PSG
PERCHLORATE STUDY GROUP

A coalition of aerospace, defense,
chemical and allied industries

July 2, 2007

US Environmental Protection Agency
Office of Water Docket (Mailcode 2822T)
1200 Pennsylvania Avenue, NW
Washington, DC 20460

RE: Comments on Regulatory Determinations Regarding Contaminants on the Second Drinking Water Contaminant Candidate List Rule
Docket EPA-HQ-OW-2007-0068

The Perchlorate Study Group (PSG) is pleased to submit comments to EPA on Docket ID No. EPA-HQ-OW-2007-0068, entitled Drinking Water: Regulatory Determinations Regarding Contaminants on the Second Drinking Water Contaminant Candidate List—Preliminary Determinations; Proposed Rule.[1]

The PSG is committed to ensuring that the best available science is made available in public debate and in the subsequent setting of regulatory standards.[2] The member companies of the PSG include Aerojet, AMPAC, ATK, and Tronox.

The PSG has worked cooperatively and effectively with the US Environmental Protection Agency (EPA) and other federal agencies, state governments, water purveyors, and other business organizations to:

- increase scientific and medical understanding of perchlorate's possible effects on human health; and,

- assess the level of perchlorate in drinking water that will pose no cognitive risk.

In seeking public comment on its Second Contaminant Candidate List (CCL 2) Preliminary Determinations, EPA has expressed particular interest in receiving information regarding the adequacy of available occurrence and exposure data with respect to making a regulatory determination for perchlorate. In addition, EPA has asked for public input on scientific analysis options that would assist the Agency in reaching a regulatory determination for perchlorate.

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[1] 72 Fed. Reg. 24015 (2007) (proposed May 1, 2007).

[2] In section 1412(b)(3)(A) of the 1996 Amendments to the Safe Drinking Water Act, Congress required EPA to use the best available science and data: "The Administrator shall use: (i) the best available, peer-reviewed science and supporting studies conducted in accordance with sound and objective scientific practices; and (ii) data collected by accepted methods or best available methods (if the reliability of the method and the nature of the decision justifies use of the data).

The PSG members are manufacturers and users of perchlorate who are actively remediating areas of past releases, and are citizens concerned with the protection of the public's health. As such, the PSG member companies have a strong and unique commitment to ensuring that the best available science is applied in regulatory decision making.

Based on its thorough evaluation of the best available science, as well as consideration of the Agency's statutory authorities, the PSG respectfully submits:

- in light of the National Academy of Sciences comprehensive review, as well as numerous, peer-reviewed studies, the Agency has more than sufficient data on perchlorate's human health effects to make a regulatory determination for perchlorate on an expedited basis; and

- the extensive scientific record indicates that establishing a drinking water standard for perchlorate would not yield a meaningful opportunity to reduce risk to human health, as required under the Safe Drinking Water Act.

ANALYSIS AND OBSERVATIONS

EVALUATING THE 3 STATUTORY CRITERIA FOR THE REGULATORY DETERMINATION PROCESS

To determine whether to regulate a contaminant with a Federal drinking water standard, EPA evaluates three Safe Drinking Water Act criteria.[3] EPA has determined that it must make an affirmative determination on all three criteria to move forward with regulation.

If the Agency determines that a regulation is appropriate, EPA can make its regulatory determination for perchlorate in two ways:

1. through its longstanding approach used in the CCL 1 rulemaking and proposed for the CCL 2 determinations; or,

2. applying supplemental or alternative approaches reflecting new scientific information, using the uniquely conservative derivation of the perchlorate reference dose (RfD) for perchlorate, as well as the exceptionally deep and authoritative scientific literature on toxicity and population exposure.

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[3] In section 1412(b)(1)(A) of the Safe Drinking Water Reauthorization Act of 1996, Congress established three criteria for use by EPA in making drinking water regulatory determinations:

(i) the contaminant may have an adverse effect on the health of persons;
(ii) the contaminant is known to occur or there is a substantial likelihood that the contaminant will occur in public water systems with a frequency and at levels of public health concern; and,
(iii) in the sole judgment of the Administrator, regulation of such contaminant presents a meaningful opportunity for health risk reduction for persons served by public water systems.

(See, 110 Stat. 1613, 1619; 42 USC. §300g-1(b)(1)(B)(ii)(II)).

No matter which approach EPA takes, the best available science runs inevitably to the conclusion that a perchlorate standard will not yield a meaningful opportunity to reduce risk to human health as required by the Safe Drinking Water Act.

EPA has more than sufficient data on perchlorate's human health effects as well as on occurrence and exposure to make a determination on perchlorate without delay. EPA is to be commended for its efforts to obtain public comment relating to the prospective use of supplemental or alternative approaches. These approaches are scientifically rigorous and up-to-date, based on the peer-reviewed literature. Our collective goal of applying the best available science would point toward their use.

Nonetheless, should the agency elect to apply an approach based strictly on toxicology and modeled exposures, we anticipate it will yield the same conclusions, albeit, after a period of unnecessary delay.

REVIEW OF THE NAS REPORT AND SUBSEQUENT PEER-REVIEWED STUDIES AFFIRMS USE OF THE RfD AS THE HEALTH REFERENCE LEVEL

EPA must often make important decisions on the basis of less information than it would wish; and perchlorate is a welcome exception.

There is extensive scientific literature, most notably a comprehensive, authoritative review of the range of peer-reviewed studies by the National Research Council of the National Academy of Sciences (NAS). The success of EPA, along with other agencies, in obtaining this review has put the Agency in an unusually well-informed position, backed by the deliberations and judgment of the nation's highest scientific body. The NAS Report, followed by the Agency's own RfD process, is supplemented by subsequent, peer-reviewed studies. Taken together, these comprise a solid basis for an EPA regulatory determination.

EPA's RfD is the best health benchmark to use as the health reference level (HRL). EPA concurred with the conclusion of the NAS panel in the adoption of the panel's recommendation as EPA's RfD. This RfD is based on the NAS panel's emphatically conservative approach of establishing the point of departure at the No Observed Effect Level (NOEL), rather than EPA's customary No Observed *Adverse* Effect Level (NOAEL). Consistent with EPA's design for RfDs, the NAS panel selected its recommended RfD to be protective of all sensitive populations. Subsequent peer-reviewed studies affirm and reinforce the conclusion that the RfD is a conservative, health protective value that protects all members of society, even the most sensitive population.

Further discussion of these studies and our comments is contained in **Attachment 1**.

USE OF ALTERNATIVE APPROACHES WOULD ENABLE EPA TO MAKE A DETERMINATION ON PERCHLORATE WITH GREATER SPEED AND SCIENTIFIC CERTAINTY

In its Support Document, EPA presents a number of alternatives for evaluating the third statutory criterion, of "meaningful opportunity for health risk reduction" for perchlorate.[4] Many of these approaches take advantage of the extensive scientific information available on perchlorate.

EPA outlines several options in its Support Document for using the superior biomonitoring data for its regulatory determination. Clearly, real-time human data can be uniquely valuable and would enable EPA to make a determination on perchlorate with greater speed and scientific certainty. Using such powerful new data, EPA can make a determination more quickly and with more scientific certainty than was possible in the past. The National Health and Nutrition Examination Survey (NHANES) biomonitoring data provides a more reliable estimate of total perchlorate exposure in the US population than the fallback of extrapolating from food data.[5]

The biomonitoring data demonstrates that total perchlorate exposure from all sources is below the EPA's health benchmark for virtually all US residents. Since drinking water exposure is a small subset of total exposure, it follows that reducing this small subset by a small amount through regulation will not meet the meaningful risk reduction criterion of the Safe Drinking Water Act.

There are two additional approaches that merit Agency consideration, further suggesting that drinking water perchlorate levels pose no meaningful risk to human health. One approach posits that it is unnecessary for EPA to adjust for total exposure because Greer *et al.*[6] and other studies relied on by the NAS panel are studies of total exposure. The last approach posits that EPA could consider the comparative effect on iodine uptake inhibition (IUI) of perchlorate exposure in drinking water to other dietary goitrogens in determining whether there is meaningful opportunity for risk reduction.

In **Attachment 2,** we discuss the supplemental or alternative approaches that EPA can adopt to directly answer the question of whether regulation of perchlorate in drinking water will result in meaningful reduction in human health risk.

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[4] US EPA Regulatory Determinations Support Document for CCL2, May 2007 [hereinafter, *CCL 2 Support Document*].

[5] Benjamin C. Blount *et al.*, *Perchlorate Exposure of the US Population, 2001-2002*, J. Expos. Sci. Envtl. Epidemiol., Oct. 2006 [hereinafter *Blount 2006c*].

[6] Monte A. Greer *et al.*, *Health Effect Assessment for Environmental Perchlorate Contamination: The Dose Response for Inhibition of Thyroidal Radioiodide Uptake in Humans*, Envtl. Health Perspectives, Sep. 2002, at 927.

BIOMONITORING DATA SUGGESTS THERE IS NO NEED TO ACCOUNT FOR PERCHLORATE EXPOSURES FROM OTHER SOURCES

In the absence of extensive biomonitoring data, EPA has historically created an HRL by multiplying the Drinking Water Equivalent Level (DWEL) of the RfD by a Relative Source Contribution (RSC) for the constituent (a factor of the proportion of exposure expected to come from water). EPA's Support Document outlines several options that EPA suggests for its RSC determination using the biomonitoring data and food surveys. If performed in a scientifically valid manner, the data shows that EPA would calculate an RSC of one (which yields an HRL of 24.5 ppb drinking water equivalent).

EPA also references other approaches to calculate the RSC that appear to be at variance with the best available scientific information, representing overly conservative departures from customary EPA policy or apparently requiring months of additional computations.

Ultimately, it appears that these approaches would yield essentially the same result: an RSC of one, which would render them duplicative.

Attachment 3 provides detailed exploration of the issues raised in this section. Our analysis finds that proper application of the best available science through any of the Agency-suggested approaches will yield the same conclusion – perchlorate in drinking water is a small fraction of total exposure. Using the most reliable of the approaches EPA outlines, the RSC factor is essentially equal to one.

EVALUATION OF POTENTIAL HEALTH EFFECTS ALONG WITH OCCURRENCE AND EXPOSURE RESULTS REVEALS THAT REGULATION OF PERCHLORATE WOULD NOT PRESENT A MEANINGFUL OPPORTUNITY FOR RISK REDUCTION

EPA establishes the HRL based on the RfD and the RSC and then compares the occurrence data to the health benchmark. Assuming an RSC of one (which yields an HRL of 24.5 ppb drinking water equivalent), the population exposed to perchlorate in drinking water above EPA's evaluative criteria – ½ and 1 times the health benchmark – are small fractions of the total population served by public drinking water systems. The populations exposed to perchlorate above these benchmarks is lower than the populations for other chemicals for which EPA has determined a drinking water standard would not reduce risk in a meaningful manner.

A comparison of occurrence data for perchlorate and relevant compounds from EPA's CCL 1 regulatory determinations and CCL2 proposed determinations reveals that perchlorate ranks as a lower opportunity for risk reduction than sodium, manganese, sulfate, and boron, all four of which EPA has made or proposed determinations not to regulate.

