- *The information presented here is preliminary and did not undergo NTP quality assurance examination. Moreover the pathology portion of this study has not yet been peer-reviewed by the NTP Pathology Working Group.*

13-WEEK DRINKING WATER TOXICITY STUDY OF SODIUM DICHROMATE DIHYDRATE IN F344 RATS AND B6C3F$_1$ MICE*

Summary of study design:

Groups of 10 male and 10 female F344 rats and of B6C3F$_1$ mice received concentrations of 0, 62.5, 125, 250, 500, or 1000 mg of sodium dichromate dihydrate / liter in their drinking water for 13 weeks. Additional groups of 10 rats of each sex were dosed similarly and used for hematology and clinical pathology studies. Water and compound consumption, survival, body and organ weights, hematology, clinical pathology and histopathology data were collected.

Rat Study Results

Water and compound consumption:

Water consumption by male and female rats decreased with increasing sodium dichromate concentration in the drinking water (Figure 1). Based on water consumption, the mean effective dose received by rats was 0, 4.7, 8.8, 16.7, 31.6, or 60.4, and 0, 5.3, 9.9, 17.8, 33.0, or 61.4 mg per kg body weight per day for males and females, respectively. Theses doses correspond to 0, 1.6, 3.1, 5.8, 11.0, or 21.1 and 0, 1.8, 3.5, 6.2, 11.5, or 21.4 mg chromium per kg body weight per day for males and females.

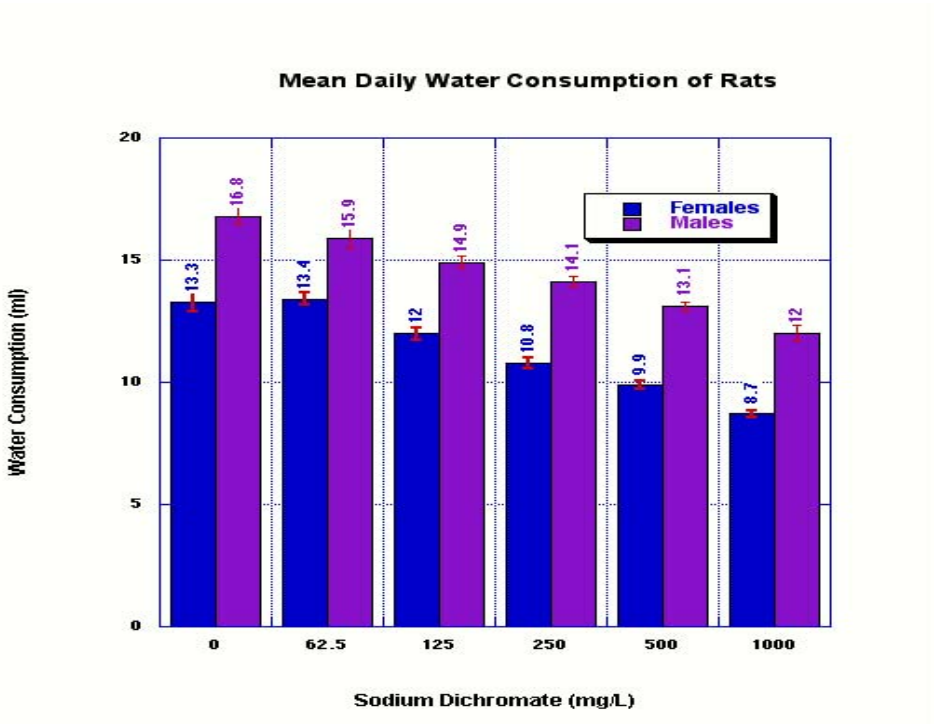
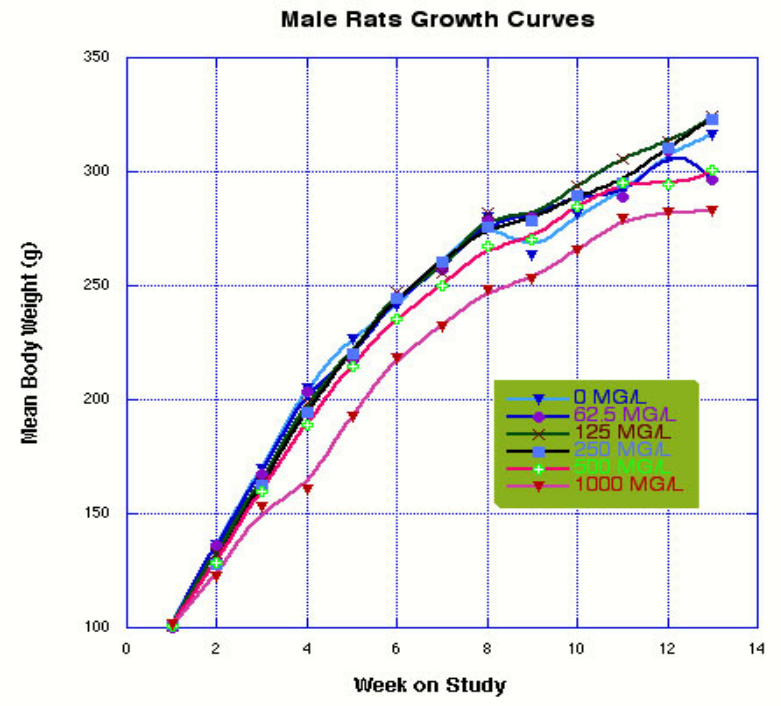


Figure 1

Survival, body weights, and relative organ weights:

All rats survived until the end of the study. The mean body weight of the highest dose group of rats was lower than that of the controls throughout the study period (Figure 2). The reduction in body weight was attributed to decreased water consumption. A significant ($p \leq 0.05$) reduction occurred in the relative weights of liver for male rats in the 500 and 1000 mg/L dose groups and spleen of male rats in the 250 and 500 mg/L dose groups. Significant increases were observed in the relative weights of testis (1000 mg/L), spleen (500, and 1000 mg/L female rats) and kidney of all dosed groups of female rats (Table 1).


Male Rats Growth Curves
Mean Body Weight (g)
Week on Study
0 MG/L
62.5 MG/L
125 MG/L
250 MG/L
500 MG/L
1000 MG/L

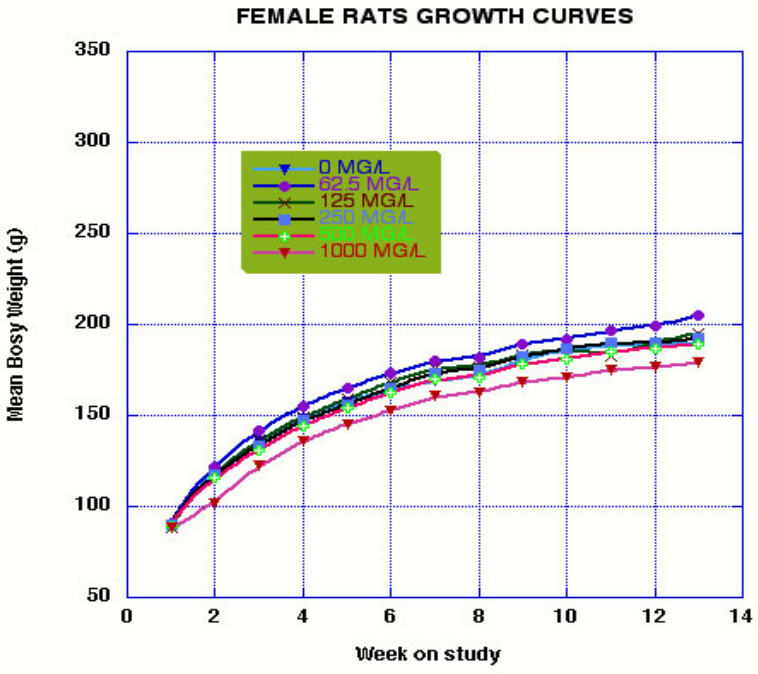

FEMALE RATS GROWTH CURVES
Mean Bosy Weight (g)
Week on study
0 MG/L
62.5 MG/L
125 MG/L
250 MG/L
500 MG/L
1000 MG/L

Figure 2

Table 1: Organ Weights and Organ-Weight-to-Body-Weight Ratios for Rats in the 13-Week Drinking Water Study of Sodium Dichromate Dihydrate[a]

	Vehicle Control	62.5 mg/L	125 mg/L	250 mg/L	500 mg/L	1,000 mg/L
n	10	10	10	10	10	10
Male						
Necropsy body wt	330 ± 8	322 ± 4	337 ± 6	330 ± 4	316 ± 3	298 ± 5**
Heart						
Absolute	0.862 ± 0.021	0.771 ± 0.028*	0.850 ± 0.020	0.867 ± 0.027	0.797 ± 0.010	0.836 ± 0.022
Relative	2.610 ± 0.024	2.392 ± 0.082*	2.526 ± 0.037	2.629 ± 0.070	2.526 ± 0.033	2.805 ± 0.058
R. Kidney						
Absolute	1.025 ± 0.025	1.014 ± 0.022	1.089 ± 0.025	1.022 ± 0.017	0.984 ± 0.011	0.964 ± 0.019
Relative	3.105 ± 0.038	3.145 ± 0.055	3.239 ± 0.066	3.103 ± 0.048	3.117 ± 0.026	3.234 ± 0.025
Liver						
Absolute	10.894 ± 0.417	10.297 ± 0.278	11.449 ± 0.377	10.508 ± 0.178	9.197 ± 0.166**	8.881 ± 0.184**
Relative	32.911 ± 0.650	31.911 ± 0.608	33.981 ± 0.749	31.904 ± 0.539	29.145 ± 0.533**	29.799 ± 0.351**
Lung[b]						
Absolute	1.349 ± 0.045	1.280 ± 0.032	1.441 ± 0.053	1.321 ± 0.045	1.223 ± 0.033[b]	1.191 ± 0.035*
Relative	4.080 ± 0.073	3.968 ± 0.072	4.276 ± 0.114	4.004 ± 0.115	3.857 ± 0.109	3.998 ± 0.102
Spleen						
Absolute	0.639 ± 0.018	0.596 ± 0.014	0.616 ± 0.015	0.596 ± 0.019	0.533 ± 0.008**	0.597 ± 0.012**
Relative	1.935 ± 0.031	1.848 ± 0.030	1.832 ± 0.036	1.806 ± 0.045*	1.689 ± 0.022**	2.004 ± 0.025
R. Testis						
Absolute	1.316 ± 0.034	1.342 ± 0.034	1.367 ± 0.045	1.369 ± 0.014	1.236 ± 0.038	1.351 ± 0.027
Relative	3.994 ± 0.103	4.158 ± 0.077	4.066 ± 0.120	4.157 ± 0.031	3.917 ± 0.122	4.536 ± 0.064**
Thymus						
Absolute	0.231 ± 0.008	0.224 ± 0.016	0.244 ± 0.013	0.248 ± 0.015	0.196 ± 0.006	0.217 ± 0.011
Relative	0.701 ± 0.029	0.694 ± 0.045	0.723 ± 0.031	0.750 ± 0.043	0.622 ± 0.021	0.727 ± 0.033
Female						
Necropsy body wt	193 ± 3	215 ± 3	199 ± 2	199 ± 2	193 ± 3	185 ± 2
Heart						
Absolute	0.573 ± 0.012	0.607 ± 0.006	0.587 ± 0.011	0.570 ± 0.015	0.570 ± 0.013	0.563 ± 0.014
Relative	2.973 ± 0.036	2.829 ± 0.041	2.946 ± 0.048	2.872 ± 0.071	2.954 ± 0.038	3.045 ± 0.057
R. Kidney						
Absolute	0.641 ± 0.020	0.712 ± 0.011*	0.708 ± 0.012*	0.705 ± 0.016	0.692 ± 0.026	0.671 ± 0.019
Relative	3.328 ± 0.091	3.315 ± 0.035	3.553 ± 0.046*	3.552 ± 0.073*	3.582 ± 0.102*	3.630 ± 0.087**
Liver						
Absolute	5.751 ± 0.130	6.028 ± 0.157	5.954 ± 0.145	5.978 ± 0.121	5.623 ± 0.195	5.599 ± 0.176
Relative	29.839 ± 0.421	28.076 ± 0.728	29.880 ± 0.661	30.117 ± 0.503	29.130 ± 0.791	30.249 ± 0.688
Lung						
Absolute	0.957 ± 0.037	0.979 ± 0.019	1.007 ± 0.035	0.947 ± 0.043	0.957 ± 0.017	0.858 ± 0.015
Relative	4.961 ± 0.153	4.561 ± 0.094	5.058 ± 0.190	4.767 ± 0.199	4.968 ± 0.094	4.645 ± 0.081
Spleen						
Absolute	0.408 ± 0.010	0.438 ± 0.009	0.431 ± 0.009	0.441 ± 0.007	0.435 ± 0.014	0.441 ± 0.005
Relative	2.120 ± 0.053	2.038 ± 0.027	2.164 ± 0.048	2.222 ± 0.026	2.253 ± 0.051*	2.387 ± 0.027**
Thymus						
Absolute	0.209 ± 0.009	0.216 ± 0.009	0.230 ± 0.007	0.219 ± 0.007	0.210 ± 0.007	0.203 ± 0.011
Relative	1.081 ± 0.040	1.005 ± 0.039	1.154 ± 0.028	1.102 ± 0.029	1.088 ± 0.033	1.100 ± 0.058

