UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JUN - 9 2005

OFFICE OF
ENVIRONMENTAL INFORMATION

Mr. David A. Smith
2210 E. Marconi
Phoenix, Arizona 85022

Re: Response to Request for Reconsideration regarding removal of documents referring to bromate in all forms as carcinogenic from all EPA Web sites, pursuant to United States Environmental Protection Agency (EPA) and Office of Management and Budget (OMB) Information Quality Guidelines – RFR # 12385A

Dear Mr. Smith:

This letter responds to your September 23, 2004, letter regarding U.S. Environmental Protection Agency (EPA) documents and their characterization of bromate carcinogenicity. EPA has treated your September 23, 2004, letter as a Request for Reconsideration (RFR) under the Agency's Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by the Environmental Protection Agency (IQGs, October 2002, located at http://www.epa.gov/quality/informationguidelines) and has followed the procedure outlined in these IQGs to evaluate the information discussed in that letter. The RFR was considered by an Executive Panel comprised of myself, the Acting Associate Administrator of the Office of Policy, Economics, and Innovation, and the Acting Assistant Administrator of the Office of Solid Waste and Emergency Response. The Panel's decision is based on a thorough review of your cited literature, and other relevant material.

Your RFR presents rebuttals to the Agency's April 28, 2004, response to your Request for Correction (RFC) that requests EPA "repair" the "errors on EPA documentation" caused by classification of bromate as a carcinogen. After careful consideration of your RFR and the Agency's information, the Executive Panel has determined that your RFR does not warrant a change to the existing classification of bromate as a probable human carcinogen at the present time. The Executive Panel reaffirms the Agency's determination in the April 28, 2004, response to your RFC that references on Agency Web pages to bromate carcinogenicity and its toxicological effects are consistent with the intent and purpose of EPA's IQGs. Greater detail on the Executive Panel's determination is provided below.

EPA has reviewed the points you presented in the RFR and has grouped them into the following four themes for purposes of this response.

Theme 1: You contend that EPA incorrectly responded to your RFC by suggesting that all soluble bromate salts have the same biological effect. Your letter stated that only potassium bromate has been shown to be carcinogenic, that there is no evidence of carcinogenicity for sodium bromate, and that the biological effects of potassium and sodium bromate salts are substantially different.

To support your RFR, you refer to the Kurokawa et al. (1990) publication that discusses the use of microbial assays to evaluate the mutagenic potential of bromate and bromate compounds. The article's authors note that unpublished results from an Ames test found that sodium bromate did not produce revertant (mutated) colonies. The Ames test is known to be a good screening test for detecting compounds with the inherent potential for inducing nucleic acid (DNA) base changes and frame shifts; however, it is not a definitive test for mutagenic potential. Kurokawa et al. (1990) also noted that negative results have been reported for potassium bromate from another microbial assay, and there is no dispute about the carcinogenic potential of potassium bromate. Because the Ames test and the other microbial assays cannot evaluate the potential of a chemical to produce clastogenicity (structural chromosal aberrations) and aneugenicity (numerical chromosomal aberrations), both EPA (Dearfield et al., 1991: Considerations in the U.S. EPA's Testing Approach for Mutagenicity. Mutation Research. 258:259 -283) and the Committee on Mutagenicity of Chemicals in Food, Consumer Products and the Environment (COM, 2000, Guidance on a strategy for testing of chemicals for mutagenicity. U.K. Department of Health, London. Available from <http://www.doh.gov.uk/com/guidance.pdf>) recommend that chemicals also be tested using an in vitro micronucleus test. If human exposure is likely, the Committee also recommends the use of a mammalian cell mutation assay and its preferred choice is the mouse lymphoma assay.

In your RFR you also cite Eckhardt et al. (1982). These researchers tested sodium bromate with the Ames test, the sex-linked recessive lethal test in *Drosophila melanogaster*, and the mouse micronucleus test. The results of the Ames test and the recessive lethal test were negative, but a significant dose-response for mutagenic activity was observed in the mouse micronucleus test. More recently, Harrington-Brock et al. (2003) found that both sodium and potassium bromate were clastogenic using the mouse lymphoma assay. In summary, Kurokawa et al. (1990) indicates that both sodium and potassium bromate can test negative for mutagenicity in a microbial cell system, and Eckhardt et al. (1982) and Harrington-Brock et al. (2003) demonstrate that each of these bromate salts yields positive results in mammalian cell systems. These results continue to support the 2001 EPA determination of bromate as a probable human carcinogen.

