January 22, 2013

Michael Baes (mbaes@oehha.ca.gov)
Pesticide and Environmental Toxicology Branch
Office of Environmental Health Hazard Assessment
California Environmental Protection Agency
1515 Clay St., 16th floor
Oakland, California 94612

Re: Proposed Public Health Goal for Perchlorate in Drinking Water

Dear Mr. Baes:

The Association of California Water Agencies (ACWA) appreciates the opportunity to comment on the proposed public health goal (PHG) for perchlorate in drinking water. ACWA represents nearly 440 public water agencies in California that collectively supply 90% of the water delivered in California for domestic, agricultural and industrial uses. Our state enjoys some of the highest water quality in the world, and local water agencies are responsible for meeting many stringent federal and state water quality regulations to ensure the water they deliver is clean and safe, including the existing drinking water standard of 6 ppb for perchlorate.

We are once again disappointed that the proposed revision to the PHG for perchlorate originally published in January 2011 and again in December 2012 did not respond to any of ACWA’s comments or stated concerns as presented in our letters dated August 29, 2008 and February 23, 2011. While the Office of Environmental Health Hazard Assessment (OEHHA) published these proposals and encouraged comments on both, there is no response to comments received by OEHHA or how it has chosen to evaluate and consider them. Since ACWA’s comments still apply to the most recent proposal, we enclose copies of the letters cited above.

In addition, we provide the following comments specifically on the December 2012 published Draft Public Health Goal for Perchlorate in Drinking Water.

Compounding of Safety Factors

OEHHA has increased the uncertainty factor applied to infants from the factor of 3 used in the 2004 PHG to a factor of 10 in the current proposed PHG based on the assumption that infants are likely to be an additional “susceptibility group,” or sensitive sub-population. This assumption appears to be based on a review done by U.S. Environmental Protection Agency’s (USEPA) Science Advisory Board (SAB) at USEPA’s request to consider “sensitive life stages” and the use of Physiologically Based Pharmacokinetic (PBPK) modeling that takes into account an increased daily water ingestion rate to body weight ratio for infants. This PBPK modeling likewise considers other groups like fetuses, preterm infants and pregnant women. However, OEHHA has compounded this increase in safety factor by also including in its PHG calculation a much higher intake level per body weight for infants of 0.237 L/kg-day. This is essentially “double counting” safety factors for the same reason...
for infants, which ACWA believes is inappropriate. ACWA believes that OEHHA must choose one safety factor or the other, but should not use both. OEHHA has calculated the PHG as follows:

\[ 0.37 \, \text{ug/kg-day} \times 0.73 \, \text{(RSC)} / 0.237 \, \text{L/kg-day} = 1 \, \text{ug/L} \]

By eliminating the 10 x safety factor and going back to the old 3 x safety factor from 2004 and still using the new “infant” consumption rate, the PHG is calculated as follows:

\[ 3.7 \, \text{ug/kg-day} \times 0.73 \, \text{(RSC)} / 0.237 \, \text{L/kg-day} = 11.4 \, \text{ug/L} \]

The alternative to this, based on OEHHA’s current discussions, is the keep to the new 10 x safety factor for consideration of infants and use the more traditional consumption rate of the average 70 kg adult of 2 liters. This would be 2 L / 70 kg = 0.0285 L/kg-day. The PHG would then be calculated as follows:

\[ 0.37 \, \text{ug/kg-day} \times 0.73 \, \text{(RSC)} / 0.0285 \, \text{L/kg-day} = 9.5 \, \text{ug/L} \]

As the above calculations indicate, removing the inappropriate “double safety factors” result in levels that are above the current PHG of 6 ug/L, in spite of the fact there is a third compounding safety factor that has existed since the debate began on perchlorate. That is the fact the National Academy of Sciences (NAS) proposed that the reference dose for perchlorate be calculated on a No Observed Effect Level (NOEL) rather than a No Observed Adverse Effect Level (NOAEL), a first time departure when considering health effects in the regulation of a drinking water contaminant. OEHHA and USEPA have both agreed with this, and OEHHA used this approach in setting the current PHG of 6 ug/L. This is an extremely conservative approach considering that the NOEL represents the inhibition of iodine uptake, while the NOAEL is the reduction in the production of thyroid hormones. It is also important to note that neither OEHHA nor USEPA has ever cited a study actually showing the “adverse effect” on humans from the consumption of perchlorate in drinking water.

**Draft SAB Report**

The 2012 draft SAB report to USEPA on consideration of the setting of a MCLG for perchlorate has several interesting comments. The SAB seems to endorse the use of a PBPK model by USEPA in developing an MCLG for perchlorate, but not the one that was proposed and reviewed by the SAB. The SAB has said that the PBPK model proposed by USEPA is inadequate and needs to be modified to correctly be used in the setting of an MCLG. Therefore, by inference, it may be premature and inappropriate at this time for OEHHA to use the 0.237 L/kg-day number in calculating a revised PHG.

The SAB has also indicated that many studies previously used by USEPA (and OEHHA) in consideration of setting an MCLG (and a PHG) are inadequate. These include Blount *et al* (2006), Brechner *et al* (2000), and Steinmaus *et al* (2010) because it relied on Blount *et al* (2006). Many of these same sentiments were expressed to OEHHA by ACWA in our prior comment letters. Since many of these studies are key to the conclusions drawn by OEHHA in the revision of the PHG for perchlorate, ACWA requests a thorough re-evaluation by OEHHA as to the quality and adequacy of
the science being considered in this effort. OEHHA staff assured ACWA members that the work conducted by OEHHA and USEPA on perchlorate health effects would reach similar conclusions, and since it appears there are significant discrepancies, we believe there must be some form of reconciliation of those differences before OEHHA finalizes its PHG for perchlorate.

Additionally, ACWA would like to express our frustration with OEHHA in the “cherry picking” of the science cited in the development of the proposed revised PHG. While OEHHA cites many studies that support its thinking, no peer reviewed studies contradicting those conclusions are discussed. One such example is a study using the National Health and Examination Survey (NHANES) 2001–2002 data set looking at the risk from multiple chemicals that can cause iodide uptake inhibition (nitrate, thiocyanate, and perchlorate). The study found that “no evidence of functional thyroid abnormality (e.g., low thyroid hormone coupled with high TSH) was seen with exposure to the combined IUI agents and enhanced estimates of thyroid function.” We have included a copy of that study with this letter for your information. As we have stated throughout this process and during the development of all public health goals, ACWA believes that a comprehensive and balanced review of the relevant science is critical to the PHG development process. This is especially true for a revised PHG for perchlorate.