* Significantly different (P≤0.05) from the control group by Williams' or Dunnett's test

** P≤0.01

[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).

[b] n=9 for the 500 mg/L group

Clinical PathologyFindings:

The hematology, clinical chemistry and urinalysis data for rats are shown in Tables 2, 3, 4 and 5. Administration of sodium dichromate dihydrate was associated with multiple hematologic changes (erythrocyte microcytosis, hypochromasia, anemia, and RBC morphology changes) that were consistent with iron deficiency and/or RBC oxidative damage. The incidence and severity of abnormal erythrocyte morphology findings (e.g., RBC fragments, keratocytes and eccentrocytes, and poikilocytes), as well as hypochromia and microcytosis, were increased in sodium dichromate dihydrate-treated rats of both sexes. Reductions in erythrocyte MCV, % reticulocyte, and reticulocyte counts, and increases in platelet counts were also observed on Day 5 for rats in all groups except the 62.5 mg/L dose group. Mild increases in WBC, neutrophil, and monocyte counts for rats in the 1000 mg/L dose group on Days 5, 23, or 93 were also considered to be related to sodium dichromate dihydrate administration and were consistent with the microscopic lesions (ulceration and inflammation) observed in the forestomach and glandular stomach. An increase in both the incidence and the severity of abnormal RBC morphology findings was observed for rats of both sexes in the higher dose groups at all time points and in rats in lower dose groups on Day 23. These abnormal findings included the presence of keratocytes, RBC fragments, and poikilocytes. The severity of these changes appeared to be lower in rats sacrificed on Day 93 than in rats sacrificed on Day 23. Treatment-related clinical chemistry findings included increases in group mean BUN values for female rats in the 500 and 1000 mg/L dose groups, decreases in group mean total protein and albumin values for rats of both sexes in the 1000 mg/L dose group, and decreases in group mean triglyceride values for rats in the 1000 mg/L dose group. All three of these changes were probably related to the decreases in water consumption observed at the higher doses and the accompanying reductions in body weight gain. Minimal to mild elevations in group mean ALT activity were observed for rats of both sexes in all dose groups and were considered to be potentially compound-related. Decreases in mean urine volumes and increases in mean specific gravity and urine creatinine were observed for rats in the sodium dichromate dihydrate-treated groups, and were consistent with the decreases in water consumption for rats in these dose groups.

Table 2: Hematology Data for Male Rats in the 13-Week Drinking Water Study of Sodium Dichromate Dihydrate

	0 mg/L	62.5 mg/L	125 mg/L	250 mg/L	500 mg/L	1,000 mg/L
n						
Day 5	10	10	10	10	10	10
Day 23	10	10	10	10	10	10
Day 93	10	10	10	10	10	10
Hematocrit (%)						
Day 5	45.8 ± 1.0	45.0 ± 0.8	45.2 ± 0.9	43.8 ± 0.8	44.6 ± 0.6	46.2 ± 0.7
Day 23	48.5 ± 0.7	45.0 ± 1.0*	34.3 ± 1.8**	28.0 ± 1.4**	24.3 ± 0.9**	21.1 ± 1.6**
Day 93	46.0 ± 0.3	45.5 ± 0.4	45.3 ± 0.3	44.9 ± 0.7	43.1 ± 0.5**	30.8 ± 1.9**
Hematocrit (spun) (%)						
Day 5	45.6 ± 1.1	45.1 ± 0.7	45.0 ± 0.8	44.0 ± 0.8	44.5 ± 0.6	45.9 ± 0.7
Day 23	48.0 ± 0.5	44.7 ± 0.7**	39.8 ± 0.8**	36.2 ± 1.0**	34.4 ± 0.5**	32.3 ± 1.1**
Day 93	45.7 ± 0.2	45.2 ± 0.4	45.2 ± 0.3	44.8 ± 0.7	42.9 ± 0.4**	36.9 ± 0.8**
Hemoglobin (g/dL)						
Day 5	15.3 ± 0.4	15.0 ± 0.2	15.1 ± 0.3	14.9 ± 0.3	15.1 ± 0.2	15.7 ± 0.2
Day 23	15.9 ± 0.1	14.2 ± 0.2**	12.0 ± 0.3**	10.9 ± 0.3**	10.3 ± 0.3**	9.2 ± 0.3**
Day 93	15.3 ± 0.1	15.2 ± 0.1	15.0 ± 0.1	14.4 ± 0.2**	13.3 ± 0.2**	10.9 ± 0.3**
Erythrocytes (10^6/dL)						
Day 5	7.27 ± 0.17	7.30 ± 0.12	7.46 ± 0.14	7.36 ± 0.13	7.43 ± 0.10	7.70 ± 0.10
Day 23	7.94 ± 0.10	8.38 ± 0.11	7.13 ± 0.35*	6.03 ± 0.28**	5.25 ± 0.19**	4.54 ± 0.33**
Day 93	8.88 ± 0.05	9.04 ± 0.09*	9.25 ± 0.07**	10.15 ± 0.22**	10.87 ± 0.07**	8.52 ± 0.45**
Reticulocytes (10^5/dL)						
Day 5	6.25 ± 0.20	5.16 ± 0.12**	3.09 ± 0.18**	1.92 ± 0.24**	1.71 ± 0.25**	0.99 ± 0.11**
Day 23	2.57 ± 0.10	4.05 ± 0.14**	3.85 ± 0.34**	3.17 ± 0.17	2.68 ± 0.13	2.72 ± 0.24
Day 93	2.27 ± 0.03	2.36 ± 0.05	2.18 ± 0.06	2.37 ± 0.07	2.32 ± 0.09	3.10 ± 0.12**
Reticulocytes (%)						
Day 5	8.65 ± 0.39	7.07 ± 0.17**	4.15 ± 0.25**	2.60 ± 0.33**	2.30 ± 0.33**	1.27 ± 0.14**
Day 23	3.26 ± 0.15	4.83 ± 0.18**	5.38 ± 0.34**	5.29 ± 0.27**	5.16 ± 0.34**	6.00 ± 0.35**

Table 2 (continued): Hematology Data for Male Rats in the 13-Week Drinking Water Study of Sodium Dichromate Dihydrate[a]

