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Sacramento

NATURAL RESOURCES DEFENSE COUNCIL

August 2, 2002

Dr. Joan E. Denton, Director
Office of Environmental Health Hazard Assessment (OEHHA)
1001 I Street
Sacramento, CA 95814

RE: Request for listing under Proposition 65 for Perchlorate

Dear Dr. Denton:

The Natural Resources Defense Council, As you Sow Foundation, Center for Environmental Health, Clean Water Action and the Environmental Working Group, hereby request that you nominate perchlorate salts to the State's Qualified Experts for listing under Proposition 65 as a developmental toxicant.

The Developmental and Reproductive Toxicants (DART) Identification Committee has the authority to list perchlorate as a chemical known to the state to cause reproductive toxicity under California Health and Safety Code § 25249.8(b) and 22 C.C.R. § 12305(b)(1). Exceptional circumstances due to the widespread exposure of California citizens to this hazardous chemical warrant an abbreviation of the typical prioritization procedures. We urge the Director to place perchlorate on the agenda of the next scheduled meeting of the DART Identification Committee following consultation with the Committee Chair, according to the abbreviated listing procedure described in OEHHA, Procedure for Prioritizing Candidate Chemicals for Consideration Under Proposition 65 by the "State's Qualified Experts," May 1997, p. 12 (visited July 23, 2002) <http://www.oehha.org/prop65/pdf/priodoc.pdf>.

As you know, OEHHA is currently already involved in evaluating the risk of perchlorate for purposes of developing a Public Health Goal in drinking water. The OEHHA draft risk assessment, as well as the U.S. EPA draft risk assessment for perchlorate, both conclude that this chemical is a developmental toxicant and that the potential for exposure is widespread. Therefore the chemical should be brought before the Developmental and Reproductive Toxicants Identification Committee in an expedited manner.

rg 71 Stevenson Street, Suite 1825
San Francisco, CA 94105
TEL 415 777-0220 FAX 415 495-5996

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Ammonium perchlorate (NH_4ClO_4), is used as an oxidizer in rocket propellants. Sodium perchlorate ($NaClO_4$) is used in explosives, and potassium perchlorate ($KClO_4$) is used in road flares and air bags. Perchlorate salts are also used in nuclear reactors and electronic tubes, in lubricating oils, leather tanning, fabrics, electroplating, aluminum refining, rubber manufacture, and the production of paints[1]. As a consequence of widespread use and water solubility, huge amounts of perchlorate have leached into surface and groundwater used as drinking water sources. Perchlorate is highly mobile in water and can persist for decades under typical ground and surface water conditions[2]. According to the California Department of Health Services (CDHS), perchlorate has been detected in 73 (10%) of 703 reporting public water systems.[3] A recent of analysis of CDHS drinking water quality monitoring data indicates that perchlorate has been detected in the drinking water of 7 million Californians.[4]

Perchlorate is a developmental toxicant with effects on the maternal and fetal thyroid gland and on fetal brain development. OEHHA's recent draft "Public Health Goal for Perchlorate in Drinking Water" focuses on the developmental toxicity of perchlorate. Perchlorate inhibits iodide transport into the thyroid by interfering with the sodium-iodide symporter (NIS). As a result, the effects of perchlorate exposure are similar to those of iodine deficiency. Even mild iodine deficiency during pregnancy has been shown to impair neuropsychological development and to reduce IQ in the child.[5]

Interference with maternal free T4 during gestation is directly related to fetal developmental disorders, particularly during the first and second trimesters. Maternal free T4 crosses the placenta and is converted to T3 in the fetal brain. T3 is critical for development of the cerebral cortex, the extrapyramidal system, and the cochlea.[6] The availability of maternal free T4 is crucial for normal fetal brain development in the first and second trimesters, as the fetal thyroid is not fully functional during that time period. Mild hypothyroidism or small decrements in maternal free T4, even within the "normal" range during the first trimester are associated with impaired neuropsychological development in the child.[7] Perchlorate's interference with iodine transport can significantly lower maternal free T4 levels during the first and second trimester of pregnancy, thereby causing developmental disorders in the offspring.

