Evaluation of the Murine Local Lymph Node Assay (LLNA) for Potency Categorization of Chemicals Causing Allergic Contact Dermatitis in Humans

J Strickland[1], P Brown[2], J Matheson[3], A Jacobs[2], T McMahon[4], D Germolec[5], D Allen[1], E Salicru[1], T Burns[1], F Stack[1], W Stokes[6]

[1]ILS, Inc., RTP, NC, USA; [2]US FDA, Silver Spring, MD, USA; [3]US CPSC, Bethesda, MD, USA; [4]US EPA, Washington, DC, USA; [5]NIEHS, RTP, NC, USA; [6]NICEATM/NTP/NIEHS/NIH/DHHS, RTP, NC, USA

ICCVAM and NICEATM jointly evaluated the usefulness and limitations of the LLNA to determine potency categorization of chemicals that may cause allergic contact dermatitis. The dose per unit skin area that induces a 5% positive response rate in the human maximization test or human repeat-insult patch test was used as the human induction threshold. Substances with induction thresholds ≤500 μg/cm^2 were classified as "strong" human sensitizers. The extent to which the LLNA EC3 (estimated concentration expected to produce a stimulation index of 3) correctly categorizes strong human sensitizers was evaluated using 136 substances with both LLNA and human data. Using EC3 ≤ 2%, the criterion adopted by the GHS, correctly categorized 52% (14/27) of the strong human sensitizers. However, nearly half (48% [13/27]) of the strong human sensitizers had an EC3 > 2% (11/27) or were negative in the LLNA (2/27). ICCVAM concludes that the LLNA can be used to categorize substances as strong sensitizers when EC3 ≤ 2% but cannot be used as a stand-alone assay to determine sensitization potency categories. Additional information is required to categorize substances as other than strong sensitizers when EC3 > 2%. To improve the accuracy of the LLNA for identifying strong sensitizers, ICCVAM encourages the development and evaluation of integrated decision strategies that consider other relevant information such as quantitative structure-activity relationships, structural alerts, peptide reactivity, *in vitro* data, human data or experience, and existing data from similar chemicals. 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); potency; hazard categorization