



# STATE OF CONNECTICUT

## DEPARTMENT OF PUBLIC HEALTH

July 18, 2007

Congressman John Dingell  
US House of Representatives  
Committee on Energy and Commerce  
Washington, DC 20515-6115

Dear Congressman Dingell,

In response to your letter dated July 6, 2007, I have reviewed the questions from the Honorable Joe Barton and the Honorable John Shimkus from the House Committee on Energy and Commerce, Subcommittee on Environment and Hazardous Materials. I appreciate the opportunity to clarify the points that they raise as provided in the attachment. Thank you once again for taking my testimony on this important public health matter. Please let me know if I can be of further assistance.

Sincerely yours,

  
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1. *Congress has traditionally relied upon the guidance, assistance, and recommendations of the National Academy to resolve questions of science, including current efforts on climate change. The National Academy panel was comprised of 15 leading scientists and physicians with the wide ranging expertise necessary to evaluate all aspects of the available science related to perchlorate. Are you suggesting that you are right and the scientists appointed by the National Academy are wrong?*

Response: I appreciate that the committee members in particular and that Congress in general has great respect for the National Academy of Science process, expertise, and quality of reports. As a member of two National Academy committees myself (Human Biomonitoring Committee, report to Congress, July 2006; Improving USEPA Risk Assessment Methods, ongoing, expected report early 2008) I see first hand the high level of scientific deliberation and expert judgement.

However, no one panel can be constructed to answer all questions and that is why it is given a specific charge. The charge to the NAS perchlorate panel was to “assess the current state of the science regarding potential adverse effects of disruption of thyroid function by perchlorate ...” and “to determine whether EPA’s findings in its 2002 draft risk assessment, *Perchlorate Environmental Contamination: Toxicological Review and Risk Characterization*, are consistent with the current scientific evidence.” Finally, the Committee was to “suggest specific scientific research that could reduce the uncertainty in the understanding of human health effects associated with ingestion of low concentrations of perchlorate.” The charge was not to redo the USEPA risk assessment but to provide a scientific assessment of its validity and areas for improvement or new research. To meet the stated charge, the construction of the commitment may have been appropriate -- of the 15 members, 10 have academic posts, mostly in clinical or basic research settings. Of the other 5 members, 4 are consultants and only one is in a public health position. The strong emphasis on clinical and research expertise was appropriate for the committee to meet its charge of determining whether USEPA got the science

right. However, this particular NAS panel overstepped the charge and actually provided its own quantitative assessment of potency, dismissing the use of benchmark dose (BMD) analysis, and employing their own set of uncertainty factors to come up with an acceptable level of exposure (0.007 ug/kg/d, which corresponds to 24.5 ug/L in drinking water). The panel was not constructed for this activity as there were no (possibly one) members with expertise in the practice of risk assessment who works in public health. The types of expert judgement required for public health risk assessment requires years of experience with data analysis, statistical approaches to variability and uncertainty and the setting of uncertainty factors. This experience is so important because standards of practice have been developed to foster consistency between chemicals, media (water, soil, air, food), and sites (Superfund, Brownfields, others). Without the proper training and experience, the risk assessment will likely have arbitrary aspects and be out of line with modern practice. That unfortunately is the way that this particular document reads. The problem is not with the Committee's knowledge base to tackle the charge; the problem is that the Committee overstepped the charge. As one might expect, those are the areas in which the NAS perchlorate report are weakest. The dismissal of the BMD approach (which was used by USEPA in its draft assessment and also used by CalEPA in its final assessment) without proper justification and the inadequate application of uncertainty factors are two of the indicators that this report is not an improvement over perchlorate risk assessments that came before or after. Regarding uncertainty factors, the Committee felt comfortable with a rather minimal UF largely on the basis that they considered perchlorate's effect as a precursor effect and not a true adverse effect. However, they did not fully account for the variability between people such that relatively low levels of perchlorate in certain individuals (women with low iodine status) can actually experience decreased thyroid function (Blount, et al, 2006), an effect that would never have been predicted by the Committee. In fact, the recent data from CDC strongly suggest that the study relied upon by the CDC, the Greer study, underappreciated human variability and sensitivity to perchlorate. Obviously if that study had been published before the NAS report was completed, it may have changed their deliberations. However, now that it is published, it is important that EPA scientists and public health officials use it to refine the perchlorate risk assessment.

I don't believe this is a question of my being right and the NAS Committee on perchlorate being wrong. Staying within the charge, the NAS Committee provided useful information that I have no concern over. However, when venturing into the risk assessment arena, the NAS panel did not bring the type of perspective and analysis that is the standard in this field. This difference in perspective is important to public health at large because when dealing with millions of Americans you are more likely to see the small percentage problems. This is less the case for clinicians and academic researchers in university settings who may be studying effects in single individuals or small numbers of experimental groups. And of course, as I am writing this, I have the advantage of having seen the 2006 CDC study which bears out the importance of human variability in response to perchlorate, a study that the NAS Committee did not have at the time.