Further explanation of our evaluation of the third statutory criteria for meaningful opportunity for risk reduction is contained in **Attachment 4**.

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CONCLUSION

In summary, EPA has an extraordinary wealth of comprehensive, authoritative scientific information relating to perchlorate's health effects, supplemented by extensive occurrence and exposure data. The Agency is therefore exceptionally well-positioned to issue a well-considered regulatory determination.

In this case, the Agency can rely on the scientific review by the NAS and its own subsequent analysis in setting a reference dose pursuant to the NAS Report. Subsequent, peer-reviewed studies provide additional information that corroborates the conclusions of the NAS and EPA.

The Agency can use its RfD as the HRL. EPA should take into account that the RfD is based on an unusually conservative point of departure, a NOEL (as opposed to the Agency's customary No Observed Adverse Effect Level), with an added safety factor of 10.

Ultimately, regardless of which approach EPA takes, the best available scientific data supports a determination that there is not a meaningful opportunity for risk reduction as required by the Safe Drinking Water Act.

The Perchlorate Study Group appreciates the opportunity to submit comments on this issue. If you have any questions regarding these comments, please do not hesitate to contact Michael Girard at (916) 355-2945.

Sincerely,

Michael Girard
The Perchlorate Study Group

Attach:

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ATTACHMENT 1

1.   *EPA has sufficient information from the National Academy of Sciences (NAS) Report on perchlorate and subsequent studies to characterize human health effects from perchlorate exposure and to identify meaningful risk reduction opportunities.*

To determine whether a contaminant poses adverse effects, EPA characterizes human health effects resulting from drinking water exposure through evaluation of peer-reviewed assessments and studies. EPA then estimates a health reference level (HRL) or health benchmark to evaluate the occurrence data. For all of the approaches, EPA's reference dose should be the HRL.

1.1   EPA's RfD is the best health benchmark to use as the health reference level.

1.1.1   For this regulatory determination, EPA has the benefit of a rigorous and independent peer review of the available science. In 2005, the NAS perchlorate panel recommended an RfD of 0.0007 mg/kg per day. The NAS panel comprised 15 leading scientists and physicians with wide-ranging expertise necessary to evaluate all aspects of the available science related to perchlorate. The NAS process occurred over a 15-month time period, providing ample time for the panel to review studies and consider oral testimony and written comments prior to issuing its conclusions and recommendations. As part of this process, the NAS panel performed an exhaustive review of the wide body of available animal and human studies as well as other scientific data relevant to understanding the health effects of perchlorate. The NAS panel noted that "emphasis was given to studies with the soundest scientific methods to draw conclusions regarding the effects of perchlorate exposure."[7]

This RfD is based on a conservative approach of establishing the point of departure at the No Observed Effect Level (NOEL), or a nonadverse effect. The NAS panel based its recommendation on the results of *Greer*, which administered controlled doses of perchlorate in drinking water to a total of 37 subjects. The panel found support for *Greer* in other human clinical studies with similar findings (*Lawrence et al.,* 2000[8]; Lawrence *et al.*, 2001[9]; *Braverman et al.*

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[7] National Academy of Sciences, *Health Implications of Perchlorate Ingestion*, 2005 [hereinafter *NAS*], at 5 (pdf version).

[8] J.E. Lawrence, *The Effect of Short-Term Low-Dose Perchlorate on Various Aspects of Thyroid Function*, Thyroid, 2000, at 659.

2005[10]). The NAS panel stated that using a NOEL as the point of departure is a more conservative and health-protective approach than EPA's customary approach of using the adverse effect.[11] The NAS panel emphasized that iodine uptake inhibition is not an adverse effect, but rather the first biochemical event in a continuum of possible effects that would not occur if exposure is at or below the NOEL.[12]

Concluding that the adverse effect of perchlorate exposure is hypothyroidism, the NAS Report stated that a healthy adult must likely have sustained exposure at a level of 0.4 mg/kg per day [14,000 parts per billion (ppb) drinking water equivalent level (DWEL)] before adverse health effects would occur.[13] Even when the intraspecies uncertainty factor of 10 is applied to account for sensitive populations, the resultant adverse health affect level would be 0.04 mg/kg per day (or 1,400 ppb DWEL).

1.1.2   The NAS's expert panelists concluded that the recommended RfD would be protective of all sensitive subpopulations.

Consistent with EPA's design for RfDs, the NAS panel selected its recommended RfD to be protective of all sensitive populations. The NAS-recommended RfD is fully protective of all sensitive populations for two major reasons. First, it breaks with EPA's practice to base the RfD on an adverse effect but rather bases it on a nonadverse event. Second, the NAS panel adjusted the NOEL downward by an uncertainty factor of 10 as an added margin of safety for the most sensitive populations, identified as fetuses of pregnant women with hypothyroidism or iodide deficiency. The NAS panel concluded that the RfD is "conservative and health protective," providing an additional level of protection for not only the most sensitive population, but all other sensitive groups as well.

The most frequent criticism of *Greer* and the NAS Report relates to unfounded concerns over the "limited" number of study participants, the study's short duration, and misidentification of the sensitive sub population. The NAS panel specifically addressed

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[9] J.E. Lawrence, *Low Dose Perchlorate (3 mg daily) and Thyroid Function*, Thyroid, 2001, at 295.

[10] Lewis E. Braverman *et al.*, *The Effect Of Perchlorate, Thiocyanate, and Nitrate on Thyroid Function in Workers Exposed to Perchlorate Long-Term*, J. Clin. Endocrinol. Metab., 2005, at 700.

[11] *NAS*, at 170-71.

[12] Id. at 166-67.

[13] Id. at 171-72.

these concerns in its report. First, it noted that while *Greer* had only seven subjects in the low-dose group, the dose-response curve was based on the results of all 37 subjects.[14] Second, the panel cited four other studies with results similar to *Greer*.[15] Third, the panel's conclusions are supported by other studies involving long-term treatment of hyperthyroidism as well as occupational and environmental exposure studies.[16] Finally, the panel restated its finding that the basis of their recommended RfD, IUI, is the initial key biochemical event in a continuum of possible effects. If IUI does not occur, than all downstream effects do not occur. Therefore, chronic exposure will have no comparatively greater effects than short-term exposure.[17]

Four members of the panel took the opportunity subsequently to reaffirm their support for the NAS Report in response to an article by two scientists criticizing the panel's scientific conclusions. The members, comprising of the NAS panel's chair and three other panel members, stated that the NAS's recommended RfD "provides a wide margin of safety for all subjects of all ages."[18]

1.1.3 EPA has concurred with the conclusion of the NAS panel in the adoption of the panel's recommendation as EPA's RfD.[19]

Explained another way, the panel's recommended point of departure includes a 57-fold safety factor from the panel's finding of the no observed adverse effect level. The panel adds a 10-fold uncertainty factor, giving the RfD a composite 570-fold safety factor. As EPA evaluates the risk reduction opportunities for perchlorate, it must remember that there is already substantial health protection explicitly embedded into the benchmark level.

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[14] Id. at 16 n.4.

[15] Id.

[16] Id.

[17] Id.

[18] Richard B. Johnston Jr. *et al.,* Envtl. Health Perspectives, Nov. 2005, at A 728-29.

[19] Susan Bodine Memorandum, *Assessment Guidance for Perchlorate*, US EPA Ofc. of Solid Waste and Emergency Response, Jan. 26, 2006 [hereinafter *Bodine Memorandum*], at 1-2: "EPA has determined that the RfD recommended by NRC and adopted by EPA represents the best available science regarding the toxicity of perchlorate. Consequently, this IRIS RfD of 0.0007 mg/kg-day is now the appropriate value for use by risk assessors and project managers."

1.1.4   The NAS Report found that the human toxicity data was more reliable, determining that available animal studies had limited utility in determining the effects of perchlorate in humans.[20]

As discussed in greater detail below, endorsement by the NAS panel of this clinical study enables EPA to take advantage of the biomonitoring data in humans that has recently become available.

1.1.5   Arguments that the EPA's RfD is not sufficiently health protective to be the health benchmark are without merit and fail to apply the best available science.

1.1.6   Some critics have argued that EPA and the NAS panel failed to consider nursing infants. The potential adverse effects arise in two ways: first, a nursing mother's sodium/iodine symporter (NIS) passes on substantial doses of perchlorate via breast milk; and, the infant receives a reduction in the amount of iodine received through breast milk due to IUI at the NIS.

The literature does not validate these concerns at environmental levels of perchlorate. A recent study on perchlorate exposure in lactating women in the Boston area revealed no significant correlation between breast milk iodine and perchlorate exposure.[21] At levels found in drinking water, perchlorate does not prevent iodine from entering breast milk in any discernable amount. In addition, regulators from the State of California found that, at a given water concentration, the internal perchlorate doses are similar in infants and in adults. Because perchlorate is not metabolized or retained by the body to a significant extent, the higher intake rate of infants is likely balanced by a higher excretion rate.[22]

Further, in determining whether an adverse risk is posed to the population, EPA does not need to adjust its RfD by body weight and drinking water consumption rates to account for infants and children. As EPA made clear in its most recent perchlorate

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[20] *NAS*, at 113: "The committee reviewed the human and animal data and found that the human data provided a more reliable point of departure for the risk assessment than the animal data…The committee recommends using clinical data collected in a controlled setting with the relevant route of exposure to derive the RfD."

[21] Elizabeth N. Pearce et al., *Breast Milk Iodine and Perchlorate Concentrations in Lactating Boston-Area Women*, J. Clin. Endocrin. Metab., Feb. 2007, at 1673.

[22] David Ting et al., *Development of a Health-Protective Drinking Water Level for Perchlorate*, Envtl. Health Perspectives, Jun. 2006, at 881.

guidance, any additional adjustments would be inconsistent with other drinking water standards and conflict with other policy goals.[23]

In the Disinfectant Byproduct rule, EPA also rejected additional safety factors for children or adjusting the standard adult body-weight/consumption parameters. For chlorite, the adverse effect of concern was neurodevelopment and the most important exposure was during pregnancy, lactation, and infancy. EPA dismissed the issues some have raised about perchlorate:

> EPA disagrees that an additional safety factor should be applied to provide additional protection for children or that drinking water consumption relative to body weight of children should be used in developing the MCLG (maximum contaminant limit goal). The MCLG presented for chlorite and chlorine dioxide are considered to be protective of susceptible groups, including children, given that the RfD is based on a NOAEL derived from developmental testing. Additionally, current methods for developing RfDs are designed to be protective for sensitive populations. The 2 liter per day water consumption and the 70 kg body weight assumptions are viewed as adequately protective of all groups.[24]

1.2   New peer-reviewed studies published since release of the NAS Report corroborate the conclusions of the NAS panel and provide important insights into the potential for meaningful risk reduction. EPA should consider these studies in its proposed regulatory determination.

1.2.1   In its Support Document, EPA provides a description of the Blount *et al.* associational study comparing perchlorate levels and lower levels of thyroid hormones.[25] It is the only paper besides the NAS peer

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[23] *Bodine Memorandum*, at 2: "[T]he Agency's practice of using the RfD to calculate a DWEL for perchlorate using a 70 kg body weight and a water consumption value of 2 L/day is further supported in this instance by the fact that the standard weight and consumption values also represent weight and consumption values relevant for protecting the most sensitive population."

