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Managing PMT/vPvM substances in consumer products through the concepts of essential-use and functional substitution: a case-study for cosmetics†

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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 consumer products. The combined application of the essential-use and functional substitution concepts has been proposed to phase out substances of concern and support the transition to safer and more sustainable chemicals, a key goal of the European Commission's Chemicals Strategy for Sustainability. Here, we first identified the market share of PMT/vPvM containing cosmetic products. We found that 6.4% of cosmetic products available on the European market contain PMT or vPvM substances. PMT/vPvM substances were most often found in hair care products. Based on their high occurrence, the substances Allura red (CAS 25956-17-6), benzophenone-4 (CAS 4065-45-6) and climbazole (CAS 38083-17-9) were selected as case-studies for assessment of their functionality, availability of safer alternatives and essentiality. Following the functional substitution framework, we found that the technical function of Allura red was not necessary for the performance of some cosmetic products, making the use non-essential. For other applications of Allura red, as well as all applications of benzophenone-4 and climbazole, the technical function of the chemical was considered necessary for the performance. *Via* the alternative's assessment procedure, which used experimental and *in silico* data and three different multicriteria decision analysis (MCDA) strategies, safer alternatives were identified for all case-study chemicals. All assessed uses of PMT/vPvM substances were thus deemed non-essential and should consequently be phased out.

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Environmental significance

Persistent, mobile and toxic (PMT) and very persistent and very mobile (vPvM) substances pose a risk to water resources worldwide, and thus also to environmental and human health. Although PMT/vPvM substances are widely used, their exact use in consumer and industrial applications is often not well known or well characterised. The essential use and functional substitution concepts have recently been developed as tools to characterise and manage the many uses of chemicals of concern. Here, as recently recommended in the literature, the two concepts are applied in combination to facilitate the transition away from using PMT/vPvM substances in cosmetic products. Minimising the use of PMT/vPvM substances in "open uses", such as in cosmetic products, will lower environmental emissions and thus human and wildlife exposure.

1 Introduction

Synthetic chemicals are present in approximately 95% of all manufactured goods and are considered as indispensable for modern societies.[1] Over 350 000 chemicals and mixtures are reportedly registered for usage and production globally.[2] Chemical production, use and disposal result, however, in pollution of the environment, affecting both human and environmental health.[3,4] Furthermore, pollution, including that from chemicals, has been identified as one out of five main drivers for global biodiversity loss.[5] Chemical pollution (now known as "novel identities") is also one of the planetary boundaries which humanity has already crossed.[6,7]

Driven by safety concerns, regulations are in place worldwide in order to reduce the risks associated with the use of chemicals. In the EU, the main chemical legislation REACH (Reg. No. 1907/2006 EC) should 'ensure a high level of

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protection of human health and the environment as well as the free movement of substances… while enhancing competitiveness and innovation'. REACH should also promote the development of alternative methods for the assessment of hazards of substances. Under REACH, substances that are persistent, bioaccumulative and toxic (PBT) and substances that are very persistent and very bioaccumulative (vPvB) are identified as substances of very high concern (SVHC), resulting in a limit or ban of their production and consumption. Current SVHC classification criteria, however, do not capture all potentially hazardous substances, including substances that negatively impact water resources. The so-called mobile substances are readily transported in water, soil layers, river banks, and aquifers, or pass through natural or artificial barriers (*e.g.* in wastewater treatment plants). When combined with persistence, these mobile substances accumulate in the aquatic environment and drinking water sources.[8–10] Mobility (*M*) has therefore been proposed as an additional hazard criterion to identify SVHCs, as substances that are mobile, persistent and toxic (PMT) or very persistent and very mobile (vPvM).[11,12]

PMT/vPvM substances are currently used in a diverse range of applications, including in cosmetic products.[10] An estimated 2320 thousand tonnes of cosmetic products are sold per year in the European Economic Area.[13] Furthermore, it has been reported that cosmetic products contain a large number of chemicals with potential hazardous properties.[14] Environmental risks are currently not taken into account for market approval of cosmetics under the Cosmetic Products Regulation (CPR, Regulation (EC) No. 1223/2009),[15] despite the use of cosmetic products contributing to the occurrence of chemicals in the environment.[13] Several improvements are expected, however, in light of the European Green Deal's Chemicals Strategy for Sustainability (CSS).[12] As part of the CSS, a new legislative proposal to amend the CPR will be presented. This will include an aim to minimise and substitute the use of chemicals that have a chronic effect on human health and the environment, and incorporation of the essential-use concept in order to phase out the most hazardous chemicals.[16]

The essential-use concept was first introduced in 1987 as part of the Montreal Protocol to phase-out ozone-depleting chlorofluorocarbons. Under the Montreal Protocol, the use of a substance is considered essential if: "(1) it is necessary for health and safety or is critical for the functioning of society; and (2) there are no available technically and economically feasible alternatives or substitutes that are acceptable from the standpoint of environment and health". More recently, the essential-use concept was proposed as a tool to guide the phase-out of PFAS.[17,18] Following this approach, uses of PFAS can be classified into three different categories: (1) essential and non-substitutable, (2) essential but substitutable by safer chemicals and (3) non-essential; and only the uses that would be judged as being essential and non-substitutable should be authorised.[17,18]

Essentiality assessments have been proposed to focus on the technical function provided by a chemical for a specific use. Hence, it was recently suggested to combine the essential-use concept with the functional substitution approach.[17,19] The identification of non-essential uses is key to prevent the continued use of hazardous substances. In order to identify uses that are substitutable, the implementation of the essential-use concept requires a sufficient understanding of the current uses of substances, but also of the availability, suitability, and hazardous properties of alternatives.[17,20] Identifying alternative non-hazardous chemicals that are functional and affordable is key to prevent regrettable substitution of chemicals.[21,22]

First described by Tickner *et al.* (2015), functional substitution aims to evaluate whether the function of a chemical is necessary for the application, and then examines through alternative assessment whether safer and effective chemicals, product/process design, or product service alternatives exist to provide a similar function.[23] By combining the essential-use and functional substitution concepts, and thus focussing on both the essentiality, function and performance of substances of concern, a solution-oriented approach is obtained that can help to effectively support the transition to safer and more sustainable chemicals.[19]

The aim of this study is to explore the potential of the combined application of the essential-use and functional substitution concepts to facilitate the phase-out of PMT/vPvM substances in cosmetic products. First, the market share of PMT/vPvM-containing cosmetic products is identified through database searches. Then, the most frequently occurring substances are selected as case-study chemicals for which an assessment is performed per use case by (1) assessing the functional use of these chemicals, (2) identifying suitable and safer alternatives through the process of alternative assessment and (3) considering whether the use of the chemical is necessary for health and safety or critical for the functioning of society, in case no suitable and safer chemical alternatives are available.

