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Hand Delivery

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EPA East - Room 6428
Attn: 8(e) Coordinator
U.S. Environmental Protection Agency
1201 Constitution Avenue, NW
Washington, DC 20004-3302



Re: TSCA 8(e) Submission for Vanadium Trioxide (CASRN 1314-34-7)

Dear Sir or Madam:

The Vanadium Producers & Reclaimers Association (VPRA) hereby submits to the United States Environmental Protection Agency (EPA) a Toxic Substances Control Act (TSCA) section 8(e), 15 U.S.C. § 2607(e), submission for preliminary results on vanadium trioxide (V_2O_3). This work is being undertaken as part of a systematic investigation to establish the relative toxicology of several vanadium compounds. A non-GLP 14-day repeated exposure nose-only inhalation study was conducted with aerosolized V_2O_3 powder with Sprague-Dawley rats in order to select exposure concentrations for a possible, subsequent subchronic inhalation toxicity study with this compound.

Six male and six female rats per group were exposed for 6 hours per day, five days per week for 14 days (10 total exposures) to V_2O_3 at concentrations of 0, 0.002, 0.02 or 0.25 mg/L with a mean particle size distribution range (MMAD) of 1.92 to 2.25 microns. Statistically significant decreases in the absolute and relative (to final body weight) spleen weight were observed in male rats at 0.25 mg/L. Statistically significant increases in the lung weights (absolute and relative to final body weight) were observed in male and female rats in the 0.02 and 0.25 mg/L groups. Bronchoalveolar lavage evidenced an increase in the number of cells in the lung for male and female rats across low, medium, and high exposure groups. Draft tables summarizing the findings are attached. These data are being reported within 30 days of December 2, 2011, the date on which these preliminary investigative results were transmitted to VPRA members.



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December 19, 2011
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For the record, previous results on this and other test materials under investigation were filed under TSCA section 8(e) on April 9, 2010, August 6, 2010, and October 7, 2010.

Sincerely yours,

A handwritten signature in cursive script, appearing to read "John Hilbert".

John Hilbert, President
Vanadium Producers & Reclaimers Association

Enclosures

14-Day Repeat Exposure Range-Finding Nose-Only Inhalation Toxicity Study with Vanadium Trioxide in Rats

Table 1: Body Weights and Food Consumption

| Concentration (mg/L) | Males | | | | Females | | | |
|---|-------|-------|------|-------|---------|-------|------|-------|
| | 0 | 0.002 | 0.02 | 0.25 | 0 | 0.002 | 0.02 | 0.25 |
| Body Weight (g): Day 8 | | | | | | | | |
| Mean | 282 | 281 | 272 | 243** | 221 | 219 | 222 | 198** |
| SD | 12.9 | 15.2 | 14.6 | 15.5 | 9.4 | 13.7 | 14.9 | 7.6 |
| N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Day 14 | | | | | | | | |
| Mean | 320 | 319 | 306 | 242** | 236 | 235 | 235 | 196** |
| SD | 12.4 | 17.8 | 15.4 | 17.0 | 11.6 | 13.5 | 20.0 | 10.9 |
| N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Body Weight Change (g): Days 1 to 8 | | | | | | | | |
| Mean | 55 | 56 | 46 | 17** | 23 | 22 | 26 | 0** |
| SD | 3.5 | 6.5 | 13.9 | 17.0 | 7.6 | 7.9 | 8.1 | 5.1 |
| N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Days 8 to 14 | | | | | | | | |
| Mean | 38 | 38 | 34 | -1** | 15 | 16 | 13 | -2** |
| SD | 3.3 | 6.3 | 7.0 | 9.5 | 7.1 | 5.5 | 7.3 | 5.4 |
| N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Days 1 to 14 | | | | | | | | |
| Mean | 93 | 94 | 80 | 16** | 38 | 38 | 39 | -2** |
| SD | 5.7 | 10.7 | 13.8 | 15.0 | 11.5 | 6.5 | 14.8 | 9.4 |
| N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Food Consumption (g): Days 1 to 8 | | | | | | | | |
| Mean | 167 | 166 | 148 | 115** | 126 | 124 | 118 | 85** |
| SD | 8.8 | 13.7 | 20.1 | 20.6 | 7.7 | 11.8 | 13.7 | 5.2 |
| N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Days 8 to 14 | | | | | | | | |
| Mean | 150 | 148 | 138 | 76** | 106 | 107 | 101 | 68** |
| SD | 8.3 | 12.3 | 13.8 | 11.9 | 7.4 | 8.5 | 12.2 | 9.7 |
| N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |

