



Consortium for in vitro Eye Irritation testing strategy

An Van Rompay¹, Els Adriaens², Nathalie Alépée³, Agnieszka Drzewiecka⁴, Przemyslaw Fochtman⁴, Katarzyna Gruszka⁴, Robert Guest⁵, Helena Kandarova⁶, Michiel Baert⁷, Jamin A. Willoughby Sr.⁸, Sandra Verstraelen¹

an.vanrompay@vito.be

¹Flemish Institute for Technological Research (VITO NV), Mol, Belgium; ²Adriaens Consulting bvba, Aalter, Belgium; ³L'Oréal Research & Innovation, Aulnay-sous-Bois, France; ⁴Institute of Industrial Organic Chemistry, Pszczyna, Poland; ⁵Envigo, Derbyshire, United Kingdom; ⁶MatTek In Vitro Life Science Laboratories, Bratislava, Slovak Republic; ⁷Ghent University, Laboratory of Pharmaceutical Sciences, Gent, Belgium; ⁸Cyprotex US, LLC, Michigan, USA.

Background

Assessment of the acute eye irritation potential is part of the international regulatory requirements for testing of chemicals. All *in vitro* assays have specific strengths and limitations whether this relates to ranges of irritancy, types of chemical classes or physical nature of the materials. Therefore, combinations of *in vitro* assays are needed for hazard identification and complex safety assessment. Today, these combinations of assays are used by individual companies as an integral part of their safety assessments, but often with limited scientific knowledge covering their own specific chemical properties/portfolio needs. This can contribute to a lack of consistency among *in vitro* test results within a battery approach or a conflict with available *in vivo* data.

Despite efforts to compare *in vitro* methods with *in vivo* data, the problem is that most of the so far proposed testing strategies for assessment of eye irritation were not evaluated with the same adequately large set of chemicals. This is consequently resulting in a lack of information on predictive capacity of the *in vitro* assays in a testing strategy. All available information confirms that the strategy is as strong as the weakest part of it.

Cefic LRI-AIMT6-VITO CON4EI project goal

The main objective of this project is to develop tiered testing strategies for eye irritation assessment for all eye irritation drivers of classifications.

In this project the irritancy potency of a set of 80 chemicals, with good quality *in vivo* Draize eye data representing the most important drivers of *in vivo* classification, will be evaluated. Following eight test methods will be included in this project: BCOP¹ (Bovine Corneal Opacity and Permeability), ICE¹ (Isolated Chicken Eye) and STE² (Short Term Exposure), all of them can distinguish Category 1 versus No Category. EpiOcular EIT² (EpiOcular Eye Irritation Test) and SkinEthicTM HCE³ (Human Corneal Epithelial) can distinguish between Not classified versus classified (Category 1/ Category 2). To distinguish between Category 1 and Category 2, the following methods are relevant to include: histopathology in association with the BCOP and ICE, EpiOcular ET-50⁴ (EpiOcular time-to-toxicity test), SMI (Slug Mucosal Irritation), and BCOP-LLBO (BCOP-laser light-based opacitometer).

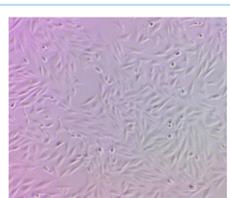
¹regulatory accepted, ²undergoing regulatory acceptance, ³mature in development, ⁴accepted by EPA for testing of antimicrobial cleaning products



BCOP



ICE



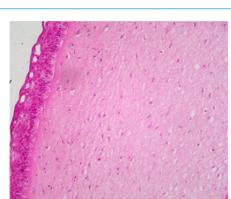
STE



SMI



BCOP-LLBO



Histopatholog
(BCOP-ICE)



SkinEthic
HCE



EpiOcular
EIT/ET50

This project will assess the reliability of these *in vitro* test methods, define applicability domains in terms of 'drivers of classification', strengths and limitations of each method.

In this way, we will be able to identify methods that will fit in a tiered approach to distinguish UN GHS classified Category 1 chemicals versus No Category chemicals and address the highest industrial gaps namely distinguish between Category 2 versus Category 1 chemicals.