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Poster: computer assisted procedures

## Implementation of *in silico* models in the cosmetic industry to face the 7th Amendment of the European Cosmetics Directive

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The 7th Amendment to the EU Cosmetics Directive has made *in vitro* and *in silico* approaches to warrant the safety of products a key issue to support regulatory dossiers and future innovation. A ban on animal testing for chemicals to be used in cosmetics comes into effect in the EU in March 2009 for acute toxicity, genotoxicity, and skin or eye irritation. For repeat-dose (or systemic exposure) toxicity, the EU ban is subject to the 2013 deadline.

Over the past years there have been considerable efforts to develop alternative methods, including *in silico* methods that would comply with regulatory constraints (OECD principles). In this context, transparent and mechanism-based approaches are needed. Progress in the area of computer science and information technology has triggered the creation of curated databases and the development of predictive models for various toxicological endpoints.

A number of commercial or free software integrate global models targeting the 2009 endpoints. From the cosmetic industry perspective, the predictive performance of such models has to be evaluated on chemical series of interest for:

- Chemical prioritization
- Mechanistic understanding
- Elaboration of regulatory dossiers by providing additional information

The purpose of the present study was to use data generated on “real-life” chemicals from the cosmetic industry to challenge some of the global models available today.

Historical in-house data obtained from the *in vivo* skin irritation, bacterial mutagenicity and *in vivo* oral acute toxicity tests, have been curated in collaboration with in-house experts for this purpose. Global models available in the Derek, MC4PC and TIMES software were evaluated for mutagenicity (Derek, MC4PC and TIMES), acute toxicity (Derek, MC4PC) and skin irritation (only Derek since ToxTree will be evaluated in the next phase of this project). Applicability domains and predictive performance were compared in order to identify potential gaps and assess the complementarities of these tools and their relevance in Integrated Testing Strategy (ITS) workflows.

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