Special Series

UV filters used in sunscreens—A lack in current coral protection?

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EDITOR'S NOTE:

This article is part of the special series "Consequences of Sunscreen Product Use on Aquatic Environments." This series documents the current state of knowledge concerning potential impacts of chemicals derived from sunscreen products on freshwater and marine ecosystems, including coral reefs. Specific topics discussed include use patterns, environmental loadings, potential exposures, toxicological effects, and future research needs.

Abstract

Ultraviolet (UV) filters used in sunscreens are among the anthropogenic substances that may enter the marine environment by both indirect (via wastewater) and direct pathways (leisure activities). Owing to the recent global decline in coral population, the impact of those UV filters on the coral health is currently under increased investigation. First results from scientists suggest that some of the filters may be toxic to various coral life stages, but an initial cross comparison with existing data from other freshwater organisms does not indicate that corals are specifically more susceptible to UV filters than other standard species. In fact, the available data leading to this conclusion is still vague and based on toxicity and bioaccumulation tests with corals, which are both still at the research stage. To facilitate a proper hazard assessment, robust experimental procedures for coral ecotoxicological studies are considered mandatory. In other words, additional steps should be taken to standardize and validate such new test systems to generate reliable results, which then can be used in regulatory decision making. Furthermore, to facilitate a more detailed and site-specific environmental risk assessment in the marine area, an application-based exposure scenario must be developed. Until these data and tools become available, environmental hazard and risk assessments may be carried out using existing data from freshwater organisms and existing tonnage-based exposure scenarios as a potential surrogate. *Integr Environ Assess Manag* 2021;17:926–939. © 2021 SETAC

KEYWORDS: Coral toxicity, environmental risk assessment (ERA), Sunscreen, UV filter

INTRODUCTION

Tropical rain forests are biodiversity hot spots on land, and coral reefs are regarded as the corresponding counterpart in the marine environment (Maragos et al., 1996; Zakaria et al., 2016). A global decline in vital coral reef communities has been observed for decades, and the speed of their degradation has increased dramatically during the past two decades. Reasons for this decline have been linked to global warming ("El Niño" effects) on a more general basis (Bruno et al., 2007; Burke et al., 2011; Glynn, 1996;

Hughes et al., 2017); however, anthropogenic pollution of marine water by untreated wastewater (nutrition load), agricultural pesticides, and increased sediment loads also contribute significantly on a more local basis (GCRMN, 2004a, 2004b). Having said that, ultraviolet (UV) filters and corresponding sunscreens have been included as potential pollutants in the debate over coral reef decline, although their impact on marine life remains unclear (Mitchelmore et al., 2021; Moeller et al., 2021).

Many people around the globe use personal care products such as toothpaste, cremes, soaps, shampoos, and sunscreens in daily life. Although these products may be categorized into leave-on or rinse-off applications, at the end of the use phase most of them end up in wastewater or may even be released directly into the environment. The latter situation is of special relevance to sunscreens because their use is mainly linked to

leisure activities such as basking on grassland or swimming in lakes, rivers, and coastal areas (Andrey, 1999). Also, fieldworkers rely on sunscreens to protect themselves from serious skin damage during daily work at places and times with high sunlight intensity (Ruppert et al., 2016). Sunscreens are complex formulations composed of several UV filters as key components (Osterwalder et al., 2014; Pawlowski & Petersen-Thiery, 2020). To provide both a full UV A and UV B range protection and a high sun protection factor (SPF), the use of several UV filters in a sunscreen formulation is required (Sohn et al., 2020). The environmental fate and ecotoxicity continue to receive scientific attention, based on the structural features of the commonly used UV filters and the fact that some have been measured in the aquatic environment (Buser et al., 2006; Danovaro et al., 2008; He et al., 2019; Matsumoto et al., 2005; Mitchelmore et al., 2019; Poiger et al., 2004). Some years previously, organic ring structures had already raised the concern that UV filters might affect the endocrine system of aquatic invertebrates and vertebrates (Kaiser et al., 2012; Kunz & Fent, 2006; Kunz & Galicia, & Fent, 2006). More recently, however, effects on coral health have become the focus of research (Lozano et al., 2020). On the other hand, inorganic UV filters such as zinc oxide (ZnO) and titanium dioxide (TiO_2) have also raised concerns related to the use of nanomaterials as well as heavy metal impurities (Franklin et al., 2007; Heinlaan et al., 2008).

In this article, we elaborate on functional aspects of UV filters used in sunscreens and review existing chemical legislation on UV filters related to the environmental aspects and impact of UV filters on the environmental profile of sunscreens. Furthermore, we discuss how coral toxicity data fit into existing marine risk assessment approaches by considering existing options for hazard and risk assessment and addressing relevant data gaps.

MATERIAL AND METHODS

Functional aspects of UV filters used in cosmetics

The functionality of UV filters used in cosmetic products such as sunscreens was reviewed in an online search using the terms "UV filter," "sunscreens," and "UV protection" in the scientific databases BIOSID and HCA Plus (2020). Legislation relevant to UV filters was evaluated by reviewing existing EU legislation (i.e., Registration, Evaluation, Authorisation and Restriction of Chemicals [REACH]), because this is still the key market for global UV filter production and approval. Furthermore, this approach also considers the approval process in the United States as another highly relevant market for sunscreen products that differs significantly from the European approval process.

The impact of UV filters on the environmental (ecotoxicological) hazard profile of sunscreen formulations, compared with other co-formulants used in sunscreens, was evaluated based on the information provided in the substance-specific REACH registration dossiers published at the European Chemicals Agency (ECHA) website (www.echa.eu). Furthermore, available hazard and risk related information were assessed and comparted with existing coral toxicity data, to evaluate the impact of the overall protection objective of the marine compartment with special focus on corals. The data retrieved from the dossiers were effect levels (50%-lethal/effective concentrations [LC/EC50], no observed effect concentrations [NOECs]) on aquatic (freshwater) organisms, applied assessment factors and the predicted no effect concentration for the marine water ($PNEC_{marine\ water}$). Furthermore, existing risk assessment approaches applied in EU chemical regulations were evaluated for their suitability to cover a direct-release scenario for UV filters used in sunscreen products.

