
Lecture: skin models as alternatives to animal testing

The application of the Phenion[®] Full Thickness Skin Model as an alternative test to predict toxic effects

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It is more than 20 years ago that epithelial equivalents have been successfully produced for clinical studies. Since then reconstructed tissue equivalents of different complexity have been established for scientific investigation as well as commercial use.

While less complex systems, like monolayers, have been extensively analysed in the nineties and the beginning of this century for their applicability in product development and the use as alternatives to animal testing, more sophisticated systems are now available for academia and industry. The Phenion[®] Full Thickness Skin Model is a skin equivalent comprising an epidermis and dermis that resembles native skin in terms of differentiation and protein production.

This talk will address the application of the Phenion[®] Full Thickness Skin Model to predict toxic effects. It has been characterised for its competency to metabolise xenobiotic compounds. Several phase I enzymes (CYP450) as well as phase II enzymes are expressed. The distribution pattern of these enzymes reflects the native situation. Therefore the Phenion[®] Full Thickness Skin Model seems to be a useful tool to show toxic effects to skin mediated by the xenobiotic metabolism.

In the field of genotoxicity the Phenion[®] Full Thickness Skin Model allows to determine transient as well as clastogenic effects, by analysing COMET induction and micronucleus formation, respectively. For the detection of micronuclei a proliferating tissue is required. Thus the detection of clastogenic effects is limited to the epidermis of the Phenion[®] Full Thickness Skin Model. Transient effects can be analysed in the epidermis as well as the dermal compartment.

The sensitising properties of compounds have been assessed *in vitro* in the past using immunocompetent cell lines or cells deriving from human peripheral blood. Coming into contact with test compounds these cells change their composition in cell surface proteins. A metabolic competent skin as first site of contact has not been considered in this context. A coculture system of the Phenion[®] Full Thickness Skin Model and immunocompetent cells might overcome the failure in predicting prohapten correctly.

The close resemblance of the Phenion[®] Full Thickness Skin Model to native skin recommends it as a promising tool to analyse different toxic effect, such as genotoxicity and sensitisation, directed to human skin.

Keywords: skin equivalent, full thickness, genotoxicity, sensitisation, xenobiotic metabolism