ICCVAM Evaluation and Recommendations on the Nonradioactive LLNA: BrdU-ELISA for Evaluating Allergic Contact Dermatitis Hazards

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ICCVAM assessed the usefulness and limitations of the LLNA: BrdU-ELISA, a nonradioactive local lymph node assay (LLNA) that measures the amount of BrdU incorporation into the DNA of proliferating lymphocytes as an indicator of potential allergic contact dermatitis (ACD) hazards. Accuracy when compared to the traditional LLNA was assessed based on data generated with 43 substances and using several different stimulation indices (SI) as decision criteria. Optimal performance was achieved using SI $\geq$ 1.6; the LLNA: BrdU-ELISA correctly identified all 32 LLNA sensitizers (0% [0/32] false negatives) and 9/11 LLNA nonsensitizers (18% [2/11] false positives). The 2 false positives had maximum SI between 1.6-1.9. There were 18 substances with repeat tests; results for 85% (11/13) of the LLNA sensitizers and 60% (3/5) of the LLNA nonsensitizers were 100% concordant among the repeat LLNA: BrdU-ELISA tests. ICCVAM concluded that the accuracy and reproducibility of the LLNA: BrdU-ELISA support its use to identify potential skin sensitizers and nonsensitizers. ICCVAM recommends SI $\geq$ 1.6 to identify potential sensitizers 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: BrdU-ELISA should be considered and used, thereby reducing animal use by up to 40%. The ICCVAM-recommended protocol formed the basis of the recently adopted OECD Test Guideline 442B for the LLNA: BrdU-ELISA. Because the LLNA: BrdU-ELISA 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: BrdU-ELISA will also eliminate the environmental hazard associated with use and disposal of radioactive materials used in the LLNA.

Keywords: allergic contact dermatitis; LLNA; nonradioactive; BrdU; ELISA; alternative methods

Poster Session: Risk Assessment and Regulatory Policy Applications