Multivariate Models for Prediction of Human Skin Sensitization Hazard

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One of ICCVAM's highest priorities is the development and evaluation of non-animal approaches to identify potential skin sensitizers. The complexity of biological events necessary for a substance to elicit a skin sensitization reaction suggests that no single alternative method will replace the currently accepted animal tests. ICCVAM is evaluating machine learning approaches to integrate relevant data based on the OECD adverse outcome pathway for skin sensitization to predict human skin sensitization hazard. We obtained data on 96 chemicals from the direct peptide reactivity assay (DPRA), human cell line activation test (h-CLAT), KeratinoSens assay, six physicochemical properties, and an *in silico* read-across prediction of skin sensitization hazard. These data were used as inputs for two machine learning approaches to predict human skin sensitization hazard, support vector machine and logistic regression, which were each applied to 12 different combinations of the input variables. Models were trained on a set of 72 substances and tested on an external set of 24 substances. The input variable set containing DPRA, h-CLAT, KeratinoSens, read-across, and log P data performed the best for both approaches: accuracy = 99% (71/72), sensitivity = 98% (50/51), and specificity = 100% (21/21) for the training set; and accuracy = 96% (23/24), sensitivity = 93% (14/15), and specificity = 100% (9/9) for the test set. This integrated approach predicted human skin sensitization hazard better than the local lymph node assay or any *in chemico*, *in vitro*, or *in silico* method alone. These results suggest that computational methods are promising tools to effectively identify potential skin sensitizers without animal testing. *This abstract does not represent EPA policy. This project was funded in whole or in part with Federal funds from the NIEHS, NIH under Contract No. HHSN273201500010C.*

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