[24] 63 FR 69404-05 (1998).

[25] Benjamin C. Blount *et al.*, *Urinary Perchlorate and Thyroid Hormone Levels in Adolescent and Adult Men and Women Living in the U.S.*, Envtl. Health Perspectives, Dec. 2006 [hereinafter *Blount 2006b*], at 1865.

review that is discussed in depth in the section on health effects. First, numerous other peer-reviewed published papers since the NAS Report provide key insights. Second, while noteworthy, *Blount 2006b* has limitations and should not alter EPA's reliance on the RfD for its regulatory determination on perchlorate based on its RfD.

1.2.2   New peer-reviewed studies support EPA's RfD as highly protective.

Five new peer-reviewed studies published since the NAS Report support the conclusion that EPA's perchlorate reference dose poses no significant risk to human health. The studies provide insight into the major science policy questions concerning perchlorate: its potential effect after long-term exposure on pregnant women and newborns, on people with moderate iodine deficiency, and on other potential sensitive subpopulations.

In addition, these studies show that perchlorate at the RfD dose comprises only a tiny fraction of total dietary IUI. Reducing the drinking water level to account for other exposures would have a corresponding, even smaller effect on total IUI. Therefore, these studies reinforce the conclusion from existing scientific evidence: a Federal drinking water standard would provide no meaningful opportunity to reduce human health risk.

Tonacchera et al., 2004[26]

In this study researchers measured the relative potency of nitrate, thiocyanate, and perchlorate to inhibit uptake of iodine. The researchers were able to measure with quantitative precision the three compounds' relative IUI potencies. They also determined that the three compounds were not synergistic – their effects were simply additive after taking the relative potencies into account.

Since nitrate and thiocyanate exposure is common via diet and lifestyle choices, the experiment provides insight into how much perchlorate adds to routine IUI. A typical diet creates a background level of 50 percent IUI. Using the *Tonacchera* relationship, drinking 200 ppb of perchlorate in 2 liters of drinking water a day adds only 0.2 percent to a nonsmoker's background level – at the level of the RfD adopted by EPA (24.5 ppb) perchlorate adds less than 0.025 percent.

This work led to two additional efforts: verifying the laboratory relationship between the three compounds in humans and

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[26] Massimo Tonacchera *et al.*, *Relative Potencies and Additivity of Perchlorate, Thiocyanate, Nitrate, and Iodide on the Inhibition of Radioactive Iodide Uptake by the Human Sodium Iodide Symporter*, Thyroid, 2004, at 1012.

translating the extensive research of thiocyanate's effect to learn about perchlorate.

Braverman, et al. 2005[27]

This study's primary goal was to verify the *Tonacchera* relationship in humans exposed to perchlorate. The best study population comprises the workers at the sole US ammonium perchlorate manufacturing plant. A previous study of these workers found no changes in thyroid function after intermittent, long-term exposure to levels equivalent to thousands of ppb in drinking water.

In this study, workers were administered radio-labeled iodine before and after their shifts at the plant. Concentrations of nitrate, thiocyanate, and perchlorate were measured in blood samples. Their actual IUI was compared to the predicted IUI from the *Tonacchera* study.

The data agreement was excellent and statistically significant. When data from other human studies (e.g., *Greer*) is added, all of the data shows a general agreement on the relationship between perchlorate dose and IUI. This study confirms that the IUI relationship is consistent across multiple human populations and can be predicted from the laboratory model.

Gibbs 2006[28]

Another use of the *Tonacchera* relationship is to apply the extensive medical literature investigating thiocyanate's thyroidal effects to draw inferences about potential thyroidal effects from perchlorate. In the developed countries, most thiocyanate exposure results from exposure to cigarette smoke. Cyanide in cigarette smoke is quickly detoxified to thiocyanate. Thiocyanate is the only substance from cigarette smoke known to affect the thyroid.

Sixteen published and peer-reviewed human studies relating serum thiocyanate concentrations and thyroid function were evaluated. The thiocyanate studies, by proxy, fill many of the gaps in the perchlorate literature. These studies included chronic exposure among pregnant women and infants, exposure in regions with varying degrees of iodine deficiency, and exposure resulting in a wide range of thiocyanate concentrations.

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[27] Braverman et al., *supra* note 10.

[28] John P. Gibbs, *A Comparative Toxicological Assessment of Perchlorate and Thiocyanate Based on Competitive Inhibition of Iodine Uptake as the Common Mode of Action*, Human Ecol. Risk Assess., 2006, at 157.

No adverse thyroid effects were observed at thiocyanate levels equivalent to 0.2 mg/kg-day or less of perchlorate (half of the NAS's stated NOAEL), even among pregnant women and neonates in regions with mild to moderate iodine deficiency. For the most sensitive subpopulation identified by the NAS panel, fetuses of pregnant women with insufficient iodine consumption, the thiocyanate literature shows that EPA's RfD is hundreds of times lower than no adverse effect levels seen in these studies.

Crump and Gibbs, 2005[29]

This study analyzes the thyroid hormone and perchlorate dose data from *Braverman* and from a previous study[30] of the same occupational cohort using the benchmark dose methodology. The statistical lower bound on the benchmark dose calculation (BMDL) has recently been favored by EPA over the No Observed Adverse Effect Level (NOAEL) in risk assessment.

The BMDLs from this combined analysis ranged from 0.18 to 0.56 mg/kg-day for decreases in free thyroxine (fT4) and from 0.36 to 0.92 mg/kg-day for increases in thyroid stimulating hormone (TSH). These BMDLs represent valid statistical lower bounds for a potential but unobserved thyroidal effect of long term perchlorate exposure in healthy, working, adult males.

These study results are consistent with the NAS statement that for adults with normal iodide intake exposure of more than 0.4 mg/kg-day for several months or longer would be required in order to cause thyroid hormone production to decline sufficiently to cause adverse health effects.

Tellez, et al., 2005[31]

This study tracks pregnant women and their newborns that are naturally exposed to perchlorate of up to 110 ppb in municipal drinking water in northern Chile. This study tracked women from early in their pregnancy to term, and measured thyroid hormone changes, perchlorate serum levels, and breast milk perchlorate and iodine concentrations.

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[29] Kenny S. Crump and John P. Gibbs, *Benchmark Calculations for Perchlorate from Three Human Cohorts*, Envtl. Health Perspectives, Aug. 2005, at 1001.

[30] Steven H. Lamm *et al.*, *Thyroid Health Status of Ammonium Perchlorate Workers: A Cross-Sectional Occupational Health Study*, J. Occup. Envtl. Med., 1999, at 248.

[31] Rafael Téllez Téllez *et al.*, *Long-Term Environmental Exposure to Perchlorate Through Drinking Water and Thyroid Function During Pregnancy and the Neonatal Period*, Thyroid, 2005, at 963.

The results show no change in thyroid hormone levels in the critical time period during pregnancy that other studies have found affects subsequent neurodevelopment in the infants. The data also confirms that breast milk iodine concentrations are not reduced. Breast milk perchlorate concentrations are comparable to drinking water concentrations, suggesting that a baby's exposure would be the same either through nursing or bottle feeding.

Among the pregnant women studied by *Tellez*, 90 percent of the women with drinking water concentrations averaging 110 ppb exceeded the RfD, yet there was no tendency toward hypothyroid findings in either the mothers during pregnancy or the infants at birth. This study supports the NAS panel's finding that the RfD is highly conservative and clearly protective of these most sensitive subpopulations.

Finally, the study concluded that the pregnant women were subject to an additional dietary source of perchlorate based on analysis of maternal urinary perchlorate excretion data.

1.2.3   In addition to these important published studies of perchlorate's relative toxicity, a major biomonitoring paper was published. In *Blount 2006c*, the authors measure perchlorate in urine samples collected from a nationally-representative sample of 2,820 persons as part of the 2001–2002 National Health and Nutrition Examination Survey (NHANES) conducted by the Centers for Disease Control and Prevention (CDC). The survey's study population is the civilian, non-institutionalized US population aged 6 years and older. The sampling design for NHANES is a complex multistage design to generate a particular sample frame. In NHANES 2001–2002, urine and serum specimens were collected from each participant. Perchlorate was detected and measured in all 2,820 participants, suggesting widespread exposure to perchlorate. The authors then estimated the daily dose of perchlorate needed to generate the observed values.

Table 1: Total Perchlorate Exposure for Different Percentiles of US Population (Daily Dose)

Percentile of US Population	Total Exposure Dose (µg/kg/day)	Factor of Safety Above RfD
5	0.02	35
50	0.064	11
95	0.234	3
99.9961	0.7	1

As shown in Table 1, total exposure is below the RfD 0.7 μg/kg/day at the 50th, 90th, 99th, and 99.99[th] percentile of the US population.

1.2.4   The *Blount 2006b* associational study should not change EPA's reliance on its RfD for making a regulatory determination on perchlorate.

Researchers analyzed the same NHANES 2001-2002 data to determine whether environmental urinary perchlorate levels are associated with changes in thyroid hormones (serum TSH and total T4) in the US. The study finds an association between lower levels of urinary perchlorate and decreased total T4 and increasing TSH in women 12 years and older with urinary iodine less than 100 μg/L. The study also found an association between lower levels of urinary perchlorate and increased TSH in women with at least 100 μg/L urinary iodine. The study found no such association in men. The study result is cause for initial pause since it finds an association at levels well below the NAS Report's no effect level of 240 ppb (DWEL).

Several limitations have been noted about the study however, including some by its authors. First, the findings of *Blount 2006b* are not suitable to show cause and are inconsistent with the conclusion of a large body of studies that have found no such effects at environmental levels. Second, the analysis is only a cross-sectional association study, whereas the studies relied on by the NAS panel were based on partially-controlled human perchlorate exposure, a more authoritative form of scientific inquiry. Third, the study measures total T4, not free T4. Fourth, due to other missing data, perchlorate could be a surrogate for an unknown variable.

The American Thyroid Association (ATA) issued a public health statement cautioning against the paper's use in making decisions on regulating perchlorate. The ATA found that free T4 is a better clinical measure of serum thyroxine. The *Blount 2006b* study fails to explain the role of other goitrogens. Thyroid autoantibodies, which have a high presence in women and act as confounders, were not measured. The study also failed to consider other confounders as well.[32] (See,

Dr. Jonathan Borak, faculty member at the Yale School of Medicine and an expert presenter to the NAS Perchlorate panel, raised concerns with *Blount 2006b* in a letter on behalf of the PSG to the California Department of Health Services. Dr. Borak identified the

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[32] American Thyroid Association Public Health Statement on Perchlorate, Dec. 13, 2006, www.thyroid.org/professionals/publications/statements/06_12_13_perchlorate.html.

following concern about the inconsistent effects of perchlorate, thiocyanate, and nitrate on IUI as found in *Blount 2006b*:

> The effects of these anions on iodine uptake have been shown repeatedly to be similar in direction and additive in magnitude . . . If decreased thyroid iodine uptake leads to alterations in thyroid hormone levels, then increasing levels of any of these anions would affect thyroid hormone levels in the same way . . . [H]owever, thyroid effects attributed to these anions were different and inconsistent. Increasing perchlorate was associated with anti-thyroid effects in women, but not in men. Thiocyanate apparently had the opposite effect; increasing thiocyanate was associated with decreased TSH, particularly in women with urine iodine <100 µg/L, who seemed most susceptible to perchlorate. (Although the Blount study only reported the effects of thiocyanate and nitrate in women, separate analyses of the NHANES data sponsored by the [PSG] indicated that similar inconsistent effects were also seen in men.[33]

Dr. Borak noted that this concern was identified in *Blount 2006b*, but no explanation was provided by the authors to explain this inconsistency. Dr. Borak concluded by appropriately maintaining that *Blount 2006b* should not be used for regulatory decision-making.