After evaluating studies that offer both perspectives, ACWA would like to request that OEHHA provide a balanced summary of each study and how it was incorporated into the technical document. We believe this information will aid those outside of OEHHA to better understand the process and how it may differ from efforts currently underway at the USEPA.

ACWA and its member agencies’ highest priority continues to be protecting public health while ensuring a reliable and affordable water supply for consumers. We look forward to continuing our work with OEHHA and the California Department of Public Health on this very important issue.

If you have questions, please contact me at 916-441-4545 or danielleb@acwa.com.

Sincerely,

Danielle Blacet
Senior Regulatory Advocate

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Urinary Nitrate, Thiocyanate, and Perchlorate and Serum Thyroid Endpoints Based on NHANES 2001 to 2002

Gretchen M. Bruce, BS, Lisa M. Corey, PhD, Jeffrey H. Mandel, MD, MPH, and Richard C. Pleus, PhD

Objective: To determine, on the basis of iodide uptake inhibition (IUI), whether associations between urinary concentrations of IUI agents (perchlorate, nitrate, and thiocyanate), as total perchlorate equivalent concentration (PEC), and serum thyroid parameters suggest functional thyroid abnormalities. Additional thyroid hormone measures were released to augment the National Health and Examination Survey (NHANES) 2001 to 2002 data set, which we used in this study. Methods: Enhanced thyroid hormone measures released to augment the National Health and Examination Survey (NHANES) 2001–2002 data set were used in this study. Multiple regression was used to assess the relationships among total thyroxine (TT4), free thyroxine, total triiodothyronine (TT3), free triiodothyronine, and thyroid-stimulating hormone (TSH) and PEC. Results: PEC was weakly and negatively associated with TT4, but not with TSH, TT3, or free T4. This association with TT4 appears to be dominated by nitrate and thiocyanate. Conclusion: No evidence of functional thyroid abnormality (eg, low thyroid hormone coupled with high TSH) was seen with exposure to the combined IUI agents and enhanced estimates of thyroid function.

Assessing risk from multiple chemicals in risk assessment is not a new concept and is one that has been endorsed by the National Academy of Sciences,1 US Environmental Protection Agency,2 and World Health Organization.3 Despite this, studies in the peer-reviewed literature often focus on the effects of a single chemical. For example, nitrate, thiocyanate, and perchlorate are among a class of chemicals that can cause iodide uptake inhibition (IUI) at sufficient dose. These three chemicals are environmentally ubiquitous and cause IUI through the exact same mechanism of action. Coexposures are common, yet previous studies have evaluated these chemicals independently, rather than additively.4,5

At sufficiently large doses for weeks or months, these agents can cause a decrease in thyroid hormones. The mechanism of action is the inhibition of iodide uptake from the blood as it competitively binds to the sodium iodide symporter (NIS), a membrane-bound protein on the basal side of the thyrocyte.5 In the thyroid, iodide is organized to produce thyroid hormones (thyroxine [tetraiodothyronine; T4] and triiodothyronine [T3]), and if thyroid iodide stores are insufficiently reduced, this could result in decreased production of thyroid hormones.6 In general, decreased thyroid hormone production causes increased release of thyroid stimulating hormone (thyrotropin [TSH]) from the anterior pituitary gland, which increases the thyroid’s ability to take up iodide and produce active thyroid hormone. The developing fetus, in particular, requires adequate thyroid hormone levels, but because the fetus is supported by maternal thyroid hormone, iodide stores in the adult thyroid prevent against short-term iodide uptake fluctuations. Iodide uptake inhibition must be reduced by at least 70% and sustained for months or longer to deplete existing stores.8 Furthermore, when iodide uptake is decreased, the body adapts by increasing the number and efficiency of NISs to pump more iodide into the thyroid.6 As an adaptive effect, IUI precedes clinical hypothyroidism by several biochemical steps.9

Nitrate and thiocyanate are less potent inhibitors of NIS activity than perchlorate; nevertheless, typical exposure levels are much higher.10 Nitrate is formed endogenously in humans and is found in drinking water and foods such as spinach and carrots. Thiocyanates are formed endogenously from cyanates in certain foods and exogenously found in smoking tobacco, and are commonly found in cruciferous vegetables. Perchlorate is environmentally ubiquitous and is naturally formed or man-made. When considering exposures to all three agents it is estimated that perchlorate is responsible for less than 1% of thyroidal IUI.10,11 The effect of perchlorate on IUI cannot be distinguished from the effects of other NIS inhibitors.10,12 It is useful to normalize the potentials of nitrate and thiocyanate to that of perchlorate to facilitate the dose addition. Relative potency factors (RPFs) for IUI at the NIS have been reported by others.8,9 These RPFs can be used to calculate a total perchlorate equivalent concentration (PEC) to provide a cumulative measure of the total IUI load contributed by nitrate, thiocyanate, and perchlorate.

The reversible inhibition of the NIS by these three agents is well documented both in vitro and in vivo.3,7 Inhibition of the NIS occurs with a sigmoidal dose–response curve—as dose increases, so does the response—and there is a threshold below which no measurable effect occurs.6 If inhibition is functionally important, reduced thyroid hormone (eg, total T4 [TT4], free T4 [fT4], total T3 [TT3], or free T3 [fT3]) would be accompanied by elevations in TSH.

Two studies reported associations between urinary perchlorate and limited serum measures of thyroid function (TSH and TT4) at perchlorate exposure levels below the no observable effect level (NOEL) for IUI identified in human volunteers in Greer et al.7 and used as the basis for the US EPA reference dose, using the National Health and Nutrition Examination Survey (NHANES) 2001 to 2002 data set.3,4 The Centers for Disease Control and Prevention (CDC) has been collecting information through NHANES since the early 1960s to assess the health and nutritional status of the US population based on age, sex, race/ethnicity, and income. NHANES 2001 to 2002 provides data for 11,039 individuals of all ages, collected between January 2001 and December 2002. NHANES 2001 to 2002 oversampled low-income persons, persons aged 12 to 19 and more than 60 years, African Americans, and Mexican Americans.15 Collected information included demographic, examination, laboratory, questionnaire, and dietary interview variables.

The NHANES 2001 to 2002 data set released in 2004 measured only TT4 and TSH. Clinically, these measures provide an

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Funding for this study was provided by the Perchlorate Study Group (PSG), a consortium of manufacturers and users of perchlorate. The PSG member companies include Aerojet General Corporation, American Pacific Corporation, Alliance Techsystems, Inc., and Lockheed Martin Corporation. Neither the PSG nor any of its member companies had any role in the conduct of the study or in the writing or editing of the article.

