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PERCHLORATE AND TCE IN WATER

HEARING

BEFORE THE

COMMITTEE ON ENVIRONMENT AND PUBLIC WORKS UNITED STATES SENATE

ONE HUNDRED TENTH CONGRESS

SECOND SESSION

MAY 6, 2008

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ONE HUNDRED TENTH CONGRESS
SECOND SESSION

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ADDITIONAL MATERIAL

PERCHLORATE AND TCE IN WATER

TUESDAY MAY 6, 2008

U.S. SENATE,
COMMITTEE ON ENVIRONMENT AND PUBLIC WORKS,
Washington, DC.

The full committee met, pursuant to notice, at 10:05 a.m. in room 406, Dirksen Senate Office Building, Hon. Barbara Boxer (chairman of the full committee) presiding.

Present: Senators Boxer, Barrasso, Bond, Cardin, Klobuchar, Whitehouse.

OPENING STATEMENT OF HON. BARBARA BOXER, U.S. SENATOR FROM THE STATE OF CALIFORNIA

Senator BOXER. Good morning. The Committee shall come to order.

Because it is a different type of schedule day today, we will have colleagues coming in all through the morning. So what I have told Senator Inhofe is that we would keep the record open when they come in, and at that time they could either put their statement in the record or give their statement. We will hold all statements to 5 minutes, and that includes all of our panelists as well. We want to thank you all for coming.

The other issue is, and I have spoken to Senator Inhofe about this as well, I have to be briefly running down to give a statement on behalf of a bill I have to create or add on to a marine sanctuary in California. The moment I have to do that, I will have to recess and come right back, so it is a little bit or a marathon-type of day for me. So thank you for your understanding.

So we will start the clock at 5 minutes.

The U.S. Environmental Protection Agency is working on a public relations campaign telling us this week that we should celebrate National Drinking Water Week. This chart is off of their website, to celebrate National Drinking Water Week. Great. It is great because when Congress passed the Clean Water Act, the Safe Drinking Water Act, and all the landmark laws, it was a moment in history that we should celebrate every year.

However, until EPA sets scientifically based health standards for dangerous tap water contaminants and strictly enforces the law, it is impossible to celebrate this Administration's drinking water record. Slogans and PR campaigns are no substitute for action.

In fact, today we will hear about EPA's particularly disturbing failures to address significant risks to our families from two widespread drinking water contaminants: perchlorate and TCE. Perchlorate is used to make rocket fuel, but when it gets into drinking

water, this toxic chemical can interfere with the thyroid and affect hormone systems which control the way the body develops. Infants and pregnant women are especially vulnerable to perchlorate.

Researchers have found that over 20 million Americans safe drinking water supplies contain perchlorate. GAO found in 2005 that there were nearly 400 sites in 35 States contaminated with perchlorate. My State of California has 106 sites. The evidence of significant exposure to perchlorate and assorted health risks has strengthened in recent years. In 2006, scientists at the CDC found, and I am quoting the CDC scientists, "Widespread human exposure to perchlorate" in the U.S. in young children. They found many women who were exposed to perchlorate in their drinking water had significant changes in thyroid hormone levels.

This isn't a game we are playing. This is the health of the American people. We know we are exposed to perchlorate from many sources, not just drinking water. A January, 2008 study by the FDA found perchlorate in 74 percent of all foods tested, including baby food.

What has the EPA done? The answer is very little. In December, 2006, EPA revoked its rule requiring some water systems to monitor for perchlorate and disclose the test results to the public. EPA said it had enough data on perchlorate. It had enough data. It didn't need to have anybody test the drinking water supplies. It didn't need to have the public know because EPA had enough data.

However, several months later, in May 2007, EPA said, oh, really, it didn't have enough data on perchlorate exposure, especially from food, to regulate perchlorate in drinking water.

Talk about speaking out of both sides of your mouth. This is the perfect case. We don't need to test anymore. We have enough information, but we can't set a standard because we don't have enough information.

Even when many water industry officials, like the American Water Works Association urge the EPA to set a perchlorate standard, EPA refused to do it, flat-out refused. EPA has issued a guidance for perchlorate cleanup. That, they have done, but based this level on a 154-pound adult whose only exposure to perchlorate is from drinking water. Now, that is the way we did it in the past. A 154-pound man, what is safe for him? And they didn't even do that because they said, we are just going to consider the perchlorate from drinking water.

This guidance fails to protect children and pregnant women. It fails to consider the fact that people also are exposed to perchlorate in other ways such as through food and milk. EPA's Children's Health Protection Advisory Committee said the clean-up guidance is "not protective of children's health and is not supported by the underlying science and can result in exposures that pose neurodevelopment risks in early life." That is EPA's own Children's Health Protection Agency. It is no wonder you hear Bush officials saying, gee, we don't really need that office anymore.

The story for TCE is unfortunately very similar. EPA proposed a risk assessment in 2001. It found the chemical could be up to 40 times more toxic than previously thought. In 2002, EPAEs Science Advisory Board commended EPA's assessment and urged the agency to proceed with revising and finalizing it. But according to press

accounts, the Department of Defense and their contractors and OMB, the Office of Management and Budget, stopped EPA from moving forward, successfully lobbied for delay, and for a National Academy of Sciences report on TCE.

Now, in 2006, the National Academy of Sciences found that evidence of TCE FEs cancer risks had grown since 2001 and recommended EPA finalize risk assessments using currently available data so that clean-ups can be made expeditiously. Yet GAO reported last week that EPA will not finalize its TCE assessment until 2010.

Where is the EPA? A shadow of its former self, doing harm to people by not acting. There are lots of words, but no action. While the Federal EPA delays or, worse, rolls back safeguards, children and families are exposed to dangerous toxic chemicals. I told EPA last week that if the Bush administration failed to protect our people, Congress will. I have two bills to protect people from perchlorate contamination. The first bill, the Perchlorate Monitoring and Right-To-Know Act, S. 24, says EPA is to restore the rule requiring that drinking water be tested for perchlorate and the results of those tests be disclosed to the public.

My second bill, the Protecting Pregnant Women and Children from Perchlorate Act, requires EPA to quickly set a perchlorate standard for drinking water that protects pregnant women and children.

I wish that everyone who has said in his or her life, our children are our future, or I love my grandchildren more than I love myself, everyone who has said that, if everyone who said that forced their elected officials who have said that to act now, it would be the best thing for our Country.

Senator Clinton, Senator Dole and myself and several colleagues also have a bill, the TCE Reduction Act, S. 1911, that would protect people exposed to TCE. Congress will not sit idly by while EPA fails to adequately protect our children. Chuck Schumer has a bill to ban bisphenol-A. Dianne Feinstein and I had a bill—it passed—to ban phthalates.

So this is what is happening because EPA does nothing. We must step in to require action that will ensure that our children and our families can turn on their taps and be assured that what comes out is safe to drink. If we can't do that, then shame on us.

Senator BOXER. Senator Barrasso.

OPENING STATEMENT OF HON. JOHN BARRASSO, U.S. SENATOR FROM THE STATE OF WYOMING

Senator BARRASSO. Thank you very much, Madam Chairman.

As you say, TCE is a carcinogenic industrial solvent. It has been used to clean engines and rocket motor parts in my home State of Wyoming, primarily by the Department of Defense. Wyoming has had an important legacy to the defense of this Country, and nuclear missile silos have been in Wyoming since the early days of the cold war. Wyoming residents are proud of this legacy, but we also believe that the Federal Government has a responsibility to leave Wyoming as clean as when they found it.

I have raised the issue, Madam Chairman, with the Army Corps of Engineers regarding TCE contamination in the city of Chey-

enne's water wells at Belvoir Ranch in Wyoming, which is west of Cheyenne. The Wyoming Department of Environmental Quality believes that this contamination is directly linked to a former nuclear missile site known as Atlas D Missile Site 4. The missile site is currently listed as a formerly utilized defense site. These sites were operational from 1960 to 1965. They were the first generation of intercontinental ballistic missiles armed with nuclear warheads.

The Army Corps of Engineers is well aware of TCE leakage from this site. In a latter to me, the Corps amazingly stated that their information does not support the conclusion that the missile site is the cause of the water contamination discovered in Cheyenne's nearby wells. The Army Corps suggests, "the potential for the existence of other contributing sources" of the contamination.

In the same letter, the Corps announced that they will now be conducting a study to determine whether there is a connection between the missile site and the wells. They will now study the historical TCE use in the area.

Well, given the rural undeveloped terrain of the area in question and the historical fact that TCE was heavily used by the military in the area, it seems clear that the Government is needlessly delaying the technical and financial assistance that the city and the State have asked for.

This problem has been studied for more than a decade. A major study was initiated in 1995 during the Clinton administration. The map that I have here shows a brown line that shows where the Army Corps believes the TCE is. However, to the right over here, you can see this dotted line that shows where the city of Cheyenne's water wells are. The series of brown boxes around this area shows where the Wyoming Department of Environmental Quality has tested the groundwater. Fourteen of the brown boxes tested positive for traces of TCE. So this has all tested positive, and this is where the Army Corps says absolutely they realize the TCE plume is moving.

Given the close proximity of the Atlas missile site to the site, common sense would conclude that there is a connection to the contamination in the city's water wells. Unfortunately, this is not how the Federal Government works. After additional meetings with the Army Corps of Engineers, I have been informed that additional testing is needed in the area between the city FEs wells and the missile site to definitively prove that there is a connection. Those tests will be occurring in the next few months and we will not know the results until the end of the year.

The city of Cheyenne and the Wyoming Department of Environmental Quality are containing the TCE, but they have been asking the Army Corps for help. It is an expensive process to clean TCE from the water. Currently, that cost is being borne entirely by Wyoming taxpayers. The Federal Government, through the Army Corps and the EPA should provide technical and financial assistance sooner, rather than later. This situation needs to be resolved quickly for the betterment of Wyoming residents.

I look forward to the testimony. Thank you, Madam Chairman.

Senator BOXER. Thank you, Senator.

Senator Whitehouse.

Senator WHITEHOUSE. Madam Chair, I will pass. We can go directly to the testimony.

Senator BOXER. Senator Bond.

OPENING STATEMENT OF HON. CHRISTOPHER S. BOND, U.S. SENATOR FROM THE STATE OF MISSOURI

Senator BOND. Thank you very much, Madam Chair. Thank you for holding this hearing today.

This hearing allows us to examine the politicization of environmental protection, attempts to roll back environmental law, and disregard sound science. Now, some may think that I am 1 day early. That is the goal of tomorrow's hearing, as I understand it. However, I would say that before stones are thrown today, we should examine the glass house some of us are living in today.

Part of the purpose of this hearing is to establish the need for a bill currently before the Senate, S. 150. That legislation would require EPA to issue regulations on perchlorate levels in drinking water. Sponsors of this legislation are well meaning, and I have no question about their motives and their concerns. They have the best interests of their constituents at heart, but they fail to acknowledge that their effort is the very definition of political regulation. It is politicians here in the Senate dictating the outcome of EPA's environmental decision making.

And yet in past months and again tomorrow, these same folks may be trying to tell us that political officials should not tell career scientists and environmental specialists what to do. Their perchlorate bill also represents a roll-back of environmental law. Ironically, Congress amended the Safe Drinking Water Act a dozen years ago to get politicians out of the business of deciding which compounds to regulate. The Safe Drinking Water Act now includes a specific process designed to protect public health. The law specifically requires risk assessment and the use of science in decision making.

Under the law, the Administrator must present information to the public and conduct a health risk reduction and cost analysis. But advocates would sweep away the environmental law and go straight to the conclusion they favor. Apparently, rolling back environmental laws are OK with them if and when they choose.

This effort also includes a minimization of the work of the National Academy of Sciences. Witnesses will tell us today why we should not follow the natural conclusions of an NAS study on perchlorate. How many times have we heard charges of heeding the advice of political figures instead of peer-reviewed science?

Indeed, 2 weeks ago an NAS study by the National Research Council was heralded when it determined that short-term exposure to ozone is likely to cause premature death in some cases. Two weeks later when the NAS is not so helpful, it becomes an inconvenient truth to be minimized or discounted.

Now, I agree with the sponsors of this hearing that we must protect the health of women and children from compounds like perchlorate. We must understand the prime pathway perchlorate is getting into the bodies of our infants and children, and put a stop to that. Studies indicate the primary route is through baby food,

dairy products and vegetables, and we need to take a hard look at regulating that.

But the decision on whether or not to regulate perchlorate in water, as with all of these technical decisions, is best left to the scientific experts, using the processes established by our environmental law. We should not do as some propose and override our environmental law, minimize peer-reviewed science, or act by political fiat.

I join with you in welcoming EPA Assistant Administrator Grumbles. I will have some questions for the record for him.

Thank you, Madam Chair.

[The prepared statement of Senator Bond follows:]

STATEMENT OF HON. CHRISTOPHER S. BOND, U.S. SENATOR FROM THE STATE OF MISSOURI

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Thank you.

Senator BOXER. Thank you very much.

Senator Bond, at our last hearing what we learned from the GAO is that indeed there is politics in the risk assessment process. That

was what GAO found within EPA, that they are shunting the scientists to the back.

I also want to say since we will be marking up two perchlorate bills in June, and so we will have another robust debate at that time, I wanted to mention that we don't set any standard. We say follow the science, but act within certain timeframe. So we don't set the standard or put politics in it. We are just trying to put the science back into it and give them a deadline because in your State and my State, and I can tell you, I know you alluded to it, people are getting very high levels of exposure.

We want to see action by the scientists. We want to see a standard set.

Senator BOND. Madam Chair, I wouldn't think you would say that NAS is putting politics in the science.

Senator BOXER. No, what I said is——

Senator BOND. I am referring to the NAS study.

Senator BOXER. I am talking about the GAO. I am reminding you that we had a full hearing on a GAO report that looked at the IRIS system and the way risk assessment is being done and the fact that EPA is trying to shunt the scientists to the back, put the DOD contractors to the front at the table, and they said it is very dangerous, GAO.

On perchlorate, what I am saying to you is, we do not set a standard. We ask the EPA to act. We will have that debate.

Senator BOND. Based on sound science.

Senator BOXER. Absolutely. So I am going to share that with you and hope maybe to win you over.

By the way, working with you on other issues, if you could talk among yourselves for a minute, I am very proud of the work we are doing on the veterans.

Senator BOND. Thank you. We do have strong bipartisan cooperation.

Senator BOXER. Yes, we do.

Senator BOND. Senator Boxer and I have been working on other things. We may have an occasional disagreement.

Senator BOXER. Once in blue moon.

Senator BOND. A slight variance here, but we work together when it comes to taking care of our wounded heroes coming home.

Thank you, Madam Chair.

Senator BOXER. We do. Thank you very much.

Mr. Grumbles, we look forward to your testimony.

STATEMENT OF BENJAMIN GRUMBLES, ASSISTANT ADMINISTRATOR FOR WATER, U.S. ENVIRONMENTAL PROTECTION AGENCY

Mr. GRUMBLES. Thank you, Madam Chair. It is an honor to be here. EPA truly appreciates the opportunity to discuss our important work on perchlorate and TCE.

Madam Chair, since you mentioned it, I do feel it is important to say that the agency strongly supports environmental education, the use of websites, and getting out the word and raising awareness about the importance of source water protection and drinking water protection, but it is not the only effort or the only tool. The regulatory tool is critically important. That is why we are proud

that over the last several years, we have moved to finalize several nationally significant and important drinking water rules.

I would also say, Madam Chairman, that it doesn't take an act of Congress for us. It didn't take an act of Congress for us to make a decision to revise the coliform rule which we are working on right now. It didn't take an act of Congress for us to issue an aircraft drinking water rule. It also didn't take an act of Congress for us to revise the lead and copper rule based on the knowledge we have learned over the last several years.

But we share a lot with you and have a lot in common in terms of the goals and using the framework of the regulatory determination process that is set out in the 1996 amendments. We are committed to using the best available science to ensure our policies continue to protect public health and the environment. We are working with other Federal agencies to gather and understand data needed to inform our decision making.

This allows us to share the considerable expertise of other senior Government scientists, as well as ensure that each agency's research and analysis benefit from the findings of counterparts who are evaluating similar issues in other agencies.

As you know, we also consult with the National Academy of Sciences when we need assistance in evaluating emerging or conflicting scientific issues. With respect to perchlorate, as has been stated, in 2005 the NAS released a report recommending a reference dose. The agency adopted that reference dose. A year later, we issued guidance for contaminated sites which recommended a revised preliminary remediation goal for perchlorate in water. It was calculated using the reference dose, which was based on the National Academy of Sciences' work. It used standard exposure values of 70 kilograms body weight and two liters of water consumed per day. This calculation provides the drinking water equivalent level, assuming no other sources of perchlorate exposure. But we understand, and we have been gathering data that indicates there are other sources of exposure.

Madam Chair, I just want to also underscore the decision we made did not continue regulation of unregulated contaminants, but not to continue the monitoring of perchlorate. We never said it is because we had enough data. What we said was we had enough data on occurrence based on the contaminant monitoring rule. We have spent the last several years gathering additional information on relative sources that contribute to the overall determination to make as to whether or not to regulate for perchlorate.

As you know, we need to know that the contaminant is likely to cause an adverse effect on the health of persons. We know that perchlorate can have an adverse effect and we are concerned about that. We have set a reference dose that is based on a more protective no-effect level and it is based on the most sensitive sub-population, which is the fetus of a pregnant woman with iodine deficiency or hypothyroidism.

Second, we need to determine if the contaminant is known or likely to occur in public water systems at a frequency and level of public health concern. The results of our regulation from monitoring of unregulated contaminants such as perchlorate dem-

onstrated that it was detected at levels above four parts per billion in 4 percent of the public water systems.

But we also have to answer the question under the statute of is there a meaningful opportunity to reduce risk if we issue a new national regulation on perchlorate. We have been spending a lot of time on that, Madam Chairman, and we have been coordinating with other agencies, CDC and in particular FDA. We find it is very important to have the total diet study from the FDA. It is the most comprehensive effort to date, we believe, on the different sources of contamination and exposure to perchlorates such as food, not just water. It provides an important additional tool for us to make our determinations.

I understand your frustration on how long the process is taking, but we believe it is important to do the work and we intend to issue a final regulatory determination before the end of 2008.

With respect to TCE, as you know, it is a different contaminant and we have already been regulating it. We have been managing the risk in drinking water for many years. Currently, there is a five part per billion standard. We began, however, reevaluating the risk assessment for TCE several years ago and we also, with other agencies, sought additional comments from the Science Advisory Board, and then following up on that, from the National Academy of Sciences.

Right now, we are evaluating TCE, both in terms of reevaluating the risk assessment based in information we have gotten from the NAS and others. The other thing, Madam Chairman, is that my office, the Water Office, is evaluating TCE under our 6-year review process under the Safe Drinking Water Act. We are analyzing new scientific and technological data and information on health effects associated with each regulated contaminant such as TCE. We are taking this very seriously and we are looking at it very closely.

The other aspect I want to add is that TCE is prevalent. It is a prevalent groundwater contaminant at hazardous waste sites, so we are concerned about vapor intrusion and when it occurs. We are working with Federal partners, State regulators, industry, academia, environmental groups and the general public to understand the rapidly developing science of vapor intrusion. We are developing recommendations for——

Senator BOXER. Mr. Grumbles, could you complete? I have let you go over a minute and a half, but if you could complete.

Mr. GRUMBLES. Yes. So we are developing recommendations for interim toxicity values with respect to vapor intrusion.

In conclusion, Madam Chair, the agency is committed to robust protection of public health from contaminants in drinking water using the science-based framework. We believe this framework is sound and respectfully request that you allow us time to complete the required analyses and determinations to ensure appropriate science-based protection of public health from these and other contaminants as envisioned by the 1996 amendments.

We are committed to making a final regulatory determination for perchlorate by the end of this year, and for TCE, as soon as the necessary analyses have been completed.

Thank you for your patience and the opportunity to discuss this with you.

[The prepared statement of Mr. Grumbles follows:]

TESTIMONY OF

BENJAMIN H. GRUMBLES
ASSISTANT ADMINISTRATOR FOR WATER
U.S. ENVIRONMENTAL PROTECTION AGENCY
BEFORE THE
ENVIRONMENT AND PUBLIC WORKS COMMITTEE
UNITED STATES SENATE

May 6, 2008

Good morning, Madam Chair and Members of the Committee. I am Benjamin H. Grumbles, Assistant Administrator for Water at the United States Environmental Protection Agency (EPA). One of Administrator Stephen L. Johnson's key principles for the Agency is using the best available science for decision-making to accelerate the pace of environmental protection in our country while maintaining our country's economic competitiveness.

We appreciate the opportunity to provide you with information about our on-going efforts to determine the need for managing potential risks posed by perchlorate and trichloroethylene.

We are working with other federal agencies to gather and understand data needed to inform our decision-making. We are committed to using the best science to ensure that our policies continue to protect public health and the environment.

Perchlorate Research and Risk Management for Contaminated Sites

EPA has been working on the science related to perchlorate for more than ten years. In 2003, EPA sent its January 2002 external review draft of the perchlorate risk assessment to the National Academy of Sciences (NAS) for review. The NAS panel released a report in January 2005 which recommended that the Agency use a reference dose (RfD) of 0.0007 mg/kg/day (0.7 µg/kg/day) based on a human study (Greer et al., 2002). The RfD is an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily oral exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of adverse effects during a lifetime. EPA endorsed their recommendation and used the NAS panel report "*Health Implications of Perchlorate Ingestion*" as the basis for establishing its RfD which was subsequently posted to the Integrated Risk Information System (IRIS) database in February 2005.

In carrying out their analysis, the NAS recommended the use of a human study (Greer et al., 2002) as the principal study. Because this study was based on healthy adult men and women, an uncertainty factor of 10 was applied to the no observed effect level (NOEL) identified from the Greer data to protect the most sensitive population, i.e., the fetuses of pregnant women who might have hypothyroidism or iodide deficiency. The NAS also indicated that deriving the RfD to prevent a nonadverse precursor effect, which would precede an adverse effect, as was done here, is a conservative and health-protective approach to perchlorate risk assessment.

In January 2006, EPA issued guidance for contaminated sites which recommended a revised preliminary remediation goal (PRG) of 24.5 ppb perchlorate in water. The PRG was calculated from EPA's RfD using standard exposure values of 70 kg body weight and 2 liters of water consumed per day. This calculation provides the drinking water equivalent level, assuming no other sources of perchlorate exposure.

PRGs are, however, not final cleanup levels, but are the starting point for identifying site-specific goals. In accordance with the National Contingency Plan, PRGs should be modified, as necessary, as more information becomes available at specific sites. This may include assessing factors such as actual and potential exposure pathways through environmental media and actual and potential exposure routes.

In addition, if a state has promulgated a drinking water standard for perchlorate (e.g., Massachusetts adopted 2 ppb as a drinking water standard), that value would be considered an Applicable or Relevant and Appropriate Requirement (ARAR) and used as the ground water cleanup level for sites in that state.

Perchlorate Risk Management for Drinking Water

The Agency has also been working to evaluate the potential risks posed by perchlorate in drinking water. The Agency has placed a high priority on making a regulatory determination for perchlorate as soon as possible and intends to make a final determination by the end of this year.

The Safe Drinking Water Act (SDWA) has an established process for determining if unregulated contaminants pose a sufficient risk to public health to warrant regulation. The law requires the Agency to develop a Contaminant Candidate List (CCL), which is a list of unregulated contaminants that may require regulation. Perchlorate was placed on the first CCL which was released in 1998 and carried on to the second CCL which was published in February of 2005. It

has also been included on the draft third CCL which was published this past February. Every five years, EPA must determine whether or not to regulate at least five contaminants from the list. EPA may also decide at any time to regulate a contaminant (whether on the list or not) if we believe it is necessary to do so to protect health.

In making a determination to regulate a contaminant under the SDWA, the law requires EPA to consider three questions:

Is the contaminant likely to cause an adverse effect on the health of persons?
Is the contaminant known or likely to occur in public water systems at a frequency and level of public health concern?
In the sole judgment of the Administrator, does regulation present a meaningful opportunity to reduce risk for persons served by public water systems?

When the Agency issued the first set of regulatory determinations for nine contaminants on the first CCL in 2003, we did not have sufficient information to make a regulatory determination for perchlorate. The Agency's risk assessment and RfD value had not yet been finalized and we were continuing to collect occurrence data from public water systems under the first round of unregulated contaminant monitoring.

In May 2007, the Agency issued a Federal Register Notice with preliminary regulatory determinations for 11 contaminants on the second CCL. The Notice also indicated that the Agency was not making a preliminary determination on perchlorate at that time because of the need to more fully characterize and understand perchlorate exposure. The Notice provided an extensive update on the Agency's review of perchlorate, including a summary of recent research, and requested comment on approaches the Agency has under consideration to help arrive at a final decision.

Health Effects

Based on the RfD, the Agency has sufficient information on health effects to answer the first question needed to inform a regulatory determination. However, as with any chemical, the Agency is continuing to review new research findings on perchlorate as they become available.

Occurrence in Drinking Water

To support our regulatory development process, the Agency requires short-term monitoring for specific contaminants under the Unregulated Contaminant Monitoring Rule program (UCMR). During the first round of this program, which included monitoring for 26 contaminants, 3,858 water systems monitored for perchlorate during a one-year period between 2001 and 2003. This monitoring was designed to provide an assessment of perchlorate occurrence in public water supplies that was representative of community water systems throughout the country.

Perchlorate was detected at levels above the minimum reporting level of 4 parts per billion (ppb) in approximately 2 percent of the more than 34,000 samples analyzed. The average concentration of the detected values was 9.8 ppb and the median concentration was 6.4 ppb. The samples in which perchlorate was detected were collected from 160 of 3,858 public water systems (4% of systems) located in 26 states and 2 territories.

We have determined that the existing data on the occurrence of perchlorate in public water supplies is sufficient to support our regulatory decision-making and, as such, it is not necessary to conduct additional perchlorate monitoring under the second round of the UCMR program, which began for 25 new contaminants this year. Additionally, monitoring under the second UCMR would not be completed until 2010 and the Agency intends to make a final determination in 2008. If necessary, EPA can require additional monitoring at a later time if new information indicates that additional sampling is warranted. If EPA determines that federal regulation of perchlorate in drinking water is necessary, on-going compliance monitoring of perchlorate would be part of any new standard.

Relative Source Contribution and Other Sources of Exposure

Before the Agency can make a determination as to whether it is appropriate to regulate perchlorate in drinking water, we need to better understand total perchlorate exposure and what

portion comes from food versus water. Because perchlorate has been found in a variety of foods, we believe that a default assumption for the relative source contribution (RSC) (i.e., exposure to perchlorate from water as opposed to food sources) may not be the best means to determine whether it is appropriate to regulate perchlorate in drinking water. We need to determine how public exposure compares to the RfD and need to determine whether setting a drinking water standard would provide a meaningful opportunity to reduce risk for people served by public water systems. We described a number of approaches in our Federal Register Notice and asked for comment on their potential utility in informing a determination.

The FDA has been conducting surveys to determine perchlorate levels in food since 2004. EPA's May 2007 Federal Register Notice described results of FDA studies and other published studies of perchlorate levels in food. The FDA's Total Diet Study (TDS) provides the most comprehensive assessment of food exposure to date and is designed to provide estimates of total food exposure by region based on a representative market basket approach. In January 2008, FDA researchers published results of their analysis in the advance online version of the Journal of Exposure Science and Environmental Epidemiology. The study found detectable levels of perchlorate in 74 percent of the 285 TDS foods (Murray *et al.*, 2007). FDA estimated the average amount of perchlorate in the diet for 14 age-gender groups. The estimates range from 0.08 to 0.39 µg/kg/day, which is between 11 and 55 percent of EPA's RfD of 0.7 µg/kg/day. Estimates for infants and children are higher, on a body-weight basis, than those for teenage and adult subpopulation groups. FDA estimates that the majority (81%) of dietary perchlorate intake by infants comes from baby foods and dairy foods. The dairy group contributes about half of the total daily intake of perchlorate by children 2, 6 and 10 years of age. Vegetables and dairy foods combined account for between 46% and 59% of the total intake of perchlorate by teenagers and adults.

We are carrying out additional analyses to better understand what happens to perchlorate once it has been ingested by an infant or young child (e.g., how quickly is it excreted). Understanding these physiologic processes is critical to our evaluation of the effects of perchlorate exposure on these subpopulations.

We are continuing to carry out the analyses evaluating exposure that are needed to inform our regulatory determination and intend to issue a final regulatory determination before the end of 2008.

Trichloroethylene

While perchlorate is an emerging contaminant, trichloroethylene, or TCE, is a contaminant that the Agency has been regulating for several years. The Agency is carrying out several efforts related to TCE – developing a final risk assessment, reevaluating the regulations controlling TCE in drinking water, and evaluating the need for standards to manage risk from vapor intrusion at contaminated sites.

Reevaluating Risks

In 1989, EPA initiated a process to reevaluate the risk assessment for TCE through the Integrated Risk Information System (IRIS) process in response to uncertainties raised by an EPA Science Advisory Board (SAB) review regarding the appropriate classification for TCE carcinogenicity. The Agency subsequently engaged in an extensive scientific outreach effort to gather a diversity of views and range of expertise. The results of these efforts were used to prepare a draft risk assessment which in 2001 underwent public review and review by the SAB. The peer review report by the SAB was completed in 2002, but due to continuing science issues as well as significant emerging new science, in 2004, EPA, along with the Department of Defense, the Department of Energy, the National Aeronautics and Space Administration and Agency for Toxic Substances and Disease Registry, asked the NAS/National Research Council to provide independent guidance on scientific issues related to TCE. On July 27, 2006, the NAS/NRC publicly released its report on these science issues, providing advice to EPA.

Unlike the review of perchlorate, the NAS did not recommend an RfD or a cancer slope factor/unit risk for the Agency to consider. The panel recommended that EPA consider several issues as part of the risk assessment development process, including, for example:

Development of a new meta-analysis of the epidemiologic data on TCE exposure and various forms of cancer, and

Consideration of multiple options for dose metrics and benchmark response values when conducting dose-response analysis of cancer and non cancer endpoints.

EPA has a multidisciplinary scientific team working on this assessment and has made this a top priority for its chemical assessment program. We currently expect to have an assessment ready for intra-agency review at the end of August and interagency review in December 2008. At this point in time, EPA is uncertain how extensive further review will need to be. This schedule is constrained by the complexity of the assessment, the size of the existing data base, and the recent availability of significant new information on modes of action relevant for TCE.

EPA's assessment team is addressing the NAS/NRC recommendations and comments previously received from all sources. Because of the complexity of this assessment, several sections of the assessment are being developed simultaneously.

Reevaluating Risk Management for Drinking Water

In 1987, EPA published a national primary drinking water regulation for TCE. The regulation established a Maximum Contaminant Level Goal (MCLG) of zero based on a cancer classification of B2, probable human carcinogen. EPA also set a Maximum Contaminant Level (MCL) of 0.005 mg/L, or 5 parts per billion (ppb), which was established based on analytical feasibility (i.e., the ability to measure the contaminant in water).

The 1996 SDWA Amendments require EPA to reassess national primary drinking water regulations every six years to determine if the regulations need to change. EPA completed its first Six Year Review in 2003 and made the decision to revise the Total Coliform Rule.

EPA is now carrying out the second Six Year Review process which will review existing national primary drinking water regulations for TCE and other regulated contaminants. As part of this review, we are analyzing new scientific and technological data and information on health effects associated with each regulated contaminant. With respect to TCE, the final risk assessment represents a key piece of information that will support any regulatory revisions. However, we are also evaluating technological information, including whether it is feasible for public water systems to reliably measure TCE in drinking water below the 5 ppb standard.

If the Agency identifies a potential health or technological basis for a revision to the drinking water regulation, this would necessitate a series of follow up analyses. For example, EPA

would need to conduct an occurrence and exposure analysis to determine if changes to the drinking water standard are likely to increase public health protection for customers served by public water systems. EPA anticipates releasing the draft results of our Six Year Review for public comment in 2009 and completing our review in 2010.

Managing Vapor Intrusion

Vapor intrusion occurs when volatile chemicals in buried wastes and/or contaminated ground water migrate from the subsurface and emit vapors into air spaces of overlying buildings.

TCE is a prevalent ground water contaminant at hazardous waste sites throughout the country. While EPA has a TCE standard for drinking water, which is also used as a clean up goal for contaminated ground water, the Agency does not promulgate standards for vapor intrusion. A site specific risk assessment approach is used at sites to determine remediation goals.

EPA is developing recommendations for interim TCE toxicity values to assess human health risk and recommending an approach for vapor intrusion pathway analysis. Absent a toxicity value in EPA's Integrated Risk Information System (IRIS)(Tier 1 information), Agency guidance provides that provisional peer reviewed toxicity values be used (Tier 2 information), and if those are unavailable, other EPA and non-EPA sources of information (Tier 3 information) be used, with priority given to information which is transparent, publicly available, and has been peer reviewed. With respect to TCE toxicity, Tier 1 and Tier 2 information is not available, so the Agency must rely on Tier 3 information. To assist EPA regions, EPA is currently developing a recommended interim TCE toxicity value, based upon Tier 3 information.

With respect to the current management of vapor intrusion, EPA worked closely with the Interstate Technology & Regulatory Council (ITRC) to develop the ITRC's January 2007 guidance, *Vapor Intrusion Pathway: A Practical Guide.* The ITRC guidance improved upon prior EPA guidance by emphasizing the importance of evaluating multiple lines of evidence when determining the potential for vapor intrusion into buildings, and therefore we believe it is an appropriate starting point for vapor intrusion investigations and for assessing and managing vapor intrusion risks.

We will also continue the dialogue on the rapidly developing science of vapor intrusion with Federal partners, state regulators, industry, academia, environmental groups and the general public to continue to improve the science of vapor intrusion prevention.

Views on Proposed Senate Legislation

We have significant concerns with the bills introduced by Senators Boxer and Clinton. With respect to drinking water our primary concern with these bills is that they return the Agency to the time before 1996 when Congress dictated the drinking water regulations developed by the Agency. EPA found it difficult to meet the regulatory development requirements associated with the 1974 SDWA and 1986 Amendments, and stakeholders, including the states that implement SDWA requirements, almost universally questioned whether the Agency was able to focus its efforts on the most significant risks to health under this approach. In passing the 1996 Amendments, the intent of Congress was to bring a risk-based, scientifically sound approach to regulatory development. The changes that Congress made to the Act ensure that the Agency appropriately addresses contaminants that pose a risk to human health and develops regulations that provide a meaningful opportunity to reduce those risks from contaminants in public water supplies.

EPA has been working to carry out the activities required by the 1996 Amendments to evaluate unregulated drinking water contaminants and determine whether they require national regulation. In doing so, we review the best available, peer-reviewed science and supporting studies to determine if a contaminant poses a risk to human health. We collect and analyze information on contaminant occurrence, including monitoring the Agency itself may require or otherwise conduct, to determine if the contaminant occurs in drinking water at a level and frequency that may pose a risk to health. We also review information to determine if there are additional sources of exposure to a contaminant other than drinking water.

While our primary concern is that the bills would require regulation without considering the data and analyses that the Agency has spent the past several years developing, and thereby subvert the public process established by the SDWA to ensure that our regulatory activities are focused where they will provide the greatest public health benefit, we are also concerned about the timeframes provided for by the bill. The SDWA provides the Agency with 24 months to propose a regulation after making a determination to regulate and another 18 months after proposal to issue a

final rule. We believe this is the minimum time necessary to promulgate regulations that includes the analyses and public process required by SDWA and the Administrative Procedures Act and are sound enough to withstand judicial scrutiny.

Conclusion

The Agency is committed to robust protection of public health from contaminants in drinking water using the science-based framework laid out in the current SDWA. We are working expeditiously to address potential risks from perchlorate and to evaluate the need for and feasibility of a stronger standard for TCE using this framework. We believe this framework is sound, and respectfully request that you allow us time to complete the required analyses and determinations to ensure appropriate science-based protection of public health from these and other contaminants, as envisioned in the 1996 amendments. As noted above, we are committed to making a final regulatory determination for perchlorate by the end of 2008, and for TCE as soon as the necessary analyses have been completed.

Thank you again for this opportunity to describe EPA's important work on perchlorate and TCE. I would be happy to answer any questions you may have.

Senator BOXER. Thank you, Mr. Grumbles.

So you are going to act at the end of 2008. Is it possible that EPA could decide not to regulate perchlorate? Is that an option?

Mr. GRUMBLES. That is an option. That is a distinct possibility and we are in the final stages of assessing the latest information we have. We would, first, before we issue a final determination, we would issue a preliminary determination and take public comment on that, Madam Chair.

Senator BOXER. OK. So it is a distinct possibility that the EPA in protecting the public may determine not to set a standard for perchlorate? Is that correct?

Mr. GRUMBLES. It is. It is a distinct possibility to make another determination as well, but that is the stage we are in.

Senator BOXER. Right. Well, that is what I hear is going to happen. That is what I hear. You have a lot of good people over there who talk to us. I am just saying if that happens, and you can look the American people in the eye and say, we are protecting you, no standard. And you have stopped testing. Why did you stop testing? Why did you tell the water systems they didn't have to test for perchlorate and let people know if perchlorate is in their water?

Mr. GRUMBLES. After the rounds of the regulations that required utilities to monitor for perchlorate, we got a robust amount of data from 3,800 systems, and we felt that is a sufficient amount of data that can help us to meet one of the three statutory requirements under the Safe Drinking Water Act.

I would note two things, Madam Chair. One is that we can still require additional contaminant monitoring if the science leads us to that result.

Senator BOXER. OK. I understand. But you think—you the agency—the Government has enough information. Don't you think that people who are drinking the water have a right to know how much perchlorate is in there? They are not stupid. They read the papers. I can imagine what is going on with TCE in Wyoming. My friend told me. People are upset.

Now, you have enough information.

Mr. GRUMBLES. But we are not saying we——

Senator BOXER. Excuse me. EPA said that, you had enough information that you didn't have to test anymore. Is that right?

Mr. GRUMBLES. Well, the important clarification is that we felt because we want to get on with the process and make a determination on whether or not to issue a new regulation, we felt we had sufficient data on one of the three elements, and that is the occurrence data. Now, that was based on various assumptions. We have never said to any utility, you should not test for it, or you should stop testing.

Senator BOXER. But you stopped requiring it.

Mr. GRUMBLES. That is correct.

Senator BOXER. OK.

Mr. GRUMBLES. With the right to re institute that if more science comes in.

Senator BOXER. You always have that right, but EPA said—and here it is, I will put it in the record—we agree with the comments that it is not clear that the agency needs additional information on the occurrence of perchlorate in drinking water.

Now, it is a year and a half since you stopped the testing. You still haven't acted. You now say you are going to act at the end of 2008, and it is a distinct possibility you could conclude you are not going to set a standard. So if that is the case, and that is what I believe is going to happen after all this folderol, there won't be a Federal standard. The States will have to do it.

People will be completely ignorant of the whole situation because they won't be protected by the Drinking Water Act by EPA and they won't have the information. It is unbelievable to me that at the minimum, at the minimum, you give people information. Let them make their judgments. Let them have the political information. Let them make it a reason to support a Senator or not support a Senator or a President or whatever. So I think keeping people ignorance is part of what this is about.

I just want to ask you something else.

Mr. GRUMBLES. But Madam Chair, I just have to say, EPA firmly supports getting as much information as we can out there on perchlorate. Now, what that means is that it is not just the occurrence measurements. It is also getting critical information about other types of exposure such as food. So we have been spending the time to get that additional information because we are concerned. It is not just water, it is food.

Senator BOXER. Mr. Grumbles, you know what? I was not born yesterday, as I keep reminding people. You just have to look at me to get it. I was not born yesterday. What is the best way to give people information? Let them know if it is in their drinking water. Isn't that a lot easier than, oh, go up on our website?

Let me ask you this. You testified that EPA's preliminary remediation goal for perchlorate clean-up is based on protecting a 154-pound adult. Shouldn't EPA lower this number to account for the larger amount of water and food that infants and children consume for their body weight compared to adults?

Mr. GRUMBLES. It has been very much a part of our discussions of the need to revisit the preliminary remediation goal as we have spent the last couple of years getting additional information, Madam Chair. So my answer to your question is that, yes, that is a distinct possibility of revising the preliminary remediation guidelines, particularly as we have gotten additional information from the Food and Drug Administration.

Senator BOXER. Well, you set the standard in 2006. This isn't like it happened many years ago. You set it to protect a 154-pound male.

Mr. GRUMBLES. Right.

Senator BOXER. And now you are saying, a little while later, a year later, because I am questioning you, well, maybe you ought to change it.

Mr. GRUMBLES. Well, everyone embraces the concept of adaptive management. We set a time as quickly as we could.

Senator BOXER. Adaptive management?

Mr. GRUMBLES. That is right.

Senator BOXER. What does that mean? What does that mean?

Mr. GRUMBLES. That means that right after the National Academy of Sciences came out with their report, the agency shortly after that adopted a reference dose. After the reference dose, the

heads of the Superfund program realized they wanted to have a preliminary remediation goal. So they went with the best information available and they made assumptions, Madam Chair, about the types of exposure.

Senator BOXER. Right. Lots of words. Lots of words.

Mr. GRUMBLES. The answer to the question is what it means is, as you get additional information about food exposure, you go back and you look at is the preliminary remediation goal the proper number at this point.

Senator BOXER. Well, let me put in the record your own Children's Health Advisory panel made up of scientists—and I wish Senator Bond was here—and doctors. I am putting this letter in the record. They told Mr. Johnson on March 8th, 2006 the new PRG is not supported by the underlying science and can result in exposures that pose neurodevelopmental risks in early life. So don't give me you are just learning this, when your own people——

[The referenced document follows:]

March 8, 2006

Stephen L. Johnson, Administrator
United States Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, D.C. 20460

RE: Perchlorate PRG and water contamination

Dear Administrator Johnson:

The Children's Health Protection Advisory Committee (CHPAC) is writing to express concern over a recent assessment guidance issued by the U.S. EPA, Office of Solid Waste & Emergency Response (OSWER). The OSWER guidance creates a groundwater preliminary remediation goal (PRG) for perchlorate at Superfund sites that is not protective of children's health. The new PRG is not supported by the underlying science and can result in exposures that pose neurodevelopmental risks in early life. The new PRG can lead to exposures that are well above USEPA's IRIS RfD for perchlorate. The CHPAC finds it disturbing that this change in the PRG was made without dissemination of a decision support document or any opportunity for public input. We recommend that OSWER lower the PRG, taking into account infant exposures and susceptibility. We also recommend that USEPA's Office of Ground Water and Drinking Water (OGWDW) develop a Maximum Contaminant Level (MCL) for perchlorate, and in the interim, issue a health advisory for potable water that takes into account early life exposures.

Background

On January 26, 2006 OSWER released a PRG that would allow remediation of perchlorate at Superfund sites to a higher level (24.5 μg/L) than the previous screening level (4-18 μg/L). This establishes a potable water PRG, which is a critical starting point for site cleanup. USEPA is required to develop PRGs in a health protective manner to enable broad future use of the site, with site-specific factors enabling the risk manager to adjust the cleanup target.

Risk of neurodevelopmental toxicity can occur from perchlorate exposure because perchlorate impairs the uptake of iodide by the thyroid, which can decrease thyroid hormone production and affect brain development. This is especially important in infants because they do not have stores of thyroid hormone, and are no longer supported by maternal thyroid hormone following birth. What may be considered by some to be a precursor effect in normal adults (inhibition of iodide uptake by the thyroid) may be an adverse effect during this sensitive life stage, especially in concert with exposure to other thyroid toxicants (e.g., PCBs, PBDEs) and because perchlorate may decrease iodine levels in human milk.

The CHPAC acknowledges that EPA's RfD incorporates a ten-fold uncertainty factor to protect the fetuses of pregnant women who might have hypothyroidism or iodide deficiency. This factor was used to account for interindividual differences that lead to uncertainty in assessing perchlorate risk. However, the uncertainty factor does not cover the types of exposure differences across life stages discussed in this letter.

The OSWER Perchlorate PRG Does Not Protect Infants and Should be Lowered

Perchlorate is a well-recognized endocrine disruptor at sufficiently high doses, targeting the thyroid and thus creating risk of neurodevelopmental toxicity. A key concern is the nursing infant because of the potentially high exposure rate associated with this pathway, and the high susceptibility at this life stage. The following points highlight the fact that nursing infants could receive daily doses that are greater than the RfD if the mother is exposed to 24.5 μg/L perchlorate in tap water. The supporting calculations are provided in the appendix to this letter.

Infant Exposures

- Perchlorate is actively transported into human milk leading to nursing infant exposure to perchlorate; current data suggest this is associated with concomitant lowering of iodide in human milk (Kirk, et al., 2005; Tellez, et al., 2005, see Appendix to this letter). Both of these factors increase the risk of neurodevelopmental toxicity due to perchlorate anti-thyroid effects occurring in the susceptible postnatal period.
- The current PRG (24.5 μg/L) would allow a nursing mother to ingest approximately 54 μg of perchlorate per day. Based upon the Chilean three-cities database (Tellez, et al., 2005), this would yield a human milk perchlorate concentration of 28 to 46 μg/L.
- **This would lead to a nursing infant exposure that is approximately 5 to 10 times higher than the perchlorate RfD.**
- This analysis does not account for variability in perchlorate exposure. Assessment of the entire population distribution would identify high-exposure individuals that would be at greater risk than currently estimated.
- Bottle-fed babies can also receive perchlorate exposure above the RfD through tap water used to reconstitute formula and juices, or directly fed to the infant. This perchlorate exposure may not be quite as high as in breast-fed infants; however, it is still a concern.

Infant are a Susceptible Population

Not only are infants more exposed, they are also susceptible to the neurodevelopmental effects of perchlorate because of the following early life factors:

- The central nervous system (CNS) is still developing but the maternal supply of thyroid hormone that was present *in-utero* is no longer available; thyroid hormone does not transfer into breast milk in significant amounts.
- The developing CNS in infants is sensitive to small deficits in thyroid hormone levels as evidenced by later indices of neurocognitive function (Oerbeck, et al., 2003; Heyerdahl and Oerbeck, 2003; Rovert and Daneman, 2003);
- Infants are not born with adequate thyroid hormone reserves and so must make new thyroid hormone on a continual basis to meet the demands of brain growth (Delange, 1998; van den Hove, et al., 1999).
- Immaturities in renal function at birth may lead to slow clearance of perchlorate, as urinary excretion is the major elimination pathway. Data from rats on perchlorate toxicokinetics in neonates (Clewell, et al., 2003) may not be highly relevant (see Appendix).

These factors, coupled with the infant exposure estimates, indicate that the PRG of 24.5 μg/L in drinking water is not protective. The PRG would produce above-RfD perchlorate exposure in infants who are susceptible to endocrine disruption and adverse neurodevelopmental impacts. While RfDs are generally considered chronic toxicity values, applying the perchlorate RfD to a shorter, critical window of susceptibility and high exposure in infancy is warranted. The OSWER cleanup PRG should apply the RfD to infants just as it is applied to pregnant women.

Lack of Consideration of an RSC

Groundwater cleanup targets are normally based upon the chemical's RfD and a relative source contribution (RSC) factor. The RSC accounts for that part of the exposure that comes from non-drinking water sources. The OSWER PRG is set without accommodation for other exposure sources. This is an obvious concern given the recent widespread detection of perchlorate in lettuce and milk (USFDA, 2004). Drinking water standard setting for perchlorate in New Jersey and Massachusetts has used an RSC of 0.2 (20% from water) while the California RSC is 0.6 (NJ Drinking Water Quality Inst., 2005; Ting, et al., 2006).

Use of an appropriate RSC could lower the PRG to a range that would ensure maternal intake of perchlorate is below a level which poses a risk of adverse neurodevelopmental outcome for the fetus and nursing infant.

The CHPAC recommends that OSWER lower the PRG considering the following points:

- The OSWER PRG ignores the higher exposure and susceptibility of infants, and could lead to nursing and bottle-fed infants being exposed to daily doses

that are well above the perchlorate RfD; the PRG needs to protect this susceptible population.

- The OSWER PRG does not account for perchlorate exposures from foods, which are in addition to drinking water. By omitting the RSC and not accounting for infant exposure, the PRG now allows for greater-than-RfD doses to the mother and her developing fetus and to nursing infants. OSWER should lower the PRG with an appropriate RSC and adjustment for exposure to infants.

The scientific issues discussed above are also central to the ongoing OGWDW deliberation of whether to set a Maximum Contaminant Level (MCL) for perchlorate. The CHPAC has been closely monitoring this deliberation for the past year and is concerned that there is still no decision about a perchlorate MCL.

OGWDW Regulatory Determination on Perchlorate

The CHPAC encourages OGWDW to establish a national drinking water standard for perchlorate, and in so doing, to fully consider both the prenatal and postnatal exposures and risks. Perchlorate has been known to contaminate groundwater at over 400 locations nationwide (GAO, 2005) and biomonitoring data demonstrate widespread exposure (Valentin-Blasini, 2005). We encourage the Agency to fully consider the particular susceptibility of the fetus as well as the infant who may be exposed through breastfeeding or reconstituted formula. We believe that technology (e.g., cleanup methods) exists to protect infants from perchlorate exposure.

Setting a federal MCL will greatly facilitate the discovery and control of drinking water contamination by this pervasive chemical. It would also help decrease a key uncertainty identified by the CHPAC: we do not know the perchlorate level in pre-constituted infant formula and other drinks. The water that goes into ready-to-use formulations is not currently required to be tested for perchlorate, although we are aware that manufacturers may purify water that goes into pre-constituted formula. Setting a federal MCL would require widespread testing of water supplies and thus provide greater confidence that both commercial and home-reconstituted infant formulations are made with water free of perchlorate contamination.

We recognize setting an MCL can be a lengthy process. In the interim, it is important for OGWDW to develop a drinking water health advisory for perchlorate. Such advisories normally factor in the RSC and can account for early life windows of high intake rate and susceptibility. A drinking water health advisory can inform the many state and federal programs that may detect perchlorate in drinking water supplies and need a public health protective guideline. The OSWER PRG is not intended for this purpose, but some risk managers may extend its use to such applications. This would be most unfortunate given the concerns expressed above that the current PRG is not protective of infants. Therefore, it is especially important for OSWER to lower the PRG and for OGWDW to develop an interim health advisory for perchlorate.

Summary and Recommendations

Perchlorate is an important endocrine toxicant because of widespread exposure and the potential for impairment of the thyroid during critical stages of brain development. The risk posed by this environmental agent is preventable by appropriate Agency action.

The CHPAC recommends that:

- OSWER lower the perchlorate PRG, using a more comprehensive risk assessment that includes postnatal exposures and health risks.
- OSWER use an RSC factor of less than 100% to account for the non-drinking water sources of perchlorate.
- OGWDW set an MCL for perchlorate that protects both the pre-and post-natal exposure periods.
- OGWDW develop an interim health advisory that addresses the early life exposure and susceptibility issues raised above.

We would be happy to discuss any of the points or recommendations raised in this letter with you or your staff. We would also like to be informed of the Agency's progress in protecting the public from perchlorate and to be provided with the documentation for any future guidance on perchlorate remediation. We thank you in advance for your consideration of these issues.

Sincerely,

Melanie A. Marty, Ph.D., Chair
Children's Health Protection Advisory Committee

Cc: Susan Bodine, Assistant Administrator, OSWER
Barry Breen, Deputy Assistant Administrator, OSWER
Benjamin Grumbles, Assistant Administrator, OW
Michael Shapiro, Deputy Assistant Administrator, OW
William Sanders, Interim Director, OCHPEE
Joanne Rodman, Assistant Director, OCHPEE

Administrator Johnson
March 6, 2006

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Administrator Johnson
March 6, 2006

Appendix

1) Relationship between iodide and perchlorate levels in human milk.

A sodium iodide transporter protein akin to that in the thyroid exists in mammary tissue. It transports iodide into human milk, and perchlorate id able to take iodide's place and be selectively pumped into milk (Clewell, et al., 2003). This can lead to nursing infant exposure to perchlorate, while at the same time leading to lower levels of iodide in milk. Kirk, et al. (2005) demonstrate an inverse correlation between perchlorate and iodide concentrations in human milk in a small number of US samples that were over 10 μg/L perchlorate. Tellez, et al. (2005) did not see a correlation, inverse or otherwise, between perchlorate and iodide concentrations in human milk across three Chilean cities with widely differing concentrations of perchlorate in drinking water. However, there does seem to be a factor that depresses iodide levels in human milk in these Chilean cities relative to the U.S. On average, Chilean human milk iodide concentrations were 40% lower than in US women in spite of the fact that iodide intake rates are known to be higher in these Chilean cities than in the US (Tellez, et al., 2005; Kirk, et al., 2005). The factor responsible for the lower-than-expected human milk iodide in Chile may be perchlorate intake as baseline (dietary) exposure to perchlorate is approximately 3 times higher in Chile as compared to the US. This is seen by comparing perchlorate biomonitoring data in Atlanta against the three Chilean cites (Valentin-Blasini, et al., 2005). The reason the Chilean cross-sectional study did not find an inverse correlation between human milk levels of perchlorate and iodide is unclear but comparisons are available only on the basis of group mean (Tellez, et al., 2005); regression analysis of the entire dataset would be a more sensitive method to determine whether there is a significant relationship between these human milk parameters in Chile. Evidence in rats for an inverse relationship between maternal perchlorate exposure and iodine levels in breast milk (Clewell, et al., 2003) supports the evidence for such a relationship in human milk.

2) Calculations of nursing infant perchlorate dose stemming from the OSWER cleanup target (24.5 μg/L) and comparison to the EPA RfD:

Nursing Infant Dose (μg/kg/d) = (μg/L in human milk/ug perchlorate ingestion-day)*[(24.5 μg perchlorate/L water)* (L water ingested/day) + (baseline US dietary ingestion rate, μg/d)]*(L human milk ingested/day/infant body weight)

Parameter values:

a) Relationship between human milk perchlorate and maternal perchlorate intake:

i) μg/L in human milk – data for the 3 Chilean cities (Tellez, et al., 2005).
Antofagasta: Cannot use the data due to extreme outlier and high variability;
Chanaral: **Mean = 18.3 μg/L**; SD = 17.7
Taltal: **Mean = 95.6 μg/L**; SD=54.6

ii) μg perchlorate excreted/g creatinine:
Antofagasta: Min: 2.9; 10th%: 8.64; 25th%: 12.96; Med: 22.7; 75th%:43.2; 90th%: 59.4; Max:: 75

Chanaral: Min: 12; 10th%: 17; 25th%: 27; Median: 37; 75th%:63; 90th%: 155; Max: 210
Taltal: Min: 20; 10th%: 45; 25th%: 70; Median: 120; 75th%:190; 90th%: 295; Max: 395

iii) μg perchlorate excreted /day = above #'s * creatinine excretion/d (1.08 g/d) (Tellez, 2005; Knuppel, 1979)
Antofagasta: Min: 3.1; 10th%: 9.3; 25th%: 14; Median: 24.5; 75th%:46.7; 90th%: 64; Max: 81
Chanaral: : Min: 13; 10th%: 18.4; 25th%: 29.2; **Median: 40**; 75th%: 68; 90th%: 167; Max: 227
Taltal: Min: 21.6; 10th%: 48.6; 25th%: 75.6; **Median: 129.6**; 75th%:205; 90th%: 319; Max: 427

Assume μg excreted/day = μg intake/day

Estimate of relationship between μg/L human milk to μg ingested/day is thus:
Chanaral: 18.3 μg/L / 40 μg/d = **0.458 (units of d/L)**
Taltal: 95.6 μg/L / 129.6 μg/d = **0.737 (d/L)**

b) Lactating mother water ingestion rate (ml/d): mean = 1189 ml/d, SD=699; 50th percentile = 1063; **90th% 2191**; 95th% = 2424 (from CSEFH, USEPA, 2000, Table 4-13)

c) Dietary perchlorate ingestion rate per day from food and other baseline sources in US (Atlanta data – Valentin-Blasini, et al., 2005)
μg perchlorate excreted/g creatinine:
Atlanta: Min: 2.5.; 10th%: 3.1; 25th%: 4.8; **Median: 7.8**; 75th%:10.0; 90th%: 16.2; Max: 20
μg perchlorate excreted /day = above #'s * creatinine excretion/d (1.08 g/d) (Tellez, 2005; Knuppel, 1979)
Atlanta: Min: 2.7; 10th%: 3.35; 25th%: 5.2; **Median: 8.4**; 75th%:10.8; 90th%: 15; Max: 21.6

d) Infant human milk consumption rate at 2 wks of age: **634 ml/d**, SD = 149.5; range = 416-922. (CSEFH, 2000; page2-4)

e) Infant body wt at 2 weeks age (kg): avged across sex:
5th% = 2.76; 25th%= 3.34; **Median = 3.69**; 75th%=4.07; 95th%=4.57

Exposure and Risk Calculations:
Nursing infant exposure dose = (0.458 or 0.737 d/L) *[(24.5 μg/L * 2.191 L/d) + 8.4 μg/d] * (0.634 L human milk/d) / 3.69 kg body wt) = **4.9 – 7.9 μg/kg/d**

RfD = 0.7 μg/kg/d

Nursing infant Hazard Index = 4.9 or 7.9 / 0.7 = 7 to 11

Note: Hazard Index is influenced by the way in which the milk to perchlorate intake ratio was calculated. The cited literature reports the mean human milk concentrations and the median urinary perchlorate; it will take a full distributional analysis to calculate the mean urinary perchlorate; this will enable the construction of a mean milk to mean intake ratio. This ratio may be slightly lower than the mean milk to median intake ratio presented above. Therefore, we round our estimate of nursing infant hazard index downward to **5 to 10 fold** pending further analysis.

3) Perchlorate Toxicokinetics in the Neonate

Perchlorate is cleared primarily via the urine with protein binding tending to retain perchlorate in serum and retard its excretion (Clewell, et al., 2003). Human infants have immature renal function and less urinary clearance of many water soluble chemicals (Morselli, 1989; Kearns and Reed, 1989, Ginsberg, et al., 2002), suggesting that slow clearance is another infant susceptibility factor to perchlorate. Rat toxicokinetic data show that in spite of higher dose rate from nursing, pups had lower perchlorate serum concentration than adult rats (Clewell et al., 2003; NAS, 2005, Appendix E). These data are of questionable relevance to human infants given the variety of cross-species differences in the ontogeny of toxicokinetic systems (Ginsberg, et al., 2004). Other factors also affect the utility of neonatal rat data from this study (Clewell, et al., 2003): a) rat dams drink 80% of the daily output of pup urine which inflates the adult dose and serum level of perchlorate relative to the neonate; b) lactating dams and pups were dosed with radioactive iodide which may affect perchlorate toxicokinetics, especially with regards to competition for serum binding sites in the neonate which has limited binding capacity. These factors discourage the use of nursing rat pup data (Clewell, et al., 2003) to describe the toxicokinetics of perchlorate in human infants.

Mr. GRUMBLES. That was another aspect to it, ma'am.

Senator BOXER. Excuse me. I am speaking. Excuse me.

You know why I get so angry with you? It is not a personal anger. It is because you say things that are not backed up by the facts. You say as you get additional information you are going to get tougher. You have that information from your own panel. They told you what you were doing was dangerous. And now you are sitting here under, I would agree, hostile questioning from me and saying, oh yes, Madam Senator, we are going to take another look at it. I just don't buy it.

Mr. GRUMBLES. I think to be fair, you ought to allow me the chance to say——

Senator BOXER. Well, let me finish. I am giving you a chance.

Mr. GRUMBLES [continuing].—that the reason, one of the areas of concern they had, and it is not just with EPA, but it was with the National Academy of Sciences, was the focus on what is the most sensitive sub-population. That wasn't the preliminary remediation goal discussion. It was focused on the reference dose and how the agency got to its DWEL, the drinking water equivalency level.

So there has been a very robust debate, Madam Chair, as to what is the most sensitive sub-population. I think part of the concern that the Children's Health Advisory group had was that we ended up adopting the perspective of the National Academy of Sciences and indeed, the fetus of a pregnant woman.

The other issue I was trying to get at and explain on adaptive management, Madam Chair, was that the preliminary remediation goal when it was set, it was also based on an assumption of the data that we had. They made the assumption that 100 percent of the contamination source would be coming from water, and we are in the agency discussing it. Well, we know that food is another significant source. So that is what I meant by the need to embrace adaptive management.

Senator BOXER. Well, I am going to turn to Senator Barrasso, but I am going to read you some more of this letter.

Mr. GRUMBLES. OK.

Senator BOXER. Because the things that you say just don't comport with the facts. Your own Children's Health Advisory Committee, made up of scientists, told you, told Stephen Johnson, told the world in this letter, that the standard you had set for the clean-up was not good enough. I said, I read before, it is not protective of children's health. And you tell me adaptive management—let's see, what does that mean? You set a standard in a low way and you get caught at it, and you get called before a Senate Committee that you might have to adapt and go back?

I am sorry. I find it cynical. Let me read the rest of this. The Children's Health Advisory Panel finds it disturbing that this change in the PRG was made without dissemination of a decision support document or any opportunity for public input. We recommend that OSWER lower the PRG, taking into account infant exposure and susceptibility. They are very concerned, and this letter states it.

You don't have to wait for anything else. These are the people that you are supposed to rely on. Supposed to rely on. So I can only say to you——

Mr. GRUMBLES. Can I say one more important——

Senator BOXER. Let me finish, please, and yes, then you can respond.

I can only say to you that your explanation here today doesn't make any sense. Oh, you have to wait for science, when your own scientists who care about children have already told you. And you have admitted you may not even set a standard for perchlorate, and you don't think that having the ordering, if you will, requiring water systems to test for perchlorate really is a good idea.

So everything I add up says to me danger, flashing red light for the public. Again, EPA, the shadow of its former self, celebrating our great drinking water, and in the back rooms here derailing what your own scientists want to do to protect kids. It is very disturbing.

Yes, sir?

Mr. GRUMBLES. Thank you. I just simply wanted to say that the relationship we have with the Children's Health Advisory Board is an important one. I said it is a distinct possibility, Madam Chair, that we might determine not to regulate perchlorate. It is also—and this is important—it is also a distinct possibility that we may issue a health advisory. And part of the dynamics that are involved in that is over the last couple of years we have gotten a lot more information, supplementing the National Academy of Sciences, about potential risks to children or infants. So that is important to us.

We also have made clear from the beginning, Madam Chair, that our goal was to make a final determination by this year, and that we had enough occurrence data. We also realize we may need to revise that approach in terms of monitoring in the future, just like with any emerging contaminant.

Senator BOXER. OK.

Mr. GRUMBLES. Thank you.

Senator BOXER. Well, I would like you to know that my State has enough information, and they do have a perchlorate standard.

Senator.

Senator BARRASSO. Thank you very much, Madam Chairman.

Thank you, Mr. Grumbles.

I think you started your testimony before you got to your written remarks, talking about that it doesn't take an act of Congress to, and then you went through a number of things, lead and copper, airline drinking water. Is that your concern with a bill like this, that we don't really need an act of Congress on this? I am kind of getting that as a sense of what you are saying here today.

Mr. GRUMBLES. We think congressional oversight of the agency as it moves through this regulatory process is critically important, but when it comes to legislating a specific decision on whether or not to regulate and to set a very aggressive timeframe schedule, we have serious concerns about that. So Senator, that is the point, is that we have concerns about a legislative directive that overrides the current regulatory framework for decision making.

Senator BARRASSO. I wanted to get back to the issue I was talking about earlier with Cheyenne, Wyoming. As the support regulatory agency, I would ask that you please look into this matter and help clear up the bureaucratic red tape so that the Wyoming

Department of Environmental Quality can get the assistance that they are requesting to help with the issues that I have addressed.

Mr. GRUMBLES. Senator, most certainly we will look into that.

Senator BARRASSO. And then with my remaining time, as you have been collecting your thoughts, is there anything else you would like to add that you haven't had a chance to say here in some of the dialog?

Mr. GRUMBLES. Well, we feel that it is important to take both perchlorate and TCE very seriously. On perchlorate, the scientific issues that surround the health effects and also if there is a meaningful opportunity to reduce risk to human health as required under the Safe Drinking Water Act, that is where we have been spending our time over the last several years because we recognize it is widespread. It does have risks to health, as the National Academy of Sciences and others have confirmed.

So we are committed to going through the process, to working with Congress, and making sure that a science-based decision is made.

On TCE, we have been regulating it for some time. We are aggressively pursuing additional guidance on vapor intrusion and the reevaluation of the risks, given the scientific issues evolving over the degree to which cancer is caused by TCE. It is a priority issue as well for us. In the Drinking Water Office, Senator, we are committed to reviewing it and other contaminants for potential further regulation under our process of the Safe Drinking Water Act.

Senator BARRASSO. So it is your concern, then, that with the current Safe Drinking Water Act and how to regulate water contaminants, that this bill may override that Safe Drinking Water Act in terms of the listing process and others?

Mr. GRUMBLES. Well, it would. It would. And we understand, and Congress has used its prerogative to direct the agency to regulate specific named contaminants in the past. We see the value, and I think many others see the value, in the 1996 framework, the 1996 Safe Drinking Water Act Amendments that said rather than identifying specific ones or having to regulate an X number by X years, you go through a systematic process.

The downside, Senator, is that systematic process can take some time because we have three statutory criteria that we need to go through. And we need to make sure pursuant to the statute that it is the best available peer-reviewed science. So it takes some time, but we think that overall it is an excellent framework and we would just urge caution to members in legislative directives that picks which of the 60 or 50 contaminants to regulate, and sets a timeframe that may be so ambitious that may not result in a legally sustainable final product.

Senator BARRASSO. So you are working with groups like the Food and Drug Administration and the Center for Disease Control, in determining what is best for our children and ways to protect them?

Mr. GRUMBLES. We have been working with them and other agencies and scientific organizations. We are spending a lot of time lately with the Food and Drug Administration and the bio-monitoring study that CDC did was an important one.

Senator BARRASSO. Madam Chair, I have no further questions.

Senator BOXER. I am going to put the rest of my questions in writing to you.

