

## Parameters for assessing the aquatic environmental impact of cosmetic products



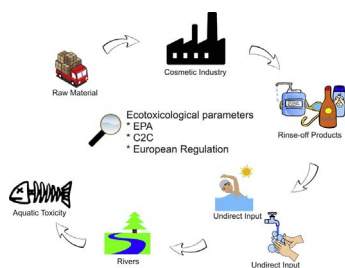
N.A. Vita<sup>a,b,\*</sup>, C.A. Brohem<sup>a</sup>, A.D.P.M. Canavez<sup>a</sup>, C.F.S. Oliveira<sup>a</sup>, O. Kruger<sup>c</sup>, M. Lorencini<sup>a</sup>, C.M. Carvalho<sup>a,b</sup>

<sup>a</sup> Grupo Boticário, Department of Safety and Efficacy Assessment, São José dos Pinhais, Paraná, Brazil

<sup>b</sup> Master's Program in Industrial Biotechnology, Positivo University [Universidade Positivo], Curitiba, Paraná, Brazil

<sup>c</sup> Grupo Boticário, Department of Technological Research, São José dos Pinhais, Paraná, Brazil

### GRAPHICAL ABSTRACT



### ARTICLE INFO

#### Keywords:

Ecotoxicity  
Raw materials  
Environmental impact  
Aquatic toxicity

### ABSTRACT

The cosmetic industry's growing concern about the impact of its supply chain on the environment, sustainability of raw materials, and biodiversity increases the need to ensure that the final product has a lower environmental impact. The objective of this review is to summarize and compare the information available from international organizations and legislation regarding the main criteria used to assess raw materials for aquatic toxicity, as well as the most suitable alternative methods for obtaining assessment parameters. Using the literature available in databases, a review of the scientific literature and international legislation, this work discusses and compares the parameters established by international organizations such as the Environmental Protection Agency (EPA) and Cradle to Cradle (C2C), as well as European legislation, namely, European Regulation 1272/2008, for assessing environmental impact. Defining the ecotoxicity parameters of the main classes of raw materials in rinse-off cosmetic products can enable the development of products that are more environmentally sustainable, prioritizing substances with less environmental impact.

### 1. Introduction

According to the definition given in European Regulation 1223/2009, a Cosmetic Product is understood as any substance or mixture intended to be placed in contact with the external parts of the human body (skin, hair system, nails, lips and external genital organs) or with the teeth and mucous membranes of the oral cavity to, exclusively or

primarily, clean them, perfume them, change their appearance, protect them, keep them in good condition or correct body odors (Regulation (EC) No 1223/2009 of The European Parliament and of The Council, 2009), and, some of the products commonly referred to as “personal care products” are cosmetics, for example, skin moisturizers, perfumes, lipsticks, shampoos, soaps, body oils, toothpastes, and deodorants (<https://www.fda.gov/ForIndustry/FDABasicsforIndustry/>

\* Corresponding author at: Grupo Boticário, Department of Safety and Efficacy Assessment, São José dos Pinhais, Paraná, Brazil.  
E-mail address: [nataliav@grupoboticario.com.br](mailto:nataliav@grupoboticario.com.br) (N.A. Vita).

ucm238796.htmhttps://www.fda.gov/ForIndustry/FDABasicsforIndustry/ucm238796.htm). After use, a significant amount of these products enter the wastewater stream and may end up in the aquatic environment (Tolls et al., 2009). Pharmaceutical and personal care products enter the aquatic environment, and their potential toxic effects on the biota, particularly on aquatic organisms, are of considerable concern (Kim et al., 2008). The presence of these products in sewer systems in different countries is measured in ng/L to µg/L, and the efficacy of removing these products through conventional treatment (flocculation, sedimentation and treatment of activated sludge) is limited (Liu and Wong, 2013).

There has been little research assessing the environmental impact of personal care products, although they are used more often and in greater concentrations than pharmaceutical products (Brausch and Rand, 2010). There is some evidence that a number of these compounds are persistent in the environment and impact organisms in different ways such as changes in reproduction and in biogeochemical cycles (Jjemba, 2004).

Many ingredients used in personal care products have become compounds of increasing environmental concern and are often detected mainly in receiving waters (Cassani and Gramatica, 2015).

Although data from some classes of raw materials are available, additional research is needed to understand the environmental concentrations, potential toxicities of mixtures, endocrine effects and bioaccumulation potentials of personal care products to accurately identify the potential risk of this type of product when it is released into the aquatic environment (Brausch and Rand, 2010).

Based on these considerations, there is a need to expand knowledge on the properties of personal care products to better understand their environmental behaviors and their sustainabilities, not only in terms of their immediate impacts on the environment but also in terms of their long-term implications and potential environmental hazard, in particular bioaccumulation, persistence and toxicity (Cassani and Gramatica, 2015).

Bioaccumulation can also occur through food capture (biomagnification); it is the most critical parameter, as raw materials with the potential to bioaccumulate can move through the entire trophic chain, generating a series of environmental impacts (Hermann et al., 2015).

Rinse-off products such as shampoos, conditioners, soaps, body oils and sunscreens are transported to a sewage treatment plant and subsequently enter rivers. The parameters related to the ecotoxicity of each raw material contained in these product categories should be analyzed to assess their environmental impact. Therefore, selecting more sustainable raw materials for the environment is essential to prioritize more sustainable cosmetic products with lower environmental impact. Thus, the cosmetic industry needs to develop more sustainable products with lower environmental impact.

Because there are no guidelines or even recommendations for how the cosmetics industry should act to produce more cosmetic products with less environmental impact, the objective of this review is to summarize and compare the information available from international organizations and legislation regarding the main criteria used to assess raw materials for aquatic toxicity and the most suitable alternative methods for obtaining assessment parameters. By analyzing the ecotoxicity generated by the main raw materials contained in rinse-off cosmetic products it will be possible to develop products that are more environmentally sustainable, prioritizing substances with less aquatic environmental impact.

## 2. Environmental impact of the main classes of raw materials used in rinse-off cosmetic products

A lot of raw materials are present in a cosmetic formulation and many have potential concerns for the environmental.

When rinse-off products such as shampoos, conditioners, soaps, body oils and sunscreens are used, they are sent directly to sewage

treatment facilities and thus to an effluent river (Brausch and Rand, 2010).

Pharmaceutical and personal care products have been found in sewage around the world, and research shows that certain products may have an impact on the environment at concentrations ranging from micrograms to nanograms per liter, with a host of potential impacts (Blair et al., 2013).

Sewage treatment is not specifically designed to remove personal care products and numerous ingredients from personal care products are found in high levels in domestic sewage after use, such as antimicrobials, synthetic fragrances, surfactants and filters. (Roberts et al., 2015).

Some classes of raw cosmetic materials are already known to have some impact on the environment, for example, sunscreens, which present a serious hazard to the environment (Sobek et al., 2013).

The analysis of parameters related to the ecotoxicity of raw materials used in rinse-off cosmetic products is of fundamental importance to prioritize the use of those that are most sustainable for the aquatic environment and have a lower environmental impact.

### 2.1. UV filters

UV (ultraviolet) filters are a broad class of substances that have received attention in the scientific press for many years. They are used in a wide range of cosmetic products to protect products and/or skin from damage caused by ultraviolet rays (Environment Agency, 2008).

To achieve high SPF and UVA values, the concentrations of filters in products have increased, and different combinations of filters have been used (Manová et al., 2012).

The use of sunscreens is regulated in many countries, although there are differences in their classification. In Europe, they are considered cosmetics, in the United States, they are considered OTC (over-the-counter) medications, and in Japan, they are considered both cosmetics and medications (Días-Cruz and Barceló, 2009).

Recent studies have shown that UV filters reach the surface of water (rivers, lakes and oceanic coast) during the release of sewage (Rodil et al., 2009a).

UV filters from sunscreen products are released into the aquatic environment both directly onto the water's surface during recreational activities and indirectly through the treatment of sewage related to household activities such as bathing, for example, after using shampoos (Rodil et al., 2009a).

UV filters are known to bioaccumulate, and recent studies have also indicated their potential for estrogenic activity (Brausch and Rand, 2010).

Organic UV filters are considered pseudo-persistent environmental contaminants, but little is currently known about their distribution and impact on aquatic environments (Vione et al., 2015).

Despite the fact that most filters have high lipophilicity (log Kow > 3), they can be washed away, ending up in the environment. Therefore, different sunscreens have been detected at ppb or ppt levels on surface waters and in sewage, with maximum concentrations in the summer (Vione et al., 2015).

Many UV filters have a high lipophilicity, and their octanol-water partition coefficient (log Kow) values are generally higher than 3 (Tsui et al., 2014). The log Kow data presented in the work of Rodil and colleagues are benzophenone-3 log Kow 3.07, octocrylene 6.88, butyl methoxydibenzoylmethane 4.51, ethylhexyl methoxycinnamate 5.80, homosalate 6.16, and ethylhexyl salicylate 5.97 (Rodil et al., 2009b).

An analysis of lake water indicated the presence of seven UV filters with concentrations between 40 ng/L for benzophenone-3 and 4381 ng/L for octocrylene. In untreated sewage, different UV filters were also detected at high concentration levels, such as octocrylene at 5322 ng/L (Rodil et al., 2009a).

Benzophenone-3, ethylhexyl methoxycinnamate, 4-methylbenzylidene camphor and octocrylene were the predominant pollutants in fish

samples from four rivers on the Iberian Peninsula. The maximum concentration was 241.7 ng/g for ethylhexyl methoxycinnamate (Ferrero et al., 2015).

