
Lecture: skin models as alternatives to animal testing

Advantages and difficulties in using 3-dimensional human skin models in toxicology and efficacy studies

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Three dimensional models of the human skin have been commercially available for use in *in vitro* studies for almost 20 years, but they have never reached their projected potential. Expectations were high that the first full thickness (epidermis plus dermis) skin tissues (produced by Organogenesis) could provide an immediate replacement to animal studies, but although the model proved useful for many investigations, it did not have universal application. Since then other manufacturers have brought skin models to the market, each with a slightly different format, each providing some advantage or disadvantage. Some models have survived, others have been discontinued or their companies have gone out of business.

Clearly human skin models are needed in our *in vitro* arsenal, but each manufacturer seems to struggle at one point or another with the same problems: shipping (especially across the oceans), customs regulations, lot-to-lot reproducibility, contamination with microorganisms, inability to cope with fluctuating demand, and many others. Tissue users can be frustrated by the cost of the product and their inability to cost effectively "test drive" and compare the various tissues. This should not continue since skin has the opportunity to act as a clear replacement for animal studies – it is a human organ that can be grown in isolation from the body yet has the potential to provide information on adsorption, irritation, corrosion, genotoxicity, phototoxicity, sensitization, pigmentation changes, etc. We must reach a point where we can use human skin models from various suppliers interchangeably. It is one of the missions of the Institute for In Vitro Sciences (IIVS) to work with many skin manufacturers so that users worldwide can be assured tissue of high quality and a known standard.

The ability to use multiple skin models is also one of the goals of recent Colipa-sponsored programs on genotoxicity and skin metabolism. In an effort to provide solutions to the animal testing ban of the 7th amendment to the Cosmetics Directive, the project is attempting to validate the use of several human skin models for the detection of both micronuclei induction (originally reported in the EpiDerm™ model [MatTek Corp., Ashland, MA, USA]) and DNA strand breaks (Comet assay) after topical application of test materials. Currently three tissue models (produced by MatTek, Skinethic and Phenion) will be compared under similar protocols for their ability to detect known skin genotoxins. Multiple laboratories are testing the different models first with direct acting carcinogens to show interlaboratory reproducibility, and then with chemicals requiring metabolic activation by the skin, e.g. cyclophosphamide and the polycyclic hydrocarbons. Considerable progress in standardizing the models has been made so far, and it is hoped that several skin models will meet the appropriate criteria so that comparable data can be easily generated in many laboratories around the world.

Keywords: skin models, irritation, corrosion, genotoxicity