

DEPARTMENT OF HEALTH AND HUMAN SERVICES**National Toxicology Program (NTP); NTP Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM); Peer Review Panel Report on the Validation Status of New Versions and Applications of the Murine Local Lymph Node Assay (LLNA): A Test Method for Assessing the Allergic Contact Dermatitis Potential of Chemicals and Products: Notice of Availability and Request for Public Comments**

AGENCY: National Institute of Environmental Health Sciences (NIEHS), National Institutes of Health (NIH).

ACTION: Request for comments.

SUMMARY: NICEATM, in collaboration with the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM), convened an independent international scientific peer review panel on March 4–6, 2008 to evaluate new versions and applications of the LLNA for assessing the allergic contact dermatitis potential of chemicals and products. The peer review panel (“the Panel”) report from this meeting is now available. The report contains (1) the Panel’s evaluation of the validation status of the methods and (2) the Panel’s comments and conclusions on draft ICCVAM test method recommendations. NICEATM invites public comment on the Panel’s report. The report is available on the NICEATM–ICCVAM Web site at http://iccvam.niehs.nih.gov/methods/immunotox/llna_PeerPanel.htm or by contacting NICEATM at the address given below.

DATES: Written comments on the Panel report should be received by July 7, 2008.

ADDRESSES: Comments should be submitted preferably electronically via the NICEATM–ICCVAM Web site at http://iccvam.niehs.nih.gov/contact/FR_pubcomment.htm. Comments can also be submitted by e-mail to niceatm@niehs.nih.gov. Written comments can be sent by mail or fax to Dr. William S. Stokes, Director, NICEATM, NIH/NIEHS, P.O. Box 12233, MD EC–17, Research Triangle Park, NC 27709, (phone) 919–541–2384, (fax) 919–541–0947. Courier address: NICEATM, 79 T.W. Alexander Drive, Building 4401, Room 3128, Research Triangle Park, NC 27709.

FOR FURTHER INFORMATION CONTACT: Dr. William S. Stokes, Director, NICEATM (919–541–2384 or niceatm@niehs.nih.gov).

SUPPLEMENTARY INFORMATION:**Background**

In January 2007, the Consumer Product Safety Commission submitted a nomination to NICEATM and ICCVAM to assess the validation status of (1) The use of the LLNA to determine potency for hazard classification purposes; (2) LLNA protocols using non-radioactive procedures; (3) the LLNA limit dose procedure; and (4) the use of the LLNA to test mixtures, aqueous solutions, and metals (*i.e.*, an updated assessment of the applicability domain of the LLNA). In June 2007, the Scientific Advisory Committee on Alternative Toxicological Methods (SACATM) endorsed these activities as high priorities for ICCVAM. NICEATM, on behalf of ICCVAM, also sought input from the public on these activities and requested data from studies using the LLNA or modified versions of the LLNA (**Federal Register** Vol. 72, No. 95, pages 27815–27817, May 17, 2007). After considering all comments received, ICCVAM endorsed carrying out these activities as high priorities. ICCVAM also developed draft LLNA performance standards to facilitate evaluation of modified LLNA protocols that are functionally and mechanistically similar to the traditional LLNA. These draft LLNA performance standards were made public and comments were requested via the **Federal Register** (Vol. 72, No. 176, pages 52130–52131, Sept. 12, 2007).

ICCVAM and NICEATM prepared draft background review documents (BRDs) that provided comprehensive reviews of available data and relevant information for each of the modifications and new applications of the LLNA. ICCVAM also developed draft test method recommendations regarding the proposed usefulness and limitations, standardized protocols, and future studies. Both the draft BRDs and draft recommendations were made available for public comment, and a public peer review meeting was announced in the **Federal Register** (Vol. 73, No. 5, pages 1360–1362, Jan. 8, 2008).

The Panel met in public session on March 4–6, 2008. The Panel reviewed the draft ICCVAM BRDs for completeness, errors, and omissions of any existing relevant data or information. The Panel evaluated the information in the BRDs to determine the extent to which each of the applicable criteria for validation and acceptance of toxicological test methods (ICCVAM, 2003) had been appropriately addressed. The Panel then considered the ICCVAM draft test method

recommendations (*i.e.*, proposed test method uses, proposed recommended standardized protocol, proposed test method performance standards, and proposed additional studies) and commented on whether the recommendations were supported by the information provided in the draft BRDs.

The Panel's conclusions and recommendations are detailed in the *Peer Review Panel Final Report: Validation Status of New Versions and Applications of the Murine Local Lymph Node Assay (LLNA): A Test Method for Assessing the Allergic Contact Dermatitis Potential of Chemicals and Products* (available at http://iccvam.niehs.nih.gov/methods/immunotox/llna_PeerPanel.htm). The draft BRDs, draft ICCVAM test method recommendations, and the draft LLNA Performance Standards are available at <http://iccvam.niehs.nih.gov/methods/immunotox/immunotox.htm>.

Request for Comments

NICEATM invites the submission of written comments on the Panel's report. When submitting written comments, please refer to this **Federal Register** notice and include appropriate contact information (name, affiliation, mailing address, phone, fax, e-mail, and sponsoring organization, if applicable). All comments received will be made publicly available on the NICEATM–ICCVAM Web site at <http://ntp-apps.niehs.nih.gov/iccvampb/searchPubCom.cfm>. In addition, there will be an opportunity for oral public comments on the Panel's report during an upcoming meeting of SACATM scheduled for June 18–19, 2008. Information concerning the SACATM meeting will be published in a separate **Federal Register** notice and available on the SACATM Web site at <http://ntp.niehs.nih.gov/go/7441>.

ICCVAM will consider the Panel report along with SACATM and public comments when finalizing test method recommendations. An ICCVAM test method evaluation report, which will include the final ICCVAM recommendations, will be forwarded to relevant Federal agencies for their consideration. The evaluation report will also be available to the public on the NICEATM–ICCVAM Web site and by request from NICEATM (see **ADDRESSES** above).

Background Information on ICCVAM, NICEATM, and SACATM

ICCVAM is an interagency committee composed of representatives from 15 Federal regulatory and research agencies that use, generate, or disseminate

toxicological information. ICCVAM conducts technical evaluations of new, revised, and alternative methods with regulatory applicability and promotes scientific validation, regulatory acceptance, and national and international harmonization of toxicological test methods that more accurately assess safety and hazards of chemicals and products and that refine, reduce, and replace animal use. The ICCVAM Authorization Act of 2000 (42 U.S.C. 285f-3, available at http://iccvam.niehs.nih.gov/docs/about_docs/PL106545.pdf) established ICCVAM as a permanent interagency committee of the NIEHS under NICEATM. NICEATM administers ICCVAM and provides scientific and operational support for 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 NICEATM–ICCVAM Web site (<http://iccvam.niehs.nih.gov>).

Additional information about SACATM, including the charter, roster, and records of past meetings, can be found at <http://ntp.niehs.nih.gov/go/167>.

References

ICCVAM, 2003, ICCVAM Guidelines for the Nomination and Submission of New, Revised, and Alternative Test Methods. NIH Publication No. 03–4508. Research Triangle Park, NC: NIEHS. Available at: <http://iccvam.niehs.nih.gov>.

Dated: May 8, 2008.

Samuel H. Wilson,

Acting Director, National Institute of Environmental Health Sciences and National Toxicology Program.

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