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[1] U.S. EPA Perchlorate Environmental Contamination: Toxicological Review and Risk Characterization Based on Emerging Information (External Review Draft). Office of Research and Development, Washington, D.C. NCEA-1-0503, 1998.

[2] Ibid

[3] California Department of Health Services, http://www.dhs.ca.gov/ps/ddwem/chemicals/perchl/perchlindex.htm, updated as of July 3, 2002.

[4] Sharp, R., Walker, B., Environmental Working Group, Rocket Science: Percholorate and the Toxic Legacy of the Cold War, July, 2001.

[5] Glorieux J, Desjardins M, Letarte J, Morissette J, Dussault JH. Useful parameters to predict the eventual mental outcome of hypothyroid children. Pediatr Res 24:6-8, 1988.

[6] Porterfield SP. Thyroid dysfunction and environmental chemicals – potential impact on brain development. Environ Health Perspect 108(Suppl. 3):433-438, 2000.

[7] Haddow JE, Palomaki GE, Allan WC, Williams JR, Knight GJ, Gagnon J, O'Heir CE, Mitchell M, Hermos RJ, Waisbren SE, Faix JD, Klein RZ. Maternal thyroid deficiency during pregnancy and subsequent neuropsychological development of the child. N Engl J Med 341:549-555, 1999.

- Adverse effects of perchlorate on the development of the fetal brain have been observed in rats.[8] In a study reported by Argus Research Laboratories, ammonium perchlorate in water was administered to female rats throughout gestation at doses of 0, 0.01, 0.1, 1 or 30 mg/kg/day. Several brain areas in the treated pups varied significantly from controls in size. Based on this data set, U.S. EPA identified a LOAEL of 0.0085 mg/kg-day for effects of perchlorate on fetal development.[9]

- Postel demonstrated that perchlorate crosses the placenta in guinea pigs and causes goiter in fetuses when administered at a level that does not cause goiter in the dam.[10]

- Another developmental neurotoxicity study of ammonium perchlorate in rats, also conducted by Argus Research Laboratories, exposed Sprague-Dawley rats via drinking water to doses of 0, 0.1, 1.0, 3.0, and 10 mg/kg/day.[11] Perchlorate was associated with brain morphological changes in the 10 mg/kg/day dose group and possibility also the 3 mg/kg/day group. The study revealed thyroid colloid depletion, hypertrophy, and hyperplasia in the 0.1 and 3 mg/kg/day dose groups, and thyroid hormone changes in the 0.1 and 1 mg/kg/day dose groups. In addition, behavioral changes were noted in the exposed animals.

- Perchlorate may also be a transplacental carcinogen. In one study, male rats from the F1 generation developed adenomas of the thyroid. These males were dosed from conception to 19 weeks of age at 30 mg/kg/day.[12]

- A study described by U.S. EPA studied the effects of perchlorate on thyroid and brain development pre- and post-natally.[13] Perchlorate was administered in drinking water to female rats prior to conception at 0, 0.01, 0.1, 1, or 30 mg/kg/day and continued throughout gestation and parturition. The thyroid weights of pups at all ages were significantly increased at 30 mg/kg/day. U.S. EPA noted that the $BMDL_{10}$ for colloid depletion was lowest in the gestation day

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[8] Argus Research Laboratories. Hormone, thyroid and neurohistological effects of oral (drinking water) exposure to ammonium perchlorate in pregnant and lactating rats and in fetuses and nursing pups exposed to ammonium perchlorate during gestation or via material milk. Protocol no. 1416-003. Argus Research Laboratories, Inc., Horsham, PA, 2001.

[9] U.S. EPA (2002). Perchlorate Environmental Contamination: Toxicological Review and Risk Characterization (External Review Draft). U.S. Environmental Protection Agency, Office of Research and Development, Washington, D.C. NCEA-1-0503.