2 Methods

An overview of the method used to determine the essentiality of specific potential PMT/vPvM substances used in cosmetic products is presented in Fig. 1. An integrated method has been developed based on the concepts of essential-use,[18] function substitution[23] and the decision tree suggested by Roy *et al.* (2022).[19] The hazard assessment of alternatives was based on ECHA[24] and OECD[25] guidances. Each step is explained in more detail below.

2.1 Identifying PMT/vPvM substances in cosmetic products

The most comprehensive analysis of PMT/vPvM substances registered under REACH has been published by the German Environment Agency in which any substance with a logarithm of the organic carbon–water partition coefficient ($\log K_{oc}$) lower than 4 is classified as being mobile.[26] In total, 211 substances have been identified as potential PMT/vPvM substances. These substances were compared with entries in the cosmetic ingredient database (CosIng) in order to identify substances which can be used in cosmetic products.[27] As of November 2021, CosIng had a total of 53 028 entries. These entries contained many substances without CAS numbers. In addition, the list

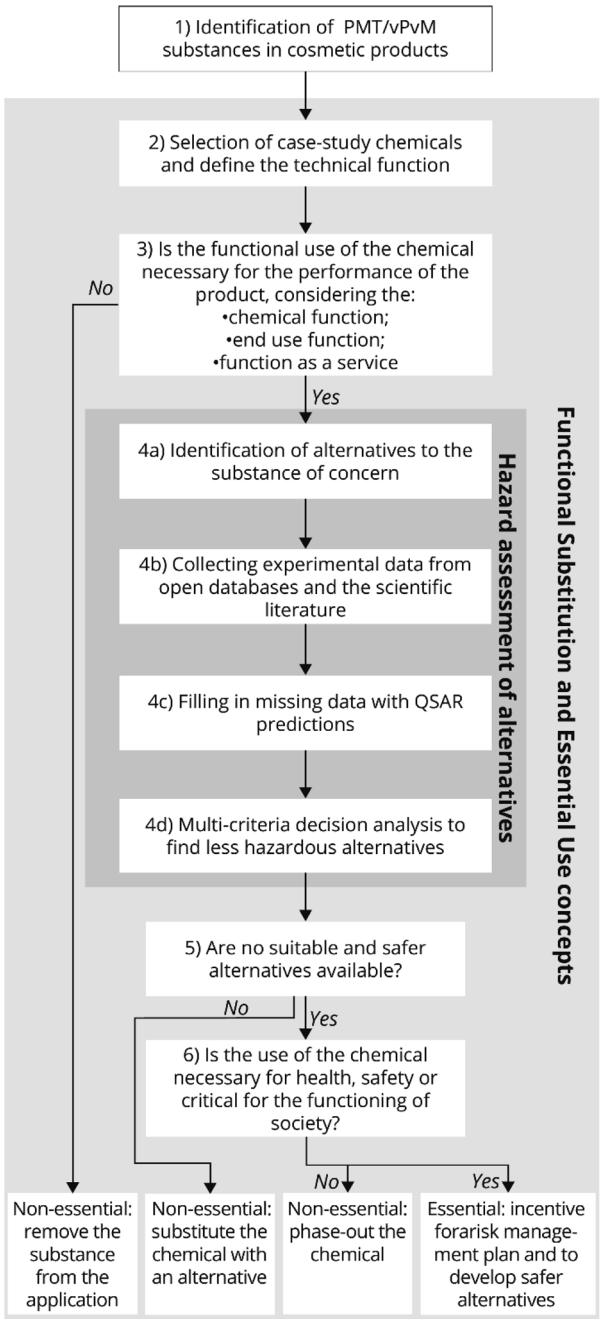

Fig. 1 Integrated methodology for the identification and assessment of chemical alternatives to PMT/vPvM substances in cosmetics, incorporating aspects from the concepts of functional substitution, essential-use and alternative assessment.[18,19,23,25]

contains substances that are mentioned twice or more, due to their multiple functions. When substances without a CAS number are removed and substances with multiple functions are merged, this results in 10 000 unique CAS numbers.

PMT/vPvM substances listed in the CosIng database were screened in The Danish Consumer Council Think Chemicals (Kemiluppen, screened in November 2021) and Cosmethics (screened in December 2021) databases to identify cosmetic products containing PMT/vPvM substances. Kemiluppen is an initiative under the Danish Consumer Council and contains information on cosmetic products available on the Danish market. A full database search was performed for this study, only leaving out outdated products as these are no longer on the market. Cosmethics is a company that has a data repository of cosmetic products. For our study, 1000 products registered in Cosmethics in 2021 were randomly selected and analysed for PMT/vPvM substances. Data beyond the publicly available information of these databases were obtained *via* personal communication with Stine Müller (Kemiluppen) and Katariina Rantanen (Cosmethics). The three highest occurring substances in the datasets were selected as case studies for the assessment of alternatives and for further analysis of essentiality.

2.2 Technical function and application of substances

The general technical function(s) provided by the case-study chemicals was derived from the CosIng database. Interviews with Gerald Renner (Cosmetic Europe) and Héloïse Le Levier (IDUN Minerals) helped to provide a better understanding of the precise technical function provided by the substances of interest and their necessity for the performance in each application.

2.3 Investigating the availability of suitable alternatives

A suitable alternative includes any type of alternative (*i.e.*, chemical, material, process and/or product alternative) which is safer for the environment and human health, and technically and economically feasible.[24] To determine whether suitable alternatives to each case-study chemical were available, an alternative assessment based on chemical hazards (PBMT) was performed following the framework described in the ECHA guidance for the preparation for application for authorisation, and the suggestions provided in the OECD guidance for key considerations for the identification and selection of safer chemical alternatives.[24,25]

2.3.1 Identification of potential alternatives. Potential chemical alternatives with a similar technical function to that of the case-study chemicals were identified *via* the CosIng database, the cosmetics ingredient database,[28] and the list of authorised substances under the CPR and approved food additives, as approved food additives can also be used in cosmetic products (Regulation (EC) No. 1333/2008). In addition, literature searches (*e.g.*, reports from industry, industry organisations and suppliers' website) were performed. Only substances with a CAS number were considered in this study.