Intertox is a health science research firm and has conducted work for the PSG and other users and/or manufacturers of perchlorate. Dr. Pleus has served as an independent expert and has provided expert testimony on the toxicology of perchlorate. Dr. Mandel has done general consulting for Lockheed Martin, unrelated to this topic.

The authors declare no conflict of interest.

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initial screen for thyroid function; nevertheless, follow-up testing is required to determine whether these changes reflect short-term fluctuations and are adaptive or whether thyroid function is impaired. Per the American Thyroid Association,16 “The free T4 fraction is the most important to determine how the thyroid is functioning . . .” and “Combining the TSH test with the fT4 of fT3 [fT4 index] accurately determines how the thyroid gland is functioning.” CDC added testing for more specific thyroid measures, including fT4, to NHANES in later years.

In 2010, CDC released a new data set providing analyses of thyroid measures from surplus sample serum saved from the NHANES 2001 to 2002 subjects.17 The samples were reanalyzed for TT4 and TSH, as well as fT4, TT3, fT3, thyroglobulin (Tg), Tg antibody, and thyroperoxidase antibody. The inclusion of these measures enables a more complete assessment of thyroid function.

The purpose of this evaluation was to assess the additive relationship among urinary nitrate, thiocyanate, and perchlorate, and serum thyroid parameters in the 2001 to 2002 data set. On the basis of the known mechanism of action, we hypothesized that serum thyroid parameters would be associated with total PEC. The assessment was made using reanalyzed measures of thyroid hormone and TSH with the addition of the free hormone measures, which best capture the active component of the hormone, and a correction for urinary creatinine to account for variation in urine dilution. The ubiquitous nature of these environmental agents and the potential impact on the newborn and/or developing fetus adds to the importance of this understanding.

METHODS

Study Design

In NHANES 2001 to 2002, perchlorate, nitrate, and thiocyanate using ion chromatography tandem mass spectrometry and for iodide using inductively coupled plasma–mass spectrometry.18 Subsequently, a bias (−4.7%) in the reported sample volumes due to the aliquoting technique used in NHANES 2001 to 2004 was discovered by CDC, and urinary analyses for perchlorate, nitrate, and thiocyanate were adjusted by a factor of 1.049 and rereleased.18 Stored NHANES 2001 to 2002 serum samples were also reanalyzed for CDC by the University of Washington, Seattle, for total and free T4, total and free T3, TSH, Tg antibodies, and thyroid peroxidase antibodies, in samples from participants older than 12 years, using immunoenzymatic assay techniques.17 An explanation for the reanalysis was not provided.

Prior to statistical analysis, urinary results were normalized for creatinine as follows:

\[ \text{Urinary ion concentration (mM/L) = (Urinary creatinine (mg/dL)/100) / \mu g anion/g Cr} \]

Statistical Analysis

Data were analyzed using Stata 11 (College Station, TX) statistical software with survey commands to account for survey design and weighting, using 2-year sample weights corresponding to the one-third subsample for urinary perchlorate, nitrate, and thiocyanate. Multivariate regression was used to identify variables associated with thyroid measures. The significance threshold was set at 0.05 (two-tailed).

Regression models were constructed separately for each thyroid measure (TSH, TT3, TT4, fT3, and fT4). The total PEC was calculated by multiplying the RPF for IU1 at the NIS for each anion by the amount of the anion in the urine, and summing the PECs for each anion. The relative molar potency of perchlorate to inhibit 1 uptake at the NIS was 240 and 15 times that of free nitrate and thiocyanate, respectively, or 150 and 8.8 on a weight basis (to extrapolate from ingested doses rather than internal serum concentrations).8 The RPF applied to ingested thiocyanate was adjusted to account for thiocyanate bound to albumin in human blood serum (50%), resulting in an RPF of 17.6.11 Thus, the equation for PEC is as follows:

\[ \text{PEC} = [\text{perchlorate}]_{\text{urine}} + [\text{thiocyanate}]_{\text{urine}} / 17.6 + [\text{nitrate}]_{\text{urine}} / 150 \]

Perchlorate equivalent concentrations were calculated using the creatinine-corrected urinary concentration of each anion.

Independent variables were selected on the basis of a hypothesis-driven approach, including demographic variables and other independent variables collected in the NHANES database that have been shown to potentially influence thyroid status. Variables considered were age (in months), sex, race/ethnicity (non-Hispanic white [referent], non-Hispanic black, Mexican American, other Hispanic, other race [including multiracial]), fasting time (in hours), body mass index (BMI), kcal (divided by 1000), serum albumin concentration (indicative of serum protein levels and involved in the transport of thyroid hormones),19 serum cotinine concentration (a biomarker of tobacco smoke exposure), serum C-reactive protein concentration (a marker of low-grade inflammation associated with overt and subclinical hypothyroidism),20,21 urinary iodide concentration, and use of medications reported to potentially impact thyroid hormone or TSH concentrations (specifically, β-blockers, furosemide, and glucocorticoid steroids and androgens). Because of their skewed distributions, urine concentrations of iodide, perchlorate, nitrate, and thiocyanate and serum concentrations of cotinine and C-reactive protein, as well as BMI and thyroid function measures, were log transformed. Correlations among variables were computed to examine possible associations among the various factors.

RESULTS

Reanalysis Using Enhanced Thyroid Hormone Data From NHANES 2001 to 2002

A total of 1960 participants aged 12 years or older had urinary perchlorate as well as TSH and TT4 measures in the “new” data set. Individuals with a reported history of thyroid disease or current use of thyroid medications (including levothyroxine and “unspecified” thyroid drugs) as well as methimazole and propylthiouracil, were excluded from analysis (77 females and 31 males). Because estrogen increases the free thyroglobulin to bind circulating T4 and T3,22 pregnant women and women currently taking estrogen-containing medications were also excluded (an additional 205 females). Six subjects with extreme TT4 or TSH levels were also removed because of the potential for intrinsic thyroid disease. These included four females (with TSH = 0.004 mIU/L and TT4 = 14.6 μg/dL; TSH = 39.776 mIU/L and TT4 = 4.4 μg/dL; TSH = 0.023 mIU/L and TT4 = 17 μg/dL; and TSH = 0.002 mIU/L and TT4 = 24.7 μg/dL) and two males (with TSH = 350.517 mIU/L and TT4 = 0.5 μg/dL and TSH = 290.60 mIU/L and TT4 = 1.8 μg/dL). The resulting data set consisted of 758 females and 883 males. Only those who had information for all covariates were included in the regression analysis (711 females and 833 males). The number of individuals, records missing, and arithmetic means for normally distributed covariates, geometric means for log normally distributed covariates, or percent in category for binary covariates, are presented in Table 1.

