Accepted Manuscript

Title: Validation of the 3D Skin Comet assay using full thickness skin models: transferability and reproducibility

Authors: Kerstin Reisinger, Veronika Blatz, Joep Brinkmann, R.Thomas Downs, Anja Fischer, Frank Henkler, Sebastian Hoffmann, Cyrille Krul, Manfred Liebsch, Andreas Luch, Ralph Pirow, A. Astrid Reus, Markus Schulz, Stefan Pfuhler

PII: S1383-5718(17)30217-6
DOI: https://doi.org/10.1016/j.mrgentox.2018.01.003
Reference: MUTGEN 402871

To appear in: *Mutation Research*

Received date: 5-7-2017
Revised date: 18-12-2017
Accepted date: 9-1-2018

Please cite this article as: Kerstin Reisinger, Veronika Blatz, Joep Brinkmann, R.Thomas Downs, Anja Fischer, Frank Henkler, Sebastian Hoffmann, Cyrille Krul, Manfred Liebsch, Andreas Luch, Ralph Pirow, A.Astrid Reus, Markus Schulz, Stefan Pfuhler, Validation of the 3D Skin Comet assay using full thickness skin models: transferability and reproducibility, Mutation Research/Genetic Toxicology and Environmental Mutagenesis https://doi.org/10.1016/j.mrgentox.2018.01.003

Validation of the 3D Skin Comet assay using full thickness skin models: transferability and reproducibility.

Reisinger Kerstin[1], Blatz Veronika[2], Brinkmann Joep[3], Downs Thomas R[4], Fischer Anja[1], Henkler Frank[3], Hoffmann Sebastian[5], Krul Cyrille[6], Liebsch Manfred[3], Luch Andreas[3], Pirow Ralph[3], Reus Astrid A[7], Schulz Markus[2] , Pfuhler Stefan[4].

[1] Henkel AG &Co KGaA, Henkelstr. 67, 40589 Düsseldorf, Germany

[2] Experimental Toxicology and Ecology, BASF SE, 67056 Ludwigshafen, Germany

[3] Federal Institute for Risk Assessment, 10589 Berlin, Germany

[4] Procter & Gamble, 8700 Mason-Montgomery Road, Mason, OH 45040

[5] seh consulting + services, Stembergring 15, 33106 Paderborn, Germany

[6] TNO, Utrechtseweg 48, 3704 HE Zeist, The Netherlands

[7] Triskelion B.V., Utrechtseweg 48, 3704 HE Zeist, The Netherlands

Corresponding author: Kerstin Reisinger

Highlights

- The 3D Skin Comet assay is a new in vitro genotoxicity assay for the dermal exposure route.
- Data of an ongoing validation exercise are presented.
- A high predictivity was obtained, i.e. 100% in 4 laboratories, 70% in the fifth.
- In parallel, a good intra- and inter- laboratory reproducibility was observed.
- The assay is intended to follow up on positive findings from standard in vitro assays.

Abstract

Recently revised OECD Testing Guidelines highlight the importance of considering the first site-of-contact when investigating genotoxic hazard. Thus far, only in vivo approaches are available to address the dermal route of exposure. The 3D Skin Comet and Reconstructed Skin Micronucleus (RSMN) assays intend to close this gap in the *in vitro* genotoxicity toolbox by investigating DNA damage after topical application. This represents the most relevant route of exposure for a variety of compounds found in household products, cosmetics, and industrial chemicals.

The comet assay methodology is able to detect both chromosomal damage and DNA lesions that may give rise to gene mutations, thereby complementing the RSMN which detects only chromosomal