

APPENDIX C

HEMATOLOGY AND CLINICAL CHEMISTRY RESULTS

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TABLE C1
Hematology and Clinical Chemistry Data for Rats in the 16-Day Gavage Study
of Benzyltrimethylammonium Chloride^a

	Vehicle Control	16 mg/kg	32 mg/kg	63 mg/kg
Male				
n	5	5	5	5
Hematology				
Automated hematocrit (%)	40.4 ± 0.6	40.3 ± 0.6	40.7 ± 1.0	40.3 ± 0.4
Manual hematocrit (%)	45.4 ± 0.7	45.8 ± 0.7	45.8 ± 1.2	45.4 ± 0.5
Hemoglobin (g/dL)	15.0 ± 0.3	15.1 ± 0.1	15.1 ± 0.3	14.8 ± 0.1
Erythrocytes (10 ⁶ /μL)	7.06 ± 0.10	7.08 ± 0.12	7.13 ± 0.20	6.99 ± 0.11
Reticulocytes (10 ⁶ /μL)	0.29 ± 0.02	0.24 ± 0.06	0.25 ± 0.04	0.46 ± 0.13
Nucleated erythrocytes/100 leukocytes	0.40 ± 0.25	0.40 ± 0.25	0.20 ± 0.20	0.40 ± 0.25
Mean cell volume (fL)	57.1 ± 0.2	56.9 ± 0.3	57.1 ± 0.3	57.6 ± 0.5
Mean cell hemoglobin (pg)	21.2 ± 0.1	21.3 ± 0.3	21.3 ± 0.2	21.3 ± 0.2
Mean cell hemoglobin concentration (g/dL)	37.1 ± 0.2	37.4 ± 0.5	37.3 ± 0.3	36.8 ± 0.2
Platelets (10 ³ /μL)	838.4 ± 15.1	820.0 ± 34.2	857.4 ± 21.1	774.0 ± 9.4
Leukocytes (10 ³ /μL)	9.10 ± 0.32	8.42 ± 0.18	8.88 ± 0.55	9.06 ± 0.40
Segmented neutrophils (10 ³ /μL)	0.86 ± 0.16	0.82 ± 0.14	0.82 ± 0.14	1.00 ± 0.14
Lymphocytes (10 ³ /μL)	8.06 ± 0.31	7.38 ± 0.26	7.91 ± 0.35	7.63 ± 0.26
Monocytes (10 ³ /μL)	0.07 ± 0.05	0.20 ± 0.09	0.10 ± 0.06	0.37 ± 0.12
Eosinophils (10 ³ /μL)	0.12 ± 0.06	0.02 ± 0.02	0.06 ± 0.04	0.06 ± 0.04
Clinical Chemistry				
Urea nitrogen (mg/dL)	24.0 ± 0.5	25.8 ± 0.4	23.0 ± 0.7	25.0 ± 0.5
Creatinine (mg/dL)	0.70 ± 0.00	0.70 ± 0.00	0.70 ± 0.00	0.70 ± 0.00
Total protein (g/dL)	6.6 ± 0.2	6.3 ± 0.1	6.6 ± 0.1	6.2 ± 0.1
Albumin (g/dL)	4.8 ± 0.1	4.7 ± 0.1	4.7 ± 0.1	4.6 ± 0.1
Alanine aminotransferase (IU/L)	48 ± 1	56 ± 4	43 ± 1	43 ± 4
Alkaline phosphatase (IU/L)	545 ± 15	553 ± 13	566 ± 16	559 ± 13
Creatine kinase (IU/L)	440 ± 81	542 ± 147	505 ± 81	444 ± 79
Sorbitol dehydrogenase (IU/L)	33 ± 2	32 ± 3	31 ± 2	32 ± 2
Serum cholinesterase (IU/L)	676.8 ± 28.8	753.2 ± 13.5	738.4 ± 23.4	789.0 ± 39.7*
Erythrocyte cholinesterase (IU/L)	530.2 ± 143.6	726.4 ± 113.2	694.4 ± 121.9	726.6 ± 71.4
Bile acids (μmol/L)	28.3 ± 4.5	28.6 ± 4.0	39.9 ± 7.2	34.5 ± 5.1

TABLE C1
Hematology and Clinical Chemistry Data for Rats in the 16-Day Gavage Study
of Benzyltrimethylammonium Chloride

	Vehicle Control	16 mg/kg	32 mg/kg	63 mg/kg
Female				
n	5	5	5	5
Hematology				
Automated hematocrit (%)	44.5 ± 0.4	42.6 ± 0.8	42.5 ± 0.4	44.2 ± 1.1
Manual hematocrit (%)	46.4 ± 0.4	45.0 ± 0.5	44.8 ± 0.4	46.2 ± 0.9
Hemoglobin (g/dL)	15.6 ± 0.1	15.2 ± 0.2	15.0 ± 0.1	15.7 ± 0.3
Erythrocytes (10 ⁶ /μL)	7.59 ± 0.08	7.24 ± 0.13	7.20 ± 0.06	7.58 ± 0.20
Reticulocytes (10 ⁶ /μL)	0.20 ± 0.03	0.22 ± 0.03	0.18 ± 0.02	0.23 ± 0.03
Nucleated erythrocytes/100 leukocytes	0.00 ± 0.00	0.80 ± 0.37	0.20 ± 0.20	0.00 ± 0.00
Mean cell volume (fL)	58.6 ± 0.2	58.9 ± 0.1	59.1 ± 0.2	58.3 ± 0.3
Mean cell hemoglobin (pg)	20.6 ± 0.2	21.0 ± 0.2	20.8 ± 0.1	20.7 ± 0.2
Mean cell hemoglobin concentration (g/dL)	35.2 ± 0.3	35.7 ± 0.4	35.2 ± 0.3	35.5 ± 0.2
Platelets (10 ³ /μL)	714.8 ± 13.5	755.2 ± 23.9	763.2 ± 14.2	710.0 ± 23.9
Leukocytes (10 ³ /μL)	9.28 ± 0.50	9.46 ± 0.19	9.38 ± 0.93	8.24 ± 0.30
Segmented neutrophils (10 ³ /μL)	1.30 ± 0.26	1.21 ± 0.22	1.17 ± 0.23	0.77 ± 0.18
Lymphocytes (10 ³ /μL)	7.72 ± 0.37	7.89 ± 0.27	8.05 ± 0.84	7.32 ± 0.44
Monocytes (10 ³ /μL)	0.19 ± 0.05	0.27 ± 0.05	0.13 ± 0.04	0.09 ± 0.05
Eosinophils (10 ³ /μL)	0.07 ± 0.03	0.10 ± 0.03	0.04 ± 0.02	0.06 ± 0.02
Clinical Chemistry				
Urea nitrogen (mg/dL)	23.8 ± 0.4	23.6 ± 0.2	22.6 ± 1.3	22.4 ± 0.8
Creatinine (mg/dL)	0.70 ± 0.00	0.68 ± 0.02	0.66 ± 0.02	0.66 ± 0.04
Total protein (g/dL)	6.0 ± 0.1	6.0 ± 0.1	5.8 ± 0.1	6.0 ± 0.1
Albumin (g/dL)	4.5 ± 0.1	4.5 ± 0.1	4.3 ± 0.1	4.4 ± 0.1
Alanine aminotransferase (IU/L)	40 ± 2	37 ± 1	37 ± 2	37 ± 1
Alkaline phosphatase (IU/L)	505 ± 8	490 ± 18	501 ± 31	518 ± 9
Creatine kinase (IU/L)	432 ± 61	272 ± 32	421 ± 70	378 ± 86
Sorbitol dehydrogenase (IU/L)	30 ± 1	28 ± 0	27 ± 2	26 ± 1
Serum cholinesterase (IU/L)	2,364.0 ± 120.6	2,577.8 ± 189.9	2,061.0 ± 123.8	2,138.4 ± 223.7
Erythrocyte cholinesterase (IU/L)	673.8 ± 175.9	400.6 ± 164.4	1,185.8 ± 193.3	819.2 ± 204.7
Bile acids (μmol/L)	29.2 ± 2.9	31.4 ± 5.2	28.5 ± 5.0	28.9 ± 6.2

* Significantly different ($P \leq 0.05$) from the vehicle control group by Dunn's test

^a Mean ± standard error. Statistical tests were performed on unrounded data. No data are available for the 125 and 250 mg/kg groups due to 100% mortality.