The potential chemical alternatives were shortlisted in order to filter out substances known (or suspected) to be hazardous. To achieve that goal, the potential alternatives were screened in the SUBSPORT database, which includes 32 lists of substances from industry, authorities and non-governmental organisations (NGOs) that are legally or voluntarily restricted, or are recommended for restriction due to their hazardous properties.[29] All the lists screened in the SUBSPORT database are listed in the ESI (SI 1).† Annex III to the CPR (listing restricted substances in cosmetic products) was used as an additional priority list to filter out substances. The ECHA database of registered

substances was screened to identify classifications under CLP (classification, focussing labelling and packaging) and C&L (classification and labelling) notifications for potential alternatives. Lastly, the REACH Annex III inventory was screened to determine if the potential alternatives are suspected to present CMR (carcinogenic, mutagenic or reprotoxic), PBT and ED (endocrine disruption) properties based on QSAR outcomes. The precise workflow, which has been followed to shortlist chemical alternatives for further assessment, is presented in the ESI (SI 1).† Other types of potential alternatives (*e.g.*, change in product and change in material) were identified based on the information collected during semi-structured interviews with Gerald Renner (Cosmetic Europe) and Héloïse Le Levier (IDUN Minerals).

2.3.2 Hazard assessment of the shortlisted alternatives. A hazard assessment was performed for the shortlisted chemical alternatives following the recommendations of the OECD guidance (OECD, 2021). To that end, 26 hazard endpoints were selected. These cover PBMT properties, consisting of environmental fate and behaviour endpoints (P = persistency, B = bioaccumulation, and M = mobility) and human health (T_{human}) and ecotoxicity (T_{env}) endpoints (SI 1†). First, experimental data were collected *via* the OECD QSAR toolbox, ECHA registration database, US EPA CompTox and EcoTox databases, and the EFSA Foodtox database.[30–33] The data set was supplemented with experimental data from open literature when possible. The search strategy is explained in more detail in SI 1.† When no experimental data were found, quantitative structure–activity relationship (QSAR) models were used to attempt to fill in data gaps. Only models fulfilling criteria, as laid down in Annex XI to the REACH regulation, were used (Regulation (EC) No. 1907/2006). To that end, models available in the OECD QSAR Toolbox and the VEGA platform were used. Only predictions from models for which the compounds of interest fall in the applicability domain were kept. An average value was calculated when multiple models were available. Predictions from classification models were transformed into quantitative data by calculating the ratio of models returning a "positive" outcome over the total number of models for which the compound of interest falls in the applicability domain (for a given endpoint). Further details on the collection of hazard data are provided in the ESI (SI 1).†

2.3.3 Comparison of the alternatives

2.3.3.1 Heatmap. Hazard profiles of each alternative were compared by using a heatmap. The range of values for each hazard endpoint was divided into four colour-coded categories. The threshold values to define the categories for each hazard endpoint were taken from Zheng *et al.* (2019), who used CLP and PBT classification criteria to assign hazard categories.[34] All threshold values used in this study are available in the ESI (SI 1).† In order to compare the hazard profiles of the potential alternatives, a score was assigned to each alternative following the recommendations of the OECD guidance. In short, for a given alternative, a score of 1 was assigned for every endpoint coloured green (low hazard), of 2 for endpoints coloured yellow (moderate hazard), of 3 for endpoints coloured orange (high hazard), and 4 for endpoints coloured red (hazard criterion exceeded). To test the sensitivity of the approach to the data gaps, three different scenarios were tested (*i.e.*, risk neutral, risk seeking, and risk averse scenarios) as has been performed in previous studies.[34,35] For the risk neutral scenario, data gaps were assigned a score of 2.5. The method to assign the score to data gaps under the other scenarios is detailed in SI 1.† The final score of the alternative was obtained by summing up the scores of each endpoint. The alternative with the lowest score was considered to be the potentially safest alternative.

2.3.3.2 MAUT and ELECTRE III. A multi-criteria analysis based on the multi-attribute utility theory (MAUT) principle was performed on the hazard endpoints based on the study by Zheng *et al.* (2019).[34] In short, the data collected for all alternatives were normalised from 0 to 1 for each endpoint considered in the assessment, with 0 corresponding to the worst level, and 1 to the best level for a given endpoint. As for the heatmap, three different scenarios were used to test the sensitivity of the approach to the data gaps. Under the risk neutral scenario, data gaps were assigned a value of 0.5. Further information on the approach is provided in the ESI (SI 1).†

The scores for P, B, M, T_{human}, and T_{env} were considered as equally important (equal weight approach) and added up to obtain a final MAUT score for a chemical. The chemical with the highest MAUT score was assumed to be the most preferred alternative. The MAUT assessment was complemented with ELECTRE III (an outranking method), for which calculations were performed according to Zheng *et al.* (2019, 2021).[34,35] The determination of the thresholds for the pairwise comparison for each endpoint is detailed in the ESI (SI 1).†

2.4 Necessity of the use of the compound of concern for health, safety, and functioning of society

As no clear criteria to evaluate the necessity of the use of a chemical for health, safety and functioning of society are available at the time of the study, only a qualitative assessment was performed.

3 Results

3.1 Occurrence of PMT/vPvM substances in cosmetic products

50 PMT/vPvM substances were identified in CosIng (SI 2†). These include REACH registered substances and the pharmaceuticals ibuprofen, naproxen, and progesterone and the biocidal active substance, triclosan. Six substances (dimethoxydiglycol, pigment orange 5, progesterone, chloroform, DMSO and methylthiophenyl morpholino isobutanone) on this list were listed as Annex II substances, meaning their use in cosmetic products is prohibited. These six substances were subsequently not considered for further analysis as they should not be present in cosmetic products. The remaining 44 substances were screened in the cosmetic product databases. Out of these substances, 21 were identified in cosmetic products. In total, 20 of these substances were found in 6.6% (897) of the cosmetic products listed in Kemiluppen, and 8 substances were found in 6.2% (ref. 62) of the cosmetic products screened

in the Cosmethics database (Fig. 2). In both databases, the product group containing the most PMT/vPvM substances was hair care products. Table S1† lists all PMT/vPvM substances which have been identified in the Cosing database along with their technical function(s), and the type of cosmetic products they are used in. Based on their high occurrence, Allura red (CAS 25956-17-6), benzophenone-4 (CAS 4065-45-6) and climbazole (CAS 38083-17-9) were selected as case-study chemicals for the assessment of alternatives and essentiality.