RESULTS

Functional aspects of UV filters used in cosmetics

The objective of anthropogenically synthesized UV filters is the protection of a respective organism or product from harmful UV rays (Radice et al., 2016; Rocholl et al., 2018; Velasco et al., 2008). This includes biobased flavonoids protecting the photosystems of plants and chemically derived organic and inorganic filters used in cosmetics (i.e., sunscreens), as well as in other applications such as plastics, textiles, paints, and home-care products (Pawlowski & Petersen-Thiery, 2020). Ultraviolet light absorption is linked to certain chemical and structural elements in the molecule: conjugated double bonds that are capable of absorbing UV light in the UV B range from 290 to 320 nm (i.e., relevant to skin burn and skin cancer) and UV A range from 320 to 400 nm (i.e., relevant to skin aging and skin cancer; Herzog, 2012; Pawlowski & Petersen-Thiery, 2020). In addition to the ability to absorb light, chemical stability is also required in order to retain sufficient efficacy during the entire time pf application (e.g., sunlight intense conditions). This time of application and the demand for chemical stability may vary from several hours (i.e., in sunscreens), to days and weeks (i.e., home-care products), and up to several years (i.e., plastics, paints). In the last named application types, UV filters typically remain in the product, avoiding significant release into the environment (OECD, 2009). In sunscreen applications, the UV filter should, per definition, stay on the human skin (e.g., "water resistant" products), although significant amounts may be released into the environment during swimming. Again, for home-care products (i.e., cleaning agents), a significant release into the aquatic environment may occur, especially if a sewage treatment plant step is missing. Further aspects related to the environmental risk assessment will be treated in more detail later in this article.

Typically, molecules containing aromatic ring structures as the UV-absorbing core are capable of combining all of these UV-absorbing aspects and, by side chain variation, the filter stability may be designed according to the specific application. Nevertheless, UV filters used in sunscreens are highly

specific substances dedicated to human health and safety (Herzog, 2012; Osterwalder et al., 2014; Pawlowski & Petersen-Thiery, 2020; Sohn et al., 2020). All cosmetic UV filters used in sunscreen applications in the EU require a safety evaluation by the Scientific Committee for Consumer Safety (SCCS) of the European Commission (EC, 2009b). Only approved filters considered as safe for human health can be used in sunscreens. However, the approval process may be different in various regions around the globe, significantly affecting the number of filters available for cosmetic use. By the end of 2020, 29 and 11 UV filters had been approved for sunscreens by the EU and the United States, respectively (EC, 2009b; FDA, US Food and Drug Administration, 2011). In the EU, UV filters in sunscreens are regulated as cosmetics, whereas in the United States, they are classified as over-the-counter (OTC) products and therefore regulated by the US Food and Drug Administration (FDA). Thus, differences in regulations and use patterns of UV filters may even affect the spatial and temporal distribution of UV filters in the environment on more local and regional scales.

Because the SCCS focuses on consumer safety, environmental safety aspects are not considered during this process. However, this point is addressed by another EU chemical legislation known as REACH, which considers all life-cycle stages, ranging from the cradle to the grave (i.e., from production to waste). So, despite their use in cosmetics and their status as organic or inorganic, UV filters are still considered "industrial chemicals" requiring a REACH registration, if they are produced in or imported to the EU at ≥1 ton/year (EC, 2006).

Environmental regulations in place and principles of environmental risk assessment

As mentioned in the previous section, REACH is considered to be the relevant EU chemical legislation that includes both human health (worker and consumer) and environmental safety aspects related to the substances' various life-cycle stages (production, formulation, professional and consumer use, waste). Currently, UV filters used in sunscreens are first marketed in the EU, before they are authorized in other countries around the globe. In the United States, however, the last time a new UV filter was approved was approximately 10 years ago (FDA, 2011), which limits the use of more recent, innovative, and eco-friendly UV filters. Therefore, EU regulations may be considered the most relevant because they are the entry path to further approval worldwide. They will be described in more detail later in this paper. The REACH registration process is substance specified and applicable to all UV filters produced in or imported into the EU at ≥1 ton/year (EC, 2006). Substance-related data requirements are tonnage based, including tests related to physicochemical properties, environmental fate, environmental and human toxicity, and the need to generate relevant data. In fact, only a minimum dataset is required for substances in the lowest tonnage level (i.e., 1–10 tons/year), whereas extensive (higher tier) data are required at the highest tonnage level (i.e., >1000 tons/year). Any data that must be generated or that already exist should preferably be conducted under good laboratory practice (GLP) and should follow accepted test guideline protocols, such as OECD, ISO, or OCSPP. Nevertheless, many data published in scientific literature might not be conducted under such conditions; the data, however, may be still of use for regulatory needs, after being accessed according to the Klimisch scoring system and considered to be valid or valid with restrictions (Klimisch et al., 1997). The entire dataset available and considered as acceptable will then be used to identify the hazard profile of the substance (Step 1). Substances with volumes >10 tons/year and classified as hazardous to the environment will move to Step 2, the environmental risk assessment (ERA). For that purpose, PNECs were derived for each environmental compartment, namely freshwater and marine water, sediment, and soil. In case of available data (i.e., marine water, sediment, soil), the PNEC is based on test results from the most sensitive species related to that environmental compartment. However, at the lower tonnage levels, where typically no marine water, sediment, and soil toxicity data were available, PNECs associated with these compartments may be derived from the $PNEC_{freshwater}$ using assessment factors (AFs) or the equilibrium-partitioning method (EPM; ECHA, 2017). In case of available data, such PNECs were based on measured effect levels (i.e., EC/LC50 values in case of short-term toxicity tests, or NOECs/EC10 values in case of long-term or chronic toxicity tests) and appropriate AFs. It can then be calculated as follows: effect level / AF = PNEC. The size of the AF correlates with the type of test and the number of tropic levels that have been tested and range from 10 000 to 10 for the marine compartment (Tables 1 and 2). When a large chronic toxicity dataset representing at least eight taxonomic groups and at least 10 species is available, a probabilistic species sensitivity distribution method (SSD) may be applied as an alternative to the AF-approach. The result is a so-called HC5 value, representing a concentration where 95% of the species are considered as protected (EC, 2011). By using an SSD approach, the applied AF can be reduced from 1 to 5 (EC, 2003; ECHA, 2008).

Although the SSD approach is regularly applied to active ingredients of plant protection products, it is hardly applicable to most UV filters owing to the absence of such large datasets.