TABLE C2
Hematology and Clinical Chemistry Data for Rats in the 13-Week Gavage Study
of Benzyltrimethylammonium Chloride^a

	Vehicle Control	12.5 mg/kg	25 mg/kg	50 mg/kg	100 mg/kg
Male					
n					
Day 3	10	10	10	10	10
Day 21	10	10	10	10	10
Week 13	10	9	10	10	10
Hematology					
Automated hematocrit (%)					
Day 3	38.4 ± 0.5	39.0 ± 0.6	37.9 ± 0.4	38.7 ± 0.4	39.1 ± 0.7
Day 21	44.3 ± 0.4	44.3 ± 0.4	44.1 ± 0.3	44.8 ± 0.5	43.5 ± 0.7
Week 13	46.8 ± 0.4	48.5 ± 0.3*	47.9 ± 0.5	46.5 ± 0.5	46.5 ± 0.4
Manual hematocrit (%)					
Day 3	42.2 ± 0.7	41.5 ± 0.7	41.2 ± 0.4	43.1 ± 0.4	42.5 ± 0.8
Day 21	47.7 ± 0.5	47.5 ± 0.7	47.0 ± 0.5	48.0 ± 0.6	47.6 ± 0.6
Week 13	48.9 ± 0.4	50.0 ± 0.4	49.5 ± 0.4	48.7 ± 0.5	48.9 ± 0.4
Hemoglobin (g/dL)					
Day 3	13.7 ± 0.2	13.8 ± 0.2	13.5 ± 0.1	13.8 ± 0.1	13.8 ± 0.2
Day 21	15.4 ± 0.1	15.6 ± 0.1	15.5 ± 0.1	15.6 ± 0.1	15.4 ± 0.2
Week 13	15.8 ± 0.1	15.9 ± 0.1	16.0 ± 0.1	15.8 ± 0.2	15.8 ± 0.1
Erythrocytes (10⁶/μL)					
Day 3	6.27 ± 0.07	6.33 ± 0.09	6.18 ± 0.06	6.28 ± 0.05	6.36 ± 0.12
Day 21	7.25 ± 0.08	7.31 ± 0.06	7.34 ± 0.05	7.28 ± 0.08	7.09 ± 0.10
Week 13	8.96 ± 0.07	9.08 ± 0.06	9.03 ± 0.09	8.71 ± 0.09	8.67 ± 0.06*
Reticulocytes (10⁶/μL)					
Day 3	0.53 ± 0.03	0.58 ± 0.02	0.54 ± 0.04	0.50 ± 0.02	0.55 ± 0.03
Day 21	0.24 ± 0.01	0.23 ± 0.01	0.20 ± 0.02*	0.20 ± 0.01**	0.21 ± 0.01**
Week 13	0.21 ± 0.01	0.24 ± 0.02	0.24 ± 0.01	0.22 ± 0.01	0.22 ± 0.01
Nucleated erythrocytes (10³/μL)					
Day 3	0.17 ± 0.05	0.13 ± 0.06	0.12 ± 0.05	0.16 ± 0.02	0.13 ± 0.03
Day 21	0.05 ± 0.03	0.04 ± 0.03	0.01 ± 0.01	0.06 ± 0.03	0.07 ± 0.03
Week 13	0.02 ± 0.02	0.04 ± 0.03	0.00 ± 0.00 ^b	0.02 ± 0.02 ^b	0.00 ± 0.00
Mean cell volume (fL)					
Day 3	61.2 ± 0.3	61.5 ± 0.3	61.3 ± 0.3	61.6 ± 0.2	61.4 ± 0.2
Day 21	61.0 ± 0.4	60.7 ± 0.4	60.0 ± 0.3	61.6 ± 0.4	61.3 ± 0.3
Week 13	52.2 ± 0.2	53.4 ± 0.1**	53.0 ± 0.2**	53.4 ± 0.2**	53.6 ± 0.1**
Mean cell hemoglobin (pg)					
Day 3	21.8 ± 0.1	21.8 ± 0.2	21.9 ± 0.1	22.0 ± 0.1	21.7 ± 0.1
Day 21	21.2 ± 0.2	21.3 ± 0.1	21.1 ± 0.1	21.4 ± 0.1	21.7 ± 0.1
Week 13	17.6 ± 0.1	17.5 ± 0.1	17.7 ± 0.1	18.1 ± 0.1**	18.2 ± 0.1**
Mean cell hemoglobin concentration (g/dL)					
Day 3	35.6 ± 0.1	35.5 ± 0.2	35.7 ± 0.2	35.7 ± 0.2	35.4 ± 0.2
Day 21	34.8 ± 0.3	35.1 ± 0.2	35.2 ± 0.2	34.8 ± 0.3	35.4 ± 0.2
Week 13	33.7 ± 0.2	32.8 ± 0.2*	33.4 ± 0.3	33.9 ± 0.2	34.0 ± 0.2
Platelets (10³/μL)					
Day 3	1,091.1 ± 30.5	1,086.9 ± 25.3	1,080.6 ± 14.8	1,025.7 ± 11.2	1,069.5 ± 26.3
Day 21	793.1 ± 19.9	807.4 ± 8.6	820.8 ± 10.4	824.7 ± 20.0	838.7 ± 28.7
Week 13	649.8 ± 10.3	640.6 ± 9.7	646.3 ± 10.8	641.4 ± 6.6	653.7 ± 13.7
Leukocytes (10³/μL)					
Day 3	8.09 ± 0.28	8.49 ± 0.24	7.70 ± 0.24	7.89 ± 0.22	8.91 ± 0.54
Day 21	11.03 ± 0.41	12.07 ± 0.30	10.78 ± 0.45	10.78 ± 0.25	10.90 ± 0.59
Week 13	11.96 ± 0.53	12.60 ± 0.61	11.90 ± 0.38	12.86 ± 0.60	11.67 ± 0.36

TABLE C2
Hematology and Clinical Chemistry Data for Rats in the 13-Week Gavage Study
of Benzyltrimethylammonium Chloride

	Vehicle Control	12.5 mg/kg	25 mg/kg	50 mg/kg	100 mg/kg
Male (continued)					
n					
Day 3	10	10	10	10	10
Day 21	10	10	10	10	10
Week 13	10	9	10	10	10
Hematology (continued)					
Segmented neutrophils ($10^3/\mu\text{L}$)					
Day 3	1.28 ± 0.21	1.14 ± 0.07	0.96 ± 0.11	0.10 ± 0.11	1.14 ± 0.08
Day 21	1.17 ± 0.07	1.37 ± 0.19	1.18 ± 0.14	1.35 ± 0.12	1.15 ± 0.14
Week 13	2.13 ± 0.17	1.59 ± 0.11*	1.56 ± 0.16 ^b	1.54 ± 0.20 ^b	1.25 ± 0.18**
Lymphocytes ($10^3/\mu\text{L}$)					
Day 3	6.69 ± 0.32	7.18 ± 0.19	6.64 ± 0.27	6.72 ± 0.18	7.57 ± 0.49
Day 21	9.55 ± 0.43	10.16 ± 0.25	9.17 ± 0.41	9.01 ± 0.27	9.49 ± 0.47
Week 13	9.06 ± 0.43	10.35 ± 0.65	9.82 ± 0.42 ^b	10.29 ± 0.61 ^b	9.97 ± 0.50
Atypical lymphocytes ($10^3/\mu\text{L}$)					
Day 3	0.04 ± 0.03	0.06 ± 0.05	0.00 ± 0.00	0.03 ± 0.02	0.00 ± 0.00
Week 13	0.22 ± 0.09	0.12 ± 0.05	0.18 ± 0.06 ^b	0.19 ± 0.09 ^b	0.16 ± 0.07
Monocytes ($10^3/\mu\text{L}$)					
Day 3	0.09 ± 0.04	0.14 ± 0.06	0.08 ± 0.02	0.14 ± 0.05	0.19 ± 0.04
Day 21	0.22 ± 0.07	0.44 ± 0.09	0.37 ± 0.09	0.36 ± 0.07	0.24 ± 0.10
Week 13	0.46 ± 0.12	0.35 ± 0.07	0.18 ± 0.05 ^b	0.53 ± 0.10 ^b	0.21 ± 0.04
Eosinophils ($10^3/\mu\text{L}$)					
Day 3	0.02 ± 0.01	0.02 ± 0.01	0.03 ± 0.02	0.02 ± 0.02	0.01 ± 0.01
Day 21	0.05 ± 0.04	0.02 ± 0.02	0.04 ± 0.02	0.04 ± 0.02	0.01 ± 0.01
Week 13	0.08 ± 0.03	0.16 ± 0.04	0.12 ± 0.04 ^b	0.11 ± 0.04 ^b	0.07 ± 0.03
Clinical Chemistry					
Urea nitrogen (mg/dL)					
Day 3	20.1 ± 0.6	19.3 ± 0.4	19.4 ± 0.3	19.8 ± 0.3	19.2 ± 0.3
Day 21	22.4 ± 1.5	21.4 ± 0.5	20.9 ± 0.3	23.4 ± 1.8	21.8 ± 0.5
Week 13	23.5 ± 0.5	24.2 ± 1.3	23.6 ± 0.6	22.6 ± 0.3	22.3 ± 0.6
Creatinine (mg/dL)					
Day 3	0.58 ± 0.01	0.59 ± 0.01	0.58 ± 0.01	0.56 ± 0.02	0.57 ± 0.02
Day 21	0.68 ± 0.01	0.67 ± 0.02	0.68 ± 0.01	0.67 ± 0.02	0.67 ± 0.02
Week 13	0.66 ± 0.02	0.69 ± 0.01	0.70 ± 0.02	0.68 ± 0.01	0.67 ± 0.02
Total protein (g/dL)					
Day 3	5.7 ± 0.1	5.8 ± 0.1	5.7 ± 0.1	5.6 ± 0.1	5.7 ± 0.1
Day 21	6.2 ± 0.1	6.2 ± 0.1	6.2 ± 0.1	6.2 ± 0.1	6.2 ± 0.0
Week 13	6.8 ± 0.1	6.8 ± 0.1	7.0 ± 0.1	6.7 ± 0.1	6.7 ± 0.1
Albumin (g/dL)					
Day 3	4.3 ± 0.0	4.4 ± 0.0	4.3 ± 0.1	4.2 ± 0.1	4.3 ± 0.1
Day 21	4.6 ± 0.1	4.5 ± 0.0	4.5 ± 0.0	4.6 ± 0.1	4.6 ± 0.1
Week 13	5.0 ± 0.0	5.0 ± 0.1	5.0 ± 0.0	4.9 ± 0.0	4.9 ± 0.0
Alanine aminotransferase (IU/L)					
Day 3	42 ± 1	41 ± 2	41 ± 2	43 ± 2	42 ± 1
Day 21	47 ± 1	50 ± 1	46 ± 1	47 ± 1	46 ± 1
Week 13	67 ± 4	60 ± 4	69 ± 5	67 ± 5	56 ± 2

TABLE C2
Hematology and Clinical Chemistry Data for Rats in the 13-Week Gavage Study
of Benzyltrimethylammonium Chloride