One additional note is that there was one dissenting opinion on the Committee that made it into the report regarding the size of uncertainty factors:

*"The RfD is derived from a study in which a group of only seven healthy adults was given 0.007 mg/kg of perchlorate daily for 14 days (Greer et al. 2002). Although two other studies had similar results, the total number of subjects is still small. In addition to the small number of subjects, no chronic exposure studies have been published. An uncertainty factor of 3 could account for the uncertainty surrounding the small number of subjects and the absence of a long-term study."*

- 2) *Isn't it true that the National Academy, in its recommendation, incorporated a 10-fold intra-species uncertainty factor to account for sensitive populations, including the fetuses of pregnant mothers with iodine deficiency or hypothyroidism?*

Response: Yes, this is true. However, as suggested by the one dissenting opinion on the Committee quoted above, this factor may not be large enough to address all the uncertainties in the perchlorate assessment. The difference between a small group of healthy volunteers tested in the Greer study (or in the occupational studies) vs. the general public in terms of iodine status, physiological status (particularly pregnancy which puts extra demands on the thyroid), medical status (e.g. preexisting thyroid

conditions) and exposure to other thyroid toxicants (PCBs, thiocyanate from cigarette smoke, nitrates in the diet, etc.) can easily span more than 10 fold. This 10 fold factor is of course a common risk assessment default for interindividual variability but should not be seen as highly conservative or a guarantee of protecting everyone. When interindividual variability is combined with the unknowns about human response to perchlorate and the substantial data gaps (e.g., longer-term testing), there is certainly wisdom in a larger than 10 fold total uncertainty factor.

This is especially the case given the uncertainty that the key endpoint from the Greer study chosen by the NAS Committee is in fact no effect level (NOEL). It was considered an effect level (LOAEL) by USEPA in the original risk assessment (2002) and by others (Ginsberg and Rice, 2005; Mass DEP, 2006). Further, CalEPA surpassed the NOEL/LOAEL level of analysis with a benchmark dose approach to show the statistically likely minimal effect level, which is below the dose chosen by the NAS as a NOEL (Ting, et al., 2006).

3) *The National Academy suggested level for perchlorate in drinking water that is based on "no observed effects" rather than the traditional approach using "no adverse effects." For regulatory and public health purposes, is a standard that uses a "no observed effects" level more conservative than a "no adverse effects" level?*

Response: First, it is incorrect to state that risk assessment traditionally only uses frankly toxic or adverse effects as a point of departure. Official USEPA guidance is to use an adverse effect or its precursor to set an RfD (USEPA, 2002). This is because of the recognition that affecting an upstream event in the steps leading towards toxicity (e.g., iodine uptake inhibition) leaves open the possibility that other exposures or events (e.g., co-exposure to anti-thyroid agents with similar mechanism or iodine deficiency) will compound the perchlorate effect and lead to an unpredictably large risk. One of the great

uncertainties in risk assessment is compounding of effect due to multiple chemical exposures. In fact, the public often loses confidence in risk assessment over the glaring “one chemical at a time” approach common to regulatory risk assessment. However, at least if we are starting from a point of no demonstrable biochemical effect that could be part of a toxic process, we are more guaranteed of no significant interactions or unpredictable risk. Therefore, the precursor effect of iodine uptake inhibition should have primacy in this risk assessment just as other precursor effects have in other risk assessments. The fact that the NAS Committee marginalized this effect on this basis again shows a lack of experience with the process. It appears that they were heavily influenced by the large degree of thyroid hormone reserve in typical adults such that a small amount of iodide uptake inhibition from low level perchlorate exposure could not plausibly have an effect on thyroid hormone status. As we learned from the CDC study (Blount, et al., 2006), this assumption is incorrect for at least 31% of US women who evidently have low iodine status and low thyroid hormone reserves. It is clear from the CDC study that the perchlorate effect is much more significant than some precursor finding with only theoretical but implausible connection to human risk.

4) *Dr. Utiger, your co-panelist, who has been a practicing physician specializing in thyroid function for 40 years, suggests that one of the best ways for people with hypothyroidism to compensate for potential perchlorate exposures is through greater dietary intake of iodine rich foods and vitamins. Yet, your testimony seems to reject these notions as inappropriate. What about your scientific background makes you more qualified to reject the health advice of this medical clinician?*

Response: Actually on this account I may not disagree very much with Dr. Utiger. Iodine supplementation is a good way to combat nutritionally-based thyroid insufficiency that is compounded by perchlorate exposure. Perchlorate is an excellent competitor for

thyroid uptake, its uptake being many times higher than iodide's. However, enough iodide can get into the thyroid if the diet is rich in this element. There is a question of how much is enough given the new data from FDA and other sources on the wide range of perchlorate concentrations in common vegetables, fruits and dairy. However, I would agree that iodide sufficiency is an important public health goal during pregnancy and nursing to combat the effects of perchlorate on the thyroid and neurodevelopment. However, equally important is diminishing perchlorate exposure where this is testable and intervention measures are available. A key arena in this regard is water supplies which are known to have substantial perchlorate contamination. Iodine supplementation will not solve the problem of environmental perchlorate because of the difficulty in getting everyone to an adequate level of education, nutrition and if necessary, supplementation. The fact that iodine intake has dropped approximately 30% in the US since the mid-1970s shows the challenge (Hollowell, et al.,1998). A combined approach to perchlorate mitigation via establishment of a health protective MCL in combination with campaigns to increase awareness about iodine during pregnancy and lactation will protect children from the harmful effects of perchlorate on brain development.

Finally, I believe the health advice of the medical clinician and public health toxicologist are both needed to move this issue forward.

## References

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