EVIDENCE ON THE DEVELOPMENTAL AND REPRODUCTIVE TOXICITY OF

Perchlorate

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Reproductive and Cancer Hazard Assessment Section
Office of Environmental Health Hazard Assessment
California Environmental Protection Agency

PREFACE

The Safe Drinking Water and Toxic Enforcement Act of 1986 (commonly known as Proposition 65, codified at California Health and Safety Code 25249.5 *et seq.*) requires the Governor to published a list of those chemicals "known to the state" to cause cancer or reproductive toxicity. The Act specifies that "a chemical is known to the state to cause cancer or reproductive toxicity if in the opinion of the state's qualified experts the chemical has been clearly shown through scientifically valid testing according to generally accepted principles to cause cancer or reproductive toxicity" (Health and Safety Code Section 25249.8(b)). The lead agency for implementing Proposition 65 is the Office of Environmental Health Hazard Assessment (OEHHA), within the California Environmental Protection Agency. The "state's qualified experts" regarding findings of reproductive toxicity are identified as members of the Developmental and Reproductive Toxicant (DART) Identification Committee of the Office of Environmental Health Hazard Assessment's Science Advisory Board (Title 22, California Code of Regulations, section 12301).

Perchlorate (ClO_4) was proposed for consideration by the Developmental and Reproductive Toxicant (DART) Identification Committee by that Committee itself. At a meeting of the DART Identification Committee held on December 4, 2002, after considering a petition from several interested parties, the Committee asked OEHHA to take perchlorate out of the usual prioritization process order and to prepare hazard identification materials as resources were available.

These hazard identification materials were compiled to provide the Committee with relevant information for use in its deliberations. The attachments listed below are being provided to the Committee either in hard copy or on compact disc. The public can obtain Attachments I, III, IV (abstract only) and V through the OEHHA website at http://www.oehha.ca.gov/prop65/hazard_ident/hiddartmats2005.html. A full copy of Attachment IV can be requested from the Proposition 65 Implementation Office at (916) 445-6900. Attachment II can be read on-line or a hard copy ordered from the National Academy Press at http://www.nap.edu/catalog/11202.html.

A public meeting of the Committee will be held on August 11, 2005, in Sacramento, California. Following discussion and Committee deliberation, the Committee will determine whether perchlorate has been clearly shown through scientifically valid testing according to generally accepted principles to cause reproductive toxicity. Written public comments should be submitted to OEHHA by July 19, 2005, in order to be considered by the Committee in advance of the meeting. During the August 2005 meeting, the public will have an opportunity to present verbal comments to the Committee.

SUMMARY OF AVAILABLE INFORMATION

Ammonium perchlorate has been and continues to be used as an oxidizer in solid rocket propellant. Sodium perchlorate is used in slurry explosive, and potassium perchlorate is used in road flares and air bag inflation systems. Large volumes of perchlorate have been disposed of in California since the 1950's. Some of this has leached into soil, and into aquifers used as drinking water sources. Perchlorate is highly mobile in aqueous systems and can persist for many decades under typical ground and surface water conditions. Because perchlorate is a ubiquitous, aqueous environmental contaminant, perchlorate hazards and risks have been reviewed by other groups. Two documents addressing the risks posed by perchlorate in drinking water – a Public Health Goal document (OEHHA, 2004; Attachment I) and a National Research Council assessment (NRC, 2005; Attachment II) – include reviews of the developmental toxicity of perchlorate. These documents are being provided to the DART IC as background for its deliberation on the developmental and reproductive toxicity of perchlorate. As discussed in the OEHHA and NRC documents (Attachments I and II), perchlorate blocks uptake of iodine by the thyroid gland which may lead to decreased synthesis of the thyroid hormones, T_3 and T_4. These thyroid hormones are critical determinants of growth and development in fetuses, infants and young children. The sensitive subpopulations identified for this chemical are pregnant women and their fetuses, lactating women, and infants.

In addition to these documents, the committee is provided with some of the original studies on the developmental toxicity of perchlorate that were reviewed by OEHHA and the NRC in developing their documents, as well as a study evaluating the female reproductive system effects of perchlorate in rodents that has just become available.

ATTACHMENTS

In order to provide the DART Identification Committee with the scientific evidence on the potential for perchlorate to cause developmental and reproductive toxicity, the following documents are being provided to the Committee either in hard copy or electronic form and are incorporated herein by this reference. They are also available through the OEHHA website at www.oehha.ca.gov/prop65/hazard_ident/hiddartmats2005.html.