Some critics have suggested that EPA should await more studies to validate this study prior to making a regulatory determination. Even if the conclusions in *Blount 2006b* are taken at face value, there would still be no meaningful risk reduction by lowering perchlorate drinking water levels. Based on the study, low levels of perchlorate occur alongside the normal range of thyroid hormone levels in US women. Since EPA uses population measures for drinking water determinations, it is important to examine how much additional perchlorate exposure would be required to put even a fraction of US women at potentially increased risk.

First, it would have to be assumed that the study identified a causational mechanism between low levels of perchlorate and low thyroid hormone levels, not the much weaker association found in the paper.

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[33] See Attachment 5, Letter from Dr. Jonathan Borak to Cal. Dept. of Health Svs., Nov. 2, 2006.

Second, assuming there is causation, using the relationship in the *Blount 2006b* paper, how large must the perchlorate dose be to "cause" a reduction of thyroid hormones in the population? To cause even one percent of US women to have clinically low levels of thyroid hormones, the perchlorate dose would have to be equivalent to well over 5,000 ppb.

As a result, even if the association was a true biological effect, validating it would have no practical impact on EPA's decision. From the representative studies of perchlorate levels in the US population and in drinking water, perchlorate concentrations are substantially below this level.

ATTACHMENT 2

2.   *Options for evaluating potential risk reduction.*

Establishing the RfD as the health benchmark provides a foundation to evaluate exposure and risk reduction opportunities. In addition to its customary, generic methods for evaluating the third statutory criterion of meaningful risk reduction, the Support Document outlines other approaches that take advantage of the best available scientific information on perchlorate. EPA should evaluate other methodologies discussed below in addition to the stated approaches to evaluate this potential for human risk reduction. With this powerful new data, EPA can make a determination with greater speed and scientific certainty than following its customary approach.

2.1   EPA's proposal to use biomonitoring data to evaluate total perchlorate exposure is a credible approach that should be adopted.

EPA outlines several options in the document for using the superior biomonitoring data for its regulatory determination. All of these proposed uses yield the same result – there is no meaningful opportunity for risk reduction from reducing perchlorate exposure from drinking water.

2.1.1   Biomonitoring is a tool to assess human exposure to chemicals by measuring the chemicals or their by-products in human tissue or specimens (e.g., blood, urine, hair). There is significant support in the scientific community for the appropriate use of biomonitoring data to determine total exposure.

Noting the increase in biomonitoring activity, Congress directed the NAS to report on the current practices and suggestions to improve the use and interpretation of biomonitoring results. The NAS issued its report last year.[34]

In its exhaustive 262-page report, the NAS biomonitoring panel surveyed the scientific designs and practices of biomonitoring studies. It found that CDC's NHANES study draws from a large study population, a wide-range of chemicals, and well-documented analytic techniques and thus is the epitome of the most scientifically rigorous biomonitoring study design and execution.

The panel endorsed and reiterated numerous scientific articles finding that adding biologic markers to risk assessments would reduce uncertainty. The report carefully evaluated how biomonitoring results can contribute to risk assessments. The strongest approaches have two necessary conditions:

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[34] National Academy of Sciences, *Human Biomonitoring for Environmental Chemicals*, 2006.

- First, appropriate biomarkers for chemicals must be identified. They must be specific to the exposure of interest and measure exposure over the range of potential adverse health effects.

- Second, there is data on biomarker-response relationships from human epidemiology studies. In other words, scientists must identify a good measure of chemical exposure and must also know how changes in that measure affect human health.

Perchlorate meets all of the NAS panel's criteria for use in risk assessment. EPA has excellent biomarkers of perchlorate exposure in humans. Since perchlorate does not bioaccumulate and is not transformed by the body, perchlorate urinary levels are an excellent measure of daily exposure. There is a strong body of scientific literature finding a dose-response relationship between the biomarker and the biologic effect of interest in humans. The NAS's perchlorate panel recommended using these human clinical studies as the basis of perchlorate toxicity evaluation.

2.1.2   The NHANES biomonitoring data provides a better estimate of total perchlorate exposure in the US population compared to extrapolating from food data. EPA explicitly recognizes this potential in the Support Document:

> While this would be the first time the Agency has used biomonitoring data to assist EPA in making a preliminary regulatory determination for a CCL contaminant, the Agency believes that estimating perchlorate exposure among large populations using urinary perchlorate excretion data may be appropriate for the following reasons:
>
> Perchlorate is not metabolized in the body and is excreted unchanged primarily via the renal pathway (*Merrill et al.*, 2005),
>
> Perchlorate does not bioaccumulate, that is, it is excreted essentially completely (*Merrill et al.*, 2005),
>
> Perchlorate has a short half-life in the human body (approximately 8 hours), simplifying the estimation of daily exposure (*Greer et al.*, 2002), and

A methodology exists that allows estimation of daily perchlorate intake from all sources (e.g., water, food) using standard creatinine adjustment factors to account for variations in urine concentration (*Mage et al.*, 2004).[35]

2.1.3   EPA should use the 2001-2002 NHANES perchlorate data to determine directly whether regulation of perchlorate in drinking water presents a meaningful opportunity for health risk reduction.

In the NHANES results, Americans 6 years and older had a 50th percentile dose of perchlorate on the sampling day equivalent to 2.2 ppb in drinking water. This dose is less than 10 percent of the conservative NOEL level that is the basis of EPA's RfD and 7,000 times lower than the NOAEL effect level in adults.[36] As shown in Table 1, only those above the 99.996 percentile of the population have total exposure above the RfD.

By all regulatory benchmarks EPA uses to determine acceptable incremental population risk, total perchlorate exposure is not a risk of concern for regulation. If total exposure is not a meaningful risk for regulatory purposes, it follows that a risk from a fraction of that total exposure – from drinking water - is even smaller. The sole effect of setting a drinking water MCL would be to reduce this already insignificant fraction.

Rarely does EPA have both toxicology and exposure measures of such high quality. To rely on the best available science, EPA must use this approach to determine that regulation of perchlorate will not lead to a meaningful reduction in human health risk.

2.2   EPA does not need to adjust for total exposure because *Greer* and other studies relied on by the NAS panel are studies of total exposure.

Crawford-Brown et al.[37] point out that there is no need to adjust EPA's RfD because the subjects from *Greer* were exposed to background levels of perchlorate in their diet. Subjects were not asked to alter their diets in any

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[35] *CCL 2 Support Document*, at 12-34, 35.

[36] The DWEL of the RfD dose, 24.5 ppb, is calculated using conservative values of the average adult. While the body weight, 70 kg, is representative of the average adult and the average pregnant female, the drinking water rate of 2 liters/day is toward the high end of all adult and toward the median of the consumption rate of pregnant women. In other words, the 50th percentile concentration should not be compared with the greater than 50th percentile value of 24.5 ppb, but should properly be compared with a higher number.

[37] Crawford-Brown *et al.*, *Intersubject Variability of Risk from Perchlorate in Community Water Supplies*, Envtl. Health Perspectives, Jul. 2006, at 975, 977.

way. To the extent that perchlorate is widely dispersed in food, their actual perchlorate exposure exceeded the administered doses by amounts equal to dietary perchlorate intake of perchlorate. The dose-response relationship in *Greer* between IUI and perchlorate overstates the true relationship by the amount equal to the amount of perchlorate and other goitrogens in food. The no effect level observed in *Greer* is thus 0.007 mg/kg-day plus the dietary goitrogen amount.

With its RfD and the new information on perchlorate's widespread occurrence in food, EPA can determine that its RfD is based on – at a minimum - a dose-response relationship between total perchlorate exposure and IUI.   Since almost all of the population has exposure below the RfD, it follows that drinking water exposure is below the total exposure and no meaningful risk reduction will occur.

2.3   EPA could consider the comparative effect on IUI of perchlorate exposure in drinking water to other dietary goitrogens in determining whether there is meaningful opportunity for risk reduction.   An important measure of whether drinking water regulation of perchlorate will have a meaningful risk reduction opportunity is to examine perchlorate's contribution to EPA's identified potential adverse health effect.   Perchlorate's sole effect on the body is inhibition of iodine uptake, the nonadverse effect used by the NAS and EPA for the RfD.   However, perchlorate is just one of many goitrogenic compounds in the diet and drinking water that inhibit iodine uptake.   Since the NAS Report stated that IUI had to be sustained at high levels for an adverse effect to occur, if reducing perchlorate in drinking water has an insignificant effect on total IUI, there can not be even the possibility of a reduction in risk.

The scientific literature allows EPA at least three approaches to place the relative contribution of perchlorate and other goitrogens into perspective. First, it is possible to measure serum levels of goitrogens and estimate the relative IUI from them in the body. Second, EPA can limit the comparison to goitrogen and perchlorate consumption to compare the external dose of IUI compounds. Finally, EPA can even more narrowly compare IUI potential of different goitrogens in drinking water. Whether considering body levels, total dietary exposure, or even drinking water exposure, perchlorate in drinking water is a small fraction of total IUI.

2.3.1   Nitrate and thiocyanate are known to share the same mode of action as perchlorate in inhibiting iodine uptake. (1) To compare their relative contribution to IUI, total exposure data for perchlorate, nitrate, and thiocyanate are needed. In May 2007, the US Food and Drug Administration (FDA) posted a Monte Carlo analysis of estimated US dietary perchlorate intake (2) as shown in Table 2 below. This preliminary exposure assessment is consistent with the results of the perchlorate biomonitoring study and affirms that virtually all population exposure to perchlorate occurs through food consumption.

Table 2: Summary of Population-Based Perchlorate Exposures from FDA 2007[38]

Population	Monte Carlo estimate using @Risk software with 5,000 iterations (µg/kg-bw/d)	
	Mean	90th Percentile
All ages 2+ Years	0.053	0.12
Children, 2-5 Years	0.17	0.34
Females, 15-45 Years	0.037	0.074

Typical serum levels of nitrate in European and other developed economies are 30-50 micromolar.[39] Serum levels increase during pregnancy and crosses the placenta with cord blood levels similar to maternal levels.[40] *Braverman* documented serum nitrate concentrations in a study of US perchlorate workers.[41] Serum nitrate concentrations from Table 2 of that study indicated a mean ± SD of 120 ± 60 micromolar nitrate among perchlorate workers and controls in southern Utah. Therefore, using the data available from European countries will underestimate the effect of nitrate in the US if the perchlorate workers are representative of the US population.

