

Web Application to Predict Skin Sensitization Using Defined Approaches

K.T. To¹, J. Strickland¹, A. Borrel¹, J. Truax¹, D.G. Allen¹, N. Kleinstreuer²

¹Inotiv, RTP, NC, United States; ²NIH/NIEHS/PTB/DTT/NICEATM, RTP, NC, United States

Defined approaches (DAs) combine data from specific information sources to predict toxicity. While certain DAs are accepted to identify potential skin sensitizers, the data interpretation procedures they use vary in logical complexity and can be time-consuming to apply manually. We have developed an open-source web application, the DASS App, to facilitate use of three DAs for skin sensitization (DASS). The app implements two validated DAs, known as the Two-out-of-Three (2o3) and the Integrated Testing Strategy (ITS), that are described in OECD Guideline 497. It also implements the Key Event 3/1 Sequential Testing Strategy (KE 3/1 STS) accepted by the U.S. Environmental Protection Agency. The three DAs available in the DASS App integrate data from three in vitro assays that represent three key events within the skin sensitization adverse outcome pathway: the direct peptide reactivity assay (DPRA), human cell line activation test (h-CLAT), and the KeratinoSens assay. To predict skin sensitization hazard, the 2o3 uses the consensus hazard across the three in vitro assays; ITS uses a scoring method with outcomes from h-CLAT, DPRA, and in silico predictions; and KE 3/1 STS sequentially evaluates outcomes from h-CLAT and DPRA. ITS can also be used to predict potency categorization. The DASS App enables users to computationally implement non-animal approaches to evaluate chemical skin sensitization without the need for additional software or computational expertise. The DASS App is available on the National Toxicology Program website at <https://ntp.niehs.nih.gov/go/40498>. This project was funded by NIEHS under Contract No. HHSN273201500010C.