For the risk characterization, the derived PNECs will be correlated with environmental concentrations. Those concentrations may be based on measured (MEC; only rarely applicable) or predicted concentrations (PECs). The latter has the advantage that, lacking valid and representative MECs, a risk characterization may be applied to each hazardous substance registered. REACH uses numerous models to calculate PECs, namely CHESAR, ECETOC TRA, EASYTRA, and EUSES, but they all rely on the same mathematical calculations and so should return the same result. The resulting risk characterization ratio (RCR = PEC/PNEC) indicates either a safe use of the substance (RCR < 1) or indicates a risk (RCR ≥

TABLE 1 Options for the derivation of the PNEC_{marine water}[a] related to data the availability (e.g., acute or chronic toxicity tests on freshwater and/or marine organisms) and the applicable assessment factor

Available data[b]	Assessment factor
L(E)C50 from short-term study of freshwater or saltwater species of three taxonomic groups (algae, crustaceans, and fish) of three trophic levels	10 000
L(E)C50 from short-term study of freshwater or saltwater species of three taxonomic groups (algae, crustaceans, and fish) of three trophic levels, and two additional marine taxonomic groups (e.g. echinoderms, mollusks)	1000
EC10 or NOEC from one long-term study of freshwater or saltwater crustaceans or fish	1000
EC10 or NOEC from two long-term studies of freshwater or saltwater species representing two trophic levels (algae and/or crustaceans and/or fish)	500
EC10 or NOEC from three long-term freshwater or saltwater species (normally algae and/or crustaceans and/or fish) representing three trophic levels	100
EC10 or NOEC from two long-term studies of freshwater or saltwater species representing two trophic levels (algae and/or crustaceans and/or fish) and one long-term result from an additional marine taxonomic group (e.g. echinoderms, mollusks)	50
EC10/NOEC from three long-term studies of freshwater or saltwater species (normally algae and/or crustaceans and/or fish) representing three trophic levels + two long-term results from additional marine taxonomic groups (e.g., echinoderms, mollusks)	10

Abbreviations: EC, effect concentration; NOEC, no observed effect concentration; PNEC, predicted no effect concentration.
[a]According to ECHA (2008) and EC (2003) modified.
[b]Effect values always refer to the most sensitive taxonomic group tested.

1) and so the need for further action. In fact, further efforts should be made to refine either PEC or PNEC or both by reducing the given uncertainty on the RCR. If, in the end, all refinement options are exhausted and still no safe use for the substance can be derived, environmental emission reduction options must be considered as part of a risk management plan. This will also apply to substances such as hexabromocyclododecane (HBCDD) identified as being persistent, bioaccumulative, and toxic (PBT), and/or very persistent and very bioaccumulative (vPvB) according to EU REACH criteria. This may also include a replacement of a certain substance by a suitable alternative demonstrating a better environmental profile (Pawlowski et al., 2021), although none of the UV filters marketed in the EU meet such criteria.

UV filter properties as key elements for environmental profiling

Ultraviolet filters are the key ingredient in sunscreen formulations, because without them UV protection will not be given. Nevertheless, several co-formulants such as sensory enhancers, thickeners, boosters and film formers, emulsifiers, emollients, and water contribute to this cosmetic product to

TABLE 2 Options for the derivation of the PNEC_{marine sediment}[a] related to data availability (e.g., acute or chronic toxicity tests on freshwater and/or marine sediment organisms) and the applicable assessment factor

Data available[b]	Assessment factor
E(L)C50 from one freshwater or marine species[c]	10 000
E(L)C50 from one freshwater or marine species[c]	1000
EC10 or NOEC from one long-term freshwater sediment species	1000
EC10 or NOEC from two long-term freshwater species representing different living and feeding conditions	500
EC10 or NOEC from one long-term marine sediment species representing different living and feeding conditions	100
EC10 or NOEC from three long-term tests on sediment species representing different living and feeding conditions	50
EC10 or NOEC from three long-term tests on sediment species representing different living and feeding conditions including a minimum of two tests with marine species	10

Abbreviations: EC, effect concentration; NOEC, no observed effect concentration; PNEC, predicted no effect concentration.
[a]According to ECHA (2008) and EC (2003) modified.
[b]Effect values always refer to the most sensitive taxonomic group tested.
[c]Also considers the results from the equilibrium-partitioning method.

facilitate its proper use (Herzog, 2012; Osterwalder et al., 2014; Pawlowski & Petersen-Thiery, 2020). The data review revealed that the environmental hazard profile of UV filters ranges from non-toxic substances (i.e., bis-ethylhexyloxyphenol methoxyphenyl triazine [BEMT], with an NOEC above the maximum solubility threshold under test conditions) to highly toxic candidates (i.e., octocrylene [OCR]; NOEC 2.3 µg/L). On the other hand, the data available on co-formulants at the ECHA website (data not shown) revealed that they are less hazardous (i.e., D-glucopyranose with EC50 27.2 [freshwater algae] and 7.03 mg/L [marine algae], respectively) or even non-hazardous (i.e., propylene glycol with EC50 [algae, *Daphnia*, fish] >100 mg/L) to the aquatic environment. Ultraviolet filters are often poorly biodegradable and have a high log P_{ow} (>4.5); co-formulants are typically readily biodegradable and have a low octanol-water partitioning coefficient (<3). Taking that into account, the environmental hazard profile of the co-formulants is much more favorable than that of the UV filters, especially compared with those that are highly toxic to aquatic organisms. Therefore, for co-formulants, available data may be sufficient to reach a conclusion on the environmental hazard profile, whereas for UV filters, additional (higher tier) testing data may be considered necessary. In contrast, UV filters often require additional data in order to obtain the full picture with regard to the hazard evaluation; therefore, several substances (i.e., OCR, ethylhexylmethoxycinnamate [EHMC], Isoamylmethoxy cinnamate [IPMC], Diethylhexyl butamido triazone [DBT]) are subject to further substance evaluation by the ECHA. Although UV filters exhibit similar physical chemical properties from a more general perspective, distinct differences in individual structural and physicochemical features result in differences in the hazard profile evaluation. In other words, small and rather water-soluble molecules (mg–µg/L range) are typically more bioavailable than larger molecules with very low water solubilities (e.g., at the ng/L range). This information is relevant when we consider acute and chronic toxicity as well as the bioaccumulation potential of substances because, typically, no specific membrane carrier systems exist in animals leading to passive log P_{ow} driven membrane transport only. Large three-dimensional structures hinder substances from passing through membranes, and the uptake is typically via the water phase only. Low concentrations in the water will facilitate an uptake of only very small amounts per time, leading to very low potential of bioaccumulation (Figure 1). Consequently, such very low water-soluble substances would require very high specific toxicity in order to result in intrinsic adverse effects in test organisms, similar to concentrations of naturally occurring and anthropogenic hormones (Länge et al., 2001; Pawlowski et al., 2004a, 2004b; Wehner & Gehring, 1995).

