In Silico Predictions of Skin Sensitization Using OECD QSAR Toolbox

J Strickland[1], N Choksi[1], D Allen[2], W Casey[3]

[1]ILS/NICEATM, RTP, NC, USA; [3]NIH/NIEHS/DNTP/NICEATM, RTP, NC, USA

Skin sensitization data are needed to develop precautionary labeling to protect workers and consumers from chemical exposures. To reduce or eliminate the use of animals for skin sensitization testing, a number of *in vitro* and *in silico* test methods have been proposed. NICEATM evaluated the utility of the OECD QSAR Toolbox for making read-across skin sensitization predictions using murine local lymph node assay (LLNA) outcomes as reference data. The Toolbox protocol identified analogs for 120 target substances (87 sensitizers and 33 nonsensitizers) using mechanism of protein binding and chemical structure schemes in the Toolbox. If protein binding alerts were not identified in a substance, auto-oxidation and skin metabolism products were predicted; a representative product with a protein binding alert was used in the evaluation. If neither parent nor products had protein binding alerts, the substance was classified as a nonsensitizer. For parent or products with protein binding alerts, *in vivo* skin sensitization data for analogs were used to predict the sensitization potential. Accuracy of the Toolbox protocol was 77% (92/120) with sensitivity = 77% (67/87) and specificity = 76% (25/33). Using only protein binding alerts in the parent compound to predict sensitization potential yielded accuracy = 69% (83/120), sensitivity = 66% (57/87), and specificity = 79% (26/33). Using only protein binding alerts in the parent or product to classify substances as sensitizers improved accuracy (82% [98/120]) and sensitivity (91% [79/87]) compared to the Toolbox protocol, but decreased specificity (58% [19/33]). Thus, potential skin sensitizers may be predicted with similar accuracy using either the Toolbox protocol or only protein binding alerts. Because the Toolbox protocol had a lower false positive rate, it will be evaluated as part of an integrated decision strategy for skin sensitization that includes *in vitro* data and physicochemical parameters. *This project was funded in whole or in part with Federal funds from the NIEHS, NIH under Contract No. HHSN27320140003C.*