Cosmetics Europe eye program: application of two defined approaches for ocular toxicity predictions based on *in vitro* bottom-up approach on 4 case studies

Abstract # 221

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Introduction

Cosmetics Europe developed two defined approaches (DA) to distinguish between the three UN GHS categories for eye hazard identification, i.e., Category 1 (Cat. 1) on "serious eye damage"; Category 2 (Cat. 2) on "eye irritation" and No Category (No Cat.) for chemicals "not requiring classification and labelling" for eye irritation or serious eye damage (UN GHS, 2019).

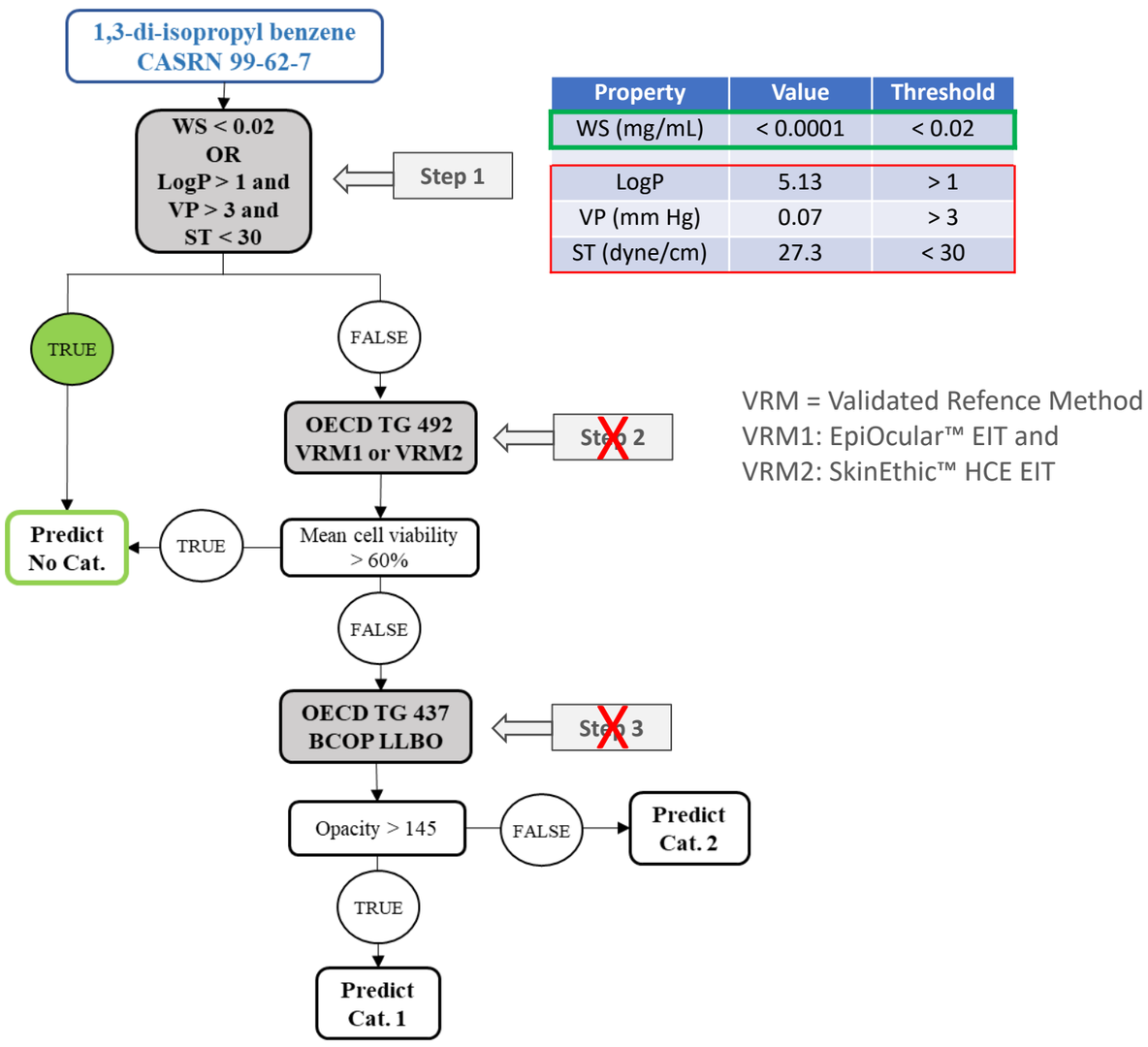
DAL-1 for non-surfactant liquids combines physicochemical properties with the results of two OECD adopted *in vitro* test methods [Reconstructed human Cornea-like Epithelium (RhCE) test method (OECD TG 492), and Bovine Corneal Opacity and Permeability (BCOP) test method (OECD TG 437)] (Alépée et al., 2019a). **DAL-2** for non-surfactant liquids combines the results of two OECD adopted *in vitro* test methods [Short Time Exposure (STE) test method (OECD TG 491) and BCOP test method (OECD TG 437] (Alépée et al., 2019b). In both DAs, the BCOP laser light-based opacitometer (LLBO) is used, as described within the OECD TG 437. The performance of the DALs is presented in poster #1043.