	Vehicle Control	12.5 mg/kg	25 mg/kg	50 mg/kg	100 mg/kg
Male (continued)					
n					
Day 3	10	10	10	10	10
Day 21	10	10	10	10	10
Week 13	10	9	10	10	10
Clinical Chemistry (continued)					
Alkaline phosphatase (IU/L)					
Day 3	708 ± 12	737 ± 17	730 ± 12	722 ± 15	700 ± 17
Day 21	533 ± 9	562 ± 17	543 ± 8	532 ± 10	544 ± 10
Week 13	270 ± 6	271 ± 8	276 ± 5	245 ± 5*	227 ± 7**
Creatine kinase (IU/L)					
Day 3	443 ± 47	577 ± 64	529 ± 38	429 ± 35	463 ± 31
Day 21	432 ± 31	457 ± 34	399 ± 20	467 ± 47	443 ± 47
Week 13	226 ± 23	255 ± 20	244 ± 14	256 ± 21	256 ± 30
Sorbitol dehydrogenase (IU/L)					
Day 3	16 ± 1	14 ± 2	15 ± 1	16 ± 1	16 ± 1
Day 21	19 ± 1	19 ± 1	20 ± 1	17 ± 1	20 ± 1
Week 13	25 ± 2	22 ± 2	24 ± 1	22 ± 1	19 ± 1**
Serum cholinesterase (IU/L)					
Day 3	859.6 ± 15.2	851.2 ± 17.9	853.5 ± 15.0	846.4 ± 14.4	904.1 ± 19.4
Day 21	692.9 ± 13.4	719.5 ± 11.1	712.4 ± 11.8	745.0 ± 32.0	777.3 ± 18.7**
Week 13	741.9 ± 20.7	760.0 ± 13.4	792.0 ± 25.2	792.5 ± 23.7	753.6 ± 16.3
Bile acids (μmol/L)					
Day 3	28.1 ± 4.2	18.0 ± 1.3	17.6 ± 1.3	23.3 ± 2.3	20.9 ± 1.6
Day 21	28.4 ± 2.9	15.6 ± 1.1*	18.6 ± 2.3	22.0 ± 2.5	26.8 ± 3.6
Week 13	19.4 ± 5.6	16.3 ± 2.7	17.3 ± 3.7	13.7 ± 0.8	17.6 ± 1.7
Female					
n					
Day 3	10	10	10	10	10
Day 21	10	10	10	10	10
Week 13	10	10	9	10	8
Hematology					
Automated hematocrit (%)					
Day 3	42.9 ± 0.4	41.7 ± 0.5	41.9 ± 0.5	40.9 ± 0.5*	42.7 ± 0.4
Day 21	45.0 ± 0.4	45.2 ± 0.6	46.1 ± 0.3	45.0 ± 0.3	45.7 ± 0.4
Week 13	45.2 ± 0.4	46.8 ± 0.3*	46.2 ± 0.4	46.4 ± 0.3	44.8 ± 0.3
Manual hematocrit (%)					
Day 3	43.9 ± 0.4	42.5 ± 0.4	43.0 ± 0.4	42.9 ± 0.4	43.9 ± 0.5
Day 21	48.6 ± 0.4	48.1 ± 0.9	49.4 ± 0.5	48.1 ± 0.6	49.7 ± 0.4
Week 13	46.1 ± 0.3	47.2 ± 0.4	46.7 ± 0.3	47.0 ± 0.4	45.8 ± 0.4
Hemoglobin (g/dL)					
Day 3	14.7 ± 0.1	14.2 ± 0.1	14.3 ± 0.2	14.1 ± 0.2*	14.7 ± 0.1
Day 21	15.7 ± 0.1	15.7 ± 0.2	16.0 ± 0.1	15.7 ± 0.1	16.0 ± 0.1
Week 13	15.3 ± 0.1	15.7 ± 0.1*	15.5 ± 0.1	15.5 ± 0.1	15.1 ± 0.1

TABLE C2
Hematology and Clinical Chemistry Data for Rats in the 13-Week Gavage Study
of Benzyltrimethylammonium Chloride

	Vehicle Control	12.5 mg/kg	25 mg/kg	50 mg/kg	100 mg/kg
Female (continued)					
n					
Day 3	10	10	10	10	10
Day 21	10	10	10	10	10
Week 13	10	10	9	10	8
Hematology (continued)					
Erythrocytes ($10^6/\mu\text{L}$)					
Day 3	6.97 ± 0.08	6.74 ± 0.06	6.78 ± 0.10	6.61 ± 0.10*	6.91 ± 0.07
Day 21	7.15 ± 0.07	7.19 ± 0.12	7.31 ± 0.05	7.10 ± 0.07	7.31 ± 0.06
Week 13	7.88 ± 0.07	8.11 ± 0.05	7.97 ± 0.07	8.00 ± 0.06	7.70 ± 0.05
Reticulocytes ($10^6/\mu\text{L}$)					
Day 3	0.28 ± 0.02	0.27 ± 0.02	0.25 ± 0.01	0.28 ± 0.01	0.30 ± 0.02
Day 21	0.14 ± 0.01	0.12 ± 0.01	0.14 ± 0.02	0.15 ± 0.01	0.14 ± 0.01
Week 13	0.18 ± 0.01	0.18 ± 0.01	0.18 ± 0.01	0.18 ± 0.01	0.19 ± 0.01
Nucleated erythrocytes ($10^3/\mu\text{L}$)					
Day 3	0.13 ± 0.04	0.05 ± 0.03	0.08 ± 0.04	0.12 ± 0.04	0.06 ± 0.02
Day 21	0.06 ± 0.02	0.00 ± 0.00*	0.01 ± 0.01	0.04 ± 0.02	0.01 ± 0.01
Week 13	0.04 ± 0.02	0.00 ± 0.00	0.01 ± 0.01	0.01 ± 0.01	0.01 ± 0.01
Mean cell volume (fL)					
Day 3	61.6 ± 0.1	61.8 ± 0.2	61.8 ± 0.3	61.9 ± 0.3	61.8 ± 0.3
Day 21	63.0 ± 0.2	62.9 ± 0.3	63.0 ± 0.3	63.4 ± 0.3	62.6 ± 0.3
Week 13	57.4 ± 0.1	57.7 ± 0.1	57.9 ± 0.1**	57.9 ± 0.1**	58.2 ± 0.2**
Mean cell hemoglobin (pg)					
Day 3	21.1 ± 0.1	21.1 ± 0.1	21.1 ± 0.1	21.4 ± 0.2	21.3 ± 0.1
Day 21	21.9 ± 0.1	21.9 ± 0.2	21.9 ± 0.1	22.1 ± 0.2	21.9 ± 0.1
Week 13	19.4 ± 0.1	19.4 ± 0.1	19.4 ± 0.1	19.4 ± 0.1	19.6 ± 0.1
Mean cell hemoglobin concentration (g/dL)					
Day 3	34.2 ± 0.1	34.2 ± 0.3	34.1 ± 0.2	34.5 ± 0.2	34.4 ± 0.2
Day 21	34.9 ± 0.1	34.8 ± 0.2	34.8 ± 0.1	34.9 ± 0.3	35.1 ± 0.2
Week 13	33.9 ± 0.1	33.7 ± 0.2	33.5 ± 0.2	33.4 ± 0.2	33.6 ± 0.2
Platelets ($10^3/\mu\text{L}$)					
Day 3	1,010.4 ± 33.0	1,056.0 ± 14.6	1,045.4 ± 20.1	1,016.0 ± 20.9	980.5 ± 24.8
Day 21	693.6 ± 15.7	696.2 ± 17.9	709.2 ± 16.2	723.9 ± 20.5	665.5 ± 12.8
Week 13	649.3 ± 13.8	653.2 ± 11.5	648.7 ± 20.6	708.8 ± 35.8	641.0 ± 16.4
Leukocytes ($10^3/\mu\text{L}$)					
Day 3	9.52 ± 0.28	9.39 ± 0.28	9.18 ± 0.26	9.24 ± 0.41	9.77 ± 0.33
Day 21	10.73 ± 0.48	10.20 ± 0.71	10.72 ± 0.58	9.71 ± 0.48	10.51 ± 0.36
Week 13	10.38 ± 0.32	9.85 ± 0.60	9.84 ± 0.42	10.71 ± 0.52	10.51 ± 0.63
Segmented neutrophils ($10^3/\mu\text{L}$)					
Day 3	1.08 ± 0.04	1.21 ± 0.11	1.23 ± 0.12	1.21 ± 0.08	1.10 ± 0.15
Day 21	1.06 ± 0.09	1.19 ± 0.15	1.02 ± 0.07	0.98 ± 0.11	1.06 ± 0.09
Week 13	1.30 ± 0.17	0.85 ± 0.11	1.72 ± 0.23	1.13 ± 0.18	1.05 ± 0.20
Lymphocytes ($10^3/\mu\text{L}$)					
Day 3	8.11 ± 0.29	7.71 ± 0.24	7.51 ± 0.29	7.53 ± 0.41	8.26 ± 0.23
Day 21	9.42 ± 0.45	8.79 ± 0.58	9.46 ± 0.61	8.57 ± 0.48	9.33 ± 0.41
Week 13	8.53 ± 0.34	8.45 ± 0.50	7.48 ± 0.41	8.84 ± 0.38	8.93 ± 0.61
Atypical lymphocytes ($10^3/\mu\text{L}$)					
Day 3	0.01 ± 0.01	0.03 ± 0.02	0.01 ± 0.01	0.01 ± 0.01	0.00 ± 0.00
Week 13	0.02 ± 0.02	0.24 ± 0.20	0.08 ± 0.04	0.13 ± 0.05	0.11 ± 0.04

TABLE C2
Hematology and Clinical Chemistry Data for Rats in the 13-Week Gavage Study
of Benzyltrimethylammonium Chloride