UV filters are generally not readily biodegradable, but they are removed from the water cycle through adsorption and photodegradation. The ecotoxicities of most of these compounds are significant (Tolls et al., 2009). Almost 50% of the UV filters studied and approved for use in cosmetics according to the European regulation and their classifications were identified as being hazardous to the aquatic environment, including butyl methoxydibenzoylmethane, classified as readily biodegradable, with an aquatic toxicity between 1 and 10 mg/L, ethylhexyl methoxycinnamate with an aquatic toxicity of 1 mg/L and BCF > 500, ethylhexyl salicylate with a toxicity from 1 to 10 mg/L and BCF > 500, and octocrylene, which is considered bioaccumulative and not readily biodegradable (Sobek et al., 2013).

A risk assessment showed that 4-methylbenzylidene camphor presented a high risk for algae, whereas benzophenone-3 and ethylhexyl methoxycinnamate presented a high risk for fish and corals in Hong Kong (Tsui et al., 2014).

According to Rodil and collaborators, all UV filters can be determined in sewage samples at concentrations between 920 and 3893 ng/g for most of the 4-methylbenzylidene camphor, octocrylene and ethylhexyl triazone UV filters (Rodil et al., 2009b).

There is also an accumulation of ethylhexyl methoxycinnamate in the food chain, with concentrations of up to 337 ng/g in fish from six Swiss rivers. The accumulation of these compounds in organisms is a problem because UV filters and their metabolites have been shown to interfere with endocrine function through the activation of environmental estrogens, both *in vitro* and *in vivo* (Tsui et al., 2014).

Ethylhexyl methoxycinnamate is one of the most widely used UVB filters in the world; it is included on the list of the highest volume chemicals in Europe, with more than 1000 tons per year. It has already been found in fish and seafood at ng/g levels, which suggests that it can bioaccumulate in the food chain. The widespread occurrence of ethylhexyl methoxycinnamate in the environment and its negative effects on health demonstrate the importance of assessing environmental persistence and transformation (Vione et al., 2015).

Benzophenone-3 (BP-3) has been widely used in sunscreens and many other consumer products, including cosmetics, is an emerging contaminant of concern in marine environments. The widespread use of BP-3 has resulted in its release into the water environment, and hence its potential impact on aquatic ecosystem is of concern (Kim and Chai, 2014; Downs et al., 2015).

BP-3 is lipophilic, photostable, and bioaccumulative, and can be rapidly absorbed via oral and dermal routes. BP-3 is reported to be transformed into three major metabolites *in vivo*, benzophenone-1 (BP-1), benzophenone-8 (BP-8), and 2,3,4-trihydroxybenzophenone (THB). BP-1 has a longer biological half-life than its parent compound and exhibits greater estrogenic potency *in vitro*. BP-3 has been detected in water, soil, sediments, sludge, and biota. BP-3 and its derivatives have been also detected in fish lipid (Kim and Chai, 2014).

## 2.2. Preservatives

Many personal care products need preservatives to increase their stability and prevent the growth of bacteria and fungi. The concentrations of preservatives in products are generally small, and thus, their concentrations in the water system are below the threshold of biocide action. Aldehydes, alcohols and acids, as well as the parabens used as preservatives, are readily biodegradable and present moderate toxicity to aquatic life, with LC/EC<sub>50</sub> values between 10 and 100 mg/L. As a result, the assessment of these substances does not indicate environmental risk (Tolls et al., 2009).

### 2.2.1. Triclosan

Triclosan is widely used as an antimicrobial agent in personal care

products such as soaps, shampoos, lotions and sunscreens. Concentrations of it have been found in sewage, and because of its hydrophobicity, its persistence has been reported in sewage and water (Roberts et al., 2015).

Triclosan, also has some environmental impact because it is highly toxic to the aquatic environment and enters the environment through the effluent sewage system. It has a log Kow of 4.8, which makes it persistent and bioaccumulative. According to Montagner et al. (2013), triclosan should be considered a priority pollutant and included in legislation in Brazil to promote the protection of the aquatic environment (Montagner et al., 2013).

According to legislation, the maximum amount of triclosan allowed in Brazil by the National Health Surveillance Agency (Agência Nacional de Vigilância Sanitária – ANVISA) is 0.3% in personal care products, cosmetics and perfumes (Resolução – RDC N° 29, 2012). In Europe, this raw material has already been banned and cannot be used in some cosmetic products according to European legislation, although is still permitted for toothpaste, hand soaps, body soaps/shower gels and deodorants (Commission Regulation (EU) N° 358/201, 2014).

The increased use of triclosan in personal care products led to an increase in its environmental levels over a short period of time. In 2006, the average concentration of triclosan in South Carolina was 0.63 ng/L; in 2008, its concentration reached 7.5 ng/L. Aquatic organisms are highly sensitive to triclosan exposure; its LC<sub>50</sub> is 0.352 mg/L (Hopper et al., 2015).

### 2.2.2. Parabens

Preservatives such as Parabens present minimal environmental risk to aquatic organisms (Brausch and Rand, 2010). Urban wastewater is one of the main sources of chemicals in aquatic environments, and parabens are not an exception to this rule. In fact, most parabens are detected in sewage. Methylparaben and propylparaben are the most abundant parabens in sewage, with values of up to 30,000 ng/L and 20,000 ng/L, respectively. Ethylparaben, butylparaben and isobutylparaben have also been detected, but at lower concentrations (Haman et al., 2014).

Parabens are widely used preservatives in cosmetics, pharmaceutical products and food. One study reported that, in 1987, more than 7000 kg of parabens was used in cosmetics, and that number has increased in the last 20 years (Brausch and Rand, 2010). In the early 2000s, the production of parabens in the European Union ranged from 10 to 100 tons per year (Haman et al., 2014).

In cosmetics alone, parabens are found in over 22,000 products, with a maximum concentration of 0.4% for each type of paraben and 0.8% in combinations (Haman et al., 2014).

Parabens are considered ideal preservatives because they have a high spectrum of antimicrobial activity, are highly stable with respect to pH changes, are relatively safe to use and are low cost. However, in 2004, a British study suggested a link between parabens and breast cancer. Previous studies have suggested that parabens are endocrine disruptors. In recent years, parabens have been criminalized, although results on the risks arising from their use are inconclusive (Haman et al., 2014).

According to Brausch and Rand (2010), there are results indicating effects on aquatic organisms that are continually exposed to parabens; however, preliminary data on environmental concentrations suggests only a minimal risk to aquatic organisms (Brausch and Rand, 2010). Furthermore, Denmark's Environmental Protection Agency assessed methylparaben and propylparaben and considered both to be readily biodegradable, with no expectation of bioaccumulation in aquatic organisms and low to moderate aquatic toxicity (Danish Environmental Protection Agency, 2015).

According to Carlsson et al. (2005), methylparaben is highly biodegradable and has no potential to bioaccumulate, and its aquatic toxicity presents LC<sub>50</sub> values that range from 10 to 100 mg/L and a PEC/PNEC of 0.0112, which is well below 1; it can thus be concluded

that there is no environmental risk (Carlsson et al., 2005). The Danish Environmental Protection Agency also concluded that methylparaben is readily biodegradable (> 90%) in the aquatic environment, has no tendency to bioaccumulate based on the log Kow value of 1.96 and is considered moderately toxic to the aquatic environment, with a LC<sub>50</sub> of 23 mg/L (Office Of Prevention Pesticides, And Toxic Substances, 2005). Finally, in a study by Haman et al., methylparaben presented a log Kow of 1.96, and propylparaben presented a log Kow of 3.04 (Haman et al., 2014).

According to Haman et al., parabens can be readily biodegradable and have an estimated half-life of between 9.6 and 35.2 h. Based on the bioconcentration factor and the log Kow calculated, the potential for bioconcentration in aquatic organisms is low for methylparaben and ethylparaben, moderate for propylparaben and high for butylparaben (Haman et al., 2014).

### 2.2.3. Phenoxyethanol

Another preservative, phenoxyethanol, which is widely used in rinse-off cosmetic formulations, was assessed by the Danish Environmental Protection Agency and was considered readily biodegradable according to OECD 301, is not expected to bioaccumulate and has low aquatic toxicity (Danish Environmental Protection Agency, 2015). Preservatives and antimicrobials are widely used in cosmetics, and their presence in river water is a concern. In 13 sites along Japanese rivers contaminated by domestic sewage or industrial effluents, the most detected preservatives were 2-phenoxyethanol, isopropylmethylphenol, resorcinol and triclosan; a maximum concentration of phenoxyethanol was detected at 14000 ng/L. The result suggests that the largest sources of 2-phenoxyethanol were cosmetics and household detergents (Kimura et al., 2014).

The results reported by Kimura et al. (2014) show a log Kow of 1.2 for 2-phenoxyethanol, 1.96 for methylparaben, 2.47 for ethylparaben, 3.04 for propylparaben, 2.91 for isopropylparaben, 3.57 for butylparaben, and 0.93 for resorcinol (Kimura et al., 2014).

### 2.2.4. Benzyl alcohol

The preservative benzyl alcohol was also assessed by the Danish Environmental Protection Agency, was considered readily biodegradable according to OECD 301, is not expected to bioaccumulate, has a log Kow of 1.1 and has a low aquatic toxicity with an LC<sub>50</sub> of 460 mg/L in fish and a PEC/PNEC of 0.1 (Danish Environmental Protection Agency, 2015).

## 2.3. Surfactants

The massive use of surfactants in detergents and cosmetic formulations and their subsequent release into aquatic systems require surfactants to be environmentally friendly (Lechuga et al., 2015). After use, surfactants and their products are mostly discarded in the treatment of sewage and then dispersed in the environment through the release of effluents onto the water's surface. Most surfactants used in personal care products are readily biodegradable, and high-volume product formulations have surfactants as an essential ingredient in all rinse-off products at relatively high concentrations. Considering their ecotoxicities and the large amounts used in products, surfactants are certainly the most relevant category of ingredients for the potential environmental impact of products (Tolls et al., 2009).

