

**Session: Regulations and Policy Implications in Toxicology  
8:30 AM – 12:00 PM, Thursday, March 19  
Ballrooms I-IV**

## **ICCVAM Performance Standards for the Murine Local Lymph Node Assay (LLNA)**

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ICCVAM develops performance standards to facilitate the efficient validation of modified versions of adequately validated alternative test methods. ICCVAM recently developed performance standards based on the ICCVAM-recommended LLNA protocol (ICCVAM 1999). The protocol was revised recently to reduce the minimum number of mice per dose group from five to four, and to provide guidance on reducing the number of positive control animals and determining the appropriate highest test dose. The performance standards include essential test method components, a minimum list of reference substances, and standards for accuracy and reliability. Essential test method components are the structural, functional, and procedural elements of a validated test method that must be included in a modified method in order for it to be evaluated using the established performance standards. Essential components of the LLNA include topical application of the test substance to the ears of mice, measurement of lymphocyte proliferation in the lymph nodes draining the area of test substance application, and use of the maximum soluble dose that does not result in systemic toxicity or excessive local irritation. The minimum list of reference substances for these LLNA performance standards includes 13 sensitizers and 5 non-sensitizers. The accuracy and reliability standards to be achieved by a modified LLNA are based on the performance of the traditional LLNA. These LLNA performance standards will facilitate rapid and efficient validation of modified LLNA protocols, such as those using non-radioactive markers of lymphocyte proliferation. New versions of the LLNA that provide improved performance or other advantages are expected to result in broader use of the LLNA, which will further reduce and refine animal use for allergic contact dermatitis assessments while ensuring human safety.

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Keywords: allergic contact dermatitis; skin sensitization; murine local lymph node assay; performance standards; alternative methods; protocol