Comparison of the DPRA with a Three-Test Battery for *In Vitro* Evaluation of Skin Sensitization

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To protect people from allergic contact dermatitis (ACD), regulatory agencies require that the results from standardized animal tests be used for hazard labeling. Such labeling warns consumers and workers of the precautions necessary to avoid exposures to substances that may cause ACD. International legislation to ban animal testing of cosmetics has spurred efforts to develop *in vitro* replacements for ACD hazard tests that use animals. NICEATM retrospectively evaluated the performance of the direct protein reactivity assay (DPRA) against that of testing strategies using three *in vitro* assays: DPRA, the human cell line activation test (h-CLAT), and KeratinoSens. The murine local lymph node assay was used as the reference test for a set of 67 unique substances. The DPRA alone generated an accuracy of 85% (57/67), a false positive rate of 22% (5/23), and a false negative rate of 11% (5/44). Using the most prevalent result for each substance from all three assays yielded an accuracy of 82% (55/67), a false positive rate of 30% (7/23), and a false negative rate of 11% (5/44). A classification tree model was also evaluated for predicting the LLNA results. A structural reactivity assessment was used to divide the 67 substances into positive and negative groups, then a recursive partitioning routine was used to generate further branches based on the *in vitro* test results. This strategy did not improve the performance of the three *in vitro* tests relative to the DPRA (accuracy = 79% [53/67]). However, based on the classification tree results, an interim testing strategy that combines the DPRA and the LLNA was proposed. This strategy could potentially reduce animal use for skin sensitization testing by up to 72% compared to testing all substances in the LLNA.