

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

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Introduction

- Defined approaches (DAs) combine data from a pre-determined set of information sources via fixed data interpretation procedures to derive toxicity predictions.
- Defined approaches for skin sensitization (DASS) have been developed (OECD 2021) to identify potential skin sensitizers by integrating non-animal test methods that represent key events in the skin sensitization adverse outcome pathway (OECD 2012).
 - Hazard identification** characterizes a chemical as either a sensitizer or non-sensitizer.
 - Potency classification** assigns a chemical to a category in an established classification scheme. In this case, classifications are established by the United Nations Globally Harmonized System for Classification and Labelling of Chemicals (GHS).
- We created the DASS App, an open-source web application that allows users to apply regulatorily approved DAs to their own data to derive skin sensitization hazard and potency predictions.
 - The DASS App can be accessed from anywhere via the web with no account creation required.
 - User support resources include context-appropriate pop-up boxes and a downloadable user guide.

Access the DASS App
<https://ntp.niehs.nih.gov/go/952311>



Figure 1. Adverse Outcome Pathway for Skin Sensitization

Across the DAs, three unique *in vitro* information sources are used, each representing a key event (KE) in the skin sensitization adverse outcome pathway:
KE1. Direct Peptide Reactivity Assay (DPRA)
KE2. KeratinoSens Assay
KE3. Human Cell Line Activation Test (h-CLAT)

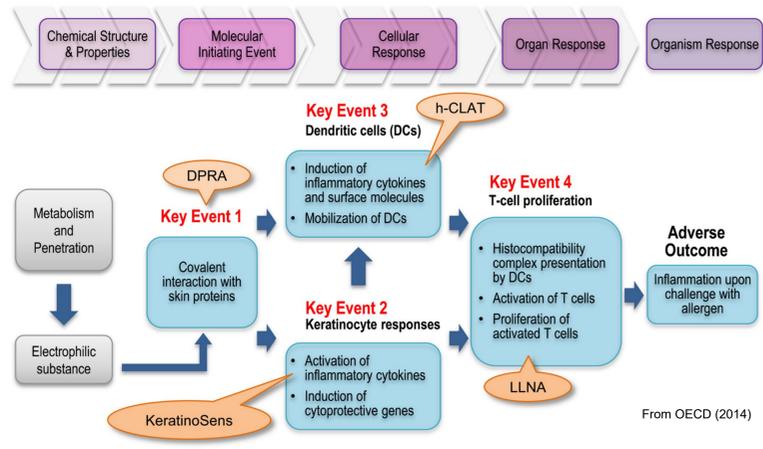
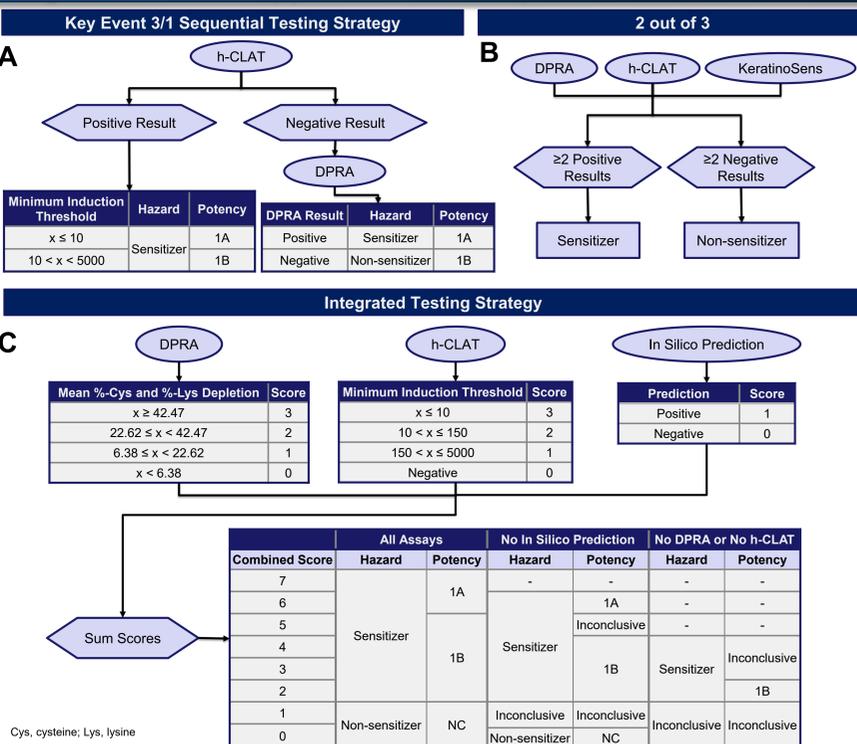