[10] Postel S. Placental transfer of perchlorate and triiodothyronine in the guinea pig. Endocrinology 60:53-66, 1957.

[11] Argus Research Laboratories. A neurobehavioral developmental study of ammonium perchlorate administered orally in drinking water to rats. Protocol no. 1613-002. Argus Research Laboratories, Inc., Horsham, PA, 1998.

[12] U.S. EPA. Perchlorate Environmental Contamination: Toxicological Review and Risk Characterization (External Review Draft). U.S. Environmental Protection Agency, Office of Research and Development, Washington, D.C. NCEA-1-0503, 2002.

[13] Ibid.

21 pups, implying that the thyroid gland is most susceptible during gestation rather than postnatally. T4, T3, and TSH were affected in the fetuses, with dose-response relationships for all hormones. Size of various brain areas was also measured in brain sections. The striatum, cerebellum, and corpus callosum all showed significant differences from control with the lowest dose of ammonium perchlorate. U.S. EPA identified a LOAEL of 0.01 mg/kg/day for the adverse effects of ammonium perchlorate on the developing brain in rats.

- In another study by Argus Laboratories, female rats were dosed at 0, 0.01, 0.1, 1.0 and 30.0 mg/kg/day ammonium perchlorate in drinking water beginning 15 days before cohabitation and continuing through the day of sacrifice. All rats were sacrificed on gestation day 21. Preimplantation loss was noted at all dose levels. OEHHA analyzed the data and found that the increase in preimplantation loss was statistically significant in the 30 mg/kg-day group compared to controls.[14] A decrease in the number of live fetuses was also reported to be statistically significant at 30 mg/kg-day, although no significant decrease was noted in the lower groups. Ossification sites per litter were also significantly reduced at 30 mg/kg-day.

- Using data from a newborn screening registry, Schwartz et al. evaluated the serum T4 and TSH levels of all newborns in California during 1996.[15] All infants were screened for serum T4 levels, and the lowest T4 groups were further analyzed for TSH. Perchlorate exposure was estimated based on zip code, concentration of perchlorate in underground water sources, water source information, and characteristics of the water distribution system. After adjustment and separation into low, medium, and high exposure groups, the study found statistically significant associations between exposure and serum thyroid hormone levels. This study controlled for most important variables and found that even an extremely low level of perchlorate exposure through drinking water consumption was associated with a decreased serum T4 in newborns in California.

The severity of these health hazards combined with the widespread exposure of the public to perchlorate through the public drinking water systems of California necessitates that perchlorate be placed on the agenda of the next scheduled meeting of the DART Identification Committee for consideration to be listed under Proposition 65. Accordingly, we hereby request that you nominate perchlorate for listing by the DART Identification Committee.

Please feel free to contact Gina Solomon at NRDC (415.777.0220) if you have any questions or require further information.

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[14] Office of Environmental Health Hazard Assessment. Public Health Goal for Perchlorate (Peer Review Draft). March 2002.

[15] Schwartz J. Gestational exposure to perchlorate is associated with measures of decreased thyroid function in a population of California neonates [thesis]. University of California, Berkeley, CA, 2001.

Sincerely,

Gina Solomon

Gina Solomon, MD, MPH
Senior Scientist
Natural Resources Defense Council
71 Stevenson Street, Suite 1825
San Francisco, CA 94105

Larry Fahn

Larry Fahn
Executive Director
As You Sow Foundation
311 California Street, Suite 510
San Francisco, CA 94104

Katie Silberman

Katie Silberman
Public Policy Advocate
Center for Environmental Health
528- 61st St, Ste. A, Oakland, CA 94609

Bill Walker

Bill Walker
Vice President/West Coast
Environmental Working Group
1904 Franklin #703
Oakland CA 94612

Marguerite Young

Marguerite Young
California Director
Clean Water Action/ Clean Water Fund
814 Mission St, Suite 602
San Francisco CA 94103