

## The SARA-ICE Model for Predicting Skin Sensitizer Potency

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The Skin Allergy Risk Assessment-Integrated Chemical Environment (SARA-ICE) model is a defined approach (DA) that provides a weight-of-evidence point of departure (PoD) and GHS potency prediction for use in skin sensitization assessments. SARA-ICE is constructed within the Bayesian statistical framework using data sourced from the Integrated Chemical Environment (<https://ice.ntp.niehs.nih.gov/>), Unilever SARA publications, and Cosmetics Europe. SARA-ICE predicts a human relevant PoD: the ED<sub>01</sub>, the dose with a 1% chance of inducing sensitization in a human predictive patch test (HPPT). The PoD can be calculated using data from HPPTs, local lymph node assays (LLNA), and new approach methodologies (NAMs). For a chemical of interest, the model returns the probability of each GHS classification conditional on the distribution of the ED<sub>01</sub>. We used the OECD DA for Skin Sensitisation (TG 497) reference data set to evaluate SARA-ICE for GHS classification accuracy. Using a probability of 0.8 as the binary classification criterion, balanced accuracy was 97% for conclusive calls relative to human classifications, but 36% of chemicals had inconclusive calls. Using a probability of 0.55 for the subcategory classification criterion, average balanced accuracy was 85% for conclusive calls versus human classifications. A case study on isothiazolinones demonstrated that SARA-ICE performed well, correctly identifying these broad-spectrum preservatives as sensitizers. SARA-ICE will be made freely available online, enabling users worldwide to easily predict human skin sensitization potency without animal testing. This project was partially funded by NIEHS under Contract No. HHSN273201500010C.