APPENDIX B 1-1

CHEMICAL INTAKE CHANGES (TWO-WEEK STUDIES:SUMMARY)

RAT:MALE

STUDY NO. : 0018
ANIMAL : RAT F344
UNIT : g／kg／d a y
REPORT TYPE : A1 2
SEX : MALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2
Control	0.000± 0.000	0.000± 0.000
1110 ppm	0.135± 0.006	0.119± 0.006
3330 ppm	0.397± 0.024	0.339± 0.021
10000 ppm	1.101± 0.052	0.921± 0.056
30000 ppm	2.982± 0.134	2.939± 0.161
90000 ppm	0.927± 0.246	-

APPENDIX B 1-2

CHEMICAL INTAKE CHANGES (TWO-WEEK STUDIES: SUMMARY)

RAT: FEMALE

STUDY NO. : 0018
ANIMAL : RAT F344
UNIT : g／kg／d a y
REPORT TYPE : A1 2
SEX : FEMALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2
Control	0.000± 0.000	0.000± 0.000
1110 ppm	0.158± 0.013	0.148± 0.016
3330 ppm	0.412± 0.026	0.377± 0.020
10000 ppm	1.112± 0.045	0.962± 0.039
30000 ppm	2.848± 0.223	2.648± 0.451
90000 ppm	1.299± 0.825	-

APPENDIX B 1-3

CHEMICAL INTAKE CHANGES (TWO-WEEK STUDIES:SUMMARY)

MOUSE:MALE

STUDY NO. : 0019
ANIMAL : MOUSE BDF1
UNIT : g／kg／d a y
REPORT TYPE : A1 2
SEX : MALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2
Control	0.000± 0.000	0.000± 0.000
1110 ppm	0.199± 0.028	0.212± 0.045
3330 ppm	0.672± 0.089	0.649± 0.064
10000 ppm	1.360± 0.216	1.395± 0.252
30000 ppm	1.614± 1.052	3.477± 0.395
90000 ppm	1.920± 0.351	5.333± 0.000

APPENDIX B 1-4

CHEMICAL INTAKE CHANGES (TWO-WEEK STUDIES:SUMMARY)

MOUSE:FEMALE

STUDY NO. : 0019
ANIMAL : MOUSE BDF1
UNIT : g／kg／d a y
REPORT TYPE : A1 2
SEX : FEMALE

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2
Control	0.000± 0.000	0.000± 0.000
1110 ppm	0.214± 0.087	0.260± 0.036
3330 ppm	0.766± 0.068	0.728± 0.076
10000 ppm	1.796± 0.318	1.750± 0.224
30000 ppm	3.505± 0.853	2.945± 0.264
90000 ppm	3.055± 1.561	-

APPENDIX B 5-1

IDENTITY AND PURITY IN THE TWO-WEEK STUDIES OF 1,4-DIOXANE

PERFORMED AT THE JAPAN BIOASSAY LABORATORY

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

Lot no.PEN6246

1.Physical properties	Determined	Literature Values
Appearance:	Clear,colorless liquid	Clear,colorless liquid
Boiling point:	101°C	101°C (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:	1μl

Results: Only one major peak

Peak No.	Retention Time(min)	Retention Time Relative to Major Peak	Area (percent of Major peak)
1	3.825	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 Litrature values.

APPENDIX B 5-2

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

AT THE JAPAN BIOASSAY LABORATORY

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

Lot no.PEN6246

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

2.Physical properties	Previous determined of test (07/19/83)	After determined of test (08/03/83)
Appearance:	Clear,colorless liquid	Clear,colorless liquid
Boiling point:	101°C	101°C

3.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	1295
1370	1370
1460	1460
1700～1740	1700～1740
2700～3000	2700～3000

4.Gas Chromatography

Instrument: Shimazu GC-9A

Column: SBS-1

Column Temperature: 80°C

Flow Rate: 20ml/min

Detector: Hydrogen flame ionization(FID)

