

Poster: skin models as alternatives to animal testing

***In vitro* micronucleus assay using a co-culture system: towards new tools for *in vitro* risk assessment of dermally applied compounds?**

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In vitro reconstructed skin models such as Episkin[®] (reconstructed epidermis) and Realskin (reconstructed full thickness: epidermis + living dermis) are biological models mimicking human skin. They are of growing interest in safety or efficacy pre-screening tests and for regulatory purposes as alternatives to animal testing (7th amendment to the European Cosmetic directive, REACH). The reduction and eventually the replacement of *in vivo* toxicity testing require the development of new complementary biological models and methods with improved ability to predict the genotoxic or other endpoint risk with *in vitro* data. This can be achieved if these new assays take into account the exposure conditions in a more relevant way than the current ones. To that end, new approaches using human reconstructed skin models for *in vitro* toxicology assessment are proposed.

The skin is the target organ for dermally exposed compounds or environmental stressors. A co-culture system using Episkin[®] or RealSkin and target cells to perform a regular micronucleus assay is used with six different compounds. This way of using human reconstructed skin for genotoxicity testing aims at improving the relevance of exposure conditions in *in vitro* genotoxicity assays for dermally applied compounds. The skin is indeed a biologically active barrier driving the exposure to compounds and their possible metabolites. The exposure of the target cells to a given substance can be assessed after topical application as was the case here. Episkin[®] and Realskin were used as a metabolically active tissue and a physiologic barrier. The test compound can be metabolized by the skin and/or by the target cells (\pm S9 if needed).

Metabolism is an important event to consider in genotoxicity and skin sensitization evaluation. Compared to cell models, a broad variety of chemicals with different physico-chemical features can be evaluated in this system (after topical or systemic application): compounds with different pH, physical state (liquids, gels, solids, formulations).

References

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