



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



March 5, 2010

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

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 September 18, 2009 request to the Administrator of EPA that the Environmental Protection Agency review the suitability of 1) the updated test method protocol for the reduced murine local lymph node assay and 2) the updated test method performance standards for the local lymph node assay (LLNA). The supporting materials for the development of these recommendations are contained in a report entitled: 1) ICCVAM Test Method Evaluation Report: The Reduced Murine Local Lymph Node Assay: An Alternative Test Method Using Fewer Animals to Assess the Allergic Contact Dermatitis Potential of Chemicals and Products (NIH Publication No. 09-6439); and, 2) Recommended Performance Standards: Murine Local Lymph Node Assay (NIH Publication No. 09-7357).

Staff in EPA's Office of Pesticide Programs for review found ICCVAM's evaluation and recommendations about the reduced LLNA assay to be technically sound and appropriate for Agency use. We 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.

OPP has already used the ICCVAM rLLNA recommendations in a draft white paper proposal to initiate a pilot for the "reduced dose" LLNA radio labeled assay. Once the pilot is initiated OPP will start accepting for review the rLLNA where it is applicable to do so. Although EPA does not have a plan in place to update the OPPTS LLNA guidelines using the updated 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 the ICCVAM rLLNA recommendations.



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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 LLNA protocol reduces the number of animals per dose group from 5 (the original) to 4 (updated protocol), based on data analyses done by ICCVAM. We appreciate the time and energy ICCVAM devotes to advancing the "three Rs" principles of reduction, refinement and replacement of animal use. We look forward to continuing interactions with ICCVAM as part of the Agency's commitment to applying the 3 R's, where possible, in Agency programs.

Sincerely,

/s/

John R. Fowle III, Ph.D., D.A.B.T.
Principal Agency ICCVAM Representative
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Office of Pesticide Programs