DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service

National Institute of Environmental Health Sciences (NIEHS); National Toxicology Program (NTP); Notice of the Availability of Agency Responses to ICCVAM Test Recommendations for the Revised Up-and-Down Procedure for Determining Acute Oral Toxicity and In Vitro Methods for Assessing Acute Systemic Toxicity

Summary

The National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) announces the availability of Federal agency responses to Interagency Coordinating Committee on the Validation of Alternative Methods

(ICCVAM) test recommendations for: (1) The revised Up-and-Down Procedure (UDP) for determining acute oral toxicity and (2) *in vitro* methods for assessing acute systemic toxicity. Pursuant to sections 3 of the ICCVAM Authorization Act of 2000 [Pub. L. 106–545 (42 U.S.C. 285l–4)], ICCVAM is required to make final ICCVAM test recommendations and the responses from agencies regarding such recommendations available to the public.

Availability of Agency Responses

The agency responses to the ICCVAM test recommendations and other current information relevant to these test recommendations are available electronically (PDF and HTML formats) on the NICEATM/ICCVAM Web site at *http://iccvam.niehs.nih.gov.* Hard copy versions of these responses can be requested by contacting NICEATM at P.O. Box 12233, MD EC–17, Research Triangle Park, NC 27709 (mail), 919–541–2384 (telephone), 919–541–0947 (fax), or *niceatm@niehs.nih.gov.*

In summary, the Federal agencies agreed that the UDP had been adequately validated as a replacement for the conventional LD50 test and indicated to the extent applicable, that they will encourage the use of *in vitro* tests for determining starting doses for acute systemic toxicity testing.

ICCVAM Recommmendations

NICEATM announced availability of the ICCVAM recommendations for the UDP on February 7, 2002 (**Federal Register** Vol. 67, No. 26, pages 5842–5844). ICCVAM recommends based upon 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, that the UDP be used instead of the conventional LD50 test to determine the acute oral toxicity hazard of chemicals for hazard classification and labeling purposes.

NICEATM announced availability of the ICCVAM recommendations for the *in vitro* methods for assessing acute systemic toxicity on September 28, 2001 (**Federal Register** Vol. 66, No. 189, pages 49686–49687). ICCVAM recommends based upon the reports, *Report of the International Workshop on In Vitro Methods for Assessing Acute Systemic Toxicity,* NIH Publication No. 01–4499, and the *Guidance Document on Using In Vitro Data to Estimate In Vivo Starting Doses for Acute Toxicity,* NIH Publication No. 01–4500, that the *in vitro* methods be considered as a tool for estimating starting doses for animal tests of acute systemic toxicity.

Background Information on ICCVAM and NICEATM

The NIEHS established the ICCVAM in 1997 to coordinate the interagency technical review of new, revised, and alternative test methods of interagency interest, and to coordinate cross-agency issues relating to the validation, acceptance, and national/international harmonization of toxicological testing methods. ICCVAM was established as a permanent interagency committee of the NIEHS under the NICEATM on December 19, 2000, by the ICCVAM Authorization Act of 2000 (Pub. L. 106–545, available at *http://iccvam.niehs.nih.gov/about/PL106545.pdf*). The Committee is composed of representatives from fifteen Federal regulatory and research agencies that use or generate toxicological information. ICCVAM promotes the scientific validation and regulatory acceptance of toxicological test methods that will improve agencies' ability to accurately assess the safety or hazards of chemicals and various types of products, while refining (less pain and distress), reducing, and replacing animal use wherever possible. NICEATM administers the ICCVAM and provides scientific and operational support for ICCVAM and ICCVAM-related activities. NICEATM and ICCVAM work collaboratively to evaluate new and improved test methods applicable to the needs of Federal agencies. Additional information about ICCVAM and NICEATM can be found at the following Web site: *http://iccvam.niehs.nih.gov.*

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Samuel H. Wilson,

Deputy Director, National Institute of Environmental Health Sciences.

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