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[38] US FDA, *Preliminary Estimation of Perchlorate Dietary Exposure Based on FDA 2005/2005 Exploratory Data*, Food and Drug Admin., May 2007 [*hereinafter FDA Perchlorate Exposure Estimate*], *available in* www.cfsan.fda.gov/~dms/clo4ee.html.

[39] *See*, E. Charmandari *et al.*, *Plasma Nitrate Concentrations in Children with Infectious and Noninfectious Diarrhea*, J. Pediatr. Gastroenterol. Nutr., Apr. 2001, at 423; T. Jo *et al.*, *Maternal or Umbilical Venous Levels of Nitrite/Nitrate During Pregnancy and at delivery*, In Vivo, Sep. – Oct. 1998, at 523; S.K. Kassim *et al.*, *Serum Nitrate and Vasoactive Intestinal Peptide in Patients with Gastroesophageal Reflux Disease*, Clin. Biochem., Nov. 2002, at 641; T. Minamino *et al.*, *Plasma Levels of Nitrite/Nitrate and Platelet cGMP Levels are Decreased in Patients with Atrial Fibrillation*, Arterioscler. Thromb. Vasc. Biol., Nov. 1997, at 3191; H. Moller *et al.*, *Nitrate Exposure from Drinking Water and Diet in a Danish Rural Population*, Int. J. Epidemiol., Mar. 1989, at 206; S. Taniuchi *et al.*, *Increased Serum Nitrate Levels in Infants with Atopic Dermatitis*, Allergy, Jul. 2001, at 693; T. Watanabe *et al.*, *Influence of Sex and Age on Serum Nitrite/Nitrate Concentration in Healthy Subjects*, Clin. Chim. Acta., Nov. 2000, at 169.

[40] T. Watanabe *et al.*, *Influence of Sex and Age on Serum Nitrite/Nitrate Concentration in Healthy Subjects*, Clin. Chim. Acta., Nov. 2000, at 169.

[41] Braverman *et al.*, *supra* note 10.

In *Gibbs* 2006, the mean ± SD serum thiocyanate among non-smokers from four US studies is approximately 30 ±18 micromolar.[42] This amount can reasonably be assumed to be entirely from diet. See table 3 below.

Table 3: Estimates of Serum Micromolar Perchlorate Concentrations Based on Perchlorate Dose from Figure 3[43]

	Dose, µg/kg-day	Serum, micromol/L
RfD	0.7	0.0142
FDA	0.340	0.0073
FDA	0.170	0.0039
FDA	0.120	0.0028
FDA	0.074	0.0018
FDA	0.053	0.0013
FDA	0.037	0.0010

EPA can readily translate how serum nitrate, thiocyanate, and perchlorate levels will contribute to IUI using the relationship established in *Tonacchera*.[44] On a serum micromolar basis, perchlorate is 240 times more potent than nitrate in inhibiting the uptake of iodine by the thyroid. Perchlorate is 15 times more potent than thiocyanate by the same measure. Using this relationship, EPA can calculate the Perchlorate Equivalent Concentration (PEC) for various serum thiocyanate and nitrate concentrations. For both dietary nitrate and dietary thiocyanate, the most likely range is considered to be 20-50 micromolar. These PEC values are presented in Table 4 and range from 1.4 to 3.5 micromolar perchlorate.

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[42] Gibbs, *supra* note 28.

[43] Id.

[44] Tonacchera *et al.*, supra note 26.

Table 4: Perchlorate Equivalent Concentrations, Micromolar (PEC) Calculated from
Tonacchera et al. **for Various Combinations of Serum Nitrate and Thiocyanate**
Concentrations that could be Anticipated from Dietary Exposures.

Serum Nitrate Micromolar	Serum Thiocyanate Micromolar			
	20	30	40	50
20	1.417	2.083	2.750	3.417
30	1.458	2.125	2.792	3.458
40	1.500	2.167	2.833	3.500
50	1.542	2.208	2.875	3.542

In contrast, the range of serum perchlorate concentrations likely to result from total (diet and drinking water) perchlorate (from Table 3) is 0.001 to 0.007 micromolar perchlorate. Thus, the range of possible contribution to the nonadverse effect of IUI of dietary perchlorate ranges from 0.03 percent to 0.5 percent of that from typical total sources of nitrate and thiocyanate.

Reducing it further will have an insignificant effect on total dietary IUI and a vanishingly small potential effect on human health risk.

2.3.2 Serum levels are the most accurate predictors to likely inhibition of iodine uptake. However, to avoid any confounding from goitrogens produced internally in the body, EPA can compare external sources of IUI potential. Existing data enables EPA to compare total dietary exposure of nitrate and perchlorate. The PSG contracted with ENVIRON International to estimate the dietary nitrate exposure for important sensitive subpopulations. Green vegetables like broccoli and lettuce are the most significant nitrate sources; the analysis includes nitrate and consumption of 21 foods. Applying the model developed for FDA to estimate food intake, the ENVIRON report uses a Monte Carlo simulation to estimate the distribution of dietary nitrate intake values for different subpopulations.

Table 5 gives the key finding of this analysis. For females aged 14 to 45, the mean dietary exposure from the 21 foods is equivalent to nearly 1,300 μg/kg-bw/day. If the ratio of perchlorate to nitrate's contribution to IUI potential is 240:1, then a daily dose of 1,300 μg/kg-bw/day of nitrate in food is equivalent to 5.4 μg/kg-bw/day of perchlorate in food. This amount of IUI potential is over 140 times greater than the median perchlorate concentration in food for

females in this age group (as given in Table 2 above). It is also 84 times greater than total perchlorate exposure for all adults (as given in Table 1). A similar calculation can be made for other groups and points along the population distribution.

In other words, the analysis examines an approximation of the most sensitive subpopulation identified by the NAS: pregnant women with mild iodine deficiency. Women of child-bearing age eat diets filled with nitrate and small amounts of perchlorate. Their nitrate consumption in this diet has 145 times the potential to reduce their iodine uptake than the perchlorate in their food. This dietary nitrate exposure has 84 times more IUI potential than all perchlorate exposure and much more than 84 times more IUI potential than perchlorate drinking water exposure. Therefore, even if a drinking water standard eliminated all perchlorate exposure, it would reduce only a small fraction of total IUI exposure in the diet.

Table 5: Mean Nitrate Intake by Women of Child-Bearing Age for 21 foods

	Ages 14-45 Females		
Food Item	Mean Nitrate Intake (µg/kg BW/day)	Percentage	Cumulative Percentage
Lettuce	522.38	40	40
Broccoli	200.63	16	56
Celery	154.85	12	68
Spinach	105.78	8	76
Potatoes	98.94	8	84
Cabbage	57.09	4	88
Greens	50.75	4	92
Green Beans	31.59	2	95
Cauliflower	22.67	2	96
Carrots	12.48	1	97
Cucumber	10.75	1	98
Corn, sweet	7.10	1	99
Peppers, sweet			
Squash, Summer			
Bacon, (any type)			
Milk			
Lima Beans	< 7	< 1 %	100
Okra			
Brussels Sprouts			
Asparagus			
Artichoke			
Total	**1292**		

2.3.3   Metropolitan Water District (MWD) results

An example: Drinking water served by the Metropolitan Water District of Southern California.

Even within drinking water, perchlorate is a small fraction of IUI. MWD imports water from the San Francisco-San Joaquin Bay Delta and the Colorado River for delivery to residents of the Southern California region. MWD has five filtration plants that receive varying portions of water from either the State Water Project or the Colorado River. According to MWD water quality test results for data collected in 2005, only one of the five filtration plants had detectable levels of perchlorate with a range from non-detect to 2.3 ppb, with the average level identified as non-detect. Working with EPA and state agencies, PSG members have invested hundreds of millions of dollars to contain and treat contaminated water entering this watershed.

This data illustrates how little perchlorate contributes even in drinking water's contribution to IUI. When looking at nitrate results collected the same year, detects were found at each of the five filtration plants with identified ranges from non-detect to 1.5 parts per million (ppm), with averages from non-detect for one plant up to 0.79 ppm.[45]

In addition, monthly sampling results for perchlorate at MWD's Lake Havasu Intake covering calendar years 2000-2007 show a steady decrease in mean annual perchlorate levels compared with an overall increase in nitrate levels. Specifically, perchlorate levels at the Lake Havasu Intake decreased from a mean annual level of 6.42 μg/L (micrograms per Liter) in calendar year (CY) 2000 to 0.38 μg/L in CY2006. MWD's CY2007 sampling results show no detects for the first four months of the year. Nitrate sampling results over the same period showed an overall increase in mean annual levels from 0.99 mg/L (milligrams per Liter) up to 1.53 mg/L in CY2006. Based on the sampling results received for CY2007 thus far, the mean nitrate levels over the first six months is 1.98 mg/L, or almost a 1 mg/L increase from its levels in CY2000.[46]

2.3.4   In summary, there are three approaches that EPA should use to determine that regulation of perchlorate in drinking water does not present a meaningful opportunity to reduce human health risk.

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[45] Metropolitan Water District of Southern Cal., *2006 Water Quality Report: 2005 Water Quality Table*, 2006.

[46] Data on perchlorate and nitrate sampling results provided by Metropolitan Water District of Southern Cal.

These approaches depend on the exceptionally rich scientific literature on perchlorate's occurrence, human exposure, and human toxicity. EPA should adopt one of these approaches so that it can move forward immediately with a proposed determination for perchlorate.

ATTACHMENT 3

3.   *Other options presented by EPA for the RSC.*

If EPA does not pursue any of the approaches discussed in Attachment 2, it can rely on its customary, generic approach to evaluate meaningful risk reduction opportunities. Under EPA's customary approach, EPA creates a HRL by multiplying the DWEL of the RfD by an RSC for the constituent. The Support Document outlines several options that EPA suggests for its RSC determination using the biomonitoring data and food surveys. If performed in a scientifically valid manner, the data shows that EPA would calculate an RSC of essentially one. The health benchmark level then would become the RfD.

3.1   Use of urinary biomonitoring total exposure value to estimate an RSC.

EPA outlines one option to use the biomonitoring data to calculate an RSC:

> EPA could use the urine data to estimate total perchlorate exposure, then subtract this exposure value from the reference dose and allow the remainder as the exposure limit for water. The allowed remainder divided by the RfD would be the RSC for drinking water.[47]

This approach has major flaws. Under this approach, EPA would calculate the RSC differently for perchlorate as opposed to all other drinking water determinations.   The approach is unnecessarily conservative and mathematically inconsistent with past practice. Put simply, in this approach EPA would double count other perchlorate exposure: once when it subtracts total exposure from the reference dose; again when it limits the drinking water exposure to this reduced amount.

This mathematical conservatism can be shown by comparing this approach to EPA's usual method. EPA calculates a maximum contaminant level (MCL) for a noncarcinogen as

$$MCL = RSC \cdot RfD$$

Where the RSC is

$$RSC = DW / (DW + Other)$$

Or, in other words, the fraction of exposure derived from drinking water as compared to total exposure to the constituent. The perchlorate biomonitoring results provide a good measure of total exposure, DW + Other.

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[47] *CCL2 Support Document*, at 12-35.