Urinary perchlorate was detected above the detection limit (0.05 μg/L) in all samples in the data set. Three nitrate measurements and four thiocyanate measurements were reported at concentrations slightly below their detection limits of 700 μg/L and 20 μg/L, respectively. Median urinary iodide concentrations were 133.9 μg/g creatinine in females and 135.6 μg/g creatinine in males. For males, significant correlations (P < 0.001), with
coefficients greater than ±0.30, were apparent when comparing age with log BMI, serum albumin, and log C reactive protein (correlation coefficients, 0.33, −0.40, and 0.40, respectively), and when comparing log C reactive protein with log BMI and serum albumin (correlation coefficients, 0.48 and −0.38, respectively). For females, significant correlations \( (P < 0.001) \), with coefficients greater than ±0.30, were apparent when comparing age with log BMI and log C reactive protein (correlation coefficients, 0.31 and 0.45, respectively) and when comparing serum albumin with log BMI and log C reactive protein (correlation coefficients, −0.35 and −0.40, respectively).

Log serum cotinine concentration (a biomarker of tobacco smoke exposure) was considered for inclusion in the models but was excluded because it was significantly \( (P < 0.001) \) correlated with both log creatinine-corrected urinary thiocyanate (correlation coefficients, 0.45 and 0.51 for males and females, respectively) and log creatinine-corrected total PEC (correlation coefficients, 0.29 and 0.31 for males and females, respectively). Thiocyanate is expected to be greater in smokers independent of dietary exposures. Significant positive \( (P < 0.001) \), simple correlations were observed between the logs of creatinine-corrected urinary perchlorate and iodide (correlation coefficients, 0.38 in males and 0.38 in females), urinary perchlorate and nitrate (correlation coefficients, 0.33 in males and 0.35 in females), and urinary nitrate and thiocyanate (correlation coefficients, 0.33 in males and 0.30 in females). Correlation coefficients between the logs of creatinine-corrected IUI agents and thyroid parameters in males and females ranged from −0.15 to 0.19 (data not shown). Because of the correlation of iodide with urinary perchlorate, the impact of iodine status was evaluated by dividing the population into lower and higher iodide groups, using the median urinary iodide level for the population as the division. Potential correlations among urinary perchlorate, nitrate, and thiocyanate were addressed by evaluating exposure as total PEC.

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In the combined population with urinary iodide less than the median and in females analyzed separately regardless of iodine status, there were no significant relationships between total PEC and any thyroid variable, in the direction expected for an IUI agent. In females with urinary iodide less than the median, there was a significant positive relationship between total PEC and FT3 (coefficient, −0.020; P = 0.028). Examination of the components of total PEC for this population revealed significant associations of FT3 with thiocyanate (coefficient, −0.014; P = 0.005), but not nitrate (coefficient, −0.007; P = 0.479) or perchlorate (coefficient, −0.0004; P = 0.954).

In the combined population and in males with urinary iodide greater than the median, total PEC was significantly negatively associated with TT4 (for combined population: coefficient, −0.057; P < 0.001; for males: coefficient, −0.049; P = 0.026). In both of these populations, TT4 was significantly associated with thiocyanate (for males, coefficient, −0.049; P = 0.026).
combined population: coefficient, −0.037; P < 0.001; for males: coefficient, −0.039; P < 0.001), and in the combined population but not in males only. TT4 was also associated with nitrate (coefficient, −0.036; P < 0.001). TT4 was not associated with perchlorate in either population. In males with urinary iodide greater than the median, there was also a significant positive relationship between total PEC and TT3 (coefficient, 0.034; P = 0.010), in the opposite direction expected for an IUI agent.

Regression analyses were also run using the logarithm of PEC calculated with NIS inhibitor levels unadjusted for creatinine level and the log of creatinine level as a separate independent variable in the model. No substantial differences in model results were obtained using this approach.

**DISCUSSION**

Using the newly released NHANES 2001 to 2002 data set for thyroid variables and urinary measures of chemical agents that cause IUI, we observed no consistent or functionally relevant association between PEC and thyroid measures, including TSH. Total PEC was associated with TT4 in the combined population, but the relationships did not remain in either males or females alone. When the impact of individual IUI agents on these thyroid variables was analyzed separately, TT4 was significantly negatively associated with both nitrate and thiocyanate but not perchlorate.

FT4 is the most important measure along with TSH to determine thyroid function.10 Because there are many influences on measured thyroid hormone, the combined effect of both of these variables is critical in the determination of functional abnormalities involving thyroid hormone status and the pituitary gland. In these analyses, total PEC was not associated with FT4 or TSH in any group.

Even with statistical significance, the correlation coefficients between variables are low. The highest $r^2$ is 0.324, which means that only a relatively small amount of variance of the dependent variables (thyroid measures) is accounted for by the explanatory variables. Similar $r^2$ values have been reported for similar analyses.3

Iodide uptake inhibition resulting from perchlorate exposure is the same as IUI caused by the other agents. In the individual study subjects, perchlorate contributed an average of only 1.2% of the total PEC measured in urine (range, <1% to 18.0%), whereas nitrate contributed an average of 74.5% (range, 2.9% to 99.0%) and thiocyanate an average of 24.0% (range, 0.6% to 96.0%). This is similar to what others have reported.10

The findings based on the new CDC data set are not consistent with the results of other reports using the initially released NHANES 2001 to 2002 thyroid measures data set.11 Using the NHANES 2001 to 2002 data, Blount et al1 reported that perchlorate measured in spot urine samples was positively associated with serum TSH and negatively associated with serum TT4 in females aged 12 years and older.

**TABLE 3.** Regression of Log TT3 and Log FT3 Measurements on Covariates in Males + Females, Males Alone, and Females Alone in NHANES 2001—2002

