
Calcium	DCPC method ³⁾	mg/dl
Inorganic phosphorus	Fiske-Subbarow method ³⁾	mg/dl
Urinalysis		
pH, Protein, Glucose, Ketone body, Bilirubin, Occult blood, Urobilinogen	Urinalysis reagent paper method ⁵⁾	

- 1) Automatic blood cell analyzer (Coulter counter SP : Coulter Electronics Inc.)
- 2) Automatic blood cell differential analyzer (Hematrak 590 : Geometric Data & Smithkline Company)
- 3) Automatic analyzer (Hitachi 705 : Hitachi, Ltd.)
- 4) Flame photometer (Hitachi 750 : Hitachi, Ltd.)
- 5) Ames reagent strips for urinalysis (Multistix, Uro-Labstix : Miles Sankyo Co., Ltd.)

APPENDIX P 2

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHMISTRY

UNITS AND DECIMAL PLACE FOR HEMATOLOGY AND BIOCHEMISTRY

	TEST ITEM	DECIMAL PLACE	UNIT
HEMATOLOGY	Red blood cell	2	$\times 10^6/u1$
	Hemoglobin	1	g/dl
	Hematocrit	1	%
	MCV	1	fl
	Platelet	0	$\times 10^3/u1$
	White blood cell	2	$\times 10^3/u1$
	Differential WBC	0	%
	Total protein	1	g/dl
	Albumin	1	g/dl
	A/G ratio	1	
BIOCHEMISTRY	T-bilirubin	2	mg/dl
	Glucose	0	mg/dl
	T-cholesterol	0	mg/dl
	Triglyceride	0	mg/dl
	GOT	0	IU/l
	GPT	0	IU/l
	LDH	0	IU/l
	ALP	0	IU/l
	LAP	0	IU/l
	CPK	0	IU/l
	Urea nitrogen	1	mg/dl
	Creatinine	1	mg/dl
	Sodium	0	mEq/l
	Potassium	1	mEq/l
	Chloride	0	mEq/l
	Calcium	1	mg/dl
	Inorganic phosphorus	1	mg/dl