The environmental risk of surfactants depends on the final concentration reached in the aquatic environment. The concentration of surfactants and, thus, their possible toxic effects are reduced by their degradation through microbial activity, which is the first transformation that occurs in the environment. Even so, toxic products released in the biodegradation process can bioaccumulate, and their long-term effects are not sufficiently well known. Furthermore, surfactant degradation depends on the conditions in which biodegradation occurs. Under aerobic conditions, most surfactants are biodegradable or readily

biodegradable. However, under anaerobic conditions, they are persistent (Lechuga et al., 2015).

Surfactants are classified as non-ionic, anionic and cationic; and the anionic surfactants are the most widely used (Cowan-Ellsberry et al., 2014).

Anionic surfactants are the most common and oldest type of surfactant, and some examples are the Sodium Laureth Sulfate; Sodium Laureth Sulfosuccinate; Sodium Lauroyl Sarcosinate, Amonium Laureth Sulfate and Alcohol Ethoxysulphates. They are readily biodegradable in water treatment and on the water's surface, limiting their potential exposure to aquatic organisms under environmental conditions. Furthermore, they have limited potential for bioaccumulation and low concentrations measured in different water compartments, and thus, this category is not expected to put organisms at risk due to the low levels of exposure and bioavailability on the water's surface (Könnecker et al., 2011; Cowan-Ellsberry et al., 2014).

Consequently, the use of these surfactants is not associated with risk to aquatic organisms because they are readily biodegradable and do not differ much in aquatic toxicity (Tolls et al., 2009).

## 2.4. Emollients

Octamethylcyclotetrasiloxane (D4), decamethylcyclopentasiloxane (D5) and dodecamethylcyclohexasiloxane (D6) are silicones present in 16% of cosmetic products, with D5 being the most widely used. According to the EPA, the use of D5 and D6 increased tenfold in the last 25 years, to more than 225,000 and 22,500 tons, respectively. In Europe, the amount of D4, D5 and D6 used annually in personal care products was estimated by the United Kingdom's Environmental Agency at 579, 17,300 and 1989 tons in 2004, respectively (Dudzina et al., 2013).

The ECHA collected and assessed a number of relevant studies on the persistence, bioaccumulation and toxicity of D4 and D5; based on the data available, they concluded that D4 meets the criteria for persistence, bioaccumulation and toxicity in the environment and is very persistent and very bioaccumulative (vPvB) due to its persistence in sediments and high bioconcentration in fish (Dudzina et al., 2013). These effects are unpredictable in the long-term and difficult to reverse. Recently, the SEAC (Committees for Socio-Economic Analysis) draft opinion confirmed that the restriction of D4 and D5 in rinse off products should be obligated in the next two years after the official publication (ECHA, 2016). Others ingredients

Epidemiologic research has revealed widespread human exposure to phthalates, a class of chemicals that appear in personal care products as a solvent and fixative in fragrances, such as the diethylphthalate. Their presence in the environment has attracted considerable attention due to their potential impacts on ecosystem functioning and on public health, because they are hepatotoxic, teratogenic, and carcinogenic by nature. (Net et al., 2015; Liang et al., 2008).

Phthalates are involved in endocrine disrupting effects, namely, upon reproductive physiology in different species of fish and mammals. They also present a variety of additional toxic effects for many other species including terrestrial and aquatic fauna and flora (Net et al., 2015).

Numerous studies indicate that phthalate esters are degraded by a wide range of bacteria and actinomycetes under both aerobic and anaerobic conditions (Staples et al., 1997).

Standardized aerobic biodegradation tests with sewage sludge inocula show that phthalate esters undergo  $\geq 50\%$  ultimate degradation within 28 days. Primary degradation half-lives in surface and marine waters range from < 1 day to 2 weeks. Longer half-lives may occur in anaerobic, oligotrophic, or cold environments (Staples et al., 1997).

Numerous experiments have shown that the bioaccumulation of phthalate esters in the aquatic and terrestrial food chain is limited by biotransformation, increasing the trophic level. Consequently, models that ignore biotransformation grossly exaggerate bioaccumulation



potential of higher molecular weight phthalate esters (Staples et al., 1997).

### 3. Most widely used criteria for assessing aquatic toxicity

The main purpose of an environmental classification is to provide information about the environmentally relevant properties of substances and how to avoid or minimize environmental exposure to hazardous substances (Tišler and Zagorc-Končan, 2003).

Because exposure to personal care products is not adequately controlled and there is a lack of information about their persistent, bioaccumulative and toxic behaviors, the safety of these substances should be carefully assessed, even before they are put on the market, to minimize their impacts on the environment and increase environmental sustainability (Cassani and Gramatica, 2015).

To assess aquatic toxicity, a limited number of relevant parameters are required by environmental organizations: acute toxicity, chronic toxicity, bioconcentration or bioaccumulation and biodegradation or persistence (Scholz et al., 2013). Aquatic toxicity tests can be categorized according to exposure time, situation, criteria of effects to be assessed and organisms to be tested (Rand, 2003).

For an initial assessment of aquatic effects, the chemical product's impact is generally assessed with only one or two species representing each of the three trophic levels, using the results of short-term toxicity tests. Toxicity to primary producers (algae), acute toxicity to primary consumers (*Daphnia* spp.) and acute toxicity to secondary consumers (fish) are thus assessed (Australian Environment Agency, 2009). Fish are one of the organisms used to monitor contaminant persistence (Kaiser et al., 2011).

The approaches currently used to assess ecological risk are based on a comparison between an exposure indicator (predicted environmental concentration or PEC) and an effect indicator (predicted no-effect concentration or PNEC) (Scientific Committee On Emerging And Newly Identified Health Risks (SCENIHR); Scientific Committee On Consumer Safety (SCCS); Scientific Committee On Health And Environmental Risks (SCENIHR, SCCS, SCHER, 2012)). The estimated risk is calculated as the ratio between these indicators (PEC/PNEC), which must be smaller than one to achieve a satisfactory result (SCENIHR; SCCS; SCENIHR, SCCS, SCHER, 2012). When the PEC exceeds the PNEC, further assessment or a risk management action must be considered (Australian Environment Agency, 2009).

Risk assessment uses the PEC, which is the concentration of a substance in the environment, based on available information about its use or the amount discarded and the PNEC, which considers environmental concentration using the EC<sub>50</sub> (effective concentration 50) of the substance, N(L)OEC or other approaches (European Centre for Ecotoxicology and Toxicology of Chemicals, 2003).

To protect human health and the environment, the European Union's REACH (Registration, Evaluation, Authorization and Restriction of Chemicals) regulation entered into force in June 2007. REACH requires that all substances produced or imported into Europe above one ton per year must be registered. Those responsible for registering the substance must provide physicochemical, toxicological and ecotoxicological information, depending on the tonnage level (Lombardo et al., 2014).

#### 3.1. Acute aquatic toxicity

Acute aquatic toxicity is a substance's intrinsic capacity to cause harm to an organism in the short-term; i.e., it is the aquatic exposure to a substance (Prevention, Pesticides and Toxic Substances United States Environmental Protection Agency (EPA), 1996). Basically, all toxicity tests are based on exposing the population of aquatic organisms to the substance being measured. These tests provide an estimate of the concentration that affects 50% of the population exposed (mortality, inhibition of mobility, interference with reproduction, reduction in

respiration, etc.). Aquatic toxicity is expressed using EC<sub>50</sub> (effective concentration) or LC<sub>50</sub> (lethal concentration) (Lechuga et al., 2015).

Aquatic toxicity is normally determined using a fish LC<sub>50</sub> after 96 h of incubation with the substance analyzed, as well as a crustacea species EC<sub>50</sub> after 48 h of incubation and/or an algal species EC<sub>50</sub> after 72 h of incubation with the substance according to Organization for Economic Co-Operation and Development (OECD) protocol 201, 202 and 203 (Rand, 2003). These species cover a range of trophic levels and are considered substitutes for all aquatic organisms (Regulation (EC) No 1272/2008 of The European Parliament and of The Council, 2008).

#### 3.2. Chronic aquatic toxicity

Chronic aquatic toxicity is a substance's intrinsic capacity to cause adverse effects in an organism during the aquatic exposure that is determined in relation to the organism's life cycle. Similar to acute toxicity, for the purposes of Cradle to Cradle, fish (vertebrates), *Daphnia* (invertebrates) and algae are chosen (Cradle To Cradle, 2012).

Chronic toxicity tests make it possible to assess the possible adverse effects of a substance under long exposure conditions at sub-lethal concentrations. In this test, the organism is exposed to at least five concentrations of the material being tested during an entire reproductive cycle (Rand, 2003). For chronic toxicity, the values studied are the NOEC (no-observed-effect concentration) and LOEC (lowest-observed-effect concentration) according to OECD 201 and 204, 211 (Office of Pollution Prevention and Toxics U.S. Environmental Protection Agency (EPA), 2011).

#### 3.3. Bioaccumulation

Bioaccumulation is a process in which a chemical substance is absorbed in an organism by all routes of exposure as occurs in the natural environment, e.g., dietary and environmental sources (Office of Pollution Prevention and Toxics U.S. Environmental Protection Agency (EPA), 2011).

Bioconcentration and bioaccumulation measure the net accumulation of a chemical within an organism as a result of uptake via exposure to the material (from either the surrounding environment only [bioconcentration] or the surrounding environment and food [bioaccumulation]). Such accumulations may eventually lead to concentration levels capable of causing toxic effects within the organism or net accumulation of the chemical to predator organisms through the food chain (biomagnification) (Jackson et al., 2016).

The bioaccumulation of a substance is affected by uptake rates, metabolism and excretion, as well as the organism's storage capacity. Accumulation can occur through the body's surface from the environment or through the capture of food (biomagnification) (Hermann et al., 2015).

