

Development of an Open-Source Integrated Test Strategy for Skin Sensitization Potency

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Regulatory authorities require testing to identify substances with the potential to cause allergic contact dermatitis so that appropriate labeling alerts users to the hazard and precautions necessary to minimize exposure. To reduce or eliminate animal use in testing, integrated test strategies (ITS) that combine *in silico* and *in vitro* test methods have been proposed. Scientists at the National Toxicology Program Interagency Center for the Evaluation of Alternative Toxicological Methods (NICEATM) and Procter and Gamble (P&G) are developing an open-source version of a previously published ITS for skin sensitization. The original ITS is based on a Bayesian network (BN ITS-2) using *in silico* and *in vitro* models that map to the OECD Adverse Outcome Pathway for skin sensitization. BN ITS-2 was developed using a commercial software package. To increase accessibility and algorithmic transparency, NICEATM and P&G developed open-source ITS-2 (OS ITS-2) with tools in R software for building and performing exact inference using a Bayesian network. R versions of widely used algorithms for supervised discretization and latent class learning were substituted for proprietary algorithms. The OS ITS-2 produced a probability distribution and resulting confusion matrix identical to that for the test data predictions in the BN ITS-2. Predictions for chemicals with varying sensitizing potential, such as chlorobenzene and citral, were evaluated using NICEATM's skin sensitization database, and value of information was assessed for the *in vitro* assays and *in silico* inputs. The OS ITS-2 provides availability, transparency, and represents a major step in allowing the ITS to be reproduced and tested, which is essential for use in a regulatory framework. The model is available on the NTP website (<http://ntp.niehs.nih.gov/go/its>).

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