Evaluation of Skin Sensitization Classification Rules to Reflect Human Potency

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Approaches currently used to subcategorize skin sensitizers into GHS subcategory 1A ("strong," using an induction dose per skin area [DSA] of 500 μg/cm^2 or less) or 1B ("other than strong," using an induction DSA greater than 500 μg/cm^2) consider only the dose inducing the skin sensitization response and not the frequency of induced sensitization in human subjects. To address this limitation, we used a data set developed to support OECD Guideline 497 to conceptualize approaches that incorporate the number of sensitized subjects, such as the DSA at which one subject is sensitized (DSA1+) or the DSA at which 5% of subjects are sensitized (DSA05). Of the 605 test results in which the test substance was active, the DSA1+ subcategorized 209 test results in GHS 1A (DSA and DSA05: 59 and 184, respectively). For substances with multiple test results, reproducibility was approximately 90% for binary classification and 80–85% for GHS subcategorization when applying a standardized weight of evidence (WoE) approach. HPPT concordance with LLNA was 44% (46/55) for binary classifications and 61–63% (28–29/46) for GHS subcategorization. Both data types, however, showed very good (91–93%, binary) or decent (76–95%, subcategory) concordance when compared to an overall WoE consensus classification. This approach to classifying and subcategorizing sensitizers improves the prediction of potency while providing good reproducibility and concordance with animal reference data. Project was funded by NIEHS under Contract No. HHSN273201500010C. The views expressed above do not necessarily represent the official positions of any federal agency.