



July 9, 2012

Mr. Thomas Carpenter  
Environmental Protection Agency  
Designated Federal Officer (DFO)  
Submitted via email to: [carpenter.thomas@epa.gov](mailto:carpenter.thomas@epa.gov)

**Re: Notification of a Public Meeting and Public Teleconference of the Science Advisory Board (SAB); Perchlorate Advisory Panel**

Dear Mr. Carpenter:

On May 30, 2012 the Environmental Protection Agency (EPA) announced notice of a public meeting and teleconference of the Scientific Advisory Board's (SAB) Perchlorate Advisory Panel (Panel)<sup>1</sup> to discuss the development of a maximum contaminant level goal (MCLG) for perchlorate. The Panel is charged with reviewing the available data and information (i.e. epidemiological data, biomonitoring data and physiologically based pharmacokinetic analysis) in support of an MCLG for perchlorate. The American Chemistry Council's (ACC)<sup>2</sup> Chlorine Chemistry Division represents the major producers and users of chlorine in North America and works to promote and protect the sustainability of chlorine chemistry processes, products and applications. We submit the following comments to the Panel regarding the scientific justification of developing an MCLG for perchlorate and provide additional comments in the attachment. We highlight several specific concerns as follows:

- **The charge questions posed to the Panel do not adequately address EPA's scientific justification to regulate perchlorate.** EPA's charge to the Panel focuses on the review of the Agency's Whitepaper titled: "*Life Stage Considerations and Interpretation of Recent Epidemiological Evidence to Develop A Maximum Contaminant Level Goal for Perchlorate*" but it does not request that Panel members review EPA's scientific justification for regulating perchlorate under the Safe Drinking Water Act (SDWA). This

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<sup>1</sup> Federal Register /Vol. 77, No. 104 /PP. 31847 - 31848

<sup>2</sup> ACC represents the leading companies engaged in the business of chemistry. ACC members apply the science of chemistry to make innovative products and services that make people's lives better, healthier and safer. ACC is committed to improved environmental, health and safety performance through Responsible Care®, common sense advocacy designed to address major public policy issues, and health and environmental research and product testing. The business of chemistry is a \$674 billion enterprise and a key element of the nation's economy. It is one of the nation's largest exporters, accounting for ten cents out of every dollar in U.S. exports. Chemistry companies are among the largest investors in research and development. Safety and security have always been primary concerns of ACC members, and they have intensified their efforts, working closely with government agencies to improve security and to defend against any threat to the nation's critical infrastructure.



is an essential issue for Panel members to consider given that, several decades of scientific data in animals and humans illustrate that perchlorate does not pose an adverse effect at current exposure levels.

- **Regulation of perchlorate under the SDWA does not provide any meaningful opportunity for health risk reduction.** In February 2011, EPA decided to regulate perchlorate under the SDWA, a decision that reversed a 2008 preliminary determination not to regulate. However, a review of the recent scientific literature and the 2005 National Research Council (NRC) report<sup>3</sup> on the health implications of perchlorate exposure indicates that perchlorate does not pose a health risk at current environmental levels. When EPA made its determination in 2008, it found that perchlorate exposure from drinking water and other sources was not at levels of public health concern.<sup>4</sup> Perchlorate was found in less than 5% of public water systems nationally and the average concentration in those systems was well below a level that would be expected to cause adverse health impacts.
- **The proposed MCLGs are overly conservative and scientifically unwarranted.** EPA has proposed to derive MCLGs for a chemical that is posing no health risk at current environmental levels. As defined by the Section 1412(b)(4)(A) of the SDWA, an MCLG is a non-enforceable goal set at *“the level at which no known or anticipated adverse effects on the health of persons occur and which allows an adequate margin of safety.”* The MCLG is normally derived from available animal or human data based on a no observable adverse effect level (NOAEL) or a lowest observable adverse effect level (LOAEL). However, in NRC’s 2005 review it departed from standard risk assessment practice and instead used a no-observed effect level (NOEL) to derive the reference value (i.e. maximum daily exposure without any appreciable risk to human health). A NOAEL is based on an adverse effect and a NOEL is based on a non-adverse effect. NRC recognized that use of a NOEL was inherently conservative and it is unfortunate that EPA has added more default assumptions and conservatism as the Agency develops its proposed MCLGs. In addition, using default body weight and water consumption rates in EPA’s MCLG calculations does not take into account the best available scientific approach or data. Instead, EPA should use the available physiologically-based pharmacokinetic (PBPK) modeling to inform and calculate any potential MCLGs. The PBPK models provide a more realistic and scientifically based estimate for relevant internal doses and their impacts on different life stages.

