Environment Agency

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UV-filters in cosmetics – prioritisation for environmental assessment

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Steve Killeen

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Head of Science

Executive summary

UV-filters are used in a wide range of products, such as plastics, rubber and cosmetics, including sunscreens. Their function is to prevent or limit damage following exposure to ultraviolet (UV) light. Recent research suggests that some of these substances might be able to interfere with endocrine systems. Given their ubiquity in society, the Environment Agency commissioned this screening project to identify whether any of these substances might be priorities for a more in-depth environmental hazard or risk assessment.

A brief survey of the uses, environmental fate, behaviour and effects of UV-filters has been undertaken, particularly concentrating on those substances that are permitted for use in sunscreens under the Cosmetic Products (Safety) Regulations 2008 and Annex VII of Directive 76/768/EEC. Only very limited information was available and the chemical identity is unclear for some substances. The UV-filters were screened using a combination of potential environmental risk (based on a simple scenario), potential PBT (persistent, bioaccumulative and toxic) and vPvB (very persistent and very bioaccumulative) properties and evidence of endocrine disruption potential. The highest priority substances for further assessment are detailed below.

CAS No	Name
118-56-9	Homosalate*
118-60-5	Ethylhexyl salicylate
131-57-7	Benzophenone-3
5466-77-3	Ethylhexyl methoxycinnamate
6197-30-4	Octocrylene
15087-24-8	3-Benzylidene camphor*
21245-02-3	Ethylhexyl dimethyl PABA*
36861-47-9/38102-62-4	4-Methylbenzylidene camphor*
70356-09-1	Butylmethoxydibenzoylmethane
71617-10-2	Isoamyl 4-p-methoxycinnamate

* Concern indicated for all three areas – risk, PBT/vPvB and endocrine disruption.

The overall priority will depend on the tonnage currently being supplied, and this information is not publicly available (there is only a broad indication of supply levels from the early 1990s). However, ethylhexyl methoxycinnamate is believed to be supplied at above 1,000 tonnes/year. A number of similar substances were notified under the Notification of New Substances Regulations (1993) and there may be some potential for grouping or read-across approaches to be developed as part of any further assessment. More information is also needed on the properties of the nano-particulate form of titanium dioxide (CAS No 13463-67-7).

Further investigation of hazard and risk can only be made in co-operation with the suppliers and their downstream users. This issue should be kept under review as more data become available under the REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) Regulation over the next few years.

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1 Introduction

Part of the Environment Agency's remit is to identify potential environmental problems, in order that appropriate action can be taken to resolve them. In the case of chemicals, there is a need to set priorities so that resources can be concentrated on those substances that might pose the highest concern for the environment.

'UV-filters' are a broad class of substances that have received attention in the scientific press for several years (for example, Jones 2001). They are used in a wide range of products including plastics, adhesives, rubber and cosmetics (such as sunscreen lotions) and are designed to protect those products (or skin, in the case of cosmetic sunscreens) from damage caused by the ultra-violet (UV) component of sunlight.

Several scientific studies have suggested that some UV-filters might interfere with the endocrine systems that control reproduction and growth, and may have a potential link to breast cancer (for example, Schlumpf *et al*. 2001; Seidlova-Wuttke *et al*. 2006; Hamann *et al*. 2006). UV-filters have also been linked to coral reef bleaching (for example, Danovaro *et al*. 2008).

Whilst the risks to human health from the use of cosmetic products are already subject to European legislation (see Chapter 2), the environmental risks from these products will not be addressed until Regulation (EC) No. 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)[1] is fully in place, which will take several years.

Given their widespread use and the fact that the majority of cosmetic products will find their way into waste water (due to washing), it is not surprising that UV-filters are found in the environment (see Chapter 5). The Environment Agency therefore commissioned this review of the available information on UV-filters in mid-2006, with the intention of making recommendations for which substances (or groups of substances) should be considered for a more detailed environmental hazard and/or risk assessment. The aim is to help set priorities for both industry and environmental regulators alike as the REACH procedures begin to take effect. It is not intended to be used as a basis for substitution decisions, and no assessment of human health hazard or risk has been performed.

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[1] See http://ec.europa.eu/environment/chemicals/reach/reach_intro.htm for more information.

2 Methods

2.1 Selection of substances

Within the European Union (EU), the substances that can be used as UV-filters in cosmetic products (such as sunscreens) are regulated by Council Directive 76/768/EEC and subsequent amendments.[2] These are implemented in the UK by the Cosmetic Products (Safety) Regulations 2008, SI 2008/1284.[3] A guidance document on implementation is also available (DTI 2005).

Annex VII of Directive 76/768/EEC was used as the starting point for this review. It covers UV-filters that are added to cosmetic sunscreen products specifically to filter out certain UV wavelengths, in order to protect the skin from the harmful effects of this radiation. It lists the maximum concentration limits for 27 UV-filters. The listed substances can also be added to other cosmetic products at levels up to the same maximum concentrations that apply to sunscreens. The list does not include other UV-filters used in cosmetics solely for the purpose of protecting the product itself from UV light (which may affect colour or odour, for example).

According to DTI 2005, UV-filters other than those listed in Schedule 7 of the Cosmetics Products (Safety) Regulations (or Annex VII of Directive 76/768/EEC) can still be used in cosmetic products provided they receive an authorisation.