I am going to just close with this. Senator Barrasso, thank you very much for showing us the TCE problem in your State. I am going to ask unanimous consent to place into the record a list of the contaminated sites throughout this Country. There are 45 States that have a problem with TCE. We need a more protective standard there.

There are also 11 Superfund sites contaminated with TCE, where human exposure is not under control. The source of this is the EPA. So you have a situation here where you have sites where human exposure is not under control and we have TCE in 45 States, 321 Superfund sites in 45 States and territories contaminated with TCE. You can't drag your feet anymore.

I would say for perchlorate, you have 35 States that have perchlorate in the water at serious levels. You already have your Children's Health Protection Advisory Committee saying you are not doing enough. You have American Water Works Association, Association of Metropolitan Water Agencies—and this gets to Senator Barrasso's point—they have urged EPA to set a perchlorate standard for drinking water. These are not environmental organizations. The American Water Works Association, the Association of Metropolitan Water Agencies, they want a standard.

I think it gets to Senator Barrasso's very important point. Is it better for EPA to act or is it better for Congress to act? Well, let me answer that question. EPA should act, if it was the Environmental Protection Agency, but they are not doing it. That is the problem. I mean, go and tell Senator Feinstein to wait until you deal with phthalates. Go and tell Senator Schumer to deal with other chemicals. People are just not going to listen, and people like Senator Barrasso, who is a very patient man, I think he wants action here in terms of clean-up for his State.

The point is, your answers—and I am speaking only for myself—are just very light. They don't give me any comfort at all. As a matter of fact, they even make me more concerned, hearing that we may not have a standard. The fact of the matter is, there are sites that are out of control here. Your own scientists have told you to act. Now, we know a couple of States have acted on perchlorate.

That is the other thing that is going to happen, Senator. The States are going to start setting standards. Right now, I know California has six, Massachusetts has two, and many other States are waiting. So we are going to have a patchwork quilt.

In the meantime, consumers of water don't know how much perchlorate is in their water because the EPA decided it wasn't necessary. So if they go down the path where they are not going to set a standard at the end of the day, which is a quote, "distinct possibility," and plus they are not requiring testing, our people are in the dark without any help, and we are talking about very dangerous chemicals here.

So thank you for coming. We will give you a bunch more questions in writing, and we call up the next panel. Thank you, sir.

Mr. GRUMBLES. Thank you.

Senator BOXER. I want to welcome panel two.

George Alexeeff is Deputy Director for Science Affairs, Office of Environmental Health Hazard Assessment from my great State of California. We welcome you.

Mike Baker is Chief, Division of Drinking and Groundwater, Ohio EPA, on behalf of the Association of State Drinking Water Administrators.

Carol Rowan West is Director, Office of Research and Standards, Massachusetts Department of Environmental Protection.

So we are going to ask you to keep your opening statements to 5 minutes, and we will begin with you, Dr. Alexeeff.

STATEMENT OF GEORGE V. ALEXEEFF, DEPUTY DIRECTOR FOR SCIENTIFIC AFFAIRS, OFFICE OF ENVIRONMENTAL HEALTH HAZARD ASSESSMENT, CALIFORNIA ENVIRONMENTAL PROTECTION AGENCY

Dr. ALEXEEFF. Thank you, Madam Chair and members of the Committee for the opportunity to testify on perchlorate and TCE in water. I am George Alexeeff, Deputy Director for Scientific Affairs for the Office of Environmental Health Hazard Assessment, which we refer to as OEHHA, in the Environmental Protection Agency of California.

As part of our duties under the California Safe Drinking Water Act, OEHHA develops public health goals, or PHGs, for drinking water. Perchlorate has been detected in hundreds of drinking water sources in California. Perchlorate inhibits the uptake of iodide, an essential nutrient, by the thyroid gland. Inadequate iodide uptake disrupts proper thyroid function. Thyroid hormones such as T4 and T3 help regulate growth and maturation of tissues, particularly the brain.

Disruption of these hormones can lead to impaired development in fetuses. Several epidemiologic studies indicate that iodide deficiency during pregnancy may affect brain development and may cause intellectual deficits in children.

Our review of the scientific literature found that the fetuses of pregnant women are the most sensitive population to perchlorate's health effects. Impairment of thyroid function in expectant mothers may affect the brain of the fetus, resulting in delayed development and decreased learning capacity.

In 2004, OEHHA published a public health goal for perchlorate in drinking water of six parts per billion. The level was adopted as the State's drinking water standard. OEHHA's draft perchlorate assessment underwent two rounds of independent peer review by the University of California scientists, as well as several public comment periods. We based our PHG on a controlled human study referred to as the Greer study, which contained the best data for assessing perchlorate's health effects. However, this study was limited because there were only 37 subjects. To ensure we did not underestimate the chemical's effects on pregnant women and fetuses, we added a tenfold margin of safety. Our PHG also took into account the higher water consumption rate of pregnant women and the potential for perchlorate exposure from food.

In 2005, the National Academy of Sciences recommended a similar approach. In 2006, the CDC released a major national study which supports the concerns that we identified. The CDC study

found that in women, perchlorate exposure was associated with changes in thyroid hormone levels. The thyroid hormone level changes were consistent with the expected effects of perchlorate. OEHHA evaluated this data and published a confirmatory article.

I will now turn to TCE. Over 350 drinking water sources in California have reportable levels of TCE contamination. Cancer is the primary health effect of concern from TCE exposure. Animal studies indicate that TCE induced liver and lung carcinomas in mice. Kidney tumors were reported in male rats. The National Toxicology Program has concluded that TCE is reasonably anticipated to be a human carcinogen.

Over the past 20 years, California has treated TCE as a carcinogen. In 1988, California listed TCE as a chemical known to the State to cause cancer. In 1990, TCE was listed as a toxic air contaminant based on carcinogenic effects. In 1999, OEHHA published a public health goal of 0.8 parts per billion of trichloroethylene in drinking water.

In developing this PHG, we reviewed the animal studies and the limited human studies. Our risk assessment confirmed that this chemical is a potential human carcinogen. We have followed the U.S. EPA cancer review process with great interest and awaited the publication of the National Academy of Sciences' report released in 2006. We note that the NAS concluded that the evidence on carcinogenic risk and other health hazards from exposure to trichloroethylene has strengthened since 2001.

I hope this summary gives you a better idea of why California has concerns about perchlorate and TCE in water, and how we have identified the level of risk to public health.

Thank you for giving me this opportunity to testify before you today.

[The prepared statement of Dr. Alexeeff follows:]

Statement of George V. Alexeeff, Ph.D., D.A.B.T.
Deputy Director for Scientific Affairs
Office of Environmental Health Hazard Assessment
California Environmental Protection Agency

Before the U.S. Senate Committee on Environment and Public Works
May 6, 2008

Thank you, Madam Chairperson and members of this Committee, for the opportunity to testify on perchlorate and trichloroethylene in water.

I am George Alexeeff, Deputy Director for Scientific Affairs of the Office of Environmental Health Hazard Assessment (OEHHA) of the California Environmental Protection Agency. I am a toxicologist by training. For over 20 years, I have worked in the field of risk assessment, evaluating the risks that chemicals in the environment pose to the public's health. I oversee a staff of scientists who evaluate the health impacts of pollutants and toxicants in the air, water and soil. As part of our duties under the California Safe Drinking Water Act of 1996, OEHHA develops public health goals (PHGs) for drinking water. Public health goals are California's equivalent to the federal MCLGs – they identify a level of a contaminant in drinking water that does not pose a health risk, and they are used by our sister agency, the California Department of Public Health, to develop California's regulatory drinking water standards.

My testimony today focuses on the public health goals we have developed to address contamination of drinking water with the chemicals perchlorate and trichloroethylene, or TCE.

Perchlorate has been detected in hundreds of drinking water sources in California, including water sources in heavily populated areas such as Riverside, San Bernardino, Los Angeles, Santa Clara and Sacramento counties. It has also been detected in the Colorado River, a major drinking source for Southern California. Our health concern is this: Perchlorate inhibits the uptake of iodide, an essential nutrient, by the thyroid gland. Inadequate iodide uptake disrupts proper thyroid function. Thyroid hormones, such thyroxine (T4) and triiodothoronine (T3), help regulate the growth and maturation of tissues, particularly the brain. Disruption of these hormones due to iodine deficiency can lead to impaired growth and development in fetuses. Several epidemiological studies indicate that iodine deficiency during pregnancy may affect brain development and may cause intellectual deficits in children. One study found that, even when the mother's iodine deficiency was borderline and the children appeared to be normal, their school achievement was impaired (Glinoer, 2001).

In our review of the scientific literature, we found that four populations are particularly susceptible to the adverse health effects of perchlorate. First, the fetuses of pregnant women are the most sensitive to perchlorate's health effects. Impairment of thyroid function in expectant mothers may affect the brain of the fetus, resulting in delayed development and decreased learning capability. The second sensitive population includes newborns and infants. They require iodide for proper brain development. The newborn may receive an inadequate amount of iodide when breast-feeding if the mother is exposed to perchlorate. In addition, the newborn may receive perchlorate in the breast milk. The perchlorate can further reduce the newborn's ability to produce the thyroid hormones needed for proper brain development. The third group includes the pregnant and lactating women themselves. These women require higher levels of iodide since they have to maintain adequate levels for themselves and their offspring. The last sensitive group includes individuals with preexisting thyroid problems.

In 2004, OEHHA published a public health goal for perchlorate in drinking water of 6 parts per billion. This level was adopted in 2007 by the California Department of Public Health as the state's drinking water standard for perchlorate.

Before publishing the final PHG, OEHHA's draft perchlorate assessment underwent two rounds of independent peer review by University of California scientists, as well as several public comment periods. We based our PHG on a controlled human study where the subjects drank specific amounts of perchlorate in their water and the effects on iodide uptake were measured (Greer et al. 2002). This study, referred to as the "Greer study," is well-regarded and contained the best data for assessing perchlorate's health effects. However, this study was limited because there were only 37 subjects. To ensure that a perchlorate assessment does not underestimate the chemical's effects on pregnant women and fetuses, we added a 10-fold margin of safety. Our PHG also took into account the higher water consumption rate of pregnant women and the potential for perchlorate exposure from food.

In 2005, the National Academy of Sciences (NAS) recommended a toxicity evaluation approach very similar to the one OEHHA used (National Research Council, 2005). They reported that the reduction of iodide uptake "is the key event that precedes all thyroid-mediated effects of perchlorate

exposure," and that focusing on the reduction of iodide uptake "is the most health protective and scientifically valid approach."

Since the publication of our PHG, the U.S. Centers for Disease Control released a major national study of over 2000 men and women which supports the concerns that we identified in our assessment of perchlorate (Blount et al. 2006). The CDC study found that in women perchlorate exposure was associated with changes in thyroid hormone levels. The thyroid hormone level changes were consistent with the expected effects of perchlorate, that is, women with higher perchlorate levels also had greater thyroid disruption. OEHHA evaluated this data and published a confirmatory article exploring further relationships between perchlorate, iodine, thyroid hormone, and other environmental chemicals (Steinmaus et al, 2007). OEHHA will consider the new data as part of our five year re-review process for PHGs.

I will turn now to trichloroethylene or TCE. Over 350 drinking water sources in California have reportable levels of TCE contamination (i.e., greater than 0.5 ppb). Cancer is the primary health concern from TCE exposure. Animal studies indicate that inhaling TCE induced liver

carcinomas in male mice and lung carcinomas in female mice. Oral exposure to TCE induced liver carcinomas in both male and female mice. Kidney tumors were reported in male rats after inhalation and after oral exposure to TCE. The National Toxicology Program has concluded that TCE is *reasonably anticipated to be a human carcinogen.*

Over the past 20 years, California has consistently treated TCE as a carcinogen in our air, water, and other programs. In April 1988, California listed trichloroethylene as a "chemical known to the state to cause cancer" (under the California Safe Drinking Water and Toxic Enforcement Act of 1986, also known as Proposition 65). In 1990, we developed a "no significant risk" level to help businesses determine when Californians must receive Proposition 65 warnings concerning exposure to TCE. Also that year, we reviewed trichloroethylene for our air toxics program and again concluded that it should be considered a carcinogen for purposes of public health protection. TCE was listed as a toxic air contaminant based on the carcinogenic effects.

In 1999, OEHHA published a public health goal (under the California Safe Drinking Water Act of 1996) of 0.8 parts per billion trichloroethylene in

drinking water. In developing this PHG, we reviewed the animal studies and the limited data from human studies. We found that the limited human data supported conclusions regarding cancer in animals, that is, the estimate based on animal data was similar to the one we obtained using data on kidney cancer from a human occupational study. Our risk assessment confirmed that this chemical is a potential human carcinogen. Our PHG of 0.8 ppb represents a one in one million risk of developing cancer after a lifetime of exposure to TCE at this level.

TCE is currently under re-review in the OEHHA drinking water program. We have followed the USEPA cancer review process with great interest, and awaited the publication of the National Academy of Sciences report, released in 2006. We note that the NAS concluded that the evidence on carcinogenic risk and other health hazards from exposure to trichloroethylene has strengthened since 2001. We expect to release our revised risk assessment document for public comment later this year.

I hope this summary gives you a better idea of why California has concerns about perchlorate and trichloroethylene in water and how we have identified

their level of risk to public health. Thank you for giving me the opportunity to testify before you today.

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Responses by George V. Alexeef to Additional Questions
From Senator Boxer

Question #1: EPA Perchlorate Level and Children. EPA has said that its preliminary remediation goal is based on a 70 kilogram, or 154 pound, adult, who is only exposed to perchlorate from drinking water. Is this scientifically sound, or should EPA base its protections on children and consider exposure from food and other sources?

For regulation of perchlorate in drinking water, pregnant women, their fetuses, and infants are the most susceptible populations, and must be adequately protected in any final rule. OEHHA uses water consumption values to ensure adequate protection of these susceptible populations, especially since women drink more water during pregnancy and children drink more water based on their body weight. OEHHA also incorporates other exposure sources in risk assessments of noncarcinogens in drinking water. This is important for noncarcinogens since toxicity is based on whether total chemical exposure, from all sources, exceeds the toxicity threshold. OEHHA usually bases a public health goal on estimated consumption from all likely sources rather than the standard assumptions for an adult male as described in the question.

Question #2: Recent Scientific Data on Perchlorate. Please describe the significance of the Food and Drug Administration and Centers for Disease Control and Prevention's latest data and studies on perchlorate.

The recent Food and Drug Administration (FDA) results on dietary exposures to perchlorate provide important supplementary data for total perchlorate exposure assessments. One of the uncertainties in assessing the drinking water risks of perchlorate has been the exposure from non-drinking water sources. Since perchlorate toxicity depends on total perchlorate exposure, drinking water and non-drinking water sources should both be considered when estimating the risk of perchlorate from any source. The identified food sources of perchlorate are consistent with the average values found in urine in the Centers for Disease Control and Prevention's (CDC's) NHANES results. However, the source of the high levels of perchlorate found in some individuals (in human breast samples as well as urine) has not yet been identified. Presumably this perchlorate is derived from minor foods not sampled in the FDA market basket survey. A detailed review of available perchlorate exposure data is being undertaken at OEHHA. The results of the review will be used in our public health goal for perchlorate as part of our drinking water assessment.

The CDC data provide an indication of a potential effect of perchlorate on thyroid hormone levels. We feel this study is extremely significant in terms of perspective on how the thyroid hormones are regulated in the body, and how the thyroid hormones are potentially affected by chemicals from the diet, drinking water, and smoking that reduce the ability of the body to utilize iodine. The study confirms previous concerns for perchlorate exposure to women with low iodine levels. The study also indicates that there is a sizable population of women with low iodine levels. Thus, perchlorate exposure must be considered in the context of susceptible populations, including women and infants who consume low amounts of dietary iodine. These

factors will be considered in our risk assessment for perchlorate in drinking water. We look forward to further discussions of these important issues with our FDA and CDC colleagues.

Question #3: Seriousness of TCE Exposure. Please describe the potential health effects from exposure to TCE vapors that can build up in indoor air from groundwater and soil that is contaminated with this chemical?

OEHHA listed TCE as a carcinogen in April 1988, under the California Safe Drinking Water and Toxic Enforcement Act of 1986, also known as Proposition 65. Trichloroethylene is classified as a probable human carcinogen, based on limited evidence in humans and sufficient evidence in animals. In the human studies there was an elevated risk for cancer of the liver and biliary tract and the modestly elevated risk for non-Hodgkin's lymphoma. In the animal studies cancer was produced when they were exposed orally or by inhalation. Of the studies finding an increase in cancer, there was an increased incidence of uncommonly occurring renal-cell tumors, an increased incidence of interstitial-cell testicular tumors, an increased incidence of lymphomas, an increased incidence of liver tumors, or increased incidence of lung tumors. While TCE vapors that build up indoors are unlikely to reach levels that could produce noncancer health effects, we estimate that they pose a cancer risk. We calculate the risk by extrapolating from the experimental animal studies (conducted at high exposure with few animals) to the much lower indoor air exposures such as might occur from vapor infiltration into a house from contaminated groundwater. Therefore the primary concern for TCE is based on the projected increased cancer risk following exposure.

OEHHA has no site-specific data to address concentrations of TCE in household air resulting from contaminated groundwater and soil, so we cannot intelligibly discuss the risk or likelihood of cancer resulting from this contamination source.

Responses by George V. Alexeef to Additional Questions
From Senator Cardin

1) The Contaminant Candidate List is growing as we are better able to detect new chemicals in our drinking water and as these new chemicals enter our environment. Based upon your work in your respective states, what is the best approach for prioritizing which emerging contaminants should be regulated?

In California, one of the first concerns regarding emerging contaminants is based on detection in ground or surface drinking water sources. Once detected, an assessment of toxicity and chemical properties, such as persistence, is helpful to place the presence of the chemical in perspective. Toxicity and properties of the chemicals, frequency of detection, concentrations, and potential impacted populations are major considerations in selection of chemicals for risk assessment. One consideration which may have been underappreciated so far is the potential for aggregate or cumulative effects. That is, if a number of chemicals appear to have similar effects, even if they are chemically dissimilar, should the potential additive or synergistic effects of the entire set of chemicals be estimated for choosing chemicals of potential regulatory interest. In California, the general approach is to evaluate the health and environmental impact of a chemical, separately from other regulatory issues. In the drinking water program, health effects are considered with other factors in setting the actual standard.

2) Should the cost of reducing the contaminant concentration factor into decisions of what is a safe level for final regulatory determination purposes?

It is important that our understanding of the health and environmental effects of a contaminant not be hampered by considerations of cost or feasibility of control. The National Academy of Sciences has spoken to this issue and indicated the importance of risk assessment without the undue influence of regulatory decisions. Thus, the ranking of chemical hazards, based on full information on the hazards associated with a given level of each chemical are necessary to provide the information needed to most efficiently manage the population risks and allocation of resources. When an actual drinking water standard is being set, cost and feasibility should be considered along with health information. In California, OEHHA develops public health goals for chemicals in drinking water, which are utilized by our Department of Public Health, along with cost and feasibility, in setting the regulatory limits for chemicals, which are known as Maximum Contaminant Levels (MCLs).

Responses by George V. Alexeef to Additional Questions
From Senator Inhofe

1. Do you think the Safe Drinking Water Act is effective? If not, how could we improve it? If so, how can you support legislation that requires EPA to establish regulation regardless if it is warranted under the Safe Drinking Water Act? For instance, if a chemical doesn't occur with a frequency and at levels of public health concern or doesn't present a meaningful opportunity for health risk reduction should it still be regulated?

In our opinion, the federal Safe Drinking Water Act is an excellent law with clear legislative intent that allows the U.S. EPA to set national health-based standards for drinking water to protect against both naturally-occurring and man-made contaminants. U.S. EPA sets scientifically-based national standards for drinking water to protect against health risks, while taking into consideration available technology and costs. California has enacted complementary legislation. It is important that our understanding of the health effects of a contaminant, and the ranking of chemical hazards, not be hampered by considerations of cost or feasibility of control. Such health information can be useful for specific contamination issues even if widespread concern for the chemical is not present. However, once the health basis is established, cost and feasibility are important factors for setting the standard. Thus, full information on the hazards associated with a given level of each chemical is necessary to provide the information needed to most efficiently manage the population risks and allocation of resources. Once standards are set they serve as important benchmarks as to whether contamination is currently present or not.

2. Since California has established an MCL for perchlorate, can you tell the committee what it costs for a municipality to become compliant? Please include average cost per well for California, including installation, changes to current infrastructure, cost of the treatment, maintenance, and cost to safely remove and dispose of any byproducts from treatment.

The MCL is established by the California Department of Public Health, while OEHHA provides the public health goal. However, in establishing the MCL, state law (H&S Code Section 116365) requires consideration of cost and feasibility regarding: the availability and

costs of analytical methods for determining the presence of perchlorate, the availability and costs of appropriate technologies for mitigating its presence, the estimated costs to the regulated water systems for contaminant monitoring and, the estimated costs for treatment to systems with sources that violate the MCL and must be treated to come into compliance. As indicated in the final statement of reasons for the California perchlorate MCL (http://www.cdph.ca.gov/services/DPOPP/regs/Documents/R-16-04 ISOR.doc): "Since the PHG of 0.006 mg/L establishes the level of no significant health risk and an MCL at this level would eliminate the potential for adverse health effects for more than half a million people at an average annual cost of only $18 per customer for affected large water systems, the Department believes that it has no alternative but to propose the MCL at this level."

3. Since treatment costs can be substantial, especially for small rural communities, shouldn't EPA's science demonstrate the importance of treatment before they require expensive treatment?

As indicated above, we find that a sound strategy to address drinking water contamination is to first establish the health basis of a potential standard and then to consider it along with cost and feasibility in setting the standard. Establishing the health basis of a potential standard would serve to demonstrate the importance of treatment. In establishing the standard, cost of treatment equipment would be considered. In some cases where the cost is prohibitive a variance can be issued. As indicated in the final statement of reasons prepared by the Department of Public Health for the California perchlorate MCL (http://www.cdph.ca.gov/services/DPOPP/regs/Documents/R-16-04 ISOR.doc): "However, the cost per service connection for small water systems at that level ranges from $300 to $1,580 per service connection per year, with an average of $540, while the total estimated population that would avoid exposure is only about 1700. The median household incomes in the areas served by these water systems range from ~$16,300 to ~$49,300. This cost versus benefit for these small systems is considerably less favorable than that for larger systems, given the small number of persons both potentially affected by exposure and having to bear the treatment costs. To address this difference, the Department is proposing to provide for variances for small water systems based on affordability criteria."

Senator BOXER. Thank you very much.
Mr. Baker, welcome.

STATEMENT OF MIKE BAKER, CHIEF, DIVISION OF DRINKING AND GROUND WATERS, OHIO ENVIRONMENTAL PROTECTION AGENCY, ON BEHALF OF THE ASSOCIATION OF STATE DRINKING WATER ADMINISTRATORS

Mr. BAKER. Thank you and good morning, Madam Chairman and Committee members. I am Mike Baker. I am Chief of the Division of Drinking and Groundwaters at the Ohio Environmental Protection Agency. I am also the President-elect of the Association of State Drinking Water Administrators, also known as ASDWA. ASDWA supports and represents the collective interests of States, territories and the Navajo Nation in our administration of national drinking water requirements. I am pleased to be here today to offer testimony on ASDWA's behalf.

Overall, ASDWA supports the fundamental construct of the Safe Drinking Water Act as it relates to determining which contaminants are likely to occur in drinking water and whose regulation would provide a meaningful opportunity for health risk reduction.

An underlying tenet of the act is that standard-setting should be driven by sound science. That includes robust data on the occurrence of contaminants, information about the abilities of these contaminants to cause health effects, information about technologies and costs to remove or reduce these contaminants, and the expected benefits of doing so.

We do appreciate this Committee's concerns about perchlorate and TCE. We are, however, concerned about the precedent of using legislative action that supersedes the provisions of the statute for a particular contaminant. Recent media stories about pharmaceuticals in personal health care products in our sources of drinking water are one example highlighting the need for a rational scientific-based approach to determining which contaminants should be regulated and at what levels.

In my own State of Ohio and a few other States, we are grappling with another type of emerging contaminants, PFOA, one of several flouropolymers used for decades by a variety of manufacturing processes. This particular compound is being detected in the environment, animals, and people around the world. Customers of an Ohio public water system contaminated by PFOA have the highest level of this chemical ever detected in humans. Clearly, we are very concerned about any of these compounds being in our drinking water at unsafe levels.

We expect to see more and more emerging contaminants. We live in a society that uses a myriad of chemicals. That fact, coupled with our increasing ability to detect contaminants at low levels, will undoubtedly raise additional concerns about the safety of our drinking water. Therefore, unless a transparent scientific approach is used, we are concerned EPA will jump from one contaminant to another based on media and political attention, rather than on meaningful public health gains.

States do agree that EPA needs to make timely decisions on contaminants of concern. Public health protection depends on sound and timely decisions. As my colleagues on this panel have and will

describe, in the absence of timely decisions by EPA, a few States can and do establish their own standards. Most States, however, simply do not have the necessary resources, nor the expertise, and we depend on EPA for timely decisions.

In the case of perchlorate and TCE, EPA should be held accountable for describing what data and information, if any, is lacking to support a regulatory decision and make decisions about whether or not to further regulate as rapidly as possible.

All of us at the Federal, State and local levels, have important roles to play to ensure people have access to safe and affordable drinking water. This includes preventing contaminants from reaching the source of our drinking water in the first place. For Congress, an important role is to ensure adequate funding to support research so that information about contaminants is available when it is needed.

We must also keep in mind regulations come with a cost burden to State drinking water programs, public water systems, and their customers. Many States and water utilities are already struggling to meet the demands of current regulations. We appreciate your support for the Drinking Water State Revolving Loan Fund and respectfully recommend more funds be appropriated to support a growing infrastructure need.

Additional Federal dollars are also needed for State drinking water programs to carry out Federal regulatory requirements. Current funding levels, which have remained at roughly the same levels for over a decade, during the same time States have had to adopt over 15 Federal regulatory requirements, is simply inadequate and needs to be increased. States and public water supplies need your support.

I thank you for the opportunity to offer testimony and would be pleased to answer any questions.

[The prepared statement of Mr. Baker follows:]

Testimony of Michael G. Baker before the
Senate Environment and Public Works Committee
May 6, 2008

Background

Good morning Madam Chairman and Committee Members. I am Michael Baker, Chief of the Division of Drinking and Ground Waters within the Ohio Environmental Protection Agency. I am also President-Elect of the Association of State Drinking Water Administrators (ASDWA). ASDWA supports and represents the collective interests of the states, territories, and the Navajo Nation in their administration of national drinking water program requirements within their states or territories. We applaud the Committee for taking up these important issues related to providing safe drinking water and are pleased to be here today to offer testimony.

States and territories are responsible for carrying out the Safe Drinking Water Act and the subsequent regulations and programs enacted to help safeguard the quality of America's drinking water. States and territories work with a number of partners to protect drinking water quality from source to tap at over 160,000 public water systems throughout the country. Our approach includes preventing pollution of sources of drinking water; administering over 90 federal contaminant regulations; and providing training, technical assistance and funding to owners and operators of public water systems. States also often implement additional state requirements, beyond the Federal minimums. The first and overarching priority of state or territorial drinking water programs is the protection of the public health of their citizens.

Support for Construct of Safe Drinking Water Act

With that brief background about who we are, what we do, and why we do it, please allow me to turn to the subject of this morning's hearing. Overall, we support the fundamental construct of the Safe Drinking Water Act as it relates to determining which contaminants are to be regulated, how those regulations will be developed, and how existing regulations are to be reviewed and periodically revised. An underlying tenant of the Act, we believe, is that environmental and public health standard-setting and review should be driven by sound science. By "sound science", we mean robust data on the occurrence of contaminants of concern in sources of drinking water; information about the ability of these contaminants to cause adverse human health effects; information about technologies and costs to remove or reduce these contaminants, and the expected benefits of doing so.

We specifically support provisions of the Act that require EPA to develop a Contaminant Candidate List and determine which contaminants on the list, if regulated, would constitute a "meaningful opportunity for health risk reduction." We also believe that, as knowledge and information change over time, existing drinking water rules should be revised, as appropriate, in order take such new information into account.

Concerns about Alternative Approaches to the SDWA

We appreciate the Committee's concerns about the contaminants being discussed today – perchlorate and TCE. We are acutely aware that these contaminants present challenges for many states, as well as for water systems and their customers. However, as a general matter, we believe the science-based decision-making processes of the Act should be allowed to function as envisioned. We are concerned about the precedent of using legislative action that supercedes the provisions of the statute for particular contaminants and contaminant categories.

There appear to be an increasing number of contaminants threatening the safety of drinking water; highlighting the need for a rational, scientific approach to determining what should be regulated and at what levels. Recent media stories about pharmaceuticals and personal care products in our surface and ground waters -- and, in some cases, in drinking water -- are just one example. In my own state of Ohio and in a number of other states, we are grappling with a different type of emerging contaminant -- "PFOA"; one of many flouropolymers used in a variety of manufacturing processes for decades to create products like non-stick cookware. This compound is being detected in the environment, animals, and people around the world. Customers of an Ohio public water system contaminated by PFOA have the highest blood levels of the chemical ever detected. Clearly, we are concerned about any of these chemicals being in our sources of drinking water.

We also expect to see more and more "emerging contaminants" in the future. We live in a society that produces and uses a myriad of chemicals. That fact, coupled with our ever increasing ability to detect and quantify contaminants, will undoubtedly educate us about new risks to the safety of drinking water. Unless a balanced, rational, and transparent approach is used, we're concerned that EPA will jump from one contaminant to another -- based on media and political attention -- rather than on the potential for meaningful public health gains.

Timeliness is Key: Recommendations for EPA from State Drinking Water Programs

While I've shared our concerns about the risks of an alternative process to contaminant regulation, states do agree that EPA needs to make timely decisions on contaminants of concern.

Most states do not have the resources or expertise to independently develop drinking water regulations and therefore look to EPA to conduct the necessary research and collect the data and information needed to make regulatory decisions. However, as my colleagues on this panel from other states have (or will) describe, in the absence of timely EPA decisions about contaminants of concern, some states can and do establish their own regulatory levels.

Public health protection depends on both sound and timely decisions. So, what is *timely* action on the Agency's part? In the case of perchlorate and TCE, EPA should be held

accountable for describing the data and information available; indicating what, if anything, is lacking to support regulatory decisions; and providing estimates of the time frames needed to finish gathering and analyzing this information. We urge EPA to gather the needed data and information as expeditiously as possible and to make decisions about whether or not to regulate (in the case of perchlorate) and whether or not to revise (in the case of TCE) as rapidly as possible. This same need applies to a number of other emerging contaminants. Resources for identifying and researching the health implications of emerging contaminants such as endocrine disrupters and fluoropolymers, for example, are critical.

Importance of Source Water Protection

The topic of "emerging contaminants" also points to a strategy we must increasingly employ in tandem with the regulatory track we've discussed thus far: namely, *source water protection.* In most cases, it's far more effective, cheaper, and protective to *prevent* contaminants from reaching sources of drinking water, in the first instance, than to identify and treat them. Key elements of a preventative approach include appropriate controls on point and non-point sources of pollution, together with wise land use decisions and "smart growth" approaches to development. There is a critical link between the protections afforded under the Clean Water Act and source water protection needed to fully achieve the goals of the Safe Drinking Water Act.

Suggestions for Congress

All of us – at the federal, state, and local levels – have important roles to play. Today's discussions underscore the need for us to stay ahead in our efforts to ensure that the American people continue to have access to water that is among the safest in the world. For Congress, an important role is to ensure adequate funding to support research and analysis so that supporting information about these complex contaminants is available when needed.

I must also note that while we support the need for new regulations to address contaminants of concern – these regulations come with a cost burden to state drinking water programs and public water systems. Many states and water utilities, especially small systems, are already struggling to meet the demands of regulations adopted since the Safe Drinking Water Act was reauthorized in 1996. We need your continued financial support of drinking water programs. We appreciate Congress' support of the Drinking Water State Revolving Loan Fund – which remains an important source of funds for thousands of drinking water systems to build new and address aging infrastructure needs. But, we respectfully recommend that more funds be appropriated in future years to help fill the large and growing infrastructure gap.

Our discussions today also highlight the need for additional federal dollars for state drinking water programs though Public Water System Supply and Supervision Grants. Current funding levels, which have remained roughly $2 million, on average, per state,

per year for the last decade, are simply inadequate for the task at hand and should be substantially increased.

Thank you for this opportunity to offer testimony. I would be pleased to answer any questions you may have.

Response by Mike Baker to an Additional Question
From Senator Boxer

1. ***Please describe the cost to states if they are required to develop their own drinking water standards for contaminants not federally regulated?***

Answer: Many, if not most, states simply do not have the capability to develop their own drinking water regulations. Those states that do have this capability essentially mimic the principal steps that EPA follows in developing drinking water regulations; albeit with additional state requirements for certain elements of the process. The cost is obviously highly variable, depending upon a number of factors, however, based on information offered by several states with medium to large populations, costs to develop state-specific drinking water rules can range from $500,000 to $4 million. An average cost to develop a state-specific rule would be approximately $1.75 million. Generally, a state-specific rule would take an average of three years from concept to completion and would require a staffing average of 3-5 full time person years. Factors that affect these costs and staffing needs include activities such as literature reviews; underlying research and/or studies; public hearings, responses to comments, and coordination with internal and external groups; data management (water quality data to determine number/size of affected utilities); laboratory sampling and analysis; peer review for risk assessment/risk management; legal analyses; and technical assistance, support, and outreach to utilities. The estimated costs, staff time, and programmatic factors do not include costs for rule implementation or compliance/enforcement.

Responses by Mike Baker to Additional Questions
From Senator Cardin

1. ***The CCL is growing as we are better able to detect new chemicals in our drinking water and as these new chemicals enter our environment. Based upon your work in your respective states, what is the best approach for prioritizing which emerging contaminants should be regulated?***

Answer: The best approach is one that leads to prioritizing, and when appropriate, regulating, those contaminants that both pose a serious threat to human health and have a high likelihood of occurring in drinking water at concentrations of concern. Our increasing ability to detect contaminants at extremely low concentrations has enabled us to have a more robust list of candidate contaminants, but detection alone does not necessarily correlate with a contaminant's ability to cause adverse human health effects in drinking water at the detected concentrations. As the Safe Drinking Water Act phrases it, contaminants should appear on EPA's Contaminant Candidate List if the contaminants "are known or anticipated to occur in public water systems, and...may require regulation." [Section 1412(b)(1)(B)(i)] If one thinks in terms placing emerging contaminants in "bins" based on their risk (i.e., potential to cause adverse human health impacts) and their likely occurrence in drinking water, we are ultimately interested in identifying those contaminants that show up in the bin in the lower right-hand quadrant of the illustration below.

Low Risk/Low Occurrence	Low Risk/High Occurence
High Risk/Low Occurence	High Risk/High Occurence

Contaminants in the upper right-hand and lower left-hand bins should be the focus of data gathering and analysis to be sure that we've "gotten it right" and that these contaminants do not merit further attention.

In general, we concur with the overall recommendations of the National Academies of Science to EPA, of a few years ago, about how to approach the CCL. The NAS recommended that EPA begin by casting a very broad "net" and considering a wide universe of contaminants that have even a remote chance of being problematic in drinking water. The NAS recommended that this list be further honed, based on the best available information, to a "pre-CCL" – i.e., a more limited universe of contaminants that would be the subject of more exhaustive data-gathering and analysis. Finally, the NAS recommended that the contaminants on the pre-CCL be modeled – based on characteristics of regulated contaminants -- to determine whether or not they met the threshold for be listed on the CCL. This winnowing process, based on the application of the best available information, is, we believe the appropriate process. The CCL should also "feed" EPA's (and other organizations') research agenda, since many of the contaminants that are identified in this process often lack the requisite health effects and occurrence information to allow the Agency to make definitive judgments about the seriousness of the contaminants. Unfortunately, there's no substitute for undertaking the tough and sometimes time-consuming research that needs to be done to elucidate information about these contaminants. However, EPA needs to move expeditiously in resolving outstanding questions about contaminants of concern. Further, the research agenda of the Agency's Office of Research and Development needs to be aligned so it that it can produce the kinds of data and information needed, at the time this information is needed. The Agency's efforts to develop, refine, and make judgments about the CCL need to be transparent, with ample opportunities for input from states, other interested parties, and the public.

2. ***Should the cost of reducing the contaminant concentration factor into decisions of what is a safe level for final regulatory determination purposes?***

Answer: The cost of reducing contaminant concentrations should *not* factor into decisions about whether or not to regulate a contaminant. That decision should be made on the basis of the above-described process, in which contaminants in the lower right-hand bin above move into the regulatory development process. The statutory test for decisions about whether to regulate a contaminant, should apply [Safe Drinking Water Act Section 1412(b)(1)], namely that:

(i) The contaminant have an adverse effect on the health of persons;
(ii) The contaminant is known to occur or there is 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 contaminants presents a meaningful opportunity for health risk reduction for persons served by public water systems.

However, once a decision to regulate a contaminant is made, the cost of treating or otherwise reducing contaminant concentrations *should* factor into the regulatory development process. In fact, the Safe Drinking Water Act (SDWA) requires, at several points in the process, that cost factors be considered. The SDWA requires that the regulatory level, the Maximum Contaminant Level (MCL), be set as close to the Maximum Contaminant Level Goal (MCLG) as *feasible*, taking cost of treatment into consideration. The SDWA also provides for an overall weighing of the projected costs and benefits of the rule and allows the Administrator to raise the MCL above the feasible level if the benefits do not justify the costs and the Administrator elects to exercise this prerogative under the Act. (This was done in the case of the MCLs for arsenic and uranium.)

Responses by Mike Baker to Additional Questions
From Senator Inhofe

1. ***Do you or the Association of State Drinking Water Administrators support legislation that singles out drinking contaminants and requires action regardless of scientific outcomes? Why or why not?***

Answer: As I mentioned during my testimony on May 6th, we support the overall science-based decision-making processes for regulatory determinations laid out in the Safe Drinking Water Act. We would be concerned about a precedent of using legislative action to supercede, for particular contaminants and contaminant categories, the provisions of the statute. Unless a balanced, rational, and transparent approach is used, we're concerned that EPA will jump from one contaminant to another -- based on media and political attention -- rather than on the potential for meaningful public health gains. An undue amount of urgency and attention paid to particular contaminants can also divert resources from the scientific process and slow down the analysis and consideration of other contaminants of concern which may, in fact, may be higher priorities on the basis of the above-discussed occurrence and health effects information. At the same time, we believe (again, as mentioned in my testimony) that EPA needs to be transparent in indicating what data and information they have about problematic contaminants, what information they lack, and what process they're using to fill those gaps. The deliberative and sometimes time-consuming science-based decision making-process should not be used as an excuse for failing to make tough decisions – once the requisite data and information are available.

2. ***You mentioned that states and water utilities are already struggling to meet the demand of current regulations. Could you explain what responsibilities states have when final federal regulations are adopted?***

Answer: There are actually three phases of state actions in connection with states adopting and implementing a new EPA rule. There are 1) pre-rule activities; 2) planning and preparation activities before the rule is effective; and 3) the ongoing compliance activities. Prior to any final rule being issued by EPA, states will participate in stakeholder meetings, provide comments on the proposed rule, and review any supporting materials to help make sure the rule is grounded in

sound science and can be effectively implemented. These pre-regulation activities also often include providing EPA with state-specific data (especially, health effects or occurrence data) related to the contaminant of concern. When the final rule is issued, state staff review the rule, including the preamble, and any accompanying fact sheets and guidance documents to determine what the rule requires and what EPA expects of water systems and states. Understanding the new rule may also involve state staff attending training sessions on rule requirements.

The state's next step will be to develop a plan for implementation. Many questions need to be answered so that the plan meets the needs of the state and the water systems, including questions about state staffing and resource needs; transitioning to the new rule; special conditions based on system characteristics; and impacts on other state programs. A key component of a state's rule implementation plan will be a training and public education plan for the rule. State staff will need to develop informational materials for distribution to water systems, conduct training for water system operators and officials, and support third party assistance providers and consultants who will also be providing assistance to water systems. Public meetings and other outreach may also be needed to inform the general public of changes that may occur as water systems adopt the rule. New rules also have an impact on a state's data system and could have a significant cost. The state's implementation plan will identify new data that must be collected and tracked resulting in a need for new reporting forms or a change in electronic reporting protocols. Modification of the state's data system to accommodate the new rule requirements may involve hiring a contractor and could require many months to plan, develop, test, and put into production. States that provide laboratory or sampling services for their smaller water systems and their own state-owned systems will have additional planning to do so they can continue to provide these services under a new rule. They may have to increase their own spending on contract services or help state labs obtain additional funding to support the new rule.

Finally, the state will write a state rule corresponding to the new federal rule and prepare the primacy application package for EPA. This package assures EPA that the state rule is at least as stringent as the EPA rule and also describes how the state will implement the rule and any special primacy requirements. All of these preparations create a significant peak in work for the state during the few years following the promulgation date of the rule and require the state to divert resources from other projects to meet the needs of rule preparation and implementation. It is during this time that much of the implementation work mentioned in the previous paragraph, such as training and data modifications actually takes place. However, the job is not over -- it is only beginning. Then, the routine work begins to ensure that systems stay in compliance with the rule. These continuing compliance activities include ongoing training and technical assistance for operators; tracking and analysis of monitoring results to evaluate compliance; review of system condition during sanitary surveys; review of engineering plans for system changes to achieve or improve rule compliance; and finally, follow-up and appropriate action in response to violations.

3. ***I'm concerned that if this legislation passes, Congress will weaken the public comment period for EPA regulation. If legislation were to pass requiring EPA to set an MCL for perchlorate in 18 months, couldn't that really limit public input into whether or not the science to regulate is appropriate and whether the suggested MCL is necessary for public health protection?***

Answer: States do believe that EPA should engage in a robust process of engaging the public and interested parties in regulations that affect them. Given the number of statutory requirements and Executive Orders governing the steps for proposing and finalizing Federal drinking water regulations, a time frame of 18 months from the time of start-up of a new rule to a final regulation seems overly optimistic. We do agree that a meaningful opportunity for pubic comment certainly must be part of the overall process and would be concerned about truncating the time allowed for that portion of the process.

Senator BOXER. Thank you very much, Mr. Baker.

And now we are going to hear from Carol Rowan West, Director, Office of Research and Standards, Massachusetts Department of Environmental Protection. Welcome.

STATEMENT OF CAROL ROWAN WEST, DIRECTOR, OFFICE OF RESEARCH AND STANDARDS, MASSACHUSETTS DEPARTMENT OF ENVIRONMENTAL PROTECTION

Ms. WEST. Thank you, Chairman Boxer and Committee members, for the opportunity to testify today on the issue of perchlorate in drinking water. As a scientist and Director of the Office of Research and Standards at the Massachusetts Department of Environmental Protection, I have spent over 15 years evaluating the toxic effect of chemicals and setting standards that are protective of public health.

I have no doubt that perchlorate is a chemical that should be regulated in the Nation's drinking water supply, given the fact that this chemical is one that affects the thyroid gland and can effect the levels of thyroid hormones that are needed for the proper development of the brain in the fetus, infants and young children. The health effects of perchlorate are well known and are based on sound science.

The Commonwealth of Massachusetts' work on perchlorate began in 2001, when perchlorate was detected in the groundwater at 600 parts per billion at the Massachusetts Military Reservation on Cape Cod. The contaminated groundwater plume migrated to nearby public water supply wells. Given the lack of Federal and State standards for perchlorate and the potential for perchlorate to affect brain development in children, we felt compelled to set a drinking water standard. We promulgated a two parts per billion perchlorate standard in 2006 based upon a thorough review of all the scientific information along with an independent review by an external scientific advisory committee.

After all of the public water supplies were tested in Massachusetts, we found a number of unanticipated situations including perchlorate levels as high as 1,300 parts per billion in one public water supply. We found that all of the contaminated public water supplies were from non-military sources of perchlorate, including blasting, fireworks and sodium hypochlorite, a chemical that is used to treat and disinfect drinking water.

As mentioned earlier, there appears to be sufficient evidence that there is widespread contamination of perchlorate in the United States. Surveys show that 26 States and two territories have perchlorate in their drinking water, and 37 States and territories have approximately 400 hazardous waste sites with perchlorate present in them.

In addition, there are new studies that demonstrate the pervasiveness of perchlorate exposures to the American public, raising issues regarding human safety. The Food and Drug Administration has found that 59 percent of the total food samples tested contain perchlorate, including baby food. The FDA estimated that children the age of 2 years old would receive the highest intake of perchlorate a day. At this age, the brain is rapidly growing and it puts these young children at risk, especially given the fact that the

amount of perchlorate from water and from food may go over the level of producing thyroid hormone level alterations that could affect brain development.

A very recent study just published on Boston women and breast milk contamination with perchlorate found that all 49 of the women tested had perchlorate, and the levels ranged from 1.3 to 411 parts per billion. And last, as mentioned earlier, the Centers for Disease Control has found through its national survey that perchlorate is pervasive in the American public and that in the high-risk group of women with low iodide intake, that they are finding alterations in thyroid hormone levels.

All of these studies indicate widespread contamination and exposure to perchlorate in both water and the food supplies of Americans. The benefits of having a national perchlorate drinking water standard are that all of the public water supplies will be tested so we will have complete information. Then action can be taken to treat the water to protect children's health. We recommend that the U.S. EPA should take a leadership role to set a perchlorate drinking water standard which protects children's health. Perchlorate contamination is a national issue and national action is needed. Federal action will lead to consistent protection of children's health across the United States. And last, the clean-up of water supplies and sites has the additional benefit of also decreasing the levels of perchlorate in food, including breast milk.

Thank you for the opportunity to testify. I will be pleased to answer any questions you might have.

[The prepared statement of Ms. West follows:]

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Written Testimony of

Carol Rowan West, MSPH

Director, Office of Research and Standards

Massachusetts Department of Environmental Protection

Before the

Senate Committee on Environment and Public Works

United States Senate

On

Perchlorate in Water

May 6, 2008

Thank you Chairman Boxer and Ranking Member Inhofe and members of the Committee, for inviting me to testify on the issue of perchlorate in drinking water. I am pleased to share with you a description of our work to set drinking water and cleanup standards for perchlorate, the process we followed, and lessons learned as they apply to this national issue.

As Director of the Office of Research and Standards (ORS) at the Massachusetts Department of Environmental Protection (MassDEP), I have spent over 15 years evaluating the health effects of toxic chemicals and working to set air, water and soil standards that are protective of public health. ORS follows the health assessment and standard setting protocols published by the U.S. Environmental Protection Agency (US EPA), and our work to set standards for perchlorate followed these standing procedures. During the course of my work on perchlorate, I chaired MassDEP's Perchlorate Workgroup comprised of senior managers from the Commissioner's Office, Drinking Water and Waste Site Cleanup Programs who dealt with all aspects of the standard setting work for perchlorate. I also chaired the external Scientific Advisory Committee on Health Effects who provided valuable input to our toxicological and standard setting work. MassDEP's goal in establishing a perchlorate drinking water standard was to protect public health, especially pregnant women and children from a compound for which no state or federal drinking water standard existed. MassDEP's process involved: (1) a rigorous scientific evaluation of the risks posed by perchlorate; (2) a comprehensive and innovative collaboration with major stakeholders; and (3) an effective outreach program to help manage the risk.

I. Establishing a Perchlorate Drinking Water Standard

a. How MassDEP became involved with perchlorate

MassDEP's experience with perchlorate began in April 2001. In July 2006, MassDEP became the first state in the nation to promulgate drinking water and waste site cleanup standards for perchlorate.

MassDEP's work on perchlorate began when it was first detected at Cape Cod's Massachusetts Military Reservation (MMR) in groundwater at 600 ppb in 2001. Perchlorate was also detected in the adjacent town of Bourne's water supply at concentrations less than 1 ppb. In response, the Bourne Water District (BWD) voluntarily shut three affected wells. Since there were no established drinking water standards for perchlorate, in March 2002, the BWD formally requested health protection guidance from MassDEP on drinking water. In order to assist the BWD, MassDEP toxicologists and risk assessors reviewed available information on the toxicity of perchlorate, including the draft United States Environmental Protection Agency's (US EPA) health assessment for perchlorate (U.S.EPA, 2002), which contained a draft reference dose and an associated drinking water limit of 1 ppb for perchlorate. This report as well as other information reviewed indicated that risks to sensitive subgroups, including pregnant women, fetuses, children and individuals suffering from hypothyroidism, could not be ruled out at perchlorate drinking water concentrations above 1

ppb. As these risks included the potential for serious adverse outcomes, including permanent neurological effects from *in utero* exposure, MassDEP provided the BWD with interim advice recommending that these sensitive subgroups be informed when perchlorate concentrations exceed 1 ppb and be advised to avoid consuming the water. The Massachusetts Department of Public Health supported this interim advice and US EPA Region 1 issued a statement indicating that the advice was health protective.

In 2003, the U.S. EPA (2002) draft document, which had already undergone extensive expert peer and public review, was forwarded to the National Academy of Sciences (NAS) for reassessment. Since it was anticipated that this review would not be complete for some time, MassDEP made a decision to set perchlorate standards so that public water supplies and sites would be cleaned up.

b. Assessment and Monitoring

MassDEP's Office of Research and standards met with its scientific advisory committee, scientists from DOD (Army, Navy, and Air Force), and members of the NAS to evaluate the health risks posed by perchlorate and to establish a reference dose[1] that would be used to establish drinking water and clean up standards. MassDEP's assessment emphasized protecting infants and addressing concerns about breast milk exposures leading to a lower and more protective reference dose than those established by other groups. MassDEP's perchlorate reference dose is 0.07 microgram per kilogram whereas the NAS value, supported by a majority of the NAS committee is 0.7 micrograms per kilogram. (see Appendix A for more detailed information on the derivation of the reference dose). The NAS committee was not unanimous regarding its recommended reference dose with a lower more health protective value also supported. When deriving the drinking water standard, MassDEP took into account that there are perchlorate exposures from food as well as water. To address this issue, MassDEP's protocol is to allow 20% of the reference dose to come from water ingestion and 80% to come from food ingestion. In this way, the reference dose is not exceeded and health is protected.

The US EPA has adopted the higher of the two NAS reference doses, which is ten times higher than MassDEP value. In addition, the US EPA Office of Solid Waste and Emergency Response translated that value into a drinking water limit of 24.5 ppb, a value that does not take into account perchlorate sources from food or infant breast milk exposures. US EPA's Children's Health Protection Advisory Committee wrote to Administrator Johnson advising that the 24.5 ppb being used at CERCLA sites is not protective of children's health (Children's Health Protection Advisory Committee Letter to Steven Johnson, 2006).

On a parallel track with the reference dose work, MassDEP's Drinking Water Program (DWP) issued regulations requiring the testing of all of the 500 plus public water supplies in the Commonwealth to determine the scope of the perchlorate problem. The results indicated perchlorate contamination above 1 ppb (MassDEP's interim guidance) in 10 community

[1] A reference dose is an estimate of daily exposure to the human population including sensitive subgroups that is likely to be without appreciable risk of deleterious effects during a lifetime.

water supplies across the state with levels as high as 1300 ppb. A major finding was that perchlorate contamination was more extensive than anticipated and that it was not solely linked to military sites. In depth site investigations demonstrated that perchlorate contamination was also associated with blasting using certain explosives, fireworks, medical manufacturing of specific devices, and due to its presence in certain drinking water treatment chemicals (sodium hypochlorite).

II. Scientific Support for a Perchlorate Standard that is Protective of Public Health

A few key studies have been published on perchlorate since the NAS report was published.

For example, researchers at the Centers for Disease Control (CDC) sampled perchlorate and thyroid hormone levels in approximately 2,800 people as part of a national survey. Perchlorate was detected in most of the samples, indicating widespread exposures.

The CDC researchers found an association between perchlorate levels and altered thyroid hormones in a subset of women with low dietary iodine intake. Thyroid hormones are necessary for normal growth and neurological (brain) development of fetuses, infants and children.

The CDC study, (Blount, et al, 2006) supports the conclusions of MassDEP's determination that perchlorate levels in drinking water should be regulated to protect public health.

The US Food and Drug Administration (FDA) conducts the Total Diet Study, which is designed to monitor the US food supply for chemical contaminants. FDA recently reported on the estimated average perchlorate intake from the contribution of specific food groups and total intake for 14 age/sex subgroups of the US population (FDA, 2008). FDA found perchlorate in a wide range of foods. 59% of the total samples analyzed contained perchlorate whereas 41% had no detectable levels. Perchlorate intake by the sensitive subgroup of infants was mainly from baby foods (81% of the total dose), which includes infant formula and dairy foods. Children with the highest total perchlorate intake per kilogram of body weight per day were children who are 2 years old. The brain is rapidly developing in young children putting them at high risk should the total perchlorate exposure impact the level of thyroid hormones needed for normal development. This study shows the importance of accounting for food exposures when setting a perchlorate drinking water standard.

A recent study on perchlorate levels in breast milk in lactating Boston-area women found measurable perchlorate levels in 100% of 49 human milk samples tested. Perchlorate levels were in the range of 1.3 ppb to 411 ppb, with a median value of 9.1 ppb.

III. Benefits of having a Perchlorate Drinking Water Standard

1. Under US EPA's Unregulated Contaminant Monitoring Rule, perchlorate was detected in 120 public water supplies in 26 states and 2 territories. According to Government Accounting Office testimony (GAO, 2007), perchlorate has been found by federal and state agencies in groundwater, surface water, soil or public

drinking water systems at almost 400 sites across the country in 37 states and U.S. territories. This extensive contamination puts our nation's children at risk. Based on MassDEP's experience with finding more perchlorate contamination problems due to uses beyond military one, these numbers might represent only the tip of the iceberg.

2. The generation of monitoring data on the presence of perchlorate in drinking water supplies allows environmental protection agencies to take steps to protect children's health. A variety of water treatment techniques are available for reducing perchlorate water concentrations to low ppb levels.
3. Knowing the sources of perchlorate can lead to pollution prevention (P2) practices. MassDEP has provided guidance to blasting and firework contractors to prevent future perchlorate ground water contamination problems (http://mass.gov/dep/water/drinking/percinfo.htm). P2 should deal effectively with the problem. MassDEP hopes that through P2 actions, we will be able to reduce monitoring requirements, which will lead to decreased expenses to public water suppliers.

IV. Recommendations

1. US EPA should take a leadership role to set a perchlorate drinking water standard, which protects public water supplies and children's health. Perchlorate contamination is a national issue and national action is needed.
2. Federal action will lead to consistent protection of children's health across the United States.
3. Federal action is more efficient and will eliminate the duplication of state efforts.
4. Cleanup of water supplies and sites has an additional benefit of also decreasing the levels of perchlorate in foods (including breast milk).

Responses by Carol Rowan West to Additional Questions
From Senator Boxer

Question #1: Costs to states of no federal standard

Please describe the importance of having a federal perchlorate drinking water standard for the public and for state government?

A federal standard for perchorate would provide important national leadership on this threat to our drinking water and would drive the clean up of numerous public drinking water supplies across the United States. Health care costs associated with the necessary treatment of adverse health effects from exposure to perchlorate in drinking water would be avoided. The costs of treatment for thyroid gland effects including hypothyroidism, goiter, behavioral and neurotoxicity effects would be avoided.

A federal health-based standard would avoid the need for individual states to set standards and would eliminate the unnecessary duplication of efforts at the state level. Having a federal standard for perchlorate would be a more cost effective approach and would avoid diverting state resources unnecessarily.

Question #2: Resources of Developing State Standard

How much time and how many resources did Massachusetts expend to develop its perchlorate drinking water standard?

Our work to set a drinking water standard for perchlorate began in 2002 and concluded in 2006. We estimate that the resources spent in establishing a state perchlorate drinking water standard was approximately equal to 9.0 Full Time Equivalents (FTEs, or person-years) at a total cost of approximately $1.35 million. Resources included expertise from toxicologists, chemists, engineers, attorneys, and program managers.

If 3 or 4 other states took on this same effort, the total costs would run from $4 to $5.4 million dollars. These enormous costs would be avoided if EPA set a federal standard for perchlorate.

Question #3: Would a federal standard or health advisory have helped Massachusetts develop such a standard?

Yes. It's likely that we would have adopted it, thereby saving over one million dollars in state funding.

Responses by Carol Rowan West to Additional Questions
From Senator Cardin

Question #1: The contaminant Candidate List is growing as we are better able to detect new chemicals in our drinking water and as these new chemicals enter our environment. Based upon your work in your respective states, what is the best approach for prioritizing which emerging contaminants should be regulated?

EPA has a good approach for prioritizing chemicals under the Unregulated Contaminant Monitoring Rule. However, it appears that EPA did not have the ability, for some reason, to regulate perchlorate such that Massachusetts had to take on the work ourselves so that we could clean up contaminated sites and drinking water supplies to protect public health.

Question #2: Should the cost of reducing the contaminant concentration factor into decisions of what is a safe level for final regulatory determination purposes?

Yes. The Massachusetts Department of Environmental Protection (MassDEP) included the costs of treatment to reduce perchlorate in drinking water during deliberations on the final standard for perchlorate. EPA also considers costs when setting Maximum Contaminant Levels (MCLs).

Responses by Carol Rowan West to Additional Questions
From Senator Inhofe

Question #1: Under the Safe Drinking Water Act can individual states set their own drinking water standards even if EPA decides not to regulate a particular contaminant? If so, then what is the problem?

Yes, MassDEP has the authority to set drinking water standards when EPA does not act. However, when multiple states have an unregulated contaminant such as perchlorate in their drinking water supplies and EPA does not act, several problems arise such as:

- *multiple states must expend large amounts of resources to set standards;*
- *states are duplicating efforts, representing wasteful spending of scare resources;*
- *the drinking water levels set by states are likely to differ numerically, resulting in different cleanup standards for industry to meet and confusion regarding what is truly the health protection level; and,*
- *interstate trans-boundary issues when higher perchlorate groundwater levels from one state migrate into a state with lower standards.*

Under US EPA's Unregulated Contaminant Monitoring Rule, perchlorate was detected in 120 public water supplies in 26 states and 2 territories. If 26 states and 2 territories set a perchlorate drinking water standard, the estimated cost to develop that would be about $38 million dollars, based on Massachusetts estimated costs to set the standard. That huge expenditure would be avoided if EPA set a federal standard.

Question #2: Since treatment costs can be substantial, especially for small rural communities, shouldn't EPA science demonstrate the importance of treatment?

Yes.

Question #3: In your response to questioning, you mention that Massachusetts had nearly all of their toxicologists working full time to come up with a perchlorate drinking water standard. Have they put this effort into other chemicals regulations? Are you concerned that over focusing the state staff on one drinking water standard might take the focus off of other, equally or more pressing contaminants?

The level of effort MassDEP expended to address perchlorate has not been necessary to date for other individual chemical regulations. Perchlorate was somewhat unusual due to the known contamination source and threat to a major regional water supply, and the high level of controversy surrounding the issue. Yes, I am concerned about the level of effort and the diversion off work on other contaminants. This is another reason why it would have been beneficial if EPA had stayed on their track to set a perchlorate reference dose in early 2003, followed by a federal drinking water standard.

Question #4: You mentioned that your study found high levels of perchlorate in human breast milk, the highest being in a woman in Boston, where there was not perchlorate in the water. If this is the case, why do you think that perchlorate regulation in drinking water is the best way to address occurrence in the population?

I believe that the perchlorate levels in the breast milk are due in significant part to perchlorate in the food supply, which in turn is a result of the presence of perchlorate in drinking water and in water used for irrigation. There are several studies that demonstrate the uptake of perchlorate from water into the food supply. A list of scientific references for these studies is attached.

In addition, the US Food and Drug Administration (FDA) which regulates contaminants in commercial food crops, has conducted national surveys and has reported perchlorate in a wide variety of food. As stated, "FDA recognizes the potential for perchlorate contamination in food through the use of contaminated irrigation water, processing water, and source waters for bottling". FDA has reported levels of perchlorate in lettuce, collards, spinach, carrots, broccoli, green beans and milk. I believe the source of perchlorate in food is from contaminated water used for irrigation.

Lastly, it is important to note that consumption of perchlorate contaminated drinking water will add to other exposures and raise the potential risks to our nation's infants.

Question #5: You mentioned that the science is settled, but omit a study by the American Thyroid Association, a group of medical doctors specializing in thyroid function, which used a state's public funds and the NAS that contradict your

findings. Are you aware of any published and peer reviewed scientific studies about what effects, if any, occur on an infant who is breast feeding based upon perchlorate exposure? I so, please share them with the Committee.

MassDEP's review of all of the pertinent perchlorate health effects studies is located in the following documents:

www.mass.gov/dep/toxics/perchlorate-toxicity-061206.doc
www.mass.gov/dep/toxics/perchlorate-addendum-061206.doc

Given the mechanism of action of perchlorate, the substantial literature documenting neuro-developmental deficits in infants born to iodine deficient mothers are of direct relevance to this issue. These are discussed at length in our report as previously cited. Additional published studies related to this issue which further support MassDEP's concern about breast milk perchlorate exposures include: 1) Ginsberg et al, 2007, which concluded that EPA's Preliminary Remediation Goal (PRG) of 24.5 parts per billion would lead to a 7-fold increase in breast milk perchlorate concentrations, causing 90% of nursing infants to exceed the National Academy of Sciences and EPA's reference dose; 2) Kirk et al, 2005 and 2007, which demonstrate that significant levels of perchlorate are present in the breast milk of nursing mothers in the U.S.; and, 3) Blount et al, 2006, which documents an association between perchlorate exposure and altered thyroid function in US women.

MassDEP. 2004. Perchlorate Toxicological Profile And Health Assessment - Final Draft. Massachusetts Department of Environmental Protection, Office of Research and Standards. Boston, MA

Andrea B. Kirk, Jason V. Dyke, Clyde F. Martin and Purnendu K. Dasgupta. 2007. Temporal Patterns in Perchlorate, Thiocycnate and Iodide Excretion in Human Milk. Environmental Health Perspectives 115 (2): 182-186

Andrea B. Kirk, P. Kalyani Martinelango, Kang Tian, Aniruddha Dutta, Erneste Smith, Purnendu K. Dasgupta. 2005. Perchlorate and Iodide in Dairy and Breast Milk. Environ Sci Technol 39: 2011-2017.

Benjamin C. Blount, James L. Pirkle, John D. Osterloh, Liza Valentin-Blasini, and Kathleen L. Caldwell
2006. Urinary Perchlorate and Thyroid Hormone Levels in Adolescent and Adult Men and Women Living in the United States. Environmental Health Perspectives 114 (12): 1865-1871

Gary L. Ginsberg, Dale B. Hattis, R. Thomas Zoeller and Deborah C. Rice (2007). Evaluation of the U.S. EPA/OSWER Preliminary Remediation Goal (PRG) for Perchlorate in Groundwater: Focus on Exposure to Nursing Infants. Environmental Health Perspectives 115 (3): 361-369

References: Accumulation of Perchlorate in Food

Jackson, A., et al. (2005) Perchlorate Accumulation in Forage and Edible Vegetation. *Journal of Agricultural and Food Chemistry.* 53, 369-373.

Sanchez, C.A. et al. (2005 Accumulation and Pechlorate Exposure Potential of Lettuce Produced in the Lower Colorado River Region. Journal of Agricultural and Food Chemistry. 53: 5479-5486.

Sanchez, C.A. et al. (2006). Potential Perchlorate Exposure from Citrus sp. Irrigated with Contaminated Water. *Analytica Chimica Acta:* 567; 33-38.

U.S. EPA. (2004). A Study on the Accumulation of Perchlorate in Young Head Lettuce. EPA/600/r-03/003.

U.S. EPA Office of Groundwater and Drinking Water. (2006). Regulatory Determination Support Document for Selected Contaminants from the Second Drinking Water Contaminant Candidate List (CCL2). Part III. What About the Remaining CCL2 Contaminants? (Draft).

Urbansky, E.T. et al. (1999). Perchlorate in the Environment. Risk Exposure for Perchlorate. *Symposia Papers Presented Before eh Division of Environmental Chemistry American Chemical Society. New Orleans. Preprints of Extended Abstracts. 39(2): 66-68.*

Yu, L. et al. (2003). Uptake of Perchlorate in Terrestrial Plants. *Ecotoxicology and Environmental Safety.*

Senator BOXER. Thank you.

Ms. West, can you explain for us what are the results of too much perchlorate in terms of the thyroid? What actually happens and how does it impact a pregnant woman and how does it affect the fetus?

Ms. WEST. When women are pregnant, they have a lot of stress on their thyroid gland. They sometimes also have a lower amount of dietary iodide in order to make thyroid hormones. So when pregnant women are exposed to perchlorate, their thyroid hormone level is reduced.

Now, the fetus depends on thyroid hormone levels from the mother, and when the mother is exposed, she may not be able to provide the necessary levels of thyroid hormone to the fetus. In early life stages of the fetus, they aren't producing any thyroid hormone whatsoever, so they are totally dependent on what the mother can deliver. So if the mother isn't making enough thyroid hormone, it is going to have an impact on the brain development of that child.

Senator BOXER. So this is very serious. You said in some systems there are 411 parts per billion that has been found?

Ms. WEST. In one breast milk sample from Boston, Massachusetts, where we do not have perchlorate in our drinking water. May we add: However, here the perchlorate exposure is from food that has taken up perchlorate from contaminated water.

Senator BOXER. Doctor, do you want to add to any of those adverse impacts, or did Ms. West pretty well cover it?

Dr. ALEXEEFF. I think she covered it very well. I would just add that perchlorate also prevents iodide from transferring to the placenta through the fetus, and also it blocks iodide transfer to breast milk for the newborn.

Senator BOXER. And that could result in developmental disabilities?

Dr. ALEXEEFF. That would add to the effect of perchlorate itself. So there is a perchlorate effect on the thyroid of either the newborn or the fetus and the mother, as well as the lower amount of iodide.

