October 5, 2011

BY ELECTRONIC MAIL
Assistant Administrator Paul Anastas
Office of Research and Development
Environmental Protection Agency
Washington, DC 20460

RE: Comments on EPA's Integrated Risk Information System Program and the Toxicological Review of Hexavalent Chromium

Dear Assistant Administrator Anastas:

The U.S. Small Business Administration (SBA) Office of Advocacy (Advocacy) has received several letters from small business representatives expressing concerns with the Environmental Protection Agency's (EPA) risk evaluation of hexavalent chromium (Cr(VI)) under the Integrated Risk Information System (IRIS). Small businesses are concerned with the scientific accuracy supporting the conclusions in EPA's Draft Toxicological Review of Hexavalent Chromium (Draft Toxicological Review), as well as EPA's intention to proceed with the Final Toxicological Review, ahead of schedule, and without relying on the most up-to-date and best available science. [1] We urge EPA to revise its current assessment after receipt of the critical new data.

Office of Advocacy

Congress established the Office of Advocacy under Pub. L. No. 94-305 to advocate the views of small entities before Federal agencies and Congress. As Advocacy is an independent body within the U.S. Small Business Administration (SBA), the views expressed by Advocacy do not necessarily reflect either the position of the Administration or the SBA.

EPA Must Regulate Based on the Best Available Science

Advocacy shares the concerns conveyed by small businesses about the Cr(VI) risk assessment under IRIS. We recognize that these concerns are based on the need of EPA to base its rule making on the best available science. President Obama in Executive Order 13563 affirms that, "our regulatory system must … be based on the best available science. It must allow for public participation and an open exchange of ideas."[2] Administrator Jackson remarked that, "Science

[1] U.S. EPA (2010). Draft Toxicological Review of Hexavalent Chromium. U.S. Environmental Protection Agency, Washington, D.C.
[2] Executive Order 13563, Improving Regulation and Regulatory Review (76 Fed. Reg. 32088) (January 18, 2011), s. 1(a).

must be the backbone of what EPA does."[3] Referring to Cr(VI) specifically, Administrator Jackson testified that, "we must always make sure our approach is based on up-to-date science," and that, "[S]cience will guide all of our actions on chromium-6."[4]

Thousands of small businesses are potentially affected by this toxicological review, including small business users of Cr(VI), and small water systems using ground water. Small businesses' primary concerns with the Draft Toxicological Review are twofold. First, data gaps prohibit EPA from accurately developing a quantitative risk assessment of the effect of Cr(VI) ingestion. Second, there is concern regarding EPA's exclusive use of the linear model in the Draft Toxicological Review and the high dose level at which Cr(VI) was tested for the 2008 National Toxicology Program (NTP) study (2008 NTP study) on which the Draft Toxicological Review is based.[5] Advocacy notes EPA accelerated its own schedule for completing the risk assessment process by two years.

The American Chemistry Council (ACC) is sponsoring the study "Mode of Action Cancer Research Project for Ingestion of Hexavalent Chromium." The results of this study are due by the end of 2011. ToxStrategies, a scientific consulting firm, is also expected to release a report by the end of 2011 on a series of studies examining the mode of action by which Cr(VI) is a carcinogenic in rodents following ingestion. Preliminary results of the latter show mounting evidence of a biological threshold for Cr(VI) toxicity. EPA has been strongly advised by small businesses and its Draft Toxicological Review peer reviewers to wait for the publication of these two studies before proceeding. Advocacy also believes that EPA's Final Toxicological Review would benefit from waiting for ongoing research to be finalized in order to consider and incorporate the best available science.

Small businesses also found insufficient basis and explanation in the Draft Toxicological Review for the singular selection of the highly conservative linear model of the exposure-response relationship for carcinogenicity in determining the reference dose and the cancer slope. Further, although the 2008 NTP study showed evidence that Cr(VI) induced cancer in rodents, the Cr(VI) concentrations administered as the basis for the Draft Toxicological Review far exceeded environmentally-relevant levels. Also, the Draft Toxicological Review assumes that Cr(VI) is a mutagenic by oral exposure, even at low doses. However, the ToxStrategies study is expected to show the effects at low doses and what amount of ingested Cr(VI) actually reaches tissues. Initial results show that Cr(VI) is not a mutagenic at low levels consistent with the current national drinking water standards, and that the human stomach has a substantial ability to reduce Cr(VI) to the non-toxic chromium-3 (Cr(III)).[6] Confirmation of a threshold would mean no cancer risk at a low dose, contrary to the EPA model.

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[3] Lisa P. Jackson. Statement to the Senate, Environment and Public Works. *Hearing on the Nominations of Lisa P. Jackson to be Administrator of the U.S. Environmental Protection Agency and Nancy Helen Sutley to be Chairman of the Council on Environmental Quality*, Hearing, January 14, 2009. Washington, D.C.

[4] Lisa P. Jackson. Statement to the Senate, Committee on Environment and Public Works. *Oversight Hearing on Public Health and Drinking Water Issues.* Hearing, February 2, 2011. Washington, D.C.

[5] U.S. HHS. (2008) National Toxicology Program Report on the Toxicology and Carcinogenesis Studies of Chromium Picolinate Monohydrate. U.S. Department of Health and Human Services, Washington, D.C.

