

## **A Proposal to Revise GHS Skin Sensitization Classification Rules to Reflect Human Potency and Support Weight-of-Evidence Assessments**

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To support development of OECD Guideline 497, Defined Approaches on Skin Sensitisation, we curated a human reference data set of 2277 human predictive patch tests (HPPT) for 1366 unique substances. We used these data and the current United Nations Globally Harmonized System of Classification and Labelling of Chemicals (GHS) criteria to assign classifications to the represented chemicals. Doing so, we noted that the classification of sensitizers into GHS subcategories 1A (at least one sensitized individual at an induction dose per skin area (DSA) of 500  $\mu\text{g}/\text{cm}^2$  or less) or 1B (at least one sensitized individual at induction DSA greater than 500  $\mu\text{g}/\text{cm}^2$ ) did not sufficiently reflect potency, as this only considers the dose used and not the fraction of sensitized test subjects. GHS also does not provide guidance on how HPPT data should be used in weight-of-evidence (WoE) assessments for potency categorization in concert with other data (e.g., animal testing or defined approaches). We propose a revision of the current GHS criteria to use an extrapolated DSA that incorporates the number of sensitized individuals, such as the DSA at which hypothetically one individual is sensitized (DSA1+) or the DSA at which hypothetically 5% of individuals are sensitized (DSA05). We also provide recommendations for determining when an HPPT result should be classified as negative and how HPPT data should be used with other relevant data in the context of WoE approaches. This project was funded with U.S. federal funds from the NIEHS, NIH under Contract No. HHSN273201500010C.