Classification of Human Reference Data for Skin Sensitization

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To support the evaluation of non-animal approaches for skin sensitization assessment, we collected data for over 2500 human predictive patch tests (human maximization test and human repeated insult patch test) from more than 1500 publications. Each test was evaluated for reliability. Results from 1900 tests considered to be sufficiently reliable were classified using the Globally Harmonized System of Classification and Labeling of Chemicals (GHS). Human predictive patch test data based on single doses makes identification of thresholds uncertain and difficult to use as reference data. To overcome this challenge, classification criteria from the GHS were extended using a decision tree to partly resolve ambiguity in the results. If individual chemicals had multiple discordant test results, a weight-of-evidence approach was used to arrive at a single classification for each chemical. This classification approach was applied to a Cosmetics Europe reference list of 128 substances to support the evaluation of defined approaches for skin sensitization proposed for inclusion in a new OECD guideline. While 79 substances could be classified, the data for 49 substances were not sufficiently reliable. Classifications for the 79 substances included: eight strong sensitizers (1A), four strong sensitizers with some likelihood of over-classification (1A-), one moderate sensitizer with some likelihood of under-classification (1B+), 28 moderate sensitizers (1B), 10 non-sensitizers with some likelihood of under-classification (NC+), and six non-sensitizers (NC). Twenty-two substances could not be classified as sensitizers or non-sensitizers, but a potential for strong sensitization could be ruled out (NC/1B). The entire human skin sensitization patch test database will be made publicly available in the future for additional evaluation of alternative skin sensitization methods and development of new models. This project was funded with federal funds from the NIEHS, NIH under Contract No. HHSN273201500010C. The views expressed above do not necessarily represent the official positions of any federal agency.

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