Attachment I. *Public Health Goals for Chemicals in Drinking Water – Perchlorate*, published by OEHHA in March 2004. The document supports OEHHA's Public Health Goal for perchlorate in drinking water. The issue of critical time periods of hypothyroxinemia and/or hypothyroidism during pregnancy and lactation and their role in increased risk for poor neuropsychological development of the fetus are discussed citing current findings in the area.

Attachment II. *Health Implications of Perchlorate Ingestion* authored by the National Research Council (NRC) and published by National Academy Press in 2005. This is the final report by the NRC Committee to Assess the Health Implications of Perchlorate Ingestion. National Research Council is an organization within the

National Academies. In its deliberations on the health effects of perchlorate in drinking water, the NAS committee considered pregnant women and their fetuses to be the most sensitive populations, and infants and developing children also to be sensitive populations.

Attachment III. Greer MA, Goodman G, Pleus RC, and Greer SE (2002). Health effects assessment for environmental perchlorate contamination: The dose-response for inhibition of thyroidal radioiodine uptake in humans. Environ Health Perspect. (110) 9; 927-937. This study, based on human trials of the effects of perchlorate exposure on iodine uptake by the thyroid, was used by OEHHA as the basis for the PHG for perchlorate, and by the NAS as the basis for estimating the Reference Dose (RfD) for perchlorate.

Attachment IV. Baldridge MG, Stahl RL, Gerstenberger SL, Tripoli V, Hutz RJ. (2004) In utero and lactational exposure of Long-Evans rats to ammonium perchlorate (AP) disrupts ovarian follicle maturation. Reprod Toxicol. 19(2):155-161. This study was published after the last meeting of the committee and was not reviewed in the NAS committee report.

Attachment Va. Report of a study conducted by Argus Laboratories entitled, *A neurobehavioral developmental study of ammonium perchlorate administered orally in drinking water to rats [report amendment: July 27]*. Protocol no. 1613-002. Argus Research Laboratories, Inc., Horsham, PA. (1998a). [Provided to the DART IC on compact disc.]

Attachment Vb. Report of a study conducted by Argus Research Laboratories entitled, *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 maternal milk*. Protocol no. 1416-003. Argus Research Laboratories, Inc., Horsham, PA. (2001). [Provided to the DART IC on compact disc.]

Attachment Vc. The following seven addenda items submitted by the authors and/or pathologist of the Argus studies to the U.S. EPA providing supplemental materials to the original reports (i.e., Attachments Va and Vb): [Provided to the DART IC on c.d.]

York, R. (1997) Genealogy of F1 generation rats (Argus protocol #1613-002), [w/TL to D Dodd 10/26/98]. Argus Research Laboratories, Inc; October 30.

York, R. G. (1998a) Update on additional items for 1613-002 [letter to Darol E. Dodd]. Horsham, PA: Argus Research Laboratories, Inc.; September 25.

York, R. G. (1998b) Protocol 1613-002 - A neurobehavioral developmental study of ammonium perchlorate administered orally in drinking water to rats. Sponsor's study

number: 7757A210-1096-25F [letter to Annie Jarabek]. Horsham, PA: Argus Research Laboratories, Inc.; October 2.

York, R. G. (1998d) Study 1613-002 - A neurobehavioral developmental study of ammonium perchlorate administered orally in drinking water to rats. Sponsor's study number: 7757A210-1096-25F [letter with attachments to Annie Jarabek]. Horsham, PA: Argus Research Laboratories, Inc.; November 5.

Consultants in Veterinary Pathology. (2001) Abbreviated morphometry report with appended thumbnails of scanned sections. Protocol 1416-003. 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 maternal milk. Murrysville, PA. (Supplement to neuropathology report on F1 generation day 10 and day 22 postpartum rats).

Garman, R. (2001b) The morphometry component of the perchlorate effects protocol [memorandum to Jean Harry]. Murrysville, PA: Consultants in Veterinary Pathology, Inc.; August 14.

Garman, R. H. (2001c) Perchlorate study [letter to Annie Jarabek regarding two topographs]. Murrysville, PA: Consultants in Veterinary Pathology, Inc.

Additional materials that may aid in the review of the reproductive toxicity of perchlorate including the Draft U.S. EPA Perchlorate Environmental Contamination: Toxicological Review and Risk Characterization (2002) are electronically available and may be downloaded/accessed at the websites below.

http://cfpub2.epa.gov/ncea/cfm/recordisplay.cfm?deid=24002

http://www.epa.gov/ncea/perchlorate/references2/