<table>
<thead>
<tr>
<th>Thyroid Measure</th>
<th>Coefficient (Males + Females = 1544)</th>
<th>Coefficient (Males = 833)</th>
<th>Coefficient (Females = 711)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\log_{10}$ TT3</td>
<td>$r^2 = 0.144$</td>
<td>$r^2 = 0.180$</td>
<td>$r^2 = 0.124$</td>
</tr>
<tr>
<td>Intercept</td>
<td>1.9858 (0.0285)</td>
<td>1.9874 (0.0979)</td>
<td>2.1300 (0.1283)</td>
</tr>
<tr>
<td>Log total PEC*</td>
<td>−0.0089 (0.0081)</td>
<td>−0.0063 (0.0095)</td>
<td>−0.0069 (0.0154)</td>
</tr>
<tr>
<td>Age, mo</td>
<td>−0.0001 (0.0000)</td>
<td>−0.0001 (0.0000)</td>
<td>−0.0001 (0.0000)</td>
</tr>
<tr>
<td>Fasting time, hr</td>
<td>0.0004 (0.0004)</td>
<td>0.0001 (0.0004)</td>
<td>0.0005 (0.0007)</td>
</tr>
<tr>
<td>Log BMI</td>
<td>0.0472 (0.0354)</td>
<td>0.0555 (0.0403)</td>
<td>0.0804 (0.0472)</td>
</tr>
<tr>
<td>Calories/1000</td>
<td>0.0009 (0.0032)</td>
<td>0.0004 (0.0040)</td>
<td>0.0097 (0.0047)</td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>−0.0111 (0.0053)</td>
<td>−0.0070 (0.0063)</td>
<td>−0.0166 (0.0084)</td>
</tr>
<tr>
<td>Serum albumin</td>
<td>0.0273 (0.0114)</td>
<td>0.0207 (0.0133)</td>
<td>0.0662 (0.0164)</td>
</tr>
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<td>Log CRP</td>
<td>0.0091 (0.0039)</td>
<td>0.0098 (0.0071)</td>
<td>0.0064 (0.0071)</td>
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<td>$\beta$-Blocker use</td>
<td>0.0103 (0.0149)</td>
<td>0.0171 (0.0183)</td>
<td>0.0104 (0.0223)</td>
</tr>
<tr>
<td>Furosemide</td>
<td>−0.0483 (0.0180)</td>
<td>−0.0722 (0.0263)</td>
<td>−0.0151 (0.0242)</td>
</tr>
<tr>
<td>GC androgen use</td>
<td>−0.0001 (0.0302)</td>
<td>−0.0028 (0.0434)</td>
<td>−0.0106 (0.0286)</td>
</tr>
<tr>
<td>$\log_{10}$ FT3</td>
<td>$r^2 = 0.272$</td>
<td>$r^2 = 0.324$</td>
<td>$r^2 = 0.244$</td>
</tr>
<tr>
<td>Intercept</td>
<td>0.3448 (0.0397)</td>
<td>0.4443 (0.0552)</td>
<td>0.4459 (0.0748)</td>
</tr>
<tr>
<td>Log Total PEC*</td>
<td>−0.0009 (0.0054)</td>
<td>−0.0045 (0.0990)</td>
<td>0.0099 (0.0087)</td>
</tr>
<tr>
<td>Age, mo</td>
<td>−0.0001 (0.0000)</td>
<td>−0.0001 (0.0000)</td>
<td>−0.0001 (0.0000)</td>
</tr>
<tr>
<td>Fasting time, hr</td>
<td>0.0007 (0.0002)</td>
<td>0.0009 (0.0003)</td>
<td>0.0005 (0.0004)</td>
</tr>
<tr>
<td>Log BMI</td>
<td>0.0558 (0.0186)</td>
<td>0.0403 (0.0278)</td>
<td>0.0268 (0.0344)</td>
</tr>
<tr>
<td>Calories/1000</td>
<td>0.0021 (0.0010)</td>
<td>−0.0004 (0.0017)</td>
<td>−0.0051 (0.0023)</td>
</tr>
<tr>
<td>Non-Hispanic white</td>
<td>−0.0087 (0.0025)</td>
<td>−0.0088 (0.0039)</td>
<td>−0.0085 (0.0039)</td>
</tr>
<tr>
<td>Serum albumin</td>
<td>0.0309 (0.0057)</td>
<td>0.0197 (0.0050)</td>
<td>0.0110 (0.0090)</td>
</tr>
<tr>
<td>Log CRP</td>
<td>0.0025 (0.0032)</td>
<td>0.0036 (0.0023)</td>
<td>0.0017 (0.0057)</td>
</tr>
<tr>
<td>$\beta$-Blocker use</td>
<td>−0.0018 (0.0068)</td>
<td>−0.0050 (0.0868)</td>
<td>−0.0054 (0.0084)</td>
</tr>
<tr>
<td>Furosemide</td>
<td>−0.0115 (0.0081)</td>
<td>−0.0124 (0.0155)</td>
<td>−0.0073 (0.0089)</td>
</tr>
<tr>
<td>GC androgen use</td>
<td>0.0063 (0.0128)</td>
<td>−0.0189 (0.0190)</td>
<td>0.0076 (0.0108)</td>
</tr>
</tbody>
</table>

$P < 0.05$ for data given in bold. BMI, body mass index; CRP, reactive protein; FT3, free T3; GC, glucocorticoid; PEC, perchlorate equivalent concentration; SE, standard error; TT3, total triiodothyronine.

$\log_{10}$ total PEC = [ perchlorate]$_{meas}$ + [ thiocyanate]$_{meas}$ /17.6 + [ nitrate]$_{meas}$ /150, μg/g creatinine.
with urinary iodide levels less than 100 μg/L. This relationship was more pronounced in current smokers. Urinary nitrate was negatively associated with TT4 only in females with urinary iodide greater than 100 μg/L, but was later reported to have no strong associations. Urinary thiocyanate was negatively associated with TSH in females with urinary iodide greater than 100 μg/L. In small subgroups of females with urinary iodide less than 100 μg/L, urinary thiocyanate was negatively associated with TT4 in a subgroup (n = 78) with urinary thiocyanate greater than 1800 μg/L and positively associated with TSH in a subgroup (n = 107) with midlevel urinary thiocyanate (751 to 1800 μg/L).2

We did not see a significant relationship between TSH and total PEC in the entire population, or in males or females analyzed separately or in these populations segregated by low and high urinary iodide concentrations. We did see a significant negative relationship between TT4 and total PEC in the entire population, but the association of the PEC variable with TT4 appears to be largely due to the contributions of nitrate and thiocyanate because TT4 was significantly negatively associated with nitrate and thiocyanate but not perchlorate. Furthermore, TT4 was only negatively associated with nitrate and thiocyanate in the subset with high urinary iodide, not the subset with low urinary iodide.