Substances with low water solubility generally have an affinity for fatty tissues and can accumulate and concentrate in tissues with a high lipid content (Rand, 2003).

Bioaccumulation is measured using the bioaccumulation factor (BAF), which is the ratio of a substance's concentration in a living organism (mg/kg) to its concentration in the environment (mg/L for aquatic systems). The potential for bioaccumulation can typically be determined using the octanol/water partition coefficient (Kow), usually reported as log Kow, according to OECD 107 or 117. While the BAF represents the bioaccumulation potential, the experimental bioconcentration factor (BCF), which is the ratio of a substance's concentration in biota to its concentration in the environment (water), provides a better measure and should preferably be used when available. The BCF is generally obtained and applied using laboratory studies (Hermann et al., 2015), and it should be determined according to OECD 305 (Rand, 2003). The BCF is a type of BAF and refers to bioaccumulation in water in laboratory tests (Cradle To Cradle, 2012).

The bioaccumulation of substances in aquatic organisms can cause

toxic effects in the long term, even when the concentrations in the water are low. The relationship between the log Kow of an organic substance and its bioaccumulation measured as a BCF in fish has considerable support in the scientific literature. The use of a cutoff value of  $\log \geq 4$  is intended to identify only those substances with a real potential for bioaccumulation. A BCF in fish of  $\geq 500$  is indicative of the potential for bioaccumulation (Regulation (EC) No 1272/2008 of The European Parliament and of The Council, 2008).

Ecological factors, including aquatic species, size (weight and length), body lipid content and sample site, can affect the bioaccumulation of substances. When the substance is not metabolized or excreted at the pace it is ingested, it accumulates, and biomagnification can occur through the trophic chain (Ferrero et al., 2015).

### 3.4. Biodegradation

Biodegradation is the period of time that a substance can exist in the environment before being destroyed (i.e., transformed) by microorganisms (Willing, 2001).

Half-life ( $T_{1/2}$ ), which is one of the values used to assess biodegradation, is the amount of time that the initial concentration of a substance takes to degrade to half in the environment (Cradle To Cradle, 2012).

Biodegradation studies are carried out for at least 28 days, and the following levels of degradation can be achieved: 70% in tests based on dissolved organic carbon and 60% of the theoretical maximum in tests based on oxygen consumption or carbon dioxide production. These levels of biodegradation should be achieved within 10 days after the start of degradation, where the result is taken as the time in which 10% of the substance was degraded (Regulation (EC) No 1272/2008 of The European Parliament and of The Council, 2008).

Degradation of organic chemicals in the environment influences exposure and, hence, it is a key parameter for estimating the risk of long-term adverse effects on biota. Degradation rates, or half-lives, are preferably determined in simulation biodegradation tests conducted under conditions that are realistic for the particular environmental compartment (e.g. STP, surface water, sediment or soil) (OECD, 2005).

## 4. Globally harmonized system (GHS) and the aquatic environment

In the European Union, the classification and labeling of hazardous chemicals is governed by Regulation (EC) No 1272/2008 on classification, labeling and packaging of substances and mixtures (the 'CLP Regulation'). The Cosmetic Regulation (EC) No 1272/2008 should ensure a high level of protection of human health and the environment (REGULATION (EC) No 1272/2008 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL).

The GHS (Globally Harmonized System of Classification and Labeling of Chemicals)

will classify and label identify hazardous chemicals and inform users about their hazards through standard symbols and phrases. They need to be harmonised to ensure good worldwide understanding and to facilitate the free flow of products (REGULATION (EC) No 1272/2008 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL). The GHS has been implemented in the EU by Regulation (EC) No 1272/2008 on classification, labeling and packaging of substances and mixtures (the 'CLP Regulation'). The CLP Regulation entered into force on 20 January 2009. The deadline for substance classification according to the new rules was in December 2010; for mixtures, the deadline was in June 2015 ([https://ec.europa.eu/growth/sectors/chemicals/classification-labelling\\_en](https://ec.europa.eu/growth/sectors/chemicals/classification-labelling_en)[https://ec.europa.eu/growth/sectors/chemicals/classification-labelling\\_en](https://ec.europa.eu/growth/sectors/chemicals/classification-labelling_en)).

The classification of hazards within the aquatic environment in the GHS is based on the impacts of substances on aquatic organisms and the ecosystems where they live, rather than on public health impacts

(Regulation (EC) No 1272/2008 of The European Parliament and of The Council, 2008).

The basic elements used to classify environmental hazard for the GHS are acute aquatic toxicity, potential for bioaccumulation, degradation and chronic aquatic toxicity. Labels should be used for substances or mixtures that meet the classification criteria in the hazard class, as shown below:

- H400: Very toxic to aquatic life (if it is classified as acute toxicity according to Regulation 1272/2008,  $LC_{50} \leq 1$  mg/L);
- H410: Very toxic to aquatic life, with long lasting effects (if it is classified as category 1 in Regulation 1272/2008,  $LC_{50} \leq 1$  mg/L, not readily biodegradable or  $BCF \geq 500$  ( $\log Kow \geq 4$ ));
- H411: Toxic to aquatic life, with long lasting effects (if it is classified as category 2 in Regulation 1272/2008,  $> 1$  to  $\leq 10$  mg/L, not readily biodegradable or  $BCF \geq 500$  ( $\log Kow \geq 4$ ));
- H412: Harmful to aquatic life, with long lasting effects (if it is classified as category 3 in Regulation 1272/2008,  $> 10$  to  $\leq 100$  mg/L, not readily biodegradable or  $BCF \geq 500$  ( $\log Kow \geq 4$ ));
- H413: May cause long lasting harmful effects to aquatic life (if it is classified as category 4 in Regulation 1272/2008, with no acute toxicity and data indicating potential capacity for aquatic environmental hazard) (REGULATION (EC) No 1272/2008 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL, 2008).

## 5. International organizations and regulation

Two organizations and one regulation were considered in reviewing the criteria for assessing environmental impact: the Environmental Protection Agency (EPA), Cradle to Cradle (C2C) and Regulation 1272/2008.

They were chosen for assessment in this work because the EPA and the European Regulation are international reference points and demonstrate the views of the United States and Europe, which are pioneers in cosmetics legislation and opinions. In addition, Cradle to Cradle is a certification organization in case there is interest in certifying a product. We thus have three different views on the subject.

The EPA's Design for the Environment (DfE) program developed assessment criteria as an alternative for evaluating hazards; it is a transparent tool to assess and differentiate between chemicals based on human and environmental hazards (Office of Pollution Prevention and Toxics U.S. Environmental Protection Agency (EPA), 2011).

Cradle to Cradle is a certification organization that assesses the entire product manufacturing process and seeks to characterize the hazards of the product's substances; in this review, the focus is only on the environment (Cradle To Cradle, 2012).

European Regulation 1272/2008 uses internationally accepted classification criteria and labeling elements to facilitate the sale of chemicals and contribute to global efforts to protect human health and the environment (Regulation (EC) No 1272/2008 of The European Parliament and of The Council, 2008).

Both programs can be used for cosmetic products because they provide analytical data for chemical substances (raw material) which are needed to assess the environmental impact of finished good. It is possible to analyze the environmental impact through the use of analysis strategies and risk quantification before the cosmetic product go to market, or reformulate a cosmetic that is already on the market but has a high environmental impact.

### 5.1. Environmental protection agency (EPA)

The EPA was proposed by President Richard Nixon and began operations on December 2, 1970. It is a United States federal government agency that was established to protect human health and the environment and writes and applies standards based on laws passed by

**Table 1**  
Criteria for Aquatic Toxicity (EPA).

	Very high	High	Moderate	Low
Acute Aquatic Toxicity (LC <sub>50</sub> or EC <sub>50</sub> mg/L)	< 1.0	1–10	10–100	> 100
Chronic Aquatic Toxicity (NOEC or LOEC mg/L)	< 0.1	0.1–1	1–10	> 10

Congress. The EPA works with industries, all levels of government and a wide variety of programs for the environment and also applies fines, sanctions and other measures (United States Protection Agency, 2015 [www.epa.gov/aboutepa/epa-history](http://www.epa.gov/aboutepa/epa-history)).

The EPA's DfE program developed assessment criteria as an alternative for evaluating hazards; it is a tool for assessing and differentiating chemicals based on human and environmental hazards. For most of the criteria were classified as “high” “moderate” and “low” risk (Office of Pollution Prevention and Toxics U.S. Environmental Protection Agency (EPA), 2011).

The EPA's DfE program can be used to evaluate the raw materials (chemicals) that are used in cosmetics to evaluate their environmental impact. With regard to the environment, the criteria used by the EPA to classify a substance are presented in Tables 1–3. It is important to mention that EPA requires toxicity data from only one of the three trophic levels.

To assess acute aquatic toxicity, substances are given hazard designations based on LC<sub>50</sub> or EC<sub>50</sub> in fish, invertebrates or algae; for chronic aquatic toxicity, they are given NOEC and LOEC values, classifying risk as very high, high, moderate and low, as shown in Table 1 (Office of Pollution Prevention and Toxics U.S. Environmental Protection Agency (EPA), 2011).

To assess persistence or biodegradation, the classification is made based on half-life or the readily biodegradable test, as described in Table 2.

To assess bioaccumulation, the criteria considered are the BAF/BCF and the log BAF/BCF, which are shown in Table 3.

When experimental BAF or BCF data are not available, the EPA suggests considering the Kow. If a substance has a log Kow of < 2, it is considered to have low bioaccumulation, and an estimated BAF or BCF is unnecessary. If log Kow data are not available, they can be estimated using the EPI (Estimation Programs Interface) suite models (Office of Pollution Prevention and Toxics U.S. Environmental Protection Agency (EPA), 2011).