3.2 Technical function provided by case-study chemicals

3.2.1 Allura red. Allura red is a red pigment used to provide colour to cosmetic products, drugs and food and beverages.[36] In the database analyses, Allura red was found in all types of cosmetic products. Some of these products aim to change the appearance of certain body parts (*e.g.* hair colour products amd make-up). In those types of products, it has been assumed that the chemical function of Allura red is necessary for the technical performance of the cosmetic product (Table 3). However, according to industry stakeholders, a pigment can also be incorporated into formulations in order to make the cosmetic product more attractive to the consumer (*e.g.* providing a red colour to a soap formulation that smells like cherries). According to industry stakeholders, similar results could be achieved by, for example, changing the colour of the packaging. Therefore, it has been assumed that the pigment is not necessary for the technical performance of the product and could be removed from the formulation.

3.2.2 Benzophenone-4. Benzophenone-4 is a so-called broad spectrum UV-filter and can adsorb both UVB and short UVA range rays,[37] and was found in all types of products. In sun care products, benzophenone-4 is added to protect the human skin from UV radiation, whilst in other products benzophenone-4 is added to protect the cosmetic product from degradation by light and therefore to increase the shelf-life. In both applications the technical function of benzophenone-4 was considered necessary for the technical performance of the cosmetic products (Table 3).

3.2.3 Climbazole. Climbazole is a halogenated preservative and exhibits a strong activity against fungi. Halogenated preservatives are commonly added to personal hygiene products.[38] However, climbazole was only found in shampoos. The chemical is also listed as an anti-seborrheic agent in anti-dandruff shampoos to treat a common chronic inflammatory skin condition called seborrheic dermatitis. Due to these chemical functions, climbazole was considered to be necessary for the technical performance of the products (Table 3).

3.3 Identifying suitable chemical alternatives

3.3.1 Identification and short listing of potential alternatives. For Allura Red at the time of the analysis, 47 substances with a CAS number that provide a red colour were allowed to be used as alternatives in cosmetic products (Annex IV to Regulation 1223/2009/EC). Some of these substances were inorganic substances, which are exempted from PBT/vPvB assessments under REACH. Hence, no information on these properties is contained in the REACH database. In addition, QSAR models cannot be used to predict the chemical properties of inorganic substances. Subsequently, only organic compounds were selected for the alternative assessment. Based on known hazard and classification data,[29–31,39] six of these colourants were shortlisted for the alternative assessment for Allura red (Table 1).

For benzophenone-4, 39 potential alternatives were selected from annex VI of the CPR (allowed UV-filters). Six of these substances were selected for the alternative assessment based on known hazard data, classification, and by compromising both low priority substances for environmental assessment[40] and UV filters with a similar absorbance compared to that of benzophenone-4.[41]

As climbazole was only found in shampoos, only its anti-seborrheic functionality was considered for which 10 potential alternatives were identified. Based on known hazard data and classification five of these substances were selected for the alternative assessment.

The exact process to shortlist chemical alternatives for further assessment is presented in SI 1,† and the collected data are shown in SI 3.† All case-study chemicals and the alternatives selected for this study are presented in Table 1, and S3.2.2† provides further information on the chemical structure and physico-chemical properties of the shortlisted alternatives.

3.3.2 Data collection of hazard endpoints for the alternative assessment. All the hazard data collected for the hazard assessment of the shortlisted alternatives are presented in the ESI (SI 4).† An overview of the type of hazard data which have been collected is presented in Fig. 3. The ECHA database of

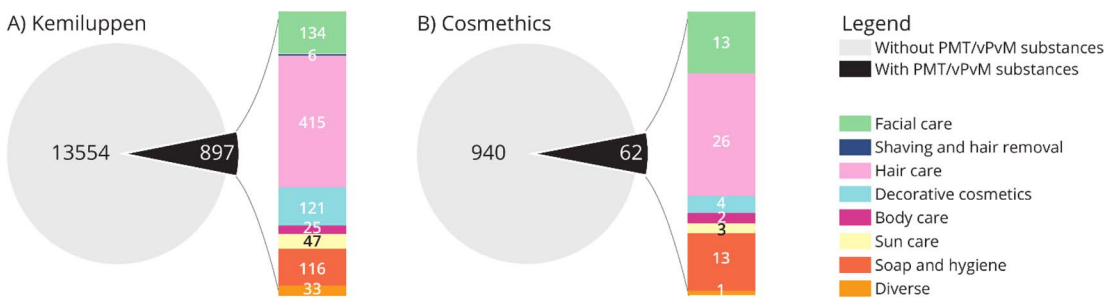

Fig. 2 Total number of cosmetic products with and without PMT/vPvM substances in the databases from (A) Kemiluppen and (B) Cosmethics.