	Vehicle Control	12.5 mg/kg	25 mg/kg	50 mg/kg	100 mg/kg
Female (continued)					
n					
Day 3	10	10	10	10	10
Day 21	10	10	10	10	10
Week 13	10	10	9	10	8
Hematology (continued)					
Monocytes ($10^3/\mu\text{L}$)					
Day 3	0.29 ± 0.09	0.42 ± 0.09	0.36 ± 0.09	0.38 ± 0.10	0.35 ± 0.09
Day 21	0.09 ± 0.05	0.09 ± 0.05	0.11 ± 0.05	0.12 ± 0.06	0.05 ± 0.03
Week 13	0.35 ± 0.07	0.37 ± 0.08	0.40 ± 0.07	0.49 ± 0.05	0.39 ± 0.11
Eosinophils ($10^3/\mu\text{L}$)					
Day 3	0.02 ± 0.01	0.01 ± 0.01	0.05 ± 0.02	0.03 ± 0.01	0.04 ± 0.02
Day 21	0.07 ± 0.02	0.06 ± 0.03	0.06 ± 0.02	0.01 ± 0.01*	0.00 ± 0.00**
Week 13	0.17 ± 0.02	0.15 ± 0.05	0.14 ± 0.04	0.10 ± 0.02	0.01 ± 0.01**
Clinical Chemistry					
Urea nitrogen (mg/dL)					
Day 3	21.7 ± 0.6	20.8 ± 0.7	19.6 ± 0.5	21.5 ± 0.5	22.6 ± 0.9
Day 21	22.8 ± 0.7	22.7 ± 0.6	21.7 ± 0.7	24.8 ± 1.4	23.4 ± 0.7
Week 13	21.2 ± 0.6	24.2 ± 0.8*	21.4 ± 0.8	21.8 ± 1.3	22.8 ± 0.7
Creatinine (mg/dL)					
Day 3	0.57 ± 0.02	0.57 ± 0.02	0.57 ± 0.02	0.58 ± 0.01	0.58 ± 0.01
Day 21	0.60 ± 0.00	0.65 ± 0.02	0.65 ± 0.02	0.64 ± 0.02	0.62 ± 0.01
Week 13	0.69 ± 0.02	0.69 ± 0.01	0.68 ± 0.02	0.69 ± 0.02	0.65 ± 0.03
Total protein (g/dL)					
Day 3	5.9 ± 0.1	5.8 ± 0.1	5.6 ± 0.1*	5.6 ± 0.0*	5.7 ± 0.1
Day 21	5.8 ± 0.0	5.8 ± 0.0	5.8 ± 0.1	5.8 ± 0.1	5.7 ± 0.1
Week 13	6.8 ± 0.1	6.7 ± 0.1	6.5 ± 0.1*	6.4 ± 0.1**	6.4 ± 0.1**
Albumin (g/dL)					
Day 3	4.5 ± 0.0	4.4 ± 0.1	4.3 ± 0.1	4.3 ± 0.1*	4.3 ± 0.0**
Day 21	4.5 ± 0.0	4.4 ± 0.0	4.5 ± 0.1	4.4 ± 0.0	4.4 ± 0.1
Week 13	5.0 ± 0.1	5.0 ± 0.0	4.9 ± 0.1	4.7 ± 0.1**	4.6 ± 0.1**
Alanine aminotransferase (IU/L)					
Day 3	37 ± 1	36 ± 1	36 ± 1	36 ± 2	36 ± 1
Day 21	36 ± 1	34 ± 1	34 ± 1	39 ± 1	39 ± 1
Week 13	42 ± 3	51 ± 4	41 ± 2	43 ± 2	48 ± 3
Alkaline phosphatase (IU/L)					
Day 3	541 ± 13	540 ± 13	537 ± 9	544 ± 13	544 ± 15
Day 21	398 ± 9	382 ± 8	400 ± 8	405 ± 13	383 ± 12
Week 13	212 ± 7	237 ± 5	235 ± 9	208 ± 6	233 ± 8
Creatine kinase (IU/L)					
Day 3	517 ± 44	574 ± 60	488 ± 44	484 ± 41	474 ± 33
Day 21	493 ± 60	505 ± 48	502 ± 29	387 ± 42	405 ± 46
Week 13	366 ± 29	311 ± 33	395 ± 25	309 ± 47	392 ± 44
Sorbitol dehydrogenase (IU/L)					
Day 3	13 ± 1	14 ± 2	13 ± 1	14 ± 1	14 ± 1
Day 21	18 ± 1	18 ± 2	19 ± 1	21 ± 1	18 ± 1
Week 13	17 ± 1	20 ± 1	15 ± 1	16 ± 2	13 ± 1

TABLE C2
Hematology and Clinical Chemistry Data for Rats in the 13-Week Gavage Study
of Benzyltrimethylammonium Chloride

	Vehicle Control	12.5 mg/kg	25 mg/kg	50 mg/kg	100 mg/kg
Female (continued)					
n					
Day 3	10	10	10	10	10
Day 21	10	10	10	10	10
Week 13	10	10	9	10	8
Clinical Chemistry (continued)					
Serum cholinesterase (IU/L)					
Day 3	1,748.3 ± 49.9	1,774.0 ± 72.4	1,701.2 ± 94.9	1,764.3 ± 95.6	1,895.4 ± 76.1
Day 21	2,525.4 ± 68.3	2,872.1 ± 127.7	2,865.9 ± 143.1	2,819.0 ± 167.2	2,781.5 ± 181.6
Week 13	4,297.5 ± 144.8	4,412.9 ± 154.0	4,034.1 ± 206.4	3,284.1 ± 134.2**	2,797.9 ± 246.9**
Bile acids (μmol/L)					
Day 3	24.1 ± 2.3	20.8 ± 2.8	17.1 ± 1.5	21.8 ± 3.2	18.1 ± 2.6
Day 21	25.9 ± 1.5	20.9 ± 1.6	18.1 ± 2.6*	28.9 ± 4.7	20.4 ± 3.4
Week 13	14.9 ± 0.9	21.8 ± 4.0	20.1 ± 2.8	35.0 ± 8.6**	27.8 ± 3.9*

* Significantly different ($P \leq 0.05$) from the vehicle control group by Dunn's or Shirley's test

** $P \leq 0.01$

^a Mean ± standard error. Statistical tests were performed on unrounded data.

^b n=9

TABLE C3
Hematology and Clinical Chemistry Data for Mice in the 16-Day Gavage Study
of Benzyltrimethylammonium Chloride^a

	Vehicle Control	63 mg/kg	125 mg/kg
Male			
n	5	5	5
Hematology			
Automated hematocrit (%)	45.0 ± 0.3	45.5 ± 0.5	45.5 ± 0.7
Manual hematocrit (%)	50.2 ± 0.4	51.4 ± 0.4	50.4 ± 0.5
Hemoglobin (g/dL)	15.8 ± 0.2	15.7 ± 0.2	15.9 ± 0.2
Erythrocytes (10 ⁶ /μL)	9.00 ± 0.08	9.09 ± 0.11	9.10 ± 0.12
Reticulocytes (10 ⁶ /μL)	0.19 ± 0.03	0.15 ± 0.02	0.18 ± 0.02
Nucleated erythrocytes/100 leukocytes	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00
Mean cell volume (fL)	50.0 ± 0.2	50.0 ± 0.2	50.0 ± 0.1
Mean cell hemoglobin (pg)	17.5 ± 0.0	17.3 ± 0.1	17.5 ± 0.1
Mean cell hemoglobin concentration (g/dL)	35.0 ± 0.1	34.6 ± 0.4	34.9 ± 0.3
Platelets (10 ³ /μL)	760.0 ± 24.3	718.6 ± 36.0	763.2 ± 38.4
Leukocytes (10 ³ /μL)	4.84 ± 0.39	4.98 ± 0.56	4.98 ± 0.54
Segmented neutrophils (10 ³ /μL)	0.53 ± 0.13	0.42 ± 0.06	0.59 ± 0.09
Lymphocytes (10 ³ /μL)	4.20 ± 0.27	4.44 ± 0.53	4.26 ± 0.44
Monocytes (10 ³ /μL)	0.08 ± 0.04	0.09 ± 0.02	0.05 ± 0.02
Eosinophils (10 ³ /μL)	0.03 ± 0.02	0.04 ± 0.02	0.08 ± 0.03
Clinical Chemistry			
Serum cholinesterase (IU/L)	5,620.2 ± 192.7	5,900.0 ± 160.0	5,941.8 ± 199.0
Erythrocyte cholinesterase (IU/L)	2,016.0 ± 185.2	1,891.4 ± 247.4	1,812.5 ± 82.1 ^b

TABLE C3
Hematology and Clinical Chemistry Data for Mice in the 16-Day Gavage Study
of Benzyltrimethylammonium Chloride

	Vehicle Control	63 mg/kg	125 mg/kg
Female			
n	5	5	4
Hematology			
Automated hematocrit (%)	44.1 ± 0.5	43.4 ± 0.5	43.9 ± 0.5
Manual hematocrit (%)	50.0 ± 0.4	49.4 ± 0.6	50.0 ± 0.9
Hemoglobin (g/dL)	15.6 ± 0.3	15.5 ± 0.2	15.4 ± 0.2
Erythrocytes (10 ⁶ /μL)	8.92 ± 0.09	8.75 ± 0.09	8.81 ± 0.14
Reticulocytes (10 ⁶ /μL)	0.22 ± 0.04	0.20 ± 0.06	0.16 ± 0.03
Nucleated erythrocytes/100 leukocytes	0.00 ± 0.00	0.00 ± 0.00	0.00 ± 0.00 ^c
Mean cell volume (fL)	49.4 ± 0.1	49.6 ± 0.2	49.9 ± 0.3
Mean cell hemoglobin (pg)	17.5 ± 0.1	17.7 ± 0.1	17.5 ± 0.1
Mean cell hemoglobin concentration (g/dL)	35.3 ± 0.3	35.6 ± 0.2	35.0 ± 0.1
Platelets (10 ³ /μL)	708.2 ± 21.8	738.6 ± 12.6	722.3 ± 22.9
Leukocytes (10 ³ /μL)	4.58 ± 0.48	5.26 ± 0.38	5.93 ± 0.49
Segmented neutrophils (10 ³ /μL)	0.64 ± 0.16	0.58 ± 0.09	0.51 ± 0.12
Lymphocytes (10 ³ /μL)	3.86 ± 0.46	4.50 ± 0.34	5.36 ± 0.37
Monocytes (10 ³ /μL)	0.05 ± 0.02	0.10 ± 0.06	0.07 ± 0.03
Eosinophils (10 ³ /μL)	0.03 ± 0.02	0.07 ± 0.02	0.00 ± 0.00
Clinical Chemistry			
Serum cholinesterase (IU/L)	8,155.8 ± 24.2	8,328.6 ± 186.0	8,038.5 ± 247.4
Erythrocyte cholinesterase (IU/L)	2,044.8 ± 443.0	2,888.2 ± 300.2	2,384.8 ± 560.3

^a Mean ± standard error. Statistical tests were performed on unrounded data. No data are available for the 250, 500, and 1,000 mg/kg groups due to 100% mortality.

