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Dr. Richard Johnston, Jr.
Chair
Committee to Assess the Health Implications of Perchlorate Ingestion
National Research Council Board on Environmental Studies and Toxicology
Committee on Toxicology
500 5th St., NW
Washington, DC 20001

Dear Dr. Johnston:

On behalf of the Center for Environmental Toxicology and the Department of Pharmacology at the University of Nebraska Medical Center, I am pleased to transmit to you 20 copies of "Perchlorate State of the Science Symposium 2003: Report of the Planning Committee and Reports of the Expert Review Panels." This report is the work product of the Perchlorate State of the Science Symposium, which we sponsored and held September 29–October 1, 2003, in Omaha, Nebraska.

My colleague Dr. Sam Sanderson and an independent expert from each of our four modules presented summaries of this work at the December 2003 meeting of the Committee in Irvine, California. At that time, you asked that we provide a copy of our written report as soon as practicable. The Planning Committee has added an overview paper setting forth the context for the Symposium: how it was organized, identification of all panelists with their expertise and affiliations, the conflict of interest disclosure statement that we used, and the complete Charge to Reviewers.

If you have any questions, or if there is any other way that we might assist the Committee in its efforts, please do not hesitate to contact me.

Sincerely,

A handwritten signature in dark ink, appearing to read 'Ercole Cavalieri'.

Ercole L. Cavalieri, D.Sc.
Professor and Director

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Perchlorate State of the Science Symposium 2003:

Report of the Planning Committee and

Reports of the Expert Review Panels

Planning Committee

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James D. Wilson, Ph.D.

Report of the Planning Committee

ABSTRACT

The Perchlorate State-of-the-Science Symposium (PS³) was designed to be an independent and impartial review of four fundamental science issues related to the potential health risks from low-level exposure to perchlorate. Researchers who performed the most important recent scientific studies published since 1999 were asked to present their work. Leading independent scientists evaluated these studies and developed consensus reports on the extent to which these studies had changed the state-of-the-science since 1999. Separate modules addressed the following questions: 1) Do rat brain morphometry studies show evidence of a neurodevelopmental hazard? 2) Do rat behavior studies show evidence of a neurodevelopmental hazard? 3) How do the available human data compare with data from animal studies? and 4) What effects in humans potentially attributable to perchlorate are adverse, adaptive, or pre-adaptive? This paper provides a brief introduction to perchlorate and a summary of the Symposium mechanics, including expert selection, conflict of interest and the Charge to reviewers. The four subsequent papers are summary reports of each expert panel that reviewed specific scientific information underlying the draft risk assessments of perchlorate prepared by various authorities. These papers are the work products of the experts and have been edited only for style by the Planning Committee.

1. INTRODUCTION

Perchlorate is the anion salt comprising the active ingredient in ammonium perchlorate, the major ingredient in solid rocket motors, fireworks, and automotive airbag inflators. It is a trace constituent of certain fertilizers and is known to be found naturally. The potassium ion of perchlorate has been used for pharmaceutical purposes for over 50 years.

Perchlorate can be detected at levels below 1 part per billion (ppb) in clean water, and has been detected at ppb levels at numerous places in the United States. As detection capability has improved, an increasing number of public and private drinking water supplies, food, and drinks have been identified as having trace levels of perchlorate.

Media reports allege that low-level perchlorate exposure may cause a host of thyroid disorders. Federal and State regulatory agencies have issued draft risk assessments concluding that low ppb-level exposures may pose potential health risks. These risk assessments have proved to be scientifically controversial, and a committee of the National Research Council is currently reviewing the underlying science to resolve these scientific disputes.

Determining “safe” levels of exposure is a practice that EPA, FDA, ATSDR, and various State environmental and health agencies perform as a precursor to setting enforceable regulatory standards. These standards usually are established under informal rulemaking such as the Administrative Procedure Act, but increasingly they are issued through guidance documents containing limited and often dated scientific information (1-4). Once disseminated, guidance documents and draft risk assessments become “influential” as defined in government-wide information quality guidelines (5,6) and are treated as authoritative by State regulatory agencies (7,8).

For perchlorate, EPA has disseminated four interim guidance documents (1-4); external review draft risk assessments in 1998 (9) and 2002 (10), and external peer review reports in 1999 (11) and 2002 (12), plus a fifth document to address the comments of peer reviewers and the public on the 2002 draft (13). EPA has proposed Reference Doses (RfD) of 0.0001 mg/kg-day (1992); 0.0001 to 0.0005 mg/kg-day (1995), 0.0009 mg/kg-day (1998), and 0.00003 mg/kg-day (2003). These RfDs translate into drinking water values of 4, 4-18, 32, and 1 ppb, respectively.

The most recent RfD proposed by EPA is derived primarily from animal studies reported to show changes in the brains of offspring whose mothers were exposed during pregnancy (14,15). EPA selected 0.01 mg/kg-day as the lowest observable adverse effect level (LOAEL) and applied a composite uncertainty factor of 300. EPA also derived an essentially identical RfD based on selected clinical data from healthy adults representing the threshold for iodide uptake inhibition, the first biochemical precursor to changes in thyroid hormones and thyroid stimulating hormone. In this alternative derivation, EPA selected 0.007 mg/kg-day as the LOAEL and applied a composite uncertainty factor of 100. Recently, California proposed a Public Health Goal of 2-6 ppb based on the same human data set, using 0.007 mg/kg-day as the LOAEL and a composite uncertainty factor of 30 (7,8).

It has been suggested that the similarities in these proposed “safe” values despite significant differences in data is evidence of scientific robustness (10,16). However, the nongovernmental RfD recommended by Strawson et al. (17), (0.006 mg/kg-day, composite UF=9; 70 ppb DWEL) could illustrate that the apparent robustness among governmental RfDs is not genuine, or that there is approximately two orders of magnitude of precautionary policy judgment embedded in the choice of uncertainty factors.

3. SYMPOSIUM MECHANICS

The present authors served as the Planning Committee for PS³. The Symposium was designed and intended to focus on underlying scientific issues rather than disputes about the most appropriate “safe” exposure level. Competing draft risk assessments were not reviewed. Three modules were developed to critically examine the quality of underlying scientific animal brain morphometry data, animal behavior data, and human clinical, occupational, and epidemiological data. A fourth module examined the array of health effects that were potentially attributable to

perchlorate and sought to characterize these effects as adverse, adaptive, or pre-adaptive. Expert panelists reviewed the critical studies, heard presentations by at least one author of each study, and interrogated the authors at length. Extensive opportunity also was provided for symposium registrants to pose questions. Expert panelists were selected by the Planning Committee in accordance with recently proposed government-wide peer review procedures (18). The symposium was held September 29—October 1, 2003, in Omaha, Nebraska.

External sponsorship and funding was provided in equal shares from federal agencies and the Perchlorate Study Group. The Society for Risk Analysis co-sponsored the event but did not provide funding. External sponsors did not participate in the selection of critical studies to review or expert panelists, or crafting the Charge to reviewers. Panelists, their fields of expertise, and their affiliations are presented in Appendix A. A conflict of interest disclosure statement is presented in Appendix B. The Charge to reviewers is presented in Appendix C. Information concerning the Symposium schedule, primary and secondary references, and additional presentations are reported elsewhere (<http://www.perchloratesymposium.com/references.asp#general>).