EPA suggests calculating the perchlorate RSC differently. It suggests a new RSCp defined as:

$$RSCp = [RfD – (DW + Other)] / RfD$$

And the potential MCL as

$$MCL = RSCp \cdot RfD$$

If EPA's approach was the same as past practice, RSCp = RSC, or

$$[RfD – (DW + Other)] / RfD \neq DW / (DW + Other)$$

It is clear that they do not equal each other. It is also clear that RSCp > RSC for the observed values in the distributions. Rearranging,

$$RfD(DW + Other) - (DW + Other)^2 > DW \cdot RfD$$

$$Other \cdot RfD - (DW + Other)^2 > 0$$

At the 50th percentile, we do not know the precise value of DW. It is certainly less than the total exposure (DW + Other), or 2.2 ppb. Using this value for DW, the above equation is greater than zero. Thus, this option would be a uniquely conservative approach in the history of EPA's drinking water program.

Most importantly, this approach would not yield meaningful risk reduction. At the 50th percentile, the calculated MCL would be 22.2 ppb. Less than 0.002 percent of the population would have any change in their drinking water exposure with this MCL. In the Support Document, EPA suggests calculating this option at the 95th percentile to get a conservative RSC of 70 percent.[48] Even using this overly conservative, unique derivation, less than 0.0036 percent of the population is above this HRL. In making other regulatory determinations, EPA has consistently decided this situation does not meet the criterion of meaningful risk reduction.[49] Since there is no health benefit from levels below the RfD, there is embedded mathematical conservatism in the approach. Exposures above the RfD are not likely to be adverse; therefore this approach also yields no meaningful health risk reduction. It would create a new, mathematically inconsistent and excessively conservative precedent for the drinking water program that will divert scarce resources from more significant threats.

3.2   Use of the urine data and Unregulated Contaminant Monitoring Rule 1 (UCMR 1) to deduce exposure from other sources.

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[48] Id.

[49] See Attachment 4, section 4.2 for a review of CCL 1 regulatory determinations.

EPA describes this approach to calculate an RSC as follows:

> Alternately, for those NHANES survey subjects served by public drinking water systems with positive detections for perchlorate, EPA could estimate the expected perchlorate dose contributed by drinking water (using individual water consumption data from the NHANES survey combined with UCMR 1 data for the area in which they live) and subtract it from the total perchlorate dose (based on urinary perchlorate excretion data) to calculate the amount contributed by food.[50]

In this approach, EPA would identify individuals from the NHANES data set and match them with the drinking water concentration in their community from the UCMR data. EPA would have a total measure of exposure in these individuals and an estimate of their drinking water exposure. EPA then states it could subtract the drinking water contribution to total exposure to estimate the total amount contributed by food.

3.2.1 Summary of the UCMR survey.

> The UCMR program is a nationally-representative statistical sample of persons served by a public drinking water system. It is a census of about 2,774 large systems (each serving more than 10,000 persons) that provide drinking water to about 80 percent of the US population served by public water systems. It also encompasses a representative sample of systems serving 10,000 or fewer persons (small systems) monitor for unregulated contaminants. These smaller water systems total approximately 65,000 systems. EPA selects a national representative sample of 800 small systems for UCMR testing.[51]

> More than 282 million people in the US of the estimated 296 million (95 percent) in 2005 are served by public water systems covered by the UCMR survey.[52]

> This analysis assumes that the concentrations measured in the UCMR 1 survey are still occurring. In fact, levels in many of the highest reported drinking water systems have significantly declined due to source control. In addition, the UCMR 1 data was collected at a

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[50] *CCL 2 Support Document*, at 12-36.

[51] 64 FR 50567 (1999).

[52] *Factoids: Drinking Water and Ground Water Statistics for 2005*, US EPA, Dec. 2006, *available in* www.epa.gov/safewater/data/pdfs/statistics_data_factoids_2005.pdf.

time when laboratory methods for measuring perchlorate were evolving. Due to interference from other compounds, laboratories must carefully analyze output to discern a sample's true perchlorate concentration. It is possible that many of the very large readings of perchlorate in the UCMR 1 sample are erroneous. EPA should validate some of the most significant sample results as part of its proposed determination.

3.2.2   EPA can make this comparison since the two surveys, the UCMR and the NHANES biomonitoring overlap in the essential features for the regulatory determination:

- Both have large sample sizes and statistically robust methodologies. The size and carefully-evaluated scientific design of both studies give confidence in the precision at the extremes of the distribution of the population. This confidence is important since perchlorate drinking water exposure only occurs at the upper end of the US population distribution.

- Both studies are nationally representative samples of their respective populations. Both study populations are essentially all Americans with some differences. While the UCMR will not cover Americans served by private wells or transient water systems, the NHANES sample includes these populations. The study of the NHANES population only includes children above the age of 6; the UCMR estimates drinking water exposure of younger children.

These differences are not material to EPA's determination. First, the study of the NHANES population includes the most sensitive subpopulations identified by the NAS Report. Second, since any drinking water standard would only apply to public water systems, the UCMR data fully encompasses the population that would receive any risk reduction from a potential EPA standard.

In the end, the principal difference is a measure of potential perchlorate input into the human body; the NHANES data is a measure of actual exposure in the human body. The NHANES data is superior as a measure of exposure since it eliminates the uncertainty concerning bottled water consumption and exposure from cooking, bathing, and other activities.

3.2.3   The publicly available NHANES data does not include information on subjects' location to perform the analysis EPA proposes. Therefore, to illustrate the potential results of this approach, suppose the two UCMR and the NHANES surveys were perfectly correlated. In other words, the person with the highest dose in the biomonitoring study also had the highest dose measured in drinking water.

In Figure 1, the two distributions are plotted as if they were 100 percent correlated. As stated above, for virtually all members of the population, total perchlorate exposure is well below the RfD. Most of the population's exposure clearly occurs from sources other than drinking water. Below the 86th percentile of the population, the UCMR survey did not detect perchlorate in drinking water below the method of detection, or 0.114 µg/kg/day. Since the mean total exposure value is well below this level, the drinking water exposure for most of the population must be below the 0.114 µg/kg/day level shown in Figure 1.

Figure 1: Comparison of Population Distribution of Total Perchlorate Exposure and Drinking Water Exposure
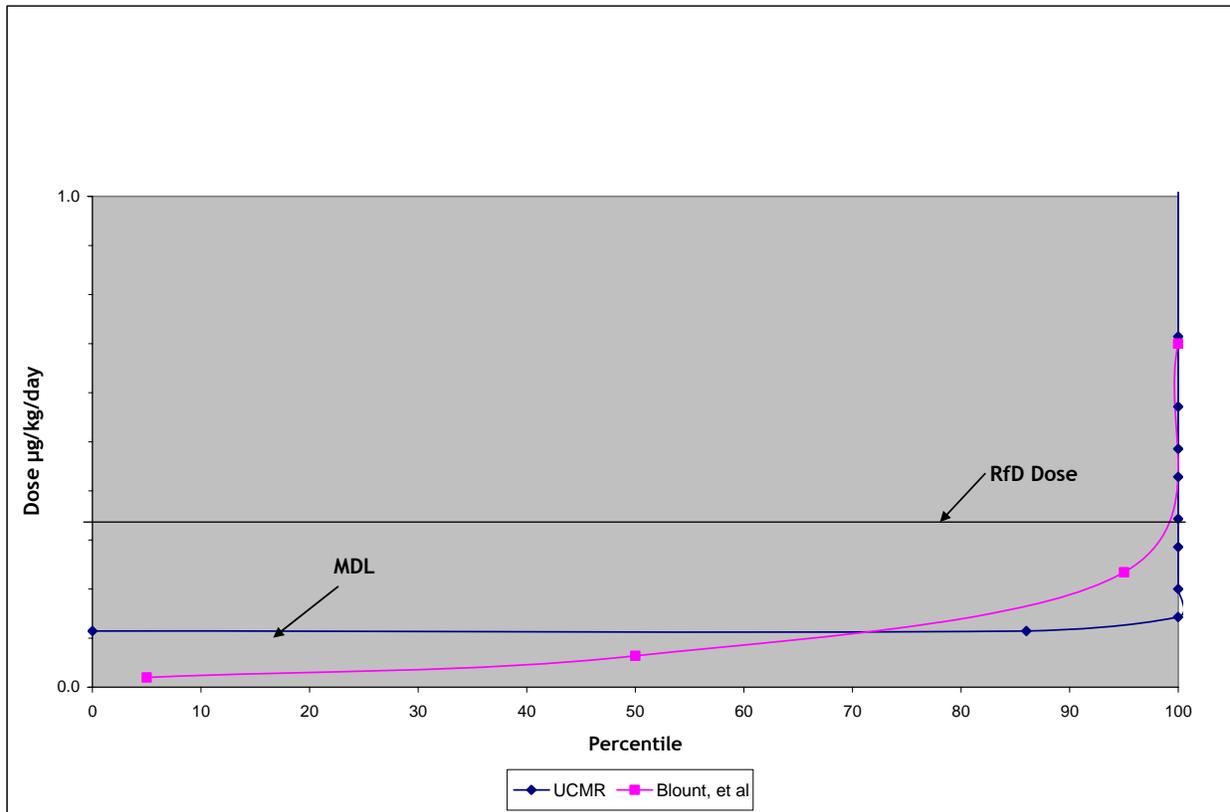
Since any relationship between the two distributions is visible only at the extreme upper end of the distribution, Figure 2 plots the relationship between the distributions in the upper 0.04[th] percentile. For simplicity, the curves are plotted and not fitted.

