April 4, 2005

The Honorable Stephen L. Johnson
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Richard B. Johnston Jr., MD
Chair
National Academy of Sciences/ National Research Council
Board on Environmental Sciences and Toxicology
Committee to Assess the Health Implications of Perchlorate Ingestion
500 Fifth Street N.W., Washington, DC 20001

RE: Perchlorate: Addressing limits for perchlorate in drinking water based on assessments that protect pregnant women, infants and children.

We are writing to you today as representatives of learning and developmental disabilities organizations and environmental health groups interested in children's healthy neurodevelopment. Our concerns relate to ongoing efforts by the US Environmental Protection Agency (EPA) to address exposures to perchlorate and the need to address exposures to perchlorate from other sources.

We understand that the EPA has established an official reference dose for perchlorate at .0007mg/kg/bw, which is consistent with the recommended reference dose (RfD), included in the National Academies' National Research Council (NRC) January 2005 report. The National Research Council's RfD was twenty times higher than the RfD from the 2002 EPA risk assessment for perchlorate of .00003 mg/kg/bw. In addition, the EPA has also established a Drinking Water Equivalent Level (DWEL) of 24.5 ppb, using adult body weight and water consumption patterns and assuming 100% of exposure through food.

We do not believe the higher RfD, or the Agency's translation of the RfD into a DWEL, is protective of infants and children. Instead, we urge the Agency to use more protective standards for drinking water by including an assessment of aggregate exposures – an acute and chronic dietary risk assessment from food and drinking water combined. It is of concern that perchlorate has been found to be present in cow's milk – a staple for children—and in food grown in areas where perchlorate is present in irrigation water.

More recently, a study published *in Environmental Science and Technology* found an average concentration of 10.5 parts per billion in 36 breast milk samples, which would alone exceed the NRC/EPA reference dose of .0007 mg/kg/day for a three kilogram baby. Although this is a small study, it is based on the same number of volunteers used in the Greer study which formed the basis for the NRC-recommended RfD.

The NRC/EPA RfD (.7ug/kg/day) would translate for adults to .7 ug x 70 kg = 49 ug/day (using EPA default values for adult weight and water consumption). The concentration of perchlorate that would deliver this dose to a 70 kg. adult would be 49 ug/2L = 24.5 ug/Liter (or ppb). This is the number reported in news articles, and set by the Agency as a Drinking Water Equivalent Level. However for an infant, the EPA calculates a consumption rate of 161 ml/kg/day. The concentration of perchlorate in the baby's fluid intake required to deliver .7ug/kg/day should translate to a DWEL of (.7ug/kg) (.161 L/kg) = 4.35 ug/L (or ppb).

In short, it was of concern that news reports extrapolated the NRC report's RfD into a drinking water limit. However it is of greater concern that the EPA has adopted these numbers without making adequate adjustments to protect pregnant women, infants and children. NRC representatives have also remarked on the need to consider aggregate exposures and infants' and children's weights and fluid consumption patterns in making public policy decisions on perchlorate, such as drinking water limits. We recommend that the EPA address this need.

In addition, we would like to make the following points regarding the health risk assessments:

- In 2002 the EPA reported multiple lines of evidence to arrive at a conclusion regarding the developmental neurotoxicity of perchlorate. This should be the endpoint of concern. The experimental data cited in the EPA analysis showed evidence of changes in brain morphology, behavior and thyroid histopathology. The Lowest Observed Adverse Effect Level (LOAEL) calculated by EPA from the DNT studies was .01mg/kg/day. Although the NRC concluded that technical mistakes rendered these data unreliable, these data may in fact be correct.

- The Crump, et. al. study reported normal thyroid levels in Chilean mothers and children exposed to perchlorate in drinking water. However, the report did not include any measure of cognitive functioning, which would be an important health outcome to consider. In addition, the NRC report concluded that the very high levels of iodide in these Chilean populations would not have out-competed perchlorate at the sodium iodide symporter (NIS) However, a comparison of the Gibbs study (perchlorate and iodide in milk in Chilean nursing mothers) and the Kirk study suggest that this lower iodide levels in American nursing mothers is being limited by perchlorate.