In addition to inclusion of nitrate and thiocyanate, our analyses differed from previous analyses of IUI agents and thyroid variables in NHANES 2001 to 2002 in several key respects. First, the data sets differed: the initially released NHANES 2001 to 2002 data set included TSH and TT4 data for 534 subjects not included in the new data release. These included 148 of the 1111 females older than 12 years evaluated in Blount et al. Second, the new analyses were conducted at a different laboratory. Comparing the results of the original and new analyses for the samples in our data set, the geometric means for TT4 are 7.73 μg/dL and 8.05 μg/dL, respectively, and for TSH are 1.34 mIU/L and 1.39 mIU/L, respectively. The old and new means for both measures differ significantly (P < 0.001). Third, the current analysis normalizes for creatinine. For chemicals with a short biological half-life (eg, perchlorate, nitrate, iodide), concentrations in spot urine samples are known to be highly variable between samples, due to within- and between-day variations in urine volume and intake of exogenous compounds. Factors shown to influence concentrations include fasting time, time of day, nature of the last meal, sample dilution, collection method, preservation method, and for TSH are 1.34 mIU/L and 1.39 mIU/L, respectively. The old and new means for both measures differ significantly (P < 0.001). The new data do not support a consistent relationship between exposure to the combination of IUI agents and thyroid measures. TT4 was associated with total PEC, but these relationships appeared to be determined by nitrate and thiocyanate. Perchlorate alone was not associated and would not be expected because the potential contribution of perchlorate to IUI is relatively low compared with nitrate and thiocyanate. No evidence of functional abnormalities in thyroid function (eg, low thyroid hormone coupled with high TSH) is seen in the enhanced data set despite the availability of more thorough measures of exposure to IUI agents and enhanced estimates of thyroid function. As the mechanism of action of perchlorate on the thyroid is well understood and exposures to NHANES 2001 to 2002 participants were below the reported NOEL for perchlorate, no effects on thyroid parameters would be expected to occur. The findings of this investigation support this understanding.

REFERENCES


February 23, 2011

Michael Baes (mbaes@oehha.ca.gov)
Pesticide and Environmental Toxicology Branch
Office of Environmental Health Hazard Assessment
California Environmental Protection Agency
1515 Clay St., 16th floor
Oakland, California 94612

Re: Proposed Public Health Goal for Perchlorate in Drinking Water

To Whom It May Concern:

The Association of California Water Agencies (ACWA) appreciates the opportunity to comment on the proposed public health goal (PHG) for perchlorate in drinking water. ACWA represents nearly 450 public water agencies in California that collectively supply 90% of the water delivered in California for domestic, agricultural and industrial uses. Our state enjoys some of the highest water quality in the world and local water agencies are responsible for meeting many stringent federal and state water quality regulations to ensure the water they deliver is clean and safe, including the existing drinking water standard of 6 ppb for perchlorate.

We have the following specific comments on the proposed PHG for perchlorate in drinking water.

Initial comment period

We are disappointed that the proposed revision to the PHG for perchlorate published in January, 2011 does not appear to respond to any of ACWA’s comments or stated concerns as presented in our letter to you dated August 29, 2008. These concerns primarily address the lack of evidence to lower the current PHG, which we feel is health protective of Californians, including sensitive subpopulations. Therefore we reiterate those comments to you below.

Overall comment

Perchlorate is a goitrogen, a chemical that blocks the uptake of iodide to the thyroid, resulting in hypertrophy of the thyroid, i.e. goiter. Sustained iodide deficiency can cause additional effects beyond goiter, including hypothyroidism and, of greatest concern, hypothyroxinemia. Maternal iodide deficiency and hypothyroxinemia during pregnancy and nursing can result in neurodevelopmental deficits in children, historically referred in its more extreme forms as
cretinism. It is this health endpoint that is the key to the determination of the current PHG. OEHHA determined that exposure to drinking water containing less than 6 ppb of perchlorate did not pose an excess public health risk of this outcome and we still believe this is accurate.

**Exposure to Perchlorate through Drinking Water**

The 2007 study by Pearce et al.\(^1\) indicates that perchlorate is actively transported into milk by nursing mothers. While this is certainly true, the study also indicates “Breast milk iodine content was significantly correlated with urinary iodine per gram creatinine and urinary cotinine, but was not significantly correlated with breast milk or urinary perchlorate.” The letter also cites Kirk et al. 2007 which did not find any correlation between perchlorate concentrations in breast milk and iodide concentrations, as did the earlier work by Kirk et al 2005\(^2\). Most interesting, Kirk et al. 2007 reported that drinking water did not appear to be a significant vector for exposure to perchlorate. The study concludes, “The fact that higher levels of perchlorate were present in milk samples from subjects’ drinking water treated by reverse osmosis indicates that drinking water is not necessarily the principal vector for perchlorate exposure.” Moreover, one of these participants (E) used a reverse osmosis system connected to a municipal water supply, which we have repeatedly analyzed: The perchlorate concentration in the feed water ranged from 0 to 4 μg/L, with rare excursions > 2 μg/L. Clearly, her perchlorate intake through drinking water would not account for the observed expression in breast milk. This fact—that drinking water is not generally an important vector for perchlorate exposure—is consistent with measurements of urinary perchlorate versus drinking-water perchlorate reported by Valentin-Blasini et al. 2005\(^3\) (emphasis added).\(^3\) These studies would not indicate that the PHG estimated by OEHHA five years ago in any way underestimated the risk.

**Blount study results**

The NGO letter submitted in 2008 cites prominently one specific study, Blount 2007\(^4\), an analysis of the NHANES 2001-2002 study. This study showed a negative association between urine perchlorate concentrations (uncorrected for creatinine) and T4 serum concentrations in women with low urine iodide concentrations. It was not shown that this actually lowered the T4 serum concentration outside of normal concentration range (5 – 12 mcg/dL). Further, Blount reports that the mean serum T4 concentration was 8.4 mcg/dL with a 95% confidence interval covering 7.97 – 8.58 mcg/dL for women aged 12 and over. This means that about 95% of the women in this study had T4 serum concentrations within 5% of the mean and well within the normal range. The study did not provide any indication that any women were hypothyroxinemic, or if they were that these women had lower iodide or higher perchlorate

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concentrations than the other women in the study. Interestingly, Blount found no correlation between iodide urine concentrations and perchlorate concentrations, which is consistent with the breast milk studies cited above. Once more, while informative, this study does not indicate that the current PHG is an underestimate or fails to provide adequate public health protection.

The Blount study found perchlorate in all participants across the United States and numerous studies indicate perchlorate is widely distributed in various food sources and ubiquitous in human exposure studies. However, the USEPA’s Information Collection Rule found perchlorate in relatively few drinking waters (Kimbrough & Parekh 2007)\(^5\) and generally in very small concentrations. This indicates, as research above supports, drinking water is a relatively minor source of human exposure to perchlorate.