Current marine risk assessment approaches and how to consider coral toxicity

As indicated previously, ERAs are well established in chemical regulations; however, the quality of the resulting RCR (safe use vs. risk) relies heavily on the quality (measured vs. predicted) and quantity (higher tier vs. lower tier) of data and the exposure scenario used. The EU has two principal approaches to ERAs in a regulatory context. The first is a tonnage-based approach (TBA), typically applied to REACH-registered substances. The second is an application-based approach (ABA), typically used for the registration of active ingredients of plant protection products and biocides (EC, 2009a, 2012). Thus, for UV filters registered under REACH, the TBA considers the yearly tonnage of a substance (confidential information), the intended uses (environmental release categories [ERCs] and specific environmental release categories [SpERCs]), and the intrinsic substance properties (phys-chem., ecotox, e-fate; Figure 2). This approach also allows for a risk characterization of the

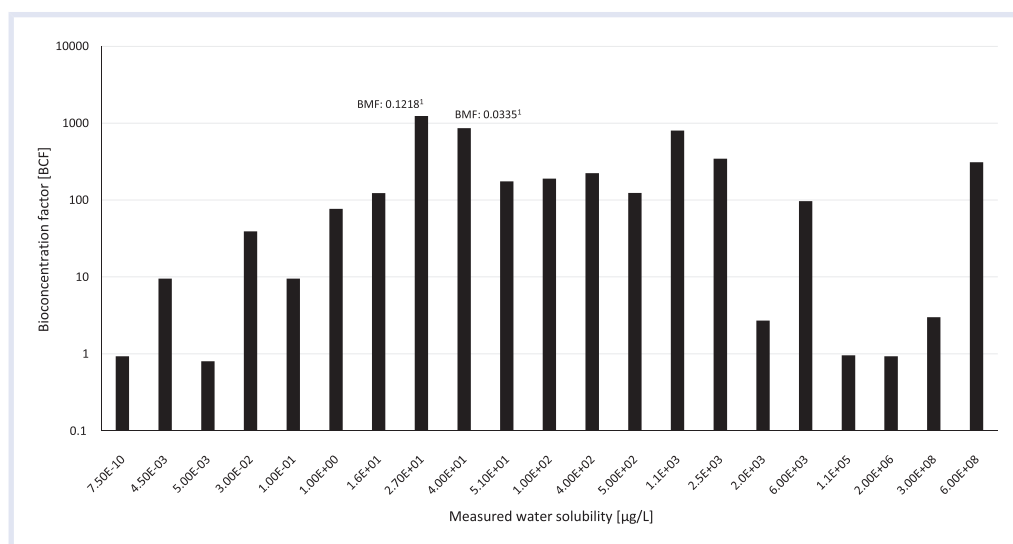**FIGURE 1** Bioconcentration factors (BCF) and associated water solubilities of 21 UV filters approved by the EU. Data were retrieved from Registration, Evaluation, Authorization and Restriction of Chemicals (REACH) Registration dossiers published at the ECHA website or from SRC EPIWIN BCFBAF Program (v3.01) calculations. [1]Indicated measured biomagnification factors (BMF) overrule even experimentally derived BCF values
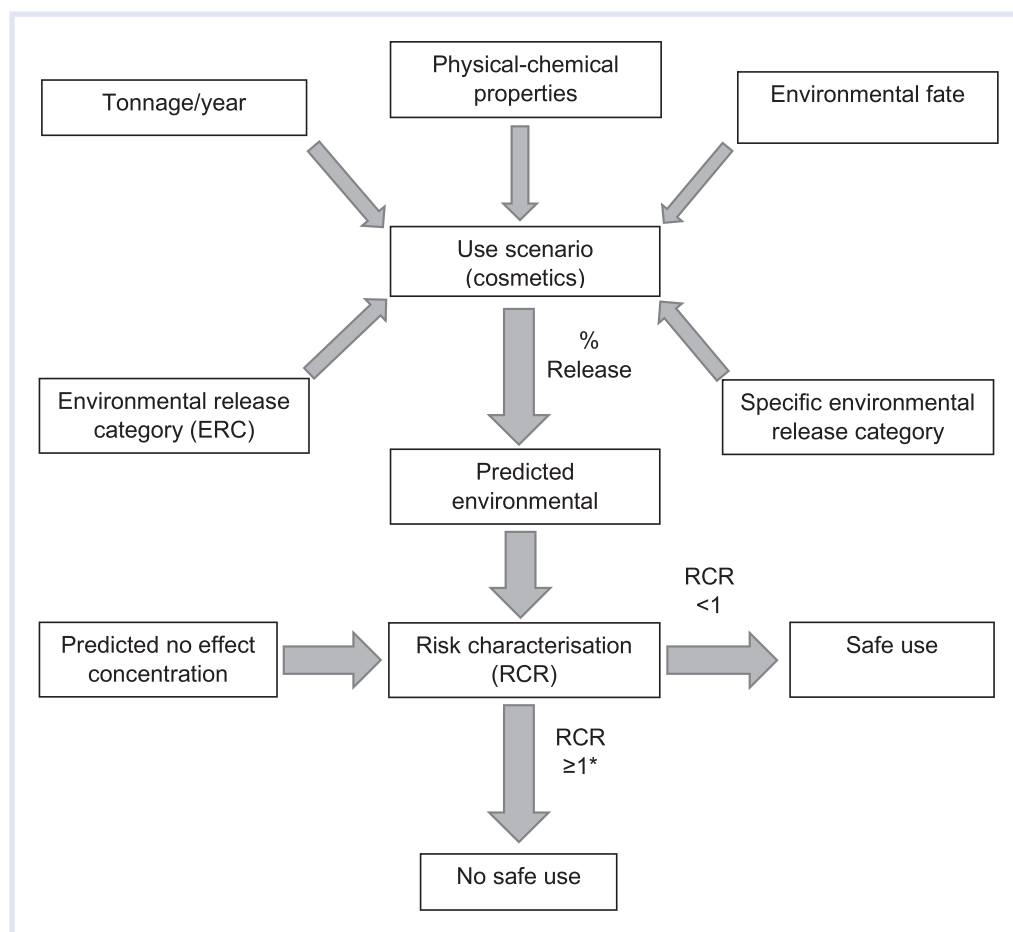
FIGURE 2 Tonnage-based approach to UV filters for release into the marine environment

