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

February 16, 1999

Ms. Carol Browner
Administrator
U.S. Environmental Protection Agency
401 M Street, S.W. (1101)
Washington, D. C. 20460-0003

Dear Ms. Browner:

I am pleased to provide you with the recently completed report: *The Murine Local Lymph Node Assay: A Test Method for Assessing the Allergic Contact Dermatitis Potential of Chemicals/Compounds* (Enclosure 1). The report describes the results of an independent peer review evaluation of the scientific validation status of this proposed test method. The review was coordinated by the Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) and the National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM).

I am pleased that your agency agreed to participate on the ICCVAM, which I established in response to P. L. 103-43 directives to NIEHS to establish criteria and processes for the validation and regulatory acceptance of toxicological test methods. The Local Lymph Node Assay (LLNA) is the first test method to undergo validation review by the ICCVAM on behalf of its 14 participating Federal agencies and programs. Independent scientific peer review, considered a prerequisite for regulatory acceptance, has now been completed for the LLNA; and the results are described in the enclosed report. The significant help that your agency staff provided for this review effort is gratefully acknowledged.

The ICCVAM and its Working Group of Federal scientists have reviewed the peer review report and fully concur with its conclusions and recommendations (Enclosure 2). The review panel that prepared the report concluded that the LLNA is a valid alternative to currently accepted guinea pig test methods for the assessment of allergic contact dermatitis (contact hypersensitivity). The ICCVAM agrees that the LLNA, when modified and used in accordance with the panel report, can be used effectively for assessment of allergic contact dermatitis potential.

The peer review of the test method was performed by a panel of international experts selected from suggestions received from Federal agencies, industry, and professional organizations. The panel considered all available information on the LLNA, including

comments and data submitted in response to a *Federal Register* Notice. The review was conducted in a public meeting where the opportunity for additional public comment was provided.

The final stage of regulatory acceptance involves determining the acceptability of the proposed method by regulatory agencies and informing the regulated community and others of the decision and its consequences regarding chemical testing under relevant regulatory authority. This is a critical last step in the ICCVAM process leading to the regulatory acceptance and use of scientifically validated new methods.

Accordingly, following your agency's review of the submission, I would ask that you inform the ICCVAM of the results of your determination of the method's acceptability, and of the steps you are taking to inform the regulated communities and others of your decision and availability of this method. I would appreciate a response regarding your agency's decision about the method by July 1, 1999. Information should be forwarded to Dr. William S. Stokes, NIEHS, P.O. Box 12233, Research Triangle Park, NC 27709, tel 919-541-7997, fax 919-541-0947, email stokes@niehs.nih.gov.

I would also like to discuss the regulatory acceptance status of the LLNA at the fall 1999 meeting of the NTP Advisory Committee on Alternative Toxicological Methods. The critical stage of regulatory acceptance was a topic of concern at a recent meeting of the Advisory Committee, which provides advice on the activities and priorities of the ICCVAM and NICEATM. I therefore invite you to send a representative to this meeting to discuss your agency's consideration of the LLNA and the overall process used by your agency to consider new methods recommended by ICCVAM.

Thank you for joining together with the NIEHS to consider this first new test method. I look forward to your agency's continued participation in these efforts to identify and adopt methods that will provide for improved protection of human health and the environment.

Sincerely yours,

/s/

Kenneth Olden, Ph. D.
Director

Enclosures

cc:
Ms. Susan Wayland, Acting AA for OPPTS, EPA
Dr. Norine Noonan, AA for ORD, EPA