

ECVAM Photopotency Feasibility Study: In Vitro Skin Model Phototoxicity Test for Determination Phototoxic Potency of Topical Phototoxins

Manfred Liebsch*, Dagmar Jírová, Kristina Kejlová, Hana Bendová, Helena Kandarova, Julian Tharmann, Dieter Traue, Horst Spielmann

[Centre for Alternative Methods to Animal Experiments – ZEBET](#) (BfR Unit 37), G-Berlin,
[National Institute of Public Health \(SZU\)](#), CZ-Prague,
[MatTek Corporation](#), MA-Ashland

Chemicals and topically applied substances (e.g. pharmaceuticals or cosmetic raw materials) absorbing light in the ultraviolet spectra have to prove their safety with regard to phototoxicity. The first step in determination of phototoxicity of these substances is to perform the validated 3T3 neutral red uptake phototoxicity test (3T3NRU-PT) (OECD TG 432). If the substance provides a negative result in the 3T3NRU-PT, in most instances no further testing is required. However, if the result is positive, the substance may be still applied topically at safe concentrations, depending on the absorption and accumulation of the chemical in the skin. Thus, additional testing might be required to obtain combined information on the phototoxicity and bioavailability of the chemical in the skin.

Ideally, confirmatory tests should be performed *in vivo* on human volunteers, but for ethical reasons, this is not acceptable if the 3T3NRU-PT has provided a positive result. Thus, to avoid confirmatory testing in animals, reconstituted human skin models are offering an attractive *in vitro* alternative approach, since such models are characterized by both skin barrier function and viable primary skin cells.

In the current study, 6 substances which provided positive results in the 3T3NRU-PT, were evaluated on the reconstructed human skin model EpiDerm in the pre-validated phototoxicity test design (Liebsch et al, 1997 and 1999). The negative result or the first non-phototoxic concentration determined by reconstructed skin model, was evaluated in a limited group of human volunteers. The results obtained in this study show, that the human skin model phototoxicity test provides concordant outcome to human response and thus represents a useful step in the sequential strategy for phototoxicity testing.

*presenting author

To be presented at the Linz 2007 – 14th Congress on Alternatives to Animal Testing, September 28-30, 2007 at the University of Linz, Austria.