The application of the DALs is illustrated with four case studies using the bottom-up approach. Within each case study, correct decisions are indicted by the green coloured circles and this will guide you to the final prediction for the chemical of interest.

DAL-1 for neat non-surfactant liquids – Case studies

Physicochemical property exclusion rules based on water solubility (WS) or a combination of octanol-water partition coefficient (LogP), vapour pressure (VP) and surface tension (ST) are used in a first step (**Step 1**) to identify liquid chemicals with no serious eye damage or eye irritation potential. The threshold values for the PCP exclusion rules are provided in the decision tree and in the tables below.

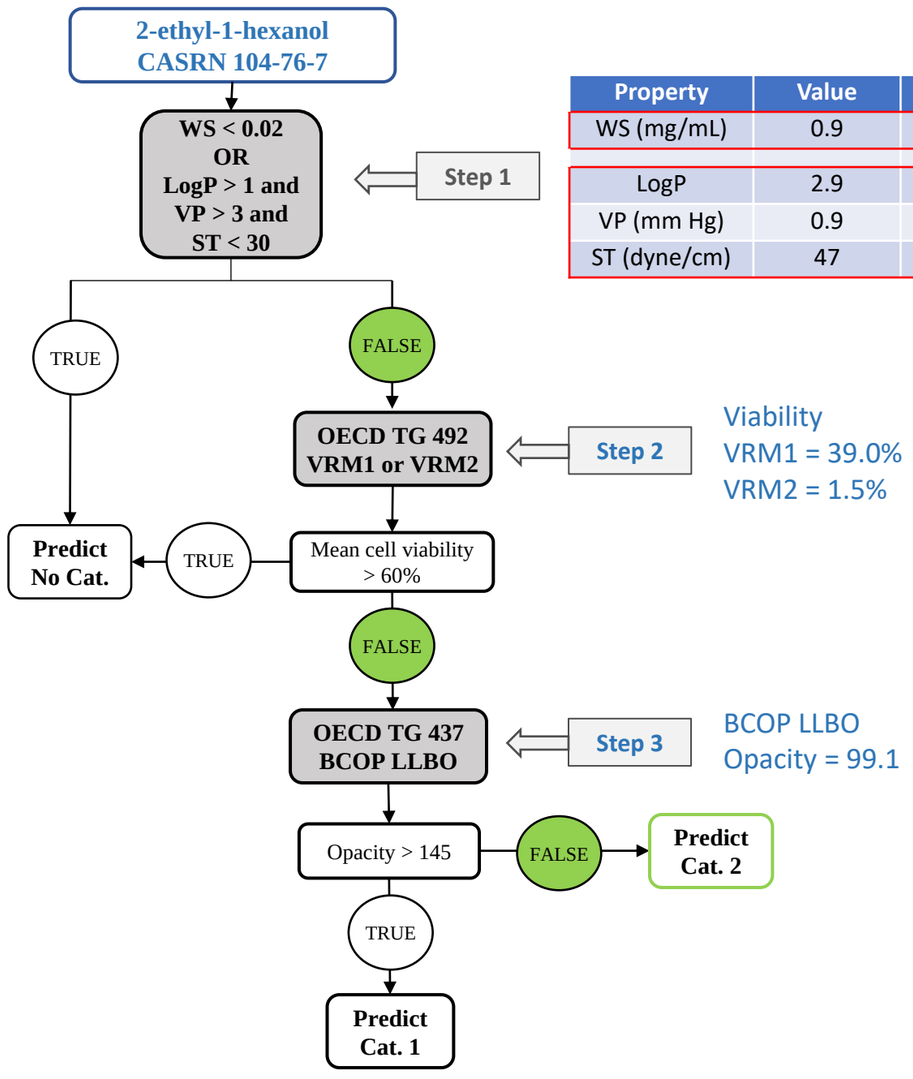
Case study 1



Property	Value	Threshold
WS (mg/mL)	< 0.0001	< 0.02
LogP	5.13	> 1
VP (mm Hg)	0.07	> 3
ST (dyne/cm)	27.3	< 30