^b n=4

^c n=5

TABLE C4
Clinical Chemistry Data for Mice in the 13-Week Gavage Study of Benzyltrimethylammonium Chloride^a

	Vehicle Control	12.5 mg/kg	25 mg/kg	50 mg/kg	100 mg/kg
Male					
n	8	10	10	10	9
Urea nitrogen (mg/dL)	27.0 ± 0.6 ^b	31.6 ± 1.6	30.3 ± 1.8	30.8 ± 1.1	30.1 ± 1.7 ^c
Creatinine (mg/dL)	0.43 ± 0.02	0.48 ± 0.02	0.46 ± 0.02	0.47 ± 0.02	0.44 ± 0.02 ^c
Total protein (g/dL)	6.1 ± 0.1 ^d	6.0 ± 0.1 ^b	5.8 ± 0.1 ^{**}	5.7 ± 0.1 ^{**b}	5.7 ± 0.1 ^{**c}
Albumin (g/dL)	4.3 ± 0.1	4.3 ± 0.1	4.1 ± 0.1	4.2 ± 0.1	4.1 ± 0.1 ^c
Alanine aminotransferase (IU/L)	40 ± 8	53 ± 20	84 ± 31	71 ± 22	37 ± 8
Alkaline phosphatase (IU/L)	91 ± 2 ^b	86 ± 4	86 ± 2	86 ± 3	84 ± 3
Creatine kinase (IU/L)	276 ± 87 ^b	255 ± 57	461 ± 113 ^b	485 ± 135	310 ± 77
Sorbitol dehydrogenase (IU/L)	47 ± 2	46 ± 1	45 ± 2	45 ± 4	45 ± 1 ^c
Serum cholinesterase (IU/L)	8,963 ± 210	8,923 ± 376	8,404 ± 107	8,380 ± 353 ^b	8,893 ± 369 ^c
Bile acids (μmol/L)	14.0 ± 1.1	13.8 ± 0.6 ^b	14.9 ± 0.8	15.2 ± 0.8 ^b	13.3 ± 0.6 ^c
Female					
n	10	10	10	10	9
Urea nitrogen (mg/dL)	26.0 ± 2.0	26.9 ± 1.2	28.9 ± 1.3	25.0 ± 1.8	26.3 ± 1.3
Creatinine (mg/dL)	0.59 ± 0.02	0.58 ± 0.02	0.60 ± 0.02	0.54 ± 0.02	0.58 ± 0.02
Total protein (g/dL)	6.0 ± 0.1	5.9 ± 0.1	5.9 ± 0.1	5.8 ± 0.1	5.8 ± 0.1
Albumin (g/dL)	4.6 ± 0.1	4.6 ± 0.1	4.5 ± 0.1	4.4 ± 0.0	4.4 ± 0.1
Alanine aminotransferase (IU/L)	34 ± 6	40 ± 9	29 ± 2	26 ± 1	36 ± 9
Alkaline phosphatase (IU/L)	139 ± 3	126 ± 6	124 ± 4	128 ± 6	125 ± 6
Creatine kinase (IU/L)	297 ± 69	615 ± 212	428 ± 55	474 ± 91	318 ± 76
Sorbitol dehydrogenase (IU/L)	47 ± 1	48 ± 3	48 ± 1	48 ± 1	46 ± 1
Serum cholinesterase (IU/L)	10,020 ± 235	10,147 ± 114	9,964 ± 179	10,080 ± 230	9,726 ± 146
Bile acids (μmol/L)	15.1 ± 0.6	15.5 ± 0.8	15.5 ± 0.5	15.2 ± 0.5	15.6 ± 0.2

* Significantly different ($P \leq 0.05$) from the vehicle control group by Dunn's test

** Significantly different ($P \leq 0.01$) from the vehicle control group by Shirley's test

^a Mean ± standard error. Statistical tests were performed on unrounded data.

^b n=9

^c n=8

^d n=5

^e n=7

APPENDIX D
ORGAN WEIGHTS AND
ORGAN-WEIGHT-TO-BODY-WEIGHT RATIOS

TABLE D1	Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats in the 16-Day Gavage Study of Benzyltrimethylammonium Chloride D-2
TABLE D2	Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats in the 13-Week Gavage Study of Benzyltrimethylammonium Chloride D-3
TABLE D3	Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice in the 16-Day Gavage Study of Benzyltrimethylammonium Chloride D-4
TABLE D4	Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice in the 13-Week Gavage Study of Benzyltrimethylammonium Chloride D-5

TABLE D1
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats in the 16-Day Gavage Study
of Benzyltrimethylammonium Chloride^a

	Vehicle Control	16 mg/kg	32 mg/kg	63 mg/kg
n	5	5	5	5
Male				
Necropsy body wt	240 ± 4	231 ± 5	233 ± 12	226 ± 8
Heart				
Absolute	0.833 ± 0.013	0.810 ± 0.016	0.828 ± 0.046	0.829 ± 0.038
Relative	3.46 ± 0.05	3.51 ± 0.06	3.55 ± 0.04	3.67 ± 0.11
R. Kidney				
Absolute	1.078 ± 0.024	1.061 ± 0.029	1.058 ± 0.081	1.011 ± 0.020
Relative	4.49 ± 0.10	4.59 ± 0.09	4.51 ± 0.14	4.48 ± 0.08
Liver				
Absolute	12.166 ± 0.302	11.288 ± 0.400	11.509 ± 0.970	10.997 ± 0.626
Relative	50.58 ± 0.70	48.82 ± 0.78	48.98 ± 1.68	48.47 ± 1.20
Lung				
Absolute	1.383 ± 0.058	1.355 ± 0.087	1.491 ± 0.104	1.314 ± 0.053
Relative	5.75 ± 0.20	5.85 ± 0.27	6.39 ± 0.30	5.82 ± 0.21
Spleen				
Absolute	0.626 ± 0.017	0.585 ± 0.020	0.605 ± 0.029	0.579 ± 0.024
Relative	2.60 ± 0.05	2.53 ± 0.05	2.60 ± 0.04	2.56 ± 0.04
R. Testis				
Absolute	1.266 ± 0.013	1.247 ± 0.026	1.231 ± 0.055	1.231 ± 0.019
Relative	5.27 ± 0.09	5.41 ± 0.14	5.28 ± 0.06	5.46 ± 0.11
Thymus				
Absolute	0.521 ± 0.010	0.501 ± 0.010	0.523 ± 0.029	0.502 ± 0.035
Relative	2.17 ± 0.06	2.17 ± 0.05	2.26 ± 0.13	2.21 ± 0.09
Female				
Necropsy body wt	137 ± 5	144 ± 5	142 ± 4	137 ± 4
Heart				
Absolute	0.548 ± 0.020	0.577 ± 0.024	0.596 ± 0.009	0.560 ± 0.021
Relative	4.01 ± 0.05	4.02 ± 0.05	4.21 ± 0.08	4.10 ± 0.12
R. Kidney				
Absolute	0.636 ± 0.031	0.655 ± 0.023	0.663 ± 0.020	0.619 ± 0.025
Relative	4.65 ± 0.12	4.57 ± 0.05	4.67 ± 0.11	4.53 ± 0.11
Liver				
Absolute	5.966 ± 0.333	6.233 ± 0.278	6.147 ± 0.219	5.771 ± 0.324
Relative	43.58 ± 1.29	43.37 ± 0.80	43.30 ± 1.00	42.09 ± 1.13
Lung				
Absolute	0.897 ± 0.041	0.985 ± 0.043	0.944 ± 0.034	0.884 ± 0.063
Relative	6.56 ± 0.13	6.88 ± 0.29	6.65 ± 0.18	6.44 ± 0.27
Spleen				
Absolute	0.401 ± 0.013	0.416 ± 0.017	0.426 ± 0.016	0.366 ± 0.021
Relative	2.93 ± 0.02	2.90 ± 0.08	3.00 ± 0.11	2.67 ± 0.07
Thymus				
Absolute	0.357 ± 0.022	0.367 ± 0.012	0.366 ± 0.008	0.353 ± 0.023
Relative	2.61 ± 0.13	2.56 ± 0.08	2.58 ± 0.09	2.58 ± 0.11

^a Organ weights (absolute weights) and body weights are given in grams; organ-weight-to-body-weight ratios (relative weights) are given as mg organ weight/g body weight (mean ± standard error). Differences from the vehicle control group were not significant by Dunnett's test. No data are available for the 125 and 250 mg/kg groups due to 100% mortality.

