**Skin Sensitization – LLNA vs GPT vs Structural Alerts as Predictors of Human Hazard**

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According to the REACH regulation, the local lymph node assay (LLNA) serves as experimental gold stan­dard for assessing the skin sensitization potential. For substances without an LLNA result but where ex­pe­ri­men­tal data of the guinea pig maximization test (GPMT) or the Buehler test are available, these (here jointly called GPT) may also be used as basis for the skin sensitization evaluation. From our newly established data base comprising 1867 organic compounds with 1077 LLNA and 989 GPT (858 GMPT and 212 Buehler) results, a subset of 101 compounds with both LLNA and GPT data can be compared with corresponding human data [1]. The results reveal a systematic difference between the prediction capability of LLNA vs GPT results re­gard­ing the human skin sensitization potential.

Whereas LLNA provides a larger fraction of false positives, GPT yields significantly more false negatives. For the subset of 37 SN2 and Michael acceptor electrophiles, combination of structural alert predictions with either LLNA or GPT results yields significantly improved classification rates regarding the human data, which demonstrates the scope of including this in silico method as further criterion in the context of assessing the skin sensitization potential of organic compounds. As an opportunity to potentially improve the structural alert performance as stand-alone tool or in combination with other information, the variation in local reactivity [2] across the respective compounds is analyzed and discussed.

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