Updated NICEATM Evaluation of the Reduced Murine Local Lymph Node Assay

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To minimize the occurrence of allergic contact dermatitis (ACD), regulatory authorities require testing to identify substances that may cause ACD. Such substances must be labeled with the hazard description and precautions necessary to minimize exposure. The murine local lymph node assay (LLNA) is an alternative test method for determining the ACD hazard potential of most types of substances. Compared to guinea pig tests, it requires fewer animals, less time, and eliminates pain and distress. The reduced LLNA (rLLNA), which uses only one high dose, further reduces animal use by 40% compared to the multidose LLNA. Based on the evaluation by ICCVAM in 2009 using 471 LLNA studies, the rLLNA was included in an updated version of the OECD Test Guideline for the LLNA (TG 429) adopted in 2010. LLNA results from 1071 published and unpublished studies, representing 664 unique substances, were obtained. Accuracy for the rLLNA was 98.5% (1055/1071), with false positive and false negative rates of 0% (0/319) and 2.1% (16/752), respectively. Sixteen false negative studies encompassed 13 substances; all produced relatively weak (SI $\leq$ 7.7) responses. This updated analysis of the rLLNA supports the conclusions and recommendations described in the 2009 ICCVAM rLLNA test method evaluation report, including the recommendation that the rLLNA should be routinely considered and used where determined appropriate. This analysis also provides further support for the use of the updated OECD TG, which is expected to significantly refine and reduce animal use for ACD hazard testing while supporting the protection of human health. ILS staff supported by NIEHS contract N01-ES-35504.