Subject: [Iccvam-all] Federal Agencies Respond to ICCVAM Recommendations on Alternative Method to Identify Chemicals Most Likely to Cause Allergic Contact Dermatitis

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The Interagency Coordinating Committee on the Validation of Alternative Methods (ICCVAM) recommended to Federal agencies that the murine local lymph node assay, or LLNA, may be used to categorize the potency of chemicals causing allergic contact dermatitis (ACD) in humans. Specifically, ICCVAM recommended that the LLNA may be used to categorize some substances as strong sensitizers, thus identifying those substances considered to have a significant potential for causing skin hypersensitivity resulting in ACD.

In today's Federal Register, the National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) announced availability of Federal agency responses to the ICCVAM recommendations. Regulatory agencies, including FDA, EPA, CPSC, and OSHA, have indicated that they will take actions in response to the ICCVAM recommendations to encourage use of the LLNA for this purpose where appropriate.

According to the U.S. Bureau of Labor Statistics, skin diseases are the most common type of occupational illness. Many of these cases arise from repeated exposures to skin-sensitizing substances, which can lead to ACD, an immunologically mediated hypersensitivity reaction. Studies have shown that ACD has a significant adverse impact on quality of life in affected individuals.

For over 10 years, the LLNA has been accepted worldwide as a valid alternative to traditionally accepted guinea pig test methods for assessing ACD hazard potential for most testing applications. The new ICCVAM recommendation provides guidance on how to use the LLNA to categorize some chemicals and products as strong skin sensitizers. However, since only half of the known strong human skin sensitizers can be identified in this way (52% or 14 out of 27), additional testing or information will be necessary to conclude that substances are not strong skin sensitizers.

Substances with the potential to cause ACD can also be categorized with the traditional test methods using guinea pigs. However, the LLNA uses fewer animals than guinea pig test methods, requires less time to perform, provides dose-response information, and, in most cases, eliminates the potential for pain and distress in the test animal. In accordance with Animal Welfare Act regulations and the Public Health Service Policy on Humane Care and Use of Laboratory Animals, the LLNA should be routinely considered when planning animal studies that evaluate whether chemicals and products are strong sensitizers in order to minimize animal use and to avoid pain and distress.

The ICCVAM evaluation is detailed in a report entitled ICCVAM Test Method Evaluation Report: Usefulness and Limitations of the Murine Local Lymph Node Assay for Potency Categorization of Chemicals Causing Allergic Contact Dermatitis in Humans (NIH Publication No. 11-7709). In June 2011, ICCVAM forwarded recommendations to Federal agencies and made these recommendations available to the public (76 FR 18639). In accordance with the ICCVAM Authorization Act of 2000 (42 U.S.C. 285l-3), agencies have notified ICCVAM in writing of their findings, and ICCVAM is making these responses available to the public.

NICEATM and ICCVAM are also currently evaluating several in vitro and in chemico methods for their potential to further reduce and eventually replace the use of animals for ACD safety testing.

The Federal agency responses to the ICCVAM recommendations and more information about the ICCVAM evaluation of the LLNA for potency categorization can be found on the NICEATM-ICCVAM website at: http://iccvam.niehs.nih.gov/methods/immunotox/LLNApotency.htm

The ICCVAM Test Method Evaluation Report is available on the NICEATM-ICCVAM website at:

http://iccvam.niehs.nih.gov/methods/immunotox/LLNA-pot/TMER.htm

The Federal Register notice announcing the availability of Federal agency responses to the ICCVAM recommendations is available at:
http://iccvam.niehs.nih.gov/SuppDocs/FedDocs/FR/FR-2012-4541.pdf

About NICEATM and ICCVAM
ICCVAM is an interagency committee composed of representatives from 15 U.S. Federal regulatory and research agencies that require, use, generate, or disseminate toxicological and safety testing information. ICCVAM conducts technical evaluations of new, revised, and alternative safety testing methods and testing strategies with regulatory applicability. ICCVAM also promotes the scientific validation and regulatory acceptance of safety testing methods and strategies that more accurately assess the safety and health hazards of chemicals and products and that reduce, refine (enhance animal well-being and lessen or avoid pain and distress), or replace animal use. NICEATM administers ICCVAM and provides scientific and operational support for ICCVAM-related activities. NICEATM also conducts independent validation studies to assess the usefulness and limitations of new, revised, and alternative test methods and strategies.

NICEATM, ICCVAM, and ICCVAM member agencies have contributed to the approval or endorsement of over 40 alternative safety-testing methods by Federal regulatory agencies and international organizations since the establishment of ICCVAM in 1997. Appropriate use of these test methods can significantly reduce animal use and improve animal welfare. Critical research, development, and validation efforts needed to further advance numerous other alternative methods have also been identified.

NICEATM and ICCVAM welcome nominations and submissions of alternative safety testing methods and testing strategies for validation studies and/or technical evaluations. Nominations and submissions are welcome from any individual or organization. Please contact NICEATM at niceatm@niehs.nih.gov for more information or to discuss a possible nomination or submission.

Additional information about other NICEATM and ICCVAM activities can be found on the NICEATM-ICCVAM website at http://iccvam.niehs.nih.gov/. Thank you for your interest and your support of NICEATM and ICCVAM.

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