

## ICCVAM Recommendations for Use of the LLNA for Evaluating the Allergic Contact Dermatitis Potential of Pesticide Formulations

J Matheson<sup>1</sup>, A Jacobs<sup>2</sup>, M Wind<sup>1</sup>, J Chen<sup>3</sup>, M Hashim<sup>3</sup>, M Lewis<sup>3</sup>, E Margosches<sup>3</sup>, D McCall<sup>3</sup>, T McMahon<sup>3</sup>, J Redden<sup>3</sup>, R Ward<sup>3</sup>, W Stokes<sup>4</sup>

<sup>1</sup>U.S. CPSC, Bethesda, MD; <sup>2</sup>U.S. FDA, Silver Spring, MD; <sup>3</sup>U.S. EPA, Washington, DC;

<sup>4</sup>NICEATM, NIEHS, RTP, NC

ICCVAM has updated its 1999 validation report on the LLNA based on a recent evaluation of the usefulness and limitations of the LLNA for assessing the skin sensitizing potential of pesticide formulations. This review was initiated because the original report did not include an analysis of the LLNA for these types of substances, and there were growing regulatory concerns that the LLNA might not identify sensitizing pesticide formulations. LLNA data from 104 formulations were included in the evaluation, most of which are water soluble and therefore were tested in an aqueous vehicle (1% Pluronic L92). Of the pesticide formulations for which LLNA and guinea pig data were available (n=23), the LLNA classified 52% (12/23) as sensitizers, while GP tests classified only 13% (3/23) as sensitizers. All three of the pesticide formulations identified as sensitizers in the GP test were also identified as sensitizers in the LLNA; there were no instances of underprediction by the LLNA. Thus, there is a greater likelihood of obtaining a positive result in the LLNA than in a GP test. These studies also provide data for aqueous solutions that emphasize the need for careful selection of an appropriate vehicle that maintains test substance contact with the skin (e.g., 1% Pluronic L92) to achieve adequate exposure when testing such substances. Based on these data, ICCVAM agreed with an international peer review panel that the LLNA could be used for testing pesticide formulations, and any other products, unless there are unique physicochemical properties that may interfere with the ability of the LLNA to detect sensitizing substances. ICCVAM recommendations are being forwarded to Federal agencies for their consideration for future regulatory acceptance. These recommendations should expand the use of the LLNA for skin sensitization testing, thereby reducing and refining animal use for this purpose.

Character Count: 2271/2300

Keywords: allergic contact dermatitis; skin sensitization; murine Local Lymph Node assay; applicability domain; alternative methods; pesticide formulations; other products; metals; aqueous solutions

Categories: Regulatory/Policy (Hypersensitivity - 2nd choice)