Taking into account data quality and uncertainty to guide informed chemical substitution of PMT/vPvM substances

Empa
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Background

- Measures are needed to protect water sources from substances that are mobile, persistent and toxic (PMT) or very persistent and very mobile (vPvM).
- PMT/vPvM substances are used in a diverse range of applications, including cosmetic products, such as the three selected case-study chemicals (Figure 1).
- Our previous research based on three case-study chemicals showed that potential safer alternatives are available, as identified through an alternatives assessment based on the concepts of essential use and functional substitution and three different multi-criteria decision analysis (MCDA) strategies [1].
- Safer alternatives were identified based on PBMT parameters. Both experimental data and QSAR data were used, but data gaps remained (Figure 2).

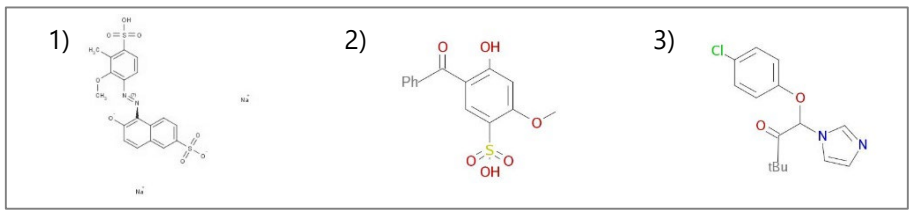

Figure 1: *The three selected case-study chemicals 1) Allura Red (colourant; CAS 25956-17-6), 2) Benzophenone-4 (UV-filter; CAS 4065-45-6) and 3) Climbazole (anti-seborrheic; CAS 38083-17-9).*

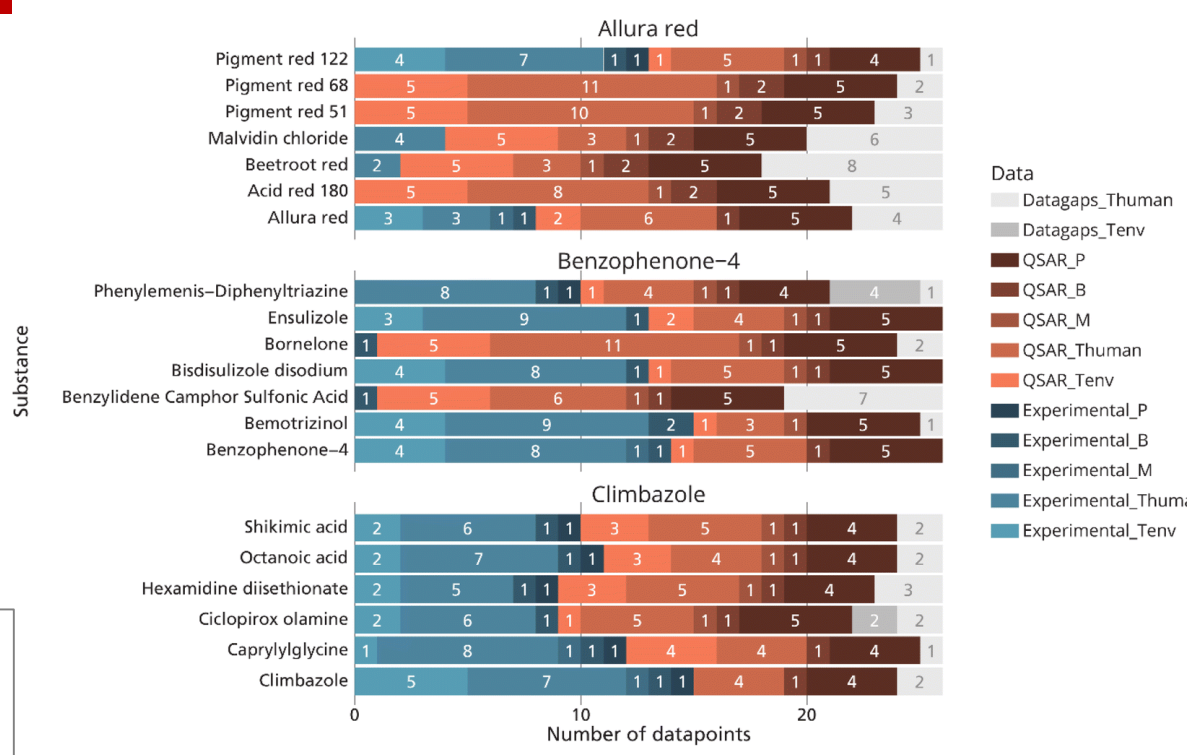

Figure 2: *Total amount of experimental data, QSAR data and data gaps for the 26 PMBT endpoints considered for the alternative assessment, consisting of environmental fate and behaviour endpoints (P = persistency, B = bioaccumulation, and M = mobility) and human health (Thuman) and ecotoxicity (Tenv) endpoints.*

Objectives

- Most experimental data from the previous study was obtained from REACH dossiers [1]. Issues regarding reliability of this data have been raised before [2].
- Modelled results also need to be interpreted with caution

→ **Incorporate reliability assessments for experimental and modelled data in order to communicate and deal with uncertainties, subsequently increasing the transparency of the alternative assessment.**

- Combination of experimental and QSAR data (Figure 2) as well as identified data-gaps needs further consideration
- Data can be less reliable when only one study for an endpoint is available. Supplementing data with a set of QSAR predictions might be more desirable instead of using one single experimental value.

→ **Combine different data sources and test different approaches to include data gaps**

- Ranking of safer alternatives is largely determined by the selected endpoints of the assessment
- Most relevant endpoints can differ per use scenario
- The application of MCDA approaches can be used to frame decision-making problems and develop a comprehensive assessment of alternatives

→ **Explore how trade-offs and different data and safety requirements for different uses can be incorporated and influence the final decision-making using MCDA**

Proposed workflow

Collect available experimental hazard data and run QSAR models

- ECHA database, Ecotox database, eChem portal, EFSA database, COSMO, ECHA IUCLID, HPVIS
- QSAR models: OECD QSAR Toolbox, Danish QSAR database, VEGA 1.2.3 platform

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Generate confidence scores and exclude data accordingly

- CRED method [3] for experimental data;
- QSAR applicability domain and expert judgement for modelled data

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Summarise the different data (types) per endpoint

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Score and/or rank the outcomes for the different hazard endpoints using MCDAs

References

[1] van Dijk et al. (2023). Environmental Science: Processes & Impacts, 25(6), 1067-1081.

[2] Ingre-Khans et al. (2019). Toxicol. Res., 8(1), 46–56

[3] Moermond et al. (2016). Environmental Toxicology and Chemistry, 35(5), 1297-1309.

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PARC Partnership for the Assessment of Risks from Chemicals

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