VRM = Validated Refence Method
VRM1: EpiOcular™ EIT and
VRM2: SkinEthic™ HCE EIT

Case study 2



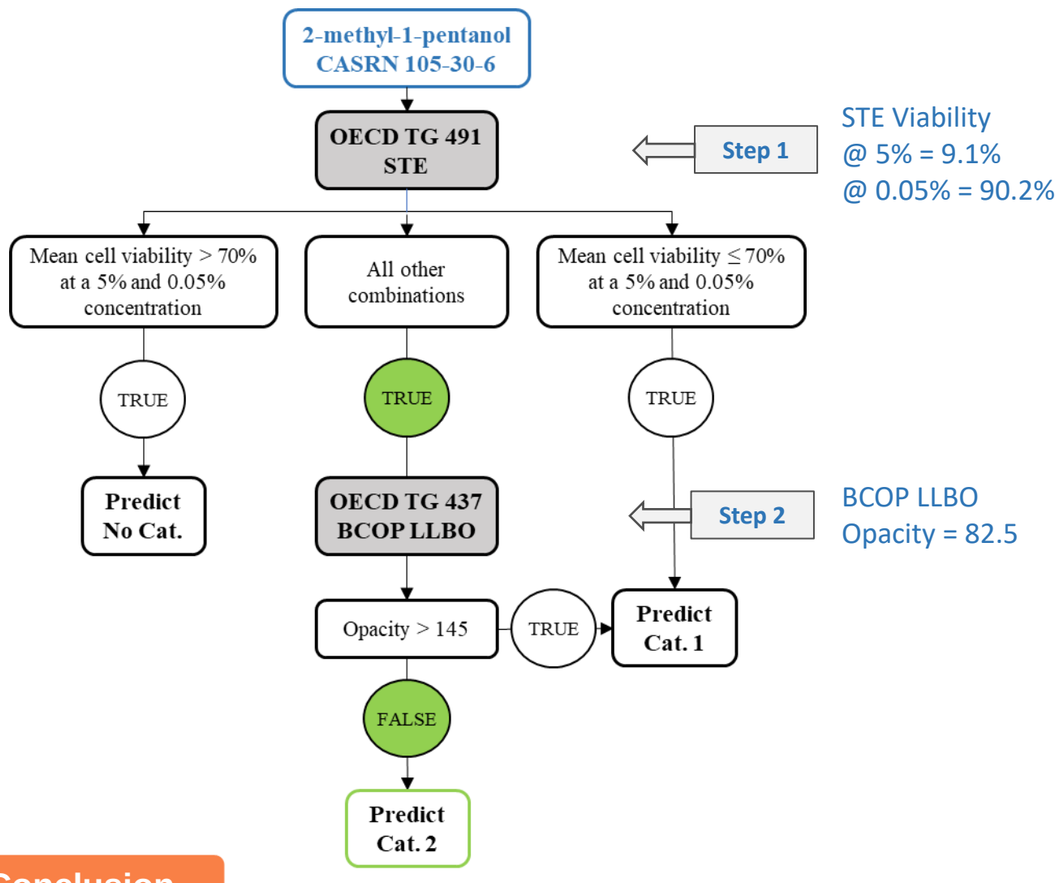
Property	Value	Threshold
WS (mg/mL)	0.9	< 0.02
LogP	2.9	> 1
VP (mm Hg)	0.9	> 3
ST (dyne/cm)	47	< 30