**Synergistic Effects**

Another important issue is the appearance of other NIS inhibitors such as thiocyanate and nitrate that might interact with perchlorate and iodine to affect thyroid hormone levels. Blount et al. 2006 found not just perchlorate but nitrate and thiocyanate in considerable concentrations. This is indeed important as the H&SC states “(C) To the extent information is available, the public health goal shall take into account each of the following factors: (i) Synergistic effects resulting from exposure to, or interaction between, the contaminant and one or more other substances or contaminants.” Both of these chemicals are also goitrogens, just like perchlorate, albeit less potent. Nitrate and thiocyanate are both goitrogens which have been shown to occur in almost all of the subjects in the NHANES 2001-2002 study (Blount et. al. 2007) and occur widely in food products. Nitrate is nearly ubiquitous in drinking water (Kimbrough & Parekh 2007). Thiocyanate is thought to be about 1/10th as potent as perchlorate but has a half-life that is considerably longer, 8 hours for perchlorate (Greer et al. 2002)\(^6\) vs. 1–6 days (Junge 1985; Schulz et al. (1979) for thiocyanate. Blount reports that the geometric mean concentration of thiocyanate among study participants was 1,200 mcg/L (95% CI 1,080 – 1,330), while the geometric mean concentration of perchlorate was 2.84 mcg/L (95% CI 2.54 – 3.18). The ratio of the geometric means is 422:1 and converting the thiocyanate into a “perchlorate equivalent concentration” (PEC), the ratio would be 42:1 thiocyanate to perchlorate. Tonacchera et al. (2004)\(^7\) determined the relative potency of perchlorate vs. nitrate to be 1:240 and for the effects of multiple goitrogens to be additive. Blount (2007) reported the geometric mean concentration of nitrate in the NHANES 2001-2002 study to be38,000 mcg/L (95% CI 35,900 – 40,300) so the ratio of the geometric means of nitrate to perchlorate would be 13,000:1.

\(^7\) Tonacchera, M.; Pinchera, A.; Dimida, A.; Ferrarini, E.; Agretti, P.; Vitti, P.; Santini, F.; Crump, K.; Gibbs, J. Relative potencies and additivity of perchlorate, thiocyanate, nitrate, and iodide on the inhibition of radioactive iodide uptake by the human sodium iodide symporter. Thyroid 14, 1012-1019, 2004
Correcting for the relative potency of nitrate, the PEC ratio of nitrate to perchlorate would be 56:1. Based on the NHANES 2001-02 study results as presented by Blount, the overall “goitrogenic burden” from perchlorate is less than 1% as compared to nitrate and thiocyanate, most of which does not come from drinking water as noted above. It is clear that co-occurring contaminants with similar health effects may have contributed more to the observed outcomes than perchlorate alone. These data do not suggest that the current PHG is excessively high.

The following comments specifically address the January, 2011 draft revised PHG for perchlorate.

Any use of ecological studies (Steinmaus et al. 2010, Buffler et al. 2006, etc.) in OEHHA’s analysis is inappropriate because these studies, by their nature, are greatly flawed in their analysis. Utilizing occurrence data from the CDPH files to assign drinking water perchlorate levels to various California populations is not appropriate because even CDPH indicates the early data is “...helpful in identifying areas in which perchlorate has affected sources of drinking water (principally wells), but they should not be interpreted as representative of water being served by public water systems.”8 Therefore, the authors could not have accurately taken these data, many of which were not treated or blended waters or even sources in service, and even remotely accurately assigned them to populations. This misunderstanding by the authors on how the monitoring results were obtained and how water systems operate has led to flawed studies that cannot be relied upon.

Additionally, ACWA objects to OEHHA increasing the uncertainty factor applied to infants from 3 to 10. This would seem arbitrary and unwarranted because OEHHA has not demonstrated actual adverse health effects correlated with perchlorate exposure. All of the connections are between perchlorate exposure and hypothesized adverse health effects. Further, there are a large number of epidemiological studies where no adverse health effects were found. The proposed PHG is based entirely on studies like Steinmaus, Greer, and Blount9 where some physiological change is measured, iodide uptake or changes in TSH levels, neither of which is adverse in and of themselves. Even in Blount and Steinmaus, the amount of change in TSH concentration measured was not outside of the normal clinical range, it was just different as compared to controls. By not addressing studies where no effects were found and the inclusion of studies showing only non-adverse health effects, several layers of uncertainty have already been built in to the calculation.

Because OEHHA has also dramatically increased the infant drinking water intake per body weight in this analysis, it is inappropriate to increase the uncertainty factor for infants when OEHHA has already accounted for so much uncertainty. Therefore, ACWA recommends that OEHHA recalculate the health protective concentration for infants as follows:

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8 http://www.cdph.ca.gov/certlic/drinkingwater/Pages/Perchlorate.aspx
\[
\frac{3.7 \text{ ug/kg-day}}{3} = 1.23 \text{ ug/kg-day}
\]

\[
1.23 \text{ ug/kg-day} \times 4.3 \text{ kg-day/L} \times 0.73 \text{ (RSC)} = 3.86 \text{ ug/L} \quad \text{rounded} = 4 \text{ ug/L}
\]

Lastly, ACWA supports the comments made by East Bay Municipal Utility District (EBMUD) regarding the incorporation of microbiological risks associated with current disinfection practices and the health risk trade-off associated with the production of perchlorate during sodium hypochlorite storage.

ACWA and its member agencies’ highest priority continues to be protecting public health while ensuring a reliable water supply for consumers. We look forward to working with you and the appropriate stakeholders as OEHHA and the California Department of Public Health address this very important issue.

If you have questions, please contact me at 916-441-4545 or danielleb@acwa.com.

Sincerely,

[Signature]

Danielle Blacet
Regulatory Advocate
August 29, 2008

Mr. Michael Baes  
PHG Project  
Pesticide and Environmental Toxicology Branch  
Office of Environmental Health Hazard Assessment  
1515 Clay Street, 16th Floor  
Oakland, CA 94612  

Subject: Comments on the Review of the Perchlorate PHG  

Dear Mr. Baes:  

The following are comments developed by the Association of California Water Agencies (ACWA) relative to the review of the Public Health Goal (PHG) for perchlorate. ACWA represents over 450 public water agencies in California that collectively supply over 90% of the water delivered in California for domestic, agricultural and industrial uses. 

We understand that the review is being undertaken at the request of several environmental groups and for purposes of the Office of Environmental Health Hazard Assessment (OEHHA) statutorily prescribed five year review of previously adopted PHGs. We appreciate the opportunity to provide these initial comments and request that the comment period be extended beyond September 1, 2008 to allow inclusion of additional comments and material as noted below. 

At the outset we request a clarification as to the procedure OEHHA plans to follow relative to the public comment period related to this review process. Is OEHHA planning on following the process for preparing a PHG that is outlined in the Health and Safety Code sections PHG (116365 (c)(3) (A) – (D)) or will it be a different process? If so, can OEHHA provide us with an outline of such a process? ACWA is concerned that it is not clear what the process is or what standards will be applied to the review as the public comment period announced by OEHHA seems too short for the preparation of cogent and useful comments. 