## 5.2. Regulation 1272/2008

Regulation No. 1272/2008 was created by the European Parliament and Council and entered into force on January 20, 2009; it concerns the classification, labeling and packaging of substances and mixtures and amends and repeals Directives 67/548/EEC, 1999/45/EC and Regulation No. 1907/2006. This regulation contributes to the GHS objective of ensuring that the same hazards will be described and labeled in the same way worldwide and complements the REACH regulation (Regulation (EC) No 1272/2008 of The European Parliament and of The Council, 2008).

To protect human health and the environment, the European Union's REACH (Registration, Evaluation, Authorization and

**Table 2**  
Criteria for Persistence/Biodegradation (EPA).

Very high	High	Moderate	Low	Very Low
½ life > 180 days	½ life of 60–80 days	½ life of 16–60 days	½ life < 16 days or “readily biodegradable”	Passes the readily biodegradable test

**Table 3**  
Criteria for Bioaccumulation (EPA).

	Very high	High	Moderate	Low
BAF/BCF	> 5000	5000–1000	1000–100	< 100
Log BAF/BCF	> 3.7	3.7–3.0	3–2	< 2

Restriction of Chemicals) regulation entered into force in June 2007. REACH requires that all substances produced or imported into Europe above one ton per year must be registered. Those responsible for registering the substance must provide physicochemical, toxicological and ecotoxicological information, depending on the tonnage level (Lombardo et al., 2014).

And there is another regulation (EC) N° 1223/2009 on cosmetic products, the safety of substances classified as carcinogenic, mutagenic or toxic for reproduction (CMR) should be assessed taking account of the exposure from all sources (cosmetics, chemicals, food, medicinal products) according to a comprehensive approach.

The regulation No. 1272/2008 is composed of internationally accepted classification criteria and labeling elements to facilitate trade and contribute to global efforts to protect human health and the environment from the effects of dangerous chemicals. The regulation ensures that the risks posed by chemicals are clearly communicated to workers and consumers in the European Union through the classification and labeling of chemicals. Before making chemicals available on the market, the industry should establish the potential risks these substances and mixtures pose to human health and the environment, classifying them according to the risks identified (Regulation (EC) No 1272/2008 of The European Parliament and of The Council, 2008).

Chemicals are classified according to their physicochemical properties, as well as their toxicological and ecological properties. Environmental classification is based on the inherent harmful potential of a substance to an organism and on its environmental fate, i.e., its degradation and bioaccumulation potential (Tišler and Zagorc-Končan, 2003).

According to the European legislation, the basic elements for classifying hazards to the aquatic environment are as follows:

- Acute aquatic toxicity,
- Potential or actual bioaccumulation,
- Degradation of the chemical product and
- Chronic aquatic toxicity.

The system for classifying substances comprises one acute classification category and four chronic classification categories. The acute and chronic classification categories are applied independently. The criteria for classifying a substance as Acute Category 1 are defined based on the acute aquatic toxicity data (EC<sub>50</sub> or LC<sub>50</sub>). The criteria for classifying a substance in the chronic category combines two types of information: acute aquatic toxicity and environmental data (biodegradability and bioaccumulation data) (Regulation (EC) No 1272/2008 of The European Parliament and of The Council, 2008).

As seen in Table 4, category 1 acute toxicity only considers values of aquatic toxicity with L(E)C<sub>50</sub> data from fish, crustaceans and algae (≤ 1 mg/L). Category 1 chronic toxicity considers aquatic toxicity with L(E)C<sub>50</sub> data from fish, crustaceans and algae (≤ 1 mg/L) and also whether the substance is not readily biodegradable and presents BCF values ≥ 500 or a log Kow ≥ 4. Category 2 chronic toxicity considers values of aquatic toxicity with L(E)C<sub>50</sub> data from fish, crustaceans and larger algae (> 1 to ≤ 10 mg/L), as well as whether the substance is not readily biodegradable and/or has BCF values ≥ 500 or a log Kow ≥ 4 or whether the chronic toxicity NOEC is > 1 mg/L. Category 3 chronic toxicity considers values of aquatic toxicity with L(E)C<sub>50</sub> data from fish, crustaceans and algae (10–100 mg/L), as well as whether the substance is not readily biodegradable and/or has BCF values ≥ 500 or a log Kow

**Table 4**

Classification categories for substances hazardous to the aquatic environment according to Regulation 1272/2008.

Category 1 Acute Aquatic Toxicity	
96 h LC <sub>50</sub> (fish)	≤ 1 mg/L and/or
48 h EC <sub>50</sub> (crustaceans)	≤ 1 mg/L
72 h EC <sub>50</sub> (algae)	≤ 1 mg/L
Category 1 Chronic Aquatic Toxicity	
96 h LC <sub>50</sub> (fish)	≤ 1 mg/L and/or
48 h EC <sub>50</sub> (crustaceans)	≤ 1 mg/L and/or
72 h EC <sub>50</sub> (algae)	≤ 1 mg/L
Additionally, the substance is not readily degradable and/or BCF ≥ 500 (or, in its absence, log Kow ≥ 4)	
Category 2 Chronic Aquatic Toxicity	
96 h LC <sub>50</sub> (fish)	> 1 to ≤ 10 mg/L and/or
48 h EC <sub>50</sub> (crustaceans)	> 1 to ≤ 10 mg/L and/or
72 h EC <sub>50</sub> (algae)	> 1 to ≤ 10 mg/L
Additionally, the substance is not readily degradable and/or BCF ≥ 500 (or, in its absence, log Kow ≥ 4), unless chronic toxicity NOEC > 1 mg/L.	
Category 3 Chronic Aquatic Toxicity	
96 h LC <sub>50</sub> (fish)	> 10 to 100 mg/L and/or
48 h EC <sub>50</sub> (crustaceans)	> 10 to 100 mg/L and/or
72 h EC <sub>50</sub> (algae)	> 10 to 100 mg/L
Additionally, the substance is not readily degradable and/or BCF ≥ 500 (or, in its absence, log Kow ≥ 4), unless chronic toxicity NOEC > 1 mg/L.	
Category 4 Chronic Aquatic Toxicity	
Cases where the data do not allow classification under the above criteria but there is some degree of concern. This includes, for example, poorly soluble substances and those that are not readily degradable and have BCF ≥ 500 (or, if not present, log Kow ≥ 4), indicating potential for bioaccumulation. They will be classified in this category unless other scientific evidence exists showing that this classification is unnecessary. This evidence includes chronic toxicity > water solubility or > 1 mg/L or evidence of ready degradation in the environment.	

≥ 4 or whether the chronic toxicity NOEC is > 1 mg/L. Finally, category 4 chronic toxicity considers cases where the data do not allow classification under the above criteria but there is some degree of concern. This includes, for example, poorly soluble substances and those that are not readily degradable and have BCF ≥ 500 (or, if not present, log Kow ≥ 4), indicating the potential for bioaccumulation; these substances will be classified in this category unless other scientific evidence exists showing that this classification is unnecessary. This evidence includes chronic toxicity NOECs > water solubility or > 1 mg/L or evidence of ready degradation in the environment (Regulation (EC) No 1272/2008 of The European Parliament and of The Council, 2008).

### 5.3. Cradle to cradle (C2C)

The Cradle to Cradle (C2C) certification program was founded in 2005 by McDonough Braungart Design Chemistry (MBDC). In 2010, William McDonough and Michael Braungart formed the Cradle to Cradle™ Products Innovation Institute, a nonprofit organization, to create a quality and innovation assessment program and to manage and administer the certification program. To date, some 400 products and 150 companies have demonstrated the accessibility and benefits of developing products according to the Cradle to Cradle certification program (Cradle To Cradle, 2012).

Cradle to Cradle is a company that certifies efforts made in eco-smart design. The Cradle to Cradle certification is a third-party seal of sustainability that requires a number of different elements to be followed:

- Use of materials that are safe for human health and the environment at all stages of use,
- Products and design systems for reusing material, such as recycling or composting,
- Use of renewable energy,

- Efficient use of water and
- Social responsibility.

Cradle to Cradle certification involves a four-level approach with basic, silver, gold and platinum levels. This certification program applies to materials, sub-assemblies and finished products. The criteria used for environmental assessment are those considered below (Cradle To Cradle, 2012).

When assessing substances, the Cradle to Cradle program uses a color-based hazard classification system.

- Green: no hazard identified.
- Yellow: borderline hazard for the given endpoint.
- Gray: no data available to determine the hazard.
- Red: considered hazardous for this specific endpoint.

The program aims to capture each substance's intrinsic hazard. The probability that a substance will be hazardous to humans or the environment depends on its intrinsic hazard, but it also largely depends on the potential exposure. Collectively, this is known as risk, which can be defined by the simple formula Hazard × Exposure = RISK. Thus, to reduce risk, both the hazard and the exposure should be reduced to reduce the likelihood of adverse effects (Cradle To Cradle, 2012).

The definitions and criteria used by Cradle to Cradle to assess the environment are shown in Table 5.

Based on the BCF, BAF or Kow values, the classification of a substance's bioaccumulation potential as green, red, yellow or gray is shown in Table 5 (Cradle To Cradle, 2012).

To determine the hazard of biodegradation, many criteria may be considered; biodegradability tests are the most suitable, and using the QSAR (quantitative structure-activity relationship) to estimate biodegradation is less accurate. Different guidelines for biodegradation were developed by the OECD, and they are used for classification criteria. Criteria for biodegradation are shown below in Table 6.

When no other data are available through studies, the QSAR is indicated for predicting the toxicity of chemicals. In particular, the ECOSAR (ecological structure-activity relationship), developed as part of the EPA's EPI suite, is used for these purposes. Typically, acute toxicity is more widely available than chronic toxicity for aquatic species and is subsequently used in many classification schemes with the appropriate combination of biodegradation and bioaccumulation data (Cradle To Cradle, 2012). The criteria for acute and chronic aquatic toxicity are shown in Tables 7 and 8, respectively.

