National Institutes of Health
National Institute of
Environmental Health Sciences
P. O. Box 12233
Research Triangle Park, NC
27709

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Memorandum

Date: May 4, 2010

To: Norman Birchfield, NCEA

From: Michelle Hooth, Study Scientist for NTP 2-Year Studies of Sodium Dichromate Dihydrate and Matthew Stout, Study Scientist for NTP Studies of Chromium Picolinate Monohydrate

Subject: NTP Review of the Draft EPA Toxicological Review of Hexavalent Chromium

We reviewed the Draft EPA Toxicological Review of Hexavalent Chromium and provide the following comments for consideration:

1. On page 18 (starting on line 18), it is stated that "Four volunteers ingesting a bolus dose of 5 mg hexavalent chromium (as $K_2Cr_2O_7$) excreted 76-82% of the total as urinary chromium…" implying high absorption (76-82%) of Cr(VI). According to the Kerger et al., 1997 publication this statement should say "…approximately 76-82% of the 14-d total amount of chromium in urine was excreted within the first 4 days….". Similarly, starting on line 21, it is stated that "In a single human volunteer….87% of the total chromium was excreted in the urine in the first 4 days." This is inconsistent with the relatively low absorption of Cr(VI) and with Paustenbach et al., 1996, where on page 455, it is stated that "The estimated average bioavailability of chromium based on urinary excretion was 2.0% of the daily dose."

2. On page 48, it is stated that "Microscopic examinations of the oral mucosa and tongue were not conducted" when describing the results of the NTP 3-month study of sodium dichromate dihydrate. Based on the neoplastic findings in the 2-year study of sodium dichromate dihydrate, the NTP conducted a retrospective analysis of the oral cavity and tongue in the 3-month F344 rat study. This pathology review revealed non-neoplastic microscopic lesions in 4 rats that were not considered treatment-related. A memo describing the conduct and results of this study is posted on the NTP website with Toxicity Report #72 (http://ntp.niehs.nih.gov/go/29184).

3. On page 75, it is stated that "Results of the hematology analyses in special study female mice (hematology was not assessed in male mice) show that exposure to sodium dichromate dihydrate in drinking water produced microcytic, hypochromic anemia (NTP, 2008). An exposure-related anemia was observed in male rats in the 2-year study. However, the changes in hematological parameters in the female mice were described as an exposure-related microcytosis, not an anemia, since decreases in hematocrit and hemoglobin were not observed.

4. On page 191, it is stated that "there are absorption, distribution, metabolism, and excretion studies, although information on internal or target organ dose of hexavalent chromium is not available". In conjunction with the 2-year cancer studies, the NTP determined chromium tissue concentrations in a number of tissues at 4 different exposure durations. These data are presented in Appendix J of Technical Report 546 (http://ntp.niehs.nih.gov/go/29323) and referred to on page 189 of the draft IRIS document.

We also reviewed the charge questions and thought they were appropriate. Please feel free to contact us for additional information or clarification.

Sincerely,

Michelle J. Hooth

Michelle J. Hooth, Ph.D., DABT

Matthew D. Stout

Matthew D. Stout, Ph.D., DABT

Cc:
Raj Chhabra, Group Leader, Toxicology Branch, NTP
John Bucher, NTP Associate Director