ACC hopes the Panel will review the more detailed comments provided in the attachment and strongly recommends that the Panel: (1) evaluate EPA’s justification for regulating perchlorate under the SDWA; (2) review the full perchlorate scientific literature and how the Agency integrated the information to derive the proposed MCLGs and; (3) discuss the use of a non-adverse effect as the point of the departure for the proposed MCLGs. If you have any questions

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<sup>3</sup> National Research Council of the National Academies. (2005) Health Implications of Perchlorate Ingestion Committee to Assess the Health Implications of Perchlorate Ingestion

<sup>4</sup> U. S. Environmental Protection Agency. (2008) Fact Sheet: Preliminary Regulatory Determination for Perchlorate. [http://www.epa.gov/safewater/ccl/pdfs/reg\\_determine2/fs\\_ccl2-reg2\\_perchlorate.pdf](http://www.epa.gov/safewater/ccl/pdfs/reg_determine2/fs_ccl2-reg2_perchlorate.pdf)



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or require additional information please feel free to contact me by phone at 202-249-6707 or via email at [Kimberly\\_Wise@americanchemistry.com](mailto:Kimberly_Wise@americanchemistry.com).

Respectfully,

Kimberly Wise, Ph.D.  
Senior Director  
Chemical Products & Technology Division  
American Chemistry Council

Attachment



## INTRODUCTION

The American Chemistry Council's (ACC) Chlorine Chemistry Division (CCD) represents major producers and users of chlorine in North America. CCD works to promote and protect the sustainability of chlorine chemistry processes, products and applications in accordance with the principles of Responsible Care®.<sup>5</sup> CCD also strives to ensure appropriate product stewardship, and, as part of our mission, address important science and policy issues related to the chemical industry, including EPA's justification and approach for deriving a maximum contaminant level goal (MCLG) for perchlorate. We strongly support the development of drinking water standards that protect public health and reflect the best available scientific evidence and appreciate the opportunity to provide comment to the EPA's Scientific Advisory Board (SAB) Perchlorate Advisory Panel (Panel). As set forth in these comments, ACC believes that the EPA has not provided adequate justification for regulating perchlorate under the Safe Drinking Water Act (SDWA) nor has the Agency provided sufficient scientific information to support the generation of overly conservative MCLGs for perchlorate based on life stages.

## COMMENTS

### **A. The charge questions posed to the Panel do not adequately address EPA's scientific justification to regulate perchlorate.**

In 2008, EPA released its preliminary determination not to regulate perchlorate under the SDWA.<sup>6</sup> EPA made this determination that regulation was not necessary because it would not provide a meaningful opportunity to reduce health risk based on its review of the available scientific literature. Since the 2008 preliminary determination the scientific literature still indicates that perchlorate does not pose a risk to human health thus it is unclear why EPA's determination has changed. The Panel is charged with reviewing the Agency's whitepaper and how best to interpret the life stage information, epidemiological and biomonitoring data and the physiologically based pharmacokinetic models. However, this charge does not request that Panel members review EPA's scientific justification for regulating perchlorate under the SDWA. This is an essential issue for Panel members to consider given that, several decades of scientific data in animals and humans illustrate that perchlorate does not pose an adverse effect to human health at current exposure levels.

### **B. Regulation of perchlorate under the SDWA does not provide any meaningful opportunity for health risk reduction.**

In 2011, EPA decided to regulate perchlorate under the SDWA based on information included in the 2005 National Research Council (NRC) Report,<sup>7</sup> a review of new scientific

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<sup>5</sup> RESPONSIBLE CARE® - The chemical industry is committed to the safe, responsible and sustainable management of chemicals through their entire life cycle, and for their intended end use. Responsible Care is the chemical industry's world-class performance initiative. Its companies are industry leaders, bound together by a commitment to address challenges and continuously improve the performance of the chemical industry.

