U.S. CONSUMER PRODUCT SAFETY COMMISSION
WASHINGTON, DC 20207

Todd Stevenson
Secretary
Office of the Secretary

Tel: 301-504-6836
Fax: 301-504-0127
Email: tstevenson@cpsc.gov

SEP - 9 2003

Dr. Kenneth Olden
Director
National Institutes of Health
National Institute of Environmental Health Sciences
P.O. Box 12233
Research Triangle Park, N.C. 27709

Dear Dr. Olden:

We are pleased to inform you, as required by the ICCVAM Authorization Act, that the US Consumer Product Safety Commission (Commission) voted unanimously on August 28, 2003 to approve the recommendations of ICCVAM that for the purpose of classification and labeling, the Revised Up-and-Down Procedure (UDP) be used instead of the conventional LD50 test to determine the acute oral toxicity hazard of chemicals. Further, the Commission also approved the recommendation to encourage the use of certain *in vitro* tests for determining the starting dose for acute systemic toxicity testing. The UDP can be used instead of the conventional LD50 for the purpose of classification for labeling under the Federal Hazardous Substances Act. (FHSA) (15 U.S.C. 1261-1278) Both the FHSA at 2(h)(2) and the supplemental definitions state that available data on human experience that indicate results different from those obtained in animals in the defined dosages or concentrations will always take precedence. This is true for both the conventional LD50 and the UDP. The briefing package sent to the Commission can be found on the Commission website (www.cpsc.gov) in the Library (FOIA) section at http://www.cpsc.gov/library/foia/foia03/brief/testing.pdf.

Sincerely,

Todd Stevenson

Todd Stevenson

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Institute of
Environmental Health Sciences
P.O. Box 12233
Research Triangle Park, N.C. 27709
Website: www.niehs.nih.gov

March 21, 2003

The Honorable Thomas H. Moore
Chairman
Consumer Product Safety Commission
Suite 724
4330 East West Highway
Bethesda, Maryland 20814

Dear Chairman Moore:

At the request of the Secretary of the Department of Health and Human Services, I am pleased to forward toxicological test recommendations from the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) for your consideration. These are the first test recommendations developed and transmitted to you pursuant to Section 3(e)(4) of the ICCVAM Authorization Act of 2000 (P. L. 106-545).

ICCVAM test recommendations on *in vitro* methods for acute systemic toxicity are based on the *Report of the International Workshop on In Vitro Methods for Assessing Acute Systemic Toxicity*, NIH Publication No. 01-4499 (Enclosure 1) and the *Guidance Document on Using In Vitro Data to Estimate In Vivo Starting Doses for Acute Toxicity*, NIH Publication No. 01-4500 (Enclosure 2). ICCVAM test recommendations are provided in the workshop report as Appendix I and applicable Federal regulations on acute toxicity are provided as Appendix F. The workshop was organized by ICCVAM and the National Toxicology Program's (NTP) Interagency Center for the Evaluation of Alternative Methods (NICEATM) and was sponsored by the Environmental Protection Agency (EPA), the National Institute of Environmental Health Sciences (NIEHS), and the NTP.

The workshop report identifies research, development, and validation activities that could advance the use of *in vitro* methods for predicting acute oral toxicity in animals and man. ICCVAM recommends that such activities should be considered along with other potential research efforts in establishing priorities. The guidance document, developed in response to workshop recommendations, describes how to use *in vitro* methods to estimate starting doses for acute oral toxicity animal tests. Preliminary data suggests that such an *in vitro* approach can further reduce the number of animals used for acute toxicity testing. ICCVAM recommends that Federal agencies consider making information about this *in vitro* approach available as one of the tools that can be used to select an appropriate starting dose for acute toxicity tests.

The workshop report, guidance document, and ICCVAM recommendations on these *in vitro* methods were made available to the public for comment via a *Federal Register* notice (Enclosure 3). Public comments (Enclosure 4) were reviewed by the ICCVAM, which recommended that they be made available to agencies along with ICCVAM test recommendations.

ICCVAM test recommendations on the revised Up-and-Down Procedure (UDP) (Appendix A of Enclosure 5) are based on the report: *The Revised Up-and-Down Procedure: A Test Method for Determining the Acute Oral Toxicity of Chemicals; Results of an Independent Peer Review Evaluation Organized by the ICCVAM and NICEATM*, NIH Publication No. 02-4501 (Enclosure 5). ICCVAM recommends that the UDP be used instead of the conventional LD50 test to determine the acute oral toxicity hazard of chemicals. When used in place of the conventional LD50, the UDP will reduce and refine animal use. Federal testing regulations for which the UDP may be applicable are provided as Appendix Q in the UDP report. The report on the Up-and-Down Procedure and ICCVAM recommendations were made available to the public for comment via a *Federal Register* notice (Enclosure 6). No comments were received.

Pursuant to Sections 4(a) and 4(d) of the ICCVAM Authorization Act, agencies are required to review ICCVAM test recommendations and notify the ICCVAM in writing of their findings, including identification of relevant test methods for which the ICCVAM test recommendations may be added or substituted, no later than 180 days after receipt of recommendations. Please send your agency's response to Dr. Kenneth Olden, Director, National Institute of Environmental Health Sciences, P.O. Box 12233, Research Triangle Park, NC 27709, tel 919-541-3201, fax 919-541-2260, email Olden@niehs.nih.gov. ICCVAM is required to make final ICCVAM test recommendations and the responses from agencies regarding such recommendations available to the public per Section 3(e)(6) of the Act. Accordingly, your response will be posted on the ICCVAM/NICEATM website at http://iccvam.niehs.nih.gov.

I appreciate your agency's participation on the ICCVAM. ICCVAM serves an important role in facilitating the scientific evaluation and adoption of test methods that will help protect human health and the environment while providing for improved animal welfare whenever possible.

Sincerely yours,

Kenneth Olden, Ph.D.
Director

Enclosures

cc:
CPSC ICCVAM Agency Representatives
Marilyn Wind, Ph.D., Vice-Chair, Principal Agency Representative
Kailash Gupta, Ph.D.
Susan Aiken, Ph.D.
Patricia Bittner, M.S.