Senator BOXER. Well, I am going to talk to Mr. Baker because I think his approach—I understand where he is coming from. I don't agree with his conclusion, but I think your mind might be open to the few things that I say here. First of all, here is the problem. To say that Congress shouldn't get involved, it is a bad precedent, I hear you. I don't want to get involved. I don't want to. Senator Klobuchar doesn't want to. Senator Lautenberg and Senator Clinton and those of us who are working on this Committee to protect our people don't want to. We want the EPA to act.

Now, we hear today from two very straightforward witnesses with no axe to grind, they are not politicians, they are experts on health, that what can happen if there is too much perchlorate in the water, it is very, very serious for a pregnant woman and her fetus, and could have devastating impacts, and for all we know probably is having devastating impacts as we speak because there is no standard.

So what happens is, we have information dating back, well, probably 20 years, but we know since 1992 EPA has talked about the proper standard for perchlorate. Listen to this. This is dated Janu-

ary 25th, 2002. I want to thank my staff for finding this out here. "A long-awaited U.S. EPA draft toxicological report issued on January 18th finds that perchlorate is likely to be more harmful to human health than previously thought." EPA, 2002. In response to the report's conclusion that perchlorate concentrations of less than one part per billion are safe for human consumption in drinking water, the California Department of Health reduced its advisory action level from 18 parts per billion to 4 parts per billion.

So the work of EPA in the past in letting folks know the danger has led to State action. Very good. But why do we hear today—and Senator Klobuchar may be shocked to hear this—that our EPA witness said—what were his words?—it is a distinct possibility that they may come out with no standard whatsoever for perchlorate.

So here is where we are, and this is where I want to talk to Mr. Baker and try to get him to see it a little bit differently. When you talk about it is a bad precedent for Congress to move in here, I say to you I don't want to go down that road, but we have already gone down that road. Senator Feinstein and I had an amendment that passed the Senate pretty overwhelmingly, I don't remember the exact vote, to ban phthalates. Why? EPA does nothing.

Are we supposed to sit back and say it is bad precedent to do this? Or are we going to protect the people? That is the issue here. I agree. Legislation to get into protecting the people chemical by chemical isn't my favorite way to go. I want to get an EPA that does something. It would be a lot easier on us here so we don't have to sit and have these kinds of hearings. We also have the Children's Health Advisory Panel tell the EPA that they are not doing enough, that they are very worried.

So you can't tell me, Mr. Baker, with all due respect, that if I care so much about my people that I am willing to push for this standard, and we are not setting the standard, we are just saying to EPA get off your delay and do this. That is what our bill says.

First, we say we should test for it and let the public know. And second, we say, you should set a standard by a date certain because this thing is going. If I told you, for example, that this President or some other President woke up some morning and just acted in my view irrationally and said, we are by executive order temporarily suspending all environmental protection laws because it is in the best national security of our Nation to do it. Let's say, you know, Presidents do things we don't agree with. Obviously, I don't think you would say, Congress, don't get involved. I mean, at some point when nothing gets done, we are accountable to the people that we represent. Now, I know that your drinking water association doesn't support having a standard set for perchlorate, but I am sure you know the American Water Works Association and the Association of Metropolitan Water Agencies has urged that EPA set a perchlorate standard. I think it is unusual to see someone who has to deal with this take this kind of attitude. I respect you and you have every right to, but if I look at Ohio, you should see, you are the 12th worst State for TCE. You have perchlorate. You have TCE and you are the 12th worst State for TCE.

So I guess what I want you to think about is this. The minute we set a standard here, you will be eligible for some clean-up funds. I agree with you completely that there is not enough fund-

ing. We are spending $5,000 a minute in Iraq, you would think we would have some funding to help you clean this up. That is a whole other debate. But I wonder if you would think about this, that by backing the EPA in this foot-dragging, you are putting off the day when you could be eligible for funds to clean up your water supply, and you are not protecting the people that you serve very well either.

So I just wonder if you would be open to reconsideration and perhaps join with the largest water utility and trade associations, two of the largest, and urge them to set a standard, EPA to set a standard.

Mr. BAKER. Madam Chairman, certainly as an administrator of a State drinking water program, along with my other colleagues that have that responsibility, we share the concern about any contaminants that are in our water supplies at an unsafe level.

One clarification, it is not ASDWA's position that we are opposed to EPA establishing a standard. It may very well be that after looking at the occurrence data through the UCMR, the studies by the NSA, the studies by the Food and Drug Administration, the information generated by other States, that a standard for perchlorate is an appropriate action.

We also believe they have the building blocks in place at this point in time to make a regulatory decision. We certainly hope and encourage them to make that decision very, very soon. So we share that, but we continue to have the concern that if we use legislative action to set the standard for perchlorate and TCE now, then with the myriad of chemicals that we know are out there, we know are starting to show up in our drinking water supplies, we know, as we are able to detect them at very low levels, we are going to raise additional questions. We just think we need to use the appropriate structure in place that we vett all of these chemicals through in making those decisions about what to regulate.

Senator BOXER. So you want them to set a standard?

Mr. BAKER. We want them to make a decision on it very quickly.

Senator BOXER. Well, good, then you should back my bill because that is exactly what we are saying. We say set a standard by a certain date.

The last thing I want to do is put into the record, and then I will turn to my colleague, an article that appeared—and this is really important—on April 28th, 2003. This whole stonewalling that we saw here from the EPA is not news. The headline in The Wall Street Journal back then was, EPA bans staff from discussing issue of perchlorate pollution. The Pentagon and several defense contractors who face billions of dollars of potential clean-up liability vehemently oppose EPA's high health risk assessment, arguing perchlorate is safe at levels 200 times higher than what the EPA says is safe. The Bush administration has imposed a gag order on the U.S. Environmental Protection Agency from publicly discussing perchlorate pollution even as two new studies reveal high levels of rocket fuel may be contaminating the Nation's lettuce supply.

[The referenced material was not received at the time of print.]

Senator BOXER. So I think the reason we were so interested in having this hearing is what you are seeing here today from the EPA is just a continuation of the stonewall. The reasons we are

going to have some action on this in June once we complete our global warming on the floor is because a lot of us have had it. We agree, Mr. Baker, they should do it. They should do it according to the science, and that is just what our bill says.

And last, last, last, thank you to California and Massachusetts. You have been leaders. I just so respect what you are doing.

Senator Klobuchar.

OPENING STATEMENT OF HON. AMY KLOBUCHAR, U.S. SENATOR FROM THE STATE OF MINNESOTA

Senator KLOBUCHAR. Thank you very much. And thank you, Chairwoman Boxer, for holding this hearing.

In Minnesota, thankfully, we haven't found a lot of perchlorate contamination, but we also haven't done a lot of testing, so it is possible we may have a problem we don't know about. I will tell you that we do have a number of TCE contamination sites, and we also have hundreds of smaller TCE contamination sites. These clean-ups have been carried out on TCE, but it has been described to me by our water experts that it takes a long time to get rid of it. No matter how many times you rinse it, it is kind of like cleaning a greasy pan with cold water. It is estimated that it will take 25 years to break down.

But I want to get to the topic you all have testified about, and follow up on some of Chairman Boxer's questions.

Ms. West, I was struck by your testimony about all of the scientific work that you have had to do in Massachusetts at the State level. One of my concerns here as I look at all of these issues, whether it is climate change or whether it is the regulation of these dangerous substances, that more and more work has been pushed to the State level without the resources to go with it, especially for instance in the climate change area. It gets absurd because you have 33 States trying to form together to do a climate registry because nothing has been done on the national level.

Could you talk a little bit about the burden that has been placed on your State? Have you gotten the resources for it in terms of trying to set some standards for perchlorate?

Ms. WEST. Well, just going back a little bit historically, back in 2003, EPA seemed to be rapidly advancing in setting a reference dose for perchlorate. I believe that in 2003 they were supposed to have a draft reference dose. So we actually were going to rely on their work, but then it got delayed so we took up our own work.

Now, the Office of Research and Standards is very fortunate. We have 11 staff toxicologists and risk assessors. We worked almost full time on perchlorate until 2006, when we promulgated our standards. The work also entailed the director of our drinking water supply program the Bureau of Waste Site Clean-Up staff and the Commissioner's office. Our four regional offices were also involved, because we had to go to cities and towns to deal with the contamination, find out what the sources were, and do clean-ups.

So it was a very large effort for us to undertake. I do think if there were Federal action that it would reduce the burden on the States having to do this type of work.

Senator KLOBUCHAR. Thank you very much. You also said something that makes a lot of sense to me. Since we know that per-

chlorate can cause developmental harm to pregnant women and children, that it would make some sense to set the standard now and refine it later, or do something, because what concerns me here is we have some scientific research, but yet nothing is happening on the EPA level. It seems to me we should err on the side of caution.

Do you want to respond to that and how you could envision this getting done?

Ms. WEST. Well, I totally agree with you. I think that there is well-known information on the health effects of perchlorate. It is based on sound science. There is much information to put together to set a drinking water standard. I look at this situation, and I say what is missing? Nothing, we have the data. We have everything that we need. We have protocols for setting drinking water standards. If we follow those and take action, I think we have all that we need.

Senator KLOBUCHAR. Dr. Alexeeff, you talked about how California set a standard and there is peer review. Do you feel that there is enough national information to move forward?

Dr. ALEXEEFF. Yes, of course we do. We are in the process now. There has been so much additional information. We are coming up on our 5-year cycle for reconsidering perchlorate, and seeing if our current standard is reflective of the actual data. So we think there was sufficient data when we set our standard in, well, both in 2004 for the goal, and then 2007 for the official State standard. Since that time, there has just been additional information supporting it.

Senator KLOBUCHAR. Dr. Alexeeff, in your written testimony, you talked about pregnant mothers and fetuses and brain development. You mentioned that studies have shown that children's performance in school can be affected. Have there been other effects on children that have been documented?

Dr. ALEXEEFF. Well, the actual way that perchlorate causes an effect is by blocking iodide from being used to make the important hormones for brain development. There is a lot of information on the importance of iodide. If we don't allow our bodies to utilize the iodide that is there, we won't have proper brain development in children. There is more than enough data showing that.

Senator KLOBUCHAR. And this is my last question here. With the California standards, you do look at that, or from other parts of the Country as well, scientific data?

Dr. ALEXEEFF. Well, to a certain extent. We looked at certainly all of the health information that was available. We are aware of the contamination in various parts of the Country, and of course a lot of our drinking water is from the Colorado River, which is one of our major concerns because it is contaminated with perchlorate as well.

Senator KLOBUCHAR. OK. Thank you very much.

Senator BOXER. Thank you, Senator.

Senator Klobuchar has said that she is going to come back, and when I have to leave, she will chair the third panel, so we should have a seamless hearing today.

Senator, thank you so much. You are always such a helpful part of this Committee. I thank you very much.

I ask unanimous consent to enter into the record recent studies describing perchlorate exposure to people and its impact on human health: statements by Professor Daniel Wartenberg and Professor Tom Zoller on TCE and perchlorate; newspaper articles describing White House and Federal agencies' interfering with the creation of protective TCE and perchlorate standards; a letter from EPA's Children's Health Protection Advisory Committee; and a scientific article criticizing EPA's perchlorate remediation goal as being unprotective. So we will put those in the record.

[The referenced documents were not received t the time of print.]

Senator BOXER. Thank you, panelists. I think you have been terrific, very direct, and very helpful.

If our final panel would please come up.

Donna Lupardo is an Assemblywoman in the State of New York; Gail Charnley, Ph.D., HealthRisk Strategies; David Hoel, Ph.D., Professor at the Medical University of South Carolina; and Richard Wiles, Executive Director, Environmental Working Group.

We welcome you all. We are very pleased to have you. I invite you to drink the water if you want to.

So we will start off with Assemblywoman Lupardo from the 126th Assembly District of New York. Thank you very much, Assemblywoman.

STATEMENT OF DONNA A. LUPARDO, ASSEMBLYWOMAN, 126TH DISTRICT, STATE OF NEW YORK

Ms. LUPARDO. Thank you, Madam Chair and members of the Committee for your commitment to this issue and for allowing me to present my remarks on this topic.

First, let me say that I am not a scientist. I am not an epidemiologist. I am simply an advocate for the community that I represent in the New York State Assembly. I represent the 126th District. It includes the city of Binghamton and the towns of Union and Vestal. Located in the town of Union is the village of Endicott, birthplace of IBM and Endicott-Johnson shoes. My remarks today reflect Endicott's long journey into the world of TCE contamination and my own journey to find answers.

Prior to my election, I was a member of the Resident Action Group of Endicott, along with Congressman Hinchey. The group helped raise public awareness about the dangers of vapor intrusion and drinking water contamination. Working together, the Endicott site was reclassified back in 2003 after it was discovered that undergroundwater contamination produced toxic vapors into people's homes and businesses.

I also served as a member of the Stakeholder Planning Committee which met regularly with members of ATSDR and our State's Department of Health and Environmental Conservation.

In Endicott, there are over 480 homes spread out over 300 acres fitted with ventilation systems designed to address chemical vapor intrusion because of a large underground plume of contamination. These vapors are the legacy of the microelectronic industry that once dominated our local economy. Fortunately for Endicott residents, there was a responsible party available. IBM was in a position to assist with the costs of not only the ventilation systems, but with pumping stations, monitoring wells, ambient air testing, and

an air stripper needed to address the contamination of wells that supply drinking water to 46,000 residents in the town of Union, including my own home in Endwell.

In August 2005, the New York State Department of Health released a Health Statistics Review for the Endicott site that documented elevated rates of testicular cancer, kidney cancer, and heart birth defects in the Endicott area. The review found that these elevated rates were statistically significant, meaning that they are unlikely to be due to chance alone. This review validated what residents had been talking about for years. Unfortunately, their fears only grew.

I also serve on the Environmental Conservation Committee in the New York State Assembly. After conducting several hearings around the State, we issued a report in 2006 entitled Vapor Intrusion of Toxic Chemicals: An Emerging Public Health Concern. One finding is particularly relevant to today's hearing.

We found that the New York State air guideline for TCE of 5.0 micrograms per cubic meter of air was not based on the most protective presumptions supported by science. In developing its guidance for TCE, our Department of Health made a number of choices that resulted in a less protective standard, including the choice not to consider epidemiologic studies used by EPA in its 2001 draft assessment, the choice not to use a new and stronger epidemiological study as a source of quantitative values, and the choice not to consider animal studies which show an association between exposure to TCE and testicular cancer, lymphoma and lung cancer based on a lack of human evidence.

As a result, TCE guideline is two orders of magnitude higher than the most risk-based concentrations for TCE in air developed by California, Colorado, New Jersey, and several EPA regional offices which range from .016 to 0.2 micrograms per cubic meter of air. New York also changed its TCE guidelines in 2003 in the middle of the IBM clean-up, leaving many homeowners confused and frustrated because they were no longer eligible for ventilation systems. They went from a 0.22 microgram to their current level of 5.0 micrograms per cubic meter of air.

Our Environmental Conservation Committee strongly recommended that our Department of Health revise its current indoor air guideline for TCE to reflect the most protective assumptions about toxicity and exposure supported by science. We believed that in the face of uncertainty regarding the threat of harm to human health posed by vapor intrusion, that the Department of Health should err on the side of caution and adopt a much more conservative approach. Unfortunately, Madam Chair, they did not.

While we are attempting to address this issue legislatively in New York State, we desperately need Federal leadership on this topic. The Toxic Chemical Exposure Reduction Act would finally provide a national primary drinking water regulation for TCE and an all important reference concentration of TCE vapor that is protective of susceptible populations, along with important health advisories. It would put an end to a confusing hodgepodge of individual State guidelines and arbitrary regulations.

As you said before, Madam Chair, we don't want to legislate this. We are running into resistance trying to legislate it, frankly.

Just a couple of points to wrap up. I am also encouraged that the legislation establishes the integrated risk information system reference concentration of TCE vapor. I am, however, deeply concerned that EPA's new interagency review process will actually increase the challenges that they face in evaluating and regulating chemicals. The IRIS data base could soon become obsolete because of the backlog of ongoing assessments. I hope that the TCE assessment does not fall prey to policy biases that overshadow good science, as you have said many times.

Senator BOXER. I am going to ask you to finish up.

Ms. LUPARDO. Yes.

Finally, the last point, I would be remiss if I did not briefly mention another related matter. It has to do with the OSHA standard. They have set an exposure limit of 100 parts of TCE per million part of air for an 8-hour workday, 40-hour workweek. Surely a separate investigation of workplace exposures is warranted, especially for communities like Endicott where many residents were exposed at home and at work.

Thank you for allowing me to testify. I am deeply grateful for your efforts.

[The prepared statement of Ms. Lupardo follows:]

US Senate Testimony: "Perchlorate and TCE in Water" **May 6, 2008**

New York State Assemblywoman Donna A. Lupardo, 126th District

My name is Donna Lupardo. First, let me say that I'm not a scientist, nor am I an epidemiologist. I am simply an advocate for the community that I represent in the NYS Assembly. I represent the 126th District which includes the City of Binghamton, and the Towns of Union and Vestal. Located in the Town of Union is the Village of Endicott, birthplace of IBM and Endicott-Johnson Shoes. My remarks today reflect Endicott's long journey into the world of TCE contamination and my own journey to find answers.

Prior to my election, I was a member of the Resident Action Group of Endicott (RAGE). Along with Congressman Maurice Hinchey, the group helped raise public awareness about the dangers of vapor intrusion and drinking water contamination. Working together, the Endicott site was reclassified in 2003 after it was discovered that underground water contamination could produce toxic vapors in people's homes and businesses.

I also served as a member of the Stakeholder Planning Committee which met on a regular basis with representatives from ATSDR and the NYS Departments of Health and Environmental Conservation.

In Endicott, there are over 480 homes spread out over 300 acres fitted with ventilation systems designed to address chemical vapor intrusion. These vapors are the legacy of the microelectronics industry that once dominated our local economy. Fortunately, for Endicott residents, there was a responsible party available. IBM was in a position to assist with the costs of not only the ventilation systems, but with the pumping stations, monitoring wells, ambient air testing, and air stripper needed to address the contamination of wells that supply drinking water to 46,000 residents in the Town of Union, including my own home in Endwell.

In August of 2005, the NYS Department of Health (DOH) released a Health Statistics Review for the Endicott site that documented elevated rates of testicular cancer, kidney cancer and heart birth defects in the Endicott area. The review found that these elevated rates were statistically significant, meaning they are unlikely to be due to chance alone. This review validated what residents had been talking about for years. Unfortunately, their fears only grew.

I also serve on the Environmental Conservation Committee of the State Assembly. After conducting several hearings around the state, we issued a report in February of 2006 entitled, "Vapor Intrusion of Toxic Chemicals: An Emerging Public Health Concern." One finding is particularly relevant to today's hearing.

We found that "the New York State air guideline for TCE of 5.0 mcg/m3 was not based on the most protective assumptions supported by science. In developing its guideline for TCE, the Department of

Health (DOH) made a number of choices that resulted in a less protective standard, including the choice not to consider the epidemiologic studies used by EPA in its 2001 draft assessment; the choice not to use a new and stronger epidemiological study as a source of quantitative values; and the choice not to consider animal studies which show an association between exposure to TCE and testicular cancer, lymphoma, and lung cancer based on lack of human evidence. As a result, DOH's guideline is two orders of magnitude higher that the most risk-based concentrations for TCE in air developed by California, Colorado, New Jersey, and several EPA regional offices which range from 0.016 to 0.2 mcg/m3." New York also changed its TCE guidelines in 2003 (from 0.22 mcg/m3 to 5.0 mcg/m3) in the middle of the IBM cleanup leaving many homeowners confused and frustrated because they were no longer eligible for ventilation systems.

The Environmental Conservation Committee strongly recommended that DOH revise its current indoor air guideline for TCE to reflect the most protective assumptions about toxicity and exposure supported by science. We believed that in the face of uncertainty regarding the threat of harm to human health posed by vapor intrusion, that DOH should err on the side of caution and adopt a much more conservative approach. Unfortunately, they did not.

While we are attempting to address this issue legislatively in NYS, we desperately need federal leadership on this topic. The "Toxic Chemical Exposure Reduction Act" that Senator Clinton has introduced in the Senate (and Congressman Hinchey in the House) would finally provide a national primary drinking water regulation for TCE, and an all important reference concentration of TCE vapor that is protective of susceptible populations, along with important health advisories. It would put an end to a confusing hodgepodge of individual state guidelines and arbitrary regulations.

I am also encouraged that the legislation establishes an Integrated Risk Information System (IRIS) reference concentration of TCE vapor. I am, however, deeply concerned that EPA's new interagency review process will actually increase the challenges that they face in evaluating and regulating chemicals. The IRIS database could soon become obsolete, because of the backlog of ongoing assessments. I hope that the TCE assessment does not fall prey to policy biases that overshadow good science.

Finally, I would be remiss if I did not briefly mention another related matter that I would hope you would address. OSHA has set an exposure limit of 100 parts of TCE per million parts of air (100 ppm) for an 8 hour workday, 40 hour work week. 100 ppm equals 500,000 micrograms/cubic meter of air. That's 100,000 times higher than the current New York standard of .5. Surely, a separate investigation of workplace exposures is warranted, especially for communities like Endicott where many residents were exposed at home and at work.

Thank you for allowing me to testify today on this most important topic. On behalf of my constituents, and all the advocacy groups in NYS, I want to express my deepest gratitude for your efforts.

Responses by Donna A. Lupardo to Additional Questions
From Senator Boxer

Question #1: Importance of a Federal Standard

Please explain in detail why it is important for your constituents to install ventilation systems in their homes due to TCE contamination.

My constituents, in the Village of Endicott, need to ventilate their homes because levels of TCE were detected in their indoor air. TCE vapor intrusion is the result of an underground plume of contaminated groundwater associated with the microelectronics industry that once thrived in Endicott. Exposure to TCE has been associated with an increased risk for testicular cancer, kidney cancer and heart birth defects. In fact, health studies in Endicott, conducted by the New York State Department of Health, confirmed that certain clusters were statistically significant – meaning that they are unlikely to be due to chance alone.

If EPA had updated its safety standard TCE exposure and set a strict new standard that considered all types of exposure to TCE, could this have helped your constituents?

Yes. Because there is no clear cut, uniform standard for TCE exposure, states have been left to set their own guidelines. Unfortunately, New York State has a guideline that is not the most protective of public health. The New York State guideline was actually changed while the Endicott site was being mitigated. As a result, many of my constituents were denied vapor intrusion systems.

Responses by Donna A. Lupardo to Additional Questions
From Senator Inhofe

1. Are you aware that TCE currently has a drinking water standard and that the contaminant goal is zero, consistent with other carcinogenetic contaminants?

Yes. That may be the case, but when TCE is present in underground water, it produces a vapor that intrudes into structures posing numerous health concerns. The need for a TCE exposure standard for indoor air is critically important as well.

2. You mention in your testimony that you're concerned that policy biases may over shadow good science. Isn't that exactly what S. 1911 attempts to do by requiring EPA to establish an MCL for TCE regardless if the scientific findings are fully vetted and complete?

We already have a preponderance of scientific evidence to support the policy outlined in the legislation.

Thank you for the opportunity to testify on this critical issue. Please do not hesitate to contact me if I can be of any additional assistance.

Senator BOXER. Thank you very much, Assemblywoman Lupardo. Dr. Charnley.

STATEMENT OF GAIL CHARNLEY, PRINCIPAL, HEALTHRISK STRATEGIES

Ms. CHARNLEY. Thank you for the opportunity to speak with you all today.

EPA has a well-established process for studying drinking water contaminant levels that has been evolving for 30 years and has resulted in one of the safest drinking water supplies in the world. The Safe Drinking Water Act and its amendments reflect the best of Congress' ability to craft statutes that are effective and sensible.

Setting drinking water standards or any other limit on human exposure to chemical contaminants requires balancing the need to be precautionary and protect public health with the need to develop an adequate factual basis to justify regulation. In other words, EPA must act to prevent health risks from drinking water contaminants, but must also determine that regulating contaminants would present a meaningful opportunity to reduce health risk.

There are costs associated both with regulating too soon when health risks turn out to be negligible, and with regulating too late after health risks have occurred. Finding the right balance is what the Safe Drinking Water Act empowers EPA to do.

There are many examples of the challenging process involved in trying to set exposure limits for substances in a world of evolving science. Perchlorate is a perfect example. Until recently, EPA's continued efforts to characterize the hazards of perchlorate have been repeatedly thwarted by peer-review panels. Perchlorate first made it onto EPA's radar screen in 1985 when it was found to be a contaminant of Superfund sites in California. Toxicity data were sparse and a provisional reference dose was adopted by EPA in 1992.

That provisional dose was replaced by a different provisional reference dose in 1995. Peer review of that provisional reference dose concluded in 1997 that it was not adequately supported by data and proposed a toxicity testing strategy. EPA listed it as an unregulated drinking water contaminant of potential concern in 1998 and released a draft risk assessment with yet another provisional reference dose.

Another peer review recommended waiting for the results of the study that had been recommended in 1997. A revised draft risk assessment was released in 2002 that incorporated the new data and proposed a fourth provisional reference dose. Peer review of that reference dose by the National Academy of Sciences resulted in a fifth reference dose, which is the one that was adopted in 2005. Of course, reference doses are advisory, not regulatory.

Meanwhile, what about the costs of regulating versus not regulating perchlorate? The Safe Drinking Water Act requires EPA to establish contaminant levels at which no known or anticipated adverse effects on the health of persons occur and which allows an adequate margin of safety. So let's ask that question: Are known or anticipated adverse effects on health occurring? One approach to answering that question is to compare EPA's reference dose to the levels we are actually exposed to.

The reference dose is the perchlorate exposure level anticipated to be without adverse effects. Based on the data from the Centers for Disease Control, we know that the average exposure to perchlorate in the U.S. is about one-tenth the reference dose and the highest exposures are about one-third the reference dose. Based on CDC and FDA data, our exposure is 10,000 times less than what the National Academy of Sciences concluded would be required to produce adverse effects in healthy adults.

The good news is that the American public is apparently not being exposed to perchlorate levels that are likely to pose a risk to our health. Does that mean we shouldn't regulate perchlorate? Not necessarily. Perchlorate occurs naturally in the environment, but is also a widespread anthropogenic contaminant and probably should be regulated. Fortunately, however, there appears to be no imminent public health threat that justifies regulating in advance of the science.

And of course, just because there is no drinking water standard at present doesn't mean that precautionary risk management measures shouldn't be taken to prevent further contamination, but I think it does illustrate how legislation compelling EPA to regulate perchlorate would run the risk of freezing the standard in place in reaction to politics, not risk-based priorities, and essentially constitutes an environmental earmark.

Former EPA Administrator Bill Reilly referred to this phenomenon as regulating based on moments of episodic panic in reaction to news stories, not science. EPA's landmark 1987 report, Unfinished Business, concluded that its priorities were influenced too much by public opinion and emphasized the desirability of setting agency priorities based on risk where possible. I believe in setting priorities based on science and directing resources where they will have a demonstrable impact on public health, and not in environmental earmarks or symbolic acts that misdirect limited resources without public health benefit.

Thank you very much. I would like to also add to the record a paper that I recently had accepted for publication in a peer-reviewed journal called Perchlorate: Overview of Risks and Regulation.

[The referenced document was not received at time of print.]

[The prepared statement of Ms. Charnley follows:]

Senate Committee on Environment and Public Works
Perchlorate and TCE in Water
6 May 2008

TESTIMONY OF GAIL CHARNLEY PhD[1]

EPA has a well established process for setting drinking water contaminant levels that has been evolving for 30 years, producing one of the safest drinking water supplies in the world. The SDWA and its amendments reflect the best of Congress' ability to craft statutes that are effective and sensible. The Act requires EPA to set priorities and provides flexible direction to consider risks, costs, benefits, feasibility, population subgroups, life stages, and public values in standard-setting.

Setting drinking water standards—or any other limit on human exposure to chemical contaminants—requires balancing the need to be precautionary and protect public health with the need to develop an adequate factual basis to justify regulation. In other words, EPA must act to prevent health risks from drinking water contaminants but must also determine that regulating contaminants would present a meaningful opportunity to reduce health risk. There are costs associated both with regulating too soon when health risks turn out to be negligible and with regulating too late, after health risks have occurred. Finding the right balance is what the SDWA empowers EPA to do.

There are many examples of the challenging process involved in trying to set exposure limits for substances in a world of evolving science. Perchlorate is a perfect example. Until recently, EPA's continued efforts to characterize the hazards of perchlorate have been repeatedly thwarted by peer review panels. Perchlorate first made it onto EPA's radar screen in 1985 when it was found to be a contaminant at Superfund sites in California. Toxicity data were sparse and a provisional reference dose was adopted by EPA in 1992. That provisional reference dose was replaced by a different provisional reference dose in 1995. Peer review of that provisional reference dose concluded in 1997 that it was not adequately supported by data and proposed a toxicity-testing strategy. EPA listed it as an unregulated drinking water contaminant of potential concern in 1998 and released a draft risk assessment with yet another provisional reference dose. Another peer review recommended waiting for the results of the studies that had been recommended in 1997. A revised draft risk assessment was released in 2002 that incorporated the new data and proposed a fourth provisional reference dose. Peer review of that assessment by the National Academy of Sciences resulted in a fifth reference dose, which EPA adopted in 2005. Of course, reference doses are advisory, not regulatory, and perchlorate as a drinking water contaminant remains unregulated by EPA.

Meanwhile, what about the costs of regulating versus not regulating perchlorate? The Safe Drinking Water Act requires EPA to establish contaminant levels at which "no known or

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anticipated adverse effects on the health of persons occur and which allows an adequate margin of safety". So let's ask the question, "Are known or anticipated adverse effects on health occurring due to perchlorate exposure and, if not, is there an adequate margin of safety?" One approach to answering that question is to compare EPA's reference dose to the levels we're actually exposed to. The reference dose is the perchlorate exposure level anticipated to be without adverse effects. Based on data from the Centers for Disease Control, we know that the average exposure to perchlorate in the US is about one-tenth the reference dose and the highest exposures are about one-third the reference dose. Based on CDC and FDA data, our exposure is 10,000 times less than what the National Academy of Sciences concluded would be required to produce adverse effects in healthy adults.

So the good news is that the American public is apparently not being exposed to perchlorate at levels that are likely to pose a risk our health. Does that mean we shouldn't regulate perchlorate? Not necessarily. Perchlorate occurs naturally in the environment but it is also a widespread anthropogenic contaminant and probably should be regulated. Fortunately, however, there is no imminent public health threat that justifies regulating in advance of the science. And, of course, just because there is no drinking water standard at present doesn't mean that precautionary risk management measures shouldn't be taken to prevent further contamination. But I think it does illustrate how legislation compelling EPA to regulate perchlorate would freeze a standard in place in reaction to politics, not risk-based priorities, and essentially constitutes an environmental earmark.

Former EPA Administrator Bill Reilly referred to this phenomenon as regulating based on "moments of episodic panic" in reaction to news stories, not science. EPA's landmark 1987 report *Unfinished Business* concluded that its priorities were influenced too much by public opinion and emphasized the desirability of setting agency priorities based on risk where possible. I believe in setting priorities based on science and directing resources where they will have a demonstrable impact on public health, and not in environmental earmarks—or symbolic acts—that misdirect limited resources without public health benefit. Thank you.

Senator BOXER. Thank you.

You are right. There is politics in the system. GAO just said it is at the risk assessment level that EPA is putting politics into the system and shunting the scientists to the back. You are right on that point. It is not here. It is there. And that is the sad thing.

We are going to skip over Dr. Hoel for a minute because I have so little time. Since I asked Richard Wiles to be here, I would like to hear his statement, if you don't mind, sir.

Go ahead.

STATEMENT OF RICHARD WILES, EXECUTIVE DIRECTOR, ENVIRONMENTAL WORKING GROUP

Mr. WILES. Thank you very much, Madam Chair. I appreciate the opportunity to testify today. I will focus my remarks today on perchlorate.

Perchlorate provides a textbook example of how a corrupted health protection system, where polluters, the Pentagon, the White House and the EPA have conspired to block health protections in order to pad budgets, curry political favor, and protect corporate profits.

With perchlorate, we have reached that rare moment in environmental health when there is nothing left to do but act. All of the pieces needed to support strong health protections are in place. Contamination of food, tap water and breast milk is widespread and well documented. We have a clear understanding of the dangers to infants, children and women of childbearing age.

A strong body of science ties perchlorate exposures to potentially very serious adverse effects on the human population, anchored by a study of more than 1,100 women by the CDC that links perchlorate levels in the population to dangerous low thyroid hormone levels in women of childbearing age.

It is rare that science provides us with such a clear picture of a pollutant's harmful effects, which have been termed consistent with causality by the CDC. It is even more unusual to have this level of evidence and to do nothing. Yet this Administration has failed to act.

Instead of action, we have delay. And worse, as exposed by this Committee last week, we have the institutionalization of a new delay strategy replete with secret White House reviews of science and a shift of public health decision making away from agencies with the expertise to agencies responsible for the pollution.

This begs the question why. The answer is the enormous magnitude of the liability. Simply put, perchlorate is an environmental and public health nightmare of epic proportions for the Department of Defense and its contractors, and rather than address it head-on and protect the public health, they have spent 50 years and millions of dollars trying to avoid it. Ninety percent of all perchlorate in the United States was manufactured for use by the DOD or NASA. Perchlorate contaminates at least 153 public water systems serving about 25 million people in at least 28 States. At least 61 DOD facilities are contaminated with perchlorate, and 35 of those are listed on the national priorities list for Superfund site designation.

Hundreds of miles of the Colorado River are also polluted with perchlorate. This not only means that the tap water of Las Vegas, Phoenix, parts of Los Angeles, and San Diego are laced with perchlorate, but it also means that much of the Nation's winter vegetable crops are contaminated because they are irrigated with perchlorate-polluted water from the Colorado River.

The goal of defense contractors and the Pentagon has been to avoid clean-up of their massive perchlorate mess regardless of the health consequences to the American people. To date, they have been largely successful. It is abundantly clear that without congressional intervention, the public will not receive the protection that is so clearly justified by the science and so obviously necessary given the widespread contamination of food, water and people.

No State health agency that has independently evaluated perchlorate supports the EPA's safe contamination level, the so-called preliminary remediation goal, PRG, of 24.5 parts per billion. California has set a drinking water standard at six parts per billion. New Jersey has proposed one at five parts per billion. Massachusetts has set a safe level at two parts per billion. But most States depend on the EPA.

EPA's own children's health experts have strongly criticized the standard. In March, 2006, the EPA's top independent science advisory group, the Children's Health Protection Advisory Committee, wrote a strong letter to EPA Administrator Stephen Johnson protesting the PRG. In the words of the committee, "The perchlorate PRG does not protect infants and children and should be lowered." The agency ignored the advice.

Five months later, in September 2006, the CDC published a landmark study on the potential health impacts of chronic perchlorate exposure. The study of 1,100 women found a statistically significant dose-dependent association between perchlorate exposure and changes in thyroid hormone levels in all women in the study. The study showed convincingly that measurable adverse health effects from perchlorate exposure are occurring in the American population at levels previously thought to be safe and at exposure levels commonly experienced by the average person.

Madam Chair, members of the Committee, the time to protect the public from perchlorate is now. We commend Senator Boxer for her leadership on the issue and urge this Committee to move quickly on S. 150, the Protecting Pregnant Women and Children From Perchlorate Act.

Thank you.

[The prepared statement of Mr. Wiles follows:]

STATEMENT OF RICHARD WILES

Executive Director
Environmental Working Group

Hearing on

Perchlorate and TCE in Water

Before the
United States Senate
Committee on Environment and Public Works

Tuesday, May 6, 2008, at 10 a.m.

Submitted for the Record

Madame Chairman, distinguished Members of the Committee: my name is Richard Wiles, and I am the Executive Director at the Environmental Working Group (EWG), a nonprofit research and advocacy organization based in Washington, DC and Oakland, California. I would like to start by thanking the members of the Committee for this opportunity to testify today. We sincerely appreciate your interest in this important public health matter.

Perchlorate provides a textbook example of a corrupted health protection system, where polluters, the Pentagon, the White House and the EPA have conspired to block health protections in order to pad budgets, curry political favor, and protect corporate profits.

With perchlorate we have reached that rare moment in environmental health when there is nothing left to do but act. All the pieces needed to support strong health protections are in place: widespread and well-documented contamination of food, tap water and breast milk (FDA 2007, Murray et al. 2008, CADPH 2008, GAO 2005, Kirk et al. 2005, Kirk et al. 2007, Pearce et al. 2007), a clear understanding of the toxicity that identifies infants, children and women of childbearing age as populations at risk (Blount et al. 2006a, Blount et al. 2006b, CHPAC 2006, Ginsberg et al. 2007, MADEP 2006a, NRC 2005, OEHHA 2004), and a strong body of science that ties perchlorate exposures to demonstrable and potentially very serious adverse effects in the human population, anchored by a study of more than 1,100 women by the Centers for Disease Control (CDC) linking perchlorate levels in the population to dangerously low thyroid hormone levels in women of childbearing age (Blount et al. 2006a, Ginsberg et al. 2007).

It is rare that science provides us with such a clear picture of a pollutant's harmful effects, which have been termed "consistent with causality" by CDC scientists. It is even more unusual to have this level of evidence and do nothing.

Yet this Administration has failed to act.

Instead of action we have delay, and worse, we have the institutionalization of a new intergovernmental delay strategy replete with secret White House reviews of science and the shift of public health decision making away from agencies with the expertise, to agencies responsible for the pollution.

This begs the question, why? The answer is the enormous magnitude of the liability. Simply put, perchlorate is an environmental and public health nightmare of epic proportions for the Department of Defense (DoD) and its contractors, and rather than address it head-on, they have spent 50 years and millions of dollars trying to avoid it.

Ninety percent of all perchlorate in the U.S. was manufactured for use by DoD or NASA (GAO 2004). Perchlorate contamination of soil or water has been found in 35 states and the District of Columbia, with known contamination of 153 public water systems, serving about 25 million people in 28 states (GAO 2005). At least 61 DoD facilities are contaminated with perchlorate; 35 of these are listed on the National Priorities List for Superfund site designation, water at 29 of these is contaminated above the EPA "safe dose" of 24.5 parts per billion (EPA 2006a). Fifteen of the remaining 26 non-NPL listed sites are also contaminated above the EPA safe dose.

Hundreds of miles of the Colorado River are polluted with perchlorate. This not only means that the tap water of Las Vegas, Phoenix, Los Angeles and San Diego are contaminated, but also that the nation's winter vegetable crops – grown in the Imperial Valley of California and southwestern Arizona and irrigated with contaminated water – often contain high levels of perchlorate (EWG 2003, FDA 2007).

The goal of defense contractors and the Pentagon has been to stop promulgation of drinking water health protections that would force them to clean up their perchlorate mess, regardless of the health consequences for the American public. To date they have been successful.

Polluters and the Pentagon Collude to Block Public Health Protections

Perchlorate is a component of solid rocket propellant (fuel) that has been known to contaminate groundwater at Defense Department facilities and manufacturing locations for at least 50 years (CADWR 1964, GAO 2004, JAWA 1957). Perchlorate inhibits the uptake of iodine to the thyroid gland, which is essential to production of normal amounts of thyroid hormone. Thyroid hormone is critical for normal growth and development and inadequate levels during fetal development and infancy can result in intellectual deficits that persist throughout life (Haddow et al. 1999, Pop et al. 1999, Zoeller 2006).

In 1962, the Manufacturing Chemists Association (MCA, now known as the industry lobby group the American Chemistry Council) formed a chemical propellant toxicity "task group", which included representatives from four companies in the solid propellant industry. Members of this committee participated in a Department of Defense working group called the Inter-Agency Chemical Rocket Propulsion Group (ICRPG), which was, according to the MCA memos, "the first time that a government agency has asked

representatives of industry to participate in this type of committee activity." The goal then was the same as now, to avoid health protections that interfered with business. As put by the MCA "our active participation in the ICRPG program should be of great help in establishing safe but realistic rules and regulations without unnecessary and excessive restrictions to industrial operations" (MCA 1962, 1965).

Thirty years later, as accumulating evidence of contamination and potential health effects raised the specter of tight drinking water standards, industry formed the Perchlorate Study Group (PSG), consisting of Aerojet, Alliant Techsystems, American Pacific/Western Electrochemical Company, Atlantic Research Corporation, Kerr-McGee Chemical Corporation, Lockheed Martin, Thiokol Propulsion Group, and United Technologies Chemical Systems. In 1992, in cooperation with the Air Force, the PSG began a high-stakes campaign to block or weaken proposed standards that has continued to this day (EWG 2001).

An extraordinary report by Environment California documents in detail the multi-million dollar, decade-long PSG campaign to manipulate science in favor of perchlorate polluters and the military (EC 2006). The agenda of PSG as expressed in an internalAerojet presentation was "to provide EPA witha scientific based argument to justify a higherRfD (safe dose) and thus a more reasonable remediationstandard." This is not a scientific research agenda, this is science designed and paid for to produce a specific outcome – a "higher" or weaker, RfD that allows higher levels of pollution in drinking water.

For the past 15 years, the PSG, DoD, and industry polluters – more recently in collusion with the White House –have run an aggressive misinformation campaign that published bogus science, blocked good science, stacked independent science panels, and even went so far as to intimidate scientific journals to rewrite articles when they thought they might be "damaging" to their position.

- **1999: DoD and the Air Force block EPA study of perchlorate in food**

  The EPA and the Air Force were key players on an inter-agency committee formed in 1998 to evaluate potential health risks from perchlorate contamination. In April of 1999 this committee met to set research priorities, deciding that a study looking at the potential uptake of perchlorate into food crops was top priority, followed by research into effects on wildlife habitat. These two studies would divide half a million dollars in funds from the Army. But the crop study was never done (Danelski and Beeman 2003).

  In June of 1999, Col. Dan Rogers of the Air Force wrote to Steven McCutcheon at the EPA's National Exposure Laboratory after his group found that greenhouse lettuce absorbed and concentrated perchlorate from irrigation water. In his email, Rogers advised McCutcheon to halt some of the lab's ongoing efforts, writing: "PLEASE, PLEASE, PLEASE do not arrange for taking or accepting samples from any of the Western states." Ninety percent of lettuce consumed in the U.S. between December and March is grown in California and Arizona with Colorado River water that is contaminated with perchlorate (EWG 2003). A few months later, Rogers wrote to EPA officials stating that no agency had permission to publish articles

on perchlorate without "complete agreement from all the executive members" of the inter-agency committee, including the Air Force, adding that "any attempt to publish would not be looked upon favorably by the DoD" (Danelski and Beeman 2003).

Years later, the Food and Drug Administration finally conducted tests on perchlorate in food and found that perchlorate contamination is widespread in the food supply (FDA 2007).

- **2002: Perchlorate Study Group tampers with article in a leading academic journal**

  When the nationally known science writer Rebecca Renner was assigned to write a story about the findings of the pivotal toxicity study on perchlorate, known as the Greer study, she wrote a piece that put the study's findings of no effects at low doses in context by also reporting the EPA's concerns that perchlorate might harm the developing fetus, and that many animal studies pointed to concerns at low levels of exposure.

  When the perchlorate industry's consultants got an advance copy of it, they concluded that the article was "potentially very damaging" to their clients and pressured the journal to rewrite it, without the consent of the author (Danelski 2004).

  According to industry documents and invoices obtained through litigation, industry consultants went back and forth with the journal's editors through at least five drafts of the article, and ultimately leveraged publication of an article that painted perchlorate in a highly favorable light. Renner was entirely unaware that her piece had been rewritten.

  Several years later, when the documents came to light and she understood what had happened, Renner was stunned. "My name was misused, and my journalistic reputation was misused," she told the Riverside Press Enterprise. "It is outrageous that my article was changed by people working for industries that have a totally vested interest and a huge stake in the outcome of this issue, and that it was changed in a covert way" (Danelski 2004).

- **2003: White House stacks National Academy of Sciences (NAS) panel with industry consultants**

  The White House, the Department of Defense, and perchlorate industry consultants had undue influence on what should have been a purely scientific review of EPA's perchlorate risk assessment by the NAS. Documents obtained by Natural Resource Defense Council through public records request show that senior White House political officials with no scientific expertise actively participated in reviewing the scientific charge sent to the National Academy of Sciences on perchlorate and that White House and Pentagon officials were involved in discussions about who should be appointed to the NAS panel (NRDC 2005).

  These groups were successful in appointing a highly biased panel, which initially included a paid industry expert witness and two other paid consultants to the

perchlorate industry. While the litigation consultant was forced to resign, the two other consultants remained on the panel. Ultimately the NAS panel recommended a safe exposure level for perchlorate that has not been supported by a single state regulatory review or any subsequent scientific research (CHPAC 2006, EWG 2007, Ginsberg et al. 2005, Ginsberg et al. 2007, MADEP 2006a, NRC 2005, NRDC 2005, OEHHA 2004).

- **2005: EPA and the NAS rely on a single, underpowered, industry funded study to set "safe" exposure level. Subsequent peer-reviewed research shows that the study authors obscured adverse effects at low doses**

  A single, tiny, industry-funded study, known as the "Greer study," is the basis of the EPA's proposed safe dose level for perchlorate. It wasn't supposed to be; EPA originally wanted also to include the results of animal studies that involved dosing pregnant rats with perchlorate to determine its effects on critical periods of development. But incredibly, the National Academy of Sciences decided that the Greer study – which dosed 37 healthy adults with perchlorate for just 14 days, and did not monitor iodide intake – was sufficient on its own to form the basis of a drinking water standard. This, in spite of the study's obvious shortcomings, including the fact that an experiment on healthy adults provides no basis for understanding perchlorate's effects on infants and children, and the fact that a study with just 37 subjects, and a very short two week duration, has very limited statistical power. Even worse, the NAS did not perform its own evaluation of the raw data, but instead relied on the industry's interpretation of the study results. (Danelski 2005, EWG 2006)

  The study's authors claimed that their data showed no effects from perchlorate in the lowest dose group. But a subsequent EPA analysis found that the study's design was so weak it had virtually no chance of detecting any kind of statistically significant effect at that dose. A peer-reviewed study published in 2005 showed that the industry's analysis of the data obscured important findings (Ginsberg and Rice 2005). These independent scientists found that four of the seven individuals in the lowest dose group had perchlorate-related reductions in iodide uptake, indicating that there was in fact an effect at this dose level. The authors noted that the Greer study data point towards "a more sensitive subgroup," a conclusion that was confirmed by the 2006 CDC study finding perchlorate-related effects on thyroid hormone levels from far lower exposures to perchlorate in women with low iodide intake (Blount et al. 2006a, Ginsberg and Rice 2005).

This campaign to distort the science and delay regulation has been largely successful. Although two states, California and Massachusetts, have set drinking water standards for perchlorate that are more protective than what DoD and perchlorate polluters want, at the federal level there has been no meaningful action to protect public health from perchlorate in water or food.

In fact, since 1996 when the Safe Drinking Water Act was last amended, the EPA has not finalized a single new health standard for any contaminant, except where ordered by the courts or the Congress (Grumbles 2007). Beginning in 2002 and every

year for the past seven years, DoD has sought a congressional exemption from all state and federal environmental laws for uses of chemical constituents in military munitions, including perchlorate (Christen 2003, CRS 2006, GAO 2008, Seelye 2002, Thacker 2004).

In 2007, the EPA formally decided not to adopt a drinking water standard for perchlorate. Unless ordered by Congress the agency is not likely to develop one until well into the next decade (EPA 2007, EPA 2008a). The EPA's current position is that it is "undertaking efforts to help the Agency determine if regulation of perchlorate in drinking water would represent a meaningful opportunity for reducing risks to human health" (EPA 2008b).

Perchlorate contaminates the drinking water of about 25 million Americans in 28 states (GAO 2005). Although two states with significant contamination problems have adopted enforceable drinking water standards, California (6 parts per billion), and Massachusetts (2 ppb), the other 26 depend on the EPA (CADPH 2008, MADEP 2006b). Most of these 26 remaining states do not have the resources or expertise either to develop health standards or to enforce them, particularly in the face of combined opposition from the Pentagon and defense contractors. These states depend on the U.S. EPA to set health standards to protect them from potent pollutants like perchlorate. This is clearly a "meaningful opportunity for reducing risks to human health," but EPA has chosen not to act.

Tap Water is the Top Public Health Priority

Perchlorate contaminates food as well as water. A 2008 study by scientists at the U.S. Food and Drug Administration (FDA) found that three quarters of 285 commonly consumed foods and beverages are contaminated with perchlorate (Murray et al. 2008). The investigation found perchlorate in 90 percent of lettuce samples and 101 out of 104 bottled milk products. Two-year-olds appear to be particularly vulnerable because they eat substantial amounts of food relative to their small size. According to FDA's results, every day, the average two-year-old will be exposed to more than half of the EPA's safe dose of perchlorate from food alone (EWG 2008, Murray et al. 2008).

EPA has repeatedly cited uncertainty about food contamination with perchlorate as a reason to delay health protections for tap water exposures (EPA 2007, Grumbles 2007). The rationale for this position has always been obscure, but in the face of these new data from FDA, food contamination can no longer be considered an obstacle, rather it must be considered the primary reason to reduce tap water exposures.

Cleaning up perchlorate pollution in tap water is the critical first step to protecting children's health from the contaminant. This is in part because it is readily achievable, but also because in most cases where tap water is contaminated it accounts for at least half, and in many cases the vast majority of exposure to perchlorate (EWG 2008).

Perchlorate contamination of food is extremely difficult to control. Water exposures, in contrast, are readily controllable. The statutory framework to control food exposures is muddled, whereas the legal framework to control drinking water exposures is

clear. From a practical perspective, it is not obvious how to reduce food exposures because the source of a substantial portion of food contamination is not known. With water the clean up technology is identified, straightforward, and effective. And ironically, cleaning up one major polluted water source, the Colorado River, will substantially reduce perchlorate levels in some of the most contaminated foods.

EWG's analysis of FDA's new data shows that very small exposures to perchlorate, as low as one part per billion (ppb) in tap water, could expose some children to an unsafe dose of the compound (EWG 2008). In this light, every proposed or final drinking water standard fails to protect at least some two-year-olds from routine, daily, unsafe exposure to perchlorate when food and water exposures are combined. A two-year-old of average size could exceed EPA's safe exposure level for perchlorate (the reference dose, or RfD) by drinking water with just 4 ppb of perchlorate contamination. A smaller child drinking more than an average amount of water will face the same risks from far lower amounts of perchlorate (EWG 2008).

A recent US Government Accountability Office (GAO) report found that 28 states had at least one public water system that was contaminated with perchlorate at 4 ppb or over (GAO 2005). New Jersey has proposed a tap water standard of 5 ppb, California allows up to 6 ppb, and the U.S. EPA has proposed a limit of 24 ppb, none of which would protect two-year-olds from being chronically overexposed to perchlorate.

Children are More Sensitive to the Harmful Effects of Perchlorate

Not only do children have higher exposures to perchlorate when compared with adults, they are also particularly susceptible to its adverse effects. Perchlorate acts by inhibiting the thyroid gland from taking up iodine from circulating blood. Because iodine is the building block for thyroid hormone, perchlorate exposure can result in decreased thyroid hormone production by the thyroid gland. Adequate circulating levels of thyroid hormone are critical to maintaining normal growth and brain development during childhood. Inadequate levels of thyroid hormones can result in stunted growth and delays in intellectual development (CHPAC 2006, Ginsberg et al. 2007, Haddow et al. 1999, Pop et al. 1999, Zoeller et al. 2002, Zoeller 2006).

Children are also especially vulnerable to perchlorate because of their unique physiology. Perchlorate acts as an inhibitor of iodine uptake by the thyroid gland. Because of their rapid growth and development, children require more iodine per unit of body weight than adults. In fact, young children require 3 times more iodine per kilogram of body weight than non-pregnant adults (WHO 1998). A thyroid toxin like perchlorate that impacts the uptake of iodine by the thyroid gland will have a greater impact on children than adults.

Children could be protected from these effects by a strong federal drinking water standard for perchlorate. But the EPA has decided that this is not needed. Meanwhile dangerous exposures continue.

EPA "Safe" Dose for Perchlorate is not Really Safe

No state health agency that has independently evaluated perchlorate toxicity has agreed that the EPA's estimate of a safe exposure level for superfund sites, the so-called Preliminary Remediation Goal (PRG) of 24.5 parts per billion (ppb), is an appropriate or safe exposure value for drinking water (EPA 2006, OEHHA 2004, MADEP 2006). California has set a drinking water standard at 6 ppb, New Jersey has proposed one at 5 ppb, and Massachusetts has set a safe level for perchlorate at 2 ppb.

EPA's own children's health experts concur. In March, 2006, the EPA's top independent scientific advisory group on children's health, the Children's Health Protection Advisory Committee, wrote a very strong letter to the EPA Administrator arguing that the 24.5 ppb PRG is not protective of children (CHPAC 2006). The agency ignored the advice of its own children's health experts and in May of 2006 responded that it was standing by the guidance (EPA 2006b).

In September of 2006, the Centers for Disease Control and Prevention (CDC) published the first major epidemiological study on the potential health impacts of chronic perchlorate exposure. This landmark study of 1,100 women, which correlated measured perchlorate in urine with thyroid hormone levels, found a statistically significant, dose-dependent association between perchlorate exposure and changes in thyroid hormone levels in all women in the study (Blount et al 2006a). This study showed convincingly that measurable adverse health effects from perchlorate exposure occur at levels previously thought to be safe, and at exposure levels commonly experienced in the population.

The effects on thyroid hormones were particularly pronounced in women with lower iodine intake. Among these women, a urinary perchlorate level of only 5 parts per billion was associated with a 16 percent change in thyroid hormone levels, compared to the median level found in the study. The authors noted that 36 percent of U.S. women have iodine intakes in the range identified as "lower" in the study (Blount et al 2006a). For about 1 in 10 of these women, if they were exposed to 5 parts per billion of perchlorate in drinking water, the resulting hormone disruption would require treatment for sub-clinical hypothyroidism, according to a consensus of clinical endocrinologists (Cooper 2004, EWG 2006).

In response to questions from Republican Congressmen Joe Barton and John Shimkus of the House Committee on Energy and Commerce challenging these findings, the CDC was extraordinarily clear: "We do not think that confirmatory analysis is necessary to validate Blount's analysis of the NHANES data," showing that perchlorate exposure is tightly linked to lowered thyroid levels in one third of American women (CDC 2007). Adding that, "Although we understand that conclusions of causality can rarely be drawn based on a single study, when viewed within the context of the available literature, the findings of the Blount study are consistent with causality."

Although the EPA assumes that exposure to 24.5 ppb perchlorate in drinking water will have no adverse effects, the CDC study established that much lower exposures were having measurable, harmful effects on women's thyroid hormone levels (Blount et al. 2006a). EPA's safe dose, or RfD, is based on questionable interpretation of

perchlorate exposure in 36 adults. The CDC study is based on real-world measured perchlorate levels in more than 1,100 women, the population of concern.

Although the CDC study did not look at perchlorate exposure in children, the findings are worrisome because children are especially vulnerable to perchlorate. The FDA study of perchlorate in food shows that children have higher baseline exposure to this contaminant from food when compared with adults (Murray et al. 2008). The combined evidence from the FDA and CDC studies shows that young children have daily perchlorate exposures from food at levels that have been shown to cause statistically significant changes in thyroid hormone levels in women with lower iodine levels (Blount et al. 2006, Murray et al. 2008, EWG 2008). This is especially concerning because any decrease in thyroid hormone levels in children can disrupt normal growth and development (CHPAC 2006, Ginsberg et al 2007, Zoeller et al 2002). If these children live in any of the 28 states in which drinking water is contaminated with perchlorate, their exposure is even greater.

Trichloroethylene, or TCE

While my testimony has focused on perchlorate, I do want to touch on trichloroethylene (TCE). TCE is a colorless, liquid metal degreaser with military, industrial, maintenance, and consumer uses. According to ATSDR, TCE is pervasive in the environment and has been found in water systems, foods and the air. According to ATSDR, inhaling or drinking TCE can lead to disorientation, coma and death. The National Toxicology Program has found that trichloroethylene is "reasonably anticipated to be a human carcinogen," the International Agency for Research on Cancer has determined that trichloroethylene is "probably carcinogenic to humans," and the National Academies of Science has found that TCE is associated with cancer in humans. TCE has also been linked to neurotoxic, developmental, reproductive and teratogenic effects (ATSDR 2003, NRC 2006).

Like perchlorate, EPA delayed setting a safe drinking water standard for TCE for years, needlessly exposing the public to this dangerous chemical. Unlike perchlorate, EPA did finally set a safe drinking water standard of 5 ppb for TCE in 1989, ten years after the issuance of nonenforceable guidance. Only then did DoD begin to take action to control TCE (Stephenson 2007). Unfortunately, the last two decades of science have shown us that the current drinking water standard does not protect public health and must be lowered.

Congressional Action is Needed

This testimony and the attached timeline document a 50-year orchestrated campaign by the Pentagon and perchlorate polluters, later joined by the White House and ultimately the EPA, to avoid public health protections from perchlorate at all costs.

It is abundantly clear that without congressional intervention the public will not receive the protection that is so clearly justified by the science, and so obviously

necessary given universal human exposure and clearly identified high-risk populations including infants, children, and women of child-bearing age and their babies.

Environmental Working Group commends Senator Boxer for her leadership on this issue and strongly urges this Committee to move quickly to pass *The Protecting Pregnant Women and Children From Perchlorate Act of 2007*, S. 150, and Senator Clinton's *Toxic Chemical Reduction Act of 2007*, S.1911. We can delay no longer – the time for action is now.

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Responses by Richard Wiles to Additional Questions
From Senator Boxer

1) Please describe in detail the extent of people's exposure to perchlorate in the U.S. and in particular, exposure of infants and children.

Exposure to perchlorate is widespread among the U.S. population; in a recent study by scientists at the CDC, detectable levels of perchlorate were found in the urine of every one of 2,820 U.S. residents (ages 6 and older) in a nationally representative sample (Blount et al. 2007). In this same study, it was found that urinary perchlorate levels in children ages 6 to 11 were 1.6 times higher than levels in adults, confirming that children have higher perchlorate exposures than adults. To my knowledge, there has not been extensive testing of urinary perchlorate levels in infants and children under the age of six.

There are also three studies from CDC and academic scientists published in the last several years in which samples of breast milk from different parts of the country were tested for perchlorate. Every single sample of breast milk in all three studies tested positive for perchlorate. While this is startling in itself, what is more troubling is that average levels in breast milk in these studies would expose a significant number of breast-fed infants to perchlorate levels above the EPA's "safe" dose or RfD (Kirk et al. 2005, Kirk et al. 2007, Pearce et al. 2007). Taken as a whole, these studies suggest that perchlorate exposure is ubiquitous among the U.S population, with exposure levels highest among breast-fed infants and children.

2) **In your opinion, what do the latest study from the Food and Drug Administration on perchlorate levels in food, and the latest CDC studies on perchlorate tell us about potential threats to pregnant women, infants, and young children?**

A recent study from the FDA found that three quarters of 285 commonly consumed foods and beverages are contaminated with perchlorate (Murray et al. 2008). According to the study, every day the average two-year-old is exposed to more than half of the EPA "safe" dose (RfD) of perchlorate from food alone. This means that young children who live in communities in the 28 states where perchlorate has also been found in tap water could potentially have dual sources of exposure; an EWG analysis of the FDA data found that perchlorate concentrations as low as 4 parts per billion (ppb) in tap water could expose the average two-year-old to levels that exceed the EPA "safe" dose (RfD) (EWG 2008). Young children are particularly vulnerable to perchlorate exposure from food and tap water contamination because they eat and drink substantial amounts of food and water relative to their small size. In other words, relative to their size and weight, they eat and drink more than the average adult.

A recent study from the CDC also raises concerns about perchlorate exposure among women of childbearing age; in this study, CDC scientists analyzed both perchlorate and thyroid hormone levels in more that 1,000 American women (Blount et al. 2006). They found that in those women with lower iodine levels (one third of American women), perchlorate exposure far below the EPA RfD was associated with significant changes in thyroid hormone levels. For a subset of women in the study with lower iodine levels, exposure to perchlorate as low as 5 ppb in drinking water was associated with decreases in thyroid hormone levels to the extent that these women would require treatment with thyroid hormone if they became pregnant in order to prevent abnormal brain development in their fetus. When the findings from this study are extrapolated to the U.S. population, EWG analysis finds that 2 million women of childbearing age are at risk for abnormal thyroid hormone levels during pregnancy (EWG 2006).

3) In your opinion, why has it taken EPA this long to create a perchlorate drinking water standard? Is it really due to scientific uncertainty?

In EWG's opinion, the delay in setting a perchlorate drinking water standard has nothing to do with scientific uncertainty. In fact, all the pieces needed to support strong health protections are in place: widespread and well-documented contamination of food, tap water and breast milk (FDA 2007, Murray et al. 2008, CADPH 2008, GAO 2005, Kirk et al. 2005, Kirk et al. 2007, Pearce et al. 2007), a clear understanding of the toxicity that identifies infants, children and women of childbearing age as populations at risk (Blount et al. 2006, Blount et al. 2007, CHPAC 2006, Ginsberg et al. 2007, MADEP 2006, NRC 2005, OEHHA 2004), and a strong body of science that ties perchlorate exposures to demonstrable and potentially very serious adverse effects in the human population, anchored by a study of more than 1,100 women by the Centers for Disease Control (CDC) linking perchlorate levels in the population to dangerously low thyroid hormone levels in women of childbearing age (Blount et al. 2006, Ginsberg et al. 2007).

It is rare that science provides us with such a clear picture of a pollutant's harmful effects, which have been termed "consistent with causality" by CDC scientists. It is even

more unusual to have this level of evidence and do nothing. Yet this Administration has failed to act.

This begs the question, why? The answer is the enormous magnitude of the liability. Simply put, perchlorate is an environmental and public health nightmare of epic proportions for the Department of Defense (DoD) and its contractors, and rather than address it head-on, they have spent 50 years and millions of dollars trying to avoid it. For the past 15 years, the Perchlorate Study Group, DoD, and industry polluters – more recently in collusion with the White House – have run an aggressive misinformation campaign that published bogus science, blocked good science, stacked independent science panels, and even went so far as to intimidate scientific journals to rewrite articles when they thought they might be "damaging" to their position. My testimony and attached timeline detail the 50-year effort at delay and distortion.

Responses by Richard Wiles to Additional Questions
From Senator Inhofe

1) Mr. Wiles, if one assumes that the CDC report is correct, then perchlorate has been found at very small levels in virtually all of us. However, according to the UCMRI data, it is only in 4 percent of the nation's drinking water systems. Isn't it premature to cast the blame and all of the burden on the nation' s drinking water systems when based on CDC and EPA data, most of the perchlorate exposure is coming from other sources?

According to a 2005 GAO report, perchlorate contaminates tap water in 28 states nationwide (GAO 2005). This leads to dual perchlorate exposure for tens of millions of people across the country where tap water contamination compounds baseline food exposures. While EWG recommends that FDA take action to decrease perchlorate exposure from food, contaminated tap water is a major source of perchlorate exposure for residents of these 28 states, and it is one that is easily identifiable and readily reduced. A drinking water standard that takes into account the most recent CDC data and widespread exposures from food contamination is a public health measure that has the potential to benefit millions of people.

Children would especially benefit from a health-protective drinking water standard. An EWG analysis of recent FDA data found that perchlorate concentrations as low as 4 parts per billion (ppb) in tap water, when added to food sources could expose the average two-year-old to perchlorate levels that exceed the EPA "safe" dose (RfD), which may not be protective enough in the first place (EWG 2008). Young children are particularly vulnerable to perchlorate exposure from food and tap water contamination because they eat and drink substantial amounts of food and water relative to their small size.

In addition, the available data on perchlorate in drinking water are based on purely voluntary testing of drinking water by local and state governments; there is no requirement to monitor perchlorate in drinking water. Despite the fact that concerns about perchlorate's effects on public health first surfaced in the 1960's, and that perchlorate has been listed on EPA's candidate contaminant list since it was first issued

in 1998, EPA has refused to regulate perchlorate in drinking water and, thus, there is no requirement that it be monitored. The truth is that we really have no idea of the extent of perchlorate contamination in our drinking water supplies. We do know, however, that adopting a tough drinking water standard is the most important single step that can be taken to protect millions from the known harmful effects of perchlorate. To fully understand the breadth of the problem, EPA must require nationwide monitoring of perchlorate in drinking water.

2) The American Thyroid Association (ATA), a professional society of 900 U.S. and international physicians and scientists who specialize in the research and treatment of thyroid diseases, reached a different conclusion about the NAS study. The ATA stated that "the NAS report is a solid review of the existing literature and the resultant recommendations appear sound being based on thorough interpretation of the available scientific data." In commenting on the CDC Blount study, on which you rely heavily in your testimony, the ATA states that "[t]hese findings are intriguing, although several features of the study may limit the immediate application to guidelines for perchlorate exposure standards." The ATA also states that "further laboratory information is necessary before the implications of the findings can be understood." Why should I believe your organization's scientific conclusions as to the health effects of perchlorate over those of the professionals at the American Thyroid Association and those of the National Academies of Science?

Since the release of the NAS report in 2005, several studies from CDC, FDA, and academic scientists have added significantly to our body of knowledge regarding perchlorate exposure among the U.S. population (Blount et al. 2006, Kirk et al. 2005, Kirk et al. 2007, Pearce et al. 2007, Murray et al. 2008, Blount et al. 2007). The important points from these studies include:

- Perchlorate exposure appears to be widespread among the US population, with exposures higher among children when compared with adults.
- Studies of breast milk suggest widespread contamination with perchlorate.
- Women with lower iodine levels appear to be particularly susceptible to the thyroid disrupting effects of perchlorate exposure.
- In women with lower iodine levels, exposure to perchlorate at levels far below the EPA RfD are associated with significant changes in thyroid hormone levels.
- Perchlorate widely contaminates food, resulting in dual perchlorate exposures among residents of 28 states where the chemical has also been found in tap water.