	0 mg/L	62.5 mg/L	125 mg/L	250 mg/L	500 mg/L	1,000 mg/L
n						
Day 5	10	10	10	10	10	10
Day 23	10	10	10	10	10	10
Day 93	10	10	10	10	10	10
Day 93	2.56 ± 0.04	2.61 ± 0.05	2.36 ± 0.06	2.34 ± 0.05	2.13 ± 0.08**	3.79 ± 0.32
Nucleated erythrocytes/100 leukocytes						
Day 5	0.20 ± 0.13	0.30 ± 0.15	0.20 ± 0.13	0.30 ± 0.15	0.10 ± 0.10	0.40 ± 0.16
Day 23	0.00 ± 0.00	0.00 ± 0.00	0.70 ± 0.26**	1.30 ± 0.40**	1.90 ± 0.64**	2.70 ± 0.78**
Day 93	0.10 ± 0.10	0.30 ± 0.15	0.10 ± 0.10	0.10 ± 0.10	0.20 ± 0.13	1.20 ± 0.29**
Mean cell volume (fL)						
Day 5	63.1 ± 0.2	61.7 ± 0.2**	60.6 ± 0.2**	59.5 ± 0.2**	60.0 ± 0.2**	60.0 ± 0.3**
Day 23	61.1 ± 0.5	53.6 ± 0.6**	48.0 ± 0.4**	46.4 ± 0.6**	46.2 ± 0.3**	46.4 ± 0.5**
Day 93	51.8 ± 0.1	50.3 ± 0.2**	49.0 ± 0.1**	44.4 ± 1.0**	39.7 ± 0.5**	36.0 ± 0.4**
Mean cell hemoglobin (pg)						
Day 5	21.0 ± 0.1	20.5 ± 0.1**	20.3 ± 0.1**	20.3 ± 0.1**	20.4 ± 0.1**	20.4 ± 0.1**
Day 23	20.1 ± 0.2	16.9 ± 0.2**	17.2 ± 0.7**	18.2 ± 0.4	19.7 ± 0.3	20.7 ± 0.6
Day 93	17.3 ± 0.1	16.9 ± 0.1**	16.2 ± 0.1**	14.2 ± 0.4**	12.3 ± 0.2**	13.0 ± 0.5**
Mean cell hemoglobin concentration (g/dL)						
Day 5	33.3 ± 0.2	33.3 ± 0.2	33.5 ± 0.1	34.1 ± 0.1**	34.0 ± 0.1**	34.0 ± 0.1**
Day 23	32.9 ± 0.4	31.6 ± 0.3	35.9 ± 1.7	39.2 ± 0.9**	42.8 ± 0.7**	44.6 ± 1.3**
Day 93	33.4 ± 0.1	33.5 ± 0.1	33.1 ± 0.2	32.0 ± 0.2**	31.0 ± 0.2**	36.3 ± 1.8*
Platelets (10^3/dL)						
Day 5	913.6 ± 28.9	943.0 ± 21.7	1,084.0 ± 51.6**	1,222.2 ± 46.4**	1,239.0 ± 43.2**	1,286.8 ± 36.2**
Day 23	745.2 ± 22.2	1,065.3 ± 67.9**	2,768.6 ± 328.5**	3,504.7 ± 235.0**	4,226.0 ± 204.5**	4,688.8 ± 242.7**
Day 93	618.6 ± 20.0	736.1 ± 11.5**	604.3 ± 24.5	909.8 ± 119.1**	1,743.1 ± 178.0**	5,123.0 ± 638.9**
Platelet estimates (10^3/dL)						
Day 23	1,302.0 ± 68.9	1,537.2 ± 102.7	1,957.2 ± 106.2**	1,900.5 ± 170.3**	1,917.3 ± 83.7**	2,083.2 ± 158.5**
Day 93	676.2 ± 32.8	674.1 ± 25.3	636.3 ± 24.1	663.6 ± 21.5	678.3 ± 29.2	783.3 ± 28.5
Leukocytes (10^3/dL)						
Day 5	9.04 ± 0.29	9.26 ± 0.27	9.33 ± 0.39	9.84 ± 0.26*	9.24 ± 0.36	11.08 ± 0.17**
Day 23	10.37 ± 0.69	10.94 ± 0.58	11.11 ± 0.38	10.37 ± 0.74	11.91 ± 0.51	11.92 ± 0.56
Day 93	8.54 ± 0.28	9.38 ± 0.55	9.01 ± 0.46	9.49 ± 0.46	10.79 ± 0.52**	11.27 ± 0.80**
Segmented neutrophils (10^3/dL)						
Day 5	0.84 ± 0.02	0.91 ± 0.03*	0.93 ± 0.04	0.89 ± 0.03	0.88 ± 0.05	1.51 ± 0.14**
Day 23	0.86 ± 0.06	0.92 ± 0.06	0.92 ± 0.05	0.76 ± 0.08	0.83 ± 0.04	1.38 ± 0.15
Day 93	1.22 ± 0.04	1.41 ± 0.05*	1.30 ± 0.06	1.47 ± 0.09**	1.27 ± 0.03	2.21 ± 0.19**
Lymphocytes (10^3/dL)						
Day 5	7.81 ± 0.28	7.99 ± 0.26	8.04 ± 0.37	8.55 ± 0.22	7.96 ± 0.30	9.09 ± 0.19**
Day 23	9.15 ± 0.58	9.66 ± 0.50	9.85 ± 0.34	9.31 ± 0.64	10.73 ± 0.49	10.12 ± 0.47
Day 93	7.02 ± 0.26	7.62 ± 0.51	7.39 ± 0.44	7.67 ± 0.41	9.09 ± 0.51**	8.70 ± 0.67*
Monocytes (10^3/dL)						
Day 5	0.21 ± 0.01	0.20 ± 0.01	0.18 ± 0.01	0.19 ± 0.02	0.20 ± 0.02	0.26 ± 0.02
Day 23	0.17 ± 0.03	0.16 ± 0.02	0.17 ± 0.01	0.14 ± 0.02	0.17 ± 0.01	0.25 ± 0.03*
Day 93	0.13 ± 0.01	0.15 ± 0.02	0.14 ± 0.01	0.19 ± 0.02*	0.19 ± 0.02**	0.19 ± 0.02**
Basophils (10^3/dL)						
Day 5	0.054 ± 0.004	0.051 ± 0.003	0.055 ± 0.005	0.070 ± 0.006	0.055 ± 0.003	0.074 ± 0.003**
Day 23	0.054 ± 0.006	0.046 ± 0.005	0.040 ± 0.004	0.035 ± 0.005	0.047 ± 0.004	0.037 ± 0.003
Day 93	0.045 ± 0.009	0.045 ± 0.004	0.041 ± 0.005	0.035 ± 0.005	0.043 ± 0.005	0.036 ± 0.003
Eosinophils (10^3/dL)						
Day 5	0.03 ± 0.00	0.02 ± 0.00	0.02 ± 0.00	0.02 ± 0.00	0.02 ± 0.00	0.02 ± 0.00
Day 23	0.05 ± 0.01	0.04 ± 0.01	0.03 ± 0.00*	0.02 ± 0.00**	0.02 ± 0.00**	0.03 ± 0.00**
Day 93	0.08 ± 0.01	0.09 ± 0.01	0.08 ± 0.01	0.08 ± 0.01	0.09 ± 0.01	0.06 ± 0.01
Large unstained cells (10^3/dL)						
Day 5	0.107 ± 0.012	0.092 ± 0.006	0.104 ± 0.009	0.120 ± 0.009	0.119 ± 0.019	0.134 ± 0.017
Day 23	0.097 ± 0.017	0.112 ± 0.011	0.112 ± 0.011	0.101 ± 0.014	0.110 ± 0.012	0.108 ± 0.008
Day 93	0.058 ± 0.009	0.062 ± 0.008	0.058 ± 0.006	0.061 ± 0.006	0.100 ± 0.015**	0.077 ± 0.007*

* significant at P≤0.05
** significant at P≤0.01
[a] Mean ± standard error. Statistical tests were performed on unrounded data

Table 3: Clinical Chemistry Data for Male Rats in the 13-Week Drinking Water Study of Sodium Dichromate Dihydrate

	0 mg/L	62.5 mg/L	125 mg/L	250 mg/L	500 mg/L	1,000 mg/L
n						
Day 5	10	10	10	10	10	10
Day 23	10	10	10	10	10	10
Day 93	10	10	10	10	10	10
Urea nitrogen (mg/dL)						
Day 5	14.6 ± 0.5	13.7 ± 0.4	14.2 ± 0.3	14.9 ± 0.3	14.8 ± 0.2	13.7 ± 0.4
Day 23	14.0 ± 0.6	14.2 ± 0.4	14.8 ± 0.4	15.5 ± 0.4*	17.2 ± 0.4**	16.5 ± 0.9**
Day 93	14.7 ± 0.3	16.9 ± 0.8	17.3 ± 1.0	16.5 ± 0.8	20.2 ± 0.5**	14.9 ± 0.4
Creatinine (mg/dL)						
Day 5	0.53 ± 0.02	0.52 ± 0.01	0.51 ± 0.01	0.51 ± 0.01	0.50 ± 0.00	0.50 ± 0.00
Day 23	0.58 ± 0.01	0.53 ± 0.02	0.57 ± 0.02	0.53 ± 0.02	0.55 ± 0.02	0.51 ± 0.01**
Day 93	0.66 ± 0.02	0.60 ± 0.02	0.63 ± 0.02	0.67 ± 0.02	0.61 ± 0.02	0.59 ± 0.01*
Glucose (mg/dL)						
Day 5	146 ± 3	145 ± 3	147 ± 2	147 ± 3	143 ± 2	140 ± 2
Day 23	148 ± 6	145 ± 3	147 ± 3	153 ± 4	148 ± 4	149 ± 2
Day 93	155 ± 10	154 ± 7	155 ± 9	154 ± 8	141 ± 5	145 ± 5
Sodium (mEq/L)						
Day 5	146 ± 0	146 ± 1	147 ± 1	147 ± 0	148 ± 0**	150 ± 1**
Day 23	145 ± 1	145 ± 1	145 ± 1	145 ± 1	145 ± 1	145 ± 1
Day 93	155 ± 1	154 ± 1	155 ± 1	155 ± 1	155 ± 1	155 ± 1
Potassium (mEq/L)						
Day 5	7.0 ± 0.1	6.9 ± 0.1	7.1 ± 0.1	7.0 ± 0.1	6.7 ± 0.1	6.7 ± 0.1
Day 23	5.5 ± 0.2	5.4 ± 0.1	5.9 ± 0.2	5.8 ± 0.1	5.8 ± 0.2	5.8 ± 0.1
Day 93	5.1 ± 0.2	5.2 ± 0.2	5.4 ± 0.1	5.2 ± 0.2	5.5 ± 0.2	5.8 ± 0.1**
Chloride (mEq/L)						
Day 5	101 ± 0	101 ± 1	102 ± 0*	103 ± 0**	104 ± 0**	105 ± 0**
Day 23	99 ± 1	100 ± 1	100 ± 0	101 ± 1	100 ± 0	101 ± 1
Day 93	106 ± 1	107 ± 1	106 ± 1	108 ± 1	107 ± 1	109 ± 1
Calcium (mg/dL)						
Day 5	12.47 ± 0.10	12.42 ± 0.14	12.36 ± 0.08	11.98 ± 0.07**	11.99 ± 0.11**	11.90 ± 0.11**
Day 23	11.85 ± 0.07	11.82 ± 0.14	11.79 ± 0.12	11.81 ± 0.09	11.70 ± 0.09	11.90 ± 0.11
Day 93	11.67 ± 0.09	11.34 ± 0.09	11.65 ± 0.09	11.49 ± 0.09	11.35 ± 0.10	11.63 ± 0.08
Phosphorus (mg/dL)						
Day 5	11.5 ± 0.1	11.8 ± 0.1	11.8 ± 0.1	11.4 ± 0.1	11.6 ± 0.1	11.2 ± 0.1
Day 23	9.8 ± 0.4	9.5 ± 0.2	9.9 ± 0.2	10.1 ± 0.2	10.6 ± 0.3*	10.6 ± 0.1**
Day 93	6.5 ± 0.2	6.6 ± 0.3	6.3 ± 0.2	6.6 ± 0.3	6.4 ± 0.1	6.8 ± 0.3
Total protein (g/dL)						
Day 5	6.0 ± 0.1	5.9 ± 0.1	6.0 ± 0.1	5.9 ± 0.1	5.8 ± 0.1	5.7 ± 0.1*
Day 23	6.1 ± 0.1	5.9 ± 0.1*	6.1 ± 0.1	5.9 ± 0.1	5.9 ± 0.1*	5.8 ± 0.1**
Day 93	6.7 ± 0.1	6.5 ± 0.1	6.7 ± 0.0	6.6 ± 0.1	6.5 ± 0.1	6.4 ± 0.1
Albumin (g/dL)						
Day 5	3.9 ± 0.0	3.9 ± 0.0	3.9 ± 0.0	3.8 ± 0.0	3.8 ± 0.0	3.7 ± 0.0**
Day 23	4.0 ± 0.0	3.9 ± 0.0	3.9 ± 0.0	3.9 ± 0.0	3.9 ± 0.0	3.8 ± 0.0
Day 93	4.3 ± 0.0	4.3 ± 0.0	4.3 ± 0.0	4.4 ± 0.1	4.4 ± 0.0	4.3 ± 0.0
Cholesterol (mg/dL)						
Day 5	112 ± 3	106 ± 2	103 ± 2**	103 ± 1**	103 ± 2**	103 ± 3**
Day 23	86 ± 3	69 ± 2**	78 ± 2	76 ± 2	71 ± 1**	77 ± 2
Day 93	89 ± 2	95 ± 2	86 ± 4	65 ± 2**	86 ± 3*	71 ± 2**
Triglycerides (mg/dL)						
Day 5	119 ± 9	111 ± 11	110 ± 7	119 ± 6	109 ± 8	112 ± 10
Day 23	212 ± 12	168 ± 7**	191 ± 9	157 ± 16**	146 ± 7**	109 ± 7**
Day 93	170 ± 9	169 ± 8	172 ± 15	170 ± 13	164 ± 12	98 ± 8**
Alanine aminotransferase (IU/L)						
Day 5	48 ± 1	55 ± 2**	69 ± 2**	73 ± 3**	73 ± 3**	70 ± 2**
Day 23	44 ± 1	63 ± 5**	65 ± 2**	69 ± 2**	75 ± 3**	67 ± 3 **
Day 93	98 ± 6[b]	274 ± 30**	461 ± 102**	447 ± 121**	740 ± 81**	191 ± 17**