marine compartment (both water and sediment); however, because this approach relies on percentage release rates only, it might greatly overestimate resulting PECs or might even exclude a direct release of UV filters into the aquatic environment through recreational activities (i.e., swimming, diving, basking). This may result in a (purely hypothetical) unsafe use, which nevertheless requires further elaboration. A most suitable refinement option is based on the ABA, dedicated to the specific use of the UV filter in sunscreens and the amount of substance released into the aquatic environment during the use in sunscreen products (Figure 3). This approach will also be able to address the direct release of UV filters from sunscreens during recreational activities. For freshwater, such an exposure scenario may be taken from the biocidal product regulation; however, this scenario relates to lakes and is dedicated to repellants (PT 19) with an assumed 100% release into the water, but not considered applicable to UV filters in their current form, because the release pattern of UV filters is significantly different (especially for water-resistant products). Nevertheless, it also considers market shares of individual substances and allows for regional differences (i.e.,

inside and outside the EU) and thus a more realistic view of any potential environmental risk. Likewise, for a marine environmental risk assessment, such an approach would be considered as much favorable, also considering regional, marine site-specific aspects (i.e., tidal activities, current), but up to this point, such an exposure scenario does not exist.

Thus, at the current stage in REACH, the environmental risk assessment of hazardous UV filters used in sunscreens relies on the highly conservative tonnage-based approach, which in addition is in the confidential part of the individual registration dossiers (owing to confidential information on the production volumes). However, the hazard data and the derived PNECs for the marine water presented in the publicly available part of the dossiers allow for cross comparison with existing coral toxicity data published in peer-reviewed scientific journals. Having said that, the hazard assessment of UV filters typically relies on three standard test organisms (i.e., algae, crustaceans, and fish). Corals or cnidaria are not among the standard test organisms in any of the worldwide chemical regulations because they are difficult to culture under constant laboratory conditions. Thus, no standardized and validated testing protocol according to internationally
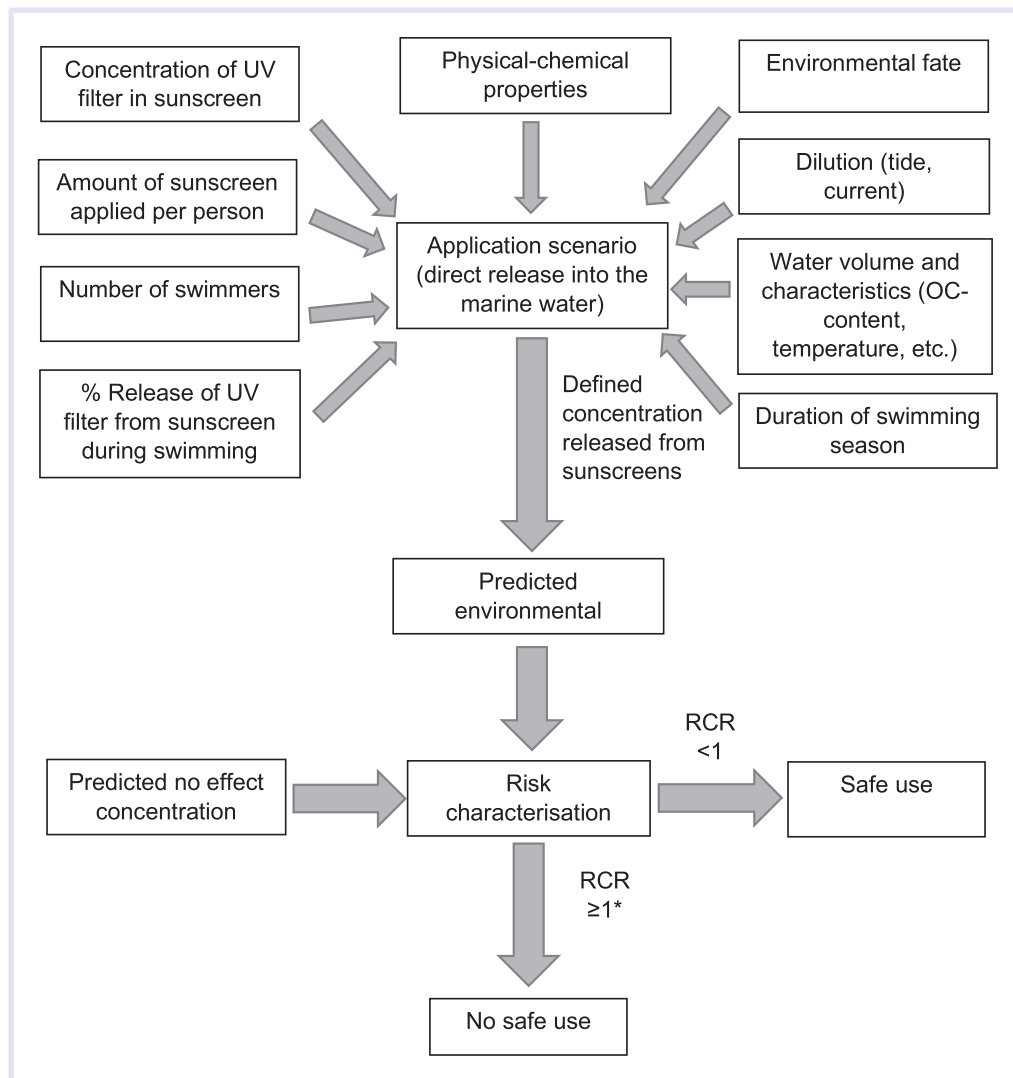
FIGURE 3 Application-based approach to UV filters for direct release into the marine environment

accepted test guidelines (i.e., OECD, ISO) exist. However, the evaluation of the currently derived $PNEC_{marine\ water}$, with existing ecotoxicological thresholds derived from toxicity tests on corals and its larvae, revealed that the effects observed in these studies may be captured in the existing risk assessment framework (Table 3). For example, the LC50 values in planulae larvae derived from 8 and 24 h exposure to benzophenone 3 (BP3) was 3.1 and 0.139 mg/L, respectively, indicating a specific high toxicity toward coral larvae (Downs et al., 2016). On the other hand, available data from the substance's REACH registration dossier concluded a $PNEC_{marine\ water}$ of 0.067 µg/L (ECHA, 2020d). Approximately 33% observed lethality in adult corals after 7 days exposure to EHMC at nominally 1000 µg/L (achieved by using a solvent) as observed in another study (He et al., 2019) is well above the known measured water solubility of 41 µg/L (ECHA, 2020b) and thus does not contribute to the toxicity of the substance. In addition, results from a fish early life stage study according to OECD 210

revealed that fish (NOEC < 46.9 µg/L) may even be more sensitive than invertebrates.