At this point, the NAS report is simply out of date with the current body of science related to perchlorate. In addition, the NAS relied heavily on a single industry funded study (the "Greer" study) to set a "safe" exposure level and subsequent peer-reviewed research shows that the study authors obscured adverse effects at low doses (Greer et al. 2002, Ginsberg and Rice 2005). Independent scientists who reviewed this industry funded research note that "the data of Greer et al point toward a more sensitive subgroup"

(Ginsberg and Rice 2005); however, this was never recognized by the study's authors, although a subsequent CDC study has identified a subgroup that is particularly vulnerable to perchlorate, namely the one third of American women with lower iodine levels (Blount et al. 2006).

3) As I understand it, having an iodine sufficient diet is one way to help counteract the effects of perchlorate on the human body and that this iodine counter transfer to breast milk as well. Yet, on April 25, 2007, Dr. Anila Jacob, an internist representing Environmental Working Group testified before the House Energy and Commerce Subcommittee on Environment and Hazardous Materials that - not withstanding expert testimony from a thyroid specialist - that iodine supplements are not sufficient and that mothers should not breast feed their children due to potential perchlorate exposure. Further, Environmental Working Group has waged a historical campaign against the use of chemicals in the production of food, yet organically-grown produce is known to have perchlorate on it. Finally, you and others at Environmental Working Group have been quoted by in the press and on Environmental Working Group's website as urging parents not to formula feed (because of bottles and protective coatings on cans). Mothers are rightly confused by Environmental Working Group' s inconsistent claims against breast feeding and formula feeding and the use of organic foods. Tell me, in the opinion of Environmental Working Group, what should America' s infants be fed?

You mention that the science is settled, but omit a study by the American Thyroid Association, a group of medical doctors specializing in thyroid function, which used a state's public funds and the NAS that contradict your findings. Are you aware of any published and peer reviewed scientific studies about what effects, if any, occur on an infant who is breast feeding based upon perchlorate exposure. If so, please share them with the Committee.

Dr. Jacob noted in her testimony that the status of iodine nutrition in the United States has a direct bearing on the susceptibility of the population to perchlorate; this is borne out by the CDC findings that show that women with lower iodine levels appear to be particularly sensitive to perchlorate. In her testimony, she does not advocate for increased iodine supplementation for the general population to counteract the effects of perchlorate exposure for the following reasons:

- CDC scientists noted in a recent analysis that iodine nutrition for the country is considered to be adequate (Caldwell et al 2005). Mandating additional iodine for the entire population could lead to overexposures and potentially significant adverse health effects.
- The Public Health Committee of the ATA, in 2006, recommended that pregnant women take prenatal vitamins that contain 150 ug of iodine but did not recommend increased iodine supplementation for the general population (ATA 2006).

EWG would like to note that while an iodine sufficient diet is one way to help counteract

the effects of perchlorate on the human body, the most health protective measure would be to prevent exposure in the first place and a stringent drinking water MCL could help do this.

While Dr. Jacob also brought up concerns about perchlorate contamination of breast milk, she did not recommend anywhere in her oral or written testimony that mothers should not breast feed their infants. In fact, EWG has consistently maintained that breast milk is the best food for infants. Public health officials and the Congress, in turn, should do everything possible to ensure that contaminants like perchlorate do not find their way to breast milk. Three different studies from independent scientists have found perchlorate in every sample of breast milk tested. A health protective MCL for drinking water is an effective means of decreasing this contamination.

While EWG has made recommendations about the types of formula packaging that would decrease a baby's exposure to the potent endocrine disruptor, bisphenol A, we encourage all mothers to breast feed their babies. Our formula recommendations are intended to assist parents who are unable to breast feed their infants.

I am unaware of the ATA study to which you are referring; I would appreciate it if the reference for the study could be forwarded to me and I would be happy to look at it.

As far as I am aware, there have not been any studies looking at health effects of perchlorate exposure on breast-fed infants. However, three independent studies consistently found perchlorate in breast milk; the mean perchlorate levels in each of these studies would expose an infant to levels that exceed the EPA RfD. In addition, the vast majority of infants in these studies would be exposed to perchlorate levels that caused significant changes in thyroid hormone levels in women with lower iodine levels.

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Senator BOXER. Thank you, sir.

Now, here is where we are. I am going to turn the gavel over to Senator Klobuchar, and Dr. David Hoel has not spoken yet. So after that point, it would go to you and then back and forth.

But I just want to say to this panel, all, thank you so very much for being here and helping us grapple with these very serious matters. Thank you very much.

Senator KLOBUCHAR.

[Presiding.] Dr. Hoel.

STATEMENT OF DAVID G. HOEL, PROFESSOR, MEDICAL UNIVERSITY OF SOUTH CAROLINA

Mr. HOEL. Thank you very much. It is an honor to be here.

I haven't testified now for many years, now that I have been at the university, which I should say for 20 years I was at the National Institute of Environmental Health Sciences. I was the Director of Risk Assessment, and that is the institute for the environment within the National Institutes of Health.

I primarily now work with radiation health effects, but have paid some attention to the chemical issues. I was a member of the SAB's panel on perchlorate and the SAB's panel on TCE, as well as a peer reviewer for the National Academies' report on TCE. So I have a little knowledge of what is going on there.

I would like to talk to you briefly about the process of setting levels for carcinogens that are used by IRIS or the EPA currently, and how these approaches are different from what is going on somewhat in Europe in the World Health Organization and so on.

Now, if we take TCE, which I will talk about, and the cancer of TCE, it is primarily kidney cancer, according to the Academy, that is the driver among the cancers. Liver cancer is equivocal and they dismissed lung cancer and so on. But taking the kidney cancer, when EPA did evaluate this and set their levels, they considered three studies—a Finnish worker study, a German worker study, and a rat study—and came up with three levels. The problem is each level disagreed by a factor of 100.

So the difference between the lowest and the highest was a factor of 10,000, which wouldn't give you much confidence in attempting to set any sort of level based on this.

What is the problem here? One is doing things by individual cancer sites in individual studies. What can be done is to do joint analyses as is done in radiation health effects. The World Health Organization and IARC recently came out with a study of 400,000 nuclear workers in 15 countries, a joint analysis. Joint analyses have also been done at IARC. I supported one financially when I was at NIH for phenoxy acid herbicides, which is a dioxin-type of exposure. They have done other studies where they bring these groups together. NCI has done some of this in radiation cancer.

Short of that, you can do med analyses, but you have to do it properly with appropriate doses and bringing in the analysis.

I am running out of time here. I am starting to lecture.

In any case, there are modern statistical methods and you will see these in the radiation business. UNSCEAR, which is the United Nations report, will be coming out this summer on the new standards for radiation health effects that are used worldwide.

Some of the new statistical methods are being done there using Bayesian techniques and uncertainties and so on.

Now, of course, my issue is to integrate the scientific laboratory understandings with the animal toxicology, with the pharmacokinetics and bring that together to come up with some intelligent risk estimates in cancer. My recommendations are, EPA should use this integrated approach and follow the advise of their SAB and the National Academy NRC Committee. It should focus on the best estimate of risk with the uncertainty on the best estimate of risk, and not just working with upper bounds. It should consider the recommendation that the National Academy gave them, and that was that the data wasn't sufficiently good for the epidemiology and they should use the animal data for setting the TCE standards, and use the human data to validate what is coming up from the animal studies.

OK, that is one issue.

The second recommendation I would make is that there is no process for developing methods in risk assessment by the EPA. It seems like they should get some quality outside advice. Maybe members from the NRC Committee could help them during the process of developing their risk estimates, as opposed to presenting the risk estimate and then getting criticisms and comments on it.

Finally, there is a basic issue of developing research programs. Senator Domenici had one for low-dose radiation effects, and that has been going on for a number of years—good basic laboratory work through the Office of Science of DOE—and similar things should be done for chemicals in our environment.

I will stop here. Thank you.

[The prepared statement of Mr. Hoel follows:]

Discussion of the Health Effects of Trichloroethylene and the Methods Used for Setting Safe Exposure Levels

Testimony of

David G. Hoel, Ph.D

Medical University of South Carolina
Charleston, South Carolina

May 6, 2008

Before the
Senate Environment and Public Works Committee

I am a University Distinguished Professor in the Department of Biostatistics, Bioinformatics and Epidemiology at the Medical University of South Carolina in Charleston. Prior to joining the university, I was employed for over twenty years at the National Institute of Environmental Health Sciences of the National Institutes of Health. There I was Director of the Division of Risk Assessment, and served for a time as Acting Scientific Director of the Intramural Research Program. I was a member of the Environmental Protection Agency's scientific panels for perchlorate and for trichloroethylene (TCE). I was a peer reviewer of the National Research Council's report on TCE.

The opinions I state today are my own.

I will comment on the process used by EPA for calculating dose levels of environmental carcinogens, with a focus on TCE. I will comment specifically on the proposed legislation S-1911, the EPA 2001 report on TCE and the National Research Council (NRC) 2006 report on TCE. I will conclude with a few recommendations.

- S-1911

I have two comments concerning the proposed legislation.

1. 3-D – This section of the bill states that the NRC study reported that there is strong evidence in a dose-dependent manner that TCE is associated with kidney cancer and leukemia in humans. The NRC committee focused on kidney, liver and lung cancer, and stated that in the future, non-Hodgkin's lymphoma (NHL) and childhood leukemia should be reviewed. I question, therefore, the inclusion of leukemia. Some of the newer studies have reported on several other cancers possibly related to TCE exposure. I have attached a brief summary of some of the reported potential adverse health effects of TCE in human studies (Hoel 2004).

2. 7-1-B – This section states that IRIS should produce a reference concentration of TCE within 180 days. My opinion is that a scientifically defensible integrated risk analysis is likely to require more than 180 days. This opinion is based upon the

following comments on the manner in which cancer risk estimation is currently conducted.

- EPA 2001 TCE Report

The EPA 2001 TCE risk assessment had a number of shortcomings that were pointed out by individual scientists and EPA's Scientific Advisory Board's TCE Advisory Panel. Although there were several health endpoints under consideration, cancer is the predominant outcome used for exposure standard setting. This is due in part to the target of one in a million lifetime cancer risk, and the assumption of a linear no threshold dose-response for carcinogens. It should be noted that the NRC report discussed this assumption and the need to validate it. The usual method for estimating cancer risk was applied to TCE. Basically, a few selected epidemiological studies and a few high dose rodent studies were individually fit to a linear dose response function in order to estimate the dose which would correspond to a lifetime risk of one in a million. Figure 1 is a reproduction of a graph of the results of this process taken from the EPA draft report, with Table 1 giving the numbers used in Figure 1.

First there is a question of the selection of epidemiological studies used for this process. EPA used three studies: Henschler (1995) kidney cancers among workers in a German cardboard factory, Anttila (1995) Finnish workers who were monitored for TSE (kidney, liver and NHL) and an ecological study of drinking water in New Jersey (NHL).

The data from animal studies was also treated in a manner similar to human studies. Using kidney cancer as the primary example, EPA gave three dose estimates. They were derived from the rat study, the German worker study and the Finnish worker study. EPA calculated the dose estimates to be (see Table 1)

3.3×10^{-3} mg/kg-d (rat)
5×10^{-5} mg/kg-d (German)
5×10^{-7} mg/kg-d (Finnish).

This represents a range in estimated dose by a factor of almost 10,000, suggesting that the process is so variable as to be meaningless. It should be noted that the most extreme result produced by EPA was from the Finnish study, which was not statistically significant, and the workers had fewer kidney tumors than were expected. It is not clear why this study was included in the analysis.

Multiple studies are often quantitatively combined using meta analysis or joint data analysis techniques. A meta-analysis was carried out by EPA (Wartenberg et al. 2000), but not used in the calculating cancer risk. The specific TCE application has been criticized in the scientific literature and most recently by the NRC 2006 report. If done correctly, with consideration of exposure, as has been done with radiation and cancer (eg. Lubin and Boice 1997), one could avoid using selected studies and their less stable risk estimates. Further Bayesian statistical methods can adjust for exposure uncertainties which vary among studies. The NRC report gives very detailed recommendations concerning the meta analysis process.

I feel that without a considerably more sophisticated analysis, which does not selectively choose individual studies and treat them independently, the low-exposure cancer risk estimates in EPA 2001 are unreliable and should not be used to set environmental standards.

- NRC 2006 TCE Report

The NRC (2006) report on TCE recommended that low dose cancer risk estimates be based on rodent bioassays and human data be used as validation of the rodent studies. This is a reasonable approach, which I support. The human epidemiological data is thought to be preferable but the very large uncertainty of exposures plus the confounding of other chemical exposures, as well as lifestyle issues, greatly decreases the value of the data for quantitative risk estimation.

Basic toxicological research focuses on a compound's mode of action (MOA); that is, how it and its metabolites affect the carcinogenesis process. Also, the use of physiologically based pharmacokinetic models (PBPK) to evaluate the relationship between routes of exposure and the formation of reactive metabolites of interest is critical to quantitative risk estimation. This information, although discussed, was not incorporated into the EPA cancer risk models. This PBPK model information, along with MOA understanding, is key to evaluating the validity of the predictability of rodent cancer effects to man. The NRC report discusses these important issues and makes specific research recommendations for improved TCE risk estimation.

An issue of increasing concern is the variability in response by various susceptible human subgroups. This is frequently discussed but rarely employed in evaluating the degree of sensitivity in subgroups. These subgroups include age, medical conditions and genetic variability. For example, Bronley-Delancey et al. (2007) measured the variability of TCE metabolism by genetic subgroups by using human hepatocytes. This basic type of human data provides guidance on possible adjustments of environmental exposure levels for genetic subgroups in the population.

All of this is important applied science which is essential to quality risk estimation, but it suffers from two problems.

First, the risk assessors are not integrating enough scientific information into their actual cancer risk estimates. There are modern statistical methods for accomplishing this. The ongoing effort in radiation carcinogenesis is one area where re-analysis is performed as new, better methods are developed, and it is a good example of scientific responsiveness to innovation.

The second issue is that there are no longer effective government programs directed at solving these issues through academic research. This work is too applied for NIH (i.e. NIH's toxicology grant study section no longer exists) and other agencies are not focused on these issues. Considering the cost of inappropriate risk estimates, in either dollars or health effects, seems foolish from a societal viewpoint.

Conclusions and Recommendations

- EPA must develop cancer risk estimates for TCE using an integrated approach following the advice of the SAB Panel and the NRC Committee. Further, it should focus on the best estimate of risk, including an estimated uncertainty. EPA should also seriously consider the NRC's recommendation of developing the risk estimates based upon the animal and laboratory studies and using the human studies as validation of their risk models.

- While developing risk estimates, EPA should consider obtaining quality outside scientific advice before and during the process, instead of waiting until the document is completed.

- EPA and other governmental agencies should sponsor the development and refinement of risk assessment methodology in general. Also, they should support key laboratory studies directed at specific problems associated with any compound, such as TCE, that is under study.

- Greater attention must be given to potentially sensitive subgroups and to adverse health outcomes other than cancer.

Figure 1

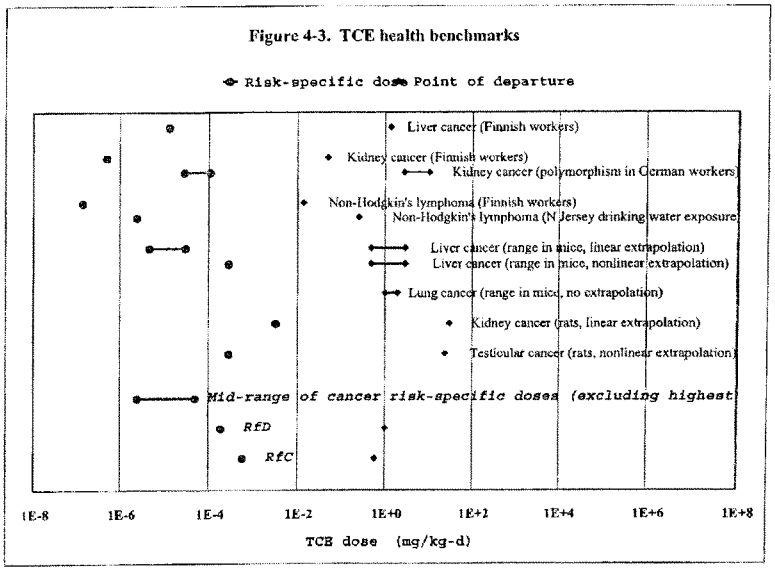

Table 1

Table 4-9. Compilation of cancer estimates

	Point of departure (mg/kg-d)	Slope factor $(mg/kg\text{-}d)^{-1}$	Risk-specific dose[a] (mg/kg-d)
Cancer estimates based on human studies			
Liver cancer			
Finnish cohort[b]	1.4[c]	7×10^{-2}	1.4×10^{-5}
Kidney cancer			
Finnish cohort[b]	0.05[c]	2×10^{0}	5×10^{-7}
German cohort	5[c]	2×10^{-2}	5×10^{-5}
Non-Hodgkin's lymphoma			
Finnish cohort[b]	0.014[c]	7×10^{0}	1.4×10^{-7}
New Jersey cohort	0.25[c]	4×10^{-1}	2.5×10^{-6}
Cancer estimates based on mouse studies			
Liver cancer			
Mechanism-based model[d]	Not applicable	8×10^{-4}	1.25×10^{-3}
Mechanism-based model[e]	Not applicable	8×10^{-2}	1.25×10^{-5}
Linear extrapolation	0.5–3.1	3×10^{-2}–2×10^{-1}	$0.5\text{–}3.1\times10^{-5}$
Nonlinear extrapolation	0.5–3.1	Not applicable	(3×10^{-4})[f]
Lung cancer[g]	1.7–4.8	Not applicable	(Not calculable)[f]
Cancer estimates based on rat studies			
Kidney cancer	33[h]	3×10^{-4}	3.3×10^{-3}
Testicular cancer	25	Not indicated	(8×10^{-4})[f]

From: EPA 2001 TCE report

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Human Exposure to TCE: Epidemiology Studies

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Trichloroethylene (TCE) is a common industrial solvent that is commonly found at low levels in drinking water. This compound has been well studied for its adverse health effects both in the laboratory and in human populations. The EPA is currently involved in reviewing their updated risk assessment analysis (1) with the likely outcome of further restricting the compound's permissible levels in drinking water.

TCE is a chemical that has been identified as being associated with or causing a wide range of adverse health effects in humans. These effects range from various cancers to neurological, developmental and autoimmune diseases as well as organ toxicities. Although there are a very wide variety of health effects from TCE, some have been more extensively studied than others. This is due in part to the specific disease interests of researchers and not necessarily due to the sensitivity of the various health endpoints in humans to TCE exposures. What follows is a summary of those health effects for which the epidemiological evidence is the strongest.

CANCER:

Traditionally and still today cancer remains the primary health endpoint used for environmental and occupational exposure standards. Epidemiological studies have shown a number of cancers to be increased from TCE and other solvent exposures including kidney, liver, non-Hodgkin's lymphoma (NHL), cervical, prostate and esophageal cancer. With these studies the major issue is separating the cancer effects of TCE from those of other solvents to which the subjects of the studies were often also exposed. Cohort and case-control studies have been carried out as well as ecological or population studies.

NHL and liver cancer are possibly the most convincing. Hansen et. al. (2) recently showed that among a cohort of male Danish workers exposed to TCE there was a statistically significant increase in NHL [SIR* = 3.5 (1.5-6.9)]. This study had good data on the exposure of the workers to TCE including both air and urine measurements of the major metabolite TCA taken since the beginning of the follow-up period. The other cohort study with actual TCA measurements was conducted by Antilla et al. (3). In this study of Finnish workers both males (2050) and females (1924) were followed from 1967 to 1992. After 10 years of exposure to TCE there was a nearly significant doubling of NHL [SIR = 2.17 (0.9-4.5)]. Of the occupational cohort studies these two have probably the most detailed information concerning the levels of TCE to which the workers were exposed. Other cohort studies reporting increases in NHL include Axelson et al. (4) [SIR = 1.6 (0.5-3.6)] and Blair et al. (5) [RR** = 2.0 (0.9-4.6)].

Case-control studies of NHL and TCE were carried out by (6) who reported a significant odds ratio [OR = 7.2 (1.3-42.0)] based on 105 cases. Also Persson et al. (7) observed an increased odds ratio of [OR=1.5 (0.6-3.7)].

For liver cancer which is the primary site of TCE metabolism Antilla et al. (3) observed a doubling of cases among the exposed [SIR = 2.3 (0.7-5.3)]. However, after 20 years of exposure this became a 6 fold increase [SIR = 6.1 (1.3-17.7)]. Also Axelson et al. (8) observed an increase [SIR = 1.4 (.4-3.6)] as did Blair et al. (9) [RR = 1.7 (0.2-16.2)]. The newer Hansen et al. (2) study reported a greater than 2 fold increase [SIR = 2.6 (0.8-6.0)]. Overall these studies all indicate an increased risk for liver cancer from TCE exposure.

Finally for women, cervical cancer is reported to be increased from TCE exposure. Hansen et al. (2) reports a significant [SIR = 3.8 (1.0-9.8)], Anttila et al. (3) found [SIR = 2.4 (1.1-4.8)], Blair et al. (9) [RR=1.8 (0.5-6.5)].

Wartenberg et al. (10) reviewed the current cancer studies and produced a meta analysis after first stratifying the studies into tiers defined by the quality and relevance of the individual studies.

* SIR = standard incidence rate. The estimate plus the 95% confidence interval is given.
** RR = relative risk.

A summary of the major cancer sites for the best cohort studies with the addition of two new studies (2), (11) is given in Table 1. It should be noticed that one site, namely kidney cancer, that has been used in risk estimation by both Cal EPA and the U.S.EPA, has only one positive study (12).

TABLE 1

Cancer Incidence Cohort Studies — SIR estimates and number of cases

Study	NHL	Liver	Kidney	Esoph.	Prostate	Cervical
Anttila	1.8 (8)	2.3 (5)	0.9 (6)		1.4 (13)	2.4* (8)
>10 yrs since exp.	2.2 (7)	3.0* (5)	1.0 (5)		1.4 (11)	1.3 (2)
Henschler			8.0* (5)			
Hansen#	3.5* (8)	2.6 (5)	0.9 (3)	4.2* (6)	0.6 (6)	3.8* (4)
Axelson	1.6 (5)	1.4 (4)	1.2 (6)		1.3 (26)	
Blair (male)	1.0 (7)	2.6 (3)	0.4 (2)		1.2 (56)	
Blair (female)	0.9 (2)		3.6 (2)			
Raaschou-Nielsen#	1.2* (96)	1.3 (34)	1.2 (76)	1.8* (23)	0.9 (163)	1.9* (62)

* $p<0.05$
# new study not included in EPA's analysis.

Cancer Mortality Cohort Studies — SMR estimates and number of cases

Study	NHL	Liver	Kidney	Esoph.	Prostate	Cervical
Blair	2.0 (28)	1.7 (4)	1.6 (15)	5.6 (10)?	1.1 (54)	1.8 (5)
Boice	1.2 (14)		1.0 (7)	0.8 (7)	1.0 (32)	
Henschler			3.3 (2)			
Morgan	1.0 (14)		1.3 (8)		1.2 (21)	
Ritz			0.7 (5)	1.2 (9)	1.4 (24)	

As with the rat model there may be an association with TCE exposure and renal cell carcinoma (RCC) with mutations in the von Hippel-Lindau (VHL) tumor suppressor gene. In a study by Brauch et al. (13) those RCC patients with high TCE exposures had a greater frequency of VHL mutations and especially a particular mutation (nucleotide 454) (see Table 2).

TABLE 2

Drinking Water Contamination and Incidence of Leukemia and NHL
Population Study of 75 New Jersey Towns

Total Leukemia	Cases		RR (95%CI)	
TCE ppb	Male	Female	Male	Female
<0.1	438	315	1	1
0.1-5.0	162	156	0.85 (0.71-1.02)	1.13 (0.93-1.37)
>5.0	63	56	1.10 (0.84-1.43)	1.43 (1.07-1.90)

NHL	Cases		RR (95%CI)	
TCE ppb	Male	Female	Male	Female
<0.1	491	504	1	1
0.1-5.0	272	226	1.28 (1.10-1.48)	1.02 (0.87-1.20)
>5.0	78	87	1.20 (0.94-1.52)	**1.36 (1.08-1.70)**

ALL	Cases		RR (95%CI)	
TCE ppb	Male	Female	Male	Female
<0.1	45	25	1	1
0.1-5.0	16	22	0.91 (0.53-1.57)	1.85 (1.03-3.70)
>5.0	3	7	0.54 (0.17-1.70)	2.36 (1.03-5.45)

NHL high grade	Cases		RR (95%CI)	
TCE ppb	Male	Female	Male	Female
<0.1	15	15	1	1
0.1-5.0	7	3	1.26 (0.51-3.09)	0.53 (0.15-1.82)
>5.0	2	9	0.61 (0.14-2.65)	2.74 (1.20-6.26)

non-Burkitt's Lymphoma
From: Cohen et al. 1994 EHP 102:556-61

In summary, these cancer epidemiology studies and others coupled with the induction of cancer in laboratory animals give a convincing argument that TCE is a human carcinogen capable of inducing cancer at several organ sites. Table 4 gives the meta-analysis estimates developed by Wartenberg et al. (10) for the cancer sites believed to be associated with TCE exposures.

TABLE 3

Association of TCE levels and mutations in the von Hippel-Lindau tumor suppressor gene among HCC patients.

			Number of patients (%) with VHL mutations		
Exposure Level	**Number Patients**	**Nucleotide #454 mut.**	**Number of mutations zero**	**one**	**two or more**
+++	17	7 (41%)	2 (11%)	4 (24%)	11 (65%)
++	24	6 (25%)	6 (25%)	15 (63%)	3 (13%)
+	3	0	3 (100%)	0	0
-	107	0	31/73(42%)	42/73 (58%)	0/73 (0%)

from: Brauch H. et al. JNCI 91:854-860 (1999)

TABLE 4

Meta Analysis of TCE Cancer Studies

SIR/SMR values with total number of cases

	Tier 1		**Tier 2**	
Cancer Site	**Incidence**	**Mortality**	**Incidence**	**Mortality**
Cervix	2.4* (8)	1.8 (5)	1.1 (1)	1.2 (13)
Esophagus		1.1 (26)		1.1 (32)
Hodgkin's	1.5 (4)	2.0* (16)		0.8 (13)
Kidney	1.7* (21)	1.2 (37)	3.7* (6)	1.3 (41)
Liver	1.9* (12)	1.7 (4)		2.0* (15)
NHL	1.5 (22)	1.2 (56)		0.9 (20)
Prostate	1.3* (95)	1.2* (131)	1.6 (7)	0.9 (72)

* $p<0.05$

from: Wartenberg et al. 2000 EHP 108 suppl.2 161-176

POPULATION CANCER STUDIES

Prompted by the well-known Woburn Study that linked childhood acute lymphocytic leukemia (ALL) with drinking water contamination by TCE and PCE, (14) studied towns in N.J. with increased TCE drinking water levels and possible associations with leukemia and lymphoma rates. Table 3 shows the results for total leukemia and NHL in general. Specific leukemia types as well as NHL stage were also analyzed. It appears that for NHL there were effects in females at the high dose group and increases but no dose response in males. A population down-stream from a contaminated industrial site was studied in Taiwan (15). Liver cancer relative risks in males were observed to be [RR = 2.57 (1.21-5.46)] with a linear trend over time for the affected areas.

DEVELOPMENTAL TOXICITY

Women exposed to TCE shortly before and during their first trimester of pregnancy have shown to have an increased incidence of malformations in their offspring. In particular congenital cardiac malformations are increased. Goldberg et al. (16) studied the specific cardiac malformations observed in the Tucson Valley where about 8% of the people were exposed to well water with excess levels of TCE. A statistically significant 3-fold increase in congenital heart disease was observed among those exposed to the TCE contamination. Importantly this increase did not persist after the contaminated wells were closed. It should also be noted that no other contaminant in excess of drinking water guidelines was identified other than TCE or its by products. Also in laboratory studies cardiac defects have been induced in chick embryos and rat fetuses by TCE exposures (17).

In an analysis of the Baltimore-Washington Infant Study Wilson et al. (18) a relative risk of RR=3.4 was observed for solvent/degreaser exposure and occurrence of hypoplastic left heart. This contaminant was present in the public drinking water and the authors did not specify what the specific chemical or chemicals in the solvent grouping were likely to be the cause of the malformations.

A second type of malformation has been observed also from TCE drinking water exposures. In a study Bove et al. (19) of drinking water contamination in 75 towns in Northern New Jersey increased odds ratios greater than 1.5 were found for TCE and central nervous system defects, neural tube defects and oral cleft defects. For levels greater than 10ppb the odds ratios were 1.7, 2.5 and 1.3, respectively. In a case control study in Finland of oral clefts it was observed that solvents were a risk factor Holmberg et al. (20-21).

These ecological studies are very suggestive of the teratogenic potential of TCE at drinking water contamination levels. It is further strengthened by the fact that in the Arizona study once the contaminated wells were closed the increased rate of malformations ceased and that animal studies have replicated the effect.

NEUROTOXICITY

TCE is well established as a neurotoxin. The State of California (22) has used the study by Vandervort et al. (23) to determine a reference standard for non-cancer chronic effects. This study of TCE exposed workers showed non-specific neurotoxicological endpoints (e.g. eye irritation, drowsiness, dizziness etc.). A drinking water and TCE study was carried out by White et al. (24). The study involved neurological testing of individuals in 3 areas with high levels of TCE present in their drinking water (Mass., Ohio and Minn.). These examinations resulted in the authors' observation that "chronic environmental exposures to solvents at surprisingly low levels (parts per billion) can be associated with significant behavioral deficits as measured by neuropsychological tests." Further the data suggested that the exposures affect the CNS and the younger individuals showed a greater range of neurological deficits. In animal studies Isaacson et al. (25) it has been shown that TCE produces a loss of myelin in the brain stem and the sheaths in the spinal cord.

HEPATOTOXICITY

TCE is metabolized primarily in the liver and as such the liver will be exposed to relatively high levels of TCE metabolites. In a study of workers exposed to TCE Chia et

al. (26) observed a disruption of peripheral endocrine function which could be the result of TCE-induced liver malfunction. The researchers also observed an effect on serum insulin levels that depended on the duration of TCE exposure Goh et al. (27). In a second study Driscoll et al. (28) of TCE exposed workers the researchers showed increased levels of plasma bile acid concentrations in the exposed workers. This effect has also been shown in laboratory rats in a dose response manner. The bile acid concentrations are likely to be a more sensitive indicator of hepatic effects of solvents than the usual liver function tests. Finally in a worker study by Nagaya et al. (29) it was suggested that exposure to low-level TCE influences hepatic functions affecting cholesterol metabolism. The U.S. EPA used the exposure values in these studies (26-27) to support their development of an RfC (reference concentration) for TCE for use in exposure stand setting.

CONNECTIVE TISSUE DISEASES

TCE has been reported to be associated with various connective diseases. A few epidemiological studies have weakly linked solvent exposures and TCE with systemic sclerosis and undifferentiated connective tissue disease (30). There has been a lack of observed dose response and also there needs to be study replication. In a case-control study of scleroderma (178 cases and 200 controls) Nietert et al. (31) found a significant odds ratio of 2.9 for solvent exposure for both cumulative exposure and high maximum intensity exposure and comparing high maximum intensity of TCE exposure the odds ratio was 3.3 (1.0-10.3). In a large case-control study of scleroderma (660 cases and 2.227 controls) Garabrant et al. (32) found increased risk in women from solvent exposures but the risk did not increase with duration of exposure. TCE exposures increased the scleroderma risk but not significantly so.

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Response by David G. Hoel to an Additional Questions
from Senator Boxer

Question. As a need to Protect Public Health, Dr. Hoel, do you agree that EPA should create drinking water standards for toxic chemicals that are widespread contaminants of drinking water and the food supply and threaten public health?

Response. Yes, the regulation of toxic chemicals in the public water supply is a major component of the EPA's mission to control the levels of toxic chemicals in the environment. The critical issue for EPA is to regulate chemicals in drinking water such that appropriate levels are set as standards. To under-regulate levels places the public's health at risk. On the other hand, over-regulation can lead to wasteful expenditure of funds that could be more effectively used for other priorities such as health and education. May I say that it is of critical importance that the EPA avail itself of the highest quality research by non-EPA scientists for the toxicants of most concern.

Responses by David G. Hoel to Additional Questions
from Senator Inhofe

Question 1. You are critical of EPA's current cancer slope for TCE. If EPA follows the NAS and SAB recommendations, should we expect that cancer slope to change? If so how do you think the slope would change? How would that affect the regulation of TCE?

Response. By incorporating the NAS and SAB recommendations, as well as the newer studies, the cancer slope should change. Without a careful evaluation, I cannot say how the slope would change. My guess is that the permissible level may be increased. I have no idea if politically the permissible drinking water levels of TCE could be relaxed if the new risk estimates indeed suggest drinking water would remain safe for consumption.

Question 2. In your opinion, is there an immediate human health risk or any information that suggests that S. 1911 is warranted?

Response. I am not aware of scientific evidence that suggests that the current drinking water standard is resulting in an immediate health risk. With respect to S. 1911, EPA should continually update their risk estimates of TCE and other important chemicals. The reason for this is that there are recent National Academy reports which evaluate recent scientific studies. If EPA re-evaluates TCE, their conclusion could easily be that the standard should be raised and not necessarily lowered. It would have been useful if the charge to the Academy had included addressing the current standard. Also, it would be useful for an Academy committee to evaluate the methodology used by EPA to establish exposure standards.

Question 3. Please explain how an advisory board works. Where do the experts come from? How are biases dealt with? Should having an advisory board member from industry automatically disqualify the recommendations from use by officials in making policy decisions?

Response. There are several types of advisory' groups that often are involved in making recommendations to the EPA:

- The National Academy of Sciences is commissioned by governmental agencies or Congress to address problems such as TCE toxicity. A specific charge is given to the Academy, and the Academy subsequently decides the composition of the committee. The members are experts in the scientific disciplines appropriate to the study and they are most often academics. The proposed membership is made public and comments concerning the membership are considered by the Academy. At the first committee meeting, each member discusses with the Academy and fellow members of the committee any possible conflicts and/or biases, both financial and intellectual. The draft report is then sent to a group for peer-review.

- The EPA Scientific Advisory Board (SAB) may be requested by the EPA to comment to the Administrator on quantitative risk estimates proposed by the agency. How often this is done, I do not know. Also, the members of the board are chosen, I believe, by the agency.

- For major issues, a special outside panel of experts is selected to answer several specific questions posed by the agency. This panel uses public comments submitted to the agency as well as the scientific literature in developing consensus answers to the questions. Also, scientific comments by individuals on the panel are often included in the panel's report. How the panel is chosen, I do not know. I have served on such panels as TCE, perchlorate, benzene and asbestos. The members of the panel often include, besides academics, members of industry, environmental groups and government. The meeting of the panel is public, with an opportunity for public statements. The report is then sent to the SAB for their comments and possible criticisms. These reviewers may have strong biases, but all of their comments are carefully considered and addressed by the committee before the report is released. An independent outside expert sees to it that the committee properly addresses peer-review comments.

  My recent experience with the Academy committees is that their charge concerns evaluation of studies and a qualitative assessment of causation for various health endpoints. The committees have not been charged with evaluating quantitative risk estimates for chemicals. This was the case for the TCE report. I should comment here that a number of years ago EPA did commission the Academy to evaluate risks of drinking water toxicants in a series of reports (Safe Drinking Water reports). We calculated quantitative risk estimates which, hopefully, were useful to the Agency in setting drinking water standards.

Question 4. Can EPA alter its internal protocols for developing risk assessments to avoid situations like perchlorate and TCE, where outside groups have given them such sound criticism?

Response. As I attempted to suggest in my written testimony, EPA should consider enlisting outside advice during the process of developing their risk assessments. This has the potential of reducing criticisms of their final product. Although this may slow the process, it has the potential for reducing the time needed to redo the analysis.

Senator KLOBUCHAR. Thank you. Thank you very much.

Assemblywoman Lupardo, I understand you represent the district where my legislative director has her home town. Is that correct? Moira Campion? Thank you for being here.

You expressed concern during your testimony about EPA's new policy on creating the IRIS risk assessments. The Government Accountability Office recently testified that the new policy would undercut the credibility of these assessments because it kept interagency comments secret. Do you think that the people that you represent, and from what you have see of this issue, that they would want an open scientific process when the Federal Government develops the safety level that would be used to protect people from TCE?

Ms. LUPARDO. There is no doubt about it, Senator. They are desperately in need of solid leadership on this topic. I have been trying everything I can at the State level, but there is resistance to micromanaging the science. That's why we are looking to the EPA for their assistance. It is frustrating to think that we can go to all this trouble and perhaps even pass this legislation, only to see it mired down in this sort of bureaucratic mess.

Senator KLOBUCHAR. Could you expand a little and explain in more detail why it is so important for your constituents to install ventilation systems in their homes due to TCE contamination?

Ms. LUPARDO. Well, after it was discovered about the underground plume of contamination, and the subsequent health studies showing elevated cancer and other risks, there was really no choice but to have these systems installed so that homes could be livable. We have almost 500 homes that are being vented.. There is even some evidence that the ambient air in that community has been affected, especially when there is heavy cloud cover, from all the venting in the community as well. So, it is extremely important that we have those systems in place. We were lucky. As I said before, we had a responsible party. Many communities do not have that luxury.

Senator KLOBUCHAR. If EPA had updated its safety standard for TCE exposure and set a strict new standard that considered all types of exposure to TCE, could this have helped your constituents?

Ms. LUPARDO. Yes, most definitely.

Senator KLOBUCHAR. How would it have helped? How would it have helped?

Ms. LUPARDO. Their situation would have certainly received much more timely attention. Also because of some arbitrary decision that was made at our State Health Department where they changed the standard mid-stream, they would have been protected by the most protective standard supported by science instead of some bureaucratic change.

Senator KLOBUCHAR. Thank you.

Ms. Charnley, do you agree with Massachusetts' perchlorate standard?

Ms. CHARNLEY. Well, do I agree with the number or the fact that they set one?

Senator KLOBUCHAR. Do you agree with the fact that they have a standard? Do you agree with the number? Both questions.

Ms. CHARNLEY. I think that they are certainly well within their prerogative to set a standard. I think that the number is too stringent. I say that because one of the things about perchlorate is that it acts by the same biological mechanism of action as, say, nitrates and thiocynates, which are present ubiquitously in our food and water. We are exposed to about 1,000 times higher doses of those substances every day based on the RfD, compared to perchlorate, but we don't seem to be worried about those.

So I think that if you regulate perchlorate, you should think about it in the larger context of the other substances that we are exposed to that act the same way, the cumulative and aggregate risks, and the larger public health context.

Senator KLOBUCHAR. And so when you commented on the standard, I think that you said it didn't have a defensible standard basis at the time. Is that right?

Ms. CHARNLEY. I think that is probably what I must have meant, yes.

Senator KLOBUCHAR. Right. And then the State of Massachusetts criticized your comments and pointed out that, and this is a quote, "a panel of independent scientists with extensive expertise in the areas of toxicology, risk assessment and epidemiology developed the proposed standard." They went on to say, "This independent committee concluded that the basis of the proposed standard was well supported and appropriate."

Ms. CHARNLEY. But they didn't consider these other possibilities. That is all.

Senator KLOBUCHAR. Since you commented on the proposed standard and you said that it did not have a defensible scientific basis, has that changed at all? Do you believe that it has a defensible scientific basis?

Ms. CHARNLEY. No, for the reasons I just stated.

Senator KLOBUCHAR. OK. Thank you.

Senator Whitehouse.

Senator WHITEHOUSE. Thank you, Madam Chairman.

I have what appears to be a Wall Street Journal article talking about the perchlorate issue from 2003. It says the following: "In another step, the White House Office of Management and Budget intervened last month to delay further regulatory action on perchlorate by referring the health debate to the National Academy of Sciences for review. Pending that study, which could take an additional 6 to 18 months, the EPA ordered its scientists and regulators not to speak about perchlorate, said Suzanne Ackerman, an EPA spokeswoman. The gag order prevented EPA scientists from commenting or elaborating Friday on two lettuce studies which show lettuce available in U.S. supermarkets appears to absorb and concentrate perchlorate from polluted irrigation water in significant amounts."

The reference to the National Academy of Sciences—I am just trying to connect the dots here. Mr. Wiles, in your testimony, you highlighted a 2003 effort by the White House to stack the National Academy of Sciences panel with industry consultants. To highlight your testimony, you said that senior White House political officials with no scientific expertise actively participated in reviewing the scientific charge sent to the National Academy of Sciences on per-

chlorate. You further said that White House and Pentagon officials were involved in discussions about who should be appointed to the NAS panel. And finally, you said that the panel initially included a paid industry expert witness and two other paid consultants to the perchlorate industry.

Is the National Academy of Sciences appointment process that you describe in your testimony the same one that I referenced in The Wall Street Journal article? Do you know?

Mr. WILES. I presume that it is, yes.

Senator WHITEHOUSE. There has just been the one National Academy of Sciences review?

Mr. WILES. Yes, there is only one report that has been done. That is correct.

Senator WHITEHOUSE. OK.

I appreciate very much Assemblywoman Lupardo's testimony about the substantive problems of exposure in her community and how hard she has had to fight to remedy them. But I am also concerned about the structural problem in and surrounding EPA of whether or not the organization itself has been polluted with politics and the extent to which it is breaking up the infrastructure that protects the integrity of its own processes.

I was surprised to read the description of the National Academy of Sciences' process. I am wondering, Mr. Wiles, if you could comment on is that unusual? What does it mean in terms of the credibility of the National Academy of Sciences? We have had my colleagues here today sort of throw out National Academy of Sciences as the Good Housekeeping seal of approval here. If it had the National Academy of Sciences imprimatur, it must be legitimate. Are we to take that with some skepticism under these circumstances? How do you put this into a large context?

Mr. WILES. I actually used to work at the National Academy of Sciences, at the National Research Council, managing these committees. I can say from experience that the influence of politics and that vested interests are having on the process now I think is unprecedented.

What we cited in our testimony was an investigation that looked at public records from the White House that showed clear intervention in the process of selecting this committee by non-scientists within the White House. You had initially three industry consultants. One was actually someone paid, who made a living as an expert witness in litigation. That person was ultimately removed.

But what happens when you have industry consultants on these panels that have to reach a consensus finding is that finding is diluted in favor of the industry's interests, which typically are financial as opposed to public health. So it is a very serious problem, but that is just the corruption of the NAS process. The influence of industry interests on the process is just a small part of the overall corruption of science that we have seen in this Administration that I think was well documented last week in a hearing that was held before this Committee.

We have seen unprecedented levels of industry influence on every scientific panel and committee from committees of the National Institutes of Health, all the way through to committees at EPA that are all designed to—they are the first line of defense that

the American public has against chemical pollution in the environment, and they have been in many respects taken over by the polluting industry under this Administration.

Senator WHITEHOUSE. Well, my time has expired, and I will end here, but it does remind me of the story about the two folks who are arguing over the merits of a particular debate. One said to the other, you know, you can have your own opinion, but you don't get to have your own facts. I think we are a little bit that way. You can have your own opinion. You can have your own policy outcome, but you shouldn't get to have your own science. That should be neutral.

I appreciate it. Thank you, Chairman.

Senator KLOBUCHAR. Senator Barrasso.

Senator BARRASSO. Thank you very much, Madam Chairman.

Dr. Hoel, if I could, you made a reference in your testimony that this bill would compel an analysis within 180 days. From a scientific standpoint, is that something that is reasonable, to put a certain number of days limit? I think you had some concerns about that.

Mr. HOEL. The reason I said I thought 180 days was a very short period was that the recommendations I was making about how to do a more scientifically credible job in this risk assessment process or carcinogens, EPA is going to have to do something a little different. I also suggested that they try to bring in some peer-reviewing during the process—advice from outside scientists and so on—so they would come up with a credible product.

Now, if you were to do that, which would be different from the way EPA has done things in the past, my guess is they could not pull it together in 180 days. You certainly probably wouldn't be able to get the quality advisors brought in considering how long it takes to do Academy of Science committees and things of that sort.

Senator BARRASSO. Do you have any estimate on what the right time figure would be if you had to insert a time figure?

Mr. HOEL. I really don't know. I was just sort of struck that if I had to arrange this from scratch with these changes, with 180 days you might have to cut some corners scientifically.

Senator BARRASSO. In your opinion, is there an immediate health risk that makes this bill necessary? For TCE?

Mr. HOEL. No. I think that if you look at the epidemiology, as the Academy had looked at, they talk about kidney cancer is the concern. They have calculated very low risk levels for TCE based on the cancer studies. But the question is, these results are coming out of Germany and there are some very high doses. Some of the workers got a continual dose of about 100 ppm of TCE in their work, with levels up to 400 to 500 ppm. The study that they did use, the top doses were I think 1,000 ppm. So there is a lot of uncertainty there, but these are very high doses, and they in fact suggest they try to find some studies where you might have some lower doses that would intersect with that.

There have been other studies, other epidemiological studies, say the one out of Denmark for TCE workers where they measured TCE in the workers. They found no increase in kidney cancer. So it is kind of mixed.

Senator BARRASSO. Dr. Charnley, if I could, you said in your testimony that legislation compelling the EPA to regulate perchlorate would freeze a standard in place in reaction to politics, not really risk-based priorities, and essentially constitutes an environmental earmark. Are you saying that such legislation if passed would basically be politics trumping science? Is that what I am hearing?

Ms. CHARNLEY. Well, I think that the priority-setting process that is in place courtesy of the Safe Drinking Water Act is appropriate. I think that there is no imminent public health threat that means we should regulate tomorrow. I think we probably should regulate, yes. But as long as there is still some discussion about relative source contributions and various other issues underway, I think that process should be completed.

Senator BARRASSO. When you talked about the average exposure in the United States to perchlorate being about one-tenth of EPA's reference dose, we are not talking about really protecting the average American? Or are we just talking about pregnant women, where the protection is needed? What should we do there?

Ms. CHARNLEY. Yes. It is the pregnant women and the developing fetus who are the sensitive sub-populations. I think that any regulation of perchlorate should take into account children's differences in exposure. There is no question about that. But I think that the studies of pregnant women have not found any impacts of perchlorate exposure on either their hormone levels or on those of their offspring. There are quite a number of recent studies that have looked at that, and I think should continue to look at that, of course. But I am not convinced that there is an imminent public health threat.

Senator BARRASSO. Thank you.

Madam Chairman, I think my time has expired. Thank you very much.

Senator KLOBUCHAR. Assemblywoman Lupardo, I was just talking to staff and I read some of the earlier information for this hearing about how the GAO is in fact very critical about the delay that is going on with EPA and how much it has made it very difficult for local units of government and States to deal with this.

Could you talk about the impact of waiting for too long in terms of the EPA acting, and what you have had to do as a result of that?

Ms. LUPARDO. We have been really working around the edges of this. We have done the best we can to protect the individuals, the hundreds and hundreds of families and individuals in our community, waiting for the Federal Government to come to our rescue and aid, and having our own Health Department resist us at every turn, to provide a more restrictive standard.

It turns out, and I am looking at the GAO highlights summary as well, that a new IRIS process is being put in place that is going to delay this even further, I just don't even know how I am going to go back and explain this to my constituents. I can appreciate what you were saying before about the 180 days. That may be too short of a timeframe perhaps, but we can't use this delaying tactic, it would seem, to further put my constituents at risk.

Senator KLOBUCHAR. Thank you.

Mr. Wiles, all the bills do is to require the EPA to use the best available science. Is that right?

Mr. WILES. That is correct.

Senator KLOBUCHAR. And we have National Academy of Science reports on both TCE and perchlorate. Aren't we at risk of just reviewing this to death at some point?

Mr. WILES. We are, not to mention that we have the CDC study of 1,100 women which I think is very unusual when you have the CDC with such a large study of exposure and adverse effects measured in the population just from ambient exposure, exposures that occur every day.

And then under questioning from Republicans in the House on the Energy and Commerce Committee, the CDC was very clear that they feel that they do not need further research to support their finding, and that the finding is consistent with causality, which is about as strong a finding as you are every going to get.

So failing to act now with such strong evidence of exposure and harm is really unprecedented and completely unwarranted.

Senator KLOBUCHAR. How would you describe, Mr. Wiles, the extent of people's exposure to perchlorate in the United States, and in particular the exposure of infants and children?

Mr. WILES. Well, according to the CDC, it is ubiquitous. In other words, everyone is exposed. I think what we heard today from earlier witnesses and what the CDC research has shown is that women of childbearing age are potentially at risk, and their developing babies are if they were to get pregnant, due to exposures that the moms have. And then breast milk is also very highly contaminated, phenomenally highly contaminated based on what earlier witnesses said.

So we have a clear danger to the public health from a compound that we know how it acts. It is not debated that perchlorate is toxic to the thyroid, that it interferes with normal thyroid function. So there literally is nothing left to do but act, and that is what this Administration does not want to do.

Senator KLOBUCHAR. Why do you think it has taken EPA so long to create a perchlorate drinking water standard?

Mr. WILES. Well, the pressure has been clearly coming from the Department of Defense, the Air Force, and defense contractors. That goes back as early as 1962 when the first group was formed to lobby, if you will, to pressure regulators into not acting to clean up groundwater supplies beginning in the 1960's. So there are at least four, if not five, decades of work on the part of DOD and contractors to avoid regulation and it continues to this day.

The difference with this Administration is that this attitude of not protecting the public health is extended all the way to the EPA now, who has adopted the Defense Department line and the Lockheed Martin line that we don't need to act.

Senator KLOBUCHAR. Last question, Mr. Wiles. Do you support the bill that Senator Clinton and others have introduced to require the EPA to use available science to create drinking water standards and publicly available data for perchlorate and to revise or create Federal standards for TCE, also using currently available data?

Mr. WILES. Absolutely. We support both bills, and we do believe that action by the Congress is clearly necessary to move this issue forward and to protect the public health.

Senator KLOBUCHAR. Thank you very much.

Mr. WILES. Thank you.

Senator KLOBUCHAR. OK. Very good.

I just want to thank our witnesses for coming. I would just point out that the GAO report is worth mentioning here in terms of their criticism of what has gone on here in terms of the delay. This is another Government agency criticizing another Government agency that we have waited for too long. As the testimony of Assemblywoman Lupardo shows, this is putting a great burden on local governments and State governments in a patchwork manner to deal with this.

The best thing that we could, as a Country, would be if the EPA acted in this area. I believe I am speaking on behalf of a number, not all, but a number of the members of this Committee. We hope that this hearing will push this, and if that doesn't work, Congress, as we said, is going to have to move forward with our legislation.

Thank you very much. This hearing is adjourned.

Background for Perchorate and TCE in Water

Senate Environment and Public Works Committee

R. Thomas Zoeller, Ph.D.

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May 6, 2008

The single-most credible report linking perchlorate exposure to potential adverse effects in the US population was published by Dr. Ben Blount and colleagues at the Centers for Disease Control (CDC) in the journal Environmental Health Perspectives in 2006 (Blount et al., 2006). The findings reported in this article were surprising because all previous studies of the effects of perchlorate exposure in humans, including that published by Greer et al. (Greer et al., 2002), did not predict this outcome. However, the CDC report is highly credible and the implications are extremely important. My opinion, represented in part in the information provided below, is that some proportion of the 4 million babies born in the US annually are being adversely affected by perchlorate exposure.

1. How does perchlorate work?

Perchlorate is a highly water-soluble compound that blocks the uptake of iodine into the thyroid gland (Dohan et al., 2007).

Iodine is essential for the production of thyroid hormone. When iodine levels are low, thyroid hormone production is impaired (Wolff, 1998).

Thyroid hormone is essential for brain development. The precise effects of low thyroid hormone depend on the developmental timing and the severity of the thyroid hormone insufficiency (Zoeller and Rovet, 2004).

Because of the exact mechanism by which perchorate works, it is predictable that high levels of perchlorate will be found in breast milk. In fact, this is now being reported (Kirk et al., 2005; Pearce et al., 2007). We can also predict that blood levels of infants drinking this milk will be higher than levels observed in their mothers. This prediction has not been tested in humans, but has been shown in experimental animals (Zoeller and Blount, unpublished).

2. What are the strengths of the CDC study?

This is the largest study to date exploring the relationship between perchlorate exposure and potential adverse consequences. Moreover, the study population was statistically representative of the US population.

This is the only study to date to measure perchlorate exposure in each *individual* study participants coupled with measures of thyroid function (and many other variables). The strength of this design cannot be overemphasized. Most importantly, it allowed the authors to determine the extent to which thyroid hormone declines for every unit of perchlorate exposure. *This provides a great deal of power when extrapolating their findings to the most vulnerable subset of the US population: infants!*

Several of the study's findings are internally consistent with what we know of the effect of perchlorate on thyroid function. Specifically:

The strength of the association between perchlorate exposure and thyroid function is stronger in women whose iodine levels are below 100 µg/L. This is predictable because perchlorate blocks iodine uptake, and if dietary iodine is already low, then the effect of perchlorate should be more severe. *Note: The women who fell into this category represented nearly 30% of the study population, so it is not trivial.*

Smoking interacts with perchlorate to cause a greater reduction in thyroid hormone levels (Steinmaus et al., 2007). Because cigarette smoke contains chemicals

(thiocyanates) that behave like perchlorate, these contaminants produce an additive effect.

Estrogen was correlated with T_4, but not with TSH. This makes sense from an endocrinological point of view.

These findings improve the confidence of this study because they demonstrate that the statistical power and approach of the study was strong enough to identify known relationships.

3. What are the implications of this study?

Everyone in the study was contaminated with perchlorate. Because perchlorate appears to be eliminated from the body relatively rapidly (Greer et al., 2002), this means that people are exposed to much more perchlorate than was being predicted before this study was published. The U.S. FDA's recent report from their "Total Diet Study" (Murray et al., 2008) verifies that perchlorate has made it into the U.S. food supply, and that children *(especially infants)* are the most exposed.

Adult women are more sensitive to the effects of perchlorate than men. This also was not predicted based on previous studies, though no one had studied this directly.

Adult women are more sensitive to perchlorate than predicted by previous studies, especially that of Greer et al. (Greer et al., 2002). Greer et al., estimated that 5.2 µg/kg-day was a "threshold" below which iodine would not be inhibited from the thyroid gland, and above which it would. Moreover, because the adult thyroid gland contains several months' worth of hormone, the NAS committee on perchlorate estimated (without scientific reference) that perchlorate would have to reduce iodine uptake by at least 75% for several months (NAS, 2005):

"Given the compensation that is known to occur in people with iodide deficiency, as discussed earlier, it is highly likely that in people with a normal iodide intake the dose of perchlorate would have to reduce thyroid iodide uptake by at least 75% for a sustained period (several months or longer) for iodide uptake and thyroid hormone production to decline enough to cause adverse health effects (equivalent to reducing dietary iodide intake by 75%). In adults, that is likely to require sustained exposure to more than 30 mg of

perchlorate per day (0.4 mg/kg per day for a 70-kg person), on the basis of the clinical studies in healthy subjects and the studies of long-term treat- ment of hyperthyroidism, both described in this chapter, and the studies of environmental exposure, described in Chapter 3 (Gibbs et al. 1998; Lamm et al. 1999; Crump et al. 2000). "

The CDC study proves that this prediction by the NAS committee was incorrect. Moreover, data available at the time of the NAS report demonstrated that as little as a 40% reduction in dietary iodide is associated with cognitive deficits in children ((Aghini Lombardi et al., 1995; Vermiglio et al., 2004)). These studies clearly imply that the developing brain is more sensitive to iodide deficiency than the NAS report suggested.

Current levels of perchlorate exposure are reducing thyroid hormone levels in infants. Although this prediction has not been directly tested, there are several scientific reasons to support this prediction.

Adult women have several month's worth of thyroid hormone stored in their gland (Greer et al., 2002), yet background levels of perchlorate exposure are linked to thyroid function.
Infants have no hormone stored in their gland (van den Hove et al., 1999).
Infants consume about six times the fluid volume (per pound of body weight) compared to adults.
Good scientific evidence indicates that breast tissue can concentrate perchlorate into milk (Dohan et al., 2007), *and studies show that there are high level of perchlorate in human breast milk* (Pearce et al., 2007).
Therefore, based on the CDC study, it is reasonable to predict that infants' thyroid function is reduced by current levels of perchlorate.

Existing studies using neonatal thyroid hormone levels are not a valid test of this prediction for the following reasons:

No one has measured perchlorate AND thyroid hormone in these neonates.
Because babies are born with a significant amount of thyroid hormone from the mother, studies of

perchlorate exposure must be performed no sooner than 10 days after birth to test the hypothesis that perchlorate is affecting the infant's thyroid (note: serum thyroid hormone in a newborn has a serum half-life of about 3.5 days (Vulsma et al., 1989; van den Hove et al., 1999). In contrast, current reports use data derived from the neonatal testing program, which takes blood from the newborn before their release from the hospital. Often, this is within one or two days of birth.

4. Neonates and Infants are highly sensitive to thyroid hormone insufficiency.

Thyroid hormone insufficiency is perhaps best documented in studies of infants with congenital hypothyroidism (CH) (for review, see (Zoeller and Rovet, 2004)). These studies are particularly useful because subjects are under continuous medical surveillance, so there is good documentation of the relationship between endogenous thyroid hormone, levels of hormone supplementation, and developmental outcome (Heyerdahl and Oerbeck, 2003; Oerbeck et al., 2003, 2005; Oerbeck et al., 2007). The neuropsychological outcome of children diagnosed with CH at birth is associated with both the severity of CH and early treatment factors (how soon thyroid hormone was administered, starting dose and serum thyroid hormone levels during the first 2 years of life). These hormone parameters were highly correlated with verbal IQ at 20 years of age, and children with CH who ultimately completed high school had a significantly higher thyroid hormone starting dose than those who did not (Oerbeck et al., 2003). Interestingly, the difference in mean starting dose between these two groups was only 2.1 µg/kg/day. Because iodine represents 65% (weight/weight) of thyroid hormone, the amount of iodine associated with that difference is only 1.37 µg/kg/day. Others have found that a difference in starting dose of only 12.5 µg/day (8.13 µg/day iodine equivalent or 2.3 µg/kg/day) was associated with a significant difference in full-scale IQ of 11 points (Selva et al., 2002; Selva et al., 2005). Thus, small differences in available thyroid hormone (and the iodine associated with it) during the first few weeks of life can have significant lifetime consequences.

These increased demands for thyroid hormone production in neonates may be compounded because adaptive mechanisms are not as robust. These mechanisms may include negative feedback

responses [i.e., thyroid-stimulating hormone (TSH) response to low T4], changes in serum binding proteins or iodothyronine transporters, or changes in deiodinases (Zoeller, 2005). Thus, a variety of adaptive mechanisms available to adults may not be available to the neonate, causing the neonate to adapt poorly to iodide uptake inhibition. Studies in rats indicate that the ability of the neonate to adapt to low iodide is poor, that compensation appears to be tissue-specific, and that humans are likely to respond in a similar manner (Pedraza et al., 2006). Mild iodide deficiency lowered thyroid hormone in the absence of an increase in TSH, suggesting that TSH may not be a sensitive index of thyroid hormone status in early life (Pedraza et al., 2006).

In summary, I believe the recent CDC study on perchlorate is the single most credible study in humans and that it has important implications for the impact of perchlorate on child health. Considering that there are about 4 millions babies born in this country every year, and that every one of them is exposed to perchlorate, we cannot ignore this CDC study or its implications.

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HAZARDOUS WASTE SITES WITH PCE/TCE DETECTION

FACILITY NAME	EPA ID#	LOCATION	TCE/PCE µg/L
Alliant Techsystems, Inc.	MDD003067121	55 Thiokol Rd. Elkton, MD 21921	
Browning-Ferris, Inc.	MDD000797365	7890 Solley Road Glen Burnie, MD 21061	TCE 17
Cytec Engineered Materials Inc.	MDD003075942	1300 Revolution Street Havre de Grace, MD 21078	
Electro-Therm Inc.	MDD043375757	Denton	
General Electric Co., Appliance Park, East	MDD046279311	9001 Snowden River Parkway Columbia, MD 21046	
GE Railcar (P&R Railcar Service)	MDD078288354	505 Blue Ball Road (Rte. 545) Elkton, MD 21922	
General Motors Truck Group	MDD003091972	2122 Broening Highway Baltimore, MD 21224	
WR Grace, Columbia	MDD074933961	7379 Route 32 Columbia, MD 21044	TCE 46.6 PCE 67.0
ISG Sparrows Point (former Bethlehem Steel)	MDD053945432	5111 North Point Boulevard Sparrows Point, MD 21219	
Safety-Kleen Corp.	MDD000737395	12164 Tech Road Silver Spring, MD 20904	TCE 44 PCE 380
Sherwin Williams Co.	MDD000215160	2325 Hollins Ferry Road Baltimore, Maryland 21230	

PCE_TCE Site Locations 5-1-08

MD-.	SITE NAME	ADDRESS	CITY	ZIP CO	COUNTY	NOTES
MD-067	FORT GEORGE G. MEADE	Fort Meade	Fort Meade	20755	ANNE ARUNDEL	
MD-428	FORT DETRICK AREA B	Rosemont Ave.	Frederick	21701	FREDERICK	
MD-032	ABERDEEN PROVING GROUNDS - EDGEWOOD AREA	off Route 40	Aberdeen	21001	HARFORD	
MD-065	ABERDEEN PROVING GROUNDS - MICHAELSVILLE AREA	off Route 40	Aberdeen	21005	HARFORD	
MD-157	U.S. ARMY PHOENIX - CONTROL	Sunnybrook Road	Jacksonville	21131	BALTIMORE	
MD-088	ANDREWS AIR FORCE BASE	Allentown Road	Camp Springs	20331	PRINCE GEORGE'S	
MD-413	Former BRANDYWINE DRMO SALVAGE YARD	Rt. 381 Brandywine Road	Andrews	20331	PRINCE GEORGE'S	
MD-057	PATUXENT RIVER NAVAL AIR STATION	Rt. 235	Lexington Park	20670	ST. MARY'S	
MD-064	NAVAL ORDANCE STATION - INDIAN HEAD	Rt. 210	Indian Head	20640	CHARLES	
MD-334	U.S. NAVAL STATION ANNAPOLIS	Annapolis Naval Complex	Annapolis	20084	ANNE ARUNDEL	
MD-482	Former FORT RITCHIE	Ft. Ritchie Road	Cascade	21719	WASHINGTON	
MD-061	Former NSWC White Oak	10901New Hampshire Ave.	Silver Spring	20903	PG/Montgomery	
MD-234	Former Nike BA-03 Phoenix Launch	Paper Mill Road	Jackson	21131	Baltimore	
Md-220	Former Nike BA-30/31 Tolchester Launch	Rock Hall-tolchester Road	Tolchester	21661	Kent	
MD-207	Former Nike-BA-43 Fort Smallwood Launch	9034 Ft. Smallwood Road	Pasadena	21122	Anne Arundel	
MD-205	Former Nike W-25 Davidsonville Launch	3737 Elmer Hagner Lane	Davidsonville	21035	Anne Arundel	
MD-230	Former Nike W-35 Croom Launch	8520 Duval Road	Upper Marlboro	20772	Prince George's	
MD-232	Former Nike W-44 Waldorf Launch	16800 Country Lane	Waldorf	20601	Charles	
MD-224	Former Nike W-93 Launch Laytonsville	5321 Riggs Road	Laytonsville	20879	Montgomery	

Environmental Working Group

Perchlorate Timeline

50 Years of Deception and Delay

1940's: Large-scale production of perchlorate begins, expanding along with the growth of the postwar military-industrial complex.

1952: Perchlorate is found to impair normal thyroid function by interfering with iodine uptake by the thyroid gland (1).

1957: Study shows that perchlorate can pass through the placenta and can affect fetal animals more seriously than adults (2).

1957: Article in the Journal of the American Water Works Association describes how "several California municipalities have experienced pollution of ground water supplies as a result of local underground disposal practices [of rocket fuel waste]" (3).

1950's - 60's: Perchlorate's inhibitory effects on thyroid hormone production are exploited by physicians to treat hyperthyroidism/Grave's disease (overactive thyroid) (4).

1960's: Reports of adverse effects of perchlorate treatment for Grave's disease begin to appear in the medical literature (5,6,7).

1962: Industry and the Department of Defense form the Inter-Agency Chemical Rocket Propulsion Group with the goal of making sure that perchlorate rules and regulations do not impose "unnecessary and excessive restrictions to industrial operations" (8).

1964: California Department of Water Resources tests groundwater in Sacramento and finds perchlorate in 34 wells at levels of up to 18,000 ppb (9).

1966: Study published showing that eleven of 76 severely ill Graves' disease patients treated with perchlorate suffered at least moderate and sometimes fatal hematological side effects (10).

Late 1960's: Physicians move on to safer and more effective treatments for hyperthyroidism (4).

1979 - 1985: Perchlorate found at Superfund sites in California (11, 12).

1992: EPA issues first provisional safe dose for perchlorate, equivalent to 4 ppb in drinking water (11).

1992: Industry launches the front group, the Perchlorate Study Group funded by Aerojet, Alliant Techsystems, American Pacific/Western Electrochemical Company,

Atlantic Research Corporation, Kerr-McGee Chemical Corporation, Lockheed Martin, Thiokol Propulsion Group, and United Technologies Chemical Systems (13).

1995: EPA's provisional safe dose raised to range equivalent of 4 ppb to 18 ppb, after industry-funded studies are submitted to EPA (11,14).

1995: EPA finds that laboratory animals developed thyroid disorders after two weeks of drinking perchlorate-laced water (15).

1997: California Department of Health Services discovers perchlorate contamination in the Colorado River while trying to develop new detection method; contamination is traced hundreds of miles upstream to a Department of Defense contractor manufacturing perchlorate. Subsequent testing finds widespread contamination in California groundwater (15).

1997: California sets action level for perchlorate in drinking water of 18 ppb (16).

1998: EPA raises provisional range to 32 ppb, even after a new study shows that perchlorate can cause health effects at lower doses than expected and has greater effects when consumed for longer periods of time (17).

