

## **DASS App: A Web Application for Applying Defined Approaches for Skin Sensitization to Predict Hazard and Potency Categorization**

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Defined approaches (DAs) are methods for evaluating data from specific information sources to derive toxicity predictions. Guideline 497 (GL 497), Defined Approaches for Skin Sensitisation (DASS), issued in 2021 by the Organisation for Economic Co-operation and Development (OECD), was the first internationally harmonized guideline to describe a non-animal approach that can be used to fully replace an animal test to identify skin sensitizers. GL 497 describes two validated DAs to identify potential skin sensitizers, the 2 out of 3 (2o3) and Integrated Testing Strategy (ITS). A third DA, Key Event 3/1 Sequential Testing Strategy (KE 3/1 STS), has been accepted by the U.S. Environmental Protection Agency. The data interpretation procedures implemented in these DAs vary in logical complexity and can be time-consuming to apply manually. Computational approaches can be used to apply the DAs more efficiently but require fluency in computational programming. We have developed an open-source web application, the DASS App, to facilitate application of these DAs by a wider audience. The DAs available in the DASS App integrate data from three in vitro assays: the direct peptide reactivity assay (DPRA), human cell line activation test (h-CLAT), and the KeratinoSens assay. These assays represent three key events within the skin sensitization adverse outcome pathway. The three DAs implement rule-based approaches for integrating multiple assay results to predict hazard and/or potency. The 2o3 predicts hazard by taking the consensus prediction across the three in vitro assays. The KE 3/1 STS first evaluates quantitative outcomes from h-CLAT to predict whether the chemical should be classified as a Strong or Weak sensitizer; if the h-CLAT is negative, DPRA results are evaluated to determine whether the chemical should be classified as a Weak sensitizer or Not Classified. The ITS predicts hazard identification and potency by scoring results from DPRA, h-CLAT, and in silico predictions. GL 497 defines two versions of ITS, using either DEREK Nexus or OECD QSAR Toolbox predictions. The ITS DA also outlines a data interpretation procedure for cases where data are only available for two information sources. When used on a test set of 150 chemicals, the DASS App generated hazard predictions in less than one second. The DASS App enables users to implement non-animal approaches to evaluate chemical skin sensitization without the need for additional software or computational expertise. The app supports upload and analysis of user-provided data, includes steps to identify inconsistencies and formatting issues, and provides hazard predictions in a downloadable format. The DASS App is available on the National Toxicology Program website at <https://ntp.niehs.nih.gov/go/40498>. This project was funded in whole or in part with federal funds from the NIEHS, NIH under Contract No. HHSN273201500010C.

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