In another case, the toxicity of both nano ZnO and soluble $ZnSO_4$ was measured in marine algae and crustacea and retrieved LC50/EC50 values ranging from 0.68 to 3.48 mg Zn/L (Wong et al., 2010). In the REACH registration dossier for ZnO, corresponding freshwater algae and crustacean EC50 values were 0.136 and 0.147 mg Zn/L (ECHA, 2020f). Corresponding lowest observed NOECs were 0.019 and 0.0078 mg Zn/L, respectively, resulting in an overall PNEC marine water of 6.1 µg Zn/L (ECHA, 2020f). This PNEC is based on an SSD by applying an assessment factor of 1 and, from a general risk assessment point of view, should also capture apparent effects in organisms (including reef building corals), which have not been tested so far. This assumption is supported by available literature data where bleaching effects in stony corals (*Acropora* sp.) exposed for 48 h to 6.3 mg/L nano ZnO occur (Corinaldesi et al., 2018). However, the latter concentration for freshwater green algae is already far greater than the above-mentioned EC50 and NOEC

TABLE 3 Overview of physicochemical properties, aquatic effects values, and applied assessment factors for the derivation PNEC$_{marine\ water}$ of UV filters[a]

UV filter INCI name (abbreviation)	CAS No.	Molecular weight (g/mol)	Water solubility (µg/L)	Log P_{ow}	GHS classification environment	Freshwater Effect level	Value (µg/L)	Marine water AF	PNEC$_{marine\ water}$ (µg/L)[1]	Minimum coral toxicity (mg/L)	Reference
4-Methyl benzylidene camphor (4MBC)	36861-47-9	254.38	1.1×10^3	5.1	Aquatic acute 1, Aquatic chronic 1	NOEC	20	500	0.04	37×10^3 [b]	Danovaro et al. (2008)
Benzophenone-3 (BP3)	131-57-7	228.25	6×10^3	3.45	Aquatic acute 1, Aquatic chronic 2	EC50	670	10 000	0.067	17	Downs et al. (2016)
Benzophenone-4 (BP4)	4065-45-6	308.31	3×10^8	0.515	Not classified	NOEC	4897	500	9.79	>1000	He et al. (2019)
Bis-ethylhexyloxyphenol methoxyphenyl triazine (BEMT)	187393-00-6	627.83	4.5×10^{-3}	>5.7	Not classified	NOEC	≥WS	N/A	No hazard identified	>1000[c]	Stien et al. (2019)
Diethylhexyl butamido triazone (DBT)	154702-15-5	766.00	<0[c]	4.12	Not classified	NOEC	≥WS	N/A	No hazard identified	>1000	Stien et al. (2019)
Ethylhexyl triazone (EHT)	88122-99-0	823.10	<1	7	Not classified	NOEC	≥WS	N/A	No hazard identified	>177[c]	Fel et al. (2019)
Terephtalidene dicamphor sulfonic acid (TDSA)	92761-26-7	562.70	$\geq 6 \times 10^8$	−1.84	Not classified	NOEC	No hazard identified	N/A	No hazard identified	>5030	Fel et al. (2019)
Drometrizole trisiloxane (DTS)	155633-54-8	501.85	No data	>4	No data	No data	No data	No data	No data	>480	Fel et al. (2019)
Butyl methoxy dibenzoyl methane (BMDBM)	70356-09-1	310.40	27	6.1	Not classified	NOEC	≥WS	N/A	No hazard identified	516[c]	Fel et al. (2019)
Ethylhexylmethoxy cinnamate (EHMC)	83834-59-7	290.41	51	>6	Aquatic chronic 2	NOEC	<46.9	100	<0.469	10	He et al. (2019)
Ethylhexyl salicylate (EHS)	118-60-5	250.34	500	6.36	Not classified	NOEC	≥WS	N/A	No hazard identified	>1000	Stien et al. (2019)
Homomenthyl salicylate (HMS)	118-56-9	262.35	400	6.34	Not classified	NOEC	≥WS	N/A	No hazard identified	>1000	Stien et al. (2019)
Methylene bis-benzotriazolyl tetramethyl butylphenol (MBBT)	103597-45-1	658.89	$<5 \times 10^{-3}$	12.7	Aquatic chronic 4	NOEC	≥WS	N/A	No hazard identified	>1000	Stien et al. (2019)

(Continued)

TABLE 3 (Continued)

UV filter INCI name (abbreviation)	CAS No.	Molecular weight (g/mol)	Water solubility (µg/L)	Log P_{ow}	GHS classification environment	Freshwater Effect level	Value (µg/L)	Marine water AF	$PNEC_{marine\ water}$[1] (µg/L)	Minimum coral toxicity (mg/L)	Reference
Octocrylene (OCR)	6197-30-4	361.49	40	6.1	Aquatic chronic 1	NOEC	2.7	100	0.027	1318[b]	Fel et al. (2019)
Titanium dioxide (TiO$_2$)	13463-67-7	79.87	100	N/A	Not classified	NOEC	>WS	N/A	No hazard identified	>6300	Corinaldesi et al. (2018)
Zinc oxide (ZnO)	1314-13-2	81.39	2.9×10^3	N/A	Aquatic acute 1 Aquatic chronic 1	NOEC	7.8	1	6.1	94	Fel et al. (2019)

Abbreviations: AF, Assessment factor; EC50, 50% effect concentration; INCI, international nomenclature of cosmetic ingredients; log P_{ow}, logarithmic partition coefficient octanol water; N/A, not applicable; NOEC, no observed effect concentration; PNEC, predicted no effect concentration; REACH, Registration, Evaluation, Authorization and Restriction of Chemicals.

[a]According to ECHA REACH registration dossiers (ECHA, www.echa.eu).

[b]Value recalculated based on 33 µl/L and a specific density of 1.108 g/cm^3.