<sup>6</sup> Federal Register /Vol. 73, No. 198 /PP. 60262 - 60282

<sup>7</sup> National Research Council of the National Academies. (2005) Health Implications of Perchlorate Ingestion Committee to Assess the Health Implications of Perchlorate Ingestion



data and stakeholder comments. EPA noted three areas as justification for its determination: (1) perchlorate may have an adverse effect on the health of persons; (2) perchlorate is known to occur or there is a substantial likelihood that it will occur in public water systems with a frequency and at levels of public health concern; and (3) regulation of perchlorate presents a meaningful opportunity for health risk reduction for persons served by public water systems. While the 2011 final determination effectively reversed the 2008 preliminary determination by the Agency not to regulate perchlorate under the SDWA it does not comport with the underlying statutory requirements necessary to regulate.

A review of the scientific literature illustrates that perchlorate is one of the most well-studied chemicals, with detailed information on the mechanism of action, dose-response, and health effects. Specifically, the 2005 NRC report included a comprehensive review of the perchlorate science which indicated that perchlorate does not pose a risk at current exposure levels. Additionally, recent animal and human studies have been published that also reinforce the NRC's findings, help reduce the uncertainty noted by the NRC and strengthen the conclusion that there are no adverse health effects from perchlorate at environmentally-relevant concentrations.

The National Health and Nutrition Examination Survey (NHANES) provides the best information available to assess actual human exposure to perchlorate from all sources, including food and water, using urinary perchlorate concentrations from a large U.S. population cohort. Based on a review by Blount et al. (2007),<sup>8</sup> the overall exposure to perchlorate from all sources based on the NHANES data is below any meaningful level of concern identified in the available scientific literature. Additionally, as noted by the EPA, in past sample collections from public drinking water systems, the Agency found that exposure to perchlorate from drinking water and other sources was not at levels of public health concern.<sup>9</sup> Perchlorate was found in less than 5% of public water systems nationally and, where perchlorate was detected, the average concentration was 9.85µg/L. These levels are several orders of magnitude below the point at which perchlorate would be anticipated to impact iodine uptake inhibition, the endpoint that EPA used to derive its proposed MCLGs (which in itself is not an adverse effect of perchlorate exposure).

### **C. The proposed MCLGs are overly conservative and scientifically unwarranted.**

EPA's decision to develop MCLGs using a no-observed effect level (NOEL) and to include additional conservatism in the calculations for several sensitive populations is unwarranted. Traditionally, chemical risk assessment and the resulting reference values are developed using data of effects on animals or humans that are viewed as adverse. However, in 2005 an NRC committee conducted a review of perchlorate health impacts and identified a clinical

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<sup>8</sup> Blount, B.C., L. Valentin-Blasini, J.D. Osterloh, J.P. Mauldin, and J.L. Pirkle. 2007. Perchlorate exposure of the U.S. population, 2001-2002. *J. Expo. Sci. Environ. Epidemiol.* 17(4):400-407.

<sup>9</sup> U. S. Environmental Protection Agency. (2008) Fact Sheet: Preliminary Regulatory Determination for Perchlorate. [http://www.epa.gov/safewater/ccl/pdfs/reg\\_determine2/fs\\_ccl2-reg2\\_perchlorate.pdf](http://www.epa.gov/safewater/ccl/pdfs/reg_determine2/fs_ccl2-reg2_perchlorate.pdf)



study involving 37 healthy men and women by Greer et al. (2002)<sup>10</sup> as the critical study from which to calculate the reference dose (RfD), the maximum daily exposure without any appreciable adverse effects to human health. The NRC's derived RfD of 0.7µg/kg/day for perchlorate was based on the NOEL corresponding to the critical effect of 1.8% inhibition of iodide uptake by the thyroid in humans. This was identified as a key biochemical event even though there are typically many biological or chemical interactions that are insufficient to induce an adverse effect.

Importantly, the NRC recognized the conservatism of its choice as stated in the NRC report, *“Using a nonadverse effect that precedes the adverse effects is a conservative, health-protective approach to the perchlorate risk assessment, and the committee’s recommendations for uncertainty factors reflect the conservatism of the approach.”* The NRC's derived RfD included an intraspecies uncertainty factor (UF) of 10 to account for differences in sensitivity between the healthy adults in the Greer study and the most sensitive population (i.e. fetuses of pregnant women who might have hypothyroidism or iodide deficiency). Additionally, the NOEL used by NRC to derive its RfD was already orders of magnitude below the levels at which adverse effects would be expected to occur from perchlorate exposure.