For Cradle to Cradle, aquatic toxicity can be assessed in fish (vertebrate), Daphnia (invertebrate) and algae because they cover a range of trophic levels in the aquatic environment and are generally representative of the aquatic flora and fauna. Furthermore, data on these species are more likely to be available because they are accepted by many regulatory organizations (Cradle To Cradle, 2012).

### 5.4. Comparison between the EPA, C2C and regulation 1272/2008

Table 9 contains a comparison between the three organizations assessed. Regulation 1272/2008 does not have as many classifications

**Table 5**  
Cut-off values for classifying bioaccumulation potential according to C2C.

Green	Yellow	Red	Grey
BCF < 100 through experimental results, QSAR log Kow < 2 or molecular weight > 1000	BCF 100–500 or QSAR results	BCF > 500 or QSAR results	No relevant data for classification. Log Kow > 2 and no further information

\*QSAR: quantitative structure-activity relationship.



**Table 6**  
Guidelines for classifying the hazard of persistence/biodegradability according to C2C.

Green	Yellow	Red	Grey
T1/2 < 30/90 days	30/90 days < T1/2 < 60/180 days	T1/2 > 60/180 days	No relevant data for classification, or substance is considered inorganic and not applicable to this parameter
Readily biodegradable (> 70% within 28 days) based on the OECD 301 protocol	< 70% based on the OECD 301 protocol	< 10% based on the OECD 301 protocol	
Readily biodegradable using QSAR results	< 60% based on the OECD 301 protocol Readily degradable within weeks using QSAR		

\*QSAR: quantitative structure-activity relationship.

as the EPA and C2C for differentiating between raw materials that are not highly hazardous to the environment. For example, to assess the biodegradation parameter, the European regulation only classifies substances that have biodegradation greater than 70%; there is no classification below that. For bioaccumulation, the classification is only for substances that are highly hazardous for this parameter, BCF > 500 and/or log Kow ≥ 4.0; it is not possible to classify the hazards of substances with lower values.

For assessing aquatic toxicity, the regulation has several classifications in categories 1–4, allowing the classification of substances with a medium to high environmental hazard; substances with a low toxicity cannot be classified (Regulation (EC) No 1272/2008 of The European Parliament and of The Council, 2008).

The EPA and C2C have similar classifications and use colors to identify the hazard. The EPA is somewhat more critical than C2C in terms of biodegradation because it considers lower half-life values in the low and moderate risk classifications. For bioaccumulation, C2C is more critical in its classifications of moderate and high risk, considering more restricted BCF values. For aquatic toxicity, both consider the same values in their assessment (Cradle To Cradle, 2012; Office of Pollution Prevention and Toxics U.S. Environmental Protection Agency (EPA), 2011).

## 6. Testing methods

### 6.1. Animal model

The animal model is the most widely used model in toxicology studies. However, the use of animals in research has been the subject of many discussions due to the large numbers of animals required and the suffering caused. The 3Rs (Reduction, Refinement, Replacement) program aims to reduce the number of animals used in research, improve study conditions to reduce suffering to a minimum, refine methodology and search for alternative methods that would ultimately replace *in vivo* tests (Cazarin et al., 2004).

For personal care products, there is regulatory pressure in many countries to reduce the number of animal tests used to assess human and environmental risk; for cosmetics specifically, their use has been banned in Europe since 2013 (Boxall et al., 2012).

**Table 7**  
Criteria for classifying acute aquatic toxicity in vertebrates, invertebrates and algae according to C2C.

Species	Green	Yellow	Red	Grey
Vertebrate (fish)	96 h LC <sub>50</sub> > 100 mg/L or by *QSAR	96 h LC <sub>50</sub> 10–100 mg/L or by QSAR	96 h LC <sub>50</sub> < 10 mg/L H400 <sup>+</sup> very toxic to aquatic life	No relevant data for classification
Invertebrate (Daphnia)	48 h L(E)C <sub>50</sub> > 100 mg/L or by QSAR	48 h L(E)C <sub>50</sub> > 10–100 mg/L or by QSAR	48 h L(E)C <sub>50</sub> < 10 mg/L or by QSAR H400 <sup>+</sup> : very toxic to aquatic life	No relevant data for classification
Algae	72/96 h 48 h L(E)C <sub>50</sub> > 100 mg/L or by QSAR	72/96 h L(E)C <sub>50</sub> > 10–100 mg/L or by QSAR	72/96 h L(E)C <sub>50</sub> < 10 mg/L or by QSAR <sup>**</sup> H400: very toxic to aquatic life	No relevant data for classification

NA: no criteria for classification.

\* QSAR: quantitative structure-activity relationship.

\*\* H400: GHS (Globally Harmonized System of Classification and Labeling of Chemicals).

**Table 8**  
Criteria for classifying chronic aquatic toxicity in vertebrates, invertebrates and algae according to C2C.

Green	Yellow	Red	Grey
Fish, Daphnia and/or Algae NOEC > 10 mg/L	Fish, Daphnia and/or Algae NOEC = 1–10 mg/L	Fish, Daphnia and/or Algae NOEC < 1 mg/L H411: Toxic to aquatic life with long-term effects H412: hazardous to aquatic life with long-term effects H413: may cause long-term effects on aquatic life	No relevant data for classification

Considerations about animal welfare have increasingly questioned ecotoxicity tests with fish and spurred efforts to develop different alternatives or refine methods. Tests with vertebrates are an integral part of identifying environmental hazards and assessing the risk of chemical substances. These tests raise concerns on ethical and economic issues and are considered inappropriate for assessing all substances that require regulatory testing (Scholz et al., 2013).

In September 2004, it became illegal to perform tests with finished cosmetic products in the European Union, and in March 2009, it became illegal to test ingredients for cosmetic products on animals and market cosmetic products that have been tested on animals in the European Union. Until March 11, 2013, there were some exceptions for toxicity tests involving repeated doses, reproductive toxicity and toxicokinetics (Directive 2004/38/EC of The European Parliament And Of The Council, 2004; Regulation (EC) No 1223/2009 of the European Parliament and of The Council, 2009). However, since March 11, 2013, there has been a complete ban on animal testing of any type for cosmetics and their ingredients.

### 6.2. *In vitro* and lower organisms

There is considerable room for using integrated strategies to predict

**Table 9**  
Classification criteria for each organization (EPA, C2C and Regulation 1272/2008).

EPA	Regulation 1272/2008						C2C							
	Classification	Acute Aquatic Toxicity mg/L	Chronic Aquatic Toxicity mg/L	Biodegradation (T1/2 life%)	Bioaccumulation BAF/BCF/log (Kow)	Classification	Acute Aquatic Toxicity mg/L	Chronic Aquatic Toxicity mg/L	Biodegradation (T1/2 life%)	Bioaccumulation BAF/BCF/log (Kow)				
Very High	< 1,0	< 0,1	< 0,1	T1/2 life > 180 days	> 5000	vPvB	NA	NA	T1/2 life > 60 days	> 5000 log kow ≥ 5	Grey	No relevant data for classification.	No relevant data for classification or log Kow > 2	
High	1–10	0,1–1,0	0,1–1,0	T1/2 life 60–180 days	5000–1000	PBT	< 0,01	NOEC < 1 mg/L	T1/2 life > 60 days	> 2000 log kow ≥ 4,5	Red	96 h LC50 < 10 mg/L	T1/2 life > 60 days	
Moderate	> 10–100	> 1–10	> 1–10	T1/2 life < 60 dias ≥16 days	< 1000–100	NA	NA	NOEC = 1–10 mg/L	30 day < T1/2 < 60 days	Yellow	10–100 mg/L	96 h LC50 10–100 mg/L	Inherently biodegradable OECD (302, 304A);	
Low	> 100	> 10	> 10	T1/2 life < 16 days or readily biodegradable	< 100 log kow < 2,0			NOEC > 10 mg/L	T1/2 < 30 days	Green	96 h LC50 > 100 mg/L	NOEC > 10 mg/L	T1/2 < 30 days	
Very Low	NA	NA	NA	readily biodegradable	NA			NA	NA	NA	NA	NA	NA	BCF < 100 or log Kow < 2 or Molecular weight > 1000

\*vPvB: very persistent and very bioaccumulative. \*PBT: persistent, bioaccumulative and toxic. \*N.A.: no criteria for classification.

**Table 10**  
Applicability of biodegradation methods.

Test	Analytical Method	Poorly Soluble Substance	Volatile Substance	Adsorbent Substance
301A: DOC Die-Away	Dissolved organic carbon	–	–	+ / –
301B: CO <sub>2</sub> Evolution (Modified Sturm Test)	Respirometry: CO <sub>2</sub> evolution	+	–	+
301C: MITI (I) (Ministry of International Trade and Industry, Japan)	Respirometry: Oxygen consumption	+	+ / –	+
301D: Closed Bottle	Respirometry: Dissolved oxygen	+ / –	+	+
301E: Modified OECD Screening	Dissolved organic carbon	–	–	+ / –
301F: Manometric Respirometry	Oxygen consumption	+	+ / –	+

aquatic toxicity, with the minimal use of tests on fish. This can be achieved by using combined methods involving *in silico* prediction and tests on cells in tissue culture and on lower organisms. PNEC levels can also be determined from the resulting data and are useful in quantitative risk assessment (Grindon et al., 2008).

To obtain data on the biodegradation, bioaccumulation and aquatic toxicity of raw materials, there are many specific *in vitro* tests for each parameter, enabling a complete environmental impact analysis, which in turn can be used to assess the acute toxicity to fish, bioaccumulation and other parameters (Scholz et al., 2013).