Table 3 (continued):Clinical Chemistry Data for Male Rats in the 13-Week Drinking Water Study of Sodium Dichromate Dihydrate

	0 mg/L	62.5 mg/L	125 mg/L	250 mg/L	500 mg/L	1,000 mg/L
n						
Day 5	10	10	10	10	10	10
Day 23	10	10	10	10	10	10
Day 93	10	10	10	10	10	10
Clinical Chemistry (continued)						
Alkaline phosphate (IU/L)						
Day 5	641 ± 11	620 ± 16	589 ± 9**	573 ± 10**	554 ± 15**	529 ± 12**
Day 23	442 ± 11	443 ± 13	421 ± 16	399 ± 5**	378 ± 8**	348 ± 19**
Day 93	181 ± 4	157 ± 6**	157 ± 3**	147 ± 3**	133 ± 4**	136 ± 4**
Creatine kinase (IU/L)						
Day 5	407 ± 23	434 ± 49	495 ± 30	486 ± 36	533 ± 43**	520 ± 21**
Day 23	586 ± 35	582 ± 62	663 ± 67	636 ± 74[b]	810 ± 73	656 ± 82
Day 93	214 ± 26	286 ± 32	291 ± 36	364 ± 23**	413 ± 16**	374 ± 44**
Sorbitol dehydrogenase (IU/L)						
Day 5	19 ± 1	20 ± 1	17 ± 1	18 ± 1	17 ± 1	17 ± 1
Day 23	20 ± 2	16 ± 1	16 ± 1	16 ± 2	16 ± 1	16 ± 1
Day 93	31 ± 2[b]	55 ± 5**	110 ± 24**	102 ± 24**	173 ± 20**	59 ± 6**
5.-Nucleotidase (IU/L)						
Day 5	40 ± 1	39 ± 1	38 ± 1	38 ± 1	37 ± 1*	33 ± 1**
Day 23	37 ± 2	33 ± 1	39 ± 2	38 ± 1	36 ± 1	39 ± 2
Day 93	42 ± 0	37 ± 1**	42 ± 1	40 ± 1	38 ± 1*	41 ± 1
Bile acids (µmol/L)						
Day 5	29.0 ± 1.6	25.9 ± 1.8	26.6 ± 1.6	32.1 ± 1.9	28.0 ± 1.7	26.5 ± 1.8
Day 23	23.4 ± 1.6	23.2 ± 2.4	29.1 ± 1.7	30.4 ± 3.1	29.8 ± 2.2	32.8 ± 1.6**
Day 93	22.0 ± 2.2	23.9 ± 3.4	34.5 ± 7.0	32.6 ± 5.3	45.3 ± 2.8**	28.1 ± 2.0**

* significant at P≤0.05
** significant at P≤0.01

Urinalysis						
n	10	10	10	10	10	9
Volume (mL/16 hr)	3.9 ± 0.4	3.5 ± 0.4	2.9 ± 0.5	3.0 ± 0.3	2.2 ± 0.2**	1.5 ± 0.2**
Specific gravity	1.047 ± 0.003	1.046 ± 0.003	1.059 ± 0.002**	1.058 ± 0.002**	1.063 ± 0.003**[b]	1.065 ± 0.005**
Creatinine (mg/dL)	85.20 ± 5.33	81.28 ± 7.84	100.32 ± 4.71	104.08 ± 4.72*	124.76 ± 5.13**	115.60 ± 10.24**
Glucose (mg/dL)	38 ± 3	32 ± 2	45 ± 4	43 ± 3	59 ± 3**	60 ± 6**
Glucose (mg/mg creatinine)	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	1 ± 0
Protein (mg/dL)	83 ± 15	88 ± 14	130 ± 16*	138 ± 13*	136 ± 11*	118 ± 14*
Protein (mg/mg creatinine)	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0	1 ± 0
Alkaline phosphatase (IU/L)	165 ± 18	136 ± 20	160 ± 12	155 ± 13	197 ± 16	172 ± 24
Alkaline phosphatase (IU/g creatinine)	195 ± 17	165 ± 12	159 ± 7	151 ± 14	158 ± 10	146 ± 11
Aspartate aminotransferase (IU/L)	6 ± 1[b]	5 ± 0	7 ± 1	8 ± 1*	12 ± 2**	12 ± 1**
Aspartate aminotransferase (IU/g creatinine)	7 ± 1[b]	7 ± 1	7 ± 1	8 ± 0	9 ± 1	10 ± 1**
N-acetyl-α-D-glucosaminidase (IU/L)	9 ± 1	10 ± 1	11 ± 0*	12 ± 1**	13 ± 1**	14 ± 1**
N-acetyl-α-D-glucosaminidase (IU/g creatinine)	11 ± 0	12 ± 1	12 ± 0	12 ± 1	11 ± 0	12 ± 1
pH	6.85 ± 0.11	6.80 ± 0.11	6.80 ± 0.08	7.05 ± 0.24	7.10 ± 0.13	7.33 ± 0.33

* significant at P≤0.05
** significant at P≤0.01

Table 4: Hematology Data for Female Rats in the 13-Week Drinking Water Study of Sodium Dichromate Dihydrate[a]

	0 mg/ L	62.5 mg/L	125 mg/L	250 mg/L	500 mg/L	1,000 mg/L
n						
Day 5	10	10	10	10	10	10
Day 23	10	9	8	9	10	9
Day 93	10	9	10	10	10	9
Hematocrit (%)						
Day 5	48.2 ± 1.3	48.4 ± 0.8	47.4 ± 1.3	46.8 ± 1.2	48.7 ± 0.6	48.5 ± 1.0
Day 23	47.7 ± 0.4	45.9 ± 0.9	35.2 ± 1.1**	29.6 ± 2.0**	24.1 ± 1.2**	19.5 ± 0.7**
Day 93	44.2 ± 0.3	45.8 ± 0.2	44.0 ± 0.2	42.8 ± 0.3*	42.8 ± 0.4*	38.4 ± 0.6**
Hematocrit (spun) (%)						
Day 5	47.8 ± 1.1	48.5 ± 0.8	47.2 ± 1.3	46.3 ± 1.3	48.3 ± 0.6	47.7 ± 1.0
Day 23	48.0 ± 0.4	46.6 ± 0.9	42.9 ± 0.8**	39.2 ±0.2**	42.6 ± 0.5**	38.3 ± 0.5 **
Hemoglobin (g/dL)						
Day 5	16.1 ± 0.4	16.2 ± 0.3	15.9 ± 0.4	15.7 ± 0.4	16.3 ± 0.2	16.4 ± 0.3
Day 23	15.9 ± 0.1	14.7 ± 0.3**	13.0 ± 0.3**	11.8 ± 0.3**	10.9 ± 0.2**	9.7 ± 0.2**
Day 93	15.2 ± 0.1	15.4 ± 0.1	14.9 ± 0.1	14.3 ± 0.1**	14.1 ± 0.2**	12.0 ± 0.2**
Erythrocytes (10^6/dL)						
Day 5	7.66 ± 0.21	7.77 ± 0.13	7.74 ± 0.20	7.68 ± 0.17	8.00 ± 0.08	8.03 ± 0.15
Day 23	7.82 ± 0.09	8.52 ± 0.14	7.22 ± 0.19	6.32 ± 0.36**	5.27 ± 0.23**	4.21 ± 0.16**
Day 93	8.30 ± 0.06	8.60 ± 0.05**	8.40 ± 0.04*	8.47 ± 0.04*	8.93 ± 0.11**	9.62 ± 0.10**
Reticulocytes (10^5/dL)						
Day 5	5.02 ± 0.18	4.27 ± 0.20*	3.30 ± 0.18**	2.22 ± 0.26**	2.37 ± 0.25**	1.23 ± 0.15**
Day 23	2.11 ± 0.09	2.71 ± 0.18	3.16 ± 0.27*	3.03 ± 0.26*	2.32 ± 0.18	2.19 ± 0.26
Day 93	1.69 ± 0.04	2.25 ± 0.08**	2.07 ± 0.04**	2.11 ± 0.07**	2.11 ± 0.07**	2.44 ± 0.18**
Reticulocytes (%)						
Day 5	6.61 ± 0.35	5.51 ± 0.23*	4.30 ± 0.24**	2.92 ± 0.34**	2.97 ± 0.33**	1.55 ± 0.20**
Day 23	2.72 ± 0.15	3.18 ± 0.23	4.40 ± 0.41**	4.78 ± 0.28**	4.43 ± 0.31**	5.10 ± 0.49**
Day 93	2.04 ± 0.05	2.60 ± 0.08**	2.47 ± 0.04*	2.51 ± 0.09**	2.37 ± 0.10	2.52 ± 0.17*
Nucleated erythrocytes/100 leukocytes						
Day 5	0.20 ± 0.13	0.30 ± 0.15	0.10 ± 0.10	0.10 ± 0.10	0.10 ± 0.10	0.00 ± 0.00
Day 23	0.00 ± 0.00	0.33 ± 0.24	0.38 ± 0.18	0.33 ± 0.17	0.40 ± 0.16	1.11 ± 0.39**
Day 93	0.30 ± 0.21	0.11 ± 0.11	0.40 ± 0.22	0.20 ± 0.20	0.00 ± 0.00	0.11 ± 0.11
Mean cell volume (fL)						
Day 5	63.0 ± 0.3	62.3 ± 0.3	61.2 ± 0.3**	60.8 ± 0.4**	60.9 ± 0.3**	60.4 ± 0.3**
Day 23	61.1 ± 0.4	53.9 ± 0.5**	48.8 ± 0.5**	46.6 ± 0.6**	45.7 ± 0.4**	46.5 ± 0.5**
Day 93	53.3 ± 0.1	53.3 ± 0.1	52.4 ± 0.2**	50.5 ± 0.3**	48.0 ± 0.9**	40.0 ± 0.7**
Mean cell hemoglobin (pg)						
Day 5	21.0 ± 0.1	20.8 ± 0.1	20.5 ± 0.1*	20.4 ± 0.1**	20.4 ± 0.1**	20.5 ± 0.1**
Day 23	20.4 ± 0.1	17.3 ± 0.2	18.0 ± 0.3	18.9 ± 0.7	21.0 ± 0.6	23.1 ± 0.5
Day 93	18.4 ± 0.1	17.9 ± 0.1**	17.8 ± 0.1**	16.9 ± 0.1**	15.9 ± 0.4**	12.5 ± 0.3**
Mean cell hemoglobin concentration (g/dL)						
Day 5	33.4 ± 0.2	33.4 ± 0.2	33.5 ± 0.2	33.6 ± 0.2	33.5 ± 0.2	33.9 ± 0.2
Day 23	33.3 ± 0.1	32.1 ± 0.1	37.0 ± 0.7*	40.8 ± 1.8**	45.8 ± 1.4**	49.6 ± 0.9**
Day 93	34.5 ± 0.1	33.7 ± 0.1**	33.9 ± 0.1**	33.5 ± 0.1**	33.0 ± 0.3**	31.2 ± 0.2**
Platelets (10^3/dL)						
Day 5	856.8 ± 36.4	872.1 ± 20.5	958.3 ± 34.2	1,045.8 ± 47.5*	1,003.3 ± 45.1*	1,002.1 ± 41.5*
Day 23	611.5 ± 43.7	1,156.3 ± 76.4**	2,808.8 ± 198.5**	3,295.0 ± 349.7**	4,318.4 ± 234.9**	5,132.8 ± 247.0**
Day 93	588.9 ± 17.1	605.8 ± 17.1	574.8 ± 21.3	528.2 ± 14.1	619.3 ± 55.4	1,524.9 ± 193.3**
Platelet estimates (10^3/dL)						
Day 23	1,404.9 ± 50.8	1,213.3 ± 43.4	1,433.8 ± 61.9	1,369.7 ± 61.6	1,364.6 ± 46.1	1,450.3 ± 70.1
Day 93	1,022.7±58.1	994.0 ± 55.0	997.5 ± 52.5	942.9 ± 42.5	858.9 ± 43.5	1,033.7 ± 79.9