Viability
VRM1 = 39.0%
VRM2 = 1.5%

BCOP LLBO
Opacity = 99.1

DAL-2 for non-surfactant liquids (neat and in dilution) – Case studies

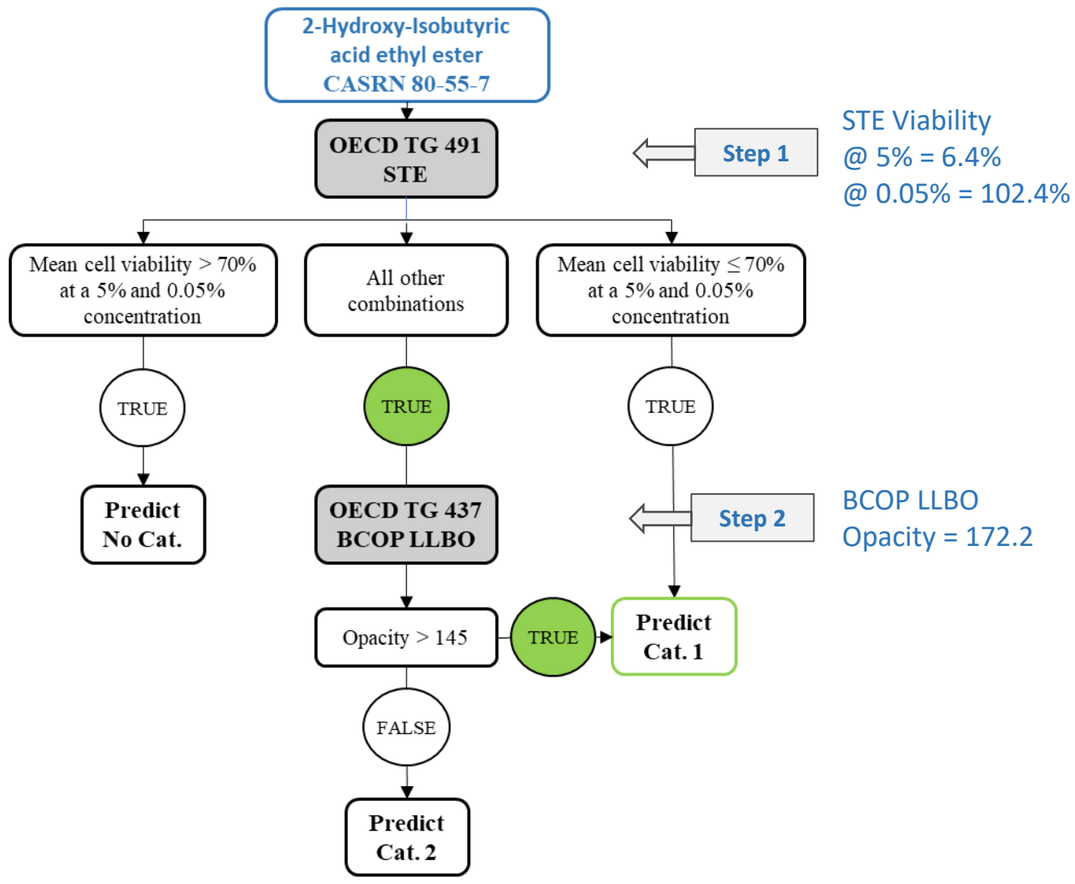
Case study 3



STE Viability
@ 5% = 9.1%
@ 0.05% = 90.2%

BCOP LLBO
Opacity = 82.5

Case study 4



STE Viability
@ 5% = 6.4%
@ 0.05% = 102.4%

BCOP LLBO
Opacity = 172.2

Conclusion

Chemical	CASRN	UN GHS	Prediction
1,3-di-isopropy benzene	99-62-7	No Cat.	No Cat.
2-ethyl-1-hexanol	104-76-7	Cat. 2	Cat. 2
2-methyl-1-pentanol	105-30-6	Cat. 2	Cat. 2
2-Hydroxy-Isobutyric acid ethyl ester	80-55-7	Cat. 1	Cat. 1

The case studies reflect 2 approaches on how to move from animal testing into an evaluation of new non-surfactant liquids ingredients based on examples of application of DAs on an Integrated Approach for Testing and Assessment for safety purposes of ingredients.

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References

Alépée N at al., 2019a. Toxicol In Vitro; 59:100-114. doi: 10.1016/j.tiv.2019.04.011.
Alépée N at al., 2019b. Toxicol In Vitro; 57:154-163. doi: 10.1016/j.tiv.2019.02.019.