A variety of testing methods have been developed by the EPA, the ISO (International Standardization Organization) and the OECD to assess the potential and hazard of substances to aquatic organisms, and they are accepted internationally. Developing uniform and standardized methods would improve the comparison of test data (Rand, 2003).

According to the United Kingdom's Environment Agency, algae and invertebrates are considered more sensitive than fish and are sufficient for estimating toxicity (Scholz et al., 2013).

To determine acute toxicity, the most widely used methodology is OECD 201B/2011, an algae toxicity test (OECD, 2002). Cell cultures have been a promising alternative for testing acute toxicity in fish. A substantial number of studies have compared the *in vitro* cytotoxicity of substances to the fish line with *in vivo* acute toxicity in fish and confirmed the usability of fish cell lines. However, fish cell lines are still not part of any regulation (Scholz et al., 2013).

Various fish primary cells and cell lines are available for aquatic ecotoxicity tests. However, one obstacle to their use and acceptability is the frequent observation of a reduced response to the same test samples compared to *in vivo* studies in fish. These tests end up being used only for screening, and they are not a full replacement for acute toxicity tests on fish (Grindon et al., 2008).

### 6.3. QSAR

Another approach to reducing the number of fish used for toxicological purposes is using QSAR to predict the bioaccumulation potential of substances (Braunbeck and Lammer, 2006). It is possible to reduce the number of animals using testing methods such as *in vitro* and *in silico* (QSAR) methods, employing intelligent testing strategies (Boxall et al., 2012).

Different alternatives are being employed to replace the use of animals and fill in the remaining data. One of these alternatives is QSAR, which reports a substance's molecular properties and requires toxicological data (from databases or directly from experimental data), forming a foundation for the development of predictive models. Predictive QSAR software offers a fast, reliable and effective analysis for assessing toxicity when there are limited conventional data (Kruhlak et al., 2006).

Several software tools aid in the application of QSAR to predict environmental effects, such as VEGA ([www.vega-qsar.eu](http://www.vega-qsar.eu)), Petoxtox and Petrorisk ([www.concawe.be](http://www.concawe.be)), Multicase ([www.multicase.com](http://www.multicase.com)), EPI SUITE ([www.epa.gov/opptintr/exposure/pubs/episuite.htm](http://www.epa.gov/opptintr/exposure/pubs/episuite.htm)), Toxtree ([www.source-forge.net/projects/toxtree](http://www.source-forge.net/projects/toxtree)) and many others. With

financial support from the European Union, the OECD developed the OECD QSAR Toolbox ([www.qsartoolbox.org](http://www.qsartoolbox.org)) (Scholz et al., 2013).

The EPA offers integrated tools that, in the absence of data, enable analysis through analogues and estimated values from models such as the EPI suite (Environmental Protection Agency EPI Suite, 2015). The EPI suite is a set of programs based on physicochemical and environmental properties that was developed by the EPA and includes the following programs: KOWWIN™ (estimates the log octanol-water partition coefficient), BIOWIN™ (estimates aerobic and anaerobic biodegradability), BioHCwin (estimates biodegradation half-life), WSKOWWIN™ (estimates the octanol-water partition coefficient), WATERNT™ (estimates water solubility), BCFBAF™ (estimates the bioconcentration factor, BCF and BAF), HYDROWIN™ (estimates hydrolysis and half-life), and ECOSAR, which estimates ecotoxicity as well as acute and chronic aquatic toxicity. This tool has a database of over 40,000 chemicals (<http://www2.epa.gov/tsca-screening-tools/epi-suite-estimation-program-interface>).

### 6.4. Analytical methods

The OECD's biodegradation test has six methodological variations and can be used according to the physical characteristics of the substance being tested, as shown in Table 10 (OECD, 1992). Below are the six methods:

- 301 A: DOC Die-Away,
- 301 B: CO<sub>2</sub> Evolution (Modified Sturm Test),
- 301 C: MITI (I) (Ministry of International Trade and Industry, Japan),
- 301 D: Closed Bottle 301,
- 301 E: Modified OECD Screening and
- 301 F: Manometric Respirometry.

The above methods are similar in many respects; in all tests, the test substance provides the sole source of organic carbon and is diluted in a test medium containing a relatively low concentration of biomass. In all tests, a non-analytical and non-specific method is used to follow the course of biodegradation. This has the advantage of making the methods applicable to a wide variety of organic substances, and there is no need to develop specific analytical procedures. These methods also respond to any biodegradation residue or biotransformation products; an indication of the extent of the ultimate biodegradation is provided (OECD, 1992).

The ideal method can be chosen according to the characteristic of the substance, depending on whether it is poorly soluble, volatile or adsorbent, as shown in Table 10 below.

The most widely used and cited method is 301B; the principle of the test is to assess the degradation of the raw material for 28 days by determining the carbon dioxide produced. The sample is incubated in amber vials containing a mineral medium and inoculum for 28 days, and readings are taken on predetermined days, titrating the CO<sub>2</sub> dissolved in barium hydroxide until the turning point. In parallel, negative controls are assessed. The result is provided in percent sample biodegradability (OECD, 1992).

There is a clear need to develop alternative methods for assessing the bioaccumulation of thousands of chemicals that must be evaluated in the coming years, taking integrated testing strategies into consideration (Scholz et al., 2013).

Currently, the BCF is determined using OECD 305; in general, this method is expensive and time consuming, and the basic protocol requires at least 108 fish per substance (Scholz et al., 2013). Most of the current alternatives are QSAR and log Kow (Scholz et al., 2013).

To determine bioaccumulation in aquatic organisms without the use of animals, one available alternative is to determine the octanol-water partition coefficient, usually reported as log Kow, according to OECD 107/1995 (OECD, 1995).

## 7. Conclusions

Currently, only large companies in the cosmetics sector communicate the conduction of ecotoxicological assessments to minimize the impact of their products on aquatic environments but this information is not commonly spread by companies.

Additional research is needed to understand the environmental concentrations, potential toxicity of mixtures in the environment and bioaccumulation potential of personal care products to accurately identify their potential risk to the aquatic environment. According to the literature cited in this work, there is evidence that some of these compounds are persistent in the environment, affecting organisms in different ways. It is thus necessary for all classes of raw materials used in rinse-off products to be analyzed for their environmental impact through the use of analysis strategies and risk quantification, as there may be differences between raw materials belonging to the same class.

This review indicates the need to develop an integrated and standardized strategy that enables an assessment of cosmetic raw materials in addition to the identification of potential risks to the aquatic environment. The criteria established by the most important international organizations, allied with the alternative biotechnological methods currently available, point toward establishing an analysis of environmental impact, allowing the selection or replacement of raw materials according to their environmental impact and thus generating cosmetic products that are more sustainable for the environment.

## Financial support

Grupo Boticário.