1999: External peer review of EPA's "safe" dose concludes that more research is needed before an official EPA level could be set (18).

1999: EPA lists perchlorate under the federal Unregulated Contaminant Monitoring Rule, with monitoring beginning in January of 2001 (19).

2000: Arizona state health department finds a significant increase in abnormal thyroid hormone levels in infants whose mothers drank perchlorate-tainted water from the Colorado River while pregnant (20).

2002: EPA issues a revised "safe" dose of perchlorate, equivalent to 4 ppb, based on animal studies showing effects at very low levels. California revises its action level to 4 ppb (16).

2002: Greer et al publish findings after studying effects of varying doses of perchlorate on 37 health volunteers; according to study authors, the statistical no observed level (NOEL) is 0.007 mg/kg/day (21).

2002: Beginning this year and every year since, DoD seeks a congressional exemption from all state and federal environmental laws for uses of chemical constituents in military munitions, including perchlorate.

2004: FDA publishes study on perchlorate food contamination, finds extensive contamination of the nation's food supply (22).

2005: The National Research Council of the National Academies of Science publishes its technical review of perchlorate (Health Implications of Perchlorate Ingestion). EPA

used information from the review to set reference dose (RfD) for perchlorate of 0.0007 mg/kg/day, equivalent to 24.5 ppb (23).

2005: Scientists from Texas Tech University test 36 breast milk samples from 18 states for perchlorate and find contamination in every sample (24).

2005: Government Accountability Office (GAO) report details perchlorate contamination of drinking water supplies in 28 states, at concentrations ranging from 4 ppb to over 420 ppb (25).

2006: EPA Superfund office issues guidance without public comment recommending a drinking water equivalent level (DWEL) of 24.5 ppb at hazardous waste sites (26).

2006: EPA's Children's Health Protection Advisory Committee (CHPAC) writes EPA administrator arguing Preliminary Remediation Goal (PRG) is not protective of infants (27).

2006: EPA responds that it is standing by the PRG (28).

2006: EPA's response to questions from the House Energy and Commerce Committee identify 61 DoD facilities contaminated with perchlorate. Thirty-five are listed on National Priority List (NPL). Twenty-nine of these sites had sampling results exceeding EPA's RfD of 24.5 ppb. Of the 26 non-NPL sites, 15 sites exceed EPA's proposed RfD (29).

2006: Massachusetts becomes the first state in the U.S. to set drinking water standard for perchlorate (2 pbb), based on animal and human studies (30).

2006: CDC scientists publish two studies using NHANES data, representing the first large epidemiological studies to investigate relationship between perchlorate exposure and thyroid hormone levels (31,32). Key findings include:

- Perchlorate is found in the urine of every one of 2,820 U.S. residents (ages 6 and older) in a nationally representative sample.
- Children ages 6 to 11 are exposed to an average of 1.6 times more perchlorate than adults.
- Perchlorate exposure at levels significantly lower than the EPA RfD of 24.5 ppb are associated with a lowering of thyroid hormone levels in women who are iodine insufficient (one third of American women).

2007: Rebutting questions from Republican Congressmen Joe Barton and John Shimkus of the House Committee on Energy and Commerce challenging these findings, the CDC states bluntly "...the findings of the Blount (thyroid) study are consistent with causality." "We do not think that confirmatory analysis is necessary to validate Blount's analysis using the NHANES data" (33).

2007: Scientists from CDC and academia publish two studies confirming widespread contamination of breast milk with perchlorate (34, 35).

2007: California sets drinking water standard for perchlorate (6 ppb) based on human studies (36).

2008: FDA publishes study finding that three quarters of nearly 300 commonly-consumed foods and beverages are contaminated with perchlorate (37).

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Urinary Perchlorate and Thyroid Hormone Levels in Adolescent and Adult Men and Women Living in the United States

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Background: Perchlorate is commonly found in the environment and known to inhibit thyroid function at high doses. Assessing the potential effect of low-level exposure to perchlorate on thyroid function is an area of ongoing research.

Objectives: We evaluated the potential relationship between urinary levels of perchlorate and serum levels of thyroid stimulating hormone (TSH) and total thyroxine (T_4) in 2,299 men and women, ≥ 12 years of age, participating in the National Health and Nutrition Examination Survey (NHANES) during 2001–2002.

Methods: We used multiple regression models of T_4 and TSH that included perchlorate and covariates known to be or likely to be associated with T_4 or TSH levels: age, race/ethnicity, body mass index, estrogen use, menopausal status, pregnancy status, premenarche status, serum C-reactive protein, serum albumin, serum cotinine, hours of fasting, urinary thiocyanate, urinary nitrate, and selected medication groups.

Results: Perchlorate was not a significant predictor of T_4 or TSH levels in men. For women overall, perchlorate was a significant predictor of both T_4 and TSH. For women with urinary iodine < 100 μg/L, perchlorate was a significant negative predictor of T_4 ($p < 0.0001$) and a positive predictor of TSH ($p = 0.001$). For women with urinary iodine ≥ 100 μg/L, perchlorate was a significant positive predictor of TSH ($p = 0.025$) but not T_4 ($p = 0.550$).

Conclusions: These associations of perchlorate with T_4 and TSH are coherent in direction and independent of other variables known to affect thyroid function, but are present at perchlorate exposure levels that were unanticipated based on previous studies.

Key words: exposure, iodine, NHANES, perchlorate, thyroid, thyroxine, TSH. *Environ Health Perspect* 114:1865–1871 (2006). doi:10.1289/ehp.9466 available via *http://dx.doi.org/* [Online 5 October 2006]

Perchlorate is an inorganic anion used for a variety of products such as road flares, explosives, pyrotechnics, and solid rocket propellant (Mendiratta et al. 1996). Perchlorate can also form naturally in the atmosphere, leading to trace levels of perchlorate in precipitation (Dasgupta et al. 2005). Natural processes are considered to concentrate perchlorate in some locations such as regions of west Texas (Dasgupta et al. 2005) and northern Chile (Urbansky et al. 2001). A combination of human activities and natural sources has led to the widespread presence of perchlorate in the environment. As of November 2005, perchlorate was detected in drinking water samples from 4.1% of community water supplies in 26 different states, with levels ranging from the method detection limit of 4 μg/L to a maximum at 420 μg/L [U.S. Environmental Protection Agency (EPA) 2005]. Most of this drinking-water contamination is likely due to contaminated source waters, although in rare instances perchlorate formation has been reported to occur in water distribution systems (Jackson et al. 2004). Additionally, perchlorate exposure from the diet is probable because of the contamination of milk (Kirk et al. 2005), vegetables (Sanchez et al. 2005), fruit (Sanchez et al. 2006a), grain (Sanchez et al. 2006b), and forage crops (Jackson et al. 2005). Perchlorate contamination has also been reported in dietary supplements and flavor enhancers (Snyder et al. 2006).

Trace levels of perchlorate in the environment leads to human exposure. Direct measurement of perchlorate in biological samples collected from people [National Research Council (NRC) 2005] is considered an excellent assessment of their exposure. We recently assessed perchlorate exposure in a nationally representative sample of 2,820 U.S. residents, ≥ 6 years of age, who participated in the National Health and Nutrition Examination Survey (NHANES) during 2001 and 2002 (Blount et al. 2006).

Environmental perchlorate exposure is of potential health concern because much larger doses of perchlorate have been shown to competitively inhibit iodide uptake (Greer et al. 2002; Wyngaarden et al. 1953). Populations with low intake of iodine or increased demand for iodine may be more vulnerable to inhibition of iodide uptake. Sustained inhibition of iodide uptake can lead to hypothyroidism, although perchlorate-induced changes to thyroid function have not been previously demonstrated in any human population exposed to perchlorate, even at doses as high as 0.5 mg/kg body weight per day (NRC 2005). The thyroid plays a crucial role in energy homeostasis and neurologic development. Hypothyroidism can lead to metabolic problems in adults and abnormal development during gestation and infancy (Braverman and Utiger 2000). Severe hypothyroidism due to iodine deficiency during pregnancy is a preventable cause of cretinism, a permanent cognitive impairment of the developing fetus (Glinoer 2000). Mild hypothyroidism during pregnancy has been associated with subtle cognitive deficits in children (Haddow et al. 1999; Klein et al. 2001), leading the NRC to recommend that consideration be given to adding iodide to all prenatal vitamins (NRC 2005). Therefore, we examined relationships between urinary perchlorate and serum thyroid hormones in men and women, ≥ 12 years of age, who participated in NHANES 2001–2002.

Subjects and Methods

Study design. NHANES is conducted by the National Center for Health Statistics of the Centers for Disease Control and Prevention (CDC). This survey is designed to assess the health and nutrition status of the civilian, noninstitutionalized U.S. population. NHANES uses a complex multistage probability sampling designed to be representative of the U.S. population based on age, sex, race/ethnicity, and income. Data reported in the present study were collected using an extensive household interview addressing health conditions and health-related behaviors and a standardized physical examination including medical blood and urine tests, which were conducted in mobile examination centers. NHANES 2001–2002 was conducted in 30 locations throughout the United States. Overall, the

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The authors declare they have no competing financial interests.

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survey interview response rate was 83.9% and the exam response rate was 79.6%. A full description of the NHANES survey is available on the NHANES website (CDC 2004). The study protocol was reviewed and approved by the CDC institutional review board; additionally, informed written consent was obtained from all subjects before they took part in the study.

Urinary perchlorate levels were measured by the Division of Laboratory Sciences, National Center for Environmental Health, on a representative random one-third subsample consisting of 2,820 study participants (males and females), ≥ 6 years of age (Blount et al. 2006). For ages ≥ 12 years, 2,517 persons were in the random subsample. Serum levels of thyroid stimulating hormone (TSH) and total thyroxine (T_4) were only available for 2,299 participants ≥ 12 years of age.

Demographic variables. Sociodemographic data were self-reported by study participants. Race/ethnicity was derived from self-reported questionnaire data and categorized as non-Hispanic white, non-Hispanic black, Mexican American, and "other." Each of these race/ethnicity categories was used in the regression modeling. Non-Hispanic whites were used as the referent group in regression analysis.

Laboratory methods. During the physical examinations, whole blood and spot urine specimens were collected from participants, aliquoted, and stored cold (2–4°C) or frozen until shipment. Whole blood was collected into a red-top 15-mL Vacutainer tube, mixed, allowed to clot 30–45 min, and centrifuged; approximately 1 mL serum was stored frozen in a cryovial for future analysis for TSH and T_4. Serum samples collected in 2001 were assayed for TSH and T_4 by the Coulston Foundation (Alamogordo, NM) using a microparticle enzyme immunoassay for the quantitative determination of TSH, and a Hitachi 704 chemistry analyzer (Hitachi Chemical Diagnostics, Mountain View, CA) for the quantitative determination of T_4 (CDC 2003). Serum samples collected in 2002 were assayed for TSH and T_4 by Collaborative Laboratory Services (Ottumwa, IA) using a chemiluminescent immunoassay (Access Immunoassay System; Beckman Instruments, Fullerton, CA) (CDC 2003). The National Center for Health Statistics evaluated the TSH and T_4 data sets from the two laboratories and determined that the values are comparable across the 2 years.

Surplus urine samples from NHANES 2001–2002 were shipped on dry ice to the Division of Laboratory Sciences and analyzed for perchlorate, thiocyanate, and nitrate using ion chromatography tandem mass spectrometry (Blount et al., 2006; Valentin-Blasini et al. 2005). These samples were stored frozen (–70°C) for up to 4 years before perchlorate analysis. Experiments evaluating storage at –70°C for > 2 years indicated no changes in urinary levels of this analyte (Blount et al. 2006). Reported results for all assays met the division's quality control and quality assurance performance criteria for accuracy and precision [similar to specifications outlined by Westgard et al. (1981)]. Urine samples from the same study participants had previously been analyzed for iodine using inductively coupled plasma mass spectrometry (Caldwell et al. 2005).

Statistical analysis. Initial multiple regression analysis found perchlorate to be a significant predictor of both T_4 and log TSH in women, but perchlorate did not predict either T_4 or log TSH in men (data not shown). Therefore, we present subsequent analysis focused on women.

Of the 1,318 women ≥ 12 years of age, 92 had missing TSH and T_4 values, leaving 1,226. Of these 1,226 women, 91 were excluded from analysis because they reported a history of thyroid disease or current use of thyroid medications, leaving 1,135 women. Of these 1,135 women, 3 had extreme values of T_4 and/or TSH and were excluded. One of these women had a total T_4 of 27 μg/dL and a TSH of 0.04 IU/L. This woman was clearly hyperthyroid and thus was excluded from the analysis. Two other women had very high TSH levels (43 and 68 IU/L) and were excluded. Of the remaining 1,132 women, 21 had missing perchlorate measurements, leaving a sample size of 1,111 women.

The major design variables for NHANES are age, sex, race/ethnicity, and income related to the poverty level. The values of these variables for the initial 1,318 women and the final 1,111 women, respectively, are as follows: mean age, 41.6 and 39.8 years; percent non-Hispanic whites, 70.8% and 69.4%; percent non-Hispanic blacks, 11.8% and 12.5%; percent Mexican Americans, 7.0% and 7.0%; and percent below the poverty level, 13.9% and 14.9%.

We chose covariates for the multiple regression analyses that are known to be or likely to be associated with T_4 or TSH. We selected a broad number of covariates to evaluate the independence of the perchlorate relationship. These covariates were age, race/ethnicity, body mass index (BMI), serum albumin, serum cotinine (a marker of tobacco smoke exposure), estimated total caloric intake, pregnancy status, postmenopausal status, premenarche status, serum C-reactive protein, hours fasting before sample collection, urinary thiocyanate, urinary nitrate, and use of selected medications.

For these covariates, Table 1 provides means (or geometric means if lognormally distributed) for continuous variables, percent in category for categorical variables, and number of missing results for each covariate. Thyroid

Table 1. Means and percent in category for covariates used in the multiple regression, women ≥ 12 years of age, NHANES 2001–2002.[a]

Variable	No.	No. missing	Arithmetic mean (95% CI)	Geometric mean (95% CI)	Percent in category (95% CI)
Age (years)	1,111	0	39.8 (38.1–41.6)		
Fasting (hr)	1,111	0	10.4 (9.85–10.9)		
Serum albumin (g/dL)	1,111	0	4.20 (4.17–4.23)		
Serum T_4 (μg/dL)	1,111	0	8.27 (7.97–8.58)		
Total kilocalories (kcal/1,000)	1,072	39	1.93 (1.87–1.99)		
BMI	1,075	36		25.6 (25.2–26.5)	
Serum cotinine (μg/L)	1,104	7		0.33 (0.23–0.48)	
Serum C-reactive protein (mg/dL)	1,111	0		0.16 (0.14–0.18)	
Serum TSH (IU/L)	1,111	0		1.36 (1.31–1.42)	
Urine creatinine (mg/dL)	1,109	2		81.4 (76.7–86.5)	
Urine iodine (μg/L)	1,111	0		126 (115–138)	
Urine nitrate (μg/L × 1,000)	1,106	5		38.0 (35.9–40.3)	
Urine perchlorate (μg/L)	1,111	0		2.84 (2.54–3.18)	
Urine thiocyanate (μg/L × 1,000)	1,104	7		1.20 (1.08–1.33)	
Race/ethnicity					
Non-Hispanic white	1,111	0			69.4 (62.9–75.4)
Non-Hispanic black	1,111	0			12.5 (7.49–19.1)
Mexican American	1,111	0			7.02 (5.14–9.34)
Other race	1,111	0			11.1 (7.04–16.3)
Medication usage					
Furosemide	1,111	0			1.98 (1.25–3.01)
Glucocorticoids and androgens	1,111	0			2.23 (1.24–3.67)
Beta-blocker	1,111	0			4.48 (3.34–5.87)
Estrogen	1,111	0			17.1 (13.2–21.7)
Other drug	1,111	0			1.04 (0.52–1.88)
Menopausal or postmenopausal	1,028	83			35.9 (30.1–41.9)
Pregnant	1,111	0			3.84 (2.74–5.21)
Premenarchal	1,019	92			1.06 (0.48–2.02)

CI, confidence interval.
[a]Excludes women with missing TSH, T_4, or perchlorate, women with history of thyroid disease or taking thyroid drugs, and three women with outlier values of T_4 or TSH (see text).

function has been previously reported to vary with the constitutional variables of age, race, sex, pregnancy, and menopause (Braverman and Utiger 2000). Serum cotinine is a marker of tobacco smoke exposure, and smoking is associated with altered thyroid function (Bertelsen and Hegedus 1994). We included serum C-reactive protein as a marker for inflammatory conditions that have been associated with alterations in thyroid function. Both total caloric intake [based on a 24-hr dietary recall survey and a U.S. Department of Agriculture (USDA) database (Food and Nutrition Database for Dietary Studies; USDA 2004)] and BMI are related to thyroid function, but the interrelationship as to cause or effect is unclear.

Serum albumin was included in our analysis as a possible surrogate for T_4 serum protein binding. NHANES 2001–2002 included total T_4 measurements but not free T_4 measurements; total T_4 varies with the concentrations of specific binding proteins. Concentrations of these proteins can change with physiologic state and health conditions. Free T_4 varies less with such protein concentration changes than does total T_4. Serum albumin accounts for 15–20% of T_4 binding, with thyroid binding protein and prealbumin (not measured in NHANES) accounting for the remaining percentage (Robbins 2000). Thyroid autoantibody measurements were not available for 2001–2002. For autoantibodies to affect the relationship between perchlorate and T_4 or TSH, presence of autoantibodies would have to correlate with perchlorate levels. We have found no such correlation in the literature and we are unaware of a rationale for such an association.

Medications known to affect thyroid function were also considered. As noted above, women taking medication containing thyroid hormone (e.g., levothyroxine) or antithyroid drugs (e.g., methimazole or propylthiouracil) were excluded. Use of beta-blockers, estrogen formulations, steroids, and furosemide were each modeled using an indicator variable in the regressions. An "other drug" category was also modeled by an indicator variable. This "other drug" category consisted of a heterogeneous group of other medications that have possible effects on thyroid function, protein binding, or measurements, including salicylates, dopaminergics, anticonvulsants and barbiturates, narcotic analgesics, androgenic agents, lithium, and several others (a total of 28 drug codes).

We included the log of urinary creatinine in the models to adjust for variable water excretion. A nonlinear relationship was evaluated by adding the square of the log of perchlorate to final models, but it was not significant. Models were also checked for significance of interaction terms involving main effects. We examined partial regression plots to identify any unduly influential data points; no unduly influential points were found. Indicator variable coefficients in the models (e.g., for non-Hispanic blacks) were interpreted as follows: 1 = group member, and 0 = not a group member. Urine samples were collected in three sessions of the day from 0800 hours through 2200 hours. Mean perchlorate levels were not statistically different across sessions ($p = 0.49$).

We examined univariate statistics and distribution plots for each dependent and independent variable to look for outliers and to assess the distribution shape. TSH, perchlorate, cotinine, BMI, urinary thiocyanate, urinary nitrate, and C-reactive protein were $\log_{10}$-transformed to normalize their distributions.

Regression models, including log of perchlorate as one of the predictor variables, were constructed separately for thyroxine and log of TSH. For the initial phase of analysis, we used ordinary least-squares regression (OLS) (SAS Proc Reg, version 9.0; SAS Institute, Cary, NC) and purposefully did not adjust for the NHANES complex survey design in order to obtain a broad group of potentially significant predictor variables. Forward stepwise and backward elimination procedures were used on both population-weighted and unweighted data. The entry p-value for forward elimination models was 0.10 and the retaining p-value for backward elimination was 0.10 in order to identify significant and borderline significant predictors. The forward stepwise and backward elimination approaches produced models that were generally in good agreement.

This OLS analysis produced a generous list of significant and borderline-significant variables for regression analysis using SUDAAN (version 9.0.1; Research Triangle Institute, Research Triangle Park, NC), which provides an analysis that adjusts for the complex survey design. SUDAAN regression models were tested using a manual backward elimination approach starting with the variables obtained from the OLS regression modeling. Selected variables that were excluded in the SUDAAN backward elimination process were added to the final model to ensure they were not significant. The stability of the perchlorate coefficient was monitored during the SUDAAN backward elimination process.

In the main SUDAAN regression analysis, we used population weights to represent women ≥ 12 years of age in the U.S. population for the years 2001 and 2002. In addition, we performed separate regression analyses with SUDAAN using unweighted data and verified that regression coefficients were in good agreement with those obtained using population weights. Reported regression model results in the tables use the population-weighted analysis.

Women were categorized based on a urinary iodine cut point of 100 μg/L and analyzed separately. The 100 μg/L cut point was used based on the World Health Organization (WHO) definition of sufficient iodine intake in populations (WHO 1994). The WHO noted that the prevalence of goiter begins to increase in populations with median urinary iodine < 100 μg/L. A urine iodine level of 100 μg/L represents about the 36th percentile of urinary iodine concentrations in women living in the United States (Caldwell et al. 2005). Women with lower iodine intake could be more vulnerable to perchlorate's effects to impair iodine uptake. From this analysis, the significance of urinary perchlorate as a predictor of thyroid function in women was found to be largely determined by women with urinary iodine < 100 μg/L. Consequently, we report here results for women divided into groups based on urinary iodine levels.

Compared to the use of average multiple spot urine measurements or 24-hr urine specimens, the use of a single spor urine for perchlorate and iodine measurement has more imprecision in estimaring true urine levels (Andersen et al. 2001). This imprecision is a source of random error (not bias) and therefore decreases statistical power to detect an association between perchlorate and either TSH or T_4 compared to these other urine collection approaches.

Results

For all women ≥ 12 years of age, multiple regression analysis found urinary perchlorate to be a significant predictor of serum TSH and a significant predictor of serum T_4 (data not shown). Because low iodine levels had potential to affect the relationship of perchlorate with T_4 and TSH, women with urinary iodine < 100 μg/L were analyzed separately from women with urinary iodine ≥ 100 μg/L. Results of this analysis are presented in Tables 2 and 3 for T_4 and in Tables 4 and 5 for TSH.

For women with urinary iodine < 100 μg/L, multiple regression analysis found perchlorate to be a significant predictor ($p < 0.0001$) of T_4 with a coefficient for log perchlorate of −0.8917. The result of regression of T_4 on perchlorate and urinary creatinine without other covariates yielded a coefficient of −0.8604 ($p < 0.0001$). Perchlorate was also a significant predictor ($p = 0.0010$) of log TSH with a coefficienr of 0.1230. The result of regression of log TSH on perchlorate and urinary creatinine without other covariates found a coefficient of 0.1117 ($p = 0.0031$). The signs of these coefficients are coherent, with increased perchlorate associated with less producrion of T_4 and an increase in TSH to stimulate additional T_4 production. For women with urinary iodine ≥ 100 μg/L, perchlorate was not a significant predictor of T_4 ($p = 0.5503$) but remained a significant predictor of log TSH ($p = 0.0249$). The regression analysis results

in Tables 2–5 include variables that were borderline significant ($0.05 \leq p < 0.10$) to give ample opportunity for other variables to explain variance and better evaluate the independence of the perchlorate effect.

Regression results for men (not shown) indicated that perchlorate was not a significant predictor of either T_4 or log TSH. This finding also held when examining men with urinary iodine levels < 100 μg/L.

From the regression coefficients for women with urinary iodine < 100 μg/L, we calculated the predicted effect size (i.e., the change in T_4 and TSH) for different levels of perchlorate exposure. We chose perchlorate levels corresponding to the 5th, 10th, 25th, 50th, 75th, 90th, and 95th percentiles of urinary perchlorate in women ≥ 12 years of age. The minimum and maximum perchlorate values are observed results for this population sample; they are not estimates of the 0th and 100th percentiles for the U.S. population. As such, they would be expected to change in another population sample. The effect size was calculated from the difference between the minimum level of perchlorate measured in women and the level of perchlorate corresponding to the specific percentile. For example, the 50th percentile of urinary perchlorate for women was 2.9 μg/L and the minimum level was 0.19 μg/L. Increasing exposure from 0.19 μg/L to 2.9 μg/L would result in a predicted decrease in T_4 of 1.06 μg/dL.

For TSH, one more step is needed in the calculation. Because TSH was modeled as log TSH, the change in TSH from a given change in perchlorate depends on the starting level of TSH. In our calculations we used the approximate 50th and 90th percentiles of TSH as starting points to estimate the predicted perchlorate effect size for TSH. Results of these calculations for T_4 and TSH are presented in Table 6. For comparison, the normal range is 5–12 μg/dL for T_4 and 0.3–4.5 IU/L for TSH.

To search for a threshold for the perchlorate relationship with T_4 and TSH, piecewise regression models (Neter et al. 1985) were fit to the data. No inflection point was found for the perchlorate relationship with T_4 or TSH. However, statistical power is limited to detect such a threshold, if present.

Table 2. Regression of serum T_4 on perchlorate and covariates for women ≥ 12 years of age with urine iodine < 100 μg/L, NHANES 2001–2002.

Independent variable	Coefficient	SE	*p*-Value
Intercept	8.6508	0.5428	< 0.0001
Log (urinary perchlorate)	−0.8917	0.1811	< 0.0001
Log (urinary creatinine)	0.6697	0.3338	0.0391
Estrogen use	1.5117	0.4421	0.0007
Log (C-reactive protein)	0.8249	0.1774	< 0.0001
Mexican American[a]	0.6296	0.3684	0.0876
Menopause	−0.5908	0.2578	0.0221
Pregnant (by test)	0.7389	0.3662	0.0439
Total kilocalorie intake (÷ 1,000)	−0.3334	0.1173	0.0046
Premenarche	0.6401	0.2722	0.0189

Dependent variable: serum T_4 ($n = 348$; $R^2 = 0.240$).
[a]Referent group for race is non-Hispanic white.

Table 3. Regression of serum T_4 on perchlorate and covariates for women ≥ 12 years of age with urine iodine ≥ 100 μg/L, NHANES 2001–2002.

Independent variables	Coefficient	SE	*p*-Value
Intercept	10.6652	1.2345	< 0.0001
Log (urinary perchlorate)	0.2203	0.3687	0.5503
Log (urinary creatinine)	1.3138	0.7183	0.0677
Estrogen use	0.8278	0.2722	0.0024
Log (C-reactive protein)	0.5783	0.1247	< 0.0001
Mexican-American[a]	0.5763	0.2522	0.0225
Pregnant (by test)	1.6175	0.3334	< 0.0001
Log (urinary nitrate)	−1.1215	0.4994	0.0249
Hours of fasting	0.0290	0.0156	0.0630

Dependent variable: serum T_4 ($n = 724$; $R^2 = 0.149$).
[a]Referent group for race is non-Hispanic white.

Table 4. Regression of serum TSH on perchlorate and covariates for women ≥ 12 years of age with urine iodine < 100 μg/L, NHANES 2001–2002.

Independent variables	Coefficient	SE	*p*-Value
Intercept	0.2654	0.1183	0.0403
Log (urinary perchlorate)	0.1230	0.0373	0.0010
Log (urinary creatinine)	−0.0954	0.0761	0.2103
Beta-blocker use	0.1861	0.0595	0.0016
Estrogen use	−0.0918	0.0404	0.0233
Premenarche	0.1288	0.0262	< 0.0001

Dependent variable: log of serum TSH ($n = 356$; $R^2 = 0.061$).

Table 5. Regression of serum TSH on perchlorate and covariates for women ≥ 12 years of age with urine iodine ≥ 100 μg/L, NHANES 2001–2002.

Independent variables	Coefficient	SE	*p*-Value
Intercept	−0.6948	0.3415	0.0600
Log (urinary perchlorate)	0.1137	0.0506	0.0249
Log (urinary creatinine)	−0.1198	0.0910	0.1884
Age in years	0.0025	0.0006	< 0.0001
Log (BMI)	0.4812	0.1348	0.0004
Non-Hispanic black[a]	−0.1125	0.0335	0.0008
Log (urinary nitrate)	0.1087	0.0591	0.0660
Log (urinary thiocyanate)	−0.0816	0.0352	0.0206

Dependent variable: log of serum TSH ($n = 697$; $R^2 = 0.145$).
[a]Referent group for race is non-Hispanic white.

Discussion

Increased urinary perchlorate was associated with increased TSH and decreased T_4 for women with urinary iodine levels < 100 μg/L, a group possibly more susceptible to competitive inhibition of thyroid iodine uptake by perchlorate. The statistically significant associations of urinary perchlorate with decreased serum T_4 and increased serum TSH were consistent with competitive inhibition of iodide uptake.

For women with urine iodine ≥ 100 μg/L, perchlorate was also a statistically significant predictor for TSH but not for T_4. Greater iodine intake may have diminished the effect of perchlorate on T_4 in these women. The significant association with TSH, but not with T_4, in this group may be due to the greater sensitivity of TSH to impairment of thyroid function; that is, normal T_4 levels are maintained by increasing TSH to compensate for impaired thyroid function.

Predicted changes in serum TSH and T_4 with increasing perchlorate exposure (Table 6) can span a notable portion of the normal medical range of TSH and T_4 values. Compared with a urine level of 0.19 μg/L, urinary perchlorate of 13 μg/L (95th percentile) yields a predicted decrease in T_4 of 1.64 μg/dL. The normal range for T_4 is 5–12 μg/dL. A similar exposure would increase TSH by 2.12 IU/L for a woman starting with a TSH level of 3.11 IU/L (90th percentile for TSH in

women ≥ 12 years of age). The normal range for TSH is 0.3–4.5 IU/L. Effect size estimates that start with the 90th percentile of TSH have more uncertainty than estimates starting with the 50th percentile because the predicted TSH levels fall further from the central portions of the original data.

The mechanism of perchlorate's effect is competitive inhibition of iodide uptake by the thyroid (Clewell et al. 2004; Wolff 1998). Based on this mechanism, individuals with less iodide available to compete with perchlorate may be more vulnerable to impaired iodide uptake. Chronically impaired iodide uptake could lead to changes in serum thyroid hormones, consistent with the increased TSH and decreased T_4 we find associated with increased perchlorate exposure in women with urinary iodine < 100 μg/L. The WHO (2004) has identified median urinary iodine levels ≥ 100 μg/L as indicating sufficient iodine intake for a population. Based on concerns about adequate iodine intake, the NRC (2005) recently recommended that consideration be given to adding iodine to all prenatal vitamins.

In the present study, perchlorate was not found to be a significant predictor of T_4 or TSH in men. Previous studies report that women have a much higher risk of goiter than do men, especially in populations with marginal iodine intake (Laurberg et al. 2000). The increased vulnerability of women may partially be caused by increased susceptibility to autoimmune thyroid disease in women, the increased demands on the thyroid during pregnancy, or the effect of estrogens on thyroid function. Estradiol has been shown to block TSH-induced sodium/iodide symporter (NIS) expression in the FRTL5 rat follicular cell line (Furlanetto et al. 1999). Impaired NIS expression could lead to reduced ability of the thyroid follicular cells to import iodide, and thus an increased vulnerability to NIS-inhibitors such as perchlorate. Also, estrogens increase T_4-binding globulin and thus increase the demand for T_4 so that free T_4 levels can remain constant.

Covariates in the regression models predicted T_4 and TSH levels in a manner generally consistent with previous studies. We found that estrogen use was a significant, independent, and positive predictor of T_4 in both low and sufficient iodine models of women ≥ 12 years of age, but was not a significant predictor in either of the TSH models. Similar to estrogen use, pregnancy was a significant or borderline significant predictor of T_4 but not TSH. Both estrogen use and pregnancy raise estrogen levels, increase thyroid binding proteins, and increase serum T_4 concentrations (Glinoer 1997). Menopause lowers estrogen levels and was a significant predictor of T_4 in the regression for women with urinary iodine levels < 100 μg/L.

In NHANES III (1988–1994), non-Hispanic blacks were reported to have lower TSH than other groups, and Mexican Americans had higher T_4 levels than non-Hispanic blacks and whites (Hollowell et al. 2002). The models for TSH and T_4 in the present study were consistent with these previous findings concerning race/ethnicity. Non-Hispanic blacks have also been shown to have lower urinary perchlorate levels than non-Hispanic whites, although the reason for this difference is not known (Blount et al. 2006). Age was positively associated with TSH in women with urinary iodine levels ≥ 100 μg/L, but not significant for women with urinary iodine levels < 100 μg/L. A positive association of age and TSH was seen in NHANES III and other studies (Canaris et al. 2000; Hollowell et al. 2002).

BMI was significant in the TSH model for women with urinary iodine levels ≥ 100 μg/L, and total caloric intake was significant in the T_4 model for women with urinary iodine levels < 100 μg/L. Thyroid function clearly has an effect on BMI, as seen clinically and documented in populations (Nyrnes et al. 2006). The reverse is also true, because BMI and total caloric intake can influence the hypothalamic–pituitary–thyroidal axis, although usually at the extremes of body weight and caloric intake (Acheson et al. 1984; Burger et al. 1987; Danforth et al. 1979; Loucks et al. 1992; Loucks and Heath 1994). Total caloric intake in NHANES is a 24-hr recall of food intake. Depending on how well recent intake reflects long-term intake, total caloric intake may parallel the effect of BMI, which was not seen in the present study. Increased caloric intake is known to increase thyroid hormone disposition through deiodination pathways (Burger et al. 1987; Danforth et al. 1979), increasing the conversion of T_4 to the active form, triiodothyronine (T_3), and increasing conversion of T_3 to inactive forms. The effect of changes in calories and carbohydrate composition of the diet on thyroid disposition may have different short- and long-term effects on T_3 and T_4 levels. In the present study, hours of fasting before sample collection was a borderline significant predictor in one regression model: T_4 in women with sufficient iodine. Fasting for 60 hr can reduce TSH in humans, but fasting for shorter periods has unknown effects on thyroid function.

Beta-blocker drugs are commonly used to treat hypertension and other cardiovascular conditions. Beta-blockers inhibit the conversion of T_4 to the more active form, T3, and increase serum TSH (Kayser et al. 1991). Use of these drugs was positively associated with TSH in the regression for women with urinary iodine < 100 μg/L. Serum C-reactive protein was positively associated with T_4 in women in each of the iodine groups. C-reactive protein is an acute phase reactant protein increased in many inflammatory conditions in response to production of tissue-generated cytokines, particularly interleukin-6, and has been used as a marker for both specific and systemic low-level inflammation conditions. It is unclear if C-reactive protein is associated with thyroid function other than thyroiditis (Jublanc et al. 2004; Pearce et al. 2003; Tuzcu et al. 2005). However, the stimulus for C-reactive protein, interleukin-6, has a firm inverse relationship with serum T_3 in nonthyroidal illnesses. Also, C-reactive protein and serum T_4 binding proteins are synthesized by the liver; C-reactive protein may vary with an unrecognized health or physiologic condition that affects the synthesis of both proteins. The association of C-reactive protein and T_4 in our study is unclear.

Other variables that are known to possibly affect thyroid function or measurements were not significant predictors in the regression models, including the categories of medications (other than estrogen use and beta-blockers), serum albumin, and serum cotinine. Generally, other medication categories were small and unlikely to have significant effects. Serum albumin did not appear in the final models. Factors such as estrogen use that increase protein binding of thyroid hormones may have accounted for variance in T_4 due to protein binding that serum albumin may have otherwise explained. Serum cotinine is a marker of tobacco smoke exposure, and

Table 6. Predicted change in serum T_4[a] and serum TSH[b] levels based on changes in urinary perchlorate levels in women ≥ 12 years of age, with urine iodine < 100 μg/L, NHANES 2001–2002.

Change in urine perchlorate[d]	Change in T_4 (μg/dL)	Change in TSH (IU/L)[c]	
		Initial TSH of 1.40 IU/L (50th TSH percentile)	Initial TSH of 3.11 IU/L (90th TSH percentile)
0.19 to 0.65 μg/L (5th percentile)	0.48	0.23	0.51
0.19 to 0.92 μg/L (10th percentile)	0.61	0.30	0.67
0.19 to 1.6 μg/L (25th percentile)	0.83	0.42	0.93
0.19 to 2.9 μg/L (50th percentile)	1.06	0.56	1.24
0.19 to 5.2 μg/L (75th percentile)	1.28	0.70	1.56
0.19 to 9.0 μg/L (90th percentile)	1.49	0.85	1.89
0.19 to 13 μg/L (95th percentile)	1.64	0.95	2.12
0.19 to 100 μg/L (maximum)	2.43	1.63	3.61

[a]Normal range for T_4: 5–12 μg/dL. [b]Normal range for TSH: 0.3–4.5 IU/L. [c]Depends on initial TSH level. [d]Minimum level measured, 0.19 μg/L.

smoking is associated with altered thyroid function (Belin et al. 2004; Bertelsen and Hegedus 1994). However, tobacco smoke also contains other factors that can inhibit TSH secretion (Bartalena et al. 1995), and perhaps is an explanation for the absence of an association of serum cotinine with either TSH or T_4.

Cyanide in tobacco smoke is metabolized to thiocyanate, a competitive inhibitor of iodide uptake (Tonacchera et al. 2004). Also, nitrate from dietary sources and from formation by intestinal bacteria can compete with iodide. *In vitro* studies indicate that perchlorate is a more potent inhibitor of human NIS, with potencies 15, 30, and 240 times greater than thiocyanate, iodide, and nitrate, respectively (Tonacchera et al. 2004). Thus, the ability of NIS to transport adequate amounts of iodide depends on the relative concentrations of these competing anions. Based on the relative concentrations of perchlorate, nitrate, and thiocyanate likely to be found in human serum, several researchers have predicted that nitrate and thiocyanate are more likely than perchlorate to impair thyroid function (DeGroef et al. 2006; Gibbs 2006). Thiocyanate-induced NIS inhibition is a plausible explanation of the association of smoking with goiter in populations with low iodine intake (Knudsen et al. 2002) and is analogous to the association of perchlorate exposure with thyroid hormone levels observed in our study. However, in women with urinary iodine levels ≥ 100 μg/L, urinary thiocyanate was negatively associated with serum TSH, a direction unexpected based on a mechanism of NIS inhibition. The explanation for this is unclear. Urinary nitrate was negatively associated with serum T_4 in women with urinary iodine levels ≥ 100 μg/L, a direction consistent with inhibition of NIS. Goitrogenic effects of nitrate intake in animal studies have been observed (Wyngaarden et al. 1953), but there are few studies in humans.

Recently the NRC (2005) evaluated the potential health effects of perchlorate ingestion. Based on studies of long-term treatment of hyperthyroidism and clinical studies of healthy adults, the NRC panel estimated that a perchlorate dose of > 0.40 mg/kg/day would be required to cause hypothyroidism in adults, although lower doses may lead to hypothyroidism in sensitive subpopulations (NRC 2005).

Comparison of our results to previous studies requires consideration of *a*) target population group studied, *b*) estimated dose of perchlorate, *c*) duration of exposure to perchlorate dose, and *d*) sample size (statistical power). First, for men, we found no relationship with perchlorate and T_4 or TSH. This finding is in general agreement with predicted effects of this level of perchlorate exposure based on reported studies of exposure in men. Lawrence et al. (2000) administered 10 mg perchlorate daily (~ 0.14 mg/kg) to iodine-sufficient adult males for 14 days and found a 10% decrease in radioactive iodine uptake (RAIU), but with no change in TSH or free T_4.

Greer et al. (2002) administered perchlorate to 16 male and 21 female volunteers for 14 days, and found increasing RAIU inhibition for doses between 0.02 and 0.5 mg/kg/day, with no perchlorate-related change in TSH or free T_4. An unknown number of women in that study may have had urinary iodine < 100 μg/L, but if the women were typical of the U.S. population (Caldwell et al. 2005), the predicted number of women with low urinary iodine would be 7–8. Braverman et al. (2006) administered perchlorate to 13 iodine-sufficient male and female volunteers at daily doses of 0.5 mg and 3 mg for 6 months, and found no change in RAIU, TSH, or free T_4. Two other studies have also found that workers exposed to perchlorate intermittently for long periods did not have significant changes to serum TSH or T_4 levels (Braverman et al. 2005; Lamm et al. 1999). These study populations were either exclusively (Braverman et al 2005) or predominantly (Lamm et al 1999) male.

For women, only two perchlorate studies have focused on women or included a large percentage of women. A recent study of 184 pregnant Chilean women, with mean urinary perchlorate levels near the 99th percentile for women in NHANES 2001–2002, found no perchlorate relationship with thyroid function (Tellez et al. 2005). Of these 184 women, 181 had mean urinary iodine levels ≥ 100 μg/L and only 3 had mean levels < 100 μg/L. Therefore, the results of Tellez et al. (2005) would compare to the present results for women with urinary iodine levels ≥ 100 μg/L. Urinary iodine levels in the Chilean study population (median 269 μg/L) were higher than urinary iodine levels found in the NHANES 2001–2002 population [median 168 μg/L; 95% confidence interval, 159–178 μg/L]. The Chilean women (Tellez et al. 2005) were also pregnant, which increases the variability in T_4 and TSH. This increased variability would make an association between perchlorate and thyroid function harder to find. The second study with a large percentage of women was Greer et al. (2002) discussed above. These two studies are compared with the present study in Table 7.

Table 7 indicates that our study is the first to target and separately analyze results for women with lower levels of urinary iodine, a potentially susceptible population. A second special attribute of the present study is the much larger sample size of women, affording more statistical power to detect a potential effect. By averaging over many women, the current data likely represents a good approximation of a population steady-state exposure to perchlorate that women have had for a long period of time. If a mid- to long-term exposure is needed for perchlorate to affect thyroid function, this data would have a better opportunity to detect that effect than study designs using short-term exposures. The influence of duration of exposure merits further study.

Accurate assessment of exposure is critical to detect biochemical end points potentially related to exposure. Our laboratory recently developed an improved method for measuring urinary perchlorate, which enhances individual perchlorate exposure assessment (Valentin-Blasini et al. 2005). The use of this new urinary perchlorate measurement strengthens the ability of the present study to detect potential associations with T_4 and TSH.

The present study has the general limitations of a cross-sectional analysis. Therefore, the relationship between urinary perchlorate and thyroid function was examined with attention to the potential influences of chance, bias, or confounding. Perchlorate (as with any of the significant predictor variables) could be a surrogate for another unrecognized determinant of thyroid function. We also assumed in this analysis that urinary perchlorate correlates with levels in the thyroid stroma and tissue, a kinetically distinct compartment. This would be the case in a population with stable, chronic exposures, which is likely but not certain in this population. A large sample size helps to average such potential kinetic differences. Finally, a measurement of free T_4 would be an improvement to the study.

Table 7. Comparison of perchlorate studies targeting women or including a high percentage of women.

	Greer et al. (2002)	Tellez et al. (2005)	Present study
No. of females studied	21 (37 total subjects)	184	1,111
No. of females with urine iodine < 100 μg/L	Unknown (estimate 7–8)	3[a]	348, T_4 analysis 356, TSH analysis
Females with urine iodine < 100 μg/L analyzed separately	No	No	Yes
Perchlorate dose and duration of exposure	Up to 0.5 mg/kg/day for 14 days	Long-term environmental exposure	Long-term environmental exposure
Comments		All women pregnant, increasing variability of T_4 and TSH	

[a]Average of one to three spot urine samples.

Conclusions

Urinary perchlorate is associated with an increased TSH and decreased total T_4 in women ≥ 12 years of age with urine iodine levels < 100 μg/L in the U.S. population during 2001–2002. For women with urine iodine levels ≥ 100 μg/L, urine perchlorate is a significant predictor of TSH but not T_4. These effects of perchlorate on T_4 and TSH are coherent in direction and independent of other variables known to affect thyroid function, but are found at perchlorate exposure levels that were unanticipated based on previous studies. Further research is recommended to affirm these findings.

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JONATHAN BORAK & COMPANY, INC.

Specialists in Occupational & Environmental Health

May 20, 2008

Honorable James M. Inhofe
Ranking Member,
Senate Committee on Environment and Public Works
United States Senate
Washington, DC 20510-6175

Dear Senator Inhofe:

Thank you for your letter of May 15, 2008 in which you asked me to comment on current concerns and debates regarding the health effects of perchlorate, particularly with respect to its presence in the nation's water supplies.

Allow me first to introduce myself. I am Clinical Professor of Epidemiology & Public Health and Associate Clinical Professor of Medicine at the Yale University School of Medicine and director of Yale's Interdisciplinary Risk Assessment Forum. I am a member of the Editorial Boards of *Journal of Occupational and Environmental* Medicine, *Journal of Occupational and Environmental Hygiene*, and *Occupational Medicine*. I have published numerous books, book chapters and research papers on the toxicology of environmental contaminants. I have written, spoken and taught on the science of perchlorate for the past six years in the context of my university activities and as a paid advisor to the Perchlorate Study Group and its member companies. My full CV is attached to this letter.

Please note that this letter is a response to your request for information; I do not mean to advocate whether or how perchlorate should be regulated. My hope is that by correcting some often repeated errors concerning the findings of recent scientific research, my comments can help to clarify some of the perchlorate-related confusion and misinformation about which you wrote. The information presented below is not a matter of opinion, but of established and reviewable scientific fact. I have provided the necessary links and references so that the factual correctness of my statements can be independently verified.

1. The Perchlorate database. There is an unusually extensive database on the health effects of perchlorate, reflecting the fact that it has been used medicinally at high doses for more than 50 years. That database has been the subject of recent, critical reviews by a panel of the National Academy of Sciences (NAS) and by the Agency for Toxic

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Substances and Disease Registry (ATSDR).[1,2] The NAS and ATSDR conclusions remain current and relevant today; the more recent reports summarized below affirm and expand those conclusions.

2. The recent FDA report on perchlorate in food. Recent public statements have erroneously characterized the findings of a 2008 report by FDA scientists who measured the content of perchlorate and iodine in US diets.[3] Some have claimed that the FDA data show that perchlorate exposure from food, combined with exposure from water, exceeds established safe levels. The facts indicate otherwise. The FDA study, which considered food intake of Americans from 6-months to greater than 75-years of age, provided no evidence that anyone is exposed to unsafe perchlorate levels from food; a recent EPA study provided complementary evidence for drinking water.

- In 2005, a panel of the National Academy of Sciences (NAS) concluded that perchlorate caused no observable health effects, adverse or otherwise, at levels as high as 0.007 mg/kg/day, equivalent to drinking water levels of 245 parts per billion (ppb). To ensure an adequate margin of safety for even potentially vulnerable subpopulations (e.g., pregnant and nursing mothers and their children) the NAS panel applied a ten-fold safety factor, resulting in a perchlorate Reference Dose of 0.0007 mg/kg/day, equivalent to a drinking water level of 24.5 ppb. That Reference Dose was subsequently adopted by EPA[4] and ATSDR,[5] and endorsed as "conservative" by FDA.[6] I regard the Reference Dose as a conservative, health-protective exposure limit.

- That Reference Dose was based on perchlorate doses administered to study subjects over-and-above whatever background exposures they had from diet and drinking water. In other words, study subjects almost certainly had total perchlorate exposures greater than the doses administered in that study. Thus the

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[1] National Research Council: *Health Implications of Perchlorate Ingestion*. National Academy Press, 2005. (http://books.nap.edu/catalog.php?record_id=11202).

[2] ATSDR: *Toxicological Profile for Perchlorates (Draft for Public Comment)*, 2005. (http://www.atsdr.cdc.gov/toxprofiles/tp162.html)

[3] CW Murray et al: US Food and Drug Administration's Total Diet Study: Dietary intake of perchlorate and iodine. *J Expo Sci Environ Epidemiol*, 2008. (http://www.nature.com/jes/journal/vaop/ncurrent/pdf/7500648a.pdf).

[4] EPA: *Integrated Risk Information System*, 2005. (http://cfpub.epa.gov/ncea/iris/index.cfm?fuseaction=iris.showQuickView&substance_nmbr=1007)

[5] ATSDR has adopted this Reference Dose as its chronic oral MRL. *Minimal Risk Levels for Hazardous Chemicals*, 2008. (http://www.atsdr.cdc.gov/mrls/).

[6] "NAS Committee ... recommended a perchlorate reference dose ... the reference dose is conservative." FDA: *Perchlorate Questions and Answers*, 2007. (http://www.cfsan.fda.gov/~dms/clo4qa.html).

Reference Dose derived from the study findings incorporates an even larger and more health-protective margin of safety than that specifically described by NAS and EPA. That extra margin of safety is an additional reason that I regard the Reference Dose as conservative and health-protective.

- The FDA study measured the perchlorate contents of a broad selection of foods comprising the US diet. In turn, upper bound estimates of perchlorate intake were determined for infants, children and adults. For all age/sex groups, the FDA estimated that daily dietary perchlorate intake was well below the Reference Dose.

- In a complementary study, EPA reported tests of 34,193 water samples from US public water systems; only 637 samples (1.86%) had perchlorate levels ≥4 ppb.[7] Half of those 637 samples (i.e., 319) were in the range of 4-6.4 ppb. Thus, perchlorate levels were ≤6.4 ppb in over 99% of water samples; the distribution of samples with more than 6.4 ppb perchlorate was not described.

- Total perchlorate intake reflects both diet and drinking water ingestion. EPA has described the interdependence of those two exposure sources and the likelihood that combined exposures would exceed the perchlorate Reference Dose (see Exhibit 6.9.f in [7]). In light of the FDA findings, it is probable that even if drinking water perchlorate levels exceeded 12-20 ppb, total perchlorate exposures would not exceed the Reference Dose.

Taken together, the results of the FDA diet study and the EPA water study provide no evidence that individuals ingest perchlorate at daily doses exceeding the Reference Dose and they further indicate that there is little or no likelihood that such ingestions would occur.

3. The recent FDA report also evaluated the iodine content of the US diet. The FDA study findings indicate that dietary iodine consistently exceeded current Estimated Average Requirements. This is of particular importance because FDA has also determined:

> "the impacts of perchlorate exposure will vary depending upon an individual's iodine sufficiency."[8]

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[7] Office of Water: *The Analysis of Occurrence Data from the First Unregulated Contaminant Monitoring Regulation (UCMR1) in support of Regulatory Determinations for the Second Drinking Water Contaminant Candidate List* (EPA 815-D-06-008); EPA, 2006. (http://www.epa.gov/safewater/ccl/pdfs/reg_determine2/report_ccl2-reg2_ucmr1_occurrencereport.pdf).

[8] US FDA: *2004-2005 Exploratory Survey Data on Perchlorate in Food* (Update 2007). (http://www.cfsan.fda.gov/~dms/clo4data.html).

In other words, the impact of perchlorate is reduced in individuals with sufficient iodine intake. The FDA findings emphasize that the US diet is iodine sufficient, which is consistent with recent CDC findings.[9] The FDA study also found that most perchlorate-containing foods contain relatively higher levels of iodine. Accordingly, it can be expected than anyone eating a perchlorate-rich diet would also ingest higher than usual levels of iodine, thus ensuring both relative and absolute iodine sufficiency.

These findings provide additional reassurance that there is little or no likelihood that dietary perchlorate intake could result in adverse effects.

4. The "CDC Study." A study published in late 2006 by Blount and colleagues,[10] sometimes referred to as the "CDC study", has been often misrepresented in the public debate on perchlorate. Some have wrongly asserted that this study found perchlorate caused adverse effects on human health; that is not correct. I discuss below three key points that should govern how it is considered and discussed in the context of perchlorate regulation:

- The Blount study neither found nor discussed a causal link between perchlorate exposure and abnormal thyroid function. The terms "cause" and "causal" are not used anywhere in the text. Instead the authors repeatedly refer to "associations", i.e., statements indicating a statistical relationship of uncertain direction and relevance.[11]

- None of the subjects in the Blount study had abnormal thyroid function. Subjects with a history of thyroid abnormalities and those with abnormal thyroid tests were specifically excluded. Thus, the study did not (and could not) comment on thyroid dysfunction.

- The results of the Blount study are inconsistent with accepted principles of thyroid science. Perchlorate is only one of a number of molecules that exert similar effects upon the thyroid, i.e., competitive inhibition of iodine uptake by the Sodium/Iodide Symporter (NIS). Other such molecules include nitrate and thiocyanate. The effects of these molecules have been shown repeatedly to be similar in direction and additive in magnitude. In the Blount study, however,

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[9] National Center for Health Statistics: *Iodine Levels, United States, 2000*; CDC, 2007. (http://www.cdc.gov/nchs/products/pubs/pubd/hestats/iodine.htm)

[10] BC Blount et al: Urinary perchlorate and thyroid hormone levels in adolescent and adult men and women living in the United States. *Environ Health Perspect* 114:1865-1871, 2006. (http://www.ehponline.org/members/2006/9466/9466.pdf).

[11] The distinction between causation and association is a critical concern of epidemiology. (e.g., KJ Rothman, S Greenland: *Modern Epidemiology*; Lippincott-Raven, 1998, pp. 7-28).

thyroid effects attributed to these molecules were different and inconsistent, a fact the authors described as "unexpected ... the explanation for this is unclear". I agree that the reported associations are inconsistent, contradictory, and not explicable by known physiology. Because of such inconsistency, these study data must be viewed with caution.

- I am not alone in raising concerns about the Blount study. The American Thyroid Association, for example, concluded that the study findings were "intriguing", but limited in their application to the setting of exposure standards.[12] A particular issue of concern was the inexplicable finding that perchlorate-associated effects were not seen for the other goitrogens included in the study.

The Blount study raises interesting hypothesis, but it is not adequate to test those hypotheses, it does not document any adverse effects, and it is inconsistent with well-accepted principles of the relevant physiology.

5. Children's Health Protection Advisory Committee (CHPAC) letter. The CHPAC letter reviewed a number of perchlorate-related issues of potential relevance to nursing infants. However, that letter was written more than two years ago and it necessarily fails to consider more recent reports and data relevant to its concerns.

- Consider the statement that "perchlorate may decrease iodine levels in human milk", which is further discussed in Appendix 1 of the letter. That statement is based on the findings of one small study of milk samples from 23 women.[13] Moreover, the conclusion of an inverse relationship between perchlorate and iodine levels derived from an analysis of only six of those 23 samples (see Figure 4). By contrast, a reanalysis of those data that was subsequently published found that iodine levels were actually greater in the 12 milk samples with highest perchlorate, as compared to the 12 milk samples with lowest perchlorate.[14] In other words, there was apparently no inverse relationship between breast milk perchlorate and iodine. That reanalysis was not cited in the CHPAC letter.

- Likewise, the CHPAC letter did not consider the 2007 findings of a study that measured perchlorate and iodine levels in the milk of 57 lactating Boston-area women.[15] No correlation was found between breast milk perchlorate and iodine

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[12] ATA Public Health Statement: *Update on the Question of Perchlorate Exposure and Potential Effects* ...; 2006. (http://thyroid.org/professionals/publications/statements/06_12_13_perchlorate.html).

[13] Kirk et al: Perchlorate and iodide in dairy and breast milk. *Environ Sci Technol* 39:2011-2017, 2005.

[14] Lamm S et al.: Comment on "Perchlorate and iodine in dairy and breast milk". *Environ Sci Technol* 39:5900-5901, 2005.

[15] Pearce EN et al: Breast milk and perchlorate concentrations in lactating Boston-area women. *J Clin Endo Metab* 92:1673-1677, 2007.

> levels. Such a lack of correlation seemingly corroborates the Chilean findings reported earlier by Tellez et al.,[16] which were discounted in the CHPAC letter.

Unfortunately, the CHPAC letter only came to my attention in the last few days and I have not had sufficient time to research and update the various other issues that it raises. It is apparent that although the letter may have fairly reflected the science when it was written, it is now out-of-date. Perhaps I will be able to augment my comments at some future time, when it has been possible to more carefully review and update the relevant details.

6. Perchlorate does not cause cancer in humans. I am aware that some individuals have proposed that perchlorate exposure causes various types of human cancer, but I am aware of no evidence that supports such claims. To the contrary, the weight of evidence argues that perchlorate is not a human carcinogen.

The possibility that perchlorate might be carcinogenic in humans was comprehensively reviewed by the NAS, which found insufficient epidemiological evidence to support that possibility. I am not aware of any evidence to the contrary that has been published since the report. Moreover, the NAS found that the evidence was not sufficient to suggest that a link between perchlorate and human cancer was even plausible:[17]

> "The committee questions the biologic plausibility of thyroid cancer as a likely outcome of perchlorate exposure."

EPA reached similar conclusions:[18]

> "EPA thus concludes that perchlorate is not likely to be carcinogenic to humans, at least at doses below those necessary to alter thyroid hormone homeostasis."

ATSDR cited the above NAS and EPA statements and affirmed that there is no evidence of perchlorate-induced human cancers:[19]

> "Cancer has not been reported in humans with exposure to perchlorate."

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[16] Tellez et al: Long-term environmental exposure to perchlorate through drinking water and thyroid function during pregnancy and the neonatal period. *Thyroid* 15:963-975, 2005.

[17] National Research Council: *Health Implications of Perchlorate Ingestion.* National Academy Press, 2005. (http://books.nap.edu/catalog.php?record_id=11202), p.10.

[18] EPA: *Integrated Risk Information System*, 2005. (http://cfpub.epa.gov/ncea/iris/index.cfm?fuseaction=iris.showQuickView&substance_nmbr=1007).

[19] ATSDR: *Toxicological Profile for Perchlorates (Draft for Public Comment)*, 2005. (http://www.atsdr.cdc.gov/toxprofiles/tp162.html); p. 114.

Notwithstanding the claims that have sometimes been made, there is no scientific evidence that perchlorate exposure causes human cancer.

In Summary

The ongoing public debate about environmental perchlorate exposure has led to misstatements and misinterpretations of the relevant scientific findings. The current state of knowledge should be clear:

- There is no evidence of excessive perchlorate in the US diet and little likelihood that routine perchlorate ingestion would exceed the EPA and NAS Reference Dose.
- There is no evidence that perchlorate is a human carcinogen.
- There is evidence that the US diet contains sufficient iodine, and sufficient iodine intake is protective against effects that might result from perchlorate excess.

In short, there is no evidence that environmental perchlorate exposure causes human injury. Likewise, I am not aware of any evidence that environmental perchlorate exposure causes abnormal human development. This does not mean that concerns for its potential harms are wrongheaded. To the contrary, it is appropriate that public health concerns be voiced and it is necessary that public health agencies evaluate and monitor exposures that are perceived as potentially serious threats to the public health.

On the other hand, such concerns do not justify misinterpretation or misrepresentation of scientific findings and evidence. Unfortunately, such misinterpretations and misrepresentations have sometimes characterized the ongoing perchlorate debate.

I hope that you find the information presented above to be responsive to your request. Please do not hesitate to contact me if I can be of further assistance to you or the committee.

Yours truly,

Jonathan Borak, MD, FACP, FACOEM, FRCP(C)

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Perchlorate: Overview of Risks and Regulation

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Running title: Perchlorate risks and regulation

Key words: perchlorate, health risk assessment, environmental regulation, risk management, thyroid hormones

Abbreviations: DDE, *p,p'*-dichlorophenyldichloroethylene; NAS, National Academy of Sciences; NHANES, National Health and Nutrition Evaluation Survey; PCBs, polychlorinated biphenyls; PCDDs, polychlorinated dibenzo-*p*-dioxins; PCDFs, polychlorinated dibenzofurans; T_3, triiodothyronine; T_4, thyroxine; TEQ, toxic equivalent; TSH, thyroid stimulating hormone; RfD, reference dose; US EPA, US Environmental Protection Agency; US FDA, US Food and Drug Administration

ABSTRACT

The extent to which perchlorate, which occurs naturally and as an industrial contaminant, should or should not be regulated has become controversial. This review examines a number of inconsistent conclusions that have been drawn based on thyroid hormone serum concentrations, urinary iodine concentrations, and perchlorate exposure among women participating in the 2000-2001 National Health and Nutrition Examination Survey (NHANES) and based on the body of epidemiologic and clinical evidence reporting no associations between effects on thyroid hormones and similar or much higher levels of perchlorate exposure. For example, studies associating perchlorate with thyroid effects at low exposures did not control for anti-thyroid agents with modes of action that differ from that of perchlorate, such as some organochlorines. Available evidence does not support a causal relationship between changes in thyroid hormone levels and current environmental levels of perchlorate exposure but does support the conclusion that the US Environmental Protection Agency's reference dose (RfD) for perchlorate is conservatively health-protective. However, potential perchlorate risks are unlikely to be distinguishable from the ubiquitous background of naturally occurring substances present at much higher exposures that can affect the thyroid via the same biological mode of action as perchlorate, such as nitrate and thiocyanate. Risk management approaches that account for both aggregate and cumulative exposures and that consider the larger public health context in which exposures are occurring are desirable.

Introduction

Perchlorate is a substance that has recently been receiving prominent legislative and regulatory attention in the US by both federal and state governments. Initially identified as a groundwater contaminant associated primarily with rocket fuel spillage, perchlorate is now found to be ubiquitous. Widespread human exposure to both anthropogenic and naturally occurring perchlorate occurs primarily via ingestion. Like several other dietary goitrogens, perchlorate can interfere with iodine uptake by the thyroid gland, potentially disrupting thyroid hormone levels responsible for regulating many of the body's metabolic and developmental functions. Because thyroid hormones are critical for normal fetal and neonatal development, perchlorate has the potential to pose a risk to children although no specific cases have been identified, even in areas where exposure occurs to high levels of naturally occurring perchlorate. Because there are incomplete data on perchlorate's potential risks, however, the US Environmental Protection Agency (US EPA) has developed a precautionary limit on lifetime exposure intended to prevent adverse effects that might have an impact on the developing child. The adequacy of that exposure limit is debated, with some stakeholders believing it is too stringent and others believing it is not stringent enough.

This article provides an overview of the scientific basis for the controversy, exploring what is known about perchlorate exposure and effects and describing its risks in the context of potential risks from other iodine-uptake-inhibiting goitrogens as well as goitrogens that do not inhibit iodine uptake. In particular, the apparent discrepancy between the reported associations

between exposure and effects at current low, background levels of exposure in the US and the reported absence of effects at much higher levels of exposure is discussed.

Hazard and dose-response assessment

Concern about potential human health risks from perchlorate in food and drinking water results from the observation that perchlorate has a great affinity for the sodium (Na^+)/iodide (I^-) symporter, the protein responsible for transporting iodide into the thyroid gland for the purpose of synthesizing thyroid hormones. As a result of that affinity, perchlorate can block the transport of iodide into thyroid follicular cells. When less iodide is available with which the thyroid can generate the hormones thyroxine (T_4) and triiodothyronine (T_3), the production of thyroid stimulating hormone (TSH) by the pituitary is increased. This homeostatic mechanism in turn stimulates the production of more T_3 and T_4 so that concentrations of thyroid hormones sufficient for the body's needs are maintained, even in situations with reduced levels of available iodide. According to a National Academy of Sciences (NAS) report evaluating the effects of perchlorate, "Compensation for iodide deficiency or other perturbations in thyroid hormone production . . . is the rule" (NAS/NRC 2005).

If the thyroid gland is deprived of adequate iodide over a long period of time, as occurs in areas where dietary iodide intake is insufficient, conditions such as goiter (enlarged thyroid) and even mental retardation may result. In particular, thyroid hormones are essential for skeletal and neurodevelopment and severe iodide intake deficiency during pregnancy (< 20 μg/day) or during

infancy can result in children with profound neurodevelopmental and physical deficits. By competing with iodide for the sodium/iodide symporter, perchlorate can interfere with thyroid function, leading to increased TSH and decreased T_3 and T_4, which—if not compensated for—has the potential to interfere with fetal development. There have been no reports indicating that perchlorate exposure has harmed public health or interfered with fetal development—that relationship is inferential—but epidemiologic studies demonstrating or refuting a causal relationship between perchlorate exposure and fetal harm are lacking for women with inadequate dietary iodine.

Nonetheless, a number of epidemiologic studies suggest that, at current environmental perchlorate levels, exposure is unlikely to pose developmental or other risks for women with adequate dietary iodine. For example, a prospective longitudinal study of drinking water perchlorate exposure and pregnancy outcomes for 307 women in Chile failed to show an effect on thyroid hormone serum concentrations, milk iodine concentrations, or fetal development at perchlorate concentrations up to 114 µg/L drinking water (Téllez Téllez et al. 2005). A study of 313 women from areas in Israel where well water perchlorate contamination was between 42-340 µg/L and mean serum perchlorate concentrations were about 1-6 µg/L found no effect on serum T_4 concentrations in newborns compared to 843 women in areas with lower serum perchlorate concentrations (Amitai et al. 2007). An ecological study of 342,257 newborns in California also failed to find an association between perchlorate concentrations in drinking water and the prevalence of congenital hypothyroidism or increased serum TSH concentrations (Buffler et al. 2006). Crump et al. (2000) evaluated thyroid hormone concentrations and TSH

production in 9,784 newborns and 162 school-age children in three cities in Chile with no, some (5-7 µg/L), or high (100-120 µg/L) drinking-water perchlorate concentrations and with similar characteristics in terms of socioeconomic status, ethnicity, and urinary iodine levels. No effects attributable to perchlorate exposure were observed.

A number of occupational studies have evaluated the effects of adult perchlorate exposure on thyroid hormone concentrations and reported no effects, but generally involved small numbers of subjects with adequate dietary iodine. For example, a study of 29 male workers exposed occupationally to high concentrations of airborne perchlorate demonstrated average iodide uptake inhibition of 38% but no effect on thyroid hormones (Braverman et al. 2005). A similar study evaluated 37 workers in the same plant and also reported no effect of long-term perchlorate exposure on a variety of determinants of thyroid health at doses up to about 0.5 mg/kg (Lamm et al. 1999). Intentional dosing studies involving short-term perchlorate exposure (up to two weeks) have also produced iodine uptake inhibition with no effect on serum hormone concentrations. For example, a study involving 21 healthy female volunteers and 16 healthy male volunteers saw a dose-dependent decrease in thyroid radioiodide uptake during two weeks of daily perchlorate administration, but no effect on thyroid hormone serum concentrations, even with a 67% reduction in iodide uptake (Greer et al. 2002). A no-observed-effect level of 0.007 mg/kg/day (equivalent to about 240 µg perchlorate/liter drinking water) based on iodide uptake inhibition was identified from that study. A more recent prospective, double-blind, randomized trial involving 17 healthy male and female volunteers saw no effect on thyroid function, including iodide uptake or serum concentrations of thyroid hormones,

following six months of perchlorate administration at doses up to 3 mg/day (Braverman et al. 2006).