Injection Volume: 1μl

Results: Only one major peak

Date	Retention Time(min)	Retention Time Relative to Major Peak	Area (percent of Major peak)
07/19/83	3.825	1.00	100
08/03/83	3.812	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 B 5-3

RESULTS OF ANALYSIS OF FORMULATED DRINKING WATER

IN THE TWO-WEEK STUDIES OF 1,4-DIOXANE

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

(Rat)

	Concentration of 1,4-Dioxane in drinking water for Taget Concentration(ppm)				
Date Mixed	90000 (a)	30000 (a)	10000 (a)	3330 (a)	1110 (a)
07/29/83	89991 (99.7)	29997 (100.3)	9999 (92.2)	3319.67(91.9)	1033 (93.0)

(a) Determined as a percent of taget

(Mouse)

	Concentration of 1,4-Dioxane in drinking water for Taget Concentration(ppm)				
Date Mixed	90000 (a)	30000 (a)	10000 (a)	3330 (a)	1110 (a)
07/30/83	89307 (99.2)	28097 (93.7)	9403 (94.0)	3219 (96.7)	1061 (95.6)

(a) Determined as a percent of taget

APPENDIX B 5-4

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

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

(Rat)

Date Mixed	Concentration of 1,4-Dioxane in drinking water for Taget Concentration(ppm)		
	30000 (a)	10000 (a)	1110 (a)
07/29/83	29997 (92.2)	9999 (92.2)	1033 (93.9)
08/02/83	28637 (95.5)	9319 (93.2)	1037 (93.4)

(a) Determined as a percent of taget

(Mouse)

Date Mixed	Concentration of 1,4-Dioxane in drinking water for Taget Concentration(ppm)		
	30000 (a)	10000 (a)	30000 (a)
07/30/83	28097 (93.7)	9403 (94.0)	23337 (93.7)
08/03/83	28280 (94.3)	9582 (95.8)	28280 (94.3)

(a) Determined as a percent of taget

APPENDIX C 1

CHEMICAL INTAKE CHANGES (THIRTEEN-WEEK STUDIES: SUMMARY)

RAT: MALE

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

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2	3	4	5	6	7
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
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

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

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8	9	10	11	12	13
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
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

APPENDIX C 2

CHEMICAL INTAKE CHANGES (THIRTEEN-WEEK STUDIES: SUMMARY)

RAT: FEMALE

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

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2	3	4	5	6	7
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
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

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

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8	9	10	11	12	13
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
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

APPENDIX C 3

CHEMICAL INTAKE CHANGES (THIRTEEN-WEEK STUDIES: SUMMARY)

MOUSE: MALE

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

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2	3	4	5	6	7
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
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

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

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8	9	10	11	12	13
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
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

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 CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 1	2	3	4	5	6	7
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
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

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

CHEMICAL INTAKE CHENGES (SUMMARY)
ALL ANIMALS

Group Name	Administration (weeks) 8	9	10	11	12	13
Control	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000	0.000± 0.000
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

APPENDIX O 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	Determined	Literature Values
Appearance:	Clear,colorless liquid	Clear,colorless liquid
Boiling point:	101°C	101°C (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:	1μl

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 Litrature values.

APPENDIX O 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	Previous determined of test (07/16/84)	After determined of test (10/25/84)
Appearance:	Clear,colorless liquid	Clear,colorless liquid
Boiling point:	101°C	101°C

3.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	1295
1370	1370
1460	1460
1700～1740	1700～1740
2700～3000	2700～3000

4.Gas Chromatography

Instrument: Shimazu GC-9A

Column: SBS-1

Column Temperature: 80°C

Flow Rate: 20ml/min

Detector: Hydrogen flame ionization(FID)

Injection Volume: 1μl

APPENDIX O 3

RESULTS OF ANALYSIS OF FORMULATED DRINKING WATER

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

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 det ermine of test Values.Impurity was not detected in test substance by Gas chro matography.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 O 4

RESULTS OF STABILITY 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)

	Concentration of 1,4-Dioxane in drinking water for Taget Concentration(ppm)				
Date Mixed	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

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