- The NRC based the .0007 mg/kg/day RfD on a study wherein adults were administered doses of perchlorate and the inhibition of iodine uptake was measured. An uncertainty factor (UF) of 10 was used to account for the susceptibility of sensitive subpopulations. We support an additional UF of 3 because the No Observed Adverse Effect Level (NOAEL) identified – the low-dose of the Greer study – was very poorly powered as a point estimate of a no effect level. In fact, a power calculation shows that radioactive iodine uptake would have to be changed by 40% to have been measurable in that study.

- Clinical experimental studies cannot be conducted on children for ethical reasons. Therefore in order to assess safety for children, there is a need to respect, and rely on, the experimental animal data to understand the potential for increased susceptibility to the chemical during developmental stages.

- The NRC makes two unfounded assumptions critical to the establishment of a safe level of perchlorate exposure in a neonate. First is that iodide uptake inhibition must be severe – 75% – for a long period. There is simply no quantitative data to support this assumption, which likely accounts for the lack of citation for this assumption in the NAS report. Second is that neonates can compensate for iodide insufficiency. Again, there are no quantitative data to support this statement, and again, the NRC report contains no citations to defend these statements.

- The NRC notes that in the clinical study, there was compensation over time to thyroid perturbations via neuroendocrine feedback mechanisms to reset to new functional levels. However, the 1994 Cohen study noted that recalibration of the hypothalamic/pituitary/thyroid (HPT) axis during fetal exposure enhances susceptibility to additional exposures in later life. In addition, this study also suggested that extensive and/or repetitive insults to the neuroendocrine system will eventually limit the extent to which the system can respond to change.[1]

- The NRC noted that there were no prospective data on unborn children. However a study by Haddow et.al might be noteworthy in this regard. This retrospective study measured thyrotropin (TSH) levels in 25,216 stored serum samples from pregnant women. Women with either mild and treated, or undiagnosed, hypothyroidism gave birth to children with measurable deficits in various neurological realms, including attention, language and school performance at age seven compared to the children of mothers with normal thyroid levels during pregnancy.[2] In addition, these data are consistent with the extensive studies of Evelyn Man (Yale) in the 60's, and more recently of Victor Pop[3].

In April 1997 Executive Order 13045 (62 FR 19885) required all federal regulatory agencies to consider the environmental effects on children of their actions. Under this Executive Order, each agency must submit an evaluation of the regulation's effects on children's health when submitting an action. The NAS report, in our opinion did not direct sufficient attention, or give sufficient weight, to the evidence regarding developmental effects. We urge the EPA to base drinking water standards on infants and children's size and consumption patterns; and to consider seriously the points raised in this submission regarding the health risk assessments, in order to protect pregnant women, infants and children from hazardous levels of exposure to perchlorate.

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[1] Cohen IR. (1994) Addressing alterations in the neuroendocrine system: Some examples of methods and pitfalls Teratology; 49, (5):359.

[2] Haddow, JE; Palomaki, BS; Walter, CA; Williams, JR; Knight, GJ; Gagnon, J; O'Heir, CE; Mitchell, ML; Hermos, RJ; Waisbren, SE; Faix, JD; &Klein, RZ. (1999) Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. The New England Journal of Medicine, 341 (8) 549- 555.

[3] Pop VJ, Brouwers EP, Vader HL, Vulsma T, van Baar AL, de Vijlder JJ (2003) Maternal hypothyroxinaemia during early pregnancy and subsequent child development: a 3-year follow-up study. Clin Endocrinol (Oxf) 59:282-288 9-155, and Pop VJ, Kuijpens JL, van Baar AL, Verkerk G, van Son MM, de Vijlder JJ, Vulsma T, Wiersinga WM, Drexhage HA, Vader HL (1999) Low maternal free thyroxine concentrations during early pregnancy are associated with impaired psychomotor development in infancy. Clin Endocrinol (Oxf) 50:149-155.

Respectfully submitted,

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