Perchlorate has been used therapeutically to treat hyperthyroidism, including 12 pregnant women who received doses of 600-1,000 mg/day throughout most of their pregnancies. One infant had a slightly enlarged thyroid gland but the effect disappeared shortly after birth; no other effects on the infants were observed (Wenzel & Lente, 1984). Evidence from therapeutic use of perchlorate for more than a year supports the conclusion that moderate doses of perchlorate given chronically do not cause hypothyroidism (NAS/NRC 2005).

Other ecological, occupational, and clinical studies have also failed to support an association between perchlorate concentrations in water supplies and adverse thyroid effects in children or adults. Several more detailed reviews of studies evaluating the potential effects of perchlorate exposure on human health are available (Braverman 2007, NAS/NRC 2005, Soldin et al 2001). The National Academy of Sciences perchlorate report concluded, based on studies involving both clinical and environmental exposures, that long-term, sustained exposure to more than 30 mg/day (equivalent to about 15,000 µg/L drinking water) would be required to produce adverse effects in healthy adults (NAS/NRC 2005).

Until recently no studies have specifically evaluated thyroid function related to perchlorate exposure in iodine-deficient or hypothyroid women, the groups that would be expected to be most vulnerable (NAS/NRC 2005). In a recent study, Pearce et al. (2007a)

evaluated 398 European women with lower urinary iodine concentrations (< 100 µg/liter) during the first trimester of pregnancy who were exposed to perchlorate at levels similar to those in the US and found no effects on maternal thyroid function associated with perchlorate. That result suggests that urinary iodine concentrations < 100 µg/liter do not confer susceptibility to perchlorate. The urinary concentration of iodine considered deficient is < 50 µg/liter and the most recent NHANES data indicate that about 7% of pregnant women in the US have urinary iodine concentrations < 50 µg/liter (Caldwell et al. 2005). However, NHANES data also showed no differences in thyroid hormone levels when women with urinary iodine concentrations < 50 µg/L were compared to women with higher urinary iodine concentrations (based on serum TSH and T_4 concentrations) (Soldin et al. 2005). That observation is consistent with the fact that even large reductions in iodine intake are adequately compensated for by the thyroid.

More recent concerns about perchlorate result from a study suggesting that there might be an interaction between iodine deficiency and the effects of perchlorate. In that study, Blount et al. (2006a) reported statistical correlations between increasing urinary perchlorate concentrations, increasing serum concentrations of TSH, and decreasing serum concentrations of T_4 in women but not in men. The authors used multiple regression analysis to evaluate data on urinary perchlorate and iodine concentrations and on serum concentrations of TSH and T_4 for 2,299 men and women who participated in the National Health and Nutrition Examination Survey (NHANES) during 2001-2002.

When Blount et al. (2006a) separated the women into higher (≥ 100 µg/L) and lower (<

100 µg/L, n ≈ 350) iodine groups, they found a significant positive association between perchlorate and TSH and a significant negative association between perchlorate and T_4 in the low iodine group only, although both hormone concentrations remained within the normal range. The directions of those associations are consistent with perchlorate's anti-thyroid activity but are surprising given the low levels of perchlorate involved and the studies described above reporting no effects at much higher exposure levels. However, statistically significant associations were also reported between serum hormone concentrations and a variety of other independent variables, indicating that thyroid function is likely to be affected by many important factors. For example, the R^2 value reported by Blount et al. for the association between T_4, perchlorate, and other covariates for lower-iodine women, 0.240, indicates that of the covariates evaluated showing associations with significance < 0.05, perchlorate accounts for only about 3% of the variation seen in T_4 values for that population. Significantly, a recent reanalysis of the same data adjusted urinary iodine concentrations for creatinine, which better reflects 24-hour urine iodine excretion than do the unadjusted urinary iodine concentrations used by Blount et al. (2006a). After that adjustment, the lower-urinary-iodine-status women no longer showed a negative association between urinary perchlorate concentrations and T_4 (Lamm et al. 2007).

The positive association of perchlorate with TSH for all women regardless of iodine status reported by Blount et al. (2006a) is also surprising and, if causal, is inconsistent with the idea that adequate iodine intake prevents effects associated with sodium/iodide symporter competitors. The NHANES data also show a positive association between perchlorate and iodine (Figure 1) and between iodine and TSH (Soldin et al. 2005). The positive association

between perchlorate and TSH reported by Blount et al. (2006a) is thus to be expected because natural sources of iodine co-occur with natural sources of perchlorate (hence the positive association, see exposure discussion below) until synthetic sources of perchlorate predominate and a plateau is reached. So, because there is a positive association between urinary iodine and perchlorate at lower levels because they co-occur naturally, and there happens to be a positive association between urinary iodine and serum TSH in the NHANES data, it is logical that there would be a positive association between urinary perchlorate and serum TSH, but no particular reason to conclude that perchlorate is causally responsible for the increase in TSH. Furthermore, the R^2 value of 0.061 reported by Blount et al. (2006a) for the association between TSH, perchlorate, and other significant covariates for lower-iodine women indicates that perchlorate accounts for only about 1% of the variation seen for TSH in that population.

Even the lower-iodine women in the NHANES database have adequate iodine for normal thyroid function. Because adequate iodine intake would be expected to ameliorate any potential effects of perchlorate, even in the lower-iodine women, another possibility is that an antithyroid agent with a mechanism unrelated to iodine uptake inhibition could explain the associations observed by Blount et al. (2006a). Blount et al. did not control for goitrogens with non-iodine-related modes of action so it is possible, given the adequate iodine status of the women in the NHANES study, that the presence of goitrogens with a mode of action unrelated to iodine uptake inhibition, such as some organochlorines, is responsible for the effects seen.

A number of widespread contaminants such as bisphenol A, polychlorinated biphenyls

(PCBs), and polybrominated diphenyl ethers have been characterized as goitrogens and reported to have anti-thyroid activity via mechanisms unrelated to iodine uptake (Brucker-Davis 1998, McLanahan et al. 2007, Talsness et al. 2007). Those substances' anti-thyroid activity has been attributed to their ability to react with thyroid hormone receptors and affect thyroid-hormone-regulated gene expression (Zoeller 2007) or with aryl hydrocarbon hydroxylase receptors and induce enzymes associated with T_4 metabolism (Chevrier et al. 2007). Turyk et al. (2007) used the same NHANES database as Blount et al. but added the data from 1999-2000 and evaluated the relationships between total PCBs or total toxic equivalents [TEQs; includes PCBs, polychlorinated dibenzo-*p*-dioxins (PCDDs), and polychlorinated dibenzofurans (PCDFs)] with thyroid hormones. A negative association was reported for PCB/PCDD/PCDF TEQs with T_4, with stronger effects seen in women than in men. A positive association with TSH was seen in women over 60 only. Chevrier et al. (2007) measured 34 PCB congeners in the serum of 285 pregnant women and TSH concentrations in their children's blood shortly after birth. A positive association was observed for neonatal TSH and maternal levels of PCB congeners grouped by their ability to induce microsomal enzymes, but not total PCBs or dioxin-like PCB TEQs. Schell et al. (2008) found a positive association between TSH and persistent PCBs and a negative association with free T_4 and PCBs among adolescents from the Akwesasne Mohawk Nation who had not been breastfed. Despite higher postnatal PCB exposures, no such relationships were seen among those who had been breastfed. A positive relationship between DDE and TSH has been reported in some studies (e.g., Rylander et al. 2006) but not others (e.g., Schell et al. 2008). Figure 2 compares the NHANES relationships between TSH and DDE, total dioxin-like compounds (primarily PCBs), and perchlorate. In each case, a positive correlation is seen for

women.

The reports of associations between thyroid hormone concentrations and PCBs, TEQs, other organochlorines, or perchlorate are subject to similar limitations. As with perchlorate, earlier studies of PCBs, PCDDs, and PCDFs generally reported associations with changes in thyroid hormone concentrations only at exposure levels much higher than those evaluated by Turyk et al. (2007) and Chevrier et al. (2007), although those reported associations are inconsistent and involve increasing hormone concentrations associated with exposure in some studies and decreases in others. Blount et al. (2006a) did not control for non-iodine-inhibiting goitrogens and the PCB/TEQ studies did not control for iodine-inhibiting goitrogens. None of the studies demonstrate a causal relationship between PCBs, PCDDs, PCDFs, or perchlorate and changes in thyroid hormone concentrations because all three are cross-sectional studies reflecting a single point in time. Such studies are appropriate for estimating mean values but lead to overestimation of the number of people at the tails of the distribution (Andersen et al. 2001, Givens et al. 2007), distorting the true dose-response relationship. All three studies conflict with the weight of the evidence based on results of a significant number of studies involving much higher levels of exposure. All three studies are uncontrolled for the normal fluctuations in hormone concentrations that occur throughout the day in response to various stimuli, although that shortcoming may be compensated for by the large sample sizes. Finally, in all three studies, the changes reported remained within the normal range for thyroid hormones so do not constitute adverse effects and are unlikely to have clinical significance. Nonetheless, those studies are useful for hypothesis generation and suggest the need for additional mechanistic and dose-

response research.

Exposure assessment

Perchlorate occurs both naturally and as an environmental contaminant. Most environmental perchlorate has been attributed to its use as an oxidizer in propellants used by solid fuel rockets and missiles (US EPA 2002). Since the 1950s poor disposal practices have resulted in soil and groundwater contamination. Perchlorate is also used in air bag inflators, lubricating oils, leather finishing, electroplating, rubber manufacture, and other manufacturing processes (US EPA 2002). Massachusetts reported that the primary contributors of perchlorate to environmental media in that state were blasting agents, military munitions, fireworks, and, to a lesser extent, hypochlorite (bleach) solutions (MA DEP 2005). Traces of perchlorate are found in natural materials used as fertilizers, such as Chilean saltpeter, kelp, fishmeal, hanksite, potash ore (sylvinite), and playa crust (Orris et al. 2003).

Detection of perchlorate in groundwater in regions with no historical use of rocket fuels or other potential anthropogenic sources, its occurrence in parallel with iodate, and its presence in rain and snow samples led to the suspicion that perchlorate is formed atmospherically. Dasgupta et al. (2005) demonstrated perchlorate formation by a number of atmospheric processes and concluded that a natural perchlorate background of atmospheric origin must exist.

Whether of natural or anthropogenic origin, human exposure to perchlorate is thought to

occur primarily through ingestion (NAS/NRC 2005). Perchlorate has been detected in public water systems (US EPA 2005a) and also in groundwater, including groundwater in areas with no history of industrial or agricultural use (Dasgupta et al. 2005). Low levels of perchlorate can also be found in drinking water supplies disinfected with sodium hypochlorite (MA DEP 2005). Biomonitoring data evaluating the relative contributions of different sources to perchlorate exposure suggest that the diet is an important source, however (Blount and Valentín-Blasini 2007). El Aribi et al. (2006) tested food and water samples from around the world and found detectable levels of perchlorate in all foods tested. In the US, perchlorate concentrations in foods sampled ranged from 0.094 to 19.29 µg/kg (mean, 0.252) and tap water samples ranged from 0.072 to 2.983 µg/L. California-grown lettuce and spinach have been reported to contain perchlorate at levels ranging from 0.6 to 6.4 µg/kg (Seyfferth and Parker 2006). Mean concentrations of perchlorate in cow's milk from US supermarkets in 11 states and human milk samples from 18 states were reported to be 11 and 92 µg/L, respectively (Kirk et al. 2005). In a sample of lactating women in Boston, milk perchlorate concentrations ranged from 1.3 to 411 µg/L and no correlation with milk iodine levels was seen (Pearce et al. 2007b). Groundwater monitoring data from California show concentrations ranging from below the limit of detection to 100 µg/L (CA DPH 2007). A number of other reports can be found describing perchlorate concentrations in various foods and beverages, many of which are described in detail in US EPA (2006).

The 2006 Total Diet Study conducted by the US Food and Drug Administration (US FDA), which involves analysis of nutrients and chemical contaminants in 280 different foods,

now includes perchlorate as one of the analytes, so is expected to provide data supporting comprehensive dietary intake estimates. Based on data from 27 foods, the US FDA has made a preliminary estimate of average daily perchlorate intake in the US of 0.053 µg/kg/day (US FDA 2007), similar to that estimated on the basis of urinary perchlorate measurements, 0.066 µg/kg/day (Blount et al. 2006a), and 10,000 times less than the daily intake concluded by the National Academy of Sciences perchlorate report to be required to produce adverse effects in healthy adults following long-term exposure (NAS/NRC 2005). The extent to which perchlorate intake can be attributed to natural versus anthropogenic sources is not known.

Risk characterization and regulation

Due to its biological mode of action, exposure to perchlorate during pregnancy in the absence of adequate iodine nutrition at doses high enough to result in insufficient maternal thyroid hormone concentrations could pose a risk of fetal developmental toxicity. To prevent such a risk, the 2005 National Academy of Sciences report evaluating human health risks from perchlorate recommended an exposure limit considered to be without adverse effects over a lifetime of oral exposure, or reference dose (RfD), of 0.0007 mg/kg/day (NAS/NRC 2005). That RfD was adopted by US EPA in February 2005 (US EPA 2005b) and was based on the study of Greer et al. (2002) involving perchlorate-induced inhibition of radioactive iodide uptake in human volunteers. The no-observed-effect level in that study, 0.007 mg/kg/day, was divided by an uncertainty factor of 10 to protect the most vulnerable individuals, the fetuses of hypothyroid pregnant women. Other uncertainty factors were considered unnecessary because of the

conservative (i.e., health-protective) choice of an outcome that does not constitute an adverse effect. The NAS report reasoned that inhibition of iodide uptake by the thyroid is the key biochemical event in the continuum of possible effects of perchlorate exposure and would precede any adverse effects of perchlorate exposure. That reasoning has been challenged on the basis that because iodide uptake inhibition is not in itself an adverse effect and that no adverse effect on thyroid hormones had been seen by Greer et al. (2002), its choice as the basis of the RfD is inconsistent with established reference dose methodology (M. Dourson, personal communication; Barnes & Dourson 1988). A more supportable RfD might be developed using the data from pregnant women in Chile and Israel, the potentially susceptible group of interest, which produced a no-observed-adverse-effect level of approximately 0.03 mg/kg/day.

Despite its having adopted an RfD, US EPA has not yet chosen to regulate perchlorate in drinking water by developing a maximum contaminant level, explaining that more information on sources of perchlorate exposure is needed to determine the relative source contribution of drinking water to total exposure (US EPA 2006). The US Congress is considering two pieces of legislation, one that would compel US EPA to establish a drinking water standard for perchlorate and one that would compel US EPA to determine whether perchlorate should be regulated. Meanwhile, the states of Massachusetts and California have adopted drinking water standards for perchlorate of 2 μg/L and 6 μg/L, respectively.

Understanding the apparent inconsistencies between the associations observed for perchlorate and thyroid hormone levels at low concentrations reported by Blount et al. (2006a)

using the NHANES data and the absence of effects at much higher perchlorate exposure levels in the epidemiologic and other human studies is critical to assessing risk for the purpose of establishing regulatory limits on perchlorate exposure. Upon closer examination, however, there apparently are no significant inconsistencies between those observations. The changes reported by Blount et al. remained within the normal range of thyroid hormone concentrations and are unlikely to be causally related to perchlorate at those levels of exposure for the reasons discussed above. The absence of a causal relationship is supported by the results of Lamm et al. (2007), who found no association between perchlorate and T_4 when urinary iodine concentrations were adjusted for creatinine, by the results of Pearce et al. (2007a), who failed to find associations between thyroid hormone serum concentrations and urinary perchlorate in low-iodine-status pregnant women in Europe, and by the weight of evidence provided by previous epidemiologic and clinical studies reporting effects only at much higher levels of exposure, albeit in healthy adults. The women in the NHANES database do not appear to be representative of hypothyroid or subclinically hypothyroid women; however, as evidenced by the fact that there are no differences in thyroid hormone concentrations when women with urinary iodine concentrations < 50 µg/L are compared to women with higher urinary iodine concentrations (Soldin et al. 2005).

It is also interesting to note that the perchlorate doses derived from the NHANES data compare favorably with the US EPA RfD; that is, the majority of perchlorate doses in the general US population do not exceed the RfD. Blount et al. (2006b) estimated a total daily perchlorate dose for each adult in the NHANES database they evaluated, finding a median dose of 0.066 µg/kg/day (about one tenth of the US EPA RfD) and a 95th percentile of 0.234 µg/kg/day (about

one third of the US EPA RfD). Eleven adults (0.7%) in that study had estimated perchlorate exposures in excess of the RfD (0.7 µg/kg/day). Of course, exceeding an RfD does not indicate that a person is "at risk". Reference doses are not bright lines or threshold values for adverse effects; they are set far below exposure levels associated with adverse effects. US EPA is careful to point out that, while exposure at or below a reference dose indicates that a health risk is unlikely, people who are exposed to a substance above its reference dose should not be considered at risk: ". . . exceeding the [reference dose] is not a statement of risk" (US EPA 2004) and ". . . It is . . . important to note that the [reference dose] does not define a bright line, above which individuals are at risk of adverse effect" (US EPA 2005c). In any case, the RfD was derived from a non-adverse effect. Based on US EPA's RfD, current environmental exposures to perchlorate in the US thus do not appear to pose a risk of developmental toxicity.

Because hypothyroid pregnant women are the sensitive group of interest in terms of potential perchlorate risk, it is useful to determine the extent to which hypothyroidism is prevalent. In the United Kingdom about 1-2% of pregnant women are reported to be overtly hypothyroid and another 2.5% have subclinical hypothyroidism, defined as raised TSH but normal T_4 (Anonymous 2006). The prevalence of subclinical hypothyroidism among US women in the general population has been reported to be 4-10%, with 2-5% of those cases progressing to overt hypothyroidism annually (Papi et al. 2007). Casey et al. (2005) reported that 2.3% of a cohort of 17,298 pregnant women in Texas tested before 20 weeks' gestation had subclinical hypothyroidism, while 0.2% of those had overt hypothyroidism. Between 50-80% of hypothyroidism is attributed to chronic autoimmune thyroiditis (Papi et al. 2007), however, not

iodine insufficiency; because of its mode of action, perchlorate would not be expected to contribute to risk in such cases. Of course, hypothyroid pregnant women are already at risk of effects on the fetus due to the fact of their hypothyroidism alone; measurable additional risk from normal background intakes of perchlorate (around 4 µg/day, see previous discussion of exposure) seems unlikely.

Complicating attempts to assess risks from or establish regulatory limits for perchlorate is the fact that perchlorate exposure does not occur in isolation from exposure to other goitrogens, or anti-thyroid agents, that have the same iodine uptake inhibition mode of action as perchlorate. In particular, nitrates and thiocyanates are ubiquitous in the diet and occur in such quantities and with such potencies that determining the additional contribution to risk made by small exposures to environmental perchlorate is potentially impossible (De Groef et al. 2006).

In vitro studies comparing the relative abilities of perchlorate, nitrate, and thiocyanate to inhibit cellular iodine uptake show that, after adjusting for biological half-life, perchlorate is half as potent as thiocyanate and 240 times as potent as nitrate (De Groef et al. 2006). Given those relative potency estimates, comparing perchlorate's RfD to those for nitrates and thiocyanates is instructive. Nitrate's RfD is 1.6 mg/kg/day (US EPA 1991) and cyanide's (the active portion of thiocyanates) is 0.02 mg/kg/day (US EPA 1993). Taking into account their relative potencies, the RfDs for nitrate and thiocyanate are 100 times and 50 times higher than the perchlorate RfD, respectively. Those differences could be interpreted to imply that perchlorate is 50 to 100 times safer than suggested by its RfD or that nitrate and thiocyanate are 50 to 100 times more

dangerous than implied by their RfDs. On that basis, for an adult in the US eating a US Department of Agriculture recommended diet, the average daily intake of nitrates and thiocyanates combined is equivalent to 0.5 mg/kg/day perchlorate (De Groef et al. 2006), 1,000 times greater than the perchlorate RfD.

Of course, RfDs are determined based on many factors in addition to the level of exposure anticipated to produce adverse effects, reflecting the nature and adequacy of the underlying data, so comparing them can be misleading. Comparing RfDs for perchlorate, cyanide, and nitrate highlights an unreasonable regulatory inconsistency but is not really the appropriate comparison for the purposes of drawing conclusions about relative and cumulative risks. The RfDs for the three goitrogens are derived from different biological effects—reduced iodine uptake by the human thyroid for perchlorate (not in itself an adverse effect), blue baby syndrome for nitrate, and a 1955 study in rats that produced no adverse effects for cyanide. The highest doses of each goitrogen that failed to produce an effect were divided by different "uncertainty factors"—intended to protect sensitive individuals or to compensate for the use of animal instead of human data—to derive their RfDs. As a result, the respective RfDs are not really comparable. A more appropriate comparison might be based on the highest doses that fail to produce adverse effects on the thyroid, which themselves will vary according to iodine status. Nonetheless, any potential effects of low exposures to perchlorate are likely to be undetectable against a natural goitrogen background exposure 1,000 times higher than perchlorate's exposure limit. As yet, however, human health risk assessment continues to focus on single chemicals in isolation, with the notable exceptions of PCBs, dioxins, some pesticides, and polycyclic aromatic

hydrocarbons.

Discussion

It is generally the case that data useful for evaluating a substance's human health risks are incomplete. As a result, regulatory decisions about limiting risks are based on science to the extent feasible but, of necessity, also on policy judgments. Regulatory limits are thus neither "right" nor "wrong" scientifically, although some may reflect the weight of the scientific evidence better than others. The data available on perchlorate risks appear at first to be inconsistent, with thyroid effects associated with current low levels of exposure from the NHANES data but no effects seen in other studies at much higher levels of exposure. Three explanations for the discrepancy are possible. One explanation is that the effect seen in the NHANES data is attributable to another substance that co-occurs with perchlorate but affects the thyroid via a different biological mode of action, perhaps PCB/PCDD/PCDF TEQs or some other substance as yet to be identified, for which evaluations of the NHANES data were not controlled. Another explanation is that the reported effects are statistical artifacts because perchlorate naturally co-occurs with iodine and there is an association between iodine and TSH in the NHANES data and because the negative association with T_4 cannot be detected when urinary iodine concentrations are adjusted for creatinine. Of course, despite numerous indications to the contrary, a third explanation is that the cross-sectional NHANES associations are causally related after all and, for as-yet-to-be-determined reasons, the large and consistent body of clinical and epidemiologic evidence that failed to detect similar associations or detected

them only at much higher exposures is wrong. All three explanations are consistent with the conclusion that the US EPA RfD for perchlorate is conservatively health-protective.

While a conservatively health-protective perchlorate RfD is desirable as a precautionary matter, considering perchlorate's RfD in the context of the other iodine-uptake-inhibiting goitrogens to which we are exposed ubiquitously, also primarily through the diet, suggests that it may be unnecessarily stringent. The relative exposure levels and potencies of nitrate and thiocyanate, in particular, are likely to swamp any effects potentially attributable to perchlorate. That inconsistency illustrates the need for risk assessment approaches that can account for both aggregate and cumulative exposures and for risk management approaches that can consider the larger public health context in which exposures are occurring.

In its Framework for Cumulative Risk Assessment, US EPA expresses the hope that attempts focus on the combined effects of more than one agent or stressor may generate interest in a wider variety of nonchemical stressors than do traditional risk assessments (US EPA 2003a). In other words, instead of focusing on the potential effects of individual chemical exposures in isolation, we may start looking at public health in terms of the broader definition of environment. The World Health Organization defines environment as including "both the direct pathological effects of chemicals, radiation and some biological agents, and the effects (often indirect) on health and well-being of the broad physical, psychological, social and aesthetic environment which includes housing, urban development, land use and transport" (WHO 1989). The proportion of disease that is attributable to chemical exposures is thought to be relatively small

against the backdrop of socioeconomic conditions, behavioral factors, psychological factors, infectious agents, nutrition, and other considerations. Indeed, US EPA acknowledges that "One of the greatest challenges to elucidating the connection between environmental exposure and disease is the fact that exposure to an environmental pollutant or stressor is rarely the sole cause of an adverse health outcome . . . Other factors include, for example, diet, exercise, alcohol consumption, heredity, medications, and whether other diseases are present . . . Also, different people have different vulnerabilities . . . All these factors make it difficult to establish a causal relationship between exposure to environmental pollutants and disease outcome . . ." (US EPA 2003b).

In view of our incomplete knowledge of the complex inter-relationships among multiple chemical and non-chemical, environmental and non-environmental stressors, a holistic approach to public health protection is a distant hope, probably dependent on our eventual understanding of how molecular and cellular pathways can be perturbed in ways that lead to toxicity (NAS/NRC 2007). While we eagerly anticipate that day, we can in the meantime evaluate health risks more holistically and with improved logic in the smaller spheres where it is currently possible to do so. Assessing and regulating potential risks from substances like perchlorate within the larger context of simultaneous exposure to the naturally occurring background of goitrogens with the same mode of action would be a logical start.

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The author has no conflict of interest related to the substance of this article.

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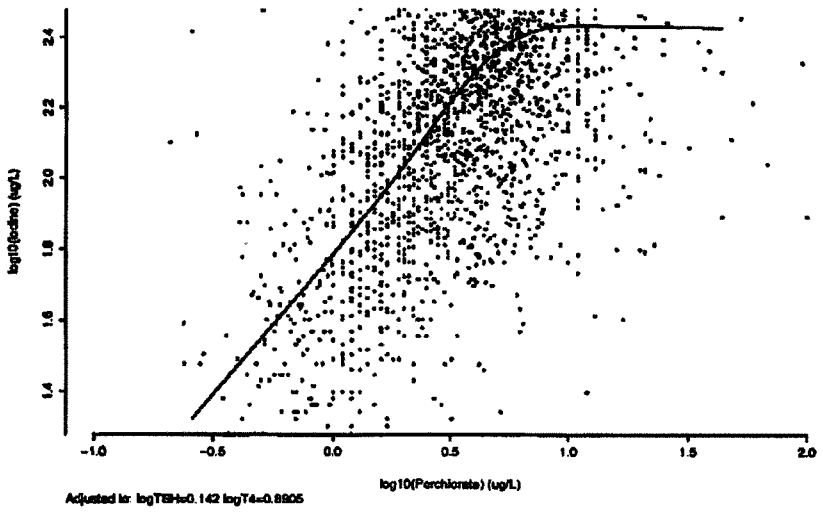
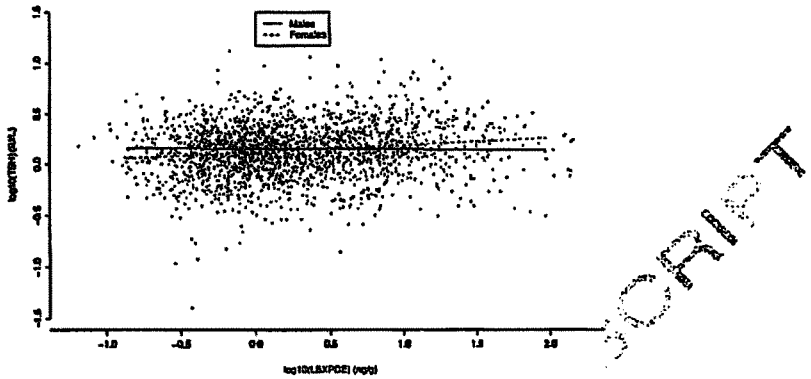
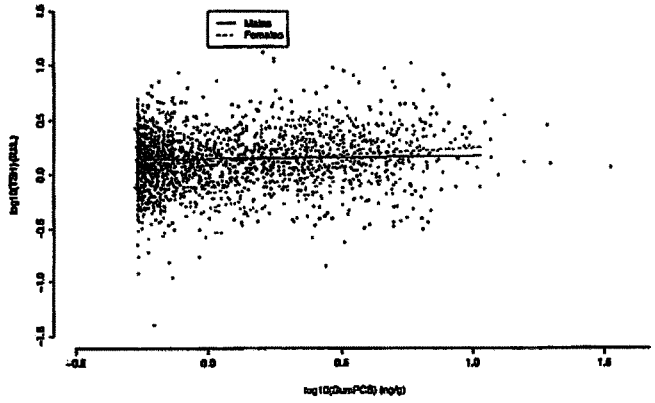


Figure 1. Relationship between iodine and perchlorate controlled for T_4 and TSH [$R^2 = 0.36$].

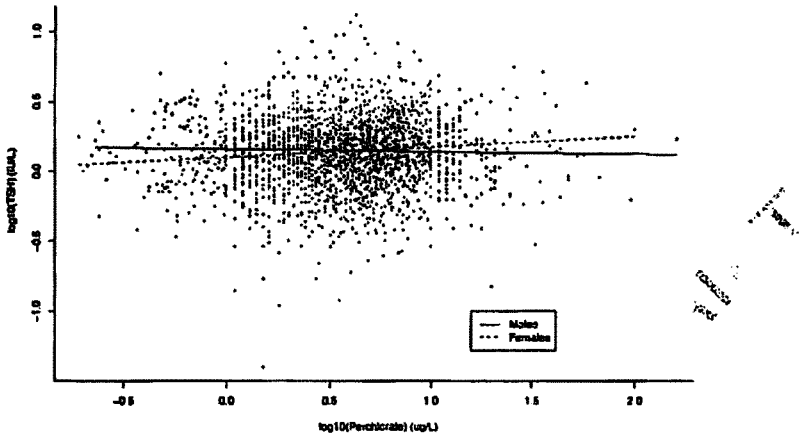
Source: Drawn from the original NHANES data by the Bio-Statistical Center of the Catholic University of Leuven



(a)



(b)



(c)

Figure 2. Relationship between TSH and DDE (a) [$R^2 = 0.01$], total PCBs (b) [$R^2 = 0.009$] or perchlorate (c) [$R^2 = 0.006$] by gender. Source: Drawn from the original NHANES data by the Bio-Statistical Center of the Catholic University of Leuven

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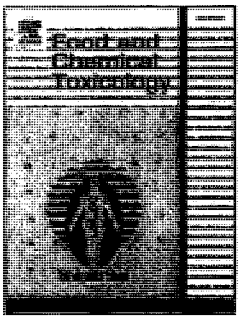

Perchlorate: Overview of Risks and Regulation

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United States Senate Committee on Environment and Public Works
FULL COMMITTEE Hearing on Trichloroethylene
Tuesday, May 6, 2008

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Professor and Chief of Environmental Epidemiology, Department of Occupational and Environmental Medicine, Robert Wood Johnson Medical School, University of Medicine and Dentistry of New Jersey

Madame Chairman, members of the Committee, I am very pleased to have been asked to provide testimony to you on the possible adverse human health effects of trichloroethylene (TCE). I provide my perspective as a research scientist who wrote a report for the US Environmental Protection Agency (EPA) on the epidemiologic evidence on the possible carcinogenicity of TCE for their planned risk assessment in 2000, and have conducted original research on TCE since then. The results of my research for EPA's state of the science review, and my subsequent research, provide compelling data in support of the view that TCE causes cancer and other serious health problems in humans, and is supported by experiments in which animals were exposed to TCE and developed a variety of cancers and also birth defects. In light of these data, and the large number of people being exposed to TCE through contaminated ground water, and vapors from water that infiltrates into the air in their homes, I feel it is urgent that actions be taken to prevent disease through remediation these situations so as to reduce or eliminate exposures. Even in the town in which I live, Skillman, New Jersey, TCE has been found in groundwater that was being used as a primary drinking water source by some residents, and had to be remediated. It also was found in the next town over, Hopewell, New Jersey. Indeed, TCE is one of the most commonly found contaminants, occurring in numerous groundwater supplies as well as in more than 850 Superfund sites nationwide, often as the result of inappropriate or illegal dumping.

TCE is a manufactured organic chemical discovered in the 1864 and first manufactured in Germany in the 1900s. It was used as an analgesi and anesthetic in 1920s and 1930s, as a drying cleaning agent until 1960, and has been used frequently as a solvent and to remove grease from metal machine parts, among other uses.

There are a wide range of adverse health effects that have been attributed to TCE. Results of human and animal studies show that TCE can affect the central nervous system (CNS), the liver, the kidney, the reproductive systemand the developing organism, including associations with cardiac birth defects. Studies on laboratory animals have shown that TCE causes cancer and birth defects, and human epidemiologic studies, particularly those in which populations of workers have been exposed to TCE, show elevated rates of cancer, especially kidney cancer, liver cancer, non-Hodgkin lymphoma, and more recently lung and esophageal cancer, and possibly birth defects and development disorders.

My work on TCE began in 1997 when I was awarded a competitive grant by the US Environmental Protection Agency, as part of their reassessment, to evaluate the epidemiologic evidence for making inferences of cancer hazards and risks for exposure to TCE. With colleagues, I conducted a detailed review of more than 80 relevant scientific publications and summarized the results in a peer reviewed paper that was published in Environmental Health Perspectives.[1] We concluded that evidence of excess cancer rates among occupational cohorts with the most rigorous exposure

assessment was compelling, reporting an average 50% elevation in risk for kidney cancer (RR-1.7, 95% CI 1.1-2.7), a nearly doubling of risk for liver cancer (RR=1.9, 95% CI 1.0-3.4), and a 50% elevation of risk for non-Hodgkin lymphoma (RR=1.5 95% CI 0.9-2.3) as well as elevated risks for cervical cancer, Hodgkin disease, and multiple myeloma. In 2000, on the basis of the work I did for EPA, I was asked to summarize the data on the carcinogenicity of TCE for the 10th Annual Report on Carcinogens issue by the National Institute of Environmental Health Sciences' National Toxicology Program (NTP), and provided a similar perspective.[2] Since that review, there have been several additional publications that provide additional evidence supporting the association between occupational TCE exposure and several types of cancer in humans, most notably kidney cancer, liver/biliary cancer, non-Hodgkin lymphoma, esophageal adenocarcinoma, and to a lesser extent Hodgkin disease and cervical cancer.[3-7] One of these reports, on a cohort in Denmark, was particularly notable in that they used biomarkers (measures of biological material from the study subjects) to more accurately document and quantify TCE exposure in these workers, and their subsequent cancers.[3] Others researchers presented data from toxicological studies suggesting a specific mechanism by which TCE causes genetic alterations and eventually cancer, for example for kidney cancer via somatic mutations in the so-called von Hippel-Lindau (VHL) tumor suppressor gene.[8-13]

TCE has been identified as an animal carcinogen by many scientific and public health agencies including the Center for Disease Control's Agency for Toxic Substances and Disease Registry (ATSDR), USEPA, California Environmental Protection Agency (CAL

EPA), the Work Health Organization's International Agency for Research on Cancer (IARC), and NTP. In animal studies, oral doses of TCE have induced liver tumors in mice, and kidney tumors in male rats, oral doses of TCE metabolites (TCA, DCA, and CH) have induced liver tumors in mice and DCA has induced liver tumors in rats, inhaled TCE has induced liver cancers, lung cancers, and malignant lymphomas in mice, and kidney cancers and testicular tumors in rats (NYS 2006). The recent review conducted by the National Academy of Sciences suggests particular concern for vulnerable populations such as children.

Further, TCE has also been shown to be associated with human non-cancer health effects, such as nervous system disorders, liver toxicity, end-stage renal disease, and adverse birth outcomes including birth defects. The recent review conducted by the National Academy of Sciences suggests particular concern for vulnerable populations such as children.

One example of the concern surrounding exposure to TCE is a recent Health Consultation conducted by the New York State Department of Health, in conjunction with ATSDR, in Endicott, NY (2006). In this community, in which vapors of TCE from contaminated groundwater seeped into people's homes through a process called vapor intrusion, the researchers found excess kidney cancer, cardiac birth defects and excess low birth weight births. The researchers cautiously note that, "although this type of study cannot prove whether there is a causal relationship between VOC exposure in the study area and the increased risk of several health outcomes observed, it does serve as

a first step in providing guidance for further health studies and interventions." The data are consistent with the epidemiology and animal studies discussed above.

In summary, since any exposure to a carcinogen is believed to increase an individual's risk of developing cancer and, in the interest of preventing unnecessary cases of cancer, I urge you to limit or prevent all exposures to TCE in accordance with the data discussed above. I believe that the data are sufficiently consistent and clear to warrant prudent and aggressive action for prevention and/or reduction of exposure at this time.

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Evaluation of the U.S. EPA/OSWER Preliminary Remediation Goal (PRG) for Perchlorate in Groundwater: Focus on Exposure to Nursing Infants

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NIEHS
National Institute of Environmental Health Sciences
National Institutes of Health
U.S. Department of Health and Human Services

Evaluation of the U.S. EPA/OSWER Preliminary Remediation Goal (PRG) for Perchlorate in Groundwater: Focus on Exposure to Nursing Infants

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Article Descriptor: Risk Assessment

Running Title: Evaluation of Perchlorate PRG

Key Words: Drinking Water, Neurodevelopment, Nursing Infants, Perchlorate, PRG, Thyroid Hormone

Abbreviations

CH: congenital hypothyroidism

FDA: Food and Drug Administration

IRIS: Integrated Risk Information System

MCL: Maximum Contaminant Level

NAS: National Academy of Science

OSWER: U.S. EPA's Office of Solid Waste and Emergency Response

PBDE: polybrominated diphenyl ether

PCB: polychlorinated biphenyl

PRG: preliminary remediation goal

RfD: reference dose

RSC: relative source contribution

SD: standard deviation

T_3: triiodothyronine

T_4: thyroxine

TSH: thyroid stimulating hormone

U.S.EPA: United States Environmental Protection Agency

Outline

ABSTRACT

Background: Perchlorate is a common contaminant of drinking water and food. It competes with iodide for uptake into the thyroid, thus interfering with thyroid hormone production. U.S. EPA's Office of Solid Waste and Emergency Response set a groundwater preliminary remediation goal (PRG) of 24.5 ug/L to prevent exposure to pregnant women that would affect the fetus. This doesn't account for greater exposure that is possible in nursing infants, and for the relative source contribution (RSC), a factor normally used to lower the PRG due to non-water exposures.

Objectives: To assess whether the OSWER PRG is protective of exposures to infants from breastfeeding, and to evaluate the perchlorate RSC.

Methods: Monte Carlo analysis was used to simulate nursing infant exposures associated with the OSWER PRG when combined with background perchlorate.

Results: The PRG can lead to a 7 fold increase in breast milk concentration, causing 90% of nursing infants to exceed the RfD (average exceedance 2.8 fold). Drinking water perchlorate must be below 6.9 ug/L to keep the median, and below 1.3 ug/L to keep the 90^{th} % nursing infant exposure below the RfD. This is 3.6-19 fold below the PRG. Analysis of biomonitoring data suggests an RSC of 0.7 for pregnant women, and 0.2 for nursing infants. Recent data from CDC suggest that the RfD itself needs to be reevaluated because of hormonal effects in the general population.

Conclusions: The OSWER PRG for perchlorate can be improved by considering infant exposures, by incorporating an RSC, and by being responsive to any changes in the RfD resulting from the new CDC data.

Introduction

Perchlorate is a powerful oxidant that is used in rocket fuel, munitions, blasting operations, and fireworks (NAS 2005). Environmental contamination has occurred at military installations, at facilities that make perchlorate, and at various construction sites from the blasting of bedrock to build roads or homes. In addition, there are natural sources of perchlorate such as fertilizer produced in certain regions (e.g., Chilean nitrate), evaporite soils, and atmospheric sources (Dasgupta et al. 2005; Orris et al. 2003). Its high water solubility and environmental persistence have led to contamination of groundwater, with detection increasing in recent years as analytical methods have improved (GAO 2005). There are no federal drinking water standards for perchlorate, although a number of states have recently developed or proposed values in the 2-6 ug/L range (MADEP 2006; New Jersey Drinking Water Quality Inst. 2005; Ting et al. 2006). These drinking water targets are intended to prevent perchlorate's neurodevelopmental effects resulting from its anti-thyroid action.

Perchlorate can impair thyroid function by inhibiting the uptake of iodide, thereby reducing the amount of iodide stored in the thyroid and available for hormone production (NAS 2005; Ting, et al. 2006). In those who have adequate iodide intake and stores of thyroid hormone, this impairment can be overcome with little to no consequence (Braverman et al. 2005). However, gestation can be a vulnerable period due to increased nutritional demands for iodide in the mother and due to the critically important role of thyroid hormone for fetal brain development (NAS 2005). The U.S. EPA reference dose (RfD) of 0.0007 mg/kg/d, as adopted from a report from the National Academy of Science (NAS 2005; U.S. EPA 2005), is intended to protect the general public, including vulnerable life stages such as in utero development, from perchlorate's anti-thyroid effects. This RfD has been used in at least one case to derive a drinking water limit for perchlorate (New Jersey Drinking Water Quality Inst. 2005), whereas other states have used more stringent toxicity values to set a drinking water limit (MADEP 2006; Ting et al. 2006). The case for a lower RfD has also been made by others (Ginsberg and Rice

2005). Recent data from CDC indicate a low dose effect of perchlorate, particularly on women with low iodine intake, and thus suggest a need to lower the RfD (Blount et al. 2006a).

The current paper does not focus on the issue of the appropriateness of the U.S. EPA RfD, but evaluates whether a groundwater cleanup guideline issued by U.S. EPA's Office of Solid Waste and Emergency Response (OSWER) would result in keeping exposure below the RfD for all vulnerable segments of the population. The OSWER guideline, released January 2006, sets a groundwater preliminary remediation goal (PRG) of 24.5 ug/L for Superfund sites containing perchlorate. Whereas this level corresponds to the amount that would deliver the RfD for a 70 kg adult ingesting 2 liters/day, it is not necessarily protective of nursing and bottle-fed infants who consume more liquid per body weight than adults (U.S. EPA 2002). A recent analysis calculated perchlorate doses that were above the RfD for infants drinking reconstituted formula made with water containing perchlorate at 24 ug/L, the OSWER PRG (Baier-Anderson et al. 2006). Further, based upon a limited breast milk biomonitoring dataset, Kirk et al. (2005) estimated that nursing infants could receive doses above the RfD even without considering the added exposure associated with the OSWER PRG.

Our primary objective is to evaluate the perchlorate dose to nursing infants resulting from maternal ingestion of water contaminated by perchlorate at the OSWER PRG of 24.5 ug/L. As explained below and described elsewhere (Baier-Anderson 2006), infants are likely to also be highly susceptible to perchlorate. The OSWER PRG did not explicitly consider exposure during this life stage.

An additional objective is to evaluate whether the OSWER PRG is protective of the pregnant mother and her developing fetus. Exposure to the fetus is dependent upon the mother's intake of perchlorate from both diet and drinking water. In setting drinking water Maximum Contaminant Levels (MCLs), U.S. EPA routinely applies a Relative Source Contribution (RSC) to allow for the possibility that not all exposure will come from water, recognizing the importance of keeping the total exposure dose (e.g., water

plus diet) below the RfD. The default RSC is 0.2, meaning that only 20% of the RfD would be allowed to come from drinking water. In the case of the OSWER PRG for perchlorate, the groundwater target is set at the water concentration that corresponds to the RfD, in effect, setting the RSC to unity. This appears to be contrary to the emerging database on perchlorate content of foods, which shows that perchlorate is common in the diet (El Aribi et al. 2006; FDA 2004). The limited human biomonitoring data suggest widespread exposure, with dietary perchlorate appearing to be a key source (Kirk et al. 2005; Valentin-Blasini et al. 2005). This indicates a need for careful consideration of the RSC. This paper provides a means to do this by analyzing the available human biomonitoring data.

Some may be less concerned about exceedance of the RfD because it is based on a precursor effect, inhibition of iodide uptake by the thyroid. This implies that the RfD prevents a biochemical change that precedes a more serious toxic effect, and thus is not itself a critical health endpoint. This assumption lacks support as there are no data that show how much iodide uptake inhibition is needed to affect thyroid function. This relationship is likely to be dependent on a number of host-specific factors. For example, recent observations by Blount et al. (2006a) demonstrate that women in the lowest category of iodine intake were most sensitive to perchlorate's effects on thyroid hormone production. Analogous to the low iodine women in the Blount, et al., study, neonates are likely to be a sensitive lifestage because of perchlorate's direct effects on the thyroid and it's ability to limit iodine transfer into breastmilk, thereby reducing infant intake of this nutrient (Kirk et al. 2005; Tellez et al. 2005; see below). Moreover, the simultaneous exposure to other breast milk contaminants (e.g., PCBs, PBDEs, dioxins) that can disrupt thyroid function by others modes of action, may interact with perchlorate in infants. Therefore, limiting perchlorate exposure should be a critical public health target not only during pregnancy but also in infants. This rationale is further described below.

Literature Review: Why Focus on Perchlorate Effects in Infants?

If the perchlorate mechanism of action is not relevant to the postnatal period, or if this period is considerably less sensitive than the in utero period, then application of the RfD to this period would be inappropriate. Therefore, this analysis begins with a literature review describing factors that may affect susceptibility to perchlorate during the postnatal period. Since there is no indication that the perchlorate mechanism of action should differ across life stages, our review focuses upon the ability of neonates to compensate for perchlorate-induced decreases in thyroid hormone synthesis.

Sensitivity of Newborns to Thyroid Disruption and Altered Brain Development

During the in utero period the fetal brain undergoes critical developmental stages that are supported by the maternal supply of thyroid hormone, T_4 (Howdeshell 2002). Maternal T_4 is an important source of thyroid hormone for the fetus throughout gestation. It is the only source during the first trimester (Howdeshell 2002; Morreale de Escobar 2001), and remains an important complement during late gestation when it contributes approximately 30% to the fetal supply of T_4 (Vulsma et al. 1989)

The importance of maternal T_4 has been demonstrated in babies with congenital hypothyroidism who appear normal at birth because of ample maternal hormone during gestation (Vulsma et al. 1989). In contrast to the fetus, the newborn can no longer rely upon maternal hormone as a buffer against inborn biosynthetic deficiencies or external stressors. The only means for hormone transfer from the mother is breast milk; however, breast milk contains very little thyroid hormone (van Wassenaer et al. 2002). Therefore, the neonate must synthesize its own supply of T_4 to maintain normal growth and development. As described below, there are a number of factors that make neonatal thyroid status more vulnerable to perturbation than in adults or the fetus.

First, the serum half life of T_4 is approximately 7-10 days in adults (Chopra and Sabatino 2000), but is approximately 3 days in neonates (Lewander et al. 1989; van den Hove et al. 1999). Thus, the rate of replacement of T_4 (i.e., T_4 secretion from the thyroid gland) must be considerably higher in early life to maintain steady-state levels. Second,

the adult thyroid gland stores a large quantity of thyroid hormone in the form of thyroglobulin; this quantity is estimated to be enough to maintain normal levels of circulating hormone for several months (Greer et al. 2002). In contrast, the neonatal gland stores very little T_4; the amount stored has been estimated at less than that required for a single day (Savin et al. 2003; van den Hove et al. 1999). These differences in thyroid hormone status between adults and neonates indicate that the functional reserve available to adults is virtually absent in neonates. Any reduction in thyroid hormone synthesis in the neonate will result in a reduction in circulating levels, whereas this is clearly not true for the adult. The combined storage deficiency and rapid hormone turnover in neonates necessitates a high rate of T_4 synthesis to keep up with the daily demand for thyroid hormone. This, in turn, is dependent upon an adequate supply of iodide. Given these demands on the neonatal thyroid, it is likely that perchlorate-induced inhibition of iodide uptake has a greater impact in neonates than in utero or at other life stages. This is consistent with a recent study of 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) in rats which showed that postnatal (lactational) exposure produced greater thyroid disruption than exposure during the in utero period (Nishimura et al. 2005). While rats have a different developmental time frame than humans, and TCDD's mechanism of thyroid disruption differs from perchlorate, the rat findings suggest an important postnatal window of vulnerability to thyroid toxicants. The concern for postnatal effects is magnified with perchlorate due to its potential to also interfere with iodide excretion into breast milk as discussed below.

Considering these factors, it is critical to understand the degree to which iodide uptake must be inhibited in neonates to cause a reduction in thyroid hormone synthesis. However, this relationship has not been explored in neonates and is not well understood in adults. The National Academy of Science perchlorate report (NAS 2005) provided the following estimate: "To cause declines in thyroid hormone production that would have adverse health effects, iodide uptake would most likely have to be reduced by at least 75% for months or longer." However, to our knowledge, no human or animal data exist that directly support this estimate. Epidemiological studies in regions of mild deficiency provide indirect estimates of the degree to which iodide must be reduced before adverse

consequences occur. Specifically, these studies show that iodine intake that is 40-50% of that recommended by the World Health Organization is associated with adverse consequences in infants and children, including lower IQ and an increased incidence of attention deficit disorder (Aghini Lombardi et al. 1995; Vermiglio et al. 2004). The authors speculate that this association is caused by thyroid hormone insufficiency secondary to moderately low iodine intake. While the relationship between perchlorate-induced iodide uptake inhibition and thyroid function is still poorly understood, it is likely that the degree of inhibition required to affect hormone status is less than 75%. This conclusion is supported by the recent observation that urinary perchlorate levels that are commonplace in the general population are associated with changes in thyroid hormone levels in U.S. women (Blount et al. 2006a).

Insight into the sensitivity of neonates to thyroid hormone insufficiency is perhaps best documented in studies of infants with congenital hypothyroidism (CH) (for review, see Zoeller and Rovet 2004). These studies are particularly useful because subjects are under continuous medical surveillance so there is good documentation of the relationship between endogenous thyroid hormone, levels of hormone supplementation, and developmental outcome (Heyerdahl and Oerbeck 2003). The neuropsychological outcome of children diagnosed with CH at birth is associated with both the severity of CH and early treatment factors (how soon T_4 was administered, starting dose and serum T_4 levels during the first two years of life). These T_4 parameters were highly correlated with verbal IQ at age 20, and children with CH who ultimately completed high school had a significantly higher T_4 starting dose than those who did not (Oerbeck et al. 2003). Interestingly, the difference in mean starting dose between these two groups was only 2.1 μg/kg-day. Because iodine represents 65% (w/w) of T_4, the amount of iodine associated with that T_4 difference is only 1.37 μg/kg-day. Others have found that a difference in starting dose of only 12.5 μg/day (8.13 ug/day iodine equivalent or 2.3 ug/kg/d) was associated with a significant difference in full scale IQ of 11 points (Selva et al. 2002; 2005). Thus, small differences in available thyroid hormone (and the iodine associated with it) during the first few weeks of life can have significant lifetime consequences.

These increased demands for thyroid hormone production in neonates may be compounded because adaptive mechanisms are not as robust. These mechanisms may include negative feedback responses (i.e., TSH response to low T_4), changes in serum binding proteins or iodothyronine transporters, or changes in deiodinases (Zoeller 2005). Thus, a variety of adaptive mechanisms available to adults may not be available to the neonate, causing the neonate to adapt poorly to iodide uptake inhibition. Studies in rats indicate that the ability of the neonate to adapt to low iodide is poor , that compensation appears to be tissue-specific, and that humans are likely to respond in a similar manner (Pedraza et al. 2006). In this study, mild iodide deficiency lowered T_4 in the absence of an increase in TSH, suggesting that TSH may not be a sensitive index of thyroid hormone status in early life (Pedraza et al. 2006).

In summary, the data needed to perform quantitative risk assessment for perchlorate in neonates are limited. However, there is ample reason to expect the neonatal period to be highly sensitive to perchlorate-induced iodide uptake inhibition. The neonate receives very little thyroid hormone from breast milk and so must depend upon the function of its own thyroid gland in the absence of stored hormone. Further, it is confronted with more rapid hormone turnover. This situation is compounded by the vulnerability of brain development to even small deficits in thyroid hormone levels during this period. Impairment of iodide uptake by perchlorate has been described as a precursor effect in adults, largely because of stored hormone and homeostatic mechanisms that can compensate for the perchlorate-induced biochemical perturbation (NAS 2005). The recent CDC data suggest that there may be many women in whom these compensatory mechanisms are inadequate even at background levels of perchlorate (Blount et al. 2006a). The consequences in neonates may be more significant and lead to long-term risks for neurocognitive deficits.

Lack of epidemiology studies that assess perchlorate effects in breast fed infants

A number of studies have addressed the association between perchlorate levels in drinking water and thyroid status of the neonate or child (Brechner et al. 2000; Buffler et

al. 2006; Crump et al. 2000; Kelsh et al. 2003; Lamm 2003; Lamm and Doemland 1999; Li et al. 2000a,b; Schwartz 2001; Tellez et al. 2005). Most of these studies have failed to find an adverse relationship, although there are a few exceptions. Interpretation of this body of evidence is difficult because the studies suffer from the fact that they were of ecological design, and because no information is provided on an exposure route of primary concern to neonates, breastfeeding. Regarding limitations due to ecological design, the levels of perchlorate actually consumed were not known in any of the studies. This has the potential to bias results toward the null, especially in the case of perchlorate due to its prevalence in the diet (El Aribi et al. 2006; FDA 2004). This leads to the potential for exposure misclassification as studies typically categorized exposure simply on the basis of perchlorate levels in a common water supply. This limitation applies to infant exposures that come from breast milk and to post-weaning exposures where perchlorate can come from the child's diet and drinking water. While it would not affect studies involving bottle-fed infants during the first months of life, we are not aware of any studies which have specifically evaluated this category of receptor.

. None of the studies addressed the exposure under consideration in the present analysis: exposure to the nursing infant through breast milk. In any of the studies it is likely that some infants were breastfed and others were not. Without this specified, one cannot analyze the relationship between nursing exposure to perchlorate and thyroid status. Several studies performed in the western US examined the association between perchlorate in drinking water and neonatal thyroid hormones (Brechner et al. 2000; Buffler et al. 2006; Kelsh et al. 2003; Lamm 2003; Lamm and Doemland 1999; Li et al. 2000a,b; Schwartz 2001). This includes three studies which followed infants past the neonatal period: Li et al. (2000a) examined TSH levels at 2-7 and 8-30 days of age in a small subset of children with low T_4 levels; Li et al. (2000b) examined T_4 levels in infants as a function of age from day 1 to 60 examined cross-sectionally based upon residence in Reno (no perchlorate in drinking water) compared to Las Vegas (perchlorate in drinking water); and Brechner et al. (2000) examined TSH levels between 0 and 132 days of age in Yuma (with perchlorate in the drinking water) vs. Flagstaff (no perchlorate). The Li et al. studies did not find an association with perchlorate exposure while the Brechner et al. study did. Aside from limitations of ecological design and lack

of information on nursing exposure, these studies were limited in other respects. For example, Li et al. (2000a) measured TSH in only a small fraction of infants for whom T_4 levels were at the low end of the distribution, thereby examining a subsample of infants that was not representative of the population. Additionally, TSH levels were treated as a dichotomous variable based on a definition of clinical disease, even though levels were available for analysis as a continuous variable. The Li et al. (2000b) study of infants out to 2 months of life suggests that levels of perchlorate of up to 15 ug/L in Las Vegas did not affect T_4 levels. However, the Las Vegas drinking water perchlorate levels fluctuated widely during this time and so it is difficult to draw conclusions about perchlorate exposure based upon city of residence. The Brechner et al. (2000) study has been questioned on the grounds that Flagstaff represents an inappropriate reference location because of its much higher elevation (Lamm 2003).

The Chilean series of studies (Crump et al. 2000; Tellez et al. 2005) were the most detailed but shared the deficiencies and inconsistencies described above for the US studies. Although neonates and first- and second-grade school children were evaluated, there were no measurements during infancy and no information on breastfeeding exposure. These studies were analyzed as ecological studies even though biomonitoring data were available in one case (Tellez et al. 2005). However, the biomonitoring data were not used to test associations between perchlorate and hormone status or goiter. There was no evidence for a perchlorate-related difference in TSH, T_3 or T_4, based upon city of residence, but the incidence of goiter in children was greater in the two cities with the higher levels of perchlorate in water. For the history of thyroid disease in the family, the high-perchlorate city (Taltal) had a significant increase compared to the reference city (Antofagasta). The environmental and biomonitoring data from the Chilean study is described further in Methods. As pointed out below, the high iodide intake in these Chilean cities may have affected the outcome of their study.

Overall, the epidemiology studies do not provide a body of evidence for determining whether perchlorate will affect thyroid status or neurodevelopment in infants. Therefore, the mechanistic and developmental information described in other

sections of this paper are critical in evaluating whether the postnatal period is likely to be vulnerable to perchlorate.

Toxicokinetic Considerations in the Neonate

Perchlorate is cleared unchanged in the urine although protein binding can retain perchlorate in serum and retard its excretion (Clewell, et al, 2003; Yu et al. 2002). Biomonitoring studies have capitalized on this excretory pathway as urinary perchlorate is an excellent biomarker for the general public (Blount et al. 2006c). However, there are no data on the efficiency of perchlorate excretion in early life stages in humans and only limited data in rats. In general, human infants have immature renal function and less urinary clearance of many water soluble chemicals (Ginsberg et al. 2002; Kearns and Reed 1989; Morselli 1989). This suggests that slower clearance may be another factor for increased vulnerability to perchlorate. However, data from pre-weanling rats suggest the opposite as rat pups had a higher perchlorate dose than their mothers, but had lower serum concentrations (Clewell et al. 2003; NAS 2005, Appendix E).

The rat data are of questionable relevance to human infants given the variety of cross-species differences in the ontogeny of toxicokinetic systems (Ginsberg et al. 2004). Regarding perchlorate, cross-species extrapolation of chemical fate is affected by apparent differences in plasma protein binding and renal clearance between rats and adult humans as simulated in well calibrated toxicokinetic models (Clewell et al. 2003; Merrill et al. 2005). The relevance of the neonatal rat data (Clewell et al. 2003) to human infant dosimetry is also affected by the fact that: a) rat dams drink nearly all of the urine excreted by their pups, which inflates the serum level of perchlorate relative to the pup; b) lactating dams and pups were dosed with radioactive iodide which may affect perchlorate toxicokinetics, especially with regards to competition for serum binding sites. Another uncertainty is the manner in which iodine intake may affect perchlorate toxicokinetics and how this may differ across species and life stages. These uncertainties prevent one from drawing conclusions on the role of perchlorate toxicokinetics to affect dosimetry and risk in human infants.

Added risk factor: potential lowering of breast milk iodide

An additional reason to highlight nursing infants as a vulnerable period is that perchlorate risks may be magnified in this group by causing a concomitant decrease in breast milk iodide levels. The sodium iodide symporter that is expressed in the thyroid gland is also expressed in lactating mammary gland. It transports iodide into breast milk with perchlorate able to take iodide's place and be selectively pumped into breast milk (Clewell et al. 2003). This can lead to exposure to perchlorate in nursing infants, while at the same time leading to lower levels of iodide in breastmilk. This has been demonstrated in rats where perchlorate exposure to nursing dams resulted in decreased levels of iodide in milk (Clewell et al. 2003). It is expected that this effect on breast milk iodide will be modified by variations in dietary iodine intake. However, the interaction between perchlorate and iodine ingestion on breast milk content of iodide has not been studied in rats or humans. Perchlorate may also impair iodine excretion into breast milk in humans as suggested by data showing an inverse correlation between perchlorate and iodide concentrations in breast milk in a small number of US samples that were over 10 ug/L perchlorate (Kirk et al. 2005). Tellez et al. (2005) did not see a correlation, inverse or otherwise, between perchlorate and iodide concentrations in breast milk across 3 Chilean cities with widely differing concentrations of perchlorate in drinking water. However, there does seem to be a factor that depresses iodide levels in breast milk in these Chilean cities relative to the U.S. On average, Chilean breast milk iodide concentrations were 40% lower than in US women in spite of the fact that iodide intake rates are known to be higher in these Chilean cities than in the US (Tellez et al. 2005; Kirk et al. 2005). The factor responsible for lower-than-expected breast milk iodide levels in Chile may be that baseline (dietary) exposure to perchlorate is approximately 3 times higher in Chile than in the US (Valentin-Blasini et al. 2005).

The reason the Chilean cross-sectional study did not find an inverse correlation between breast milk levels of perchlorate and iodide is unclear, but comparisons were performed only on the basis of group mean (Tellez et al. 2005). Regression analysis of the entire dataset would be a more sensitive method to determine whether there is a

significant relationship between these breast milk parameters in Chile. Further, the greater intake of iodide in Chile may have ameliorated the perchlorate effect on breast milk iodide. Overall, the potential for perchlorate intake by lactating women to lower the iodide content of breast milk provides additional rationale to consider this lifestage to be of prime concern for human risk assessment and standard setting.

Methods Used in Current Analysis

Calculations of infant exposure to perchlorate involve either fixed inputs, generally the central tendency value, or inputs that take the form of a distribution of values. Monte Carlo simulation analyses are used to present the variability distributions for nursing exposure under baseline conditions (dietary perchlorate only) and with the added exposure associated with the OSWER groundwater cleanup target of 24.5 ug/L. The overall exposure equation is:

$$\textit{Nursing Infant Dose (ug/kg/d)} = (BM_{perc}/U_{perc}SF)*[\,(\textit{Baseline } U_{perc}) + (\textit{Added } U_{perc})] * (\textit{L breast milk ingested-day/infant body weight}) \quad [1]$$

Where:

$BM_{perc}/U_{perc}SF$: breast milk perchlorate-to-urinary perchlorate slope factor (ug/L per ug/g creatinine) as derived from the Chilean three-cities study (Tellez et al. 2005)

Baseline U_{perc}: baseline perchlorate excretion in the U.S. from diet (no drinking water exposure) (ug perchlorate/g creatinine) taken from NHANES 2001-2002 biomonitoring data for 15-44 year old women (Blount et al. 2006c). As described below, this is included in Monte Carlo simulations as a lognormal distribution.

Added U_{perc}: increase in urinary perchlorate (ug/g creatinine) from tap water ingestion at the OSWER groundwater PRG of 24.5 ug/L. This was calculated as follows:

U_{perc}= *(24.5 ug perchlorate/L water)*(L water ingested/d)*(1/1.165 g creatinine /d)* [2]

Where:

Liters of water ingested by lactating women was entered as a normal distribution with a mean of 1.189 L/d, SD = 699 (U.S. EPA 2002)

g creatinine excretion/d based upon data from 10 women of child-bearing age (Lentner 1981).

L breast milk ingested-day/infant body weight: neonate consumption rate estimated at 2 weeks of age to capture the average over the first month of life; input as a normal distribution with mean 171.8 ml/kg-d; SD = 26.46 (U.S. EPA 2002)

The following sections provide additional details on the parameters needed to calculate infant exposure to perchlorate via breast milk.

1. Relationship between urinary and breast milk perchlorate ($BM_{perc}/U_{perc}SF$) - Urinary perchlorate is a reasonable index of the rate of perchlorate intake under conditions of frequent and relatively uniform exposure in which pseudo-steady state toxicokinetics are achieved. The biomonitored populations in Chile are exposed on a daily basis to perchlorate in the diet and drinking water and so it is reasonable to assume that their blood concentration is relatively stable and approaching steady state. The urinary concentration-to-intake dose interconversion is facilitated by the fact that excretion of unchanged parent compound is the main means of elimination. Three different Chilean cities were studied having a wide range of perchlorate exposure via drinking water as shown in Table 1 (Tellez et al. 2005). This table also shows the urinary and breast milk perchlorate data for these cities. The breast milk statistics for Antofagasta do not include one outlier subject who had very high breast milk perchlorate (1042 ug/L).

Linear regression was used to relate the mean concentrations of perchlorate in breast milk to urine across the three cities. The regression line was weighted by the inverse of the variance in the data for each city. The line was forced through the origin since it can be expected that with zero intake by the mother (and thus no perchlorate in urine), there should also be none in breast milk. The size of the sampled groups differed considerably between the urinary and breast milk measurements (Table1). The lack of paired measurements from the same individuals precludes a more precise analysis of the correlation between these parameters

2. Baseline Urinary Perchlorate Concentration in the US Population Without Drinking Water Exposure (***Baseline*** U_{perc}) – Urinary perchlorate concentrations were measured in a randomized sample (N=2818) intended to be representative of the U.S. general population age 6 years of age and up, as part of the NHANES 2001-2002 biomonitoring campaign (Blount et al. 2006c). This is a large expansion on the earlier perchlorate biomonitoring dataset published by CDC from a convenience sample of 61 adult residents of Atlanta, Georgia (Valentin-Blasini 2005). The larger dataset includes results for 662 women, aged 15-44. This subsample was selected as the baseline population to evaluate nursing exposures. Although a baseline population of nursing mothers would have been ideal, NHANES did not obtain a sizeable or representative sample from this group. The urinary data for the sample of 662 women, as well as the urine biomonitoring data from the Chilean cities appear to be lognormally distributed as evidenced by the fit of the data to regression lines in log probability plots for each city (Figure 1) (for background on probability plots see Hattis and Burmaster 1994). Therefore, dietary perchlorate intake inferred from urinary perchlorate data from Atlanta were input as a lognormal distribution to represent baseline perchlorate exposure for Monte Carlo analysis.

The group sampled by NHANES is assumed to represent baseline perchlorate exposure that comes from the diet without a substantial contribution from drinking water. NHANES did not obtain drinking water perchlorate data. However, a small pilot study conducted by CDC measured urinary perchlorate in conjunction with drinking water

perchlorate and dietary factors for 27 subjects in Atlanta (Blount et al. 2006b). Drinking water perchlorate averaged only 0.11 ug/L (range <0.05-0.25 ug/L) for these 27 individuals, a small contribution given that these subjects were excreting approximately 5 ug perchlorate/day. The importance of diet in determining urinary perchlorate was shown by dividing the group into those who ate one or fewer vs three or more servings of dairy or leafy green vegetables. The higher servings group had an average urinary perchlorate that was 1.8 fold higher. Figure 2 shows urinary perchlorate for all 27 Atlanta subjects compared to the 662 women sampled by the NHANES 2001-2002. The log probability plot shows a reasonable correspondence between these datasets. The Atlanta sample had a higher median but the two populations converged at the upper end of the distribution. Since the Atlanta distribution was not materially affected by drinking water intake, Figure 2 suggests that the NHANES distribution, even at the upper end, is what can be expected from diet alone. Therefore, we considered the NHANES urinary perchlorate distribution for these women as a reasonable baseline for projecting the added impact of drinking water at the OSWER PRG.