[6] In the "Peer Review Workshop for EPA's Draft Toxicological Review of Hexavalent Chromium, Reviewer Post-Meeting Comments", Dr. Anatoly Zhitkovich, a reviewer, notes that, "the ability of gastric juices to reduce/detoxify chromium-6 is generally accepted in the field." Dr. Janusz Byczkowski, also a reviewer, notes that the gastrointestinal fluids in humans have a higher reductive capacity than those of mice and concluding that humans

EPA Peer Reviewers Heavily Criticize Draft Toxicological Review

EPA assembled a panel of nine peer reviewers to review and comment on the Draft Toxicological Review.[7] Notably, seven of the nine scientists concluded EPA had not demonstrated that ingestion of Cr(VI) caused cancer.[8] Five of the reviewers advised EPA to wait for the results of the upcoming studies to be released before proceeding.

One reviewer, Dr. Joshua W. Hamilton states, "In this reviewer's strong opinion…Cr(VI) is highly unlikely to act via a mutagenic mode of action in vivo." Hamilton calls the finding that Cr(VI) acts via a mutagenic mode of action (MOA) by all routes of exposure "illogical" for several reasons, including based on the emerging data from the ACC-sponsored MOA and other studies.[9]

Dr. John Pierce Wise, also a reviewer, states that, "the document gives the impression that the MOA was predetermined."[10] Both Wise and Hamilton recognize that MOA is the most important point of the 2008 NTP study, "since the choice of a mutagenic MOA then drives all other considerations in this document."

Wise finds further that the study was flawed, "because only very high doses were considered…there is concern that it may not reflect events at lower doses." Wise strongly recommends that, "The EPA is in the unique position that a study that repeats the one above and extends it to lower doses is almost completed. The EPA should wait for the final results of that study to make the most informed analysis."

An Opportunity for EPA to Improve IRIS

Advocacy also shares the concerns of small businesses over the objectivity and level of scientific rigor underlying EPA's IRIS program. Advocacy notes that the National Academy of Sciences' (NAS) April 2011 independent scientific review of EPA's draft IRIS assessment of formaldehyde sharply critiqued the IRIS program for persistent failures to provide objective scientific evidence to support its conclusions.[11] NAS stated, "The IRIS program falls short of meeting the benchmarks of objectivity, scientific accuracy and transparency necessary to

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should, "be less vulnerable than mice to the adverse GI effects of oral exposure to Cr+6." Dr. Zhitkovich also remarks, however, that there is a disagreement over the completeness of the detoxification process. Such disagreement should give rise to patience in the review process so that EPA has access to the most up-to-date scientific data.

[7] U.S. EPA (2011). Peer Review Workshop for EPA's Draft Toxicological Review of Hexavalent Chromium, Reviewer Post-Meeting Comments. U.S. Environmental Protection Agency, Washington, D.C.

[8] "EPA Faces New pressure on Chromium 6 Cancer Risk After Panel Critique." July 29, 2011. Retrieved from http://insideepa.com.

[9] Joshua W. Hamilton. Peer Review Workshop for EPA's Draft Toxicological Review of Hexavalent Chromium, Reviewer Post-Meeting Comments. U.S. Environmental Protection Agency, Washington, D.C., p A-13.

[10] John Pierce Wise. Peer Review Workshop for EPA's Draft Toxicological Review of Hexavalent Chromium, Reviewer Post-Meeting Comments. U.S. Environmental Protection Agency, Washington, D.C., p A-98.

[11] NAS. (2011). Review of EPA Formaldehyde April 8 2011 Committee to Review EPA's Draft IRIS Assessment of Formaldehyde. National Academy of Sciences, Washington, D.C.; *see also* U.S. EPA. "EPA's Draft Health Assessment for Formaldehyde Needs Improvement", Press Release, April 8, 2011.

ensuring high quality, reliable assessments."[12] EPA should strengthen both the peer review process at EPA and the IRIS procedures.

In a July 2011 press release, EPA pledged to improve the IRIS program as part of an ongoing effort initiated in 2009 to achieve its goal of, "providing high quality science-based human health assessments used to inform the agency's decisions on protecting public health and the environment."[13] Any delay in the process that results from EPA waiting a few months longer on Cr(VI) will no doubt be significantly outweighed by the benefits from a more robust data base to uphold informed regulatory decisions.

Advocacy believes that by moving back the deadline for a final assessment of the scientific data, by assessing all available science, including the most recent studies, and by rewriting the Draft Toxicological Review, that EPA can demonstrate that sound science is indeed the backbone of the IRIS program.

If my office can be of any further assistance, please contact me or Sarah Bresolin Silver at (202) 205-6790 or sarah.bresolin@sba.gov.

Sincerely,

/s/

Winslow Sargeant, Ph.D.
Chief Counsel for Advocacy

/s/

Sarah Bresolin Silver
Assistant Chief Counsel
Office of Advocacy

Copy to: The Honorable Cass R. Sunstein, Administrator
Office of Information and Regulatory Affairs
Office of Management and Budget

[12] NAS. (2011). Review of EPA Formaldehyde April 8 2011 Committee to Review EPA's Draft IRIS Assessment of Formaldehyde. National Academy of Sciences, Washington, D.C. from Cal Dooley. Letter to Administrator Lisa P. Jackson, April 19, 2011. Retrieved from http://www.americanchemistry.com/Policy/Regulatory-Reform/ACC-Letter-to-Administrator-Jackson-re-IRIS-41911.pdf.

[13] U.S. EPA. (2011). EPA Strengthens Key Scientific Database to Protect Public Health [Press release]. Retrieved from http://yosemite.epa.gov/opa/admpress.nsf/d0cf6618525a9efb85257359003fb69d/a3fcd60838197067852578cb00666c4d!OpenDocument.