

Comparison of Human Patch Test and 3D Human Skin Model Results with Classification of Chemicals based on Rabbit Draize Test

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Efforts to replace the *in vivo* rabbit Draize test for skin irritation have been underway for many years and various *in vitro* protocols have been assessed. However, one key difficulty in determining the validity of any particular protocol/prediction model is that the *in vivo* rabbit data is both scarce and often of limited utility for the prediction of the biological effect in man.

In the current study, using the 4h human skin irritation patch test, we examined 15 irritants and 10 non irritants. The outcome of human patch test was compared with results obtained with reconstructed epidermis model EpiDerm using two *in vitro* skin irritation protocols. Of the 15 tested chemicals reported to be irritating in the rabbit, only 5 substances were found to be significantly irritating in human skin to merit the R38 classification. Using the EpiDerm test protocol evaluated in the ECVAM skin irritation validation study (15 min exposure), 7 out of 15 rabbit irritants were identified as R38 with one false negative prediction compared to human data. With the modified protocol (60 min exposure, 10 of 15 rabbit irritants were classified as R38, without the false negative outcome compared to 4h human patch test results.

Consequently, when approaching validation of alternative methods, existing human data should be taken into consideration, as only those may provide a final judgment about the predictive ability of a new alternative method. The *in vitro* models derived from human skin cells, if used in appropriate test designs and optimized by reference to human hazard data, may prove to be more useful than the animal tests for the prediction of human hazard from previously untested substances.

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