TABLE D2
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats in the 13-Week Gavage Study of Benzyltrimethylammonium Chloride^a

	Vehicle Control	12.5 mg/kg	25 mg/kg	50 mg/kg	100 mg/kg
Male					
n	10	10	10	10	10
Necropsy body wt	338 ± 8	337 ± 8	336 ± 8	340 ± 5	311 ± 9
Heart					
Absolute	1.018 ± 0.030	1.010 ± 0.024	1.000 ± 0.024	1.016 ± 0.025	0.953 ± 0.028
Relative	3.02 ± 0.05	3.00 ± 0.04	2.98 ± 0.05	2.99 ± 0.06	3.07 ± 0.03
R. Kidney					
Absolute	1.266 ± 0.049	1.274 ± 0.044	1.307 ± 0.092	1.238 ± 0.036	1.208 ± 0.041
Relative	3.74 ± 0.07	3.78 ± 0.07	3.89 ± 0.24	3.64 ± 0.08	3.89 ± 0.05
Liver					
Absolute	12.136 ± 0.423	12.671 ± 0.412	11.893 ± 0.277	12.146 ± 0.262	11.409 ± 0.459
Relative	35.88 ± 0.50	37.58 ± 0.69	35.46 ± 0.34	35.78 ± 0.60	36.66 ± 0.73
Lung					
Absolute	1.540 ± 0.040	1.473 ± 0.045	1.503 ± 0.045	1.515 ± 0.042	1.388 ± 0.054
Relative	4.57 ± 0.08	4.37 ± 0.07	4.48 ± 0.09	4.46 ± 0.09	4.47 ± 0.10
R. Testis					
Absolute	1.459 ± 0.043	1.380 ± 0.036	1.385 ± 0.063	1.443 ± 0.029	1.423 ± 0.043
Relative	4.32 ± 0.07	4.11 ± 0.12	4.15 ± 0.21	4.25 ± 0.05	4.58 ± 0.02
Thymus					
Absolute	0.328 ± 0.016	0.343 ± 0.023	0.341 ± 0.022	0.360 ± 0.017	0.295 ± 0.012
Relative	0.97 ± 0.04	1.01 ± 0.05	1.02 ± 0.06	1.06 ± 0.05	0.96 ± 0.04
Female					
n	10	10	9	9	8
Necropsy body wt	190 ± 3	198 ± 4	193 ± 3	193 ± 4	187 ± 4
Heart					
Absolute	0.704 ± 0.011	0.679 ± 0.012	0.674 ± 0.016	0.693 ± 0.013	0.670 ± 0.014
Relative	3.71 ± 0.04	3.43 ± 0.05**	3.49 ± 0.05*	3.60 ± 0.07	3.59 ± 0.06
R. Kidney					
Absolute	0.716 ± 0.015	0.730 ± 0.020	0.710 ± 0.012	0.750 ± 0.014	0.730 ± 0.025
Relative	3.77 ± 0.07	3.68 ± 0.06	3.68 ± 0.05	3.90 ± 0.06	3.91 ± 0.10
Liver					
Absolute	6.435 ± 0.144	6.532 ± 0.221	6.449 ± 0.129	6.715 ± 0.204	6.731 ± 0.221
Relative	33.82 ± 0.32	32.92 ± 0.81	33.47 ± 0.54	34.79 ± 0.54	36.00 ± 0.68*
Lung					
Absolute	1.156 ± 0.048	1.184 ± 0.033	1.147 ± 0.037	1.195 ± 0.050	1.121 ± 0.045
Relative	6.06 ± 0.17	5.97 ± 0.13	5.97 ± 0.24	6.20 ± 0.24	6.00 ± 0.17
Thymus					
Absolute	0.263 ± 0.010	0.276 ± 0.014	0.263 ± 0.010	0.251 ± 0.013	0.257 ± 0.012
Relative	1.38 ± 0.04	1.39 ± 0.06	1.36 ± 0.04	1.30 ± 0.05	1.37 ± 0.06

* Significantly different ($P \leq 0.05$) from the vehicle control group by Williams' or Dunnett's test

** Significantly different ($P \leq 0.01$) from the vehicle control group by Dunnett's test

^a Organ weights (absolute weights) and body weights are given in grams; organ-weight-to-body-weight ratios (relative weights) are given as mg organ weight/g body weight (mean ± standard error).

TABLE D3
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice in the 16-Day Gavage Study
of Benzyltrimethylammonium Chloride^a

	Vehicle Control	63 mg/kg	125 mg/kg
Male			
n	5	5	5
Necropsy body wt	26.4 ± 0.7	26.0 ± 0.5	26.1 ± 0.6
Heart			
Absolute	0.132 ± 0.005	0.130 ± 0.003	0.131 ± 0.003
Relative	5.00 ± 0.11	5.00 ± 0.06	5.01 ± 0.05
R. Kidney			
Absolute	0.249 ± 0.012	0.246 ± 0.007	0.255 ± 0.008
Relative	9.41 ± 0.22	9.43 ± 0.13	9.76 ± 0.11
Liver			
Absolute	1.456 ± 0.049	1.416 ± 0.044	1.437 ± 0.042
Relative	55.03 ± 0.66	54.35 ± 1.03	54.94 ± 0.64
Lung			
Absolute	0.180 ± 0.007	0.184 ± 0.007	0.194 ± 0.006
Relative	6.80 ± 0.20	7.08 ± 0.35	7.42 ± 0.18
Spleen			
Absolute	0.069 ± 0.003	0.067 ± 0.003	0.067 ± 0.003
Relative	2.61 ± 0.06	2.57 ± 0.08	2.57 ± 0.07
R. Testis			
Absolute	0.106 ± 0.002	0.103 ± 0.001	0.103 ± 0.004
Relative	4.03 ± 0.16	3.96 ± 0.07	3.94 ± 0.14
Thymus			
Absolute	0.054 ± 0.003	0.049 ± 0.004	0.051 ± 0.005
Relative	2.04 ± 0.13	1.87 ± 0.16	1.96 ± 0.20
Female			
n	5	5	4
Necropsy body wt	21.2 ± 0.4	21.9 ± 0.5	22.4 ± 0.1
Heart			
Absolute	0.120 ± 0.003	0.118 ± 0.005	0.118 ± 0.002
Relative	5.66 ± 0.11	5.40 ± 0.14	5.28 ± 0.09
R. Kidney			
Absolute	0.169 ± 0.007	0.173 ± 0.002	0.173 ± 0.007
Relative	7.96 ± 0.22	7.90 ± 0.12	7.75 ± 0.32
Liver			
Absolute	1.073 ± 0.043	1.136 ± 0.025	1.209 ± 0.017*
Relative	50.51 ± 1.35	51.88 ± 0.69	54.12 ± 1.04
Lung			
Absolute	0.171 ± 0.007	0.162 ± 0.008	0.150 ± 0.009
Relative	8.07 ± 0.23	7.38 ± 0.25	6.72 ± 0.36*
Spleen			
Absolute	0.078 ± 0.003	0.078 ± 0.004	0.076 ± 0.004
Relative	3.67 ± 0.12	3.56 ± 0.09	3.40 ± 0.20
Thymus			
Absolute	0.062 ± 0.003	0.064 ± 0.005	0.064 ± 0.007
Relative	2.94 ± 0.14	2.91 ± 0.21	2.84 ± 0.29

* Significantly different ($P \leq 0.05$) from the vehicle control group by Williams' or Dunnett's test

^a Organ weights (absolute weights) and body weights are given in grams; organ-weight-to-body-weight ratios (relative weights) are given as mg organ weight/g body weight (mean ± standard error). No data are available for the 250, 500, and 1,000 mg/kg groups due to 100% mortality.

TABLE D4
Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice in the 13-Week Gavage Study
of Benzyltrimethylammonium Chloride^a

