



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460



OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

December 10, 2010

Rear Admiral William S. Stokes, Director, National Toxicology
Program Interagency Center for the Evaluation of Alternative Toxicological Methods
National Institute of Environmental Health Sciences
P.O. Box 12233, Mail Code K2-16
Research Triangle Park, NC 27709

Dear Dr. Stokes:

This letter is in response to Dr. Linda S. Birnbaum, Director, National Institute of Environmental Health Sciences June 10, 2010 request to the Administrator of EPA that the Environmental Protection Agency review the suitability of test method recommendations for the LLNA: BrdU-ELISA and the LLNA: DA, two nonradioactive versions of the murine local lymph node assay (LLNA), and an expanded LLNA applicability domain. The supporting materials for the development of these recommendations are contained in reports entitled: 1) ICCVAM Test Method Evaluation Report on the Mouse Local Lymph Node Assay: BrdU-ELISA A Nonradioactive Alternative Test Method to Assess the Allergic Contact Dermatitis Potential of Chemical and Products (NIH Publication No. 10-7552); 2) ICCVAM Test Method Evaluation Report on the Murine Local Lymph Node Assay: DA A Nonradioactive Alternative Test Method to Assess the Allergic Contact Dermatitis Potential of Chemical and Products (NIH Publication No. 10-7551); and, 3) ICCVAM Test Method Evaluation Report on Using the Mouse Local Lymph Node Assay for Testing Pesticide Formulations, Metals, Substances in Aqueous Solutions, and Other Products (NIH Publication No. 10-7512).

Staff in EPA's Office of Pesticide Programs found ICCVAM's evaluation and recommendations about the reduced LLNA assay to be technically sound and appropriate for Agency use. Although EPA does not have a plan in place to update the OPPTS LLNA guidelines using the updated nonradioactive ICCVAM LLNA test method protocol or performance standards, it is our hope that OECD will soon undertake a revision of the LLNA guideline informed by these ICCVAM recommendations.

We appreciate ICCVAM's recommendations that the LLNA now may be used to test most chemicals and products for allergic contact dermatitis potential. The Program will use these recommendations and other scientific findings to improve our testing guidelines and to inform our discussions with the regulated community, and general public, to promote public health protection and the refinement, reduction and ultimate replacement of animals for testing.

The U.S. Environmental Protection Agency (EPA) appreciates the opportunity to review these materials, and it acknowledges the enormous amount of work that went into the evaluation and peer review. EPA further notes that the updated nonradioactive LLNA protocol not only reduces the number of animals under test but that it eliminates the need for the use of radioactivity. We are committed to advancing the "three Rs" principles of reduction, refinement and replacement of animal use, where possible, in Agency programs.

Sincerely,

/s/

John R. Fowle III, Ph.D., D.A.B.T.
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