Table 1 Overview of the studied case-study chemicals and short-listed alternatives and their Chemical Abstract Service (CAS) registry number. Further details of the assessed substances are presented in Table S2-2

Use case	Chemical name	CAS number
Pigment	**Allura red**	**25956-17-6**
	Malvidin chloride	643-84-5
	Beetroot red	7659-95-2
	Pigment red 51	5850-87-3
	Pigment red 68	5850-80-6
	Acid red 180	6408-26-0
	Pigment red 122	980-26-7
UV-filter	**Benzophenone-4**	**4065-45-6**
	Ensulizole	27503-81-7
	Benzylidene camphor sulfonic acid	56039-58-8
	Bisdisulizole disodium	180898-37-7
	Bemotrizinol	187393-00-6
	Bornelone	2226-11-01
	Phenylemenis-diphenyltriazine	55514-22-2
Anti-seborrheic	**Climbazole**	**38083-17-9**
	Octanoic acid	102731-54-4
	Caprylylglycine	14246-53-8
	Shikimic acid	138-59-0
	Ciclopirox olamine	41621-49-2
	Hexamidine diisethionate	659-40-5

registered substances was the most important source for collecting experimental data. No or few experimental data were found for substances not registered under REACH. QSAR models were used to fill in missing data, but some data gaps for human and environmental toxicity endpoints still remain for all substances. Data gaps were mainly found for acute and chronic toxicity for exposure *via* inhalation and dermal application. More information on how hazard data were harmonised and predictions from QSAR models were handled are presented in the ESI (SI 1).†

3.3.3 Heat map and scoring based on regulatory criteria. The heat map shows that all assessed chemicals obtained at least one red endpoint, indicating that none of the chemical alternatives can be considered as "non-hazardous" according to current (regulatory) criteria (Fig. 4). When looking at the total obtained hazard scores, the most favourable alternative for Allura red is Beetroot red with a score of 44.5. Beetroot red obtained the fewest number of red indicators, but also has most data gaps. Allura red, as well as all assessed alternatives, were assigned a red indicator for mobility. Moreover, with the exception of Beetroot red, all substances were assigned multiple red indicators for persistency.

For benzophenone-4, all substances were assigned at least one red indicator for persistency and, except for bemotrizinol, the mobility hazard criterion was met for all substances. The lowest total hazard score of 37 was obtained for ensulizole, making this the most preferred alternative.

Climbazole and potential alternatives were all assigned a red indicator for mobility as well. The lowest hazard score was obtained for shikimic acid, which obtained a score of 36.5.

Heat maps for the other scenarios (*i.e.* risk seeking and risk averse scenarios) to test the sensitivity of the approach to the data gaps are available in the ESI (SI 5).† This, however, did not change the ranking of the most favourable alternative compared to the case-study chemical.

3.3.4 Multi-attribute utility theory and ELECTRE III. All the data and results of the MAUT and ELECTRE III methods are available in the ESI (SI 5, Tables S5.2 and S5.3).† In agreement

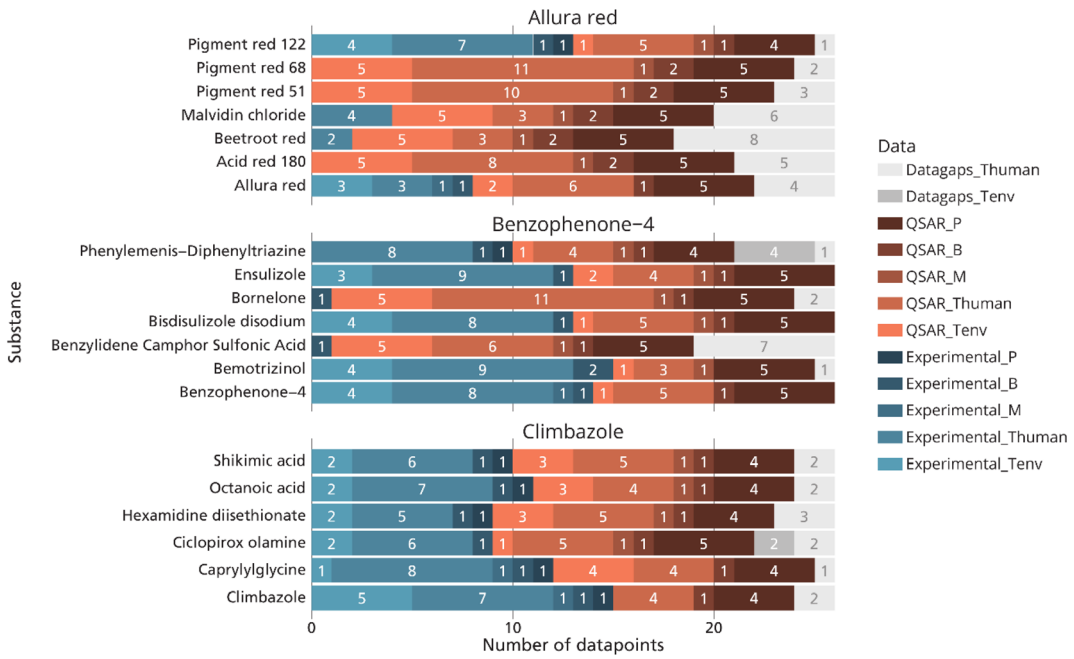

Fig. 3 Total amount of experimental data, QSAR data and data gaps for the 26 PMBT endpoints considered for the alternative assessment, consisting of environmental fate and behaviour endpoints (P = persistency, B = bioaccumulation, and M = mobility) and human health (T_{human}) and ecotoxicity (T_{env}) endpoints.

Fig. 4 Heat map and total hazard score of the three case-study chemicals and their potential alternatives for the *P* (persistency), *B* (bio-accumulation), *M* (mobility), human toxicity (T_{human}) and ecotoxicity (T_{env}) endpoints. The thresholds for the colour codes were based on ref. 34 and the scores were based on ref. 25 Colour codes indicate whether a hazard criterion is exceeded according to current regulatory standards and a very high hazard (red) is assigned. When hazard criteria fell below regulatory standards a high (orange), moderate (yellow) or low (green) hazard level is assigned. Chemicals with lower hazard scores compared to the case-study chemical are potentially safer alternatives.

with the heat-map, the MAUT analysis also showed that for every case-study chemical a safer alternative is available (Fig. 5). In order to test the sensitivity of the approach, the assigned value for data gaps was varied under the 'risk averse' and 'risk seeking' scenarios. This, however, did not seem to change the ranking of alternatives compared to the case-study chemical, as shown in the ESI.†

Similar ranking of the alternatives was furthermore observed in the ELECTRE III method, which was performed to complement MAUT results. From Fig. 5, it can be observed that, even though the total MAUT score is higher for some potential alternatives, the individual criteria do not always have a better score. For example, benzophenone-4 has a *P* score of 0.51, but most assessed alternatives are more persistent based on the available data, and therefore have a lower *P* score.

