Web Application to Classify and Subcategorize Skin Sensitizers Using Human Data

A. Unnikrishnan[1], K. T. To[2], M. Herzler[3], D. Germolec[4], E. Reinke[1], N. Kleinstreuer[5]

[1]Inotiv, RTP, NC, United States; [2]ICF, Reston, VA, United States; [3]BfR, Berlin, Germany; [4]NIH/NIEHS/DTT/STB/NICEATM, RTP, NC, United States; [5]NIH/NIEHS/DTT/NICEATM, RTP, NC, United States

Current approaches that use human data to assign skin sensitizers to United Nations Globally Harmonized System of Classification and Labelling of Chemicals (GHS) potency subcategories overlook the number of sensitized test subjects, potentially leading to an underestimation of potency. To address this concern, human predictive patch tests (HPPT) data collected to support evaluation of non-animal approaches were used to develop a modified approach for assigning skin sensitization potency subcategorizations based on GHS. The modified classification approach improves upon previous methods by considering the number of sensitized human test subjects and addressing uncertainty in assay results. Additionally, the approach includes a weight-of-evidence method to consolidate multiple HPPT results into a single GHS classification for each chemical. However, the approach involves complex decision tree logic that may be challenging for most users. To allow a broad audience of users to apply this modified approach to their own HPPT data, we have developed an open-source R Shiny-based web application, HPPT App. The app provides an interactive platform that imports user-submitted HPPT data and applies the modified GHS classification approach to classify and subcategorize skin sensitizers. To classify a substance for skin sensitization hazard, the app first derives the two response values defined within the modified approach: DSA1+, which indicates the dose that sensitizes one test subject, and DSA05, which indicates the dose that sensitizes 5% of test subjects. The app then assigns classifications for each test result. Under standard GHS classification rules, a substance can be classified as a strong sensitizer (1A), a weak sensitizer (1B), or not classified (NC). The HPPT App enables a modified classification approach, addressing uncertainty by defining borderline ranges to assign ambiguous classifications in cases where the data show no evidence of strong sensitization (NC/1B) or provide no information for classifying skin sensitization (NC/1). It provides classifications for each substance based on three different classification modes. Depending on the input data, the app may provide a binary classification (Category 1 [sensitizer] vs. NC [nonsensitizer]) or may be able to classify sensitizers as Category 1A or Category 1B sensitizers. Derived response values (DSA1+ and DSA05) and measures of classification reproducibility are also provided. The app output is provided as interactive tables that can be sorted, filtered, and downloaded. Additionally, the app website provides support documentation including information on the classification methodology, navigation guidance, and contact details. The HPPT app works with various types of data, such as test results from ingredients in consumer goods and cleaning products, highlighting its robust classification performance, applicability, and impact. This project was funded in whole or in part 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.