



Genotoxicity Screening Using the EpiDerm Human 3D Model – Skin Specific Micronucleus Assay

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Safety assessment of new products for human use requires genotoxicity testing to insure 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. Dermally exposed substances require a test which determines skin-specific genotoxicity. Starting in 2009, manufacturers of cosmetics products will need to assess genotoxicity using non-animal methods. Thus, industrial organizations such as COLIPA are actively pursuing development of Micronucleus Assay (MNA) for dermally exposed chemicals.

EpiDerm forms a 3D skin-like tissue that is highly reproducible and contains 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 ul topical doses of test material given 24 hours apart in the presence of 3 ug/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 (0.08% +/-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, 3 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.

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