## References

- Australian Environment Agency, 2009. Environmental Risk Assessment Guidance Manual for Industrial Chemicals. Published by the Environment Protection and Heritage Council (February, 2009).
- Blair, B., et al., 2013. Pharmaceuticals and personal care products found in the Great Lakes above concentrations of environmental concern. *Chemosphere*, United States 93 (July), 2116–2123.
- Boxall, A., et al., 2012. Pharmaceuticals and personal care products in the environment: what are the big questions? *Environ. Health Perspect.* 120 (September (9)).
- Braunbeck, T., Lammer, E., 2006. Fish Embryo Toxicity Assays. Prepared for German Federal Environmental Agency, Dessau (March).
- Brausch, M.J., Rand, M.G., 2010. A review of personal care products in the aquatic environment: environmental concentrations and toxicity. *Chemosphere*, United States 1518–1532.
- Carlsson, C., et al., 2005. Are Pharmaceuticals Potent Environmental Pollutants? Part II: Environmental Risk Assessments of Selected Pharmaceutical Excipients. *The Science of the Total Environment*, Sweden, pp. 88–95 (June).
- Cassani, S., Gramatica, P., 2015. Identification of potential PBT behavior of personal care products by structural approaches. *Sustain. Chem. Pharm.* 1 (November), 19–27.
- Cazarin, K., et al., 2004. Redução, refinamento e substituição do uso de animais em estudos toxicológicos: uma abordagem atual. *Brazilian J. Pharm. Sci. Brasil* 40 (September (3)).
- Commission Regulation (EU) N° 358/201 of 9 April 2014. Amending Annexes II and V to Regulation (EC) N° 1223/2009 of the European Parliament and of the Council on Cosmetic Products. April, 2014.
- Cowan-Ellsberry, C., et al., 2014. Environmental safety of the use of major surfactant classes in north america. critical reviews in. *Environ. Sci. Technol. United States* 44, 1893–1993.
- Cradle To Cradle, 2012. Material Health Assessment Methodology Cradle to Cradle Certified™, Product Standard Version 3.0.
- Días-Cruz, M., Barceló, D., 2009. Chemical analysis and ecotoxicological effects of organic UV-absorbing compounds in aquatic ecosystems. *Trends Anal. Chem.* 28, 708–717.
- Danish Environmental Protection Agency, 2015. Survey and Health and Environmental Assessment of Preservatives in Cosmetic Products N° 138. Ministry of Environmental and Food, Copenhagen.
- Directive 2004/38/EC of The European Parliament And Of The Council of 29 April 2004. *Official Journal of the European Union*, April, 2004.
- Downs, C., et al., 2015. Toxicopathological effects of the sunscreen UV filter, oxybenzone (benzophenone-3), on coral polypae and cultured primary cells and its environmental contamination in Hawaii and the U.S. Virgin Islands. *Arch. Environ. Contam. Toxicol.* 265–288.
- Dudzina, T., et al., 2013. Concentrations of cyclic volatile methylsiloxanes in European cosmetic and personal care products: prerequisite for human and environmental exposure assessment. *Environ. Int.* 62 (October), 86–94.
- ECHA – European Chemicals Agency. Committee for Socio-economic Analysis concludes on restricting D4 and D5. Available in: <https://echa.europa.eu/-/committee-for-socio-economic-analysis-concludes-on-restricting-d4-and-d5>. (Accessed 22 November 2017).
- Environment Agency, 2008. UV-Filters in Cosmetics – Prioritization for Environmental Assessment. Environment Agency, Rio House Waterside Drive, Aztec West, Almondsbury (December).
- Environmental Protection Agency EPI Suite, 2015. Available in: <http://www2.epa.gov/tsc-screening-tools/epi-suite-estimation-program-interface>. (Accessed 25 October 2015).
- European Centre for Ecotoxicology and Toxicology of Chemicals, 2003. Environmental Risk Assessment of Difficult Substances, Technical Report No. 88. Brussels, June.
- European Commission, 2017. Available in: [https://ec.europa.eu/growth/sectors/chemicals/classification-labelling\\_en](https://ec.europa.eu/growth/sectors/chemicals/classification-labelling_en). (Accessed 06 July 2017).
- Ferrero, P., et al., 2015. UV Filters bioaccumulation in fish from Iberian river basins. *Sci. Total Environ.* 518–525.
- Food and Drug Administration, 2017. Available in: <https://www.fda.gov/ForIndustry/FDABasicsforIndustry/ucm238796.htm>. (Accessed 06 July 2017).
- Grindon, C., et al., 2008. Integrated decision-tree testing strategies for environmental toxicity with respect to the requirements of the EU REACH legislation. *ATLA, United Kingdom* 36 (Suppl. 1), 29–42.
- Haman, C., et al., 2014. Occurrence, fate and behavior of parabéns in aquatic environments: a review. *Water Res.* 68, 1–11.
- Hermann, H., et al., 2015. Aquatic ecotoxicity of Lanthanum – a review and na attempt to derive water and sediment quality criteria. *Ecotoxicol. Environ. Saf.* 124 (November), 213–238.
- Hopper, T.L., et al., 2015. Accumulation of triclosan from diet and its neuroendocrine effects in Atlantic croaker (*Micropogonias undulatus*) under two temperature Regimes. *Mar. Environ. Res.* 112 (September), 52–60.
- Jackson, M., et al., 2016. Comprehensive review of several surfactants in marine environments: fate and ecotoxicity. *Environ. Toxicol. Chem.* 35 (May), 1077–1086.
- Jjemba, K., 2004. Excretion and ecotoxicity of pharmaceutical and personal care products in the environment. *Ecotoxicol. Environ. Saf.* 113–130.
- Kaiser, D., et al., 2011. Ecotoxicological effect characterisation of widely used organic UV filters. *Environ. Pollut.* 163 (December), 84–90.
- Kim, S., Chai, K., 2014. Occurrences, toxicities, and ecological risks of benzophenone -3, a common component of organic sunscreen products: a mini-review. *Environ. Int.* 143–157.
- Kim, J.W., et al., 2008. Acute toxicity of pharmaceutical and personal care products on freshwater crustacean (*Thamnocephalus platyurus*) and fish (*Oryzias latipes*). *J. Toxicol. Sci. Jpn.* 34 (December), 227–232.
- Kimura, K., et al., 2014. eof preservatives and antimicrobials in Japanese rivers. *Chemosphere* 107 (February), 393–399.
- Könnecker, G., et al., 2011. Environmental properties and aquatic hazard assessment of anionic surfactants: physico-chemical, environmental fate and ecotoxicity properties. *Ecotoxicol. Environ. Saf.* (April), 1445–1460.
- Kruhlik, N., et al., 2006. Progress in QSAR toxicity screening of pharmaceutical impurities and other FDA regulated products. *Adv. Drug Deliv. Rev.* 59 (November), 43–55.
- Lechuga, M., et al., 2015. Acute toxicity of anionic and non-ionic surfactants to aquatic organisms. *Ecotoxicol. Environ. Saf.* 125 (November), 1–8.
- Liang, D.W., et al., 2008. Phthalates biodegradation in the environment. *Appl. Microbiol. Biotechnol.* 80, 183–198.
- Liu, J.L., Wong, M.H., 2013. Pharmaceuticals and personal care products (PPCPs): a review on environmental contamination in China. *Environ. Int.* 59 (July), 208–224.
- Lombardo, A., et al., 2014. Optimizing the aquatic toxicity assessment under REACH through an integrated testing strategy (ITS). *Environ. Res.* 135 (September), 156–164.
- Manová, E., et al., 2012. Organic UV filters in personal care products in Switzerland: a survey of occurrence and concentrations. *Int. J. Hyg. Environ. Health* 216 (August), 508–514.
- Montagner, C.C., et al., 2013. Occurrence and Potential Risk of Triclosan in Freshwaters of São Paulo, Brazil—The Need for Regulatory Actions. *Environmental Science and Pollution Research International*, Berlin (August).
- Net, S., et al., 2015. Occurrence, fate, behavior and ecotoxicological state of phthalates in different environmental matrices. *Environ. Sci. Technol.* 49 (March), 4019–4035.
- Organization For Economic Co-operation and Development (OECD). Guideline for testing of chemicals Ready Biodegradability (301 B). July, 1992.
- Organization For Economic Co-operation and Development (OECD). Guidelines for the testing of chemicals Partition Coefficient (n-octanol/water): Shake Flask Method 107.



- July 1995.
- Organization For Economic Co-operation and Development (OECD). Guidelines for the testing of chemicals Freshwater Alga and Cyanobacteria, Growth Inhibition Test 201. July, 2002.
- Organization For Economic Co-operation and Development (OECD). Guideline for testing of chemicals proposal for revised introduction to the OECD Guidelines for testing Chemicals. Section 3 Part 1: Principles and strategies related to the testing of degradation of organic chemicals. April, 2005.
- Office of Prevention Pesticides, and Toxic Substances. United States Environmental Protection Agency Washington (EPA). Inert Reassessment of Methyl p-Hydroxybenzoate (methylparaben). Washington, DC, p. 1–15. September, 2005.
- Office of Pollution Prevention and Toxics U.S. Environmental Protection Agency (EPA). Design for the Environment Program Alternatives Assessment Criteria for Hazard Evaluation. United States of America, August, 2011.
- Prevention, Pesticides and Toxic Substances United States Environmental Protection Agency (EPA). Ecological Effects Test Guidelines. Washington, April, 1996.
- Rand, G.M., 2003. *Fundamentals of Aquatic Toxicology: Effects, Environmental Fate and Risk Assessment*, second edition. CRC Press, Taylor and Francis Group, Florida.
- Regulation (EC) No 1272/2008 of The European Parliament and of The Council of 16 December 2008. Official Journal of the European Union. December, 2008.
- Regulation (EC) No 1223/2009 of The European Parliament and of The Council of 30 November 2009 on cosmetic products. Official Journal of the European Union. November, 2009.
- Resolução – RDC Nº 29, de 1º de junho de 2012. Regulamento Técnico Mercosul sobre a Lista de Substâncias de Ação Conservante Permitidas para Produtos de Higiene Pessoal, Cosméticos e Perfumes. Brazil, July 2012.
- Roberts, J., et al., 2015. Pharmaceuticals and personal care products (PPCPs) in Australia's largest inland sewage treatment plant, and its contribution to a major Australian river during high and low flow. *Sci. Total Environ.* 541 (October), 1625–1637.
- Rodil, R., et al., 2009a. Non-porous membrane-assisted liquid–liquid extraction of UV filter compounds from water samples. *J. Chromatogr.* 1216 (April), 4887–4894.
- Rodil, R., et al., 2009b. Pressurised membrane-assisted liquid extraction of UV filters from sludge. *J. Chromatogr.* 1216 (October), 8851–8858.
- Scenihr (Scientific Committee ON Emerging And Newly Identified Health RISKS) SCCS (SCIENTIFIC COMMITTEE ON CONSUMER SAFETY); SCHER (SCIENTIFIC COMMITTEE ON HEALTH AND ENVIRONMENTAL RISKS). Addressing the New Challenges for Risk Assessment. Brussels, October, 2012.
- Scholz, S., et al., 2013. A European perspective on alternatives to animal testing for environmental hazard identification and risk assessment. *Regul. Toxicol. Pharm.* 67 (October), 506–553.
- Sobek, A., et al. In the shadow of the Cosmetic Directive—Inconsistencies in EU environmental hazard classification requirements for UV-filters. *The Science of the Total Environment*. Department of Applied Environmental Science (ITM), Stockholm University, 10691 Stockholm. Sweden, p. 461–462, May, 2013.
- Staples, C., et al., 1997. The environmental fate of phthalate esters: a literature review. *Chemosphere* 35 (August), 667–749.
- Tišler, T., Zagorc-Končan, J., 2003. Aquatic Toxicity of Selected Chemicals as a Basic Criterion for Environmental Classification. National Institute of Chemistry, Faculty of Chemistry and Chemical Technology, University of Ljubljana, Slovenia (March).
- Tolls, J., et al., 2009. Environmental safety aspects of personal care products—a European perspective. *Environ. Toxicol. Chem.* United States 28, 2485–2489.
- Tsui, et al., 2014. Occurrence, distribution and ecological risk assessment of multiple classes of UV filters in surface waters from different countries. *Water Res.* China 6 (September), 55–65.
- United States Protection Agency, 2015. Available in: [www.epa.gov/aboutepa/epa-history](http://www.epa.gov/aboutepa/epa-history). (Accessed 02 February 2015).
- Vione, D., et al., 2015. The role of direct photolysis and indirect photochemistry in the environmental fate of ethylhexyl methoxy cinnamate (EHMC) in surface waters. *Sci. Total Environ.* 537 (August), 58–68.
- Willing, A., 2001. Lubricants based on renewable resources ± an environmentally compatible alternative to mineral oil products. *Chemosphere*, Germany 43, 89–98.