



Genotoxicity Testing Using the Micronucleus Assay in the EpiDerm™ Human 3D Skin Model

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ABSTRACT

Safety assessment of new products for human use requires genotoxicity testing to ensure their non-carcinogenicity. Current assays are based on non-human cell systems and result in low specificity due to the lack of human-like metabolism and low relevance to the target organs. Starting in 2009, manufacturers of cosmetics products will need to assess genotoxicity using non-animal methods. Since skin has the highest exposure to many cosmetic and personal care products, a skin model will better reflect human exposure and metabolism. Thus, industrial organizations such as COLIPA are actively pursuing development of Micronucleus Assay using a human 3D skin model to serve as a "reporter" tissue for genotoxicity safety assessments.

EpiDerm forms a 3D skin-like tissue that is highly reproducible and contains an epidermis-like barrier. Also, EpiDerm possesses human in vivo-like biotransformation capabilities including CYP450, GST, and UDP enzymatic activity. The EpiDerm MNA protocol utilizes two 10 µl topical doses of test material given 24 hours apart in the presence of 3 µg/ml of Cytochalasin-B in the medium. Cells are harvested from the tissue 24 hours after the last dose. This protocol results in the generation of a reproducible population of binucleated cells (43.9% +/-7.6) with a low background frequency of micronucleated cells (0.07% +/-0.08). We have shown dose-related, statistically significant increases in micronuclei induction for 3 model genotoxins and for 5 out of 6 rodent skin genotoxins. In addition, 4 non-genotoxic chemicals have been evaluated and shown to be negative. Finally, 2 genotoxins that require metabolic activation were also positive in the MNA.

In conclusion, the MNA that utilizes EpiDerm with inherent metabolic activity holds excellent promise to predict genotoxicity while avoiding animal welfare issues.

To be presented at the 6th World Congress on Alternatives & Animal Use in the Life Sciences, August 21-25, 2007, Tokyo, Japan