

CERM Sensitization Prediction Approach



Multiple regulatory agencies have been taking a very conservative approach on sensitization in recent months. In particular, EPA has recently taken the stance that any substance with concerns for dermal sensitization will also be flagged for respiratory sensitization. The results of these very conservative assumptions are often restrictions on physical forms of end use formulations or products, harsh respiratory protection requirements, or limitations on consumer products. In many cases the requirements are sufficient to make some, if not all, of the intended uses or products non-viable.

In many cases, if sensitization concerns arise, there is no facile method to address the concerns through testing, read-across, or single predictive methods. To help address this, CERM has put into practice use of a weight of evidence, multiple model approach to predicting sensitization. The process involves read-across from available analog data, multiple screening model outputs, as well as professional review and interpretation of these results. We can also model metabolism, as well as bioavailability if necessary, to clarify results, and we look for similar analogs with *in vitro* or *in vivo* data. Taken together, this results in a robust prediction of sensitization potential.

CERM's sensitization prediction protocol is an ensemble approach using read-across and modeling predictions, followed by expert review of the results. The review includes evaluation of the predictions from a toxicological and chemical reactivity standpoint.

Read-Across

CERM will search for available data on structural or functional group analogs. This will help give a baseline concern for the class of chemicals or functional groups.

Representative Models Utilized

CERM will utilize multiple available modeling programs to predict sensitization and related characteristics. Models may include: SwissADME or the CDC Finite Dose Skin Permeation Calculation to predict skin penetration; Toxtree, a structural alert system; Pred-Skin, this model trained on human data; Tox Profiler, this model predicts immunotoxicity as well as molecular mechanisms and can help predict false positives; OECD QSAR Toolbox, this suite of models includes a Standard Skin Sensitization Workflow and can be very predictive for the base compound and metabolites; OEHHA Model, which predicts respiratory sensitization. Other models can be incorporated where appropriate.

Expert Review

Our expert chemists and toxicologists will compile and review the results to help provide clarity and accuracy. We will evaluate the weight of the evidence and provide as accurate a prediction as possible.

Please feel free to contact us for more information.

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