It is critical that the process for re-evaluating the PHG be transparent, equitable, based on new, sound science. It must also provide ample opportunity for the public to comment. 

In addition, we have the following technical comments: 

1) Perchlorate is a goitrogen, a chemical that blocks the uptake of iodide to the thyroid, resulting in hypertrophy of the thyroid, i.e. goiter. Sustained iodide deficiency can cause additional effects beyond goiter, including hypothyroidism and, of greatest concern, hypothyroxinemia. Maternal iodide deficiency and hypothyroxinemia during pregnancy and nursing can result in neurodevelopmental deficits in children, historically referred in its more extreme forms as cretinism. It is this health endpoint that is the key to the determination of the current PHG. OEHHA determined that exposure to drinking water containing less than 6 ppb of perchlorate did not pose an excess public health risk of this outcome. 

2) The NGO’s letter made a case that recent research would indicate that a much lower number than 6 ppb would be justified. However, ACWA does not agree that this is the case based on the studies
cited. The letter cites the 2007 study by Pearce et al. 2007\(^1\) indicating that perchlorate is actively transported into milk by nursing mothers. While this is certainly true, the study also indicates “Breast milk iodine content was significantly correlated with urinary iodine per gram creatinine and urinary cotinine, but was not significantly correlated with breast milk or urinary perchlorate.” The letter also cites Kirk et al. 2007 which did not find any correlation between perchlorate concentrations in breast milk and iodide concentrations, as did the earlier work by Kirk et al 2005\(^2\). Most interesting, Kirk et al. 2007 reported that drinking water did not appear to be a significant vector for exposure to perchlorate. The study concludes, “The fact that higher levels of perchlorate were present in milk samples from subjects’ drinking water treated by reverse osmosis indicates that drinking water is not necessarily the principal vector for perchlorate exposure.” Moreover, one of these participants (E) used a reverse-osmosis system connected to a municipal water supply, which we have repeatedly analyzed: The perchlorate concentration in the feed water ranged from 0 to 4 μg/L, with rare excursions > 2 μg/L. Clearly, her perchlorate intake through drinking water would not account for the observed expression in breast milk. This fact—that drinking water is not generally an important vector for perchlorate exposure—is consistent with measurements of urinary perchlorate versus drinking-water perchlorate reported by Valentín-Blasini et al. 2005\(^3\) (emphasis added).\(^3\) These studies would not indicate that the PHG estimated by OEHHA five years ago in any way underestimated the risk.

3) The letter cites prominently one specific study, Blount 2007\(^4\), an analysis of the NHANES 2001-2002 study. This study showed a negative association between urine perchlorate concentrations (uncorrected for creatinine) and T4 serum concentrations in women with low urine iodide concentrations. It was not shown that this actually lowered the T4 serum concentration outside of normal concentration range (5 – 12 mcg/dL). Further, Blount reports that the mean serum T4 concentration was 8.4 mcg/dL with a 95% confidence interval covering 7.97 – 8.58 mcg/dL for women aged 12 and over. This means that about 95% of the women in this study had T4 serum concentrations within 5% of the mean and well within the normal range. The study did not provide any indication that any women were hypothyroxinemic, or if they were that these women had lower iodide or higher perchlorate concentrations than the other women in the study. Interestingly, Blount found no correlation between iodide urine concentrations and perchlorate concentrations, which is consistent with the breast milk studies cited above. Once more, while informative, this study does not indicate that the current PHG is an underestimate or fails to provide adequate public health protection.

4) The NGO letter makes extensive references to numerous studies indicating that perchlorate is widely distributed in various food sources and ubiquitous in human exposure studies. Although not indicated in the letter, this indicates, as research above supports, drinking water is a relatively minor source of human exposure to perchlorate. The Blount study found perchlorate in all participants across the United States while the USEPA’s Information Collection Rule found perchlorate in relatively few drinking waters (Kimbroough & Parekh 2007) and generally in very small concentrations.

5) Along the same lines, the NGO letter notes that the Blount 2007 study found not just perchlorate but nitrate and thiocyanate in considerable concentrations. This is indeed important as the H&SC states “(C) To the extent information is available, the public health goal shall take into account each of the following factors: (i) Synergistic effects resulting from exposure to, or interaction between, the contaminant and one or more other substances or contaminants.” Both of these chemicals are also

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goitrogens, just like perchlorate, albeit less potent. Nitrate and thiocyanate are both goitrogens which have been shown to occur in almost all of the subjects in the NHANES 2001-2002 study (Blount 2007) and occur widely in food products. Nitrate is nearly ubiquitous in drinking water (Kimbrough & Parekh, 2007). Thiocyanate is thought to be about 1/10th as potent as perchlorate but has a half-life that is considerably longer, 8 hours for perchlorate (Greer et al. 2002) vs. 1–6 days (Junge 1985; Schulz et al. 1979) for thiocyanate. Blount reports that the geometric mean concentration of thiocyanate among study participants was 1,200 mcg/L (95% CI 1,080 – 1,330), while the geometric mean concentration of perchlorate was 2.84 mcg/L (95% CI 2.54 – 3.18). The ratio of the geometric means is 422:1 and converting the thiocyanate into a “perchlorate equivalent concentration” (PEC), the ratio would be 42:1 thiocyanate to perchlorate. Tonacchera et al. (2004) determined the relative potency of perchlorate vs. nitrate to be 1:240 and for the effects of multiple goitrogens to be additive. Blount (2007) reported the geometric mean concentration of nitrate in the NHANES 2001-2002 study to 38,000 mcg/L (95% CI 35,900 – 40,300) so the ratio of the geometric means of nitrate to perchlorate would be 13,000:1. Correcting for the relative potency of nitrate, the PEC ratio of nitrate to perchlorate would be 56:1. Based on the NHANES 2001-02 study results as presented by Blount, the overall “goitrogenic burden” from perchlorate is less than 1% as compared to nitrate and thiocyanate, most of which does not come from drinking water as noted above. It is clear that co-occurring contaminants with similar health effects may have contributed more to the observed outcomes than perchlorate alone. These data do not suggest that the current PHG is excessively high.

ACWA reserves the right to provide additional comments as new information is introduced. Specifically we encourage OEHHA to review and consider in its analysis the forthcoming study being finalized by the American Water Works Association (AWWA) (a re-review of the NHANES report on perchlorate). We anticipate that this study will be available in the next 30-60 days. Following our review of this document and others being finalized at this time we may submit further comments for your consideration.

Thank you for the opportunity to provide comments. If you have any questions regarding this matter, please contact me at 916-441-4545. We look forward to working with you and your staff in this important endeavor.

Sincerely,

Danielle Blacet
Regulatory Advocate

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