DEPARTMENT OF HEALTH AND HUMAN SERVICES

National Toxicology Program (NTP) Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM); Draft Performance Standards for the Murine Local Lymph Node Assay: Request for Comments

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

ACTION: Request for comments.

SUMMARY: The Murine Local Lymph Node Assay (LLNA) is the first alternative test method evaluated and recommended by the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM). It was subsequently accepted by regulatory authorities to determine the allergic contact dermatitis potential of chemicals and products. In January 2007, the U.S. Consumer Product Safety Commission (CSPC) submitted a nomination requesting that NICEATM and ICCVAM assess the validation status of (1) The LLNA as a stand-alone assay for potency determination for hazard classification purposes; (2) modified LLNA protocols; (3) the LLNA limit test; (4) the use of LLNA to test mixtures, aqueous solutions, and metals; and (5) the applicability domain for LLNA. In order to facilitate the review of the modified LLNA protocols, ICCVAM proposed developing performance standards for the LLNA. In May 2007, a **Federal Register** notice was published (Vol. 72, No. 95, pages 27815–27817, May 17, 2007) requesting comments and data relevant to these nominated activities. In June 2007, the Scientific Advisory Committee on Alternative Toxicological Methods (SACATM) endorsed the nominated activities as high priorities for ICCVAM. In response to SACATM comments, along with those provided by the public in response to the previous **Federal Register** notice, ICCVAM also endorsed these activities as high priorities. ICCVAM subsequently prepared draft performance standards for the LLNA and now requests public comments on this draft document, which is available on the NICEATM/ICCVAM Web site at: (*http://iccvam.niehs.nih.gov/methods/immunotox/immunotox.htm*) or by contacting NICEATM (see **FOR FURTHER INFORMATION CONTACT** below).

DATES: Submit comments on or before October 29, 2007.

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

FOR FURTHER INFORMATION CONTACT: Other correspondence should be directed to Dr. William S. Stokes (919–541–2384 or *niceatm@niehs.nih.gov*).

SUPPLEMENTARY INFORMATION:

Background

The LLNA is an alternative test method used for skin sensitization testing that reduces the number of animals needed, reduces the time required for testing, and can substantially reduce or avoid pain and distress associated with traditional guinea pig testing methods. The LLNA was the first alternative test method evaluated and recommended by ICCVAM and based on the recommendations of ICCVAM and an independent scientific peer review panel, the LLNA has been accepted by U.S. and international regulatory authorities as an alternative to the guinea pig maximization test and Buehler test for assessing allergic contact dermatitis (EPA 2003; ISO 2002; OECD 2002). Since 2003, ICCVAM has routinely developed performance standards for test methods; however, because the concept of performance standards was not developed by ICCVAM until 2003, they were not developed during the ICCVAM evaluation of the LLNA in 1998 (NIH Publication No. 99–4494, available: (*http://iccvam.niehs.nih.gov/docs/immunotox_docs/llna/llnarep.pdf*).

In January 2007, CSPC submitted a nomination requesting that NICEATM and ICCVAM assess the validation status of (1) The LLNA as a stand-alone assay for potency determination for classification purposes; (2) modified LLNA protocols; (3) the LLNA limit test; (4) the use of LLNA to test mixtures, aqueous solutions, and metals; and (5) the applicability domain for LLNA. ICCVAM endorsed the nomination and also decided to develop performance standards to facilitate evaluation of modified LLNA protocols to the traditional LLNA. In May 2007, a **Federal Register** notice was published requesting comments and data relevant to these activities (Vol. 72, No. 95, pages 27815–27817, May 17, 2007; available,

http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/FR/FR_E7_9544.pdf). In June 2007, SACATM endorsed these activities as high priorities for ICCVAM. In response to SACATM comments, along with those provided by the public in response to the previous **Federal Register** notice, ICCVAM endorsed these activities, including the development of performance standards, as high priorities. ICCVAM subsequently prepared draft performance standards for the LLNA, which are available on the NICEATM/ICCVAM Web site at: (*http://iccvam.niehs.nih.gov/methods/immunotox/immunotox.htm*).

These draft test method performance standards are proposed to evaluate the performance of LLNA test methods that incorporate specific modifications to the measurement of lymphocyte proliferation in the traditional LLNA. These modifications focus specifically on incorporating non-radioactive procedures to evaluate lymphocyte proliferation in the draining auricular lymph nodes rather than incorporation of radioactivity (i.e., ^{3}H-thymidine), which is used in the traditional LLNA.

Public comments received in response to the draft LLNA performance standards will be considered by ICCVAM during development of a revised draft version of this document. A public meeting is planned for early 2008 where an international, independent, peer review panel will evaluate the revised draft LLNA performance standards and review the other nominated LLNA related activities. Following this meeting, the recommendations of the peer review panel will be made available for public and SACATM comment. ICCVAM will consider the panel report and public and SACATM comments in preparing final LLNA performance standards.

Request for Public Comments

NICEATM invites the submission of written comments on the draft LLNA performance standards. 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 by the deadline listed above will be placed on the NICEATM/ICCVAM Web site (*http://ntp-apps.niehs.nih.gov/iccvampb/searchPubCom.cfm*) and made available to the peer review panel and ICCVAM.

Background Information on ICCVAM and NICEATM

ICCVAM is an interagency committee composed of representatives from 15 federal regulatory and research agencies that use or generate toxicological information. ICCVAM conducts technical evaluations of new, revised, and alternative methods with regulatory applicability and promotes the scientific validation and regulatory acceptance of toxicological test methods that more accurately assess the safety and hazards of chemicals and products and that refine, reduce, or replace animal use. The ICCVAM Authorization Act of 2000 (42 U.S.C. 285*l*–3, available at *http://iccvam.niehs.nih.gov/about/PL106545.htm*) establishes 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 is available on the following Web site: *http://iccvam.niehs.nih.gov.*

Dated: September 5, 2007.

Samuel H. Wilson,

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

[FR Doc. E7–18011 Filed 9–11–07; 8:45 am]

BILLING CODE 4140–01–P