Figure 2. Defined Approach Data Interpretation Procedures

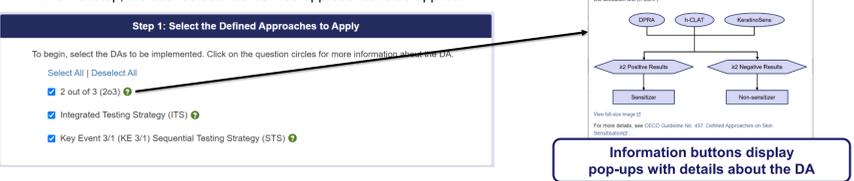


The Defined Approaches

- Two DAs from Guideline 497 (Organisation for Economic Co-operation and Development; OECD) are available in the DASS App:
 - The **2 out of 3 (2o3)** DA predicts skin sensitization hazard using the majority outcome among the DPRA, h-CLAT, and KeratinoSens assay (Fig. 2B). The 2o3 DA does not predict potency.
 - The **Integrated Testing Strategy (ITS)** DA predicts skin sensitization hazard and potency by scoring results from the DPRA and h-CLAT, as well as *in silico* predictions from either the OECD QSAR Toolbox or Derek Nexus (Fig. 2C). ITS includes multiple scoring schemes to derive predictions when data are available from only two of the information sources.
- The DASS App also includes a DA that has been accepted by the U.S. Environmental Protection Agency (EPA) for predicting hazard (EPA 2018):
 - The **Key Event 3/1 Sequential Testing Strategy (KE 3/1 STS)** DA (Nukada 2013, Takenouchi 2015) predicts skin sensitization hazard and potency by first evaluating results from the h-CLAT and then evaluating results from the DPRA (Fig. 2A). EPA accepts results from the KE 3/1 STS only for hazard classification, but the DASS App also provides potency classification predictions.

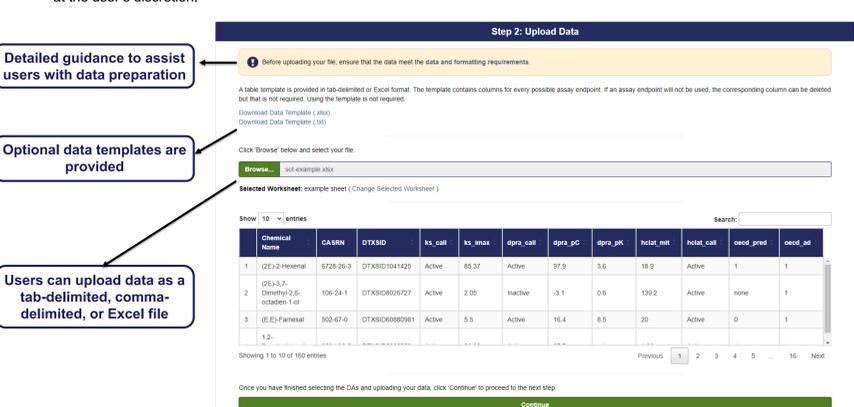
Step 1: Select DAs

- The DASS App is organized into step-by-step modules.
- In the first step, the user selects the defined approaches to be applied.