3.3.5 Comparison of MCDA approaches. The final ranking of the potential alternatives according to the three multicriteria decision analysis (MCDA) approaches considered in this study is shown in Table 2. In the cases of the pigment and the UV-filter, although the final ranking of the alternatives differs according to the MCDA method which is being used, it is possible to identify one substance which is consistently ranked first in both cases (*i.e.* Beetroot red in the case of Allura Red; E\ensulizole in the case of benzophenone-4). Furthermore, it is also possible to identify substances which are consistently ranked lower than the substance to phase-out (*i.e.* Pigment red 51 and Acid red 180 in the case of Allura Red; benzylidene camphor sulfonic acid, bornelone, and phenylemenis-diphenyltriazine in the case of benzophenone-4). In the case of the anti-seborrheic, four potential alternatives (*i.e.*, octanoic acid, caprylylglycine, shikimic acid, and ciclopirox olamine) are consistently ranked higher than climbazole with every MCDA approach considered. However, none of these potential alternatives is ranked first with all of the methods.

3.4 Chemical management step based on functionality and essentiality

The technical function of Allura red was not considered necessary for the performance of some cosmetic products, and it is thus considered as non-essential. The chemical should therefore be removed from those cosmetic products where its function is unnecessary (Table 3). For other applications of Allura red, as well as all applications of climbazole and benzophenone-4, the technical function of the chemical was considered necessary for the desired performance of the cosmetic products. Even though no hazard-free alternatives exist, potentially better alternatives were identified for all case-study chemicals in the alternative assessment of hazards. This assessment indicated that Allura red, benzophenone-4 and

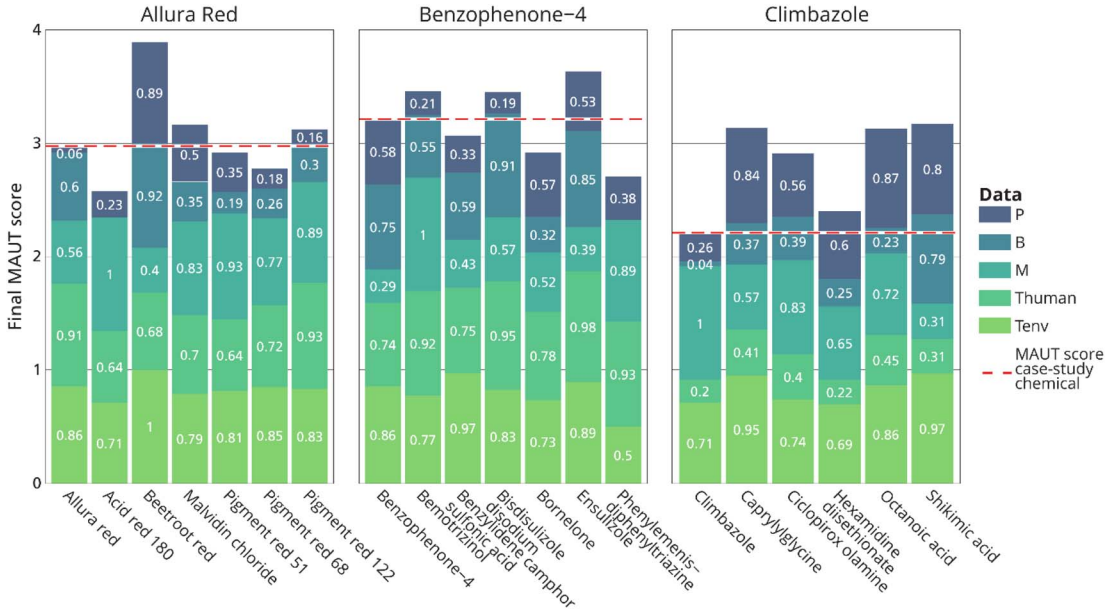

Fig. 5 Results of the MAUT assessment of the three case-study chemicals and shortlisted alternatives. The target line shows the total MAUT score for the case-study chemical, and alternatives with a higher score are potentially safer alternatives. (P = persistency, B = bioaccumulation, and M = mobility) and human health (T_{human}) and ecotoxicity (T_{env}) endpoints.

Table 2 Final ranking of the potential alternatives according to the heatmap, MAUT, and ELECTRE III approaches for the safest (ranked 1) and least safe (ranked 6 or 7) substances

Use case	Chemical name	Heatmap OECD scoring	MAUT	ELECTRE III
Pigment	**Allura red**	**2**	**4**	**3**
	Malvidin chloride	4	2	2
	Beetroot red	1	1	1
	Pigment red 51	6	5	5
	Pigment red 68	4	6	3
	Acid red 180	7	7	7
	Pigment red 122	3	3	5
UV-filter	**Benzophenone-4**	**2**	**4**	**3**
	Ensulizole	1	1	1
	Benzylidene camphor sulfonic acid	5	5	7
	Bisdisulizole disodium	2	3	5
	Bemotrizinol	4	2	2
	Bornelone	7	6	5
	Phenylemenis-diphenyltriazine	6	7	3
Anti-seborrheic	**Climbazole**	**6**	**6**	**5**
	Octanoic acid	3	2	1
	Caprylylglycine	2	3	2
	Shikimic acid	1	1	4
	Ciclopirox olamine	4	4	2
	Hexamidine diisethionate	5	5	6

climbazole can be substituted. Following the concept of essential-use, the use of these chemicals of concern is considered as non-essential for these products, as they can be substituted.

4 Discussion and conclusion

4.1 PMT/vPvM substances in cosmetics

Our analysis revealed that approximately 6.4% of all cosmetic products contain PMT or vPvM substances, and that these substances have a wide variety of functions in cosmetics. The highest share of PMT/vPvM substances was found in hair care products, followed by facial care products. The list of (potential) PMT/vPvM substances from Arp and Hale (2019) was used as a starting point in this study which classified substances as mobile if the $\log K_{oc}$ is 4.5 or lower.[26] In the proposed CLP revision, the mobility criterion, however, is set as $\log K_{oc} \leq 3$,[42] so a more stringent analysis can be considered. Thus, the list from Arp and Hale (2019)[26] might not provide an accurate overview of all relevant PMT/vPvM substances. Previous studies

Table 3 Summary table of the approach by Roy *et al.* (2022)[19] to assess the functionality and essentiality of the case-study chemicals in cosmetic products in order to identify appropriate management actions