Table 4 (continued): Hematology Data for Female Rats in the 13-Week Drinking Water Study of Sodium Dichromate Dihydrate[a]

	0 mg/ L	62.5 mg/L	125 mg/L	250 mg/L	500 mg/L	1,000 mg/L
n						
Day 5	10	10	10	10	10	10
Day 23	10	9	8	9	10	9
Day 93	10	9	10	10	10	9
Leukocytes (10^3/dL)						
Day 5	9.53 ± 0.46	9.36 ± 0.35	9.34 ± 0.37	9.50 ± 0.53	9.88 ± 0.48	10.00 ± 0.37
Day 23	9.66 ± 0.50	10.77 ± 0.42	12.07 ± 0.63*	11.17 ± 0.95*	11.76 ± 0.29*	12.01 ± 0.33**
Day 93	7.09 ± 0.45	7.16 ± 0.29	7.59 ± 0.25	7.25 ± 0.55	8.03 ± 0.40	10.91 ± 0.58**
Segmented neutrophils (10^3/dL)						
Day 5	0.94 ± 0.05	0.94 ± 0.05	0.97 ± 0.06	0.98 ± 0.06	1.00 ± 0.06	1.35 ± 0.08**
Day 23	0.98 ± 0.05	1.10 ± 0.07	0.98 ± 0.05	0.83 ± 0.10	0.81 ± 0.03	1.40 ± 0.08*
Day 93	1.26 ± 0.09	1.04 ± 0.04	1.23 ± 0.05	1.31 ± 0.11	1.47 ± 0.11	2.83 ± 0.22**
Lymphocytes (10^3/dL)						
Day 5	8.18 ± 0.38	8.04 ± 0.30	8.00 ± 0.33	8.13 ± 0.47	8.46 ± 0.41	8.15 ± 0.32
Day 23	8.32 ± 0.46	9.28 ± 0.36	10.65 ± 0.56**	9.96 ± 0.84*	10.57 ± 0.27**	10.16 ± 0.31**
Day 93	5.55 ± 0.37	5.81 ± 0.28	6.06 ± 0.23	5.63 ± 0.46	6.19 ± 0.32	7.60 ± 0.46*
Monocytes (10^3/dL)						
Day 5	0.22 ± 0.03	0.21 ± 0.02	0.20 ± 0.02	0.22 ± 0.02	0.23 ± 0.02	0.26 ± 0.01
Day 23	0.16 ± 0.01	0.18 ± 0.02	0.22 ± 0.02*	0.17 ± 0.02	0.18 ± 0.01	0.24 ± 0.02**
Day 93	0.12 ± 0.01	0.14 ± 0.01	0.14 ± 0.01	0.15 ± 0.01*	0.18 ± 0.02**	0.26 ± 0.02**
Basophils (10^3/dL)						
Day 5	0.063 ± 0.007	0.054 ± 0.006	0.054 ± 0.003	0.057 ± 0.005	0.063 ± 0.006	0.071 ± 0.009
Day 23	0.061 ± 0.005	0.054 ± 0.006	0.059 ± 0.005	0.044 ± 0.006	0.049 ± 0.004	0.050 ± 0.003
Day 93	0.034 ± 0.002	0.042 ± 0.003	0.047 ± 0.007	0.049 ± 0.010	0.049 ± 0.006	0.056 ± 0.008
Eosinophils (10^3/dL)						
Day 5	0.04 ± 0.01	0.03 ± 0.00	0.02 ± 0.00	0.03 ± 0.00	0.02 ± 0.00	0.03 ± 0.00
Day 23	0.06 ± 0.00	0.06 ± 0.00	0.05 ± 0.01*	0.05 ± 0.01	0.03 ± 0.00**	0.04 ± 0.01**
Day 93	0.06 ± 0.00	0.07 ± 0.01	0.05 ± 0.01	0.06 ± 0.01	0.06 ± 0.01	0.07 ± 0.01
Large unstained cells (10^3/dL)						
Day 5	0.100 ± 0.017	0.099 ± 0.008	0.084 ± 0.008	0.096 ± 0.010	0.101 ± 0.009	0.140 ± 0.011**
Day 23	0.081 ± 0.008	0.100 ± 0.009	0.110 ± 0.021	0.112 ± 0.014	0.119 ± 0.016*	0.123 ± 0.007**
Day 93	0.067 ± 0.006	0.066 ± 0.005	0.069 ± 0.005	0.070 ± 0.008	0.088 ± 0.008*	0.093 ± 0.013

* significant at P≤0.05
** significant at P≤0.01
[a] Mean ± standard error. Statistical tests were performed on unrounded data

Table 5: Clinical Chemistry Data for Female Rats in the 13-Week Drinking Water Study of Sodium Dichromate Dihydrate

	0 mg/ L	62.5 mg/L	125 mg/L	250 mg/L	500 mg/L	1,000 mg/L
n						
Day 5	10	10	10	10	10	10
Day 23	10	9	8	9	10	9
Day 93	10	10	10	10	10	10
Urea nitrogen (mg/dL)						
Day 5	13.2 ± 0.3	13.8 ± 0.4	13.9 ± 0.4	14.1 ± 0.4	14.9 ± 0.5**	15.1 ± 0.2**
Day 23	17.1 ± 0.4	17.6 ± 0.6	19.0 ± 1.3	18.6 ± 0.9	18.6 ± 0.5	18.2 ± 0.5
Day 93	16.4 ± 0.3	19.8 ± 0.6**	17.2 ± 0.4*	18.6 ± 0.6**	19.0 ± 0.7**	20.7 ± 0.8**
Creatinine (mg/dL)						
Day 5	0.51 ± 0.01	0.50 ± 0.00	0.50 ± 0.02	0.47 ± 0.02	0.48 ± 0.01	0.48 ± 0.02[b]
Day 23	0.57 ± 0.02	0.50 ± 0.02**	0.50 ± 0.00**	0.49 ± 0.01**	0.49 ± 0.01**	0.47 ± 0.02**
Day 93	0.55 ± 0.02	0.51 ± 0.02	0.53 ± 0.02	0.53 ± 0.02	0.54 ± 0.02	0.52 ± 0.01
Glucose (mg/dL)						
Day 5	146 ± 5	141 ± 4	145 ± 4	141 ± 6	135 ± 3	130 ± 5*
Day 23	149 ± 4	144 ± 6	146 ± 8	146 ± 6	149 ± 3	140 ± 3
Day 93	139 ± 6	134 ± 3	144 ± 7	152 ± 6	146 ± 7	144 ± 8
Sodium (mEq/L)						
Day 5	144 ± 1	144 ± 1	144 ± 1	145 ± 0	145 ± 0	146 ± 0
Day 23	147 ± 1	146 ± 1	147 ± 0	146 ± 1	146 ± 0	145 ± 1**
Day 93	147 ± 1	147 ± 0	145 ± 1	147 ± 1	148 ± 1	146 ± 1
Potassium (mEq/L)						
Day 5	6.4 ± 0.1	6.2 ± 0.2	6.4 ± 0.2	6.3 ± 0.2	6.5 ± 0.2	6.2 ± 0.2
Day 23	5.3 ± 0.1	5.5 ± 0.2	6.0 ± 0.1**	5.7 ± 0.2	5.6 ± 0.2	5.8 ± 0.1*
Day 93	4.7 ± 0.2	5.2 ± 0.1	5.0 ± 0.1	4.9 ± 0.1	5.0 ± 0.1	5.1 ± 0.1
Chloride (mEq/L)						
Day 5	100 ± 1	100 ± 0	101 ± 1	102 ± 1*	101 ± 0	102 ± 1**
Day 23	102 ± 1	102 ± 1	103 ± 1	103 ± 1	102 ± 0	103 ± 1
Day 93	102 ± 1	101 ± 0	100 ± 1	103 ± 1	103 ± 1	103 ± 1
Calcium (mg/dL)						
Day 5	12.89 ± 0.13	12.53 ± 0.12*	12.45 ± 0.13*	12.35 ± 0.20*	12.33 ± 0.15*	12.10 ± 0.09**
Day 23	12.03 ± 0.09	11.82 ± 0.14	11.81 ± 0.12	11.69 ± 0.10	11.76 ± 0.08	11.62 ± 0.10
Day 93	11.65 ± 0.10	11.46 ± 0.09	11.78 ± 0.08	11.46 ± 0.09	11.60 ± 0.10	11.30 ± 0.06
Phosphorus (mg/dL)						
Day 5	11.2 ± 0.2	10.9 ± 0.2	11.0 ± 0.2	11.1 ± 0.3	11.5 ± 0.2	10.4 ± 0.3
Day 23	8.9 ± 0.2	9.6 ± 0.3	9.5 ± 0.3	9.3 ± 0.3	10.0 ± 0.3**	10.0 ± 0.2**
Day 93	4.8 ± 0.3	5.7 ± 0.4	5.0 ± 0.3	4.1 ± 0.3	4.8 ± 0.4	5.5 ± 0.3
Total protein (g/dL)						
Day 5	5.9 ± 0.1	5.8 ± 0.1	5.7 ± 0.1	5.7 ± 0.1	5.7 ± 0.1	5.7 ± 0.0
Day 23	6.2 ± 0.1	6.1 ± 0.1	6.0 ± 0.2	5.9 ± 0.1*	5.9 ± 0.1*	5.7 ± 0.1**
Day 93	6.9 ± 0.1	6.5 ± 0.1**	6.9 ± 0.1	6.7 ± 0.1	6.7 ± 0.1	6.3 ± 0.1**
Albumin (g/dL)						
Day 5	3.9 ± 0.1	3.9 ± 0.0	3.9 ± 0.1	3.9 ± 0.1	3.9 ± 0.1	3.8 ± 0.0
Day 23	4.2 ± 0.1	4.1 ± 0.1	4.1 ± 0.1	4.0 ± 0.1*	4.1 ± 0.0	3.9 ± 0.0**
Day 93	4.8 ± 0.1	4.5 ± 0.0*	4.8 ± 0.1	4.7 ± 0.1	4.7 ± 0.1	4.4 ± 0.1**
Cholesterol (mg/dL)						
Day 5	106 ± 3	104 ± 4	98 ± 3	103 ± 3	104 ± 3	95 ± 4 Day
Day 23	87 ± 2	86 ± 2	79 ± 6	82 ± 4*	78 ± 1**	78 ± 3**
Day 93	95 ± 2	111 ± 4	94 ± 2	87 ± 2	83 ± 2*	79 ± 2**
Triglycerides (mg/dL)						
Day 5	110 ± 12	115 ± 8	102 ± 9	86 ± 6	99 ± 8	116 ± 14
Day 23	94 ± 12	89 ± 7	95 ± 10	85 ± 11	63 ± 5	78 ± 8
Day 93	139 ± 18	116 ± 10	98 ± 9	81 ± 4**	76 ± 7**	59 ± 6**
Alanine aminotransferase (IU/L)						
Day 5	43 ± 2	56 ± 2**	70 ± 3**	81 ± 1**	80 ± 2**	81 ± 3**
Day 23	33 ± 1	48 ± 4**	65 ± 4**	74 ± 4**	71 ± 2**	74 ± 3**
Day 93	64 ± 5	437 ± 68**	218 ± 27**	245 ± 30**	246 ± 37**	248 ± 22**