** = significantly different from corresponding control at $p < 0.01$ (ANOVA/Dunnett's or Kruskal-Wallis/Dunn Tests)

Table 2: Final Body Weight and Organ Weights

| Concentration (mg/L) | Males | | | | Females | | | |
|--|--------|--------|--------|---------|---------|--------|---------|---------|
| | 0 | 0.002 | 0.02 | 0.25 | 0 | 0.002 | 0.02 | 0.25 |
| Fasted Final Body Weight (g): Day 15 | | | | | | | | |
| Mean | 283 | 284 | 273 | 215** | 208 | 208 | 206 | 172** |
| SD | 12.1 | 14.2 | 13.8 | 17.8 | 8.1 | 12.5 | 17.5 | 8.6 |
| N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Organ Weights (g): Absolute Kidney Wt. | | | | | | | | |
| Mean | 2.335 | 2.428 | 2.417 | 1.812** | 1.623 | 1.660 | 1.683 | 1.472 |
| SD | 0.1632 | 0.2677 | 0.2829 | 0.1022 | 0.0926 | 0.1349 | 0.1669 | 0.1222 |
| N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Absolute Lung Wt. | | | | | | | | |
| Mean | 1.384 | 1.718 | 1.859* | 2.145** | 1.183 | 1.285 | 1.666** | 1.927** |
| SD | 0.0771 | 0.1834 | 0.1498 | 0.3054 | 0.1061 | 0.1268 | 0.0850 | 0.1842 |
| N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Relative Lung Wt. | | | | | | | | |
| Mean | 0.49 | 0.61 | 0.68** | 1.00** | 0.57 | 0.62 | 0.81** | 1.12** |
| SD | 0.031 | 0.052 | 0.068 | 0.164 | 0.043 | 0.034 | 0.065 | 0.082 |
| N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Absolute Spleen Wt. | | | | | | | | |
| Mean | 0.662 | 0.713 | 0.601 | 0.381** | 0.502 | 0.466 | 0.541 | 0.382* |
| SD | 0.1080 | 0.1420 | 0.0697 | 0.0516 | 0.0410 | 0.0791 | 0.0699 | 0.0819 |
| N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Relative Spleen Wt. | | | | | | | | |
| Mean | 0.23 | 0.25 | 0.22 | 0.18* | 0.24 | 0.22 | 0.26 | 0.22 |
| SD | 0.031 | 0.047 | 0.021 | 0.026 | 0.018 | 0.037 | 0.038 | 0.040 |
| N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Relative Brain Wt. | | | | | | | | |
| Mean | 0.66 | 0.67 | 0.71 | 0.88** | 0.88 | 0.89 | 0.90 | 1.04** |
| SD | 0.031 | 0.022 | 0.029 | 0.072 | 0.020 | 0.060 | 0.064 | 0.067 |
| N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Relative Testes Wt. | | | | | | | | |
| Mean | 1.09 | 1.04 | 1.12 | 1.35** | n/a | n/a | n/a | n/a |
| SD | 0.075 | 0.040 | 0.090 | 0.135 | | | | |
| N | 6 | 6 | 6 | 6 | | | | |
| Relative Liver Wt. | | | | | | | | |
| Mean | 2.95 | 3.04 | 2.90 | 3.38 | 2.77 | 3.05 | 3.11 | 3.30** |
| SD | 0.204 | 0.422 | 0.189 | 0.849 | 0.039 | 0.384 | 0.324 | 0.127 |
| N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |

All relative organ weights were calculated relative to the final body weight of the animals.

