

IATA for skin sensitization potential – 1 out of 2 or 2 out of 3?

David Roberts¹, [Grace Patlewicz](#)²

¹School of Pharmacy and Biomolecular Sciences, Liverpool John Moores University, Liverpool L3 3AF, United Kingdom.

²National Center for Computational Toxicology, Office of Research and Development, U.S. Environmental Protection Agency, RTP, NC

patlewicz.grace@epa.gov

To meet EU regulatory requirements and to avoid or minimize animal testing, there is a need for non-animal methods to assess skin sensitization potential. Given the complexity of the skin sensitization endpoint, there is an expectation that integrated testing and assessment approaches (IATA) will need to be developed which rely on assays representing key events in the pathway. Three non-animal assays have been formally validated: the direct peptide reactivity assay (DPRA), the KeratinoSens™ assay and the h-CLAT assay. At the same time, there have been many efforts to develop IATA with the “2 out of 3” approach attracting much attention whereby a chemical is classified on the basis of the majority outcome. A set of 271 chemicals with mouse, human and non-animal sensitization test data was evaluated to compare the predictive performances of the 3 individual non-animal assays, their binary combinations and the ‘2 out of 3’ approach. The analysis revealed that the most predictive approach was to use both the DPRA and h-CLAT: 1. Perform DPRA – if positive, classify as a sensitizer; 2. If negative, perform h-CLAT – a positive outcome denotes a sensitizer, a negative, a non-sensitizer. With this approach, 85% (LLNA) and 93% (human) of the non-sensitizer predictions were correct, in contrast to the ‘2 out of 3’ approach which had 69% (LLNA) and 79% (human) of non-sensitizer predictions correct.

The views expressed are those of the authors and do not necessarily reflect the views or policies of the U.S. Environmental Protection Agency.