Figure 2: Comparison of UCMR and NHANES Distribution at the Extreme Upper End
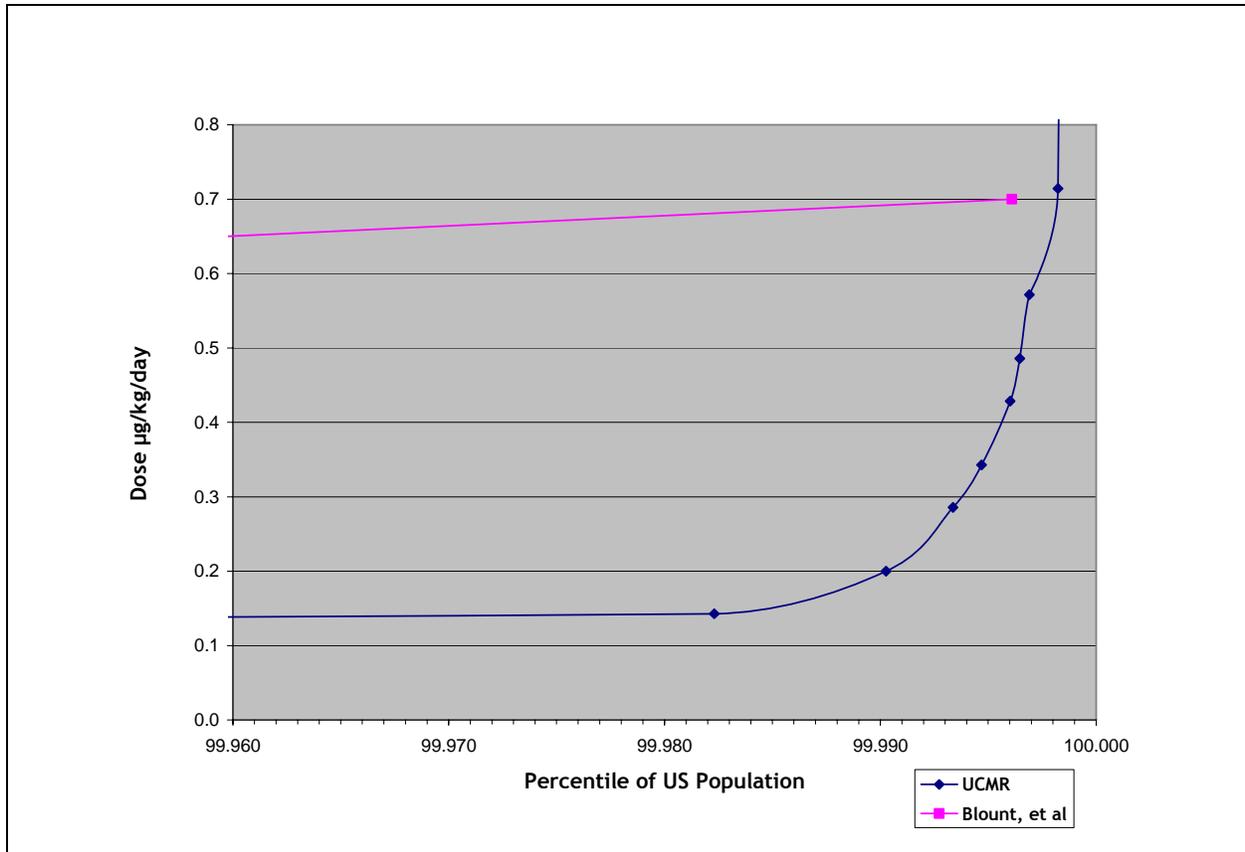
As EPA states elsewhere in the Support Document, EPA should first compare these two measures within a set of individuals to determine whether reduction in their drinking water exposure would present a meaningful opportunity to reduce risk.[53]

Visually, there is no obvious relationship between the two curves in this region, diminishing the prospect that drinking water is a major determinant of total perchlorate exposure. If the assumption that the two curves are 100 percent correlated is relaxed, a comparison of the data would show even less obvious connection. This qualitative comparison is consistent with all the other analyses that drinking water is a very small contributor of perchlorate exposure for at least 99.99 percent of the population.

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[53] *CCL 2 Support Document*, at 12-35.

The disadvantage of this approach is that it throws out a lot of the data, creating an artificially low RSC. While it is understandable that EPA would want to find a measure of drinking water concentration for the NHANES participants to match with their total exposure measure, this approach is only effective at the extreme high-end of the population distribution. Therefore, this approach excludes the overwhelming majority of the population that has low or zero perchlorate drinking water exposure. A biased RSC would not only set troubling precedents and divert scarce resources; it also ultimately would still yield a result EPA would find does not provide meaningful risk reduction.

More importantly, EPA would be expending a lot of effort and time on a tangential investigation. Rather than try to subdivide the total exposure, EPA can simply rely on the plain meaning of the biomonitoring results – total exposure including drinking water exposure, is below the appropriate health benchmark. There is no adverse risk to human health from total exposure or drinking water levels.

3.3   Use of urinary biomonitoring data from exclusive bottled water drinkers to estimate RSC.

As with the comparison of the UCMR data to the NHANES individuals, this approach is another method to identify drinking water exposure of specific biomonitoring study participants. EPA states this methodology would generate a fairly reliable estimate of the expected contribution of other sources to total perchlorate exposure.

EPA states correctly that bottled water contains essentially no perchlorate. FDA has collected bottled water samples nationwide at different retail locations. While no information is available as to whether FDA followed a specific sampling protocol, FDA reports that the samples represent different varieties of bottled water including artesian water, well water, distilled water, drinking water, purified water, and spring water. The agency tested 51 bottled water samples and found perchlorate levels in two of those samples, or a rate of less than four percent. The levels of the two detections are extremely low, 0.45 ppb and 0.56 ppb. No detectable levels of perchlorate were found in the remaining 49 bottled water samples.[54]

While the data is not available on the individuals in the biomonitoring study to know which ones drink only bottled water, if bottled water contains less perchlorate than public water supplies, the entire distribution of total perchlorate provides a conservative predictor of the bottled water subsample.

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[54] *Perchlorate Exposure Estimate, supra* note 38.

Assuming the actual value in the samples is ½ of the bottled water detection level of 0.20 ppb and assuming the data is representative of all bottled water, the mean perchlorate level in bottled water would be 0.12 ppb. Since only two of the 51 samples had values above the level of detection, this estimate is highly dependent on the assumption of the true value for the non-detects.

With this estimated average bottled water concentration, it is still only five percent of the total perchlorate exposure at the 50th percentile of the biomonitoring distribution. For bottled water drinkers, food is the source of at least 95 percent of their average perchlorate exposure. EPA would derive an RSC of essentially one. Thus, reducing the estimated five percent derived from drinking water exposure amount by a small amount through an MCL would make no meaningful -- if any -- change to total exposure. Since total exposure is well below the conservative RfD, no risk reduction would result from this miniscule reduction in potential exposure.

3.4   Use FDA's food data.

EPA also suggests that it is considering using food survey data for its RSC calculation. Customarily, the next step in the process would involve EPA undertaking the process of calculating food contribution to total exposure from FDA's food sampling results and exposure modeling estimates. This process could take several months.

FDA began sampling in December 2003 for the presence of perchlorate in various foods, milk, and bottled water following reports of perchlorate residue in lettuce. FDA did not release the results of its "Phase I" sampling effort until November 2004. FDA moved into its Phase II effort that involved sampling an expanded array of fruits, vegetables, and beverages in 2004; however, the results were not available until late May 2007. Therefore, based upon the lengthy timeframes required to complete past sampling and analyses efforts, there is no certainty as to when the more comprehensive food data will be available.

There are several disadvantages of this approach, however:

- The biomonitoring data is a better indicator of total exposure than estimates calculated from data from food sampling and total dietary surveys.

- Total Dietary Survey data will take another year to collect and analyze. The biomonitoring data is already available.

- While the sampling design is adequate for the median consumer, the enormous variety of food combinations creates the possibility of very large variations in potential perchlorate consumption. As expected, there is less statistical confidence at the extremes of the distribution. Put another way, it is possible to assume extremely unusual consumption patterns that may

represent a tiny fraction - even no one – of the population. In the face of this uncertainty, EPA has only rarely moved away from its RSC default of 20 percent. This default is clearly scientifically incorrect in the face of all the studies documenting perchlorate's occurrence in food.

- As stated above, perchlorate in food is only a small contributor to IUI, the nonadverse affect EPA is using as the health benchmark. The United Kingdom has posted a similar analysis for dietary intake of nitrate of about 50 mg/day.[55] This level is consistent with other peer-reviewed studies.[56] Based on the relative potencies of nitrate and perchlorate, the iodine inhibition from nitrate alone in the typical UK diet is more than 50 times greater than the inhibition of iodine uptake from perchlorate in the US diet.

- There is no reason to presume that nitrate in the US diet is any different than the UK diet. Should EPA determine that perchlorate is a chemical of concern as a goitrogen; another avenue for EPA to evaluate is further regulation of nitrates and other goitrogens, as appropriate.

- Finally, based on the results of FDA's preliminary exposure assessment, the ultimate RSC from the food data will be essentially one. At the 90th percentile in FDA's exposure assessment, the estimated food dose is 0.12 µg/kg/day. The 86th percentile population level of the UCMR results in a perchlorate dose at the detectible level of 0.114 µg/kg/day. Assuming the distributions are highly correlated, the RSC would essentially be one. Further sampling by FDA will only increase the estimated food dose.

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[55] *Food Surveillance Information Sheet*, United Kingdom Ministry of Agriculture, Fisheries and Food, *et al.*, Sep. 1998, *available in* http://archive.food.gov.uk/maff/archive/food/infsheet/1998/no163/tables.htm.

[56] *See*, A. Petersen, & S. Stoltze, *Nitrate and Nitrite in Vegetables on the Danish Market: Content and Intake*, Food Addit. Contam., Jul 1999, 16(7):291-9; G. Ysart *et al., Dietary Exposures to Nitrate in the UK*, Food Addit. Contam., Dec. 1999, at 16(12):521-32.

ATTACHMENT 4

4. *Evaluating meaningful risk reduction using EPA's customary, generic approach.*

As shown in the last section, if EPA follows its customary approach to evaluate the potential for meaningful risk reduction from a potential perchlorate drinking water MCL and uses consistent methods, the RSC contribution will be essentially one (which yields an HRL of 24.5 ppb drinking water equivalent).

For perchlorate, EPA should calculate the HRL based solely upon the RfD with an RSC of 1 to account for the conservative nature of the RfD. As noted above, the NAS panel calculated its recommended RfD based upon a NOEL of 0.007 mg/kg per day and then applied a full intraspecies factor of 10 to account for all sensitive populations. As EPA is aware, this approach is more conservative than EPA's normal approach of calculating the RfD based upon the NOAEL or LOAEL.[57] When calculating potential HRLs for perchlorate in its CCL 2 preliminary determinations document, EPA's customary approach fails to acknowledge the fact that the perchlorate RfD is based upon the more conservative NOEL versus EPA's traditional use of the NOAEL or LOAEL.[58] This more conservative calculation should be factored into EPA's determination.[59]

EPA then compares this HRL to perchlorate occurrence data in drinking water to evaluate the percent of the population exposed to perchlorate above fractions of the HRL. Using a HRL of 24.5 ppb, the question then is how perchlorate compares to other regulatory determinations EPA has made.

4.1 EPA proposed to continue the approach it used in the CCL 1 determination for the CCL 2 contaminants.

For the CCL 2 determination, EPA should use the evaluation criteria under the CCL 1 regulatory determinations to determine whether a meaningful opportunity to regulate health risk exists. EPA's regulatory evaluation process follows the recommendations on a protocol from EPA's stakeholder advisory panel, the National Drinking Water Advisory Council (NDWAC). To assist EPA in evaluating the third statutory criteria, the NDWAC protocol recommended "that EPA consider estimating the national population exposed above half the

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[57] *See, CCL 2 Support Document*, at 2-9: "[the RfD] can be derived from either a NOAEL or LOAEL, or benchmark dose, with uncertainty factors applied to reflect limitations of the data used."

[58] Id. at 12-31, Exhibit 12-3 at 12-32.

[59] *See,* Joan Strawson *et al.*, Envtl. Health Perspectives, Nov. 2005, at A729: "In contrast, the approach the NRC actually used was a nonstandard approach for developing an RfD based on the inhibition of iodine uptake, a distant precursor to the critical effect. This nonstandard approach yields a safe dose, but it is not an RfD, by definition, because, according to the NRC's own scheme, it is not based on the critical effect or its known and immediate precursor."

health reference level (or benchmark) and the national population exposed above the health reference level (or benchmark)."[60]

EPA used this approach for evaluating substances in its CCL 1 regulatory determinations. This approach allows EPA's decision-making process to be replicated and therefore provides greater transparency and objectivity into the Agency's final decisions rendered on the third statutory criterion. It also has the support of major stakeholders and has been subject to public comment. EPA should use a similar evaluation process for its CCL 2 regulatory determinations.

