



National Institutes of Health
National Institute of
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MEMORANDUM

DATE: March 17, 2010

TO: The Interagency Coordinating Committee on the Validation of Alternative Methods

FROM: Director, National Institute of Environmental Health Sciences and the National Toxicology Program

SUBJECT: NIEHS Response to ICCVAM Test Recommendations on New Versions and Performance Standards for the Local Lymph Node Assay

On September 18, 2009, at the request of the Secretary of the Department of Health and Human Services, I forwarded toxicological test recommendations from the Interagency Coordinating Committee on the Validation of Alternative Methods (ICVAM) to 14 Federal agencies for their consideration. The recommendations were developed and transmitted pursuant to Section 3(e)(4) of the ICCVAM Authorization Act of 2000 (42 U.S.C. 285l-3). Pursuant to Sections 4(a) and 4(d) of the ICCVAM Authorization Act, agencies are required to review ICCVAM test recommendations and notify ICCVAM in writing of their findings, including identification of relevant test methods for which the ICCVAM test recommendations may be added or substituted. This memorandum provides the NIEHS response to ICCVAM regarding the test recommendations.

NIEHS has reviewed the ICCVAM test recommendations relevant to the murine local lymph node assay (LLNA), a test method used to assess the potential for chemicals and products to cause allergic contact dermatitis (ACD). ICCVAM recommendations were provided for an updated LLNA protocol, a reduced LLNA procedure (rLLNA), and LLNA test method performance standards. Recommendations for the updated test method protocol and the rLLNA are provided in the report, *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). The LLNA test method performance standards are provided in the report, *Recommended Performance Standards: Murine Local Lymph Node Assay* (NIH Publication No. 09-7357).

NIEHS agrees with the ICCVAM test recommendations for the updated LLNA test method protocol and agrees that the updated protocol should be used in place of the LLNA test method protocol recommended by ICCVAM in 1999. The updated LLNA test method protocol will reduce the number of animals required compared to the original recommended LLNA protocol by 20% and will provide for more consistent and reproducible testing results.

NIEHS also agrees with the ICCVAM test recommendations for routine consideration and use of the rLLNA to determine the ACD potential of chemicals and products. Using the rLLNA where appropriate can reduce animal use by 40% for each test compared to the multiple-dose LLNA.

NIEHS also agrees with the ICCVAM recommendations for LLNA test method performance standards. These performance standards can be used to more efficiently evaluate the validity of modified test methods that are similar to the traditional LLNA.

NIEHS is not a regulatory agency and therefore does not promulgate regulatory testing requirements or guidelines for which the ICCVAM recommendations may be applicable. However, NIEHS does conduct allergic contact dermatitis testing as part of its National Toxicology Program activities. NIEHS and the NTP will routinely consider the updated LLNA test method protocol and the rLLNA and use these when determined scientifically appropriate.

NIEHS scientists and the NIEHS Institutional Animal Care and Use Committee (IACUC) have been informed about the availability of the updated LLNA test method protocol and the rLLNA and advised that these alternative methods should be routinely considered when planning animal studies to evaluate the allergic contact dermatitis hazard potential of chemicals and products in order to minimize animal use and to avoid pain and distress. The NIEHS IACUC has also been asked to ensure that these alternative methods are always considered whenever applicable in accordance with the Public Health Service Policy on Humane Care and Use of Laboratory Animals and applicable USDA Animal Welfare Act Regulations and to ensure that the methods are used when determined appropriate.

NIEHS appreciates ICCVAM's comprehensive evaluation of these alternative safety testing methods. NIEHS remains highly committed to the development, validation, and regulatory acceptance of scientifically sound alternative safety testing methods that will support improved protection of people, animals, and the environment while providing for improved animal welfare.

/s/

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cc:

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