Further, the results of several chronic studies using the potassium and sodium salts of halogens and other anions have been reported as not showing carcinogenic potential. Sodium chloride (mean daily dose of 154 mg/kg/day or 2.46 mg/kg/day) administered as the control vehicle in a study of the carcinogenicity of dichloroacetate in male rats did not show an increased prevalence or multiplicity of renal cell tumors (DeAngelo, AB et al., Toxicology, 114: 207-221, 1996). Sodium fluoride in the diet (4-25 mg/kg; Maurer, JK et al, J. Natl. Cancer Inst.,

82:1118-1126, 1990) or administered in drinking water (25-175 mg/L; Bucher, JR et al, Int. J. Cancer, 48: 733-737, 1991) was not carcinogenic in male or female rats. Monosodium glutamate administered to male and female F344 rats at 0.6-5% of the diets failed to increased any proliferative or neoplastic lesions in the urinary tract though urinary analysis showed increased sodium and decreased potassium levels in the urine (Shibata, MA et al., Food Chem. Toxicol. 33: 383-391, 1995). Potassium iodide at concentrations of 10-1000 ppm in the drinking water of male and female F344 rats was not reported to increase the incidence of renal cell tumors (Takegawa, K, Food Chem. Toxicol, 38:773-781, 2000).

Thus, the Panel's review reaffirms the following about the chemistry of potassium bromate and sodium bromate, as stated in EPA's RFC response: that available scientific information supports the position of mutagenic potential existing for both the sodium and potassium salts, and that the bromate ion is a probable human carcinogen.

Theme 2: EPA and other entities (World Health Organization, Health Canada) have characterized the bromate ion as a carcinogen. Your letter stated that EPA decided that bromate is a carcinogen, and the other entities agreed without critical evaluation.

An Integrated Risk Information System (IRIS) assessment was conducted for bromate in 2001 (http://www.epa.gov/iris). This assessment, which includes both internal and extensive peer review, represents the Agency's consensus opinion. The IRIS assessment provides a thorough review of the available toxicological data and presents a weight of evidence approach to the determination that bromate is a probable human carcinogen by the oral route of exposure. As listed below, other agencies made their determinations *before* the EPA IRIS assessment was complete.

Agency review found that:

- EPA's Maximum Contaminant Level Goal (MCLG) (zero) and MCL (10 ppb) for bromate (1998) were developed through the regulatory process. That process included both external and internal peer reviews, as well as a public comment period. The MCLG of zero is based on the fact that bromate is assessed to be a probable human carcinogen; this assessment went through external and internal peer review and public comment process. The MCL is based on the technical achievability of reducing contaminant levels during drinking water treatment processes.

- The International Agency for Research for Cancer (IARC) determined that potassium bromate is "possibly carcinogenic to humans" and belongs in "Group 2B" in 1986.

- Health Canada determined that bromate is a possible human carcinogen in 1999.

- The WHO determined that bromate is a "possible human carcinogen" in 2000; this WHO assessment was conducted by a panel of international experts.

Theme 3: You contend that EPA's response to your RFC suggests that since essential elements such as potassium, taken in recommended concentrations, are non-toxic, then the bromate ion must be toxic. Your letter challenged the characterization of EPA's response to your RFC, that the potassium ion cannot be bad because it is an essential element.

EPA continues to believe that essential elements are not toxic in the normal physiological concentration range. It was not the Agency's intent to state that an essential element, in this case potassium, cannot be bad at any concentration. The concentration of potassium from treatment levels in rodent bioassays was within the animal's normal body concentrations. Therefore, the Agency has concluded that the effects seen in the various toxicity tests using potassium bromate are due to the bromate ion.

Theme 4: You contend that EPA's response to your RFC suggests that EPA and the United States Food and Drug Administration (FDA) did their own mutagenicity study and found bromate to be a mutagen. Your letter stated that EPA and FDA conducted an assay to prove that sodium bromate is toxic, but that the study is flawed because it did not follow guidelines.

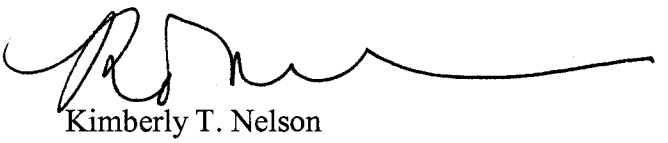
Agency review determined that:

- EPA and FDA conduct studies routinely to clarify issues about toxicants.
- This particular study is a standard mutagenicity assay that is routinely conducted.
- The study indicated no difference between potassium bromate and sodium bromate.

In addition, Agency scientists contacted Dr. Martha Moore, Director of the Division of Genetic and Reproductive Toxicology at the FDA National Center for Toxicological Research. That laboratory developed this mutagenicity assay and created the guidelines for conducting it with appropriate controls to discern interference from background levels of potassium, sodium, and bromate. Dr. Moore confirmed that the assay was done in her laboratory and that the study guidelines were followed.

The Executive Panel therefore reaffirms the Agency's determinations in the April 28, 2004, response to your RFC. EPA is committed to upholding the quality of information that we provide to the public as well as that which supports Agency decision-making processes. Thank you for your inquiry.

Sincerely,



Kimberly T. Nelson
Assistant Administrator and
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