Testing Strategies for UN GHS Classification for Serious Eye Damage/Eye Irritation of Chemicals: Cosmetics Europe Analysis.

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Introduction

A core part of the Cosmetics Europe (CE) eye programme focusses on data integration/evaluation of testing strategies/approaches for identification of serious eye damage/eye irritation of chemicals that can be advocated for external/regulatory acceptance. To enable this, CE curated an initial database of chemicals for which in vivo and partial in vitro data exist. This database was used for selection of 80 chemicals tested in in vitro test methods in the CEFCI CONAEI project. After integration of all in vitro data on an industry platform level, remaining data gaps were identified. CE completed in vitro testing to fill these data gaps resulting in a comprehensive in vivo/in vitro database of more than 110 chemicals to date. Building on proposed CONAEI testing strategies, CE has analysed the comprehensive database to determine the robustness of such testing strategies and to identify where opportunities exist for refinement.

Materials and methods

A set of 110 up to 130 chemicals was tested with seven test methods. Distribution of the 130 chemicals (73 liquids & 57 solids) according to the Drivers of Classification as defined by Barroso et al. (2017; definition see poster abstract #516) is shown in the barplot.

In order to identify which test method (original or optimized) was most suitable as a first step in a Top-Down (identification of Cat 1) or Bottom-Up (identification of No Cat) approach (Scott et al., 2010), the performance of each individual test method was assessed by comparing the prediction results with the existing proposed UN GHS classification (data not shown). Next, the most promising test methods were combined into a testing strategy. The performance of the testing strategy was evaluated in terms of correct predictions and the predictive capacity (predictive value).

Performance of two step Top-Down testing strategy (Tab)

Results & Discussion

The predictive value (PV) of a TS is influenced by (1) the prevalence (true distribution of eye effects) in a specific population of chemicals and (2) the accuracy of the TS. The values presented in the Table are based on the accuracy of TS Fig 2, Opt 2.

Top 1st test method

- BCP LLBO (Opacity/Permeability: 145/2)
  - 77% sensitivity

Bottom 2nd test method

- OECD TG 492 RhCE
  - 71% specificity

Assuming a random selection of 100 chemicals from a population with prevalence of outcomes distributed according to substances tested with the OECD TG 405 in REGA registrations (2008-2014) (Luechtefeld et al., 2017) and applying TS Fig 2 Opt 2, the following predictive values are obtained.

- Negative PV: 98% of the test outcomes are correct (correspond with an in vivo No Cat)
- Cat 1 and Cat 2 PVs: 57% and 28% of test outcomes are correct, respectively
- Overall, under predictions will be very low
- The TS tends to result in over-classification, in vivo Cat 2 predicted as Cat 1 and in vivo No Cat predicted as Cat 2

Adriaens et al., 2014. Retrospective analysis of the Draize test for serious eye damage/eye irritation: importance of understanding the in vivo endpoints under UN GHS EU CLP for the development and evaluation of in vivo test methods. Arch. Toxic. 80:701-723

Barroso et al., 2017. Cosmetics Europe compilation of historical serious eye damage/eye irritation in vivo data analyzed by drivers of classification to support the selection of chemicals for development and evaluation of alternative methods/strategies. For the Draize test Reference database (DRDB). Arch. Toxic. 91: 521-547


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