International Acceptance of the Nonradioactive LLNA: DA for Evaluating Allergic Contact Dermatitis Hazards

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ICCVAM and NICEATM jointly evaluated the nonradioactive LLNA: DA, which measures ATP content as an indicator of lymphocyte proliferation, for identifying potential allergic contact dermatitis (ACD) hazards. Accuracy was calculated by comparing results to the traditional radioactive LLNA for 44 substances using different stimulation indices (SI) as decision criteria. SI $\geq$ 1.8 generated optimal performance; 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 maximum SI for the three false positives ranged from 1.8-2.5. Fourteen substances had multiple LLNA: DA tests: 80% (8/10) of the LLNA sensitizers and 75% (3/4) of the LLNA nonsensitizers were concordant. Based on these results, ICCVAM concluded that the accuracy and reliability of the LLNA: DA supported its use for identifying potential ACD hazards and recommended SI $\geq$ 1.8, since there were no false negatives when compared to the traditional radioactive LLNA. Additionally, when dose-response information is not required or negative results are anticipated, ICCVAM recommended using a single-dose reduced LLNA: DA, thereby reducing animal use by 40%. In July 2010, the LLNA: DA was adopted by OECD as Test Guideline 442A. Availability of this international test guideline will allow more institutions to take advantage of the reduction and refinement benefits afforded by a LLNA since there is no requirement for radioactive reagents and the hazards associated with their use and disposal. The views above may not represent the official position of any government agency. ILS staff supported by NIEHS contract N01-ES-35504.

Topic area: I-11 Safety Testing for Skin Sensitization Hazards: Recent Three Rs Advances

Keywords: allergic contact dermatitis; skin sensitization; murine local lymph node assay (LLNA); nonradioactive; hazard categorization