Table 5 (continued): Clinical Chemistry Data for Female Rats in the 13-Week Drinking Water Study of Sodium Dichromate Dihydrate

	0 mg/ L	62.5 mg/L	125 mg/L	250 mg/L	500 mg/L	1,000 mg/L
n						
Day 5	10	10	10	10	10	10
Day 23	10	9	8	9	10	9
Day 93	10	10	10	10	10	10
Alkaline phosphate (IU/L)						
Day 5	535 ± 14	494 ± 13*	477 ± 13**	453 ± 11**	452 ± 14**	410 ± 15**
Day 23	357 ± 6	329 ± 6*	318 ± 11**	297 ± 4**	287 ± 6**	237 ± 10**
Day 93	166 ± 5	196 ± 5	124 ± 3**	113 ± 3**	111 ± 2**	107 ± 4**
Creatine kinase (IU/L)						
Day 5	370 ± 36	442 ± 50	458 ± 28	536 ± 54*	540 ± 49*	544 ± 52*
Day 23	397 ± 45	436 ± 56	638 ± 110	530 ± 72	561 ± 70	549 ± 105
Day 93	197 ± 23	311 ± 94	265 ± 23	296 ± 24**	359 ± 23**	432 ± 48**
Sorbitol dehydrogenase (IU/L)						
Day 5	23 ± 1	20 ± 1	20 ± 1	19 ± 1	19 ± 2	19 ± 1
Day 23	19 ± 1	18 ± 1	16 ± 1	14 ± 1**	13 ± 1**	15 ± 1**
Day 93	22 ± 2	101 ± 17**	65 ± 10**	81 ± 13**	96 ± 20**	103 ± 12**
5.-Nucleotidase (IU/L)						
Day 5	42 ± 1	39 ± 1	38 ± 1	37 ± 1*	39 ± 2	35 ± 1**
Day 23	55 ± 2	53 ± 2	56 ± 2	53 ± 3	56 ± 2	53 ± 2
Day 93	43 ± 1	41 ± 1	42 ± 1	41 ± 1	44 ± 2	49 ± 1
Bile acids (umol/L)						
Day 5	21.5 ± 1.7	20.2 ± 1.6	21.0 ± 1.4	24.3 ± 1.8	21.8 ± 1.8	20.0 ± 1.4
Day 23	22.9 ± 1.7	23.4 ± 1.9	19.9 ± 1.6	27.5 ± 1.5	27.5 ± 1.5	26.9 ± 4.0
Day 93	19.7 ± 2.5	50.4 ± 6.0**	39.9 ± 4.3**	35.3 ± 3.5	45.3 ± 5.6**	38.7 ± 3.2*

* significant at P≤0.05
** significant at P≤0.01

Urinalysis

n	10	9	8	9	6	7
Volume (mL/16 hr)	2.7 ± 0.3	2.6 ± 0.3	1.9 ± 0.3	1.4 ± 0.2**	1.0 ± 0.2**[b]	0.8 ± 0.1**[b]
Specific gravity	1.054 ± 0.003	1.059 ± 0.004	1.082 ± 0.009**	1.079 ± 0.006**	1.092 ± 0.008**[b]	1.087 ± 0.010**[d]
Creatinine (mg/dL)	89.28 ± 6.33	88.93 ± 5.33	118.30 ± 8.44*	110.49 ± 5.36*	112.27 ± 11.34*	122.69 ± 8.816**
Glucose (mg/dL)	28 ± 2	30 ± 2	46 ± 4**	42 ± 2**	50 ± 5**[c]	52 ± 5**
Glucose (mg/mg creatinine)	0 ± 0	0 ± 0	0 ± 0*	0 ± 0**	0 ± 0**	0 ± 0**
Protein (mg/dL)	35 ± 3	37 ± 4	56 ± 6*	48 ± 4*	60 ± 9*[c]	59 ± 7**
Protein (mg/mg creatinine)	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0	0 ± 0
Alkaline phosphatase (IU/L)	104 ± 10	95 ± 10	114 ± 13	113 ± 9	100 ± 15[d]	94 ± 11[d]
Alkaline phosphatase (IU/g creatinine)	116 ± 7	113 ± 14	96 ± 9	102 ± 5	92 ± 14	79 ± 10*
Urinalysis						
n	10	9	8	9	6	7
Aspartate aminotransferase (IU/L)	7 ± 1	6 ± 1	7 ± 1	10 ± 1	12 ±1**[b]	11 ± 1**[d]
Aspartate aminotransferase (IU/g creatinine)	8 ± 1	7 ±1	6 ± 1	10 ± 2	10 ± 1	8 ± 1
N-acetyl-α-D-glucosaminidase (IU/L)	9 ± 1	9 ± 1[d]	13 ± 1**	12 ± 1**	12 ± 1**[d]	13 ± 1**[d]
N-acetyl-α-D-glucosaminidase (IU/g creatinine)	10 ± 0	11 ± 0[d]	11 ± 0	11 ± 1	11 ± 1	10 ± 1
pH	7.10 ± 0.16	7.06 ± 0.27	6.94 ± 0.15	7.17 ± 0.31	7.78 ± 0.31[b]	7.75 ± 0.38[d]

* Significantly different (P≤0.05) from the control group by Dunn's or Shirley's test
** P≤0.01
[a] Mean ± standard error. Statistical tests were performed on unrounded data.
[b] n=9
[c] n=7
[d] n=8

Pathology findings:

Results of the histopathological evaluation are summarized in Table 6. The principal site of toxicity for sodium dichromate dihydrate in rats was the stomach. This is consistent with the irritant and caustic properties of sodium dichromate dihydrate.

Gastric lesions of mild to moderate severity consisting of focal ulceration, occurred at the junction of the glandular and non-glandular stomach of all male and all female rats the 1000 mg/L dose groups. None was observed in the controls. Cystic degeneration of glands occurred in the stomach wall at the border of the areas of ulceration predominantly near the junction of the forestomach and glandular stomach. Mitotic figures were noted in the squamous and glandular epithelial cells near the areas of ulceration, and acanthosis was prominent in the squamous epithelium bordering the ulcer. A prominent mixed inflammatory response was noted in the stomach wall and was characterized by pronounced infiltration of eosinophils and proliferation of granulation tissue. This response extended from the base of the ulcer to near the serosal surface of the stomach. A statistically significant neutrophil leukocytosis that occurred in male and female rats in the 1000 mg /L dose group correlated well with the inflammatory lesions in the stomach wall.

Histiocytic hyperplasia of the pancreas was observed at increased incidence in rats receiving sodium dichromate dihydrate in the drinking water. The lesion was characterized by multiple foci of histiocytes and varying degrees of lymphoid hyperplasia.

Table 6: Lesion Incidence in Rats the 13-Week Drinking Water Study of Sodium Dichromate Dihydrate

Dose Group	Control	62.5 mg/L	125 mg/L	250 mg/L	500 mg/L	1000 mg/L
Male						
Glandular Stomach[a]	10	NE	NE	NE	10	10
Focal Ulceration[b]	0				0	6
Cystic Degeneration	0				0	8
Glands hyperplasia	0				0	2
Forestomach	10	NE	NE	NE	10	10
Epithelium, Hyperplasia	0				0	10
Ulcer	0				0	3
Lymph Node, Pancreatic	10	10	10	10	10	10
Histiocytic Hyperplasia	0	4	2	4	4	7
Ectasia	0	0	0	0	1	10
Female						
Glandular Stomach	10	NE	NE	NE	10	10
Focal Ulceration	0				0	10
Cystic Degeneration	0				0	10
Forestomach	10	NE	NE	NE	10	10
Epithelium, Hyperplasia	0				0	10
Pancreas	10	10	10	10	10	10
Histiocytic Hyperplasia	1	8	7	6	5	10

[a] Number of animals examined
[b] Number of animals with the lesion

Mouse Study Results

Water and compound consumption:

Water consumption of male and female mice decreased with the increase in sodium dichromate concentration in their drinking water (Figure 4). Based on water consumption, the mean effective dose received by mice was: 0, 9, 15, 26, 45, or 86, and 0, 9, 15, 27, 44, or 75 mg per kg body weight per day for males and females.

These doses correspond to 0, 3.1, 9.1, 15.7, or 30.0, and 0, 3.1, 9.4, 15.4, or 26.2 mg chromium per kg body weight per day for males and females.

