Skin Sensitization Testing of Mixtures Without Animals

Judy Strickland[1*], Jim Truax[1], Marco Corvaro[2], Raja Settivari[3], Joseph Henriquez[4], Jeremy McFadden[4], Travis Gulledge[5], Victor Johnson[5], Sean Gehen[4], Dori Germolec[6], David G. Allen[1], Nicole C. Kleinstreuer[6]

[1]ILS, Research Triangle Park, NC, USA; [2]Corteva, Rome, Italy; [3]Corteva, Newark, DE, USA; [4]Corteva, Indianapolis, IN, USA;[5]Burleson Research Technologies, Inc., Morrisville, NC, USA; [6]NIH/NIEHS/DNTP/NICEATM, Research Triangle Park, NC, USA

*Presenting author

Skin sensitization testing is a regulatory requirement for safety evaluations of pesticides in multiple countries. Globally harmonized test guidelines that include in chemico and in vitro methods reduce animal use, but no single assay is recommended as a complete replacement for animal tests. Defined approaches (DAs) that integrate data from multiple non-animal methods are accepted, but these DAs were evaluated with mono-constituent substances. This may limit their applicability to multi-constituent substances such as pesticides. This analysis evaluated rule-based DAs for hazard and/or potency categorization of skin sensitization for agrochemical formulations. To obtain data for the analysis, we tested 27 formulations using the direct peptide reactivity assay (DPRA), the KeratinoSens™ assay, and the human cell line activation test (h-CLAT). Balanced accuracy (BA) of the DAs for predicting skin sensitization hazard in vivo ranged from 56% to 73%. The best performing DA for GHS potency classification had a correct classification rate of 52%. KeratinoSens had the highest performance for predicting in vivo hazard outcomes (BA = 81% vs. 62% for DPRA and 56% for h-CLAT), which was higher than any of the DAs. These results demonstrate that non-animal test methods have utility for evaluating the skin sensitization potential of agrochemical formulations. Further investigation will be required to determine whether DAs can outperform individual assays for predicting in vivo sensitization hazard of pesticide formulations in general. This project was funded with federal funds from the NIEHS, NIH under Contract Nos. HHSN273201500010C and HHSN273201400017C; Corteva funded the DPRA and KeratinoSens testing.