Case-study chemical	Cosmetic products in which the chemical is present, ordered per product group	Technical function of the substance in the cosmetic products	Is the functional use of the chemical necessary for the performance of the product?	Are there no alternatives available?	Is the use of the chemical necessary for health, safety or critical for the functioning of society?	Management of the substance in a product
Benzo phenone-4	Bath and body products: body wash/shower gel, body scrub, body oil, and bath salt	UV protection	Yes, find drop-in chemical replacement	No	Not relevant	Substitute
	Facial care: cleansers		Yes, find drop-in chemical replacement	No	Not relevant	Substitute
	Hair care: conditioner, hair spray, shampoo, and styling cream					
	Hands and nails: hand wash		Yes, find drop-in chemical replacement	No	Not relevant	Substitute
	Make-up: lipstick/lip gloss/lip pencil		Yes, find drop-in chemical replacement	No	Not relevant	Substitute
	Suncare: self-tanning, and suncream/lotion/gel		Yes, find drop-in chemical replacement	No	Not relevant	Substitute
Climbazole	Hair care: shampoo	Anti-dandruff agent	Yes, find drop-in chemical replacement	No	Not relevant	Substitute
Allura red	Bath and body products: shower gel, and bath bomb	Colourant	No, redesign product or packaging	Not relevant	Not relevant	Remove from application
	Facial care: cleansers, eye makeup remover, face mask, lip balm, and scrub/peeling		No, redesign product or packaging	Not relevant	Not relevant	Remove from application
	Hair care: conditioner, hair spray, shampoo, hair colour, and hair mask		Hair colours: yes, find drop-in chemical replacement	No	Not relevant	Substitute in hair colour
			All other products: no, redesign product or packaging			Remove from all other formulations
	Foot care: foot wash/bath		No, redesign product or packaging	Not relevant	Not relevant	Remove from application
	Fragrances: parfum/eau de toilette/body mist		No, redesign product or packaging	Not relevant	Not relevant	Remove from application
	Hands and nails: hand disinfection, hand wash, and nail polish remover		No, redesign product or packaging	Not relevant	Not relevant	Remove from application
	Make-up: pressed powders, (foundation, bronzer, primer, blush and eye make-up), eyebrow pencil, eyeliner, lipstick/lip gloss/lip pencil, mascara, and nail polish		Yes, find drop-in chemical replacement	No	Not relevant	Substitute

Table 3 (*Contd.*)

Case-study chemical	Cosmetic products in which the chemical is present, ordered per product group	Technical function of the substance in the cosmetic products	Is the functional use of the chemical necessary for the performance of the product?	Are there no alternatives available?	Is the use of the chemical necessary for health, safety or critical for the functioning of society?	Management of the substance in a product
	Mouth/toothcare: mouthwash and toothpaste		No, redesign product or packaging	Not relevant	Not relevant	Remove from application
	Suncare: self-tanning, suncream/lotion/gel, and sunspray		No, redesign product or packaging	Not relevant	Not relevant	Remove from application

ranked PMT/vPvM substances based on their emission potential to the environment[43] or their mobility through waste water treatments.[44] Half of the PMT/vPvM substances identified in the CosIng database are listed on these prioritisation lists (Table SI2.1†). This emphasises that, whilst we selected the most frequently occurring PMT/vPvM substances in cosmetics based on data from Kemiluppen and Cosmethics, many other relevant substances, uses and consequent emissions need to be addressed in future studies.

4.2 Assessing functionality and identifying alternatives

In this study, only chemical-by-chemical substitution was assessed as no assessment could be performed to compare chemicals to other types of alternatives for functional substitution, such as a change of material and system changes.[23] It is key that an alternative chemical provides the same chemical function to preserve the overall performance of products, whilst lowering hazards. An extensive search was conducted to identify candidate alternatives with a known chemical function. However, this search might not be exhaustive as other, perhaps better, alternatives exist that are not listed in open databases. In addition, inorganic substances and substances without a CAS number were purposely left out as no hazard data were available. The other identified substances were short-listed based on already known hazard and classification data.[29–31,39] Chemicals that are not classified as hazardous under current regulations are, however, not necessarily safer compared to classified chemicals, as effects of many chemicals are not sufficiently studied, both in the scientific literature and within REACH due to varying information requirements based on the annual tonnage.[45–47] In addition, information on the specific end function (*i.e.* function of the chemical in the product) is often unknown, for many types of chemical uses. Information contained in the CosIng database provided a generic function such as a UV filter, but detailed information on the functionality (such as the UV absorbance spectrum) is not given. Approaches to predict chemical function based on structural and physicochemical descriptors exist,[48,49] but to our knowledge only provide generic classifications. Hence, better open data on the different uses and functionalities of chemicals in products would be helpful in the future to support chemical substitution.

4.3 Collection and evaluation of hazard data

Most experimental data used in our study was obtained from REACH dossiers, and no, or only a few, experimental endpoints were found for substances not registered under REACH. Data contained in REACH dossiers, however, are not always compliant, and issues regarding REACH data reliability have been raised before.[50,51] Future studies assessing safer alternatives using REACH data might therefore need to incorporate reliability assessments in order to communicate and deal with uncertainties, which will subsequently increase the transparency of the alternative assessment.[52,53] Experimental data can furthermore be less reliable when only one study for an endpoint is available. In these cases, it might be better to use a set of QSAR predictions to define an endpoint instead of using

this single experimental value.[54] However, for many endpoints no experimental data were found and QSAR methods were used for all chemicals in order to fill in data gaps. Modelled results also need to be interpreted with caution, especially when results from different QSARs could not be combined as only one model for a specific endpoint was available. Thus, it is also important to generate confidence scores for QSAR results to reflect uncertainties in alternative assessments.[55] Future studies need to better explore how both experimental and QSAR data can be combined in MCDAs and how confidence scores can be incorporated into these approaches. Furthermore, data gaps were found for all chemicals and included in the MCDA approaches by assigning standard scores. Methods on how to handle data gaps can influence the alternative assessment outcomes greatly.[56] However, there is not yet an agreed method on how this should be done.[21,57] Data gaps were mainly found for long-term exposure endpoints, emphasising the need of data generation and/or developments of *in silico* methods in these areas.