Another source of information on possible UV-filters used in cosmetics products is the International Nomenclature of Cosmetics Ingredients (INCI). This indicative list was published in the Official Journal of the European Commission in 1996 and updated in 2006.[4]

A more general search of the internet was also made for information on other substances that are used to protect many other product types against the weathering or degradation that can result from exposure to UV radiation. When used in this way, the substance is more commonly known as a UV- or light-stabiliser – the term 'UV-stabiliser' will be used in this report. This internet search concentrated on the websites of four or five known major European suppliers of functional additives for polymers and coating systems.

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[2] A consolidated text of the Directive, including all relevant amendments, can be obtained from http://ec.europa.eu/enterprise/cosmetics/html/consolidated_dir.htm.

[3] Available from http://www.opsi.gov.uk/si/si2008/uksi_20081284_en_1#l1g9.

[4] Commission Decision 2006/257/EC of 9 February 2006 amending Decision 96/335/EC establishing an inventory and a common nomenclature of ingredients employed in cosmetic products. OJ L97, 05.04.2006, p 1. See also http://ec.europa.eu/enterprise/cosmetics/inci/inci_2006.pdf.

The chemicals identified on these sites were then cross-checked against the European chemical Substances Information System (ESIS) database[5] to determine whether:

- they were either HPV (high production volume) or LPV (low production volume) chemicals;[6] and
- there were any further suppliers within the EU.

The data available in ESIS refer to the commercial situation in the early to mid-1990s and so are bound to be somewhat out of date.

The identity of some of the chemicals found in this search is considered confidential by the suppliers (and this information is summarised in a Confidential Appendix), but a generalised summary of the findings is given in Section 3.3.

2.2 Substance property information

The ESIS database and confidential International Uniform ChemicaL Database (IUCLID)[7] were used to retrieve datasets on those substances that are listed as HPV or LPV chemicals. (Any substance not listed this way is either a new substance and so had to be notified under the Notification of New Substances Regulations, 1993, or a polymer, or is almost certainly not commercially important in Europe.) No IUCLID file was available for one of the HPV chemicals.[8] It should be noted that the entries in the IUCLID database consist of unvalidated data submitted by industry during the early 1990s.

Information was also taken from Safety Data Sheets available on the internet. Where relevant (such as because of an important data gap), estimates for the substance properties were made using the US Environmental Protection Agency's EPIWIN v3.12 program.[9] Such estimates are included where a structure for the substance was available and the program gave a result. The validity of the estimation method for any particular substance was generally not considered for this screening exercise. An exception to this is that a comment is made whenever ecotoxicity was predicted using the octanol-water partition coefficient (log K_{ow}) and the K_{ow} value lay outside the model's range. In general, the estimates are likely to be most accurate for simple structures.

Note: The EPIWIN software predicts long-term toxicity using a chronic toxicity value (Chv). This is understood to represent the geometric mean of the lowest observed

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[5] Available from http://ecb.jrc.it/esis/

[6] HPV chemicals were produced or imported by a company in amounts greater than 1,000 tonnes/year. LPV chemicals were produced or imported in amounts between 10 and 1,000 tonnes/year.

[7] Formerly available from the European Chemicals Bureau.

[8] No IUCLID data sheet was available in the stand-alone version of the confidential IUCLID nor the ESIS database. The ESIS database gives a IUCLID export file for this substance, but this caused an error when attempting to import it into IUCLID.

[9] Available from http://www.epa.gov/oppt/exposure/pubs/episuitedl.htm

effect concentration (LOEC) and the no observed effect concentration (NOEC). For this report, the Chv has been assumed to represent a prediction of the NOEC.

In addition, searches of the published literature were undertaken using the PubMed database for information on the endocrine effects of UV-filters and available monitoring data.[10]

Note: This review is based on readily available information only. No evaluation or validation of substance property data has been carried out. This should be taken into account when considering the conclusions of this report and is particularly important for data related to complex issues such as endocrine disruption potential.

2.3 EUSES calculations

A very crude risk assessment has been performed to assess the possible risks from the use of UV-filters. The associated assumptions are outlined in the following sections.

2.3.1 Quantities on the market

Little or no information is currently available on the amounts of UV-filters used in the UK or indeed in Europe. The following assumptions have been made in the absence of any other information.

Total amount used in the EU:	10,000 tonnes/year for HPV chemicals 500 tonnes for LPV chemicals (or where it is unclear whether a chemical is HPV or LPV).
Total amount used in UK/region:	1,000 tonnes/year for HPV chemicals 50 tonnes/year for LPV chemicals.

2.3.2 Uses

It is assumed that 100 per cent of the total amount of each UV-filter on the UK market is used in personal care products. Where it is clear that a substance is also used in polymer applications, a default calculation for a local polymer-processing site has been made (this use therefore makes no contribution to the regional release in this scenario). It should be noted that this is a worst case approach, but it at least allows a reasonable comparison to be made between different substances.

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[10] Available from http://www.ncbi.nlm.nih.gov/pubmed/

2.3.3 Emission estimates

Production

For production sites, the default methods from the Technical Guidance Document (TGD) