ICCVAM Evaluation and Recommendations on the Nonradioactive LLNA: DA for Evaluating Allergic Contact Dermatitis Hazards

J Matheson[1], A Jacobs[2], M Wind[1], P Brown[2], R Ward[3], E Margosches[3], W Stokes[4]

[1]U.S. CPSC, Bethesda, MD; [2]U.S. FDA, Silver Spring, MD; [3]U.S. EPA, Washington, DC; [4]NICEATM/NTP/NIEHS/NIH/DHHS, RTP, NC

ICCVAM assessed the usefulness and limitations of the LLNA: DA, a nonradioactive local lymph node assay (LLNA) that measures ATP content as an indicator of lymphocyte proliferation and, in turn, potential allergic contact dermatitis (ACD) hazards. Accuracy when compared to the traditional LLNA was assessed based on data generated with 44 substances and using several different stimulation indices (SI) as decision criteria. Optimal performance was achieved using SI $\geq$ 1.8; the LLNA: DA correctly identified all 32 LLNA sensitizers (0% [0/32] false negatives), and 9/12 LLNA nonsensitizers (25% [3/12] false positives). The 3 false positives had maximum SI between 1.8-2.5. There were 14 substances with repeat tests; results for 80% (8/10) of the LLNA sensitizers and 75% (3/4) of the LLNA nonsensitizers were 100% concordant among the repeat LLNA: DA tests. ICCVAM concludes that accuracy and reproducibility of the LLNA: DA support its use to identify potential skin sensitizers and nonsensitizers. ICCVAM recommends SI $\geq$ 1.8 to identify ACD hazards since there were no false negatives relative to the LLNA. In testing situations where dose-response information is not required, or negative results are anticipated, ICCVAM recommends that the single-dose reduced LLNA: DA should be considered and used, thereby reducing animal use by up to 40%. The ICCVAM-recommended protocol formed the basis for the recently adopted OECD Test Guideline 442A. Because the LLNA: DA does not require radioactive reagents more institutions can take advantage of the reduction and refinement benefits afforded by the LLNA compared to traditional guinea pig methods for ACD testing. The LLNA: DA will also eliminate the environmental hazard associated with use and disposal of radioactive materials used in the LLNA.

Keywords: allergic contact dermatitis; LLNA; nonradioactive; ATP; alternative methods

Poster Session: Risk Assessment and Regulatory Policy Applications