4.4 Comparing and selecting safer alternatives

We were able to show that safer alternatives for Allura red, benzophenone-4 and climbazole exist, based on an assessment of hazards. However, none of the assessed alternatives fully satisfy the criteria for the set of 26 hazard endpoints, meaning that no 'hazard-free' alternatives are available. For the MCDA approaches, endpoints were selected based on OECD recommendations and weighed using an equal weighing approach. As the vast majority of low molecular weight substances that are neutral or weak to non-polar will be either bioaccumulative or mobile,[58] many chemicals will receive similar scores for the combined bioaccumulation and mobility criteria. A few polar, ionisable or ionic substances can, on the other hand, be classified as both bioaccumulative and mobile, as is the case for some PFAS (*e.g.* perfluorooctanoic acid (PFOA)). Furthermore, a classification of a substance as bioaccumulative or mobile should not be reason for concern alone, but should always be combined with persistency; the higher the persistence of a substance, the higher the concern for potential long-lasting effects on human health and the environment.[59] The MCDA method used in this study can thus be refined by applying higher weights to the most important endpoints, such as persistency.

The relevance of other individual hazard endpoints varies according to the chemical and product type. A certain hazard might sometimes even be needed for the functionality of a chemical. For example, poorly degradable (*i.e.* persistent) UV-filters have a higher efficacy as they can protect the skin from UV radiation for a longer time.[60] In addition, certain hazards are legally allowed for one use, but not for another. Category 1 and 2 CMR substances can, for example, be used in cosmetic products if the Scientific Committee on Consumer Safety deems the reasonably foreseen uses as safe (Art. 15 Regulation (EC) No. 1223/2009). Different stakeholders need to be involved in order to refine alternative assessments by *e.g.* selecting relevant endpoints, weighing endpoints in MCDAs and dealing with trade-offs.[21,57,61,62]

It is furthermore important to note that the present analysis solely focused on hazard assessments of the potential alternatives compared to the substances of concern. Further work is needed to characterise the relevant exposure routes for humans and the environment resulting from the use of the alternatives. This might change the level of concern for the assessed alternatives. Such an assessment could be performed qualitatively, as outlined in the OECD guidance.[25]

4.5 MCDA approaches for chemical alternative assessments

In this study, three different MCDA approaches were used to compare hazards and select a safer alternative to the case-study chemicals, which generally yielded similar results in identifying the top ranked alternatives. Even though the combined use of multiple MCDA approaches has been advised,[63] it might not always be feasible to use multiple (complex) methods due to time and other resource constraints. Limitations and benefits of the heatmap, MAUT and ELECTRE approaches have previously been documented.[34] We also found the heat map to be the most helpful in rapidly comparing burden-shifting of hazards across case-study chemicals and potential alternatives, and by applying the OECD scoring approach a hazard ranking is obtained by which the most preferred chemical is identified. This ranking, however, is for a large part determined by the toxicity to human health, relating to 12 out of 26 endpoints. This is circumvented by using aggregated scores for PBMT, as performed for the MAUT and ELECTRE ranking. Of these two methods, the MAUT method is the most user friendly. The ELECTRE method is an outranking technique where superior performance in some criteria can compensate for inferior performance in other criteria. Even though ELECTRE is best able to deal with data uncertainty, a potential downside, however, is that the method does not always reflect the magnitude of relative superior or under performance of individual criteria.[21] Selection of the most suitable approach will depend greatly on the information needs of decision makers, but guidance is currently lacking to select and successfully implement MCDA approaches.[64,65]

4.6 Managing hazardous substances in cosmetic products

Following the combined application of the concepts of functional substitution and essential-use,[19] none of the assessed uses of PMT/vPvM substances were found to be essential. Starting with considerations of the function, some uses of Allura red were found not to be needed for the performance of cosmetic products. For other uses of Allura red and all uses of benzophenone-4 and climbazole, as the chemical function was considered necessary for product technical performance, the essentiality depended on the availability of suitable alternatives. As safer alternatives are available, the use of the PMT/vPvM substances was non-essential and should be substituted.[18] This also meant that the question whether the use of the chemical is necessary for health, safety or functioning of society did not need to be answered. It might, however, be argued that,

based on essentiality criteria defined earlier,[17,18] the use of hazardous substances in cosmetic products can always be classified as non-essential. Given that chemical risks are currently not adequately managed due to the many different chemicals and uses existing,[6,66] discussions about the essentiality of chemical uses might help to decide whether the continued widespread use of chemicals for certain uses is desirable in the first place.

4.7 Looking beyond chemical hazards

This work focussed mainly on the hazard assessment of chemical alternatives due to data limitations regarding the technical and economic feasibility. These other aspects should, however, be included in order to make an informed choice on the substitution of chemicals. The technical and economic feasibility of a specific alternative can depend highly on the type of actor performing the alternative assessment, and on the type of product in which the compound of concern is used. Similarly, due to lack of open data and resources, the availability of an alternative can be dependent on the actor who is attempting to phase-out a hazardous substance and could therefore not be evaluated with certainty in the context of this study.

Human health and the environment might not sufficiently be protected when only hazards are considered,[67,68] emphasising the need to include exposure assessments. In order to estimate emission and exposure, information on the different uses of chemicals and their volume in products is needed. However, to our knowledge this information is not yet openly available, and modelling approaches will be needed instead, *e.g.* to estimate chemical weight fractions.[68,69] Furthermore, it is important to consider environmental impacts beyond chemical effects, as emphasised by *e.g.* the planetary boundaries concept and the ambition laid down in the CSS to transition towards safe and sustainable chemicals.[12,70] Environmental impact assessments covering the whole product life-cycle can potentially be used to obtain a complete overview of all potential advantages and disadvantages of using a certain substance.[67,71]

As alternative assessments are a core element to phase out hazardous substances *via* the essential-use concept, it is key that these methods combine hazard-based considerations with broader life-cycle impacts to prevent burden shifting and assure that chemicals are used in a safe and sustainable manner. Such assessments might affect the ranking of most preferred alternatives found in this study. For example, beetroot red was in our analysis the best alternative to Allura red. However, the use of plant extracts in consumer products can result in a larger environmental footprint due to increased water depletion and CO_2 emissions.[72,73] Incorporation of sustainability assessments will add an additional layer of complexity to chemical assessment. Further methods are therefore required that combine safety and sustainability considerations in an accessible and transparent way.

Conflicts of interest

There are no conflicts to declare.

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