[c]Solvent used; value above known water solubility (WS).

of 0.136 and 0.019 mg/L, respectively (ECHA, 2020f). Furthermore, in the same dossier, the range of NOECs referring to marine algae toxicity tests range from 0.0078 to 0.67 µg/L, based on the dissolved ZnO concentration and, again, does not indicate any higher specific toxicity of the substance to either corals or its associated symbionts. In contrast, Corinaldesi et al. (2018) also observed no significant effect using 6.3 mg/L of the nanoform of TiO_2 in an identical test setup for 48 h, thus agreeing with the corresponding REACH dossier, revealing an EC10 and an EC50 for green algae of >2 and >50 mg/L, respectively (ECHA, 2020e).

Based on these examples, it remains unclear whether the coral holobiont (i.e., corals and associated symbionts) is a taxon that is more sensitive than other standard organisms used in OECD guideline conform testing. Although suitable toxicity data on corals related to UV filters are scarce, other classes of substances (e.g., active ingredients of plant protection products) have already been investigated intensively and thus facilitate a comparable toxicity assessment. Therefore, on a more general basis, only defined effect levels (e.g., LC/EC50) relating to a clearly visible and adverse finding (e.g., mobility and mortality in daphnids and fish, respectively, or growth inhibition in bacteria and algae) can be compared. Physiological aspects, although deemed to be much more sensitive, typically lack adversity and are highly variable (as indicated by high standard variations). Therefore, they are very difficult to judge as stand-alone criteria. Ultraviolet filters belong to various classes of substances (i.e., benzophenones, cinnamates, triazines), although they do share a comparable functionality. Thus, smaller and rather water-soluble molecules (e.g., BP3 or 4-methyl benzylidene camphor [4MBC]) are more likely to be taken up (even by corals) and may lead to physiological responses in the organism via processes such as biotransformation, detoxification, and elimination than larger, poorly soluble and poorly bioavailable substances (e.g., ethylhexyl triazone [EHT] or BEMT) (Arnot et al., 2018). It can be expected that no substance-specific transport system for UV filters exists in organisms, but unspecific translocation involving adaptations of physiological processes are in place. In vertebrates, both liver and kidney are the key players for both biotransformation and excretion of substances, respectively (Arnot et al., 2018). Therefore, measured concentrations of substances being metabolized via liver biotransformation enzymes are highest in that specific organ, whereas in other parts of the organisms (like filet in fish, fat tissue in higher vertebrates) concentrations are rather low (Arnot et al., 2018; Gago-Ferrero et al., 2013; Molins-Delgado et al., 2018). In many invertebrates, such as crustaceans or mollusks, the functionality of the liver is replaced by other organs such the midgut gland (Storch & Welsch, 1999). In other invertebrates, such as porifera or corals, however, no dedicated organs exist simply because of the rather simpler organization level of the body plan (Storch & Welsch, 1991). On the other hand,

lower organismic complexity may even facilitate a simpler excretion procedure on a cellular level (e.g., exocytosis; Storch & Welsch, 1994). Those "depuration products," although being measured in some cases, should not be considered for the bioaccumulation assessment of the target substances. Thus, a more differentiated chemical analysis of various tissues would provide a more detailed picture of a substance's distribution in the organism. However, it also requires a very comprehensive and profound analysis of the results, considering all aspects of the substance´s behavior and the organism's capabilities for biotransformation. Nevertheless, bioaccumulation data on invertebrates including corals are scarce and difficult to compare with standardized fish bioaccumulation data. Further elaboration of standardized testing methods on corals would certainly help to understand the bioaccumulation behavior of UV filters in this type of organism related to available fish bioaccumulation data.

DISCUSSION AND CONCLUSION

Corals are a keystone species and the framework builders of corals reefs, which represent one of the most diverse marine ecosystems on the planet. Coral reefs provide multiple services to humankind, such as coastal protection, food, and income through tourism (Burke et al., 2011). Located at the transition zone between terrestrial and marine habitats, coral reefs are subject to both direct and indirect naturally and anthropogenic-related impacts coming from upstream wastewater streams. The impact from anthropogenic sources has been increasing in past decades owing to general population growth, agriculture, coastal development, and increased tourism (Burke et al., 2011). Especially in geographical regions where biological wastewater treatment plants (WWTPs) and sludge incineration has not yet been implemented, the impact is more or less unavoidable. In many coastal countries, especially developing ones with limited financial resources, wastewater is continuously released into the coastal area, bringing both nutrients and potentially toxic chemicals into the ecosystem. Although lacking regular WWTPs, some countries use natural sand filtration of wastewater as an inexpensive alternative, a practice which may help to treat low volumes of wastewater. However, over time, nutrients (e.g., nitrates, phosphates, organic carbon loads) will even be released into the ocean, promoting the growth of fast growing filamentous and macroalgae rather than slow growing reef building corals (Burke et al., 2011). Nevertheless, biological wastewater treatment systems and sand filtration are relevant measures to remove lipophilic UV filters from the wastewater stream because of their high absorption capacity. In addition, sludge incineration will finally degrade the filters to carbon dioxide. Considering these aspects, a more holistic approach to wastewater management in coastal countries, especially those with extensive coral reef habitats, is required to improve overall water quality.

Rapid degradation of filters may help to lower environmental concentrations (e.g., in the case of EHMC or BP3); however, the risk also exists that toxicity to aquatic organisms may occur as the degradation products are considered to be bioavailable. On the other hand, non-degradable UV filters may remain in the aquatic environment for a long time (i.e., ZnO, TiO$_2$, BEMT, EHT). If they are not bioavailable as a result of their large molecular size and very low water solubility, they might have little biological relevance. Available toxicokinetic studies in rats confirm that some UV filters (i.e., 1,3,5-triazine, 2,4,6-tris((1,1'-biphenyl)-4-yl)- and methylene bis-benzotriazolyl tetramethyl butylphenol [MBBT]), having very low water solubilities at the ng/L range and exhibiting higher molecular weights, are not taken up by the organism after both dermal and oral exposure (ECHA, 2020a, 2020c). However further data may be needed to facilitate a more robust weight of evidence approach.