Modeling the contribution of maternal water ingestion to urinary perchlorate was accomplished by combining the expected perchlorate exposure associated with a normal distribution of daily water consumption with the lognormal distribution of baseline urinary perchlorate. Correction was made for creatinine excretion rate per day as described above. These equations also assume that perchlorate ingested per day is equal to perchlorate urinary excretion per day under pseudo-steady state conditions. The Monte Carlo simulations were done in triplicate runs of 5000 trials each.

Results

Evaluation of the Impact of the OSWER Groundwater PRG on Exposures and Risks to Nursing Infants

The relationship between perchlorate exposure, as estimated from urinary perchlorate excretion, and perchlorate in breast milk, is shown in Figure 3 across the

three Chilean cities. This is the only dataset that provides both parameters for the same population. The regression line for these three cities (weighted by inverse variance of the mean of each datapoint) provides a slope of 0.387 (ug/L breast milk per ug/g creatinine). The line is less influenced by the Taltal results than by the other data points because of the large uncertainty in the mean breast milk concentration for the Taltal data.

This slope was used to convert urinary perchlorate to breast milk perchlorate for the baseline U.S. population distribution as derived from the 668 women sampled by NHANES. The distribution of breast milk perchlorate in this baseline population is shown in Figure 4, which has a simulated mean and SD of 1.63 ± 1.5 ug/L. The vast majority of the baseline population (> 90%) would be expected to have measureable perchlorate in breast milk at a detection limit of 0.4 ug/L (detection limit from Kirk et al., 2005). This agrees with the high rate of detection seen in the limited breast milk data currently available (Kirk et al. 2005). Figure 4 also shows the total perchlorate in breast milk after adding to the baseline a daily tap water exposure of 24.5 ug/L (the OSWER PRG). The distribution is shifted approximately 7 fold to the right with a new mean and SD of 11.45± 5.7. The 99th percentile value is 25.2 ug/L.

These breast milk concentrations were then used to simulate nursing exposure in infants within the first month of life as represented by the intake rate per body weight for two-week-old infants. The resulting exposure dose for both the baseline and (+) OSWER drinking water scenarios is presented in Figure 5. The two distributions are quite distinct with the lognormal baseline distribution overlapping only about 30% of the (+) drinking water distribution. Figure 5 also shows the U.S. EPA/IRIS RfD (0.7 ug/kg/d). The RfD is surpassed at approximately the 95th% percentile of the baseline population and at the 15th percentile of the (+) drinking water distribution. The average nursing infant exposure dose for the baseline population is 40% of the RfD while the average for the (+) 24.5 ug/L drinking water scenario is 2.8 fold greater than the RfD. The 95th percentile of the (+) drinking water distribution exceeds the RfD by 5.4 fold. These results suggest that perchlorate exposure associated with the OSWER PRG, in conjunction with background dietary exposure, results in exposures to nursing infants in

excess of the RfD for the great majority (85%) of the population. In fact, the upper end of the baseline distribution is also above the RfD.

Table 2 shows the baseline distribution of nursing infant exposure as projected from the NHANES dataset, along with the perchlorate drinking water targets that would satisfy the RfD at different percentiles of the distribution. Adherence to the RfD would require a groundwater cleanup level of 6.9 ug/L for the 50th percentile of the baseline distribution, and 1.3 ug/L at the 90th percentile.

Evaluation of the RSC Needed to Protect In Utero Development and Nursing Infants

A key consideration in setting the PRG is whether a relative source contribution (RSC) term is needed to protect sensitive life stages (in utero, post-natal) and what the value should be. This depends upon the extent of non-drinking water exposure to perchlorate relative to the perchlorate RfD. In this section we use the NHANES data for 668 women to provide an indication of dietary contribution to perchlorate exposure for RSC consideration.

Table 3 shows the daily exposure dose in adults implied by the urinary excretion data from NHANES (Blount et al. 2006c). When considering central estimates from the NHANES study, dietary exposure appears to constitute approximately 10% of the RfD. At the 95th percentile, diet is still only 32% of the RfD, which would support an RSC of 0.7 in the case of pregnant women. This is considerably larger than the default RSC of 0.2 commonly used in drinking water risk assessments.

These estimates pertain to adult baseline (dietary) exposure as a percentage of the RfD. Review of Figure 5 indicates that baseline exposure of nursing infants is 40% of the RfD for average exposure and it exceeds the RfD at the 95th percentile. Therefore, baseline dietary exposure of the mother produces a nursing infant based RSC in the range

of 0.6 (average case) to 0 (no allowance for drinking water exposure). This latter estimate of the nursing infant-based RSC is because the RfD is exceeded at the 95th percentile of exposure in the maternal diet-to-breastmilk-to-nursing infant pathway.

Discussion

The OSWER PRG is an important guidance for the Superfund program in that it establishes the initial groundwater target that, if surpassed, would attract the attention of site managers and health officials. It is not necessarily the final cleanup level as it can be increased or decreased based upon site-specific considerations. The factors presented in this paper have little to do with site-specific features but rather address exposure and toxicity issues relevant to all sites where there is potential for groundwater ingestion by pregnant women, nursing mothers, and infants. The higher dose rate received by nursing infants and the contribution of diet to total perchlorate dose are key considerations, and represent an opportunity for improving the scope and public health protectiveness of the PRG.

Our literature review and analysis indicate that there are toxicodynamic and toxicokinetic reasons to consider early postnatal life as a particularly vulnerable time for perchlorate toxicity. Further, this life stage has not been adequately assessed in perchlorate epidemiology studies. This is a critical issue, because as suggested elsewhere (Baier-Anderson 2006; Kirk et al. 2005) and as presented in this paper, infants can have greater perchlorate exposure than other life stages from ingestion of reconstituted formula or breast milk. This provides an imperative to evaluate nursing infants in risk assessments of perchlorate in drinking water.

The current analysis incorporates data on urinary and breast milk perchlorate concentrations into a Monte Carlo analysis of the distribution of intake of perchlorate by nursing infants at the OSWER PRG. Our simulations indicate that 85% of nursing infants can be expected to exceed the RfD, with the average exceedance 2.8 fold. In fact, the perchlorate drinking water concentration needs to be below 6.9 ug/L to keep the

50th percentile nursing infant below the RfD. The corresponding value for the 90th percentile infant is 1.3 ug/L. . These drinking water concentrations are 4 to 19 fold below the OSWER PRG and are more in line with proposals for regulating perchlorate in groundwater in a number of states (MADEP 2006; New Jersey Drinking Water Quality Inst. 2005; Ting et al. 2006). Ideally, one would develop a perchlorate groundwater target that keeps 95% of nursing infants below the RfD, but this would require a target of <1 ug/L. Comparison of Tables 2 and 3 shows that perchlorate doses are expected to be approximately 3 fold higher in nursing infants than in adult women.

Use of biomonitoring data to evaluate the RSC in adult women found that dietary perchlorate likely represents 32% of the RfD when considering the 95th percentile of the NHANES distribution. This corresponds to an RSC of 0.7, which is somewhat higher than the RSC applied by California EPA (0.6) (Ting et al. 2006). However, the RSC would be in the range of 0.6 to 0 when considering the baseline exposure of nursing infants from mother's diet-only intake of perchlorate. Thus, protection of nursing infants from perchlorate would require an RSC at least as low as the default often used in setting drinking water standards, 0.2. The lack of an RSC in OSWER's PRG derivation in effect assumes 100% of the daily perchlorate exposure comes from drinking water, omitting the contribution from diet. Thus, there is considerable room for re-evaluation of the PRG. It should be noted that the RSC estimate is based upon a particular RfD. Obviously, if the RfD were lower, then the baseline (dietary) exposure would constitute a larger fraction, necessitating a decrease in the RSC. For example, using benchmark dose analysis from the Greer et al. (2002) dataset, California EPA derived a perchlorate toxicity point of departure that is approximately 2 fold lower than that used in the IRIS RfD (Ting et al. 2006). Based upon this toxicity value, the RSC estimate would need to be cut in half. Further, recent evidence from the same NHANES/CDC dataset described above indicates an effect on thyroid hormone status in adult women at perchlorate intake levels that are below the RfD (Blount et al. 2006a). Table 3 above shows the average intake of women in the NHANES study to be approximately 10 fold below the IRIS RfD. This is likely in the range of perchlorate effect levels given that Blount et al. (2006a) found the thyroid hormone effect along a continuous function with perchlorate dose that

spanned the center of the exposure distribution. Therefore, future evaluations of the RSC will need to take into account any changes in the RfD that may occur as the human dose-response is reanalyzed.

Uncertainties

The current analysis requires knowledge of baseline exposure to perchlorate via non-drinking water sources, primarily the diet. The recent biomonitoring dataset developed as part of NHANES 2001-2002 (Blount, et al. 2006c) provides a very useful starting point for estimating the population distribution of dietary perchlorate intake. The comparison against biomonitoring results from 27 Atlanta residents who had minimal perchlorate in their tap water (Figure 2) indicates that the NHANES distribution is likely a reasonable estimation of background (dietary) exposure. What is less certain is the conversion of the urinary biomonitoring level to intake dose for these subjects. This is a key starting point for perchlorate risk assessment. The central assumption is that the amount of perchlorate excreted per day equals the amount ingested in the biomonitored individuals. This is true if these individuals are near or at steady state. In such cases the daily exposure can be viewed as a maintenance dose which keeps body stores at a relatively constant level i.e., no net accumulation or loss. This occurs in people whose exposure rate is fairly uniform, a situation that can be expected for perchlorate since it is present in a variety of foods (El Aribi et al. 2006; FDA 2004). This approach for relating urinary biomonitoring data and intake rate has also been used for other chemicals at or near steady state such as phthalates (Koch et al. 2003; Kohn et al. 2000; Koo et al. 2002) and chlorpyrifos (Rigas et al. 2001).

A caveat with this application of biomonitoring data is that it depends upon urinary excretion data normalized per gram of creatinine, which is multiplied by the creatinine excretion rate per day to yield the daily perchlorate excretion rate. However, the creatinine excretion rate per day is not typically measured in individual subjects but rather a central population estimate is used as in the current analysis. This does not account for the considerable inter-individual variability in creatinine excretion as seen in

an analysis of NHANES III data (Barr et al. 2005). This source of variability is not expected to bias the analysis in a particular direction but could be incorporated into future Monte Carlo analyses by including the creatinine excretion rate as a distribution rather than a fixed central estimate.

It is useful to contrast estimates of perchlorate dietary ingestion in the NHANES dataset with those developed elsewhere. Data from the three Chilean cities suggest that dietary perchlorate is consistent across the three cities, 20-35 ug/d on average, or 0.3 to 0.5 ug/kg/d (Tellez et al. 2005). This is approximately 5 fold above the average intake rate we calculated for 15-44 year old women sampled by NHANES, 0.075 ug/kg/d (Table 3). This is consistent with there being higher perchlorate in soil, fertilizer, and locally grown foods in Chile than in the US (Crump et al. 2000; El Aribi et al. 2006).

Another area of uncertainty is the conversion of biomonitored levels of perchlorate in urine to breast milk perchlorate. We utilized the only available dataset that provides both urinary and breast milk biomonitoring data, the Chilean data from three cities (Tellez et al. 2005). The strength of this dataset is that it captures a wide range of perchlorate exposures. However, the number of subjects for which breast milk data were available is considerably smaller than the number of subjects for which urinary data were available. The lack of pair-matched results meant that the correlation could only be determined on a population mean basis, relying on only three data points, one for each city, rather than the individual datapoints. Although the line in Figure 3 represents a reasonable best fit across the three cities, a more robust and comprehensive analysis would have been possible if individual, pair-matched data were available.

A potentially greater uncertainty in using the Chilean data to represent the urinary-to-breast milk relationship is that this relationship may be different in the U.S. While iodide supplementation in these Chilean cities has decreased in recent years, iodine intake in Chile still appears to be higher than in the U.S. (Tellez et al. 2005). This may affect, via substrate competition, the distribution of perchlorate into various compartments into which it is actively transported. Just as high perchlorate impairs

iodide excretion into breast milk (see above), it is also possible that high iodide decreases perchlorate entry into breast milk. This would cause a shallower breast milk to urinary perchlorate slope in Figure 3 and underpredict nursing infant exposures in the U.S. That this may be the case is presented in Figure 6, which compares breast milk perchlorate simulated from the NHANES data vs actual data from Kirk et al. (2005). The actual data were collected from 36 women across 18 states in the U.S. Both distributions appear lognormal with the bulk of the results below 10 ug/L. However, the Kirk et al. distribution is shifted to the right of the NHANES-based simulation (Kirk et al. median = 3.3 ug/L; NHANES simulation median = 1.2), and there are numerous high end individuals in the Kirk dataset not predicted by the simulation. The higher perchlorate levels in the Kirk et al. dataset may be due to greater perchlorate intake from the diet or drinking water than in the NHANES subjects, although there is no reason to think that the Kirk, et al. population was biased towards high exposure individuals. A distinct possibility is that the slope between breast milk and urinary perchlorate is greater in the U.S. than in Chile, causing our simulations of nursing exposure and risk to be an underestimate. This would also lower the OSWER groundwater PRG needed to keep nursing infants below the current RfD. More studies are needed that define perchlorate levels in U.S. breast milk and that explore the interaction between iodide and perchlorate at the mammary symporter.

Conclusions

The neonate may be particularly vulnerable to perchlorate toxicity because of a number of factors described in this paper. This means that the OSWER PRG of 24.5 ug/L should be evaluated in light of neonatal exposures. Baseline exposure as simulated from NHANES biomonitoring data, takes up a substantial fraction of the RfD in nursing infants, which does not allow much additional perchlorate exposure from drinking water. In this regard, the OSWER PRG could result in perchlorate exposures that exceed the RfD in a high percentage of nursing infants. This is generally true for pregnant women because an RSC was not used in OSWER's PRG calculation. Proposed drinking water standards set for perchlorate by a number of states (New Jersey, Massachusetts,

California) are in the range of 2-6 ug/L, well below the OSWER PRG. We recommend that OSWER re-evaluate the perchlorate PRG in light of the early life exposure and RSC factors raised in this paper. In addition. recent data from CDC on perchlorate's effects on thyroid status in adult women (Blount et al. 2006a) need to spur followup studies and become incorporated into future perchlorate risk assessments.

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Table 1. Biomonitoring Results (mean ± SD) for 3 Chilean Cites

(adapted from Tellez et al. 2005)

	Antofagasta	Chanaral	Taltal
Tap Water Perchlorate (ug/L)	Not detected (<4)	5.82 ± 0.63	114 ± 13.3
Urinary Perchlorate[a]	28.4 ± 22	80.2 ± 129.6	135.5 ± 95
N	61	53	59
Breast Milk Perchlorate (ug/L)	7.7 ± 7.5[b]	18.3 ± 17.7	95.6 ± 54.6
N	13	16	25

[a]Urinary perchlorate in units of ug/gram creatinine.

[b]The Antofagasta breast milk data reflect one less sample than reported by Tellez et al. due to an outlier in this group. The mean was recalculated by multiplying the original mean (81.6ug/L) by the original N (14), subtracting the outlier (1042 ug/L) and then dividing by the new N (13). Variability in this group was assumed to be on a par with that in Chanaral.

Table 2

Drinking Water Targets for Different Percentiles of the Perchlorate Exposure Distribution[a]

Percentile	Baseline Nursing Infant Exposure (ug/kg/d)	Drinking Water Target (ug/L) to Maintain Infant at RfD
0.5	0.028	over 24.5
1	0.034	over 24.5
2	0.042	over 24.5
5	0.058	over 24.5
10	0.076	over 24.5
25	0.122	12.4
50	0.206	6.9
75	0.347	3.8
90	0.562	1.3
95	0.744	---[b]

[a]Baseline distribution is that derived for the NHANES dataset. This is overlaid with the distribution of maternal exposure to perchlorate and transfer to nursing infant.

[b]There is no drinking water concentration that can satisfy this condition because the baseline exposure is already above the RfD for a nursing infant.

Table 3

Percentage of the IRIS RfD Taken Up by Non-Drinking Water Sources in 15-44 Year Old Women Sampled in NHANES 2001-2002[a]

	Urinary Output (ug/g creatinine)	Maternal Dose (ug/kg/d)[b]	% RfD[c]
NHANES 50th %	2.97	0.056	8
NHANES Average	4.0	0.75	11
NHANES 90th %	8.4	0.16	23
NHANES 95th %	12.1	0.23	32

[a]Urinary perchlorate data adapted from Blount et al. 2006c.
[b]Converted from perchlorate in urine based upon daily creatinine excretion of 1.165 g and adult female body weight of 62 kg
[c]IRIS RfD established in 2005 is 0.7 ug/kg/d.

Figure Legends

Figure 1. Lognormal Probability Plots of the Distributions of Urinary Perchlorate Excretion in 3 Chilean Cities and the United States

Figure 2. Comparison of Urinary Perchlorate (ug/g creatinine) between Atlanta Sample of 27 Adults vs National Sample of Women 15-44 Years Old

Figure 3. Mean Breast Milk Perchlorate Concentration in Relation to Mean Urine Perchlorate Excretion. Data adapted from Tellez et al. 2005; inverse invariance-weighted straight line constrained to pass through the origin.

Figure 4. Simulated Cumulative Distribution of Breast Milk Concentrations for Baseline and OSWER PRG Scenarios

Figure 5. Daily Doses from Nursing Infant Exposure to Perchlorate Under Baseline and (+) Drinking Water Scenarios

Figure 6. Breast Milk Perchlorate Simulated from NHANES Data vs Actual Data Reported by Kirk et al. 2005.

Figure 1

Lognormal Probability Plots of the Distributions of

Urinary Perchlorate Excretion in 3 Chilean Cities and the United States

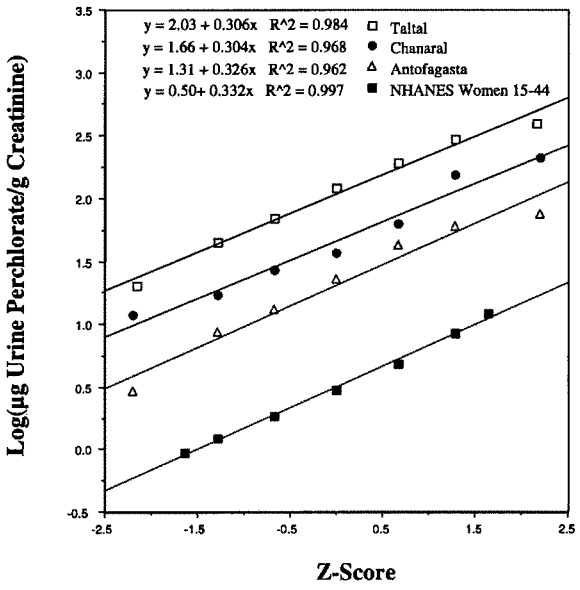


Figure 2

Comparison of Urinary Perchlorate (µg/g Creatinine) Between Atlanta Sample of 27 Adults vs National Sample of Women Age 15-44

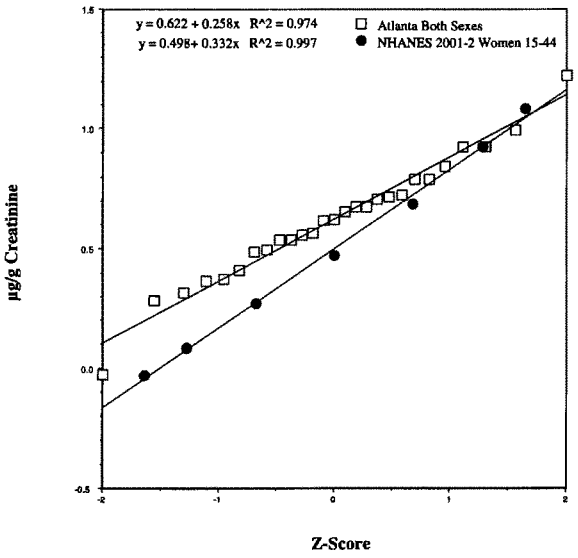
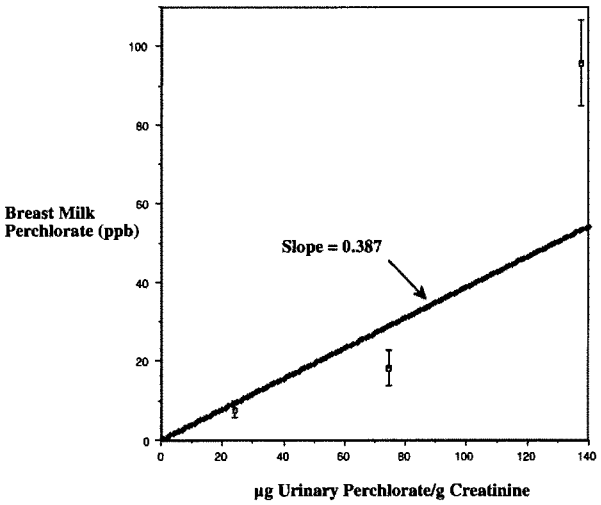


Figure 3

Mean Breast Milk Perchlorate Concentration in Relation to Mean Urine Perchlorate Excretion.



[1]Data of Tellez et al. 2005; inverse invariance -weighted straight line constrained to pass through the origin.

Figure 4
Simulated Cumulative Distribution of Breast Milk Concentrations for Baseline and OSWER PRG Scenarios

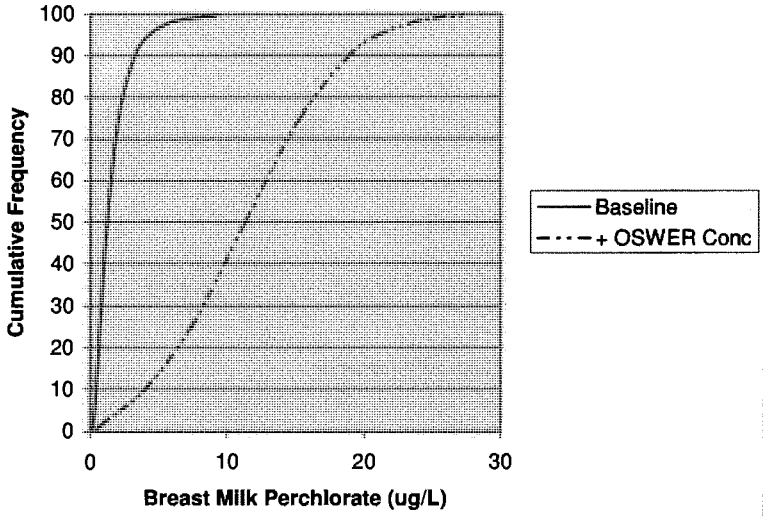


Figure 5
Daily Doses from Nursing Infant Exposure to Perchlorate Under Baseline and (+) Drinking Water Scenarios

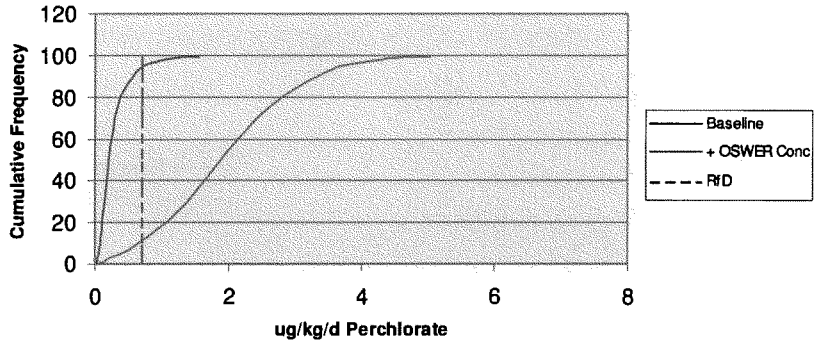
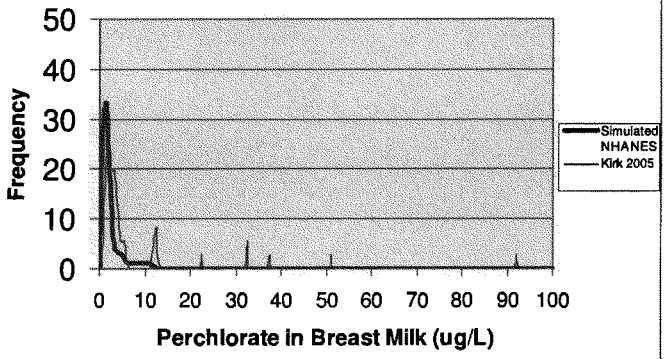


Figure 6
Breast Milk Perchlorate Simulated from NHANES Data vs Actual Data Reported by Kirk et al. 2005



THE NATION; How Environmentalists Lost the Battle Over TCE Series: First of two parts; [HOME EDITION]

Ralph Vartabedian. **Los Angeles Times.** Los Angeles, Calif.: Mar 29, 2006. pg. A.1

Abstract (Summary)
California EPA regulators consider TCE a known carcinogen and issued their own 1999 risk assessment that reached the same conclusion as federal EPA regulators: TCE was far more toxic than previous scientific studies indicated.

Rodents fed TCE develop liver and kidney cancer, and humans exposed to TCE show elevated rates of many types of cancer and birth defects. But industry experts fire back that evidence on TCE is still weak. Just because rats and mice get cancer from high levels of TCE doesn't prove that humans will get cancer from low levels of TCE, they say. And the epidemiological research is less convincing than animal studies, they say.

By 2004, the matter was out of the EPA's hands. The National Academy of Sciences received a $680,00 contract from the Energy Department to study TCE -- a decision dictated by a working group at the White House. The briefings to the national academy on how to evaluate TCE were given by White House staff as well as the EPA.

Full Text (3349 words)

CORRECTION: SEE CORRECTION APPENDED; Risks of solvent: Due to an editing error, an article in Wednesday's Section A about the regulation and dangers of the industrial solvent trichloroethylene, or TCE, quoted Alex A. Beehler, the Pentagon's top environmental official, as saying: "We are all forgetting the facts on the table. Meanwhile, we have done everything we can to curtail use of TCE." Beehler actually said, "We are all for getting the facts on the table."

After massive underground plumes of an industrial solvent were discovered in the nation's water supplies, the Environmental Protection Agency mounted a major effort in the 1990s to assess how dangerous the chemical was to human health.

Following four years of study, senior EPA scientists came to an alarming conclusion: The solvent, trichloroethylene, or TCE, was as much as 40 times more likely to cause cancer than the EPA had previously believed.

The preliminary report in 2001 laid the groundwork for tough new standards to limit public exposure to TCE. Instead of triggering any action, however, the assessment set off a high-stakes battle between the EPA and Defense Department, which had more than 1,000 military properties nationwide polluted with TCE.

By 2003, after a prolonged challenge orchestrated by the Pentagon, the EPA lost control of the issue and its TCE assessment was cast aside. As a result, any conclusion about whether millions of Americans were being contaminated by TCE was delayed indefinitely.

What happened with TCE is a stark illustration of a power shift that has badly damaged the EPA's ability to carry out one of its essential missions: assessing the health risks of toxic chemicals.

The agency's authority and its scientific stature have been eroded under a withering attack on its technical staff by the military and its contractors. Indeed, the Bush administration leadership at the EPA ultimately sided with the military.

After years on the defensive, the Pentagon -- with help from NASA and the Energy Department -- is taking a far tougher stand in challenging calls for environmental cleanups. It is using its formidable political leverage to demand greater proof that industrial substances cause cancer before ratcheting up costly cleanups at polluted bases.

The military says it is only striving to make smart decisions based on sound science and accuses the EPA of being unduly influenced by left-leaning scientists.

But critics say the defense establishment has manufactured unwarranted scientific doubt, used its powerful role in

the executive branch to cause delays and forced a reduction in the margins of protection that traditionally guard public health.

If the EPA's 2001 draft risk assessment was correct, then possibly thousands of the nation's birth defects and cancers every year are due in part to TCE exposure, according to several academic experts.

"It is a World Trade Center in slow motion," said Boston University epidemiologist David Ozonoff, a TCE expert. "You would never notice it."

Senior officials in the Defense Department say much remains unknown about TCE.

"We are all forgetting the facts on the table," said Alex A. Beehler, the Pentagon's top environmental official. "Meanwhile, we have done everything we can to curtail use of TCE."

But in the last four years, the Pentagon, with help from the Energy Department and NASA, derailed tough EPA action on such water contaminants as the rocket fuel ingredient perchlorate. In response, state regulators in California and elsewhere have moved to impose their own rules.

The stakes are even higher with TCE. Half a dozen state, federal and international agencies classify TCE as a probable carcinogen.

California EPA regulators consider TCE a known carcinogen and issued their own 1999 risk assessment that reached the same conclusion as federal EPA regulators: TCE was far more toxic than previous scientific studies indicated.

TCE is the most widespread water contaminant in the nation. Huge swaths of California, New York, Texas and Florida, among other states, lie over TCE plumes. The solvent has spread under much of the San Gabriel and San Fernando valleys, as well as the shuttered El Toro Marine Corps base in Orange County.

Developed by chemists in the late 19th century, TCE was widely used to degrease metal parts and then dumped into nearby disposal pits at industrial plants and military bases, where it seeped into aquifers.

The public is exposed to TCE in several ways, including drinking or showering in contaminated water and breathing air in homes where TCE vapors have intruded from the soil. Limiting such exposures, even at current federal regulatory levels, requires elaborate treatment facilities that cost billions of dollars annually. In addition, some cities, notably Los Angeles, have high ambient levels of TCE in the air.

An internal Air Force report issued in 2003 warned that the Pentagon alone has 1,400 sites contaminated with TCE.

Among those, at least 46 have involved large-scale contamination or significant exposure to humans at military bases, according to a list compiled by the Natural Resources New Service, an environmental group based in Washington.

The Air Force was convinced that the EPA would toughen its allowable limit of TCE in drinking water of 5 parts per billion by at least fivefold. The service was already spending $5 billion a year to clean up TCE at its bases and tougher standards would drive that up by another $1.5 billion, according to an Air Force document. Some outside experts said that estimate was probably low.

After the EPA issued the draft assessment, the Pentagon, Energy Department and NASA appealed their case directly to the White House. TCE has also contaminated 23 sites in the Energy Department's nuclear weapons complex -- including Lawrence Livermore National Laboratory in the Bay Area, and NASA centers, including the Jet Propulsion Laboratory in La Canada Flintridge.

The agencies argued that the EPA had produced junk science, its assumptions were badly flawed and that evidence exonerating TCE was ignored. They argued that the EPA could not be trusted to move ahead on its own and that top leaders in the agency did not have control of their own bureaucracy.

Bush administration appointees in the EPA -- notably research director Paul Gilman -- sided with the Pentagon and agreed to pull back the risk assessment. The matter was referred for a lengthy study by the National Academy of Sciences, which is due to issue a new report this summer. Any resolution of the cancer risk TCE poses will take years and any new regulation could take even longer.

The delay tactics have angered Republicans and Democrats who represent contaminated communities, where residents in some cases have elevated rates of cancer and birth defects but no direct proof that their illness is tied to TCE.

Half a dozen members of Congress last year wrote to the EPA, demanding that it issue interim standards for TCE, instead of waiting years while scientific battles are waged between competing federal agencies. EPA leaders have rejected those demands.

"The evidence on TCE is overwhelming," said Dr. Gina Solomon, an environmental medicine expert at UC San Francisco and a scientist at the Natural Resources Defense Council. "We have 80 epidemiological studies and hundreds of toxicology studies. They are fairly consistent in finding cancer risks that cover a range of tumors. It is hard to make all that human health risk go away."

But Raymond F. DuBois, former deputy undersecretary of Defense for installations and environment in the Bush administration, said the Pentagon had not been willing to accept whatever came out of the EPA, though it cared a great deal about base contamination.

"If you go down two or three levels in EPA, you have an awful lot of people that came onboard during the Clinton administration, to be perfectly blunt about it, and have a different approach than I do at Defense," DuBois said. "It doesn't mean I don't respect their opinions or judgments, but I have an obligation where our scientists question their scientists to bring it to the surface."

The military has virtually eliminated its use of TCE, purchasing only 11 gallons last year, said Beehler, an attorney who used to head environmental affairs for Koch Industries Inc., a large industrial conglomerate in Wichita, Kan.

In its fight against the 2001 risk assessment, the Pentagon has gone to the very fundamentals of cancer research: toxicology, the study of poisons; and epidemiology, the science of how diseases are distributed in the population. This scientific approach has worked better than past arguments that cleanups are a costly diversion from the Pentagon's mission to defend U.S. security.

A few months after the 2001 draft risk assessment came out, an Air Force rebuttal charged that the EPA had "misrepresented" data from animal and human health studies.

It said "there is no convincing evidence" that some groups of people, like children and diabetics, are more susceptible to TCE, a key part of the EPA's report. And it said the EPA had failed to consider viewpoints from "scientists who believe that TCE does not represent a human cancer risk at levels reasonably expected in the environment."

But comments such as these are outside the scientific mainstream. Other federal agencies have also expressed grave concern about TCE and some experts say it is only a matter of time before the chemical is universally recognized as a known carcinogen.

"Do I think TCE causes cancer? Yes," said Ozonoff, the Boston University TCE expert. "There is lots of evidence. Is there a dispute about it? Yes. Whenever the stakes are high, that's when there will be disputes about the science."

The 2001 risk assessment found TCE was two to 40 times more likely to cause cancer than was found in an assessment conducted in 1986, a wide range that reflected many scientific uncertainties. Because cancer risk assessments are not an exact science, federal regulators have historically exercised great caution in protecting public health.

The California EPA, the nation's largest and best-funded state environment agency, assessed TCE in 1999 and also found reason for concern. Its risk assessment fell in the middle of the EPA risk range, according to the study's author, Joseph Brown.

Rodents fed TCE develop liver and kidney cancer, and humans exposed to TCE show elevated rates of many types of cancer and birth defects. But industry experts fire back that evidence on TCE is still weak. Just because rats and mice get cancer from high levels of TCE doesn't prove that humans will get cancer from low levels of TCE, they say. And the epidemiological research is less convincing than animal studies, they say.

The U.S. still uses about 100 tons of TCE annually, a fraction of the consumption before the mid-1980s, when it was first classified as a probable carcinogen. It was once widely used in consumer products, such as correction fluid for typewriters and spot cleaners.

"If TCE is a human carcinogen, it isn't much of one," said Paul Dugard, a toxicologist at the Halogenated Solvents Industry Alliance Inc., which represents TCE manufacturers. "People exposed at low levels shouldn't be concerned.

"EPA's philosophy is still one of being super conservative and that is being pushed back against."

EPA officials were braced for such a controversy when the TCE assessment was issued and quickly convened a scientific advisory board to review the work. The board included public health officials at state agencies, academics and chemical industry scientists.

About one year later, the board issued its findings, praising the risk assessment and urging the EPA to implement it as quickly as possible. But the board also suggested some changes, including stronger support for its calculations of TCE's health risks and a clearer disclosure of its underlying assumptions.

The report, particularly the request for additional work, was interpreted as a serious problem by Gilman, the EPA research director.

He said the board's findings represented a "red flag" and "raised very troubling issues," all of which were key arguments by Gilman and others for stopping the assessment.

But members of the scientific advisory team dispute Gilman's interpretation, saying they felt the 2001 risk assessment was good science and their recommended changes amounted to normal commentary for such a complex matter.

"I thought by and large we supported the EPA and that its risk assessment could be modified to move forward," said Dr. Henry Anderson, the chairman of the scientific advisory board and a physician with the Wisconsin Division of Public Health. "That movement to shuttle the issue to the National Academy of Sciences was nothing like what we had in mind."

By 2004, the matter was out of the EPA's hands. The National Academy of Sciences received a $680,00 contract from the Energy Department to study TCE -- a decision dictated by a working group at the White House. The briefings to the national academy on how to evaluate TCE were given by White House staff as well as the EPA.

The White House originally formed the working group -- made up of officials from the Pentagon, Energy Department and NASA -- in 2002 to combat the EPA's assessment of another pollutant, perchlorate. That group stayed in business to fight the TCE risk assessment. The group was co-chaired by officials in the Office of Management and Budget and the White House Office of Science and Technology Policy. The officials declined requests for interviews.

Given the controversy and stakes involved, the issue was bound to end up with National Academy of Sciences, said Peter Preuss, director of the National Center for Environmental Analysis, the EPA organization that produced the 2001 risk assessment. "It got very difficult to proceed," Preuss said.

The lead author of the 2001 health risk assessment, V. James Cogliano, agreed that the findings ran into trouble when Defense Department officials went to the White House. "Most of it was behind the scenes," said Cogliano, now a senior official at the International Agency for Research on Cancer in Lyon, France.

He added: "The degree of opposition was not surprising given the degree of economic interests involved."

The political maneuvering marked a significant change, Cogliano said. In the 1980s, Defense Department officials accepted every possible safeguard recommended by the EPA for incinerators to burn nerve gas and other chemical weapons, he recalled.

At that time, Defense Department officials said, "You put in every margin of safety, because we want to be sure it will be safe," he said. "There was no argument. There is a different spirit today."

Every health risk assessment is also getting more technically complex and more bureaucratically difficult, Preuss said.

When the EPA issued its first health risk assessment in 1976, it ran four pages and it was based in large part on studies that counted "bumps and lumps" on animals subjected to possible carcinogens. By contrast, EPA scientists now must show not only that a substance causes tumors, but the internal biological processes that are responsible. And the work is subject to greater scrutiny.

"It is true that there is more interagency review now of our work," Preuss said. "We have a couple steps where we send our assessments to the White House and they distribute them to other agencies. Each year, additional steps are taken."

All of the EPA's travails -- the toughened scientific demands, the loss of authority, the interagency battles -- have clearly taken a heavy toll and diminished the agency's stature.

"Inside the Beltway, it is an accepted fact that the science of EPA is not good," said Gilman, now director of the Oak

Ridge Center for Advanced Studies in Tennessee, which conducts broad research on energy, the environment and other areas of science. Gilman said an entire consulting industry has sprung up in Washington to attack the EPA and sow seeds of doubt about its capabilities.

The delays in assessing TCE have also left many contaminated communities with few answers.

"My constituents who live at a recently named Superfund site ... are forced to live everyday with contaminated groundwater, soil and air and can't afford to wait the years it would take for the results of your outsourced re-review," Rep. Sue W. Kelly (R-N.Y.) told EPA officials at a hearing last year.

"I have talked to a lot of sick people," said Rep. Maurice D. Hinchey (D-N.Y.), whose district includes hundreds of homes contaminated by TCE vapors, traced to an IBM Corp. factory. IBM has paid for air filtration systems for 400 homes, but has balked at more funding based on uncertainty over the health risk. "These people are deeply frustrated and increasingly angry," Hinchey said.

Meanwhile, many environmentalists are discouraged by what they view as a virtual emasculation of the EPA in this battle.

"The general public has no idea this is happening," said Erik Olson, a lawyer at the Natural Resources Defense Council. "The Defense Department has succeeded in undermining the basic scientific process at EPA. The DoD is the biggest polluter in the United States and they have made major investments to undercut the EPA."

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(BEGIN TEXT OF INFOBOX)

The military and TCE

About 1,400 Defense Department sites across the nation are contaminated with trichloroethylene, or TCE, including military bases and depots. The map shows sites that have some of the heaviest contamination or were studied for possibly causing health hazards. A sampling of problems nationwide:

Contaminated sites

McClellan Air Force Base, Sacramento:

The Pentagon is cleaning up 12 different TCE plumes affecting about 25% of the former base's property. About a half dozen public water wells have been shut and the cleanup is expected to continue for decades.

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F.E. Warren Air Force Base, Cheyenne, Wyo.:

TCE was discovered at 13 decommissioned Atlas missile silos in Wyoming, Colorado and Nebraska. Contamination at some of the sites reached 3,500 parts per billion. TCE polluted an aquifer that Cheyenne, Wyo., planned to use as a municipal water source.

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Twin Cities Army Ammunition Plant, Arden Hills, Minn.:

A TCE plume covered 25 square miles and spread to private residential wells. The water supply for a nearby trailer park contained 720 parts per billion TCE. The site is now undergoing a cleanup under Superfund program supervision.

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Stratford Army Engine Plant, Stratford, Conn.:

Elevated TCE vapors were discovered in several buildings the Army planned to lease to private concerns. Federal health authorities judged the vapors too high for general public exposure. A cleanup is underway.

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El Toro Marine Corps Air Station, Irvine, Calif.:

TCE contaminated the groundwater under the base, now closed, which long ago complicated plans to reuse the property for private housing and a public park. The government will retain about 900 contaminated acres to continue cleanup for the indefinite future.

•

Kelly Air Force Base, San Antonio:

TCE use at the shuttered aircraft repair depot contaminated a shallow aquifer that has migrated about 4 miles off the base, through a low-income neighborhood. Health authorities have found elevated rates of cancer and birth defects in the neighborhood.

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Anniston Army Depot, Anniston, Ala.:

Extremely high concentrations of TCE, up to 200,000 parts per billion, were found by government investigators in groundwater under the depot, which included a number of dumps, a plating plant and other industrial activities. TCE levels above allowable drinking water standards have been found at springs and wells on the base.

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Camp Lejeune, N.C.:

Tens of thousands of Marine families were exposed to TCE in the base's drinking water supply. A preliminary study has found elevated rates of leukemia among children conceived at the base. The TCE was discovered in 1980 but not disclosed until 1985.

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Sources: Agency for Toxic Substances and Disease Registry, U.S. Environmental Protection Agency, Natural Resources News Service, Associated Press, California Department of Toxic Substances Control. Graphics reporting by Tom Reinken, Ralph Vartabedian

[Reference]
Message No: 17431

[Illustration]
Caption: GRAPHIC: MAP: The military and TCE; CREDIT: Los Angeles Times; PHOTO: AGENCIES AT ODDS: Environmental lawyer Erik Olson says the Pentagon has undercut how the EPA functions.; PHOTOGRAPHER: Karen Ballard For The Times; PHOTO: PUSHING BACK: Raymond DuBois, a former Defense Department official, said the Pentagon cares about cleaning up pollution but isn't willing to simply accept whatever comes out of the Environmental Protection Agency on base contamination.; PHOTOGRAPHER: Karen Ballard For The Times

Credit: Times Staff Writer

Indexing (document details)

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The Washington Post

Dangers of Rocket Fuel Chemical Downplayed; [FINAL Edition]

Rob Stein. **The Washington Post.** Washington, D.C.: Jan 11, 2005. pg. A.03

Abstract (Summary)
At high doses, perchlorate can interfere with the thyroid gland, which helps regulate many bodily functions. Animal studies have suggested it could cause thyroid tumors. In children, the thyroid plays a major role in development, raising fears that exposure to perchlorate by pregnant women and young children could cause brain damage.

The committee said it concluded that perchlorate was much less likely to cause thyroid tumors in humans than the EPA had determined because humans are much less susceptible to disruption of thyroid functions and formation of thyroid tumors than are rats, the subjects of earlier studies.

The committee based its conclusions largely on a 2002 study in which healthy men and women were given daily doses of perchlorate for two weeks without experiencing any signs of significant thyroid dysfunction -- a finding supported by four other studies of healthy subjects, the committee said. To set a safe threshold, the committee recommended using an "uncertainty factor" of 10 and permitting only one-tenth of the highest doses used in that study.

Full Text (842 words)

A chemical from rocket fuel that has seeped into drinking-water supplies nationwide is safe at higher doses than federal environmental officials hed concluded, according to a report released yesterday.

The chemical, perchlorate, can be ingested safely at doses more than 20 times those deemed safe by the Environmental Protection Agency, an expert panel convened by the National Academy of Sciences concluded.

The conclusion was praised by defense contractors facing potentially billions of dollars in cleanup costs but denounced by environmental activists, who accused the Defense Department, defense industry and White House of exerting undue influence on the panel.

The assessment is considered crucial for the EPA, which is establishing the first national standards for the pollutant, and for dozens of states that have been setting their own standards for cleaning up military and industrial sites to try to safeguard drinking water.

"[This] should protect even the most sensitive populations," said Richard B. Johnston Jr. of the University of Colorado School of Medicine in Denver, who chaired the panel.

Perchlorate is used in a variety of industrial processes, but contamination in the United States comes primarily from rocket fuel. Concern has been rising about its safety in recent years as the substance was detected in soil and drinking water around the country.

Perchlorate has been found in at least 35 states, and more than 11 million people have significant levels in their drinking water. The Food and Drug Administration also recently found the substance in milk and lettuce.

At high doses, perchlorate can interfere with the thyroid gland, which helps regulate many bodily functions. Animal studies have suggested it could cause thyroid tumors. In children, the thyroid plays a major role in development, raising fears that exposure to perchlorate by pregnant women and young children could cause brain damage.

The health concerns prompted the EPA to begin drafting the first national standard for safe levels, and in 2002 the agency concluded in a draft assessment that perchlorate levels in drinking water should be no higher than 1 part per billion. That prompted protests from the Defense Department and defense contractors, which face potentially billions of dollars in cleanup costs.

They maintained that the substance posed no danger even at levels several hundred times as high.

In an attempt to resolve the dispute, the federal government asked the National Research Council, an arm of the National Academy of Sciences, to convene an expert panel to examine the issue.

After spending months reviewing all available scientific evidence, the 15-member panel concluded that humans could safely ingest levels as high as 0.0007 milligrams per kilogram of body weight, which is more then 20 times the dose of 0.00003 milligrams per kilogram that the EPA had recommended. The committee did not translate that into parts per billion of drinking water.

The committee said it concluded that perchlorate was much less likely to cause thyroid tumors in humans than the EPA had determined because humans are much less susceptible to disruption of thyroid functions and formation of thyroid tumors than are rats, the subjects of earlier studies.

"The committee concludes that the development of thyroid tumors, as an ultimate result of perchlorate-caused inhibition of thyroid iodide uptake, is unlikely in humans," the report said.

The committee based its conclusions largely on a 2002 study in which healthy men and women were given daily doses of perchlorate for two weeks without experiencing any signs of significant thyroid dysfunction -- a finding supported by four other studies of healthy subjects, the committee said. To set a safe threshold, the committee recommended using an "uncertainty factor" of 10 and permitting only one-tenth of the highest doses used in that study.

But environmental activists denounced the findings and released documents that they said showed the committee had been subject to unprecedented pressure by the White House and Defense Department.

"The Defense Department's job is to protect Americans, not threaten our health, but these documents show that it is conspiring with its contractors and the White House to twist the science and avoid cleaning up a chemical that threatens our children's health," said Erik D. Olson of the Natural Resources Defense Council. "We've never seen such a brazen campaign to pressure the National Academy of Sciences to downplay the hazards of a chemical."

The Pentagon referred questions to the White House, which, along with an academy official, dismissed the accusations.

"The academy has an outstanding reputation for objectivity, which is why the administration sought their analysis," said Deputy White House Press Secretary Trent Duffy. "This administration always says decisions should be made on sound science, and they're the experts," he said of the National Academy of Sciences.

The EPA will incorporate the panel's findings in its deliberations as it formulates a national standard, a White House official said.

The nation's largest defense contractor praised the report.

"Lockheed Martin believes the . . . review process is highly credible and we feel the [academy] is in a position to make the best recommendation based on the available science," the company said in a statement.

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THE WALL STREET JOURNAL.

Ground War: Inside Pentagon's Fight to Limit Regulation of Military Pollutant; Rocket Fuel Got Into Water The Issue: At What Level Does It Pose Health Risk; The Meaning of a Rat Study

Peter Waldman. Wall Street Journal. (Eastern edition). New York, N.Y.: Dec 29, 2005. pg. A.1

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Abstract (Document Summary)

Chemicals don't necessarily affect rats and humans the same way. Still, the test results would be considered "adverse effects" under EPA policy, the agency's team leader, Ann Jarabek, warned the defense interests. She told them the results would tend to reduce the level of perchlorate exposure the EPA ultimately would deem safe.

Perchlorate users and the Pentagon said the chemical was safe in drinking water at 200 times the safe limit the EPA wanted, that is, at up to 200 parts per billion. The Pentagon's Mr. [Raymond DuBois] appealed in early 2003 to the White House Office of Management and Budget, which referees inter-agency disputes. Given the strict limit the EPA was pushing, he says, "I said, 'Time out!' "

Several senior EPA staffers believe the agency would be better off with no perchlorate cleanup policy than with this one, emails reviewed by The Wall Street Journal show. "We got a very ugly set of comments from Office of Management and Budget last week that eviscerated the guidance" to be given to cleanup officials in the field, one senior EPA staffer emailed a colleague this fall. "Doing nothing was better than accommodating those comments." EPA spokeswoman Eryn Witcher said the policy is still undergoing internal deliberation.

Full Text (2363 words)

Four years ago, while U.S. troops were toppling the Taliban in Afghanistan, the Environmental Protection Agency lobbed a different sort of bombshell at the Defense Department. EPA scientists recommended strictly regulating a chemical that is a key component of munitions, but that has seeped into drinking-water supplies.

The EPA said it had determined that the chemical, called perchlorate, endangers babies' brain development when present even at trace levels. As a prelude to possible formal regulation, it proposed declaring that a safe level of the chemical in drinking water would be just one part per billion. That's an amount so minute it wouldn't even have been detectable a few years ago.

Pentagon officials were aghast. Defense suppliers had discharged massive quantities of the chemical into soil and streams during the Cold War, and they still need it for weaponry. Such a strict limit could mean the Pentagon and defense contractors would have to clean up scores of water sources in 35 states and even the mighty Colorado River, with its water flow of 67,000 gallons a second at the Hoover Dam.

Fearing both costs and possible curbs on arms production, the Pentagon took its case to the White House, which told the EPA to stand down while an outside scientific panel looked at the issues. The panel then issued a middle-ground report that has left some senior EPA scientists deeply unhappy and the Pentagon still pressing for the minimum possible cleanup.

The standoff, involving two high-profile federal agencies, shows how the burgeoning science of low-dose chemical exposure is raising both the stakes and the stratagems in today's pollution fights. There's no question perchlorate interferes with the body's ability to make thyroid hormone, a substance that everyone needs but babies especially so. The question is how much exposure it takes to do harm. The controversy has intensified with science's growing ability to detect and test chemicals at extraordinarily low exposure levels.

The appeal to the White House was just one of the several moves by defense interests in a long struggle with the EPA over whether and how to regulate perchlorate. Among other tactics: Perchlorate users financed a study of the chemical's health effects -- then undermined their own study when results went against them.

Perchlorate, used chiefly in solid rocket fuel, first polluted groundwater decades ago at a munitions plant outside Sacramento, Calif., triggering years of resistance by the plant's operator to state regulatory efforts. Then in 1997, after technical breakthroughs allowed detection of the chemical at far lower levels than before, it began to be found in water supplies in Southern California.

EPA scientists traced one plume up the Colorado River aqueduct to Las Vegas. There they found the source in an old plant that once manufactured the missile propellant. The soil beneath was tainted and the chemical was seeping into the river.

In the human body, perchlorate blocks the thyroid gland from absorbing iodide, which the gland needs to make thyroid hormone. The Pentagon and defense industry say such interference isn't dangerous, at least so long as it's only partial, because most adults produce plenty of the hormone.

The EPA, however, focused on fetuses and infants. They need thyroid hormone every day, because it is critical during brain development. And unlike adults, they can't store a supply. Because risk levels weren't well understood, the EPA and the Pentagon agreed in the late 1990s to cooperate to find answers. Several defense contractors, linked in what was called the Perchlorate Study Group, agreed to pay for new research.

The centerpiece was a $3 million experiment involving 3,000 mother, infant and fetal rats. Pregnant rats and pups were fed varying levels of perchlorate for several months. Scientists then dissected the rats' thyroid glands and brains. Researchers started with the rats that got the largest dose of perchlorate, intending to work downward until they found a dose so small that it had no effect.

They never found such a dose. Even at the lowest dose tested -- 0.01 milligrams per kilogram of rat weight per day -- the scientists saw a pattern of altered growth in several regions of the baby rats' brains. They also saw effects on their thyroid cells and hormone output.

Chemicals don't necessarily affect rats and humans the same way. Still, the test results would be considered "adverse effects" under EPA policy, the agency's team leader, Ann Jarabek, warned the defense interests. She told them the results would tend to reduce the level of perchlorate exposure the EPA ultimately would deem safe.

Sponsors of the study then did something unusual. Instead of submitting the final results of the study to the EPA, the defense companies that paid for the study commissioned a critique of their own research. They hired a consulting firm, which asked five academic scientists to study the study.

A few months later, in May 2001, the defense contractors delivered to the EPA a 200-page critique of their own study. It found fault with the study's design, with the handling of rat pups, with what the pups were fed and with the way rat brains were sliced and preserved. Conclusion: They said the multimillion-dollar study they financed was highly flawed.

The agency's chief of neurotoxicology, William Boyes, says he had never seen sponsors of a study attack their own work. "Usually," he says, they either "stand behind their data or they go back and do another study."

Also puzzling: The head of the consulting firm the defense industry hired to critique the original study had been that study's science adviser.

This consultant is Michael Dourson, who leads a nonprofit science consulting firm called Toxicology Excellence for Risk Assessment, or TERA. Dr. Dourson says the critique wasn't an attempt to discredit the rat study, but simply to explain its "biological significance."

The laboratory that had done the rat study says it stood ready to do it over if necessary to correct any flaws identified. But the defense industry didn't ask the lab, Argus Research Laboratories in Horsham, Pa., to do it over. Asked why not, an executive of one major user of perchlorate, the Aerojet missile unit of GenCorp Inc., said it was because EPA guidelines regarded animal studies as inferior to human ones anyway. So, he said, the industry had by this time decided to focus on human research.

In early 2002, the EPA, equipped with the rat study's final results and also the critique of it, issued a draft risk assessment for perchlorate, proposing a safe limit for the chemical in drinking-water supplies. This would constitute the first step toward possible regulation, which can occur only after further study, including a cost-benefit analysis. The EPA's proposed safe limit was quite strict: a mere one part per billion.

Pentagon officials felt sandbagged. The defense industry paid for the rat study in the expectation that they would hear privately from the EPA about any problems it presented. Instead, they learned at the same time as the public of the strict safe limit the EPA now wanted.

"All of a sudden, up on the screen popped this one parts per billion standard -- where did that come from?" says Raymond DuBois, a former deputy U.S. undersecretary of defense who's now acting under secretary of the army. This limit, he says, "had no consistent scientific confirmation."

EPA officials, asked why they didn't warn the industry the strict proposal was impending, said that while they cooperate with industry on research, the job of setting safe exposure levels is theirs alone.

"Perchlorate is now among the better understood compounds," says Paul Gilman, the EPA's former chief scientist. "At some point, the agency had to step inside itself as a regulatory body and determine the weight of the evidence."

The furor the EPA had stirred was soon evident at a gathering known as a peer-review workshop, where a panel of scientists discussed the proposal. The workshop took place in early 2002 in Sacramento, near the site of decades of groundwater perchlorate pollution from an Aerojet missile factory.

The session was tumultuous, featuring environmentalists, regulators, consultants and lobbyists. Among the speakers was La Donna White, president of an African-American doctors' group, who said the EPA proposal would divert funds from "real health issues" affecting blacks and "scare the public." She later repeated her points in an op-ed essay in a local newspaper -- and in a news release put out by a lobbying group for perchlorate users, the Council on Water Quality.

Dr. White, a family physician, says she had learned about the issues from a guest at one of her medical-society meetings, Eric Newman. He is a lobbyist for a Sacramento firm that has lobbied on perchlorate matters for defense contractors. Dr. White says she didn't know he was a lobbyist when he asked her to speak to the EPA. She didn't reply to an email asking whether anyone had helped her draft her perchlorate commentaries -- two of which misspelled her first name. Mr. Newman didn't return messages left for him.

Perchlorate users and the Pentagon said the chemical was safe in drinking water at 200 times the safe limit the EPA wanted, that is, at up to 200 parts per billion. The Pentagon's Mr. DuBois appealed in early 2003 to the White House Office of Management and Budget, which referees inter-agency disputes. Given the strict limit the EPA was pushing, he says, "I said, 'Time out!' "

The White House told the EPA to halt further action on the chemical, and arranged for the EPA and three other agencies to sponsor further review by the National Research Council, a federally funded group that vets issues for the government and others. The council, in turn, named a panel of scientists, who did a wide-ranging assessment that included public hearings in 2003 and 2004.

At the hearings, the EPA came in for harsh criticism from perchlorate users and consultants working for them. An Air Force colonel, Daniel Rogers, termed the EPA's work "biased, unrealistic and scientifically imbalanced." Col. Rogers also said perchlorate is critical to U.S. security because while highly explosive, it is stable during handling and storage. Besides missiles, it is used in various battlefield weapons and flares and in munitions for training.

In January 2005, the National Research Council panel announced its conclusions. It called the rat research inconclusive and said perchlorate's key effect of blocking iodide from entering the thyroid gland, and thereby interfering with production of thyroid hormone, was not in itself dangerous. Still, it said, exposure to perchlorate should be restricted because of the high stakes for babies.

The panel recommended a maximum safe exposure level of 0.0007 milligrams per kilogram of body weight per day, based on a small study of human volunteers. For an adult drinking a normal amount of water, that would permit about 24 parts per billion of perchlorate in drinking water -- assuming people ingested no perchlorate from any source except water.

In fact, however, the EPA's working assumption in such cases is that drinking water accounts for only 20% of people's exposure to a waterborne contaminant. Recent studies indicate that small amounts of the chemical are in a wide variety of fruits and vegetables, possibly from irrigation water, as well as in some dairy products and breast milk.

Some EPA staffers assumed their agency would reduce the safe level in drinking water well below 24 ppb to adjust for several factors, including exposure through food. Instead, the EPA quickly adopted the panel's assessment as its own, eschewing the internal and external peer reviews that normally precede a formal EPA listing of a safe level for a chemical.

An EPA spokeswomen said no additional reviews were needed before adopting the 24 ppb safe limit because of extensive internal and external scrutiny of the chemical done several years ago. She also said it was natural to use the National Research Council's conclusion as the EPA's own because the EPA was among those who sponsored the review.

Some state agencies criticized both the National Research Council assessment and the EPA for quickly adopting it. Massachusetts complained to the EPA that the research-council panel had based its analysis on a study of just seven adults, rather than on babies. Massachusetts reaffirmed its own health advisory that is as strict as the safe limit the EPA envisioned in 2002: one part per billion in water. Meanwhile, two regulators from Connecticut and Maine wrote a science-journal commentary accusing the EPA of superseding its own scientific judgment with a flawed review by an outside body.

Today, Pentagon and White House officials are drafting new guidance for toxic-site cleanup officials. Intended to go out under the EPA's name, the guidance under consideration would effectively fix the cleanup standard for federal pollution sites at 24 ppb. The result is that many water bodies with less perchlorate than that would escape cleanup.

Several senior EPA staffers believe the agency would be better off with no perchlorate cleanup policy than with this one, emails reviewed by The Wall Street Journal show. "We got a very ugly set of comments from Office of Management and Budget last week that eviscerated the guidance" to be given to cleanup officials in the field, one senior EPA staffer emailed a colleague this fall. "Doing nothing was better than accommodating those comments." EPA spokeswoman Eryn Witcher said the policy is still undergoing internal deliberation.

All the skirmishing thus far still doesn't determine whether the federal government ever will actually regulate perchlorate with a mandatory water standard. To help decide that, the EPA plans to test drinking-water supplies nationwide over the next several years. It is also monitoring blood and urine screenings and tests of food, to measure Americans' exposure from sources other than drinking water.

The arms industry thinks even the safe limit of 24 parts per billion is far too strict. It notes that the National Research Council said the effect on the thyroid wasn't itself adverse to health, but merely could possibly lead to ill effects, in a chain of events. Says Dr. Dourson, the defense-industry consultant: "The committee chose a precursor to a precursor to an adverse effect in the development of its safe dose."

THE WALL STREET JOURNAL.

Leading the News: EPA Bans Staff From Discussing Issue of Perchlorate Pollution

By Peter Waldman. Wall Street Journal. (Eastern edition). New York, N.Y.: Apr 28, 2003. pg. A.3

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Abstract (Document Summary)

Perchlorate pollution in drinking water has become a major concern in some 20 states across the country, after an EPA recommendation last year that found perchlorate in drinking water poses dangers to human health, particularly to infant development, in concentrations above one part per billion. The Pentagon and several defense contractors, who face billions of dollars in potential cleanup liability for perchlorate pollution, vehemently oppose that EPA health-risk assessment, arguing perchlorate is safe in drinking water at levels 70 to 200 times higher than what the EPA says is safe. In January, U.S. Sen. James Inhofe, (R., Okla.) chairman of the Senate's Environment and Public Works Committee, weighed in on the industry's side with a long list of questions and criticisms of the EPA's report. The White House recently proposed a bill in Congress, in the name of military "readiness," that would effectively exempt the Pentagon and defense industry from much of their potential liability for perchlorate cleanup.

Using private funding, the environmental group paid Texas Tech University, of Lubbock, Texas, to test 22 lettuce samples purchased in January and February in the San Francisco Bay Area. It chose the two winter months because nearly 90% of the nation's winter lettuce supply is grown in the desert in Southern California and Arizona with perchlorate-tainted irrigation water from the Colorado River. The results: Four of the 22 samples tested were found to contain perchlorate in excess of 30 parts per billion, with the highest -- "mixed organic baby greens" -- registering 121 ppb. After a flurry of mathematical extrapolations, the group concluded that 1.6 million U.S. women of childbearing age -- the population of greatest concern -- are exposed daily to more perchlorate than the EPA's recommended safe dose from winter lettuce alone.

Full Text (1033 words)

The Bush administration has imposed a gag order on the U.S. Environmental Protection Agency from publicly discussing perchlorate pollution, even as two new studies reveal high levels of the rocket-fuel component may be contaminating the nation's lettuce supply.

The lettuce studies, one published today by a nonprofit environmental group and one in final preparation by an EPA laboratory in Athens, Ga., address a crucial question in the current process of developing a federal drinking-water standard for perchlorate: whether Americans are ingesting the chemical from food sources in addition to drinking water. The answer, according to both studies, strongly suggests they are, which means that any eventual drinking-water standard will have to be that much stricter to account for the other sources of perchlorate exposure.

Perchlorate pollution in drinking water has become a major concern in some 20 states across the country, after an EPA recommendation last year that found perchlorate in drinking water poses dangers to human health, particularly to infant development, in concentrations above one part per billion. The Pentagon and several defense contractors, who face billions of dollars in potential cleanup liability for perchlorate pollution, vehemently oppose that EPA health-risk assessment, arguing perchlorate is safe in drinking water at levels 70 to 200 times higher than what the EPA says is safe. In January, U.S. Sen. James Inhofe, (R., Okla.) chairman of the Senate's Environment and Public Works Committee, weighed in on the industry's side with a long list of questions and criticisms of the EPA's report. The White House recently proposed a bill in Congress, in the name of military "readiness," that would effectively exempt the Pentagon and defense industry from much of their potential liability for perchlorate cleanup.

In another step, the White House Office of Management and Budget intervened last month to delay further regulatory action on perchlorate, by referring the health debate to the National Academy of Sciences for review, according to people familiar with the matter. Pending that study, which could take an additional six to 18 months, the EPA ordered its scientists and regulators not to speak about perchlorate, said Suzanne Ackerman, an EPA spokeswoman.

The gag order prevented EPA scientists from commenting or elaborating Friday on the two lettuce studies, which show lettuce, available in U.S. supermarkets, appears to absorb and concentrate perchlorate from polluted irrigation water in significant amounts. Other scientists familiar with the studies said both are limited in scope and are only suggestive, not conclusive, on the question of whether Americans are consuming perchlorate in food.

According to these scientists, definitive data on the perchlorate content in U.S. produce -- specified as a top EPA and Pentagon research priority in the late 1990s -- were supposed to have been available at least two years ago. But in 2000, after much time and effort had gone into designing a perchlorate study plan with the U.S. Department of Agriculture's Pesticide Data Program, the Defense Department refused to fund the roughly $215,000 needed to collect vegetables for sampling, said Comell Long, who heads perchlorate research on food sources for the Air Force.

"In a perfect world, wa would have thet farm gate data now" on vegetable content, Mr. Long said. "Everybody thought it was a good idea."

Mr. Long attributed the Pentagon's decision not to fund the study to bureaucratic issues involving budget cycles. Some environmentalists, however, say the Defense Department simply didn't want to know if perchlorate was in the U.S. food supply because of liability concems.

"If they can spend $1 million on a cruise missile, it seems kind of ridiculous they won't spend $200,000 to see if our food is contaminated with rocket fuel," said Renee Sharp, a staff scientist with Environmental Working Group in Oakland, Calif., which initiated its own lettuce study instead.

Using private funding, the environmental group paid Texas Tech University, of Lubbock, Texas, to test 22 lettuce samples purchased in January and February in the San Francisco Bay Area. It chose the two winter months because nearly 90% of the nation's winter lettuce supply is grown in the desert in Southern California and Arizona with perchlorate-tainted irrigation water from the Colorado River. The results: Four of the 22 samples tested were found to contain perchlorate in excess of 30 parts per billion, with the highest -- "mixed organic baby greens" -- registering 121 ppb. After a flurry of mathematical extrapolations, the group concluded that 1.6 million U.S. women of childbearing age -- the population of greatest concern -- are exposed daily to more perchlorate than the EPA's recommended safe dose from winter lettuce alone.

"We don't claim this study is conclusive," said Ms. Sharp, its primary author. "We're saying, 'Isn't it scary we only took 22 samples and found so much perchlorate in four of them?'"

The EPA's own study, which was completed and peer-reviewed several weeks ago but has yet to be publicly released pending final adjustments, showed that lettuce grown in a greenhouse with perchlorate-contaminated water absorbs and concentrates the chemical at varying rates depending on leaf location. The study, reviewed by The Wall Street Journal, found the outer leaves of the lettuce, which the study's authors wrote are usually not eaten, concentrated perchlorate by a factor of 17 to 28, meaning the outer leaves contained 17 to 28 times more perchlorate in them than did the water used to irrigate the plants. The concentration factor for the "emerging head" -- the part people usuelly eet -- was three to nine, tha study found.