* = significantly different from corresponding control at $p < 0.05$ (ANOVA/Dunnett's or Kruskal-Wallis/Dunn Tests)

** = significantly different from corresponding control at $p < 0.01$ (ANOVA/Dunnett's or Kruskal-Wallis/Dunn Tests)

n/a = not applicable

Table 3: Bronchiolar-Alveolar Lavage Fluid Analysis

| Concentration (mg/L) | Males | | | | Females | | | |
|---|-------|-------|-------|-------|---------|-------|-------|-------|
| | 0 | 0.002 | 0.02 | 0.25 | 0 | 0.002 | 0.02 | 0.25 |
| BAL Fluid Chemistry 719-LD/LD (IU/L) | | | | | | | | |
| Mean | 36 | 132* | 215** | 158** | 36 | 60 | 178** | 144** |
| SD | 11.2 | 56.8 | 57.4 | 98.4 | 6.0 | 14.7 | 32.2 | 84.7 |
| N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Differential cell counts: Segmented Neutrophils | | | | | | | | |
| Mean | 14.2 | 29.5* | 15.5 | 29.8* | 11.0 | 14.5 | 10.8 | 30.8* |
| SD | 9.68 | 4.68 | 4.59 | 6.55 | 3.69 | 4.55 | 3.76 | 14.01 |
| N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Lymphocytes | | | | | | | | |
| Mean | 52.7 | 25.2* | 27.2* | 23.2* | 68.3 | 35.3* | 29.8* | 23.3* |
| SD | 8.76 | 2.04 | 5.49 | 6.97 | 8.73 | 7.39 | 5.91 | 8.52 |
| N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |
| Monocytes/Macrophages | | | | | | | | |
| Mean | 33.2 | 45.3* | 57.3* | 46.7* | 20.7 | 50.2* | 59.3* | 45.2* |
| SD | 7.03 | 4.37 | 6.71 | 6.53 | 10.71 | 6.08 | 7.69 | 10.53 |
| N | 6 | 6 | 6 | 6 | 6 | 6 | 6 | 6 |

* = significantly different from corresponding control at p< 0.05 (ANOVA/Dunnett's)

** = significantly different from corresponding control at p<0.01 (ANOVA/Dunnett's)

Table 4: Bronchiolar-Alveolar Lavage Fluid Analysis – Cell viability and Total Protein (males and females combined)

| Concentration (mg/L) | | 0 | 0.002 | 0.02 | 0.25 |
|------------------------------|--|----------|-----------|-----------|----------|
| Cell Viability Cells/Lung | | | | | |
| Mean | | 5.20E+05 | 12.6E+05* | 17.6E+05* | 9.44E+05 |
| SD | | 3.57E+05 | 5.93E+05 | 8.57E+05 | 5.23E+05 |
| N | | 12 | 12 | 12 | 12 |
| Viable Cells/Lung | | | | | |
| Mean | | 4.17E+05 | 11.3E+05* | 16.0E+05* | 8.08E+05 |
| SD | | 2.44E+05 | 5.80E+05 | 8.50E+05 | 4.34E+05 |
| N | | 12 | 12 | 12 | 12 |
| Percent Viable Cells/Lung | | | | | |
| Mean | | 84.0 | 89.5 | 89.2 | 86.3 |
| SD | | 11.0 | 9.0 | 5.8 | 10.6 |
| N | | 12 | 12 | 12 | 12 |
| Total Protein | | | | | |
| Mean | | 140.43 | 335.51* | 493.61* | 364.98* |
| SD | | 17.99 | 139.48 | 189.93 | 150.52 |
| N | | 12 | 12 | 12 | 12 |

* = significantly different from corresponding control at p< 0.05 (ANOVA/Dunnett's Tests)

Please note that these data are preliminary and have not been audited.