	Vehicle Control	12.5 mg/kg	25 mg/kg	50 mg/kg	100 mg/kg
Male					
n	10	10	10	8	9
Necropsy body wt	34.9 ± 0.7	34.9 ± 1.0	34.5 ± 0.6	34.8 ± 0.9	33.9 ± 0.9
Heart					
Absolute	0.142 ± 0.003	0.146 ± 0.003	0.146 ± 0.002	0.151 ± 0.003	0.145 ± 0.003
Relative	4.06 ± 0.06	4.19 ± 0.06	4.25 ± 0.05*	4.30 ± 0.10*	4.29 ± 0.06*
R. Kidney					
Absolute	0.284 ± 0.006	0.290 ± 0.008	0.285 ± 0.006	0.311 ± 0.008*	0.297 ± 0.009
Relative	8.13 ± 0.13	8.32 ± 0.17	8.28 ± 0.16	8.82 ± 0.15**	8.77 ± 0.16**
Liver					
Absolute	1.519 ± 0.042	1.553 ± 0.049	1.534 ± 0.049	1.599 ± 0.041	1.537 ± 0.036
Relative	43.44 ± 0.61	44.48 ± 0.57	44.47 ± 0.90	45.33 ± 0.50	45.39 ± 1.00
Lung					
Absolute	0.196 ± 0.011	0.199 ± 0.008	0.198 ± 0.014	0.188 ± 0.015	0.184 ± 0.006
Relative	5.63 ± 0.32	5.71 ± 0.17	5.78 ± 0.46	5.31 ± 0.34	5.43 ± 0.18
R. Testis					
Absolute	0.119 ± 0.005	0.113 ± 0.007	0.119 ± 0.003	0.120 ± 0.005	0.120 ± 0.004
Relative	3.39 ± 0.11	3.24 ± 0.21	3.46 ± 0.07	3.39 ± 0.12	3.54 ± 0.05
Thymus					
Absolute	0.063 ± 0.009	0.045 ± 0.006	0.044 ± 0.004	0.042 ± 0.005	0.044 ± 0.005
Relative	1.80 ± 0.25	1.31 ± 0.19	1.26 ± 0.11	1.19 ± 0.14	1.31 ± 0.14
Female					
n	10	10	10	10	9
Necropsy body wt	29.1 ± 1.0	29.9 ± 0.9	28.7 ± 0.9	29.2 ± 1.3	28.2 ± 0.9
Heart					
Absolute	0.125 ± 0.002	0.128 ± 0.003	0.122 ± 0.003	0.126 ± 0.003	0.124 ± 0.003
Relative	4.31 ± 0.12	4.31 ± 0.09	4.28 ± 0.11	4.37 ± 0.12	4.40 ± 0.08
R. Kidney					
Absolute	0.193 ± 0.003	0.190 ± 0.004	0.184 ± 0.004	0.192 ± 0.006	0.184 ± 0.006
Relative	6.70 ± 0.22	6.40 ± 0.18	6.44 ± 0.14	6.64 ± 0.17	6.52 ± 0.06
Liver					
Absolute	1.168 ± 0.022	1.223 ± 0.046	1.246 ± 0.034	1.249 ± 0.055	1.208 ± 0.039
Relative	40.47 ± 1.35	40.95 ± 0.81	43.57 ± 0.50	42.95 ± 1.21	42.81 ± 0.64
Lung					
Absolute	0.187 ± 0.004	0.196 ± 0.009	0.172 ± 0.005	0.176 ± 0.006	0.176 ± 0.006
Relative	6.48 ± 0.24	6.58 ± 0.27	6.02 ± 0.12	6.08 ± 0.16	6.25 ± 0.14
Thymus					
Absolute	0.051 ± 0.003	0.054 ± 0.003	0.048 ± 0.002	0.056 ± 0.005	0.050 ± 0.004
Relative	1.77 ± 0.09	1.79 ± 0.09	1.69 ± 0.10	1.90 ± 0.12	1.78 ± 0.16

* Significantly different ($P \leq 0.05$) from the vehicle control group by Williams' or Dunnett's test

** Significantly different ($P \leq 0.01$) from the vehicle control group by Williams' test

^a Organ weights (absolute weights) and body weights are given in grams; organ-weight-to-body-weight ratios (relative weights) are given as mg organ weight/g body weight (mean ± standard error).

APPENDIX E

REPRODUCTIVE TISSUE EVALUATIONS AND ESTROUS CYCLE CHARACTERIZATION

TABLE E1	Summary of Reproductive Tissue Evaluations for Male Rats in the 13-Week Gavage Study of Benzyltrimethylammonium Chloride	E-2
TABLE E2	Estrous Cycle Characterization for Female Rats in the 13-Week Gavage Study of Benzyltrimethylammonium Chloride	E-2
TABLE E3	Summary of Reproductive Tissue Evaluations for Male Mice in the 13-Week Gavage Study of Benzyltrimethylammonium Chloride	E-3
TABLE E4	Estrous Cycle Characterization for Female Mice in the 13-Week Gavage Study of Benzyltrimethylammonium Chloride	E-3

TABLE E1
Summary of Reproductive Tissue Evaluations for Male Rats in the 13-Week Gavage Study of Benzyltrimethylammonium Chloride^a

	Vehicle Control	25 mg/kg	50 mg/kg	100 mg/kg
n	10	10	10	10
Weights (g)				
Necropsy body wt	338 ± 9	335 ± 8	340 ± 5	311 ± 9*
L. Cauda epididymis	0.1660 ± 0.0076	0.1633 ± 0.0063	0.1607 ± 0.0056	0.1582 ± 0.0078
L. Epididymis	0.4933 ± 0.0157	0.4944 ± 0.0084	0.4973 ± 0.0140	0.4828 ± 0.0149
L. Testis	1.5400 ± 0.0487	1.5126 ± 0.0259	1.5180 ± 0.0316	1.4909 ± 0.0441
Spermatid measurements				
Spermatid heads (10 ⁷ /g testis)	9.15 ± 0.42	9.51 ± 0.38	9.12 ± 0.54	9.36 ± 0.35
Spermatid heads (10 ⁷ /testis)	13.98 ± 0.56	14.35 ± 0.49	13.84 ± 0.83	13.90 ± 0.49
Spermatid count (mean/10 ⁴ mL suspension)	69.90 ± 2.78	71.75 ± 2.45	69.18 ± 4.16	69.48 ± 2.46
Epididymal spermatozoal measurements				
Motility (%)	84.66 ± 0.43 ^b	83.63 ± 0.47	83.32 ± 0.47	83.27 ± 0.40
Concentration (10 ⁶ /g cauda epididymal tissue)	427 ± 19	454 ± 21	460 ± 17	409 ± 36

* Significantly different (P<0.05) from the vehicle control group by Dunnett's test

^a Data are presented as mean ± standard error. Differences from the vehicle control group are not significant by Dunnett's test (tissue weights) or Dunn's test (spermatid and epididymal spermatozoal measurements).

^b n=8

TABLE E2
Estrous Cycle Characterization for Female Rats in the 13-Week Gavage Study of Benzyltrimethylammonium Chloride^a

	Vehicle Control	25 mg/kg	50 mg/kg	100 mg/kg
n	10	9	10	8
Necropsy body wt (g)	190 ± 3	193 ± 3	192 ± 4	187 ± 4
Estrous cycle length (days)	4.75 ± 0.13	4.44 ± 0.15 ^b	4.80 ± 0.17	4.94 ± 0.26
Estrous stages^c (% of cycle)				
Diestrus	42.5	36.1	38.3	37.5
Proestrus	14.2	20.4	17.5	18.8
Estrus	25.0	23.1	25.8	22.9
Metestrus	18.3	20.4	18.3	20.8

^a Necropsy body weight and estrous cycle length data are presented as mean ± standard error. Differences from the vehicle control group are not significant by Dunnett's test (necropsy body weight) or Dunn's test (estrous cycle length).

^b Estrous cycle was longer than 12 days or unclear in one of nine animals.

^c Evidence shows that females administered 25 mg/kg differ significantly (Wilk's Criterion, P<0.05) from the vehicle control females in the relative length of time spent in the estrous stages. Dosed females spent more time in proestrus and less time in diestrus than the vehicle control females.

TABLE E3
Summary of Reproductive Tissue Evaluations for Male Mice in the 13-Week Gavage Study of Benzyltrimethylammonium Chloride^a

	Vehicle Control	25 mg/kg	50 mg/kg	100 mg/kg
n	10	10	9	9
Weights (g)				
Necropsy body wt	34.9 ± 0.7	34.5 ± 0.6	35.5 ± 0.7	33.9 ± 0.9
L. Cauda epididymis	0.0175 ± 0.0008	0.0167 ± 0.0010	0.0173 ± 0.0010	0.0174 ± 0.0009
L. Epididymis	0.0503 ± 0.0016	0.0470 ± 0.0016	0.0514 ± 0.0020	0.0486 ± 0.0015
L. Testis	0.1106 ± 0.0044	0.1150 ± 0.0033	0.1180 ± 0.0052	0.1184 ± 0.0034
Spermatid measurements				
Spermatid heads (10 ⁷ /g testis)	15.90 ± 0.34	14.83 ± 0.44	14.25 ± 0.35*	15.10 ± 0.49
Spermatid heads (10 ⁷ /testis)	1.76 ± 0.09	1.70 ± 0.05	1.69 ± 0.09	1.78 ± 0.07
Spermatid count (mean/10 ⁻⁴ mL suspension)	55.10 ± 2.76	53.05 ± 1.47	52.64 ± 2.75	55.78 ± 2.13
Epididymal spermatozoal measurements				
Motility (%)	88.75 ± 0.31	88.42 ± 0.52 ^b	88.92 ± 0.54	87.82 ± 0.40
Concentration (10 ⁶ /g cauda epididymal tissue)	914 ± 55	925 ± 71	796 ± 117	856 ± 57

* Significantly different ($P \leq 0.05$) from the vehicle control group by Dunnett's test

^a Data are presented as mean ± standard error. Differences from the vehicle control group are not significant by Dunnett's test (tissue weights) or Dunn's test (spermatid heads per testis, spermatid count, and epididymal spermatozoal measurements).

^b n = 9

TABLE E4
Estrous Cycle Characterization for Female Mice in the 13-Week Gavage Study of Benzyltrimethylammonium Chloride^a

	Vehicle Control	25 mg/kg	50 mg/kg	100 mg/kg
n	10	10	10	9
Necropsy body wt (g)	29.1 ± 1.0	28.7 ± 0.9	29.2 ± 1.3	28.2 ± 0.9
Estrous cycle length (days)	4.00 ± 0.00 ^b	4.30 ± 0.13	4.61 ± 0.44 ^c	4.17 ± 0.12
Estrous stages (% of cycle)				
Diestrus	40.0	32.5	36.7	27.8
Proestrus	16.7	17.5	15.8	17.6
Estrus	22.5	29.2	26.7	30.6
Metestrus	20.8	20.8	20.8	24.1

^a Necropsy body weight and estrous cycle length data are presented as mean ± standard error. Differences from the vehicle control group are not significant by Dunnett's test (necropsy body weight) or Dunn's test (estrous cycle length). By multivariate analysis of variance, dosed females do not differ significantly from the vehicle control females in relative length of time spent in the estrous stages.

^b Estrous cycle was longer than 12 days or unclear in 3 of 10 animals.

^c Estrous cycle was longer than 12 days or unclear in 1 of 10 animals.