Hence, if those results are found to be applicable to winter lettuce grown with Colorado River water, which contains between three and 10 parts per billion of perchlorate, the perchlorate concentration in the edible leaves could range as high es 90 ppb -- fairly close to the 72 ppb everage perchlorate level that the Environmental Working Group

found in its supermarket survey. The group says that level, for lettuce consumers, is four times the EPA's recommended daily dose for perchlorate.

"The studies have indicated we have reason for concern," says Allen Jennings, director of the USDA's office of pesticide management policy in Washington. "That's why it's critical to get as many foods as possible from the real world to find out."

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US Food and Drug Administration's Total Diet Study: Dietary intake of perchlorate and iodine

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The US Food and Drug Administration (FDA) has conducted the Total Diet Study (TDS) since 1961, which designed to monitor the US food supply for chemical contaminants, nutritional elements, and toxic elements. Recently, perchlorate was analyzed in TDS samples. Perchlorate is used as an oxidizing agent in rocket propellant, is found in other items (e.g., explosives, road flares, fireworks, and car airbags), occurs naturally in some fertilizers, and may be generated under certain climatic conditions. It has been detected in surface and groundwater and in food. Perchlorate at high (e.g., pharmacological) doses can interfere with iodide uptake into the thyroid gland, disrupting its function. The National Academy of Sciences (NAS) has identified that "the fetuses of pregnant women who might have hypothyroidism or iodide deficiency as the most sensitive population." This study reports on intake estimates of perchlorate and iodine, a precursor to iodide, using the analytical results from the TDS. Estimated average perchlorate and iodine daily intakes as well as the contribution of specific food groups to total intakes were estimated for 14 age/sex subgroups of the US population. The estimated smallest lower bound to the largest upper bound average perchlorate intakes by the 14 age/sex groups range from 0.08 to 0.39 micrograms per kilogram body weight per day (μg/kg bw/day), compared with the US Environmental Protection Agency (EPA) reference dose (RfD) of 0.7 μg/kg bw/day. Infants and children demonstrated the highest estimated intakes of perchlorate on a body weight basis. The estimated average iodine intakes by the 14 age/sex groups reveal a lower bound (ND = 0) and upper bound (ND = LOD) range of average intakes from 138 to 353 μg/person/day. Estimated iodine intakes by infants 6–11 months exceed their adequate intake (AI), and intakes by children and adult age/sex groups exceed their relevant estimated average requirement (EAR).
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Keywords: *Total Diet Study, dietary intakes, nutritional element, iodine, perchlorate, monitoring.*

Introduction

For the last 46 years, the Total Diet Study (TDS) has been an important monitoring program that provides the US Food and Drug Administration (FDA) with baseline information on the levels of pesticide residues, chemical contaminants, radionuclides, nutrient elements, and toxic elements in the US food supply. The study involves retail purchases of foods representative of the "total diet" of the average US population, which includes baby food, beverages including bottled water, dairy, eggs, fat, oil, fruits, grains, legumes, mixtures, meat, poultry, fish, sweets, and vegetables. The study also includes the analysis of the foods for levels of specific analytes and estimation of dietary intake of those analytes by selected age/sex groups.

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FDA began the TDS mainly in response to public health concerns regarding the levels of radioactive contamination in foods from atmospheric nuclear testing. Initially, the study estimated dietary intakes of two radionuclides (strontium-90 and cesium-137), several organochlorine and organophosphate pesticides, and selected nutrients by 16- to 19-year old male subjects (Pennington and Gunderson, 1987). Since 1961, the TDS has undergone many changes and refinements — expansion of the sample collection sites and the number of foods analyzed, addition of many analytes, improvement of analytical methods, and addition of population subgroups for which intakes are estimated (Pennington and Gunderson, 1987; Pennington et al., 1996). For a complete listing of various TDS publications and a more in-depth description of the history, please go to the following website: http://www.cfsan.fda.gov/~comm/tds-toc.html.

The present assessment focuses on perchlorate and iodine, two of the many analytes studied in the TDS. In recent years, perchlorate and iodine have received a fair amount of attention in the scientific literature. Perchlorate is a chemical that is found to occur naturally in Chilean nitrate fertilizer, which has been used in the United States (Dasgupta et al., 2006). Perchlorate is also synthesized in the United States

and used as an oxidizing agent in solid rocket propellant and found in other items (e.g., explosives, road flares, fireworks, car airbags, herbicides, and so on). Since the mid 1990s, the US Environmental Protection Agency (EPA), along with other government agencies, has sought to understand and assess the potential health effects of perchlorate levels in soil, groundwater, and drinking water around the country. In 2002, EPA, along with other federal agencies asked the National Academy of Sciences (NAS) to review the relevant scientific literature and key findings underlying EPA's 2002 Toxicological Review (NAS, 2005). In 2005, the NAS (NAS, 2005) advised EPA that a reference dose (RfD) of 0.0007 milligram per kilogram body weight per day (mg/kg bw/day), based on a no-observed-effects level of 0.007 mg/kg bw/day from a study by Greer et al. (2002), with the application of an uncertainty factor of 10 would protect the most sensitive population — the fetuses of pregnant women who might have hypothyroidism or iodide deficiency. The EPA accepted the NAS recommendations for the RfD (http://www.epa.gov/iris/subst/1007.htm).

Perchlorate at high pharmacological doses (0.02, 0.1, and 0.5 mg/kg bw/day) interferes with iodide uptake into the thyroid gland and, if the inhibition is severe enough, can disrupt thyroid function. Disruption of iodine uptake may cause the thyroid to become enlarged (goiter), and, if the disruption continues, it may cause hypothyroidism. The NAS (2005) reviewed findings in regards to iodine intake and thyroid function, and the committee stated that, "Generally, thyroid hormone production is normal even when iodide intake is quite low. Hypothyroidism occurs only if daily iodide intake is below about 10 to 20 μg (about one-fifth to one tenth of the average intake in the United States). However, for pregnant women, iodide deficiency of that severity can result in major neurodevelopmental deficits and goiter in their offspring. Lesser degrees of iodide deficiency may also cause important neurodevelopmental deficits in infants and children."

Blount et al. (2007), focused on perchlorate exposure of 2820 US residents 6 years of age and older from the National Health and Nutrition Examination Survey (NHANES) during 2001–2002. All the participants were found to have detectable levels of perchlorate in their urine. From this work, Blount et al. were able to estimate a total daily perchlorate dose for adults 20 years of age and older. The total daily perchlorate dose was based on urinary perchlorate, urinary creatinine concentration, and physiological parameters predictive of creatinine excretion rates, which resulted in a median estimate of 0.064 μg/kg bw/day and 95th percentile of 0.234 μg/kg bw/day.

In another study, Blount et al. (2006) focused on urinary perchlorate and thyroid hormone levels in 2299 men and women participants who were 12 years of age and older from NHANES during 2001–2002. The investigators evaluated the potential relationship between urinary levels of perchlorate and serum levels of thyroid stimulating hormone (TSH) and total thyroxine (T4). The subjects were categorized and analyzed based on a cutoff point of 100 μg/l urinary iodine level. This value was based on the World Health Organization (WHO) definition of sufficient iodine intake in populations (WHO, 2004). Blount et al. observed that perchlorate was not a significant predictor of hormone levels for men. For women with urinary iodine levels $< 100\ \mu$g/l, perchlorate was a significant negative predictor for T4 and a positive predictor of TSH. For women with urinary iodine levels $\geq 100\ \mu$g/l, perchlorate was a significant positive predictor of TSH, but not T4. Blount concluded that the associations of perchlorate with T4 and TSH are coherent in direction and independent of other variables known to affect thyroid function, but are present at perchlorate exposure levels that were unanticipated based on previous studies. Finally, Blount et al. concluded that additional research is needed to affirm these findings.

The FDA recognizes the potential for perchlorate contamination in food through the use of some fertilizers, contaminated irrigation water, processing water, and source waters for bottle water. During 2004–2005, the FDA conducted exploratory surveys to monitor perchlorate levels in 28 types of foods and beverages consisting of bottled water, milk, fruits and fruit juices, vegetables, grain products, and seafood. The results of these exploratory surveys are found at FDA (2007), http://www.cfsan.fda.gov/~dms/clo4data.html. Since the results of these exploratory surveys focused on selected foods, the data do not provide information on the presence of perchlorate in the US food supply representing the total diet of the US population and are not included in this estimate. In 2005, FDA began testing all samples from the TDS to determine whether perchlorate is found in a broader range of foods. The TDS was determined to be an appropriate tool, since it includes all major components of the average American diet. In addition, because iodine has been analyzed in all TDS foods since late 2003, estimates of daily intakes of both perchlorate and iodine by the US population could be derived from the TDS results.

This study reports the estimated average dietary intakes of iodine based on analytical results from TDS samples collected between 2003 and 2004 and of perchlorate based on analytical results from TDS samples collected between 2005 and 2006. The total estimated daily intakes were calculated for 14 age/sex population groups from infants through adults. Also, the contributions of major food groups to total estimated intakes of iodine and perchlorate are reported.

Methods

Dietary intakes of perchlorate and iodine were estimated by combining analytical results from the TDS with food

consumption estimates developed specifically for estimating dietary exposure from TDS results (referred to as TDS diets).

Development of the TDS Food List and Diets

The following is a brief discussion of the methodology for developing both the TDS food list and diets; a more exhaustive explanation of the methodology is provided by Egan et al. (2007). The current TDS food list and diets were compiled in 2003 from the results of the US Department of Agriculture's 1994–1996, 1998 Continuing Survey of Food Intakes by Individuals (94–98 CSFII). For this survey, the data collection in 1994–1996 included individuals of all ages, and data collected in 1998 included children from birth through 9 years of age; the survey design allowed for all years of data to be combined for analysis. During the 94–98 CSFII, survey participants reported detailed consumption information on about 6000 different foods and beverages. For compiling the TDS food list, all 6000 survey foods were grouped (or aggregated) according to the similarity of their primary ingredients. Then average per capita (all individuals — eaters and noneaters alike) daily consumption amounts were calculated for each survey food, and, from each group of aggregated food codes, the food consumed in greatest was selected as the representative TDS food. In all, 285 foods and beverages were selected for the current TDS food list.

For compiling the TDS diets, the consumption amounts of all survey foods assigned to each TDS food were subtotaled to derive a TDS diet consumption amount for each TDS food. The complete set of TDS consumption amounts for each of the 14 age/sex groups is referred to collectively as the TDS diets. This approach to estimating dietary intakes assumes that the analytical profiles of the survey foods would be similar to those of the TDS foods to which they are assigned and that the TDS diets could, therefore, provide a reasonable estimate of total dietary exposure to the analytes from all foods in the diet — not from the TDS foods alone. The TDS diets do not account for consumption of water other than that used in the preparation of foods or beverages (i.e., the diets do not include drinking water from the tap although bottled water, consumed as a beverage, is included in calculations presented here). Additionally, the TDS diet for infants 6–11 months does not include consumption of breast milk, thus breastfed infants would have different exposure patterns from the estimates shown in Table 5.

TDS Sample Collection and Analyses

Total Diet Study samples are routinely collected four times a year, once in each of the four regions of the country (west, north central, south, and northeast). Each round of sample collections and analyses is referred to as a market basket. For each market basket, samples of each of the 285 foods are collected simultaneously in three cities within the region. The foods are purchased at retail from grocery stores and fast-food restaurants and are then shipped from the collecting locations to FDA's Kansas City District Laboratory in Lenexa (KS, USA). The foods are prepared table-ready prior to analyses, and salt is not added to any of TDS food prepared by the laboratory. Distilled water is used for all food preparation (e.g., washing, cooking, and beverage preparation). For each of the 285 foods, the products purchased in each of the three cities within the collection region are composited to form a single analytical sample for each regional market basket.

The estimated intakes reported in this study are based on analytical results for TDS samples collected between 2003 and 2006. Iodine was analyzed in all TDS foods from five market baskets conducted in late 2003 through 2004. For perchlorate, 54 of 57 baby foods were analyzed in four market baskets conducted in 2005; the remaining three baby foods were analyzed in only three market baskets because they were not available in the fourth market basket for 2005. The other 228 TDS foods were analyzed in 2006; of those, 128 were analyzed in four market baskets and 100 were analyzed in two market baskets. The dates and locations of each market basket are listed in Table 1.

Table 1. Dates and locations of sample collections for iodine and perchlorate results.

Market basket	Sample collection dates	Collection region and locations
2003-4	July 2003	North (Monmouth-Ocean City, NJ; Rochester, NY; Philadelphia, PA)
2004-1	October 2003	Central (Chicago, IL; Youngstown-Warren, OH; Detroit, MI)
2004-2	January 2004	West (Salt Lake City/Ogden, UT; Phoenix-Mesa, AZ; Las Vegas, NV)
2004-3	April 2004	South (Atlanta, GA; San Antonia, TX; Shreveport-Bossier City, LA)
2004-4	July 2004	North (Boston, MA; Syracuse, NY; Pittsburgh, PA)
2005-1	October 2004	Central (Kalamazoo-Battle Creek, MI; Omaha, NE; St. Cloud, MN)
2005-2	January 2005	West (Pueblo, CO; San Jose, CA; Boise City, ID)
2005-3	April 2005	South (Roanoke, VA; West Palm Beach-Boca Raton, FL; New Orleans, LA)
2005-4	July 2005	North (Hartford, CT; Bergen-Passaic, NJ; Binghamton, NY)
2006-1	October 2005	Central (Rockford, IL; Cincinnati, OH; Fargo-Moorhead, ND)
2006-2	January 2006	West (Los Angeles-Long Beach, CA; Santa Clara, CA; Seattle-Everett, WA)
2006-3	April 2006	South (Raleigh, NC; Norfolk-Virginia Beach, VA; Tulsa, OK)
2006-4	July 2006	North (Portland, ME; Nassau-Suffolk, NY; Scranton Wilkes-Barre, PA)

Table 2. FDA analytical techniques and limits for iodine and perchlorate.

Chemical name	Analytical technique	Nominal analytical limits	
		Limit of detection	Limit of quantitation
Iodine	UV-Vis	0.03 p.p.m.; for some up to 0.06 p.p.m.	0.3 p.p.m., for some up to 0.6 p.p.m.
Perchlorate	IC-TMS	1.00 p.p.b.	3.00 p.p.b.

IC-TMS, ion chromatography–tandem mass spectrometry; UV-Vis, ultraviolet–visible spectrometry.

Table 3. Description of food groups contributing to intakes.

Food groups	Includes
Baby food	All baby foods and infant formulas (excluding adult foods consumed by children). Infant formulas were samples of ready-to-eat products
Beverages	Beverages, including bottled water, except for fruit/vegetable juices
Dairy	All dairy products (e.g., butter, milk, cheese, and ice cream)
Eggs	Boiled egg, scrambled egg, omelet, and egg salad
Fat/oil	Vegetable fats and oils, and salad dressings
Fruits	Fruits and fruit juices
Grains	Items that are primarily grains, including cookies and pastries
Legumes	Legumes, nuts, and seeds
Mixtures	Primarily entrée items containing mixtures of meat/poultry/fish, grains, and vegetables (no predominant ingredient)
Meat, poultry, fish (MPF)	Items that are primarily meat, poultry, or fish (e.g., roasts, fried chicken, fish filets, and luncheon meats)
Sweets	Sugars, sweeteners, syrups, candy, jelly, and gelatin
Vegetables	Vegetables and vegetable juices

Iodine was measured by FDA's Kansas City District Laboratory using a method adapted from Fischer et al. (1986). The method consists of a ternary acid digestion with a determination of iodine by UV-VIS spectrophotometry through the catalysis of the $Ce + 4/As + 3$ reaction. The method for perchlorate was developed by FDA in a collaborative effort among the Center for Food Safety and Applied Nutrition, the Southeastern Regional Laboratory, and the Total Diet Research Center; the method was published by Krynitsky et al. (2006). Table 2 reports the analytical techniques, the nominal limit of detection (LOD), and limit of quantitation (LOQ). Cases in which perchlorate and iodine were found to be present in concentrations greater than or equal to the LOD but less than the LOQ were considered "trace" amounts. The LOD for perchlorate was 1.00 μg/kg, while the LOD for iodine ranged from 0.03 to 0.06 mg/kg.

Calculation of TDS Dietary Intakes

In calculating estimated intakes, the average iodine concentration per food was calculated from results of five market baskets. For perchlorate, the average concentration per food was calculated from results of either two or four market baskets, as mentioned above. To account for uncertainties associated with samples with no detectable concentrations of perchlorate or iodine (non-detects or NDs), three average concentrations were calculated for each TDS food assuming values of zero, half the LOD, and the LOD for non-detects. The three average concentrations in each food were then multiplied by the average daily consumption amount of the food for the given subpopulation group as compiled for the TDS diets to provide a range from lower bound (ND = 0) to upper bound (ND = LOD) estimated average intakes from each TDS food. Finally, estimated intakes from all TDS foods were summed to estimate the range of average total estimated daily intakes of iodine and perchlorate for each age/sex group. The estimated perchlorate intakes were compared with the EPA's RfD for perchlorate, and estimated iodine intakes were compared with the appropriate US Dietary Reference Intakes that represent average daily intake requirements (NAS, 2000). For the TDS age/sex groups other than infants, estimated iodine intakes were compared with the relevant estimated average requirements (EARs), which are defined by NAS as the nutrient intake levels estimated to meet the requirements of half the healthy individuals within a particular age/sex group. The estimated iodine intake by the TDS group of infants 6–11 months was compared with the adequate intake (AI) of 130 μg/person/day (NAS, 2000); an AI is set by NAS when there is insufficient scientific evidence to determine an EAR and is defined as the recommended average daily intake level of a nutrient that is assumed to be adequate for a group of apparently health individuals.

The contributions of major food groups to total estimated intakes of perchlorate and iodine were also calculated. TDS foods were assigned to 1 of 12 major food groups; descriptions of these food groups are provided in Table 3, and a further rationale for TDS food assignment into the 12 major food groups are explained by Egan et al. (2007). The contributions of food groups to total estimated intake were calculated from the intake estimates based on average concentrations assuming values of half the LOD for non-detects. Contributions by food groups were determined by summing the estimated intakes from all TDS foods in each of the 12 food groups, and calculating the percentage of total intake for each food group.

Results

Perchlorate

From the TDS analytical results, it is evident that perchlorate is found in a wide range of foods. Detectable levels of perchlorate were found in 625 of 1065 (59%) of the total samples analyzed and 440 of 1065 (41%) of the samples had no detectable levels of perchlorate. Of the 625 samples with detectable levels of perchlorate, 231 contained "trace" amounts (i.e., concentrations between the LOD and LOQ). As for findings in specific foods, detectable levels of perchlorate were found in at least one sample in 74% (211 of 285) of TDS foods. In contrast, perchlorate was not detected in any sample of 74 of 285 (26%) of TDS foods.

Estimated dietary intakes of perchlorate are reported in Tables 4 and 5. The percentage contributions to total estimated daily intake by food group are presented in Table 4. The majority (81%) of the estimated perchlorate intake by infants 6–11 months comes from baby foods, which includes infant formula, and dairy foods. Dairy foods contribute about half of the total estimated daily intake of perchlorate by children 2, 6, and 10 years of age. Vegetables and dairy foods combined account for between 46% and 59% of the total estimated intake of perchlorate by teenagers and adults.

Table 5 presents the lower and upper bound estimated average total daily intakes as well as intakes by food group on a per person basis. Total estimated daily intakes are also presented per kg of body weight to compare with EPA's RfD of 0.7 μg/kg bw/day. Average body weights for each

Table 4. Contribution (%) by food groups to total estimated daily intake of perchlorate for 2005–2006.

Food group	Intake (% of total)						
	Infants 6–11 months	Children 2 years	Children 6 years	Children 10 years	Teenage girls 14–16 years	Teenage boys 14–16 years	Women 25–30 years
Baby food	49	0	0	0	0	0	0
Beverage	1	3	3	4	7	7	12
Dairy	32	51	50	47	29	37	20
Egg	0	0	0	0	0	0	0
Fat/oil	0	0	0	0	0	0	0
Fruit	4	15	11	9	11	7	8
Grain	2	6	8	8	8	9	8
Legume	0	0	0	0	0	0	0
Mixture	6	8	9	10	14	12	14
MPF	1	4	6	5	7	7	11
Sweets	0	1	1	1	1	1	1
Vegetable	5	12	12	16	23	20	26
	Men 25–30 years	Women 40–45 years	Men 40–45 years	Women 60–65 years	Men 60–65 years	Women 70+ years	Men 70+ years
Baby food	0	0	0	0	0	0	0
Beverage	12	12	11	9	9	6	7
Dairy	20	17	21	17	19	23	22
Egg	0	0	0	0	0	0	0
Fat/oil	0	0	0	0	0	0	0
Fruit	5	11	8	12	9	12	12
Grain	8	8	9	8	8	8	9
Legume	0	0	0	0	0	0	0
Mixture	16	13	13	9	10	10	10
MPF	9	7	8	7	8	5	7
Sweets	0	1	1	0	0	0	0
Vegetable	30	31	29	38	37	36	33

MPF, meat, poultry, fish.

Table 5. Range of estimated lower and upper bound average perchlorate intakes for 2005–2006.

Food group	Intake (μg/person/day)						
	Infants 6–11 month	Children 2 years	Children 6 years	Children 10 years	Teenage girls 14–16 years	Teenage boys 14–16 years	Women 25–30 years
Baby food	1.1–1.3	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0
Beverage	0.00–0.1	0.0–0.3	0.0–0.4	0.0–0.5	0.02–0.8	0.0–1.1	0.2–1.2
Dairy	0.8–0.8	2.6–2.6	2.9–2.9	3.1–3.1	1.6–1.6	3.1–3.1	1.2–1.2
Egg	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0
Fat/oil	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0
Fruit	0.1–0.1	0.7–0.9	0.6–0.7	0.5–0.6	0.6–0.7	0.5–0.6	0.5–0.6
Grain	0.0–0.1	0.3–0.3	0.4–0.5	0.5–0.5	0.4–0.5	0.7–0.8	0.4–0.5
Legume	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0
Mixture	0.1–0.1	0.4–0.5	0.5–0.6	0.6–0.7	0.8–0.8	1.0–1.1	0.9–0.9
MPF	0.0–0.0	0.2–0.2	0.3–0.3	0.3–0.4	0.3–0.4	0.5–0.6	0.7–0.7
Sweets	0.0–0.0	0.0–0.0	0.0–0.1	0.0–0.1	0.0–0.1	0.0–0.1	0.0–0.1
Vegetable	0.1–0.1	0.6–0.6	0.7–0.7	1.0–1.0	1.2–1.3	1.7–1.7	1.5–1.5
Total intake	**2.4–2.7**	**4.9–5.5**	**5.4–6.1**	**6.1–6.9**	**5.1–6.1**	**7.7–9.1**	**5.4–6.8**
Total intake (μg/kg bw/day)	**0.26–0.29**	**0.35–0.39**	**0.25–0.28**	**0.17–0.20**	**0.09–0.11**	**0.12–0.14**	**0.09–0.11**
	Men 25–30 years	Women 40–45 years	Men 40–45 years	Women 60–65 years	Men 60–65 years	Women 70+ years	Men 70+ years
Baby food	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0
Beverage	0.2–1.6	0.3–1.3	0.2–1.7	0.2–1.0	0.2–1.3	0.1–0.7	0.1–0.9
Dairy	1.5–1.5	1.1–1.1	1.8–1.8	1.1–1.1	1.5–1.5	1.4–1.4	1.7–1.7
Egg	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0
Fat/oil	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0
Fruit	0.3–0.4	0.7–0.8	0.6–0.7	0.7–0.8	0.6–0.8	0.7–0.8	0.8–1.0
Grain	0.6–0.7	0.5–0.6	0.7–0.8	0.5–0.5	0.6–0.7	0.5–0.6	0.6–0.7
Legume	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0
Mixture	1.2–1.3	0.8–0.9	1.1–1.1	0.6–0.6	0.8–0.9	0.6–0.6	0.7–0.8
MPF	0.7–0.7	0.5–0.5	0.6–0.7	0.4–0.5	0.6–0.7	0.3–0.4	0.5–0.6
Sweets	0.0–0.0	0.0–0.0	0.1–0.1	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0
Vegetable	2.2–2.2	1.9–2.0	2.4–2.4	2.4–2.4	2.8–2.9	2.2–2.2	2.5–2.5
Total intake	**6.7–8.6**	**5.9–7.3**	**7.4–9.4**	**5.9–7.1**	**7.2–8.8**	**5.8–6.9**	**7.1–8.3**
Total intake (μg/kg bw/day)	**0.08–0.11**	**0.09–0.11**	**0.09–0.11**	**0.09–0.10**	**0.09–0.11**	**0.09–0.11**	**0.11–0.12**

MPF, meat, poultry, fish.
The total intake for a specific age/sex group are provided in bold.

population group were based on self-reported body weights from respondents in the 94–98 CSFII (Egan et al., 2007). Estimated perchlorate intakes by all age/sex groups are below the RfD. Children 2 years of age, with estimated lower and upper bound average intakes ranging from 0.35 to 0.39 μg/kg bw/day, have the highest total perchlorate intake per kg body weight per day. Total lower- and upper bound average intake ranges for infants 6–11 months, and children 6–10 years of age are estimated to be 0.26 to 0.29 μg/kg bw/day, 0.25 to 0.28 μg/kg bw/day, and 0.17 to 0.20 μg/kg bw/day, respectively. The estimated smallest lower bound and the highest upper bound average intakes by the other age/sex groups ranged from 0.08 to 0.14 μg/kg bw/day.

Iodine

From the TDS analytical results, it is evident that iodine is found in more than half the foods in the TDS. Detectable levels of iodine were found in at least one sample of 169 of 285 (59%) of the TDS foods, while iodine was not detected in 116 of 285 or 41% of TDS foods.

The percentage contributions by food group to total estimated daily intake of iodine are reported in Table 6. As with perchlorate, baby foods and dairy products account for nearly all (90%) of the estimated iodine intake by infants. Dairy products account for 70% or more of total estimated daily intake of iodine by children 2, 6, and 10 years of age, and 63% of total estimated iodine intake by teenage boys. For all other age/sex groups, dairy foods contribute about 50% of total estimated iodine intake. For children 2, 6, and 10 years of age, grains account for 10%, 14%, and 15%, respectively, of the total estimated daily iodine intake. Grain products contribute between 16% and 23% of total estimated iodine intake for teenagers and adults.

Table 7 reports the lower bound (ND = 0) and upper bound (ND = LOD) estimates of average iodine intakes as well as intakes by food group on a per person basis.

Table 6. Contribution (%) by food group to total estimated daily intake of iodine for 2003–2004.

Food group	Intake (% of total)						
	Infants 6–11 months	Children 2 years	Children 6 years	Children 10 years	Girls 14–16 years	Boys 14–16 years	Women 25–30 years
Baby food	56	0	0	0	0	0	0
Beverage	1	2	2	3	6	5	9
Dairy	34	73	70	70	53	63	49
Egg	2	3	2	2	2	2	4
Fat/oil	0	0	0	0	0	0	0
Fruit	2	5	3	2	4	3	3
Grain	3	10	14	15	20	16	20
Legume	0	0	0	0	0	0	0
Mixture	1	4	5	5	8	7	8
MPF	0	1	2	1	3	2	3
Sweets	0	1	1	1	2	1	2
Vegetable	1	1	1	1	2	1	2
	Men 25–30 years	Women 40–45 years	Men 40–45 years	Women 60–65 years	Men 60–65 years	Women 70+ years	Men 70+ years
Baby food	0	0	0	0	0	0	0
Beverage	10	10	9	9	8	6	6
Dairy	45	47	51	48	48	57	57
Egg	4	3	3	4	5	4	4
Fat/oil	0	0	0	0	0	0	0
Fruit	3	3	2	4	3	4	3
Grain	21	23	21	21	21	18	18
Legume	0	0	0	0	0	0	0
Mixture	11	8	7	6	7	5	5
MPF	3	3	3	4	4	3	4
Sweets	1	1	2	1	1	1	1
Vegetable	2	2	2	3	3	2	2

MPF, meat, poultry, fish.

Estimated intakes are compared to the AI or EAR relevant to the TDS population group. The lower bound (ND = 0) total estimated iodine intake by infants of 144 μg/person/day exceeds their AI for iodine (130 μg/person/day). The lower bound (ND = 0) daily estimated intakes of iodine by children are as follows: 225 μg/person/day for children 2 years, 255 μg/person/day for children 6 years, and 276 μg/person/day for children 10 years. These estimated intakes exceed the relevant EARs of 65 μg/person/day for children 1 through 8 years of age and 73 μg/person/day for children 9 through 13 years of age.

For teenage boys and girls aged 14–16 years, dairy and grain provide the highest sources of dietary iodine. These two food groups contribute 73% of total estimated intake by teenage girls and 79% of total estimated intake by teenage boys (Table 6). Teenage boys have the highest total daily estimated intake of iodine (304 to 353 μg/person/day) in comparison with the all other age/sex groups in the TDS (Table 7). Their lower bound (ND = 0) estimated iodine intake is three times their EAR of 95 μg/person/day. Like the teenage boys, the teenage girls' estimated dietary intake of iodine of 178 to 214 μg/person/day exceeds their EAR, which is also 95 μg/person/day.

For adults, dairy and grain provided the most significant sources of dietary iodine for all groups of adults (Table 6). The total estimated lower and upper bound average intakes by women 25–30 years of age range from 148 to 196 μg/person/day; for women 40–45 years of age, estimated intakes range from 145 to 197 μg/person/day (Table 7). For adult men 25–30 and 40–45 years of age, estimated iodine intakes range from 203 μg/person/day at the lower bound to 284 μg/person/day at the upper bound.

Finally, for older (60–65 and 70+ years of age) women and men, their main sources of dietary iodine are dairy and grains (Table 6). These foods account for between 69% and 75% of their total estimated daily intake. Total estimated lower and upper bound average intakes by women 60–65 years of age range from 138 to 182 μg/person/day (Table 7). Women 70+ years of age have an estimated iodine intake ranging from 154 to 192 μg/person/day. Estimated lower and upper bound average iodine intakes by both groups of older men range from 192 to 249 μg/person/day for men

Table 7. Range of estimated lower and upper bound average iodine intakes for 2003–2004.

Food group	Intake (μg/person/day)						
	Infants 6–11 months	Children 2 years	Children 6 years	Children 10 years	Girls 14–16 years	Boys 14–16 years	Women 25–30 years
Baby food	82.8–88.3	1.1–1.2	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0
Beverage	0.0–1.8	0.0–7.6	0.1–11.3	0.0–14.6	0.1–22.9	0.0–31.2	0.2–32.1
Dairy	50.8–50.8	173.9–173.9	187.9–188.0	202.5–202.6	106.0–106.0	207.9–207.9	83.2–83.2
Egg	2.5–2.5	7.1–7.1	5.1–5.1	5.5–5.5	4.4–4.4	5.9–5.9	6.0–6.0
Fat/oil	0.0–0.0	0.1–0.2	0.2–0.3	0.3–0.4	0.5–0.6	0.5–0.7	0.6–0.7
Fruit	1.6–3.1	7.9–13.8	5.8–9.7	5.4–8.7	6.3–9.3	7.1–10.1	4.2–7.4
Grain	3.6–4.1	21.5–23.5	37.1–39.5	41.6–43.9	37.5–39.7	49.6–52.6	32.3–34.8
Legume	0.0–0.1	0.1–0.4	0.2–0.5	0.2–0.5	0.1–0.6	0.2–0.6	0.2–0.6
Mixture	1.9–2.5	8.1–10.0	11.2–13.3	12.3–14.4	14.6–16.9	22.5–25.8	12.6–15.8
MPF	0.5–0.6	2.9–4.0	4.0–5.3	3.4–5.1	4.2–6.0	5.2–7.6	4.6–6.4
Sweets	0.0–0.1	1.6–2.0	2.7–3.4	3.1–4.0	2.7–3.3	2.7–3.5	2.8–3.2
Vegetable	0.6–1.1	1.0–3.1	1.2–3.9	1.3–4.6	1.2–4.7	2.3–7.1	1.4–5.8
Total intake	**144–155**	**225–247**	**255–280**	**276–304**	**178–214**	**304–353**	**148–196**
Estimated average requirement (EAR)[a]	**130 (AI)**	**65**	**65**	**73**	**95**	**95**	**95**
	Men 25–30 years	Women 40–45 years	Men 40–45 years	Women 60–65 years	Men 60–65 years	Women 70+ years	Men 70+ years
Baby food	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0	0.0–0.0
Beverage	0.1–45.5	0.2–35.5	0.1–45.7	0.4–27.7	0.1–36.2	0.2–20.9	0.1–24.9
Dairy	105.2–105.3	79.1–79.2	125.0–125.1	76.9–77.0	105.7–105.7	96.9–97.0	123.7–123.8
Egg	9.9–9.9	5.5–5.5	8.2–8.2	7.1–7.1	11.4–11.4	6.7–6.7	8.6–8.6
Fat/oil	0.7–0.9	0.7–1.0	1.0–1.3	0.6–0.9	0.7–1.0	0.5–0.7	0.6–0.8
Fruit	6.6–9.2	2.9–6.3	4.0–7.5	3.6–7.7	3.9–8.1	4.5–9.0	4.5–9.8
Grain	47.2–50.2	36.2–38.6	50.9–54.0	33.3–35.5	45.2–48.2	29.9–32.4	37.6–40.8
Legume	0.4–1.1	0.2–0.6	0.3–0.9	0.1–0.5	0.3–0.9	0.1–0.5	0.2–0.8
Mixture	22.9–26.7	12.8–15.5	15.9–19.7	7.8–10.4	13.3–16.9	7.8–10.6	9.7–13.0
MPF	6.1–9.0	4.0–6.0	5.6–8.7	5.6–7.5	7.2–9.9	4.6–6.2	7.0–9.0
Sweets	1.9–2.2	2.0–2.5	3.7–4.3	0.9–1.5	1.6–2.2	0.9–1.4	1.4–2.0
Vegetable	2.0–8.0	1.4–6.3	2.3–8.5	1.6–6.6	2.4–8.7	1.8–6.6	2.2–7.9
Total intake	**203–268**	**145–197**	**217–284**	**138–182**	**192–249**	**154–192**	**196–241**
Estimated average requirement (EAR)[a]	**95**	**95**	**95**	**95**	**95**	**95**	**95**

AI, adequate intake; MPF, meat, poultry, fish.
[a]Taken from National Academy of Sciences, Dietary Reference Intake for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc, National Academies Press, Washington, D.C., 2000.
The total intake for a specific age/sex group are provided in bold.

60–65 years of age and 196 to 241 μg/person/day for men 70+ years of age. Estimated lower bound (ND = 0) average intakes by all groups of men and women exceed the EAR for adults of 95 μg/person/day.

Discussion

This assessment provides information on major dietary sources and estimated average dietary intakes of perchlorate and iodine in the United States. Intakes estimated from the TDS diets are based on average per capita food consumption; that is, the TDS diets reflect the average amounts of foods consumed by all individuals (eater and noneaters alike) within each of the 14 age/sex groups. However, the TDS as currently designed does not allow for estimating intakes at the extremes (i.e., upper or lower percentiles of food consumption) or for population subgroups within the 14 age/sex groups that may have specific nutritional needs (e.g., the subgroups of pregnant or lactating women within the groups of women of childbearing age). Given the increased caloric needs of these two groups of women, their perchlorate and iodine intakes are likely to be somewhat higher than those of women of childbearing age as a whole as represented by the TDS population groups. We also note that children 2 years of age are estimated to consume iodine at levels that exceed the tolerable upper limit. Nevertheless, the results of this estimated dietary intake assessment of iodine and perchlorate provides a general estimation of the average iodine and perchlorate intakes by specific age/sex groups in the United States.

The perchlorate intake estimates reveal that infants and children (2, 6, and 10 years) have the highest estimated intake on a body weight basis in comparison to other TDS age/sex groups, because they consume more food per their body weight and they have different food consumption patterns. Children 2 years of age have the highest estimated average perchlorate intake ranging from 0.35 to 0.39 μg/kg bw/day, which is between 50% and 56% of the EPA RfD, with dairy foods providing about 51% of perchlorate in their diet. The estimated lower and upper bound average perchlorate intakes by infants 6–11 months and children 6 years of age range from 0.26 to 0.29 and 0.25 to 0.28 μg/kg bw/day, respectively. The infants' estimated perchlorate intake range is 37% to 41% of EPA's RfD of 0.7 μg/kg body weight per day, with dairy foods providing 32% of their total estimated intake of perchlorate. For children 6 years of age, the estimated average range of perchlorate intake is between 36% and 40% of the EPA's RfD. Children 10 years of age had estimated lower and upper bound average perchlorate intakes of 0.17 to 0.20 μg/kg bw/day, which is between 24% and 29% of the RfD.

For teenage girls 14–16 years, women 25–30 years of age, and women 40–45 years of age had the same estimated average perchlorate intake ranges of 0.09 to 0.11 μg/kg bw/day, respectively. For these three age groups (teenage girls 14–16 years of age, women 25–30 years of age, and women 40–45 years) had estimated average range of perchlorate intakes between 13% and 16% of the EPA's RfD.

The remaining seven age/sex groups displayed estimated perchlorate intakes from the smallest lower bound of 0.08 to the highest upper bound of 0.14 μg/kg bw/day, which is between 11% and 20% of the EPA's RfD. The lower bound (ND = 0) range of estimated average perchlorate intakes for eight age/sex group that consist of men and women over 20 years of age (0.08 to 0.11 μg/kg bw/day) show relative agreement with Blount et al. (2007) median estimated perchlorate dose of 0.064 μg/kg bw/day.

It could be assumed that perchlorate would be found mainly in foods with high moisture content (e.g., milk and vegetables) because of its affinity for water, but results of the TDS analyses appear to indicate that perchlorate is more widely distributed in the food supply. As noted, detectable levels of perchlorate were found in 74% of the 285 TDS food. Since this assessment is based on a small number of composite samples (two or four) per TDS food, FDA plans to continue analyzing the full range of TDS foods for perchlorate in the future to develop a more robust data set on perchlorate levels in foods.

Perchlorate and iodine levels in selected foods have been reported previously in the literature (Pearce et al., 2004; Jackson et al., 2005; Kirk et al., 2005; Sanchez et al., 2005a, b; Sanchez et al., 2006). In addition, FDA conducted exploratory surveys in 2004 and 2005 to determine perchlorate levels in selected foods. Table 8 compares the perchlorate concentrations in 10 commodities reported elsewhere with the levels found in similar TDS foods. Perchlorate results show fairly good agreement for 5 of the 10 commodities (milk, iceberg lettuce, green leaf lettuce, oranges, and grapefruit). For the other commodities (spinach, collards, cucumbers, tomatoes, and cantaloupe), perchlorate results varied considerably. Table 9 compares iodine concentrations for three foods as reported in the literature to findings in similar TDS foods. The iodine

Table 8. Perchlorate levels in selected foods.

Perchlorate levels		Concentration–wet weight (μg/kg)	
Commodity	*n* samples	Mean[a]	Source
Milk	47	2	Kirk et al. (2005)
	125	5.8	FDA exploratory samples
	8	7	FDA TDS
Lettuce, iceberg	63	7.4	Sanchez et al. (2005a)
	24	8	Sanchez et al. (2005b)
	43	8.1	FDA exploratory samples
	4	2.1	FDA TDS
Lettuce, green leaf	69	16.5	Sanchez et al. (2005a)
	24	33	Sanchez et al. (2005b)
	26	10.6	FDA exploratory samples
	2	4.4	FDA TDS
Spinach	10	85.1	Sanchez et al. (2005a)
	36	115	FDA exploratory samples
	4	40	FDA TDS
Collards	1	5	Sanchez et al. (2005a)
	13	95.1	FDA exploratory samples
	4	17.7	FDA TDS
Cucumbers	1	40	Jackson et al. (2005)
	1	770	Jackson et al. (2005)
	20	6.6	FDA exploratory samples
	4	19.1	FDA TDS
Tomatoes	1	42	Jackson et al. (2005)
	1	220	Jackson et al. (2005)
	73	13.6	FDA exploratory samples
	4	78	FDA TDS
Cantaloupe	1	1600	Jackson et al. (2005)
	48	28.6	FDA exploratory samples
	4	24.4	FDA TDS
Oranges	28	7.4	Sanchez et al. (2006)
	10	3.4	FDA exploratory samples
	4	2.7	FDA TDS
Grapefruit	15	3.3	Sanchez et al. (2006)
	4	0.5	FDA TDS

LOD, limit of detection; ND, non-detect.
[a]Mean for FDA samples are based on ND = 1/2LOD.

Table 9. Iodine levels in selected foods.

Iodine levels		Concentration–wet weight (μg/kg)	
Commodity	*n* samples	Mean	Source
Milk	47	89.2	Kirk et al. (2005)
	18	464	Pearce et al. (2004)
	20	417	FDA TDS
Infant formula	8	159	Pearce et al. (2004)
	15	136	FDA TDS
Bread	17	334	Pearce et al. (2004)
	25	312	FDA TDS

concentrations in milk reported by Kirk et al. (2005) were considerably lower than either the TDS samples or those reported by Pearce et al. (2004), but TDS iodine levels in infant formula and bread were consistent with those reported in the literature.

These TDS results increase substantially the available data for characterizing dietary exposure to perchlorate and provide a useful basis for the beginning to evaluate overall perchlorate and iodine estimated dietary intakes in the US population. The next major step is to analyze future TDS market baskets for perchlorate and iodine. More robust data sets will provide a clearer picture of estimated perchlorate and iodine intakes using not only the TDS approach to estimating intakes but also by using the analytical results from the TDS with detailed consumption data from the CSFII or NHANES surveys. Targeting the food consumption patterns based upon results from these surveys could provide an estimate of the distribution of iodine and perchlorate intakes by women of childbearing age who are pregnant and/or lactating. Data from these surveys could also be combined to develop an estimate of iodine and perchlorate intakes specifically for pregnant and lactating women, which could provide more information about the potential for perchlorate inhibition of iodide uptake by the thyroid to occur in this population subgroup.

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Sites with Trichloroethene and Perchloroethene over 5 ppb

Anne Arundel County

Annapolis Sanitary Landfill
North of MD Rt. 450, east of Rt. 97, Annapolis MD

Fort Meade Sanitary Landfill
Magazine Road, Fort George G. Meade MD 20755-5115

Millersville Municipal Landfill
389 Burns Crossing Road, Severn MD 21144-341

Baltimore County

Hernwood Sanitary Landfill
Furman's Lane, west of Hernwood Road, Hernwood MD

Norris Farm Sanitary Landfill
Trappe Road, northeast of North Point Boulevard, Dundalk MD

Parkton Sanitary Landfill
North of Stablers Church Road, east of I-83, Parkton MD

Calvert County

Barstow Sanitary Landfill
Stafford Road, west of MD Rt. 231, Barstow MD

Carroll County

John Owings Sanitary Landfill
John Owings Road, north of MD Rt. 97, Westminster MD

Charles County

Pisgah Sanitary Landfill
MD Rt. 425, one mile southwest of Pisgah MD

Frederick County

Site B Municipal Landfill
9031 Reichs Ford Road, Frederick MD 21704

Harford County

Tollgate Sanitary Landfill
Tollgate Road near US Rt. 1, Bel Air MD

Howard County

Alpha Ridge Municipal Landfill
2350 Marriottsville Road, Marriottsville MD 21104

Kent County

Nicholson Sanitary Landfill
23750 Larney Nick Road, Melitota MD

Montgomery County

Oaks Sanitary Landfill
6001 Olney-Laytonsville Road, Laytonsville MD

Prince George's County

Brown Station Road Municipal Landfill
3500 Brown Station Road, Upper Marlboro MD 20772

St. Mary's County

St. Andrews Municipal Landfill
44825 St Andrews Church Road, California MD 20619

Research

Temporal Patterns in Perchlorate, Thiocyanate, and Iodide Excretion in Human Milk

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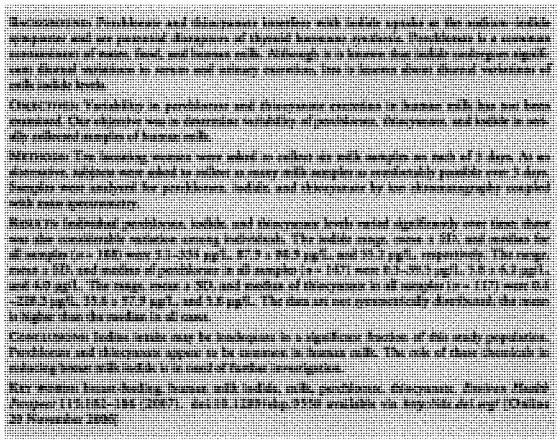

Breast milk is widely recognized as the best source of nourishment for infants (Gartner et al. 2005). Breast-feeding also fosters an infant's emotional and social well-being (Else-Quest et al. 2003; Winberg 2005). The American Academy of Pediatrics (Gartner et al. 2005), World Health Organization (WHO 2001), and the International Council of Nurses (ICN 2006) all recommend that infants be exclusively breast-fed for the first 6 months of life. It is important that milk be as free of detrimental agents as possible (LaKind et al. 2004); it is also important that the maternal diet provides the nutrients needed for high milk quality (Dorea 2002). This is especially true for iodine. Iodine deficiency is widely recognized as the leading and most readily preventable cause of mental impairment in children (Delange et al. 2001). Unlike adults, neonates do not have significant thyroxine stores (van den Hove et al. 1999). Exclusively breast-fed infants depend on their mother's milk iodine for thyroid hormone (TH) synthesis and establishment of TH stores from which they can draw TH if iodine availability falls.

Thyroid hormones and therefore iodine are essential to fetal and infant neurodevelopment. Infants born to hypothyroid- or iodine-deficient women exhibit intellectual and behavioral deficits as children (Rovet and Ehrlich 2000). Such deficits may be apparent in infants as young as 3 weeks even if the degree of early deficiency was small or transient or occurred during fetal development (Kooistra et al. 2006). The Institute of Medicine (IOM 2001) recommends an iodine intake of 110 μg/day for infants 0–6 months of age, and 130 μg/day for infants 7–12 months of age. Iodine needs of pre-term infants may be twice what is needed by full-term infants (Ares et al. 2005). Breast milk–iodine content is considered sufficient when levels are 150–180 μg/L (Delange 2004). Milk samples provided by most women in our previous study (Kirk et al. 2005) fell far short of this standard. The median iodide level in human milk from 23 donors residing in 15 different states (Kirk et al. 2005) was 33.5 μg/L, and only 4 samples fell within the recommended level. We have therefore been concerned that lactating women in the United States may not be consuming sufficient iodine to meet the needs of their breast-fed infants.

Exposure to perchlorate and other iodide transport inhibitors may increase the risk of iodine deficiency among infants. The sodium–iodide symporter (NIS) is 30-fold more selective for perchlorate than for iodide and is reportedly 9–100 times as potent as thiocyanate in inhibiting iodide uptake (Dohan et al. 2003; Tonacchera et al. 2004). Perchlorate and other iodide transport inhibitors such as thiocyanate thus likely reduce transfer of iodide to breast milk at the mammary NIS. Unless major dietary changes have occurred after the birth of her child, it is also likely that a woman with perchlorate and/or thiocyanate in her milk was similarly exposed during pregnancy, potentially reducing the pool of maternal TH needed for fetal development and reducing the ability of the fetal thyroid to produce its own hormones. For a nursing infant, the production of TH would be dually impaired: first by reduction of breast-milk iodide content and then by reduced iodide uptake by the infant thyroid. A discrimination factor of 30× at both stages amounts to 3 orders of magnitude of discrimination overall. Various aspects of brain development depend precisely on when TH deficiency occurs. An infant who had insufficient TH during fetal life might suffer delay or impairment in neurologic functions that develop *in utero*. This infant may suffer other impairments if TH deficiency occurs again, or continues, after parturition. Transient or mild hypothyroidism during fetal or infant development may result in long-standing, possibly permanent functional deficits that include learning disabilities and hyperactivity (Haddow et al. 1999; Morreale de Escobar et al. 2000; Rovet 2002, 2005; Pop et al. 1999). Some find strong links between iodine deficiency and attention deficit disorders (ADD; Vermiglio et al. 2004). In the United States, an estimated 3–5% of children (approximately 2 million) have ADD (National Institute of Mental Health 2003).

A lack of data on the variability of iodide excretion limits our ability to assess milk

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iodine levels. Most studies of human milk iodide, including our own, have been based on single samples (Ciardelli et al. 2002; Skeaff et al. 2005), although a few have examined iodide content in samples from two (Gushurst et al. 1984; Moon and Kim 1999) or three points in time (Chierici et al. 1999). These measures may not accurately portray infant intake, especially if samples were systematically collected at times when iodide content is low. The same holds for perchlorate in milk. Although perchlorate may be common in human milk, nothing is known about the temporal variation of perchlorate levels. Finally, thiocyanate, a by-product of cyanide metabolism, is also found in human milk. We describe the variation of iodide, perchlorate, and thiocyanate levels in series of human milk samples. The implications for infant development are discussed.

Materials and Methods

Ten lactating subjects were recruited and gave informed consent under a protocol approved by the Texas Tech University Institutional Review Board. Subjects were provided with precleaned 50-mL polypropylene tubes (Fisher Scientific, Fairlawn, NJ). Half the subjects were from the Texas Panhandle. One subject each was from Colorado, Florida, Missouri, New Mexico, and North Carolina. None reported being smokers or being vegetarian. All subjects were of European descent except for one woman residing in Texas who is of West African origin. Subjects were recruited through public notices and by word of mouth (subjects from previous studies, friends/associates of present and previous subjects). Subjects were of mid- to high socioeconomic status. Pregnant women were excluded from the study. All subjects reside in small cities or suburban environments except for one subject who resides in a small agricultural community. Samples were either expressed by pump and transferred from collection bags into provided collecrion tubes, or expressed manually directly into polypropylene tubes. After expression, sample tubes were placed in a supplied plastic container and stored in the donor's home freezer until transferred to out facility, where they were maintained at –20°C. Samples were thawed before processing at 1°C. Each subject was asked to pmvide six samples on each of 3 days. Alternatively, subjects were asked to provide as many samples of breast milk as comfortably possible over a series of days.

Subjects provided between six and 18 samples over an average of 4.4 days (range, 2–14 days). Days were not required to be consecutive so that inconvenience to subjects could be minimized. Subjects were asked to record dates and times of sample collections and everything they ate or drank during the days that samples were collected. Food consumption was evaluated using the U.S. Department of Agriculture's (USDA) food group tracking program "MyPyramid Tracker" (USDA 2006) and correlated with levels of perchlorate, thiocyanate, and iodide in milk. Samples were processed and analyzed by ion chromatography–mass spectrometry according to the method reported by Dyke et al. (2006).

Results

We found considerable variability in perchlorate, iodide, and thiocyanate excretion both within and among individuals. The iodide range, mean ± SD, and median for all samples (n = 108) were 3.1–334 μg/L, 87.9 ± 80.9 μg/L, and 55.2 μg/L respectively. The range, mean ± SD, and median of perchlorate in all samples (n = 147) was 0.5–39.5 μg/L, 5.8 ± 6.2 μg/L, and 4.0 μg/L. Range, mean ± SD, and median of thiocyanate in all samples (n = 117) was 0.4–228.3 μg/L, 35.6 ± 57.9 μg/L, and 5.6 μg/L. The data, based on the mean and variance, are skewed to the right. Median, rather than mean, values are therefore the preferred measure for the data set as a whole. Means and variance for individuals are reported in Table 1.

On eight occasions a subject collected milk samples before consuming any food or liquid in the morning. These were matched with a sample collected after the subject's evening meal. Student's t-test demonstrated a significant increase in perchlorate levels between ptebreakfast and postdinner samples (p < 0.03). No statistically significant difference was found for iodide or thiocyanate levels in these samples.

Milk iodine levels < 50 μg/L are considered "consistent with iodine deficiency" (Bazrafshan et al. 2005). Nearly half (46%) of all milk samples tested were below this threshold. Only 23% of the samples tested met the iodide sufficiency definition of Delange (2004). Only two of 10 donors had mean iodide levels that met the standard of iodide sufficiency when iodide concentrations were averaged. One of these subjects (C) took an iodine-containing supplemenr. Interestingly, samples from the other iodine-sufficient woman (E) also had the highest mean levels of perchlorate (21.4 ± 11.9 μg/L) and thiocyanate (149.6 ± 19.8 μg/L). Results for individual subjects are summarized in Table 1.

One subject reported exclusively using bottled spring water. The drinking water for two subjects came from a reverse osmosis–treated source; perchlorate levels in milk samples from these subjects were higher than the mean, with samples from one of the two volunteers (E) having the highest perchlorate contenr of all samples submitted (mean 21.4 μg/L, n = 10). Perchlorate in milk samples of the other subject drinking reverse osmosis–treated water (I) was also well above the median of 4.0 μg/L.

Perchlorate levels exceeded those of thiocyanate in 41% of the samples submitted. There was one sample each from two individuals in which perchlorate levels exceeded those of iodide. The iodide:perchlorate molar ratio ranged from 0.55 to 130 with a mean ± SD of 18.5 ± 21.9 and a median of 13.3. The thiocyanate:perchlorate molar ratio ranged from 0.016 to 267. The mean ± SD thiocyanate:perchlorate molar ratio was 18.2 ± 43.1, and the median value was 2.0. The iodide:thiocyanate molar ratio ranged from 0.21 to 251 with a mean ± SD of 33.4 ± 60.2 and a median of 3.0.

Table 1. Donor food intake and mean perchlorate, iodide, and thiocyanate in breast milk.

Donor	Days	No. of Samples	Vegetable	Fruit	Grain	Milk	Meat/bean	Iodide (mean ± SD)	Perchlorate (mean ± SD)	Thiocyanate (mean ± SD)
A	2	11	78	13	114	129	87	123.5 ± 107.0	2.1 ± 0.5	96.0 ± 44.2
B	4	16	62	76	73	81	119	58.9 ± 25.6	3.8 ± 2.1	7.0 ± 9.9
C	14	18	66	26	116	54	55	201.2 ± 49.7	5.5 ± 1.3	15.4 ± 53.2
D	2	11	62	77	91	15	171	24.4 ± 7.2	7.6 ± 4.7	8.6 ± 7.0
E[a]	2	8	67	118	120	55	104	182.2 ± 55.2	21.4 ± 11.9	149.6 ± 19.8
F	3	14	72	2	166	54	55	12.0 ± 7.2	1.4 ± 0.7	0.8 ± 0.5
G	3	16	28	118	64	70	43	43.5 ± 25.6	4.2 ± 3.2	3.7 ± 11.2
H	3	6	16	35	78	32	89	119.4 ± 29.8	4.4 ± 3.9	180.5 ± 42.0
I[a]	3	10	127	85	39	33	94	49.3 ± 22.8	7.3 ± 5.0	31.2 ± 16.1
J	4	6	NA	NA	NA	NA	NA	NA	8.2 ± 2.5	15.2 ± 9.4

NA, not available; data were lost through instrument malfunction, and sufficient sample for a rerun was not available. Data on food intake are reported as percentage of recommended intake by the USDA (2006).
[a]Subject uses reverse osmosis water.

Only one subject (C) reported taking an iodine-containing nutritional supplement. Figure 1 shows iodide data for samples from this subject along with data from a subject (B) not taking an iodine-containing supplement whose median iodide values was closest to the median iodide value for the entire cohort. The difference in milk iodide content is readily noticeable. Temporal variability in iodide, perchlorate, and thiocyanate levels for all subjects are shown in Figure 2A–C.

The Centers for Disease Control and Prevention (CDC) recommend that women consume 5–9 servings of fruit and vegetables daily (CDC 2006a). Only two of our donors met this recommendation (Table 1). Perchlorate levels were positively correlated (r^2 = 0.5589) with consumption of fruit and vegetables. Iodide and thiocyanate milk levels were not correlated with intake of fruit and vegetables. The unexpected lack of correlation between thiocyanate in milk and fruit/vegetable intake may be explained by high intake of soy-based nutritional supplements along with low produce intake by one subject. When data from this and another subject with unexpectedly high thiocyanate levels are removed, the correlation increases from near zero to an r^2 = 0.4758.

One donor (H) had particularly high thiocyanate levels (individual mean = 160.5 µg/L, individual median = 165.3 µg/L) when her data were compared with data from all other subjects (mean = 28.9g/L, median 5.2 µg/L) despite having the lowest level of produce intake. Although it is possible that this donor was exposed to cigarette smoke either actively or passively, she was the only subject who used soy-based nutritional beverages (mean daily intake 460 mL).

Discussion

For breast-fed infants < 12 months of age, average milk consumption is 100 mL/kg/day (Arcus-Arth et al. 2005). Three of our 10 subjects had average breast-milk perchlorate concentrations > 7 µg/L; thus for the infants of these mothers, the National Research Council (NRC) reference dose for perchlorate at 0.7 µg/kg/day (NRC 2005) will be exceeded. A more detailed analysis of breastmilk consumption as a function of age (Arcus-Arth et al. 2005), however, indicates that exposure per unit weight declines with age. Average milk intake as a function of age is available in studies by Butte et al. (1984) and Neville et al. (1988). Average infant weight as a function of age is available from the CDC (2006b); these are divided by sex—an average was used here—and the difference between the sexes is very slight. This information has been combined with our breast-milk concentration data to generate Figure 3, which shows iodide, perchlorate, and thiocyanate intake in micrograms per kilogram per day for an average-weight infant as a function of age. Each plot further shows three traces; each shows the intake of hypothetical infants consuming the mean, median, and the highest level of each species. (The mean, median, and highest values pertain to averaged data for each individual as listed in Table 1.) Figure 3A reveals that based on the median iodide content, iodine intake of our test infant population is substantially below the recommended level of 110–130 µg/day. Figure 3B indicates that if an infant of average weight, consuming an average quantity of breast milk, has a perchlorate intake corresponding to the median perchlorate content in this study, the NRC reference dose of 0.7 µg/kg/day (NRC 2005) will be exceeded for the first 2 months of his or her life. Figure 3C indicates that if perchlorate is indeed an order of magnitude or so more potent than thiocyanate in its power to inhibit iodide transport, the relative contribution of thiocyanate to iodine transport inhibition in an infant is small compared with that of perchlorate, where the infant consumes the median concentration of perchlorate and the median concentration of thiocyanate, within the limits of this study.

Single-membrane reverse-osmosis systems typically remove 80% of the perchlorate

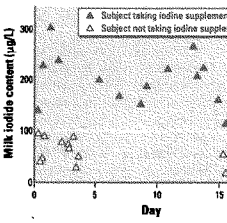

Figure 1. Iodide content of milk samples from two subjects (B, C). One has been taking an iodide supplement.

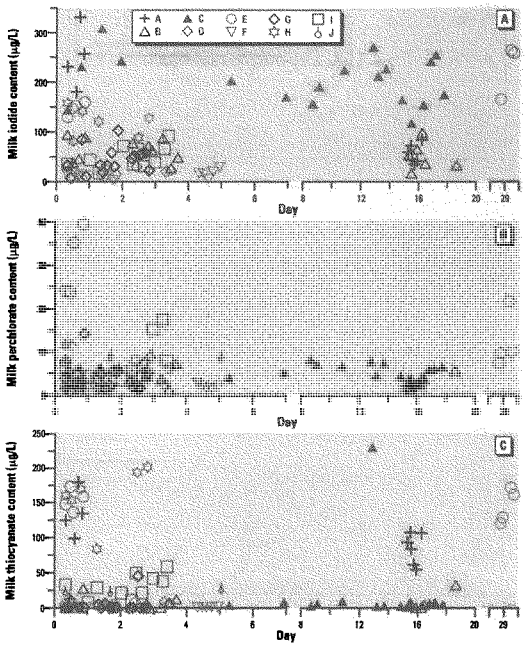

Figure 2. Temporal patterns for (*A*) iodide, (*B*) perchlorate, and (*C*) thiocyanate levels in human milk samples. Individual subjects are represented by symbols noted in key.

present (Foster Wheeler Environmental Corporation 1999). 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).

The significanr difference found between prebreakfast and postdinner perchlorate levels was not surprising, given its relatively short 8-hr half-clearance time in humans (Greer et al. 2002). Thiocyanate is thought to have a half-life of 1–6 days (Junge 1985; Schulz et al. 1979), and its excretion in milk is expected to be more stable over time.

If overall intake of iodide is sufficient, it is unlikely that milk with an occasional low iodide or high perchlorate content would pose a major risk to infants. However, the data presented here, admittedly limited, indicate that the milk of many women may not supply infants with adequate iodide, while the infants are also being exposed to significant levels of perchlorate. Such infants may be at risk of altered neurologic development due to iodine deficiency with exposure to iodide-uptake inhibitors posing an additional burden. We did not measure urinary iodine content of the subjects; this, together with breast milk iodine expression, would have allowed us an estimate of the overall iodine intake of the individual.

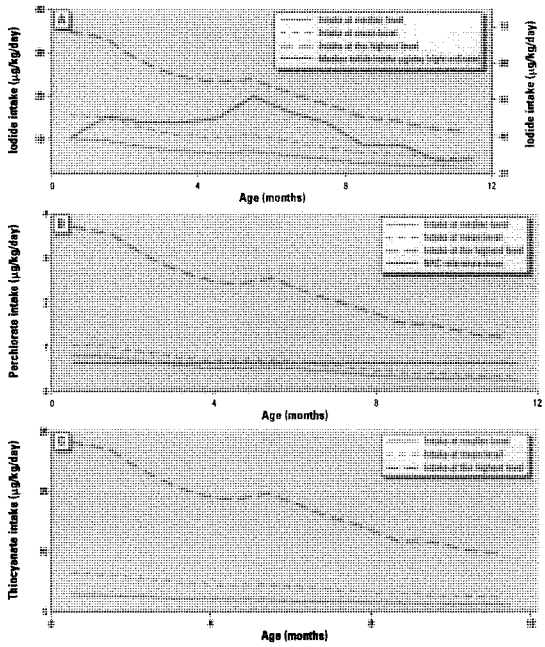

Figure 3. Projected iodide (*A*), perchlorate (*B*), and thiocyanate (*C*) intake of infants as a function of age corresponding to median, mean, and highest average values of each species in the sample population. See text for details.

The question as to whether milk iodide is low because of iodide-uptake inhibitors such as perchlorate and thiocyanate, or whether iodide levels are low simply because maternal intake is low, cannot be answered at present without the urinary data. It may be more important to base risk assessment for perchlorate exposure on the iodide:perchlorate ratio, or the ratio of iodide to "selectivity-weighted sum of iodide uptake inhibiting agents." If perchlorate uptake occurs 30 times more readily at the NIS *in vivo* as it appears to *in vitro* (Tonacherra et al. 2004), then an infant drinking milk with a ratio of 30:1 iodide:perchlorate may have an uptake ratio of 50:50 at its thyroid. If infants are able to use only half the iodide they receive in breast milk, potential iodine deficiency is a concern. For some individuals these ratios are relatively invariant on an order of magnitude scale, whereas wide variation is seen in others. The geometric mean of all the iodide:perchlorate molar ratio values is approximately 11. If the literature value for the *in vitro* results for iodide transport inhibition by perchlorate is applicable *in vivo*, then perchlorate may indeed be having a measurable effect on iodide transport. Similarly, the geometric mean of the iodide:thiocyanate and thiocyanate:perchlorate molar ratios are approximately 4.9 and 2.3, respectively, suggesting again that the effects of thiocyanate on iodide transport inhibition is less important than that of perchlorate in our sample population.

The real role, if any, of perchlorate in reduction of milk iodide levels is as yet unknown. Although there is evidence of inhibition from mathematical modeling (Almström 2006), this issue may be best examined through a controlled animal study; for a human study, at least simultaneous urinary data are needed to judge how intake affects expression. Our subjects had highly varied diets and varied timing of food intake; some used nutritional supplements and some did not. To further complicate correlations among analytes, the timing of milk sample collection was not uniform among donors or among days of individuals. The thyroid gland is adaptable and NIS expression increases when TH levels fall (Levy et al. 1997). NIS expression in the mammary gland is increased in response to prolactin, oxytocin, and β-estradiol (Tazebay et al. 2000), but it is not known whether mammary NIS is responsive to TSH (or some other signal) in a manner that would enable it to compensate for the presence of iodide-uptake inhibitors. Unfortunately, the degree to which the infant thyroid may be able cope with iodide-uptake inhibitors is also unknown.

Little is known about thiocyanate in human milk. To our knowledge, this is the first report of thiocyanate content of human milk in serial samples. Work was done on

thiocyanate excretion in human, bovine, and rat milk during the 1960s (Funderburk and Van Middlesworth 1967). These researchers also reported that dosing rats with perchlorate reduces thiocyanate excretion in milk. Laurberg et al. (2004) reported that maternal serum thiocyanate levels are strongly correlated with low milk iodide levels. Cassava, a staple food in some African regions, contains high levels of thiocyanate and may contribute to iodine deficiency. Mean thiocyanate levels in human milk from a region of northern Zaire, where cassava consumption is high, were reported at 513 μg/L (Vanderpas et al. 1984). The highest level of thiocyanate detected in our study was less than half this amount (228.3 μg/L). The mean for our cohort was approximately 6% of the mean calculated for the northern Zaire cohort.

The present research supports earlier findings that perchlorate is common, if not ubiquitous, in the milk of U.S. women. Little information has been available on the variability of perchlorate levels in milk in individuals. This lack of information has made it difficult to assess infant exposures. An apparent insufficiency of iodine in human milk is cause for concern. U.S. infants may be at risk of iodine deficiency. Whether such risk originates in dietary insufficiency or in exposure to iodide uptake inhibitors or both is not currently known. Although removal of perchlorate or other iodide transport inhibitors from U.S. food and water supplies may be a laudable goal, this does not appear to be imminent. An effort to phase in better iodine nutrition seems warranted.

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