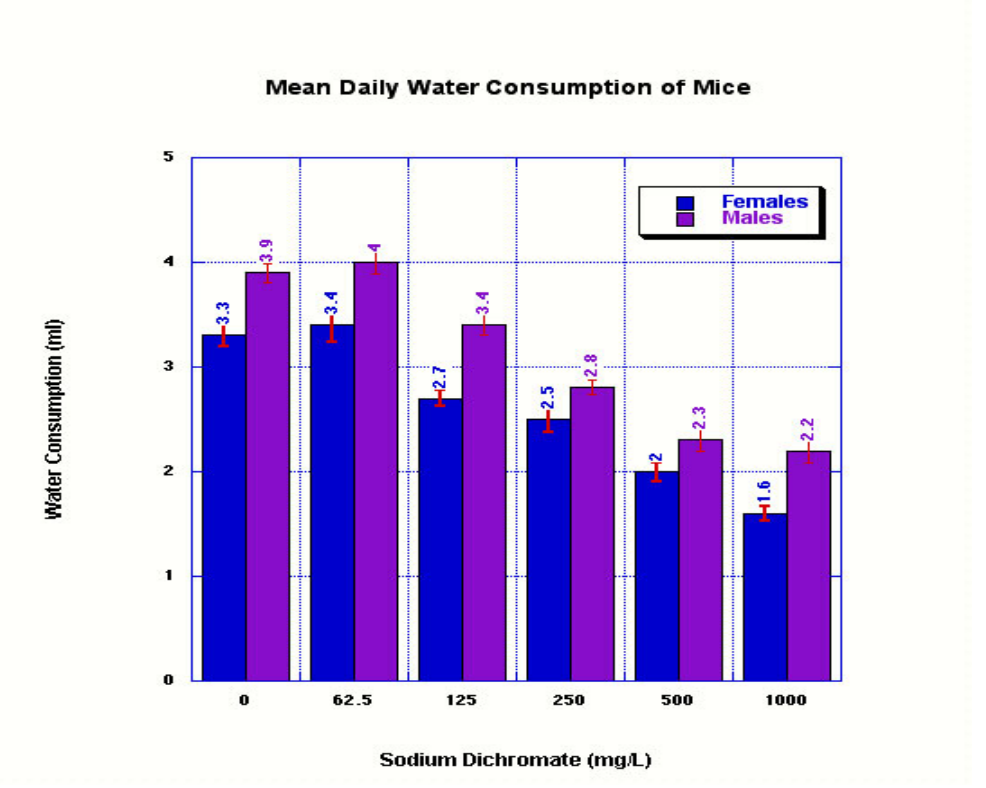
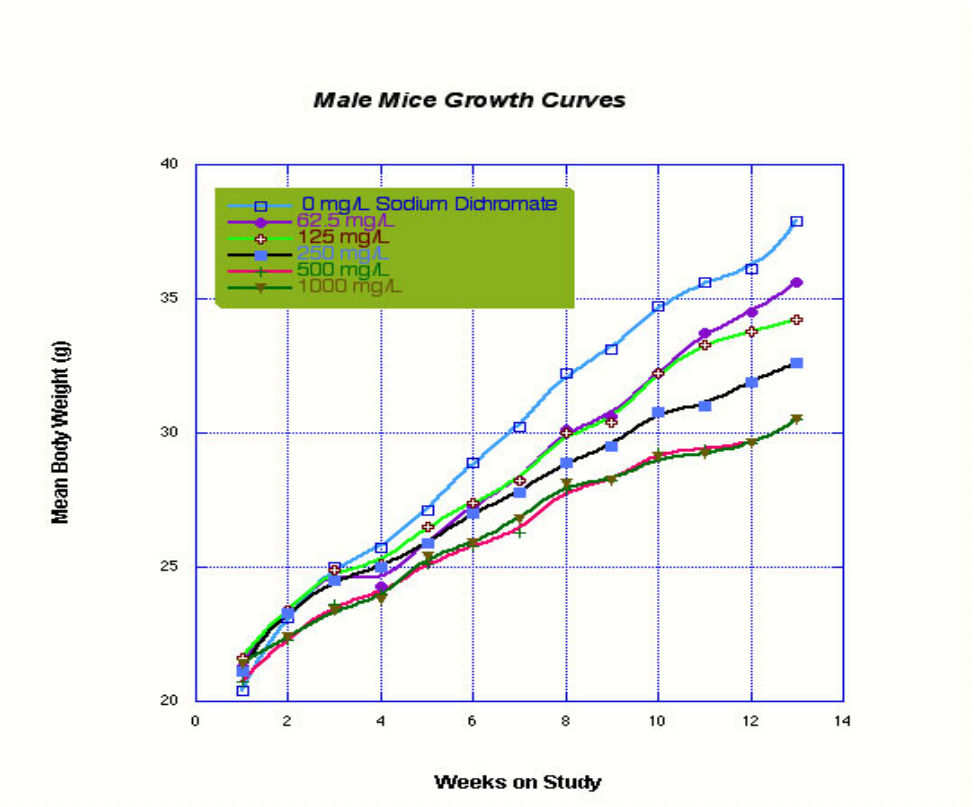


Figure 3

Survival, body weights, and relative organ weights:

All mice survived until the end of the study. Mean body weights of male mice receiving sodium dichromate dihydrate in their drinking water were lower than the controls throughout the study period. Mean body weights of females mice in the 500 and 1000 mg/kg dose groups were lower than the controls throughout the study period except for the weights on week 7 of the study (Figure 4). There is no obvious reason to explain this exception. The reduction in body weight was attributed to the decrease in water consumption. Significant ($p \leq 0.05$) increases were observed in the relative weight of heart of all dosed males, testis of males dosed with 125 mg/L or greater, spleen of 500, 1000 mg/L males, kidney of 1000 mg/L males, and thymus of 500 mg/L males and females dosed with 125 mg/L or greater (Table7).


Male Mice Growth Curves
0 mg/L Sodium Dichromate
62.5 mg/L
125 mg/L
250 mg/L
500 mg/L
1000 mg/L
Mean Body Weight (g)
Weeks on Study
40
35
30
25
20
0
2
4
6
8
10
12
14

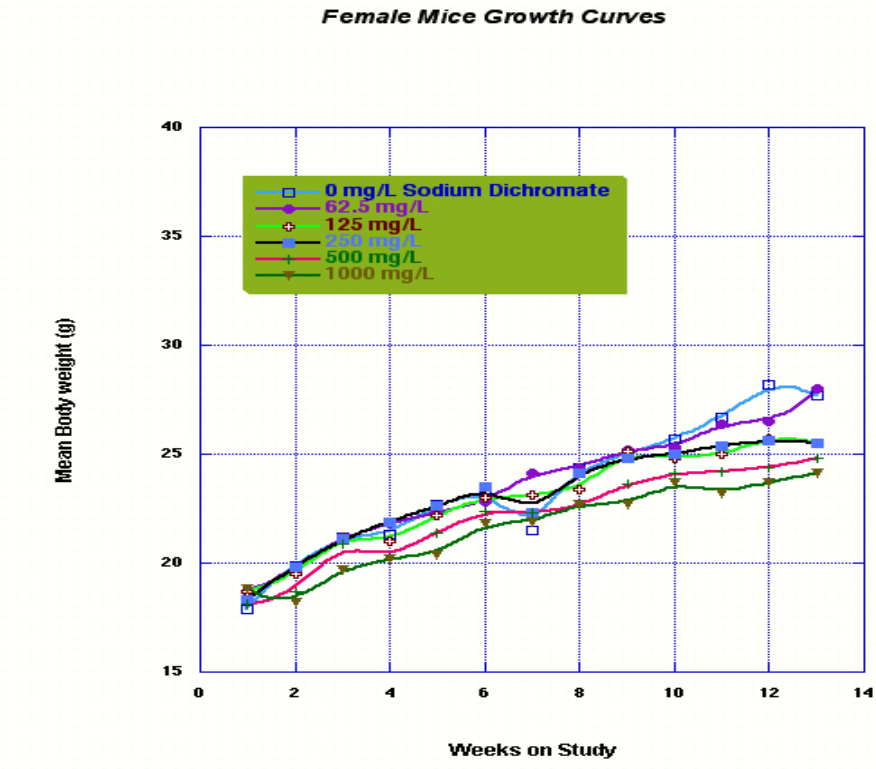

Female Mice Growth Curves
0 mg/L Sodium Dichromate
62.5 mg/L
125 mg/L
250 mg/L
500 mg/L
1000 mg/L
Mean Body weight (g)
Weeks on Study
40
35
30
25
20
15
0
2
4
6
8
10
12
14

Figure 4

Table 7: Organ Weights and Organ-Weight-to-Body-Weight Ratios for Mice in the 13-Week Drinking Water Study of Sodium Dichromate Dihydrate[a]

	Vehicle Control	62.5 mg/L	125 mg/L	250 mg/L	500 mg/L	1,000 mg/L
n	10	10	10	10	10	10
Male						
Necropsy body wt	38.9 ± 1.1	36.9 ± 0.9	35.6 ± 1.0*	33.3 ± 0.8**	31.1 ± 1.1**	31.2 ± 0.5**
Heart						
Absolute	0.148 ± 0.003	0.152 ± 0.004	0.154 ± 0.004	0.142 ± 0.006	0.141 ± 0.005	0.141 ± 0.005
Relative	3.823 ± 0.111	4.119 ± 0.066	4.356 ± 0.149*	4.271 ± 0.143*	4.540 ± 0.065**	4.542 ± 0.199**
R. Kidney						
Absolute	0.282 ± 0.008	0.282 ± 0.007	0.262 ± 0.008	0.257 ± 0.006*	0.240 ± 0.007**	0.255 ± 0.005**
Relative	7.251 ± 0.106	7.678 ± 0.292	7.429 ± 0.347	7.752 ± 0.199	7.762 ± 0.229	8.180 ± 0.074**
Liver						
Absolute	1.599 ± 0.081	1.544 ± 0.052	1.488 ± 0.052	1.403 ± 0.046*	1.330 ± 0.060**	1.339 ± 0.038**
Relative	40.931 ± 1.219	42.012 ± 1.683	41.864 ± 0.999	42.354 ± 1.577	42.777 ± 1.306	42.936 ± 0.912
Lung						
Absolute	0.244 ± 0.018	0.198 ± 0.014	0.256 ± 0.015	0.240 ± 0.019	0.222 ± 0.015	0.224 ± 0.015
Relative	6.268 ± 0.437	5.419 ± 0.461	7.254 ± 0.490	7.258 ± 0.596	7.171 ± 0.497	7.174 ± 0.459
Spleen						
Absolute	0.068 ± 0.003	0.067 ± 0.002	0.064 ± 0.002	0.064 ± 0.003	0.063 ± 0.002	0.060 ± 0.002
Relative	1.745 ± 0.050	1.820 ± 0.048	1.823 ± 0.105	1.930 ± 0.096	2.033 ± 0.059*	1.928 ± 0.070*
R. Testis						
Absolute	0.116 ± 0.001	0.118 ± 0.003	0.123 ± 0.003	0.117 ± 0.002	0.115 ± 0.005	0.115 ± 0.002
Relative	3.003 ± 0.054	3.209 ± 0.102	3.500 ± 0.187**	3.524 ± 0.054**	3.703 ± 0.164**	3.681 ± 0.079**
Thymus						
Absolute	0.033 ± 0.001	0.033 ± 0.001	0.034 ± 0.001	0.030 ± 0.001	0.031 ± 0.001	0.031 ± 0.001
Relative	0.849 ± 0.028	0.899 ± 0.034	0.953 ± 0.017	0.897 ± 0.030	0.996 ± 0.031**	1.002 ± 0.039**
Female						
Necropsy body wt	28.2 ± 0.7	28.6 ± 0.8	26.3 ± 0.7	27.1 ± 0.8	25.1 ± 0.3**	24.8 ± 0.4**
Heart						
Absolute	0.122 ± 0.003	0.117 ± 0.009	0.123 ± 0.003	0.127 ± 0.006	0.120 ± 0.003	0.111 ± 0.003
Relative	4.340 ± 0.093	4.106 ± 0.327	4.694 ± 0.128	4.708 ± 0.197	4.794 ± 0.105	4.488 ± 0.135
R. Kidney						
Absolute	0.159 ± 0.004	0.160 ± 0.003	0.154 ± 0.004	0.161 ± 0.004	0.154 ± 0.004	0.150 ± 0.003
Relative	5.658 ± 0.135	5.609 ± 0.130	5.872 ± 0.132	5.984 ± 0.187	6.159 ± 0.185	6.070 ± 0.151
Liver						
Absolute	1.151 ± 0.031	1.139 ± 0.042	1.057 ± 0.024	1.109 ± 0.037	1.041 ± 0.023*	0.990 ± 0.019**
Relative	40.964 ± 0.983	39.748 ± 0.713	40.321 ± 0.877	41.027 ± 0.737	41.538 ± 0.706	40.010 ± 0.783
Lung						
Absolute	0.206 ± 0.008	0.227 ± 0.016	0.244 ± 0.012	0.234 ± 0.016	0.217 ± 0.008	0.203 ± 0.012
Relative	7.322 ± 0.248	7.998 ± 0.639	9.302 ± 0.412*	8.670 ± 0.547	8.653 ± 0.278	8.183 ± 0.435
Spleen						
Absolute	0.074 ± 0.002	0.080 ± 0.002	0.080 ± 0.002	0.081 ± 0.004	0.071 ± 0.003	0.074 ± 0.003
Relative	2.631 ± 0.064	2.811 ± 0.102	3.061 ± 0.109*	3.002 ± 0.142	2.833 ± 0.120	2.989 ± 0.103
Thymus						
Absolute	0.035 ± 0.002	0.040 ± 0.002	0.040 ± 0.001	0.044 ± 0.002**	0.035 ± 0.002	0.039 ± 0.002
Relative	1.234 ± 0.075	1.385 ± 0.067	1.519 ± 0.029**	1.618 ± 0.058**	1.381 ± 0.071**	1.572 ± 0.066**

* Significantly different (P±0.05) from the control group by Williams' or Dunnett's test

** P≤0.01

[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).

