## Variability of Human Reference Data for Skin Sensitization

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Because humans are the primary subject of interest for regulatory safety testing, it is advantageous to have human reference data available for evaluation of new approach methodologies (NAMs) for assessing chemical safety. We have compiled such a data set for human skin sensitization potential by collecting data from the scientific literature for human predictive patch tests that used the human maximization or human repeated insult patch test protocols. We assessed the variability of these data to determine the potential impact on concordance with NAMs. We evaluated the test results based on the completeness of the study information and identified 2255 tests that were sufficiently reliable. Of these tests, we found 144 substances with at least three test results, which we considered to be the minimum number of tests needed to analyze variability. The substances included anilines, amines, aldehydes, esters, and other chemical classes. The number of results per substance ranged from 3 to 27, with a mean of 6 and a median of 4. For 20 substances, all tests were positive (at least one sensitized subject in a study); for 45 substances, all tests were negative (no sensitized subjects); and for the remaining 79 substances, both positive and negative results were obtained. There was no distinct relationship between the dose per skin area and these three groups of substances. We evaluated variability of the positive results using the calculated dose per skin area that sensitized one person (DSA1+). For the 50 substances with at least three positive tests, the mean ± standard deviation for DSA1+ ranged from 3.66 ± 5.25 to 12068.97 ± 5972.59 μg/cm$^2$, with lower mean DSA1+ representing higher skin sensitization potency. Ongoing analyses examine the impact of physicochemical properties, as well as test type, vehicle, and other protocol variables, to determine whether these parameters can explain low or high variability. This characterization provides context for defining benchmarks for the evaluation of NAMs for skin sensitization assessments. 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.

**Keywords:** chemical allergy, alternatives to animal testing, regulatory science/regulatory toxicology