EPA's review of perchlorate health impacts and its development of proposed MCLGs does not account for the large margin of safety already built into using a NOEL. By not taking this into account it implies that any measureable change would be considered adverse. This ignores the definition of NOAEL in the IRIS program, which clearly states that *“....some effects may be produced but these are not considered adverse or precursors of adverse effects.”* An adverse effect is not any known biochemical or chemical change, or even any known or measureable precursor along the pathway that could lead to some degree of perturbation. However, in EPA's proposed MCLG calculations, the Agency has applied additional default assumptions for an added layer of conservatism that is unwarranted by the data and current human exposures to perchlorate. This approach, of applying multiple layers of uncertainty to an RfD that is already based on a non-adverse effect does not provide additional health benefit.

Clearly, not giving due consideration to the inherent conservatism of using a NOEL when generating an MCLG could have far reaching implications for risk assessment. This implies that EPA's choice of a non-adverse effect does not include a large margin of safety. In essence, any chemical that initiates key events that potentially pose a downstream adverse physiological effect could be inaccurately assessed based on triggering that key event. This would unduly change the premise of risk assessment and instead focus on maintaining exposures to environmental agents below the level at which significant perturbations of these biological pathways could occur regardless of actual evidence of an eventually adverse effect. Thus if EPA decides to utilize iodine uptake inhibition as the critical effect it must ensure that any calculated MCLG accurately reflects the large margin of safety already implicit in choosing a non-adverse effect as the point of departure.

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<sup>10</sup> Greer, M.A., G. Goodman, R.C. Pleuss, and S.E. Greer. 2002. Health effect assessment for environmental perchlorate contamination: The dose response for inhibition of thyroidal radioiodide uptake in humans. *Environ. Health Perspect.* 110:927-937.



Finally, in the whitepaper, EPA has chosen to generate several proposed MCLGs utilizing water consumption rates and body weight, for various life stages. However, it seems unnecessary for EPA to derive MCLGs for perchlorate based on different life stages given the Agency's conservative RfD choice. EPA has used the NRC 2005 proposed RfD of 0.7µg/kg/day as the starting point for generation of the MCLGs and as previously noted the NRC's RfD includes a large margin of safety to account for all populations, including sensitive populations. As well, using default body weight and water consumption rates in the derivation of the MCLGs does not accurately take into account the available scientific data. Instead, EPA should use physiologically-based pharmacokinetic (PBPK) modeling to calculate any MCLG. PBPK models provide a more realistic estimate for predicting the absorption, distribution, metabolism and excretion of chemical substances in humans and animals.

EPA's 2008 determination not to regulate perchlorate considered several PBPK models. In that determination, the Agency performed a review and analysis of PBPK models discussed in the NRC 2005 report and also reviewed more recent PBPK models developed by Clewell et al. (2007).<sup>11</sup> These models estimated the levels of perchlorate absorbed through the gastrointestinal tract and subsequent distribution in the body. They also provided estimates of the internal dose and resulting iodine uptake inhibition across all life stages (including pregnant and lactating women). The Clewell et al. (2007) model predicted that perchlorate would have minimal effect on iodine uptake inhibition in all groups at 1µg/kg/day corresponding to 1.1% inhibition. This is nearly 1 ½ times higher than the proposed RfD and also uses a more conservative rate of inhibition than was proposed by NRC in 2005. EPA should not resort to the use of default body weight and drinking water consumption rates when data is available to provide more realistic estimates of probable internal exposure.

## CONCLUSION

The 2005 NRC review still remains the most comprehensive assessment of the perchlorate scientific literature. Further, the consensus of scientific evidence published after the NRC's report indicates that perchlorate does not pose a health risk at environmentally relevant concentrations. EPA has not adequately justified regulating perchlorate under the SDWA and the Agency's scientific basis for regulating perchlorate should be reviewed by the Panel prior to the development of any MCLG. Additionally, any potential regulation of perchlorate under the SDWA should not use a non-adverse endpoint as its point of departure without duly noting the large margin of safety implicitly included in using this endpoint, and any proposed MCLG should be based on the best available scientific data and methodologies.

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<sup>11</sup> Clewell RA, Merrill EA, Gearhart JM, Robinson PJ, Sterner TR, Mattie DR, Clewell HJ. Perchlorate and radioiodide kinetics across life stages in the human: using PBPK models to predict dosimetry and thyroid inhibition and sensitive subpopulations based on developmental stage. *J Toxicol Environ Health A*. 2007 Mar 1;70(5):408-28.