Clinical pathology findings:

Hematology data for mice are shown in Table 8. Administration of sodium dichromate dihydrate was associated with mild, but biologically relevant, decreases in group mean erythrocyte mean cell volume and mean cell hemoglobin values in mice of both sexes, as well as elevations in group mean RBC counts for female mice in the three highest dose groups.

TABLE 8: Hematology for Mice in the 13-Week Drinking Water Study of Sodium Dichromate Dihydrate[a]

	Vehicle Control	62.5 mg/L	125 mg/L	250 mg/L	500 mg/L	1,000 mg/L
Male						
n	10	10	10	10	10	9
Hematocrit (%)	47.7 ± 1.2	45.4 ± 0.9	47.5 ± 1.0	46.3 ± 1.0	46.3 ± 1.0	45.5 ± 1.1
Hematocrit (spun) (%)	48.3 ± 1.1	46.2 ± 0.9	48.6 ± 0.9	46.8 ± 0.7	47.5 ± 0.9	46.8 ± 0.9
Hemoglobin (g/dL)	16.3 ± 0.4	15.5 ± 0.4	16.3 ± 0.4	15.8 ± 0.3	15.6 ± 0.3	15.4 ± 0.3
Erythrocytes (10^6/dL)	10.63 ± 0.28	10.31 ± 0.22	10.97 ± 0.23	10.84 ± 0.21	10.92 ± 0.25	10.95 ± 0.25
Reticulocytes (10^6/dL)	2.99 ± 0.08	2.70 ± 0.08*	2.87 ± 0.07	2.75 ± 0.05	2.76 ± 0.07	2.80 ± 0.07
Reticulocytes (%)	2.83 ± 0.09	2.61 ± 0.06	2.62 ± 0.06	2.54 ± 0.05*	2.53 ± 0.03**	2.56 ± 0.03*
Nucleated cells/100 Leukocytes	0.10 ± 0.10	0.10 ± 0.10	0.20 ± 0.13	0.00	0.00	0.33 ± 0.24
Mean cell volume (fL)	44.9 ± 0.3	44.1 ± 0.2*	43.3 ± 0.1**	42.7 ± 0.1**	42.4 ± 0.1**	41.6 ± 0.1**
Mean cell hemoglobin (pg)	15.3 ± 0.1	15.0 ± 0.1**	14.8 ± 0.0**	14.6 ± 0.1**	14.4 ± 0.0**	14.1 ± 0.1**
Mean cell hemoglobin concentration (g/dL)	34.1 ± 0.2	34.0 ± 0.2	34.3 ± 0.1	34.1 ± 0.1	33.8 ± 0.1	33.9 ± 0.1
Platelets (10^3/dL)	891.2 ± 45.6	1,032.5 ± 44.0	931.0 ± 57.8	909.0 ± 43.7	938.0 ± 37.6	961.0 ± 34.2
Leukocytes (10^3/dL)	4.29 ± 0.62	3.63 ± 0.48	3.99 ± 0.53	3.93 ± 0.47	4.07 ± 0.73	4.41 ± 0.50
Segmented neutrophils (10^3/dL)	0.47 ± 0.05	0.44 ± 0.07	0.58 ± 0.14	0.50 ± 0.08	0.45 ± 0.05	0.43 ± 0.05
Lymphocytes (10^3/dL)	3.62 ± 0.56	3.02 ± 0.41	3.23 ± 0.45	3.26 ± 0.43	3.41 ± 0.65	3.76 ± 0.45
Monocytes 10^3/dL)	0.06 ± 0.01	0.05 ± 0.01	0.06 ± 0.01	0.04 ± 0.01	0.04 ± 0.01	0.06 ± 0.01
Basophils (10^3/dL)	0.017 ± 0.003	0.019 ± 0.005	0.014 ± 0.004	0.016 ± 0.002	0.017 ± 0.003	0.014 ± 0.003
Eosinophils (10^3/dL)	0.10 ± 0.02	0.08 ± 0.01	0.08 ± 0.01	0.09 ± 0.02	0.14 ± 0.03	0.12 ± 0.02
Large unstained cells (10^3/dL)	0.024 ± 0.005	0.012 ± 0.002	0.019 ± 0.005	0.016 ± 0.002	0.018 ± 0.006	0.019 ± 0.003
Female						
n	9	10	10	10	10	10
Hematocrit (%)	46.4 ± 0.4	46.1 ± 0.5	47.5 ± 0.6	47.1 ± 0.5	45.8 ± 0.6	45.5 ± 0.6
Hematocrit (spun) (%)	46.3 ± 0.4	46.0 ± 0.6	47.7 ± 0.5	47.0 ± 0.4	45.8 ± 0.4	45.7 ± 0.4
Hemoglobin (g/dL)	15.7 ± 0.1	15.5 ± 0.2	15.8 ± 0.1	15.6 ± 0.2	15.2 ± 0.1*	15.0 ± 0.2**
Erythrocytes (10^6/dL)	9.92 ± 0.08	9.97 ± 0.12	10.37 ± 0.12*	10.50 ± 0.11**	10.41 ± 0.12**	10.53 ± 0.14**
Reticulocytes (10^6/dL)	2.84 ± 0.29	2.64 ± 0.18	2.88 ± 0.13	3.59 ± 0.20	3.00 ± 0.13	3.03 ± 0.11
Reticulocytes (%)	2.84 ± 0.28	2.63 ± 0.17	2.78 ± 0.14	3.43 ± 0.21	2.90 ± 0.13	2.86 ± 0.11
Nucleated cells/100 Leukocytes	0.22 ± 0.15	0.10 ± 0.10	0.00	0.40 ± 0.22	0.00	0.10 ± 0.10
Mean cell volume (fL)	46.7 ± 0.1	46.3 ± 0.3	45.8 ± 0.1**	44.9 ± 0.2**	44.0 ± 0.2**	43.3 ± 0.4**
Mean cell hemoglobin (pg)	15.8 ± 0.1	15.6 ± 0.1*	15.3 ± 0.1**	14.9 ± 0.0**	14.6 ± 0.1**	14.3 ± 0.1**
Mean cell hemoglobin concentration (g/dL)	33.8 ± 0.1	33.6 ± 0.3	33.3 ± 0.2	33.1 ± 0.2*	33.1 ± 0.2*	33.0 ± 0.2*
Platelets (10^3/dL)	838.2 ± 52.4	901.1 ± 50.8	799.2 ± 31.0	769.5 ± 32.8	836.2 ± 37.7	839.5 ± 34.0
Leukocytes (10^3/dL)	5.96 ± 0.80	5.20 ± 0.49	4.39 ± 0.54	5.05 ± 0.49	5.17 ± 0.45	4.62 ± 0.70
Segmented neutrophils (10^3/dL)	0.67 ± 0.09	0.52 ± 0.06	0.39 ± 0.04*	0.52 ± 0.09	0.53 ± 0.04	0.51 ± 0.07
Lymphocytes (10^3/dL)	5.03 ± 0.71	4.47 ± 0.42	3.77 ± 0.49	4.20 ± 0.44	4.37 ± 0.41	3.91 ± 0.61
Monocytes (10^3/dL)	0.08 ± 0.01	0.07 ± 0.01	0.06 ± 0.01	0.12 ± 0.04	0.09 ± 0.01	0.07 ± 0.01
Basophils (10^3/dL)	0.024 ± 0.004	0.014 ± 0.002	0.017 ± 0.004	0.013 ± 0.003	0.019 ± 0.002	0.016 ± 0.004
Eosinophils (10^3/dL)	0.10 ±0.007	0.034 ± 0.006	0.021 ± 0.004*	0.025 ± 0.004	0.029 ± 0.005	0.027 ± 0.011*

* Significantly different (P≤0.05) from the control group by Dunn's or Shirley's test

** P≤0.01

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

Pathology Findings:

Results of the histopathological evaluation of mice are summarized in Table 9.
Sites of toxicity for sodium dichromate dihydrate in mice were the stomach and the lymph nodes. Compound-related stomach lesions were observed in the 1000 mg/L males and in the 500 and 1000 mg/L females. The lesions consisted of focal metaplasia in the glandular stomach adjacent to the limiting ridge. The focal squamous metaplasia was occasionally accompanied by slight epithelial hyperplasia of the forestomach involving the limiting ridge and a slight inflammatory response.

Histiocytic cell infiltration occurred in the tip of the villi of the duodenum of male and female mice at the 125 mg/L dose level or greater. The histiocytes occurred as plump cells resembling syncytial cells and appeared to have a slightly granular cytoplasm.

Histiocytic hyperplasia was observed in male and female mice at the 125 mg/L dose level or greater. This lesion was characterized by multiple aggregates of histiocytes in the parenchyma of the lymph nodes with morphology and staining characteristics similar to those found in the duodenum.

Table 9:Lesion Incidence in Mice in the 13-Week Drinking Water Study of Sodium Dichromate Dihydrate

Dose Group	Control	62.5 mg/L	125 mg/L	250 mg/L	500 mg/L	1000 mg/L
Male						
Stomach[a]	10	NE	NE	NE	10	10
Squamous Metaplasia[b]	0				0	4
Duodenum	10	10	10	10	10	10
Histiocytic Cell Infiltration	0	0	2	9	10	9
Mesenteric Lymph Node	10	10	10	10	10	10
Histiocytic Hyperplasia	0	0	4	8	4	8
Pancreatic Lymph Node	10	NE	NE	10	10	10
Histiocytic Hyperplasia	0			0	1	1
Female						
Stomach	10	NE	NE	10	10	10
Squamous Metaplasia	0			0	2	6
Duodenum	10	10	10	10	10	10
Histiocytic Infiltration	0	0	3	6	10	8
Mesenteric Lymph Node	10	10	10	10	10	10
Histiocytic Hyperplasia	0	0	2	6	4	8
Pancreatic Lymph Node	10	NE	NE	NE	10	10
Histiocytic Hyperplasia	0				0	1

[a] Number of animals examined
[b] Number of animals with the lesion.

Dose selection for the 2-year studies*:

Doses tentatively selected for the 2-year drinking water studies are 0, 125, 250 or 500 mg/L sodium dichromate dihydrate for rats and 0, 62.5, 125, or 250 mg/L for mice. Dose selection for rats was based on body weight depressions, decreased water consumption and/or chemical-related lesions (ulcers) observed at the glandular stomach/forestomach junction of rats receiving higher doses of the chemical in the 13-week studies. Similarly, dose selection for mice was based on body weight depression, decreased water consumption, and chemical-related lesions observed in the glandular stomach of mice receiving higher doses of the chemical in the 13-week studies. Stomach ulcers are considered life-threatening lesions and may result in decreased survival in 2-year studies.

*the doses recommended here were changed to reflect the NTP Expert Panel on Chromium recommendations" -- see the 2-year study section of the protocol (http://ntp-server.niehs.nih.gov/htdocs/Studies/HexChromium/cartoxprotocol.pdf)