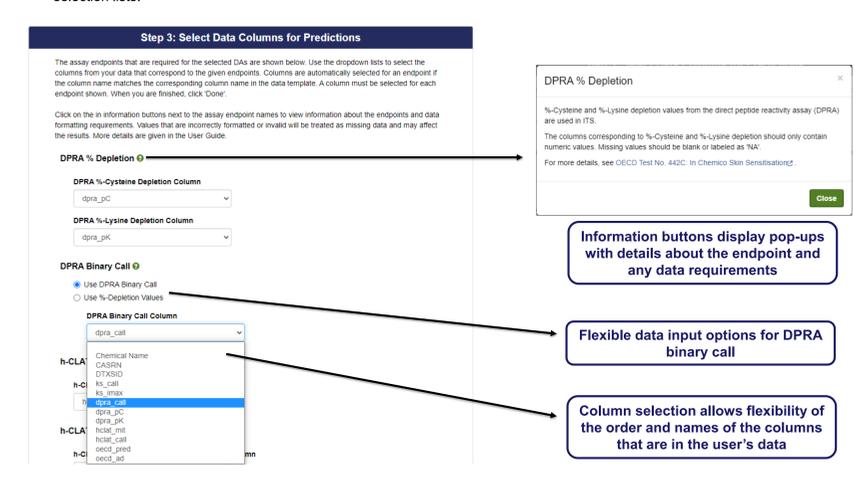
Step 2: Upload Data

- In the second step, the user uploads their data.
 - Three file formats are accepted, with support for multi-sheet Excel workbooks.
 - Data templates have defined columns for many possible data inputs and can be customized with additional metadata columns at the user's discretion.

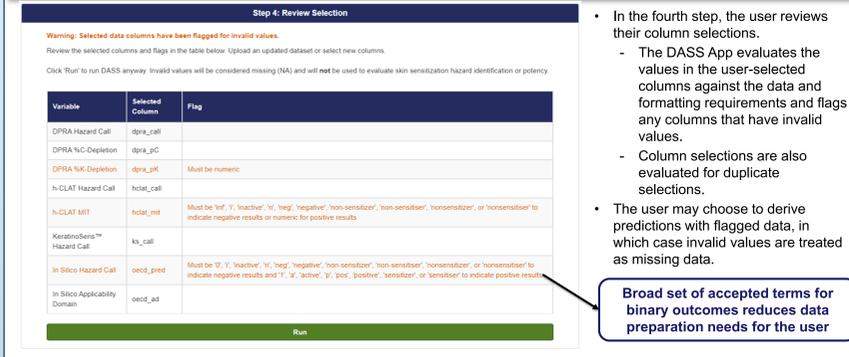


Step 3: Select Data Inputs

- In the third step, the user specifies which columns in their data correspond to the required endpoint data.
 - The DASS App evaluates the DA selections and populates the Step 3 module with the required endpoints and dropdown selection lists.

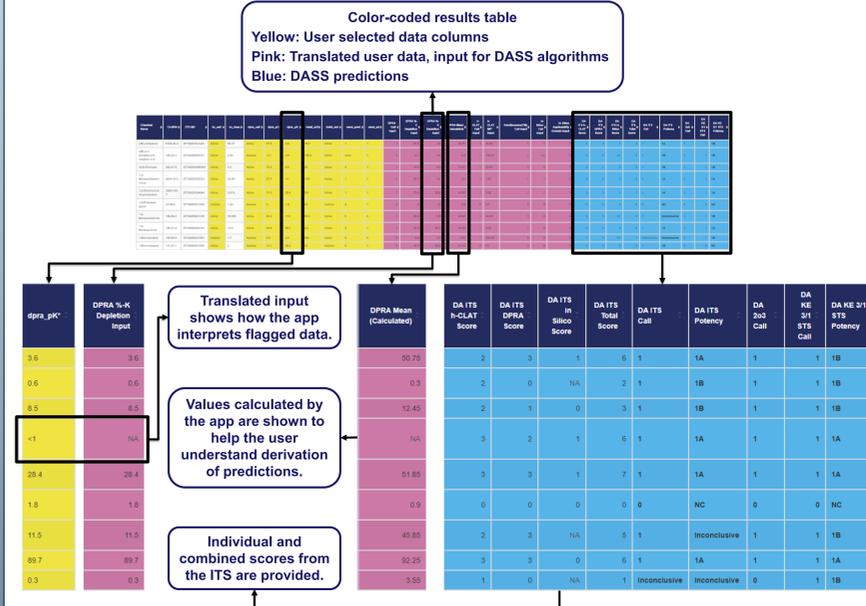


Step 4: Review Selection



Step 5: View Results

- In the final step, the user is shown a results table that can be downloaded as a tab-delimited or Excel file.
- The results table contains the user's data with DA predictions appended, along with columns that help the user to understand their results.



Summary

- We created the DASS App to facilitate the use of three accepted DAs to integrate data from non-animal methods and provide skin sensitization hazard and potency predictions.
- Data and formatting requirements are flexible, with no required column order or column names and a broad set of accepted terms for binary calls.
- The DASS App enables users to leverage computational methods to efficiently apply DAs through a user-friendly interface.

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Acknowledgments and More Information

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