Inorganic filters such as ZnO and TiO$_2$ may be considered as naturally occurring because these metal oxides exist in the environment, despite differences in their physical diameter (i.e., nano vs. non-nano), but it should be taken into account that they are also non-degradable and will remain there, in principle, forever. Stating that these inorganic filters are generally of no concern to the aquatic environment is not correct, because available acute and chronic toxicity data will have to be considered. In case of harmful substances (e.g., ZnO), environmental concentrations over time may reach ecotoxicological relevant thresholds, whereas the increase in non-hazardous substances is of little concern. A UV filter may lead to toxic effects in corals at high concentrations during laboratory studies, but MECs may be far below critical concentrations (Mitchelmore et al., 2019, 2021) or PECs might demonstrate a safe use once applied correctly. So, a substance-specific integrated hazard assessment and risk assessment are required considering all relevant and reliable data. Having said that, additional toxicity data on corals including various life stages are urgently needed, but the focus should also include substances (e.g., solvents, positive controls) in addition to UV filters to identify (constant) specific sensitivity aspects of corals as a first step. Currently available toxicity data on corals may be regarded as preliminary owing to several shortcomings (Mitchelmore et al., 2021; Moeller et al., 2021), although at this stage, they have not confirmed that corals are more sensitive than other aquatic organisms. Nevertheless, it is relevant to develop standardized test systems that are validated through international ring testing and elaborated in internationally recognized test guidelines to generate reproducible test results on corals. These results may then be used to refine/update existing environmental risk assessments of UV filters with environmental hazardous properties. In addition to coral toxicity tests, the bioaccumulation potential of UV filters in corals is another aspect that relates to potential long-term effects of a substance in living organisms. Currently, standard bioaccumulation testing in water focuses on fish, which may not allow a cross comparison with field data from corals. Therefore, it would also be useful to have such standardized and validated testing

systems for bioaccumulation at hand. However, standardization and validation processes will take a significant amount of time until approved test guidelines become available. Meanwhile, the environmental hazard and risk assessment of UV filters will be carried out based on existing data from other aquatic species and using existing tonnage-based exposure scenarios. To improve the ERAs by using a more realistic use-related scenario, further elaboration and exploration in existing application-based exposure scenarios is needed. These developments would certainly help address the potential data gaps related to UV filters, coral toxicity, and the impact on coral reef declines in the future. Meanwhile, the application of the EcoSun Pass (ESP) tool can already be used to formulate sunscreens that are more environmentally friendly (Pawlowski et al., 2021). It allows the selection of the most ecofriendly UV filter candidates by combining the environmental hazard profile of an individual UV filter with its efficacy to absorb UV light. It also considers all environmental compartments, allowing for the evaluation of aquatic toxicity and thereby leading to the exclusion of aquatoxic UV filters. The ESP evaluation is built on the available data from REACH registration dossiers, peer-reviewed scientific literature, QSARs, and expert judgment, and allows for any adjustment related to new and relevant information (including coral toxicity data). Beyond, a substance-specific evaluation carried out under REACH, the ESP tool allows for the assessment of the entire UV filter composition of various sunscreens. Therefore, it is not comparable with a quantitative, substance-specific environmental risk assessment carried out under REACH. However, taking the differences in efficacy of individual UV filters into account, the use of more efficient candidates would also reduce the concentration of filters released into the marine environment.

Moreover, an overall assessment of UV filters related to coral toxicity will be very challenging, especially for filters having water solubilities in the low ng/L range. Adequate analytical methods have to be implemented to facilitate a proper concentration control analysis in the test water. However, the composition of marine water is very complex, and high salt concentrations may interfere with detection limits of analytical methods, so that the determination of such low concentrations may not be possible at all during the entire exposure phase (e.g., remains below the limit of quantification [LoQ]). Furthermore, test substance solubility in marine water is likely below the known values of pure water. So, determination of practical water solubility is urgently needed to allow testing of concentrations up to the solubility limit under test conditions (OECD, 2019). Testing of concentrations higher than the limit of water solubility (e.g., by using a solvent) is generally not recommended (OECD, 2019) and may lead to confounding results owing to physical effects on the test organisms (e.g., agglutination of gills or antenna in daphnids). For example, some filters such as OCR form stable microemulsions in water, leading to possible physical effects on the test organism on one hand and high analytical variation in measured test concentrations on the other (Pawlowski et al., 2019). However, in the

regulatory context, both aquatic hazard and risk assessment of a substance (including UV filters) should be based on substance-intrinsic toxicity results and not on physical effects because the latter one may only occur at unrealistically high exposure concentrations. Instead of using specific analytical methods, low concentrations might be measured using radiolabeled (^{14}C) test material, which requires specific customized and cost intensive synthesis of test material. However, using ^{14}C-labeling of the test material does not allow for the identification of the environmental fate of the substance (e.g., metabolization by liver enzymes) because only radioactivity is measured. In order to include that option, additional specific analysis is required allowing for the identification of very small amounts of test material or associated transformation products (e.g., at the ng/L range).

On the risk assessment side, existing models used, for instance, in REACH are purely tonnage based, and thus may not fully cover the use of UV filters in sunscreens. An application-based lake scenario for repellents exists, but it is dedicated to freshwater and requires further refinement for UV filters. For marine risk assessment purposes, no such model exists at this stage, and so there is also an urgent need to focus on the development of such a model. This model should include various scenarios to facilitate a more site-specific (i.e., Baltic, Mediterranean, and Caribbean seas and Hawaii) marine risk assessment.

To conclude, current ecotoxicological tests with scleractinian corals (hard corals) are still considered to be at the research stage ("knowledge gathering") and upcoming tests require test method validation and standardization before they should be used in a regulatory context. For dedicated toxicity testing of UV filters, existing analytical issues related to the detection and quantification of UV filters at their solubility level in marine water must be tackled.

Many UV filters on the market already have a comprehensive set of aquatic toxicity data which allows for an adequate hazard profile of the respective substance. Once an environmental hazard has been identified, a risk characterization for the environment is considered mandatory by EU regulation (i.e., REACH) in order to demonstrate safe use or the need for further regulatory action (emission reduction). This application-based risk assessment includes marine water as well as marine sediment and can be used as a proximate for the safety assessment of corals until more application-based, site-specific risk assessment models become available.

In conclusion, the question of whether or not the use of UV filters in sunscreens is safe relies on both valid test results with corals and the availability of suitable application-based and site-specific risk assessment scenarios, supported by adequate monitoring data. The results from the risk assessment should then be the basis for any upcoming decisions on potential bans of certain UV filters.

DATA AVAILABILITY STATEMENT

All data used are either publicly available through published articles or via the ECHA webpage. Data that are not fully publicly available and used to generate Figure 1 are summarized in the Supporting Information.

SUPPORTING INFORMATION

TABLE 1. Overview of relevant background data on 24 UV filters approved by the EU.

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