4.2 A comparison of occurrence data for perchlorate and relevant compounds from EPA's CCL 1 regulatory determinations and CCL 2 proposed determinations reveals that with perchlorate ranks as a lower opportunity for risk reduction than the sodium, manganese, sulfate, and boron, all of four of which EPA has made or proposed determinations not to regulate.

Sodium

EPA decided not to regulate sodium in the CCL 1 regulatory determinations. EPA concluded that while sodium may pose adverse health risks by contributing to hypertension, there are other more effective preventative measures for reducing sodium exposure through a balanced diet and exercise. EPA also concluded that the low levels of sodium found in water systems are unlikely to significantly contribute to adverse health effects.[61]

EPA used a benchmark level of 120 mg/L for use in evaluating occurrence data. The level was derived from a 1989 NAS dietary guideline for adult intake of table salt of 2.4 g/day, to which EPA adjusted to a DWEL concentration of 1.2 g/L and applied a 10 percent RSC. EPA noted that food is a major source of sodium with reported dietary intake ranging from 1,800 mg/day up to 6,000 mg/day and that drinking water accounts for only a small contribution. EPA calculated the RSC based upon the median value in drinking water of 16 mg/L and using 4,000 mg/L for total dietary intake, found that drinking water contributes only 0.8 percent of total dietary sodium. However, when calculating RSC at the 99th percentile (500 mg/L), drinking water contributed 25 percent of daily sodium.

EPA's review of ambient water occurrence data showed that sodium occurrence in drinking water to be high, with surface and ground water detection frequencies both between 90 percent and 100 percent. EPA review of drinking water data showed that 100 percent of National Inorganic and Radionuclide Survey (NIRS) Public Water Systems (all 59,440) had sodium detects, thus affecting 100 percent of the population served or 85.6 million people.

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[60] US EPA, *Regulatory Determination Support Document for Sodium*, Jul. 2003, at 4.

[61] Id.

Approximately 23 percent of Public Water Systems (PWSs) (or 13,500) had detections greater than ½ the benchmark level of 120 mg/L, affecting 18.5 percent of the population (or 15.9 million people). Approximately 13 percent of PWSs (or 8,000) had detections greater than the benchmark level affecting 8.3 percent of the national population (or 7.1 million people).

Manganese

EPA made a determination not to regulate manganese because the Agency concluded that it does not occur in drinking water at concentrations that are of public health concern. In addition, the HRL concentration from PWSs is far less than the average daily intake from other sources.[62]

In EPA's regulatory determination for manganese, EPA identified a health reference level of 0.30 mg/L. EPA looked at median and 99th percentile concentrations to understand the middle range and high range of concentrations in ambient water through USGS National Ambient Water Quality Assessment (NAWQA) program. The 99th percentile of all concentrations was 0.63 mg/L, more than double the HRL and affecting more than 2.3 million people. The median concentration of detections was 0.001 mg/L.

EPA also looked at NIRS ground water PWSs and found that 68 percent (40,000) had detections affecting 55 percent of the population (47.5 million people). At ½ of the HRL of 0.30 mg/L, 6.1 percent of NIRS PWSs had detections greater than half the HRL (3600) affecting 4.6 percent of the population (3.9 million people). Approximately 3.2 percent (1900) of the PWSs had detections over the HRL affecting 2.6 percent of the population (2.3 million people). The median concentration was 0.01 mg/L and the 99th percentile concentration of all samples was 0.63 mg/L.

Sulfate

EPA found sulfate to occur in PWSs at levels of public health concern, however, the population of concern was "relatively small," at 1.9 million of the 202.6 million exposed.[63] EPA found that the critical effect, short-term laxative effect, is temporary and reversible. EPA set the HRL at 500 mg/L based upon the recommendation from a 1999 EPA expert panel; however, the level does not seem to incorporate an RSC. EPA noted that there was little information on dietary intake and that sulfate is unlikely to bioaccumulate through the food chain.

Occurrence estimates revealed that 87 percent of all samples showed detections with a mediation concentration of 24 mg/L and 99th percentile concentration of 560 mg/L. EPA found that 88.1 percent of the PWSs (57,299)

[62] US EPA, *Regulatory Determination Support Document for Manganese*, Jul. 2003.

[63] US EPA, *Regulatory Determination Support Document for Sulfate*, Jul. 2003.

had detects above the HRL of 500 mg/L affecting 1.8 percent or 2 million people served. EPA determined that 5 percent of the PWSs (3,229) showed detects above ½ the HRL affecting 10.2 percent or 21.8 million people served.

Boron

EPA has proposed not to regulate boron in the CCL 2 proposal, concluding that overall exposure and occurrence from surface and ground water systems are likely to fall below levels found in the NIRS data and therefore not occur at levels of concern.[64] Citing occurrence data from both the NIRS and AWWARF, the Agency found that while NIRS occurrence data for ground water systems showed detections above both the HRL and ½ of the HRL, AWWARF occurrence data for surface water systems showed no detects above either threshold. EPA remands the issue for consideration by the States based upon respective incidence of boron exposure, recommending that States consider site-specific measures in addressing exceedances.

EPA established an RfD of 0.2 mg/kg per day and an HRL of 1.4 mg/L using a 20 percent RSC. In reviewing NIRS ground water occurrence data, 81.9 percent of PWSs had detections equal to or above the MRL of 0.005 mg/L affecting 88.1 percent or 75.5 million people served. Detections greater than ½ the HRL occurred in 4.3 percent PWSs affecting 2.9 percent or 2.5 million people served. Detections greater than the HRL occurred in 1.7 percent of PWSs affecting 0.4 percent or 0.4 million people.

Perchlorate

If the RSC for drinking water is one, then according to EPA estimates in Exhibit 12-3,[65] an HRL value of 24.5 μg/L would affect between 0.12 percent and 0.36 percent of PWSs with at least 1 detection greater than 25 μg/L, affecting 0.4 million to 1 million people served. Using EPA's UCMR 1 Occurrence and Populations Estimates chart,[66] between 0.42 percent and 1.09 percent of PWSs had at least one detect with concentrations at ½ of the HRL (12 μg/L), affecting between 0.002 percent and 0.004 percent of the population served or between 1.2 million and 3.6 million people served, respectively.

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[64] *CCL 2 Support Document*, at 3-24.

[65] *CCL 2 Support Document*, at 12-32.

[66] Id.

Table 6: Comparison of Risk Opportunity Between Perchlorate and Other Compounds

	Percent of PWS with Detects	Population Percentile Above 1/2 HRL	Population Served Above 1/2 HRL (millions)
Sodium	100	18.5	15.9
Perchlorate	3.6	0.0043	1.2 - 3.6
Manganese	68	4.6	3.9
Sulfate	88.1	10.2	21.8
Boron	82	2.9	2.5

The percentage of PWSs with perchlorate detections was very low (3.6 percent) compared to the next lowest unregulated compound, manganese at 68 percent. Sodium, for example, was detected in all PWSs. Perchlorate also has one of the lowest populations served by PWSs with detections above half the HRL of 12.5 µg/L with 1.2 million to 3.6 million people. Perchlorate is well within the range of values for the evaluation criterion EPA uses. Like these other constituents, perchlorate is widely found in the diet and has minimal adverse health effects at the RfD. If EPA adopts its customary approach for the proposed regulatory determination, it should find that perchlorate does not pose a meaningful opportunity to reduce risk.

Attachment 5

JONATHAN BORAK & COMPANY, INC.

Specialists in Occupational & Environmental Health

November 2, 2006

Department of Health Services
Office of Regulations
1501 Capital Avenue, MS 0015
Sacramento, CA 95814

Re: Proposed Maximum Contaminant Limit for Perchlorate, R-16-04

Dear Sir or Madam:

At the request of the Perchlorate Study Group, I am writing to offer my perspectives as a scientist, physician, and toxicologist on a very recent perchlorate-related report by researchers at the CDC (Blount BC et al: Urinary perchlorate and thyroid hormone levels in adolescent and adult men and women living in the United States; *Environmental Health Perspectives* doi:10.1289/ehp.9466, online 5 October, 2006; the "Blount study"). This report, referred to as the "CDC study", was cited by several speakers during the October 30, 2006 public hearing on the California Department of Health Services proposed maximum contaminant level for perchlorate. For various reasons, I believe that the Blount study is not a suitable basis for regulatory decision making and should not be considered for that purpose.

By way of introduction, I am an Associate Clinical Professor of Epidemiology and Medicine at the Yale School of Medicine, Director of the Yale University Interdisciplinary Risk Assessment Forum, and a faculty member of the Yale Occupational and Environmental Medicine Program. I currently serve as Chair of the Council on Scientific Affairs of the American College of Occupational and Environmental Medicine (ACOEM), was Editor and Course Director of the ACOEM *Core Curriculum in Environmental Medicine*, and have served as a member of National Advisory Committees of the US EPA and the National Research Council.

My greatest concern is that the findings of the Blount study are inconsistent with that which is generally accepted as the basic underlying science. Perchlorate is only one of a number of anions known to compete with iodine for uptake by the thyroid; others include thiocyanate and nitrate (1-6). The effects of these anions on iodine uptake have been shown repeatedly to be similar in direction and additive in magnitude. In other words, perchlorate, thiocyanate and nitrate each competitively blocks iodine uptake, and their combined effects are additive. If decreased thyroid iodine uptake leads to alterations in thyroid hormone levels,

then increasing levels of any of these anions would affect thyroid hormone levels in the same way. (The magnitude of such effects would depend in part on the relative concentrations of each anion).

In the Blount study, however, thyroid effects attributed to these anions were different and inconsistent. Increasing perchlorate was associated with anti-thyroid effects (decreased T4 and increased TSH) in women, but not in men. Thiocyanate apparently had the opposite effect; increasing thiocyanate was associated with decreased TSH, particularly in women with urine iodine <100 μg/L who seemed most susceptible to perchlorate. Likewise, increasing levels of nitrate had no apparent effects on T4 or TSH in women with urine iodine <100 μg/L, who seemed most susceptible to perchlorate. (Although the Blount study only reported the effects of thiocyanate and nitrate in women, separate analyses of the NHANES data sponsored by the Perchlorate Study Group indicate that similar inconsistent effects were also seen in men.)

The Blount study recognized these inconsistent effects, which were described as "unexpected based on a mechanism of NIS inhibition... the explanation for this is unclear" (7). I agree with that appraisal; these associations are inconsistent, contradictory, and cannot be explained by known thyroid-related mechanisms. They probably reflect heretofore undetected bias, confounding or laboratory error and therefore the study requires controlled replication.

A dataset that is so inconsistent with the accepted science might be useful for hypothesis generating, but it cannot be used to test such hypotheses. More clearly, it provides no scientific basis for regulatory action.

Yours truly,

Jonathan Borak, MD, DABT

Associate Clinical Professor of Epidemiology and Medicine
Yale School of Medicine

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