APPENDIX F

GENETIC TOXICOLOGY

TABLE F1	Mutagenicity of Benzyltrimethylammonium Chloride in <i>Salmonella typhimurium</i>	F-2
TABLE F2	Frequency of Micronuclei in Peripheral Blood Erythrocytes of Mice Following Treatment with Benzyltrimethylammonium Chloride by Gavage for 13 Weeks	F-3

TABLE F1
Mutagenicity of Benzyltrimethylammonium Chloride in *Salmonella typhimurium*^a

Strain	Dose ($\mu\text{g}/\text{plate}$)	Revertants/plate ^b					
		-S9		+ hamster S9		+ rat S9	
		Trial 1	Trial 2	10%	30%	10%	30%
TA100	0	122 \pm 8.2	122 \pm 9.2	116 \pm 7.0	119 \pm 11.0	84 \pm 6.6	147 \pm 9.6
	100	119 \pm 12.7	128 \pm 3.7	102 \pm 1.2	130 \pm 4.9	105 \pm 7.1	128 \pm 7.1
	333	115 \pm 6.9	118 \pm 14.2	110 \pm 3.5	115 \pm 9.0	89 \pm 6.9	128 \pm 3.4
	1,000	116 \pm 11.7	116 \pm 8.2	107 \pm 8.1	113 \pm 5.7	104 \pm 8.7	136 \pm 2.5
	3,333	121 \pm 9.0 ^c	122 \pm 2.4	99 \pm 3.0	135 \pm 2.9 ^c	102 \pm 8.7	138 \pm 3.8
	10,000	65 \pm 3.7 ^c	104 \pm 4.4 ^c	103 \pm 13.5 ^c	109 \pm 6.4 ^c	91 \pm 7.8	113 \pm 7.2 ^c
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control ^d		1,389 \pm 22.6	1,485 \pm 4.8	1,125 \pm 21.5	2,231 \pm 35.7	1,883 \pm 33.0	702 \pm 16.7
TA1535	0	31 \pm 3.0	29 \pm 0.9	9 \pm 0.9	14 \pm 0.9	9 \pm 1.7	12 \pm 2.3
	100	29 \pm 0.7	30 \pm 1.0	11 \pm 3.8	8 \pm 1.0	10 \pm 1.9	13 \pm 0.0
	333	25 \pm 0.9	26 \pm 4.4	13 \pm 2.3	12 \pm 1.5	10 \pm 1.5	15 \pm 2.0
	1,000	28 \pm 1.5	37 \pm 2.2	9 \pm 1.2	10 \pm 1.7	11 \pm 0.7	11 \pm 0.7
	3,333	28 \pm 3.0 ^c	27 \pm 2.7	9 \pm 0.9	12 \pm 3.5	9 \pm 3.8	13 \pm 1.2
	10,000	22 \pm 4.8 ^c	21 \pm 1.5 ^c	9 \pm 1.5 ^c	12 \pm 0.6	11 \pm 1.5 ^c	11 \pm 2.3
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control		1,051 \pm 8.7	1,095 \pm 18.9	127 \pm 9.0	323 \pm 17.8	117 \pm 5.0	130 \pm 13.9
TA97	0	104 \pm 8.4	121 \pm 3.5	140 \pm 4.1	170 \pm 8.8	113 \pm 9.7	181 \pm 5.5
	100	113 \pm 7.0	110 \pm 7.4	143 \pm 0.3	158 \pm 8.8	126 \pm 12.1	181 \pm 4.2
	333	99 \pm 0.9	114 \pm 3.6	144 \pm 8.0	156 \pm 1.9	124 \pm 3.5	155 \pm 9.2
	1,000	112 \pm 8.3	128 \pm 5.5	139 \pm 6.9	165 \pm 6.1	133 \pm 5.3	168 \pm 11.1
	3,333	95 \pm 2.1 ^c	128 \pm 2.9	130 \pm 7.1	152 \pm 6.0 ^c	129 \pm 2.2	167 \pm 6.4
	10,000	92 \pm 5.2 ^c	100 \pm 5.6 ^c	131 \pm 2.2 ^c	172 \pm 7.8 ^c	110 \pm 4.6 ^c	174 \pm 12.8
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control		1,626 \pm 161.0	722 \pm 9.3	511 \pm 17.2	1,452 \pm 23.1	763 \pm 36.3	691 \pm 13.3
TA98	0	19 \pm 4.1	16 \pm 0.6	39 \pm 2.6	35 \pm 2.7	32 \pm 5.5	31 \pm 5.8
	100	14 \pm 1.5	14 \pm 1.7	37 \pm 3.4	27 \pm 4.4	31 \pm 1.2	29 \pm 0.9
	333	16 \pm 2.1	19 \pm 4.1	32 \pm 3.2	31 \pm 2.8	30 \pm 1.3	34 \pm 2.6
	1,000	17 \pm 2.0	17 \pm 2.4	36 \pm 2.1	34 \pm 1.2	35 \pm 1.7	30 \pm 5.8
	3,333	19 \pm 1.2 ^c	16 \pm 1.5	33 \pm 5.5	30 \pm 3.5	38 \pm 2.2	35 \pm 2.2
	10,000	14 \pm 1.0 ^c	19 \pm 3.5 ^c	34 \pm 1.2	28 \pm 1.8	31 \pm 3.8	36 \pm 1.7 ^c
Trial summary		Negative	Negative	Negative	Negative	Negative	Negative
Positive control		1,246 \pm 69.5	1,848 \pm 57.8	1,205 \pm 26.9	2,210 \pm 28.6	1,401 \pm 30.6	659 \pm 32.9

^a Study was performed at Microbiological Associates, Inc. The detailed protocol and these data are presented in Zeiger *et al.* (1988).
0 $\mu\text{g}/\text{plate}$ was the solvent control.

^b Revertants are presented as mean \pm standard error from three plates.

^c Slight toxicity

^d The positive controls in the absence of metabolic activation were sodium azide (TA100 and TA1535), 9-aminoacridine (TA97), and 4-nitro-*o*-phenylenediamine (TA98). The positive control for metabolic activation with all strains was 2-aminoanthracene.

TABLE F2
Frequency of Micronuclei in Peripheral Blood Erythrocytes of Mice Following Treatment with Benzyltrimethylammonium Chloride by Gavage for 13 Weeks^a

Compound	Dose (mg/kg)	Number of Mice with Erythrocytes Scored	Micronucleated NCEs/1,000 NCEs ^b	Pairwise P Value ^c
Male				
Water ^d		10	3.7 ± 0.6	
Benzyltrimethylammonium chloride	12.5	10	2.5 ± 0.5	0.937
	25	10	2.8 ± 0.6	0.868
	50	10	5.2 ± 0.9	0.056
	100	9	6.6 ± 1.1	0.003
			P ≤ 0.001 ^e	
Female				
Water		10	2.0 ± 0.3	
Benzyltrimethylammonium chloride	12.5	10	2.5 ± 0.6	0.228
	25	10	3.0 ± 0.3	0.078
	50	10	3.9 ± 0.3	0.007
	100	9	6.4 ± 0.6	0.000
			P ≤ 0.001	

^a Study was performed at Integrated Laboratory Systems. The detailed protocol is presented in MacGregor *et al.* (1990).

NCE = normochromatic erythrocyte

^b Mean ± standard error

^c Pairwise comparison to solvent control; significant at P ≤ 0.006 (ILS, 1990)

^d Solvent control

^e Significance of micronucleated NCEs/1,000 NCEs tested by the one-tailed trend test, significant at P ≤ 0.025 (ILS, 1990)

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TOX No.	Chemical	TOX No.	Chemical
1	Hexachloro-1,3-butadiene	28	Tetrachlorophthalic Anhydride
2	<i>n</i> -Hexane	29	Cupric Sulfate
3	Acetone	30	Dibutyl Phthalate
4	1,2-Dichloroethane	31	Isoprene
5	Cobalt Sulfate Heptahydrate	32	Methylene Bis(thiocyanate)
6	Pentachlorobenzene	33	2-Chloronitrobenzene and 4-Chloronitrobenzene
7	1,2,4,5-Tetrachlorobenzene	34	1-Nitropyrene
8	D & C Yellow No. 11	35	Chemical Mixture of 25 Groundwater Contaminants
9	<i>o</i> -Cresol, <i>m</i> -Cresol, and <i>p</i> -Cresol	36	Pesticide/Fertilizer Mixtures
10	Ethylbenzene	37	Sodium Cyanide
11	Antimony Potassium Tartrate	38	Sodium Selenate and Sodium Selenite
12	Castor Oil	39	Cadmium Oxide
13	Trinitrofluorenone	40	β -Bromo- β -nitrostyrene
14	<i>p</i> -Chloro- α,α,α -trifluorotoluene	42	1,3-Diphenylguanidine
15	<i>t</i> -Butyl Perbenzoate	43	<i>o</i> -, <i>m</i> -, and <i>p</i> -Chloroaniline
16	Glyphosate	44	<i>o</i> -Nitrotoluene and <i>o</i> -Toluidine Hydrochloride
17	Black Newsprint Ink	45	Halogenated Ethanes
18	Methyl Ethyl Ketone Peroxide	50	Cyclohexanone Oxime
19	Formic Acid	51	Methyl Ethyl Ketoxime
20	Diethanolamine	52	Urethane
21	2-Hydroxy-4-methoxybenzophenone	53	<i>t</i> -Butyl Alcohol
22	N, N-Dimethylformamide	54	1,4-Butanediol
23	<i>o</i> -Nitrotoluene, <i>m</i> -Nitrotoluene, and <i>p</i> -Nitrotoluene	58	60-Hz Magnetic Fields
24	1,6-Hexanediamine	59	Chloral Hydrate
25	Glutaraldehyde	65	3,3',4,4'-Tetrachloroazobenzene
26	Ethylene Glycol Ethers	66	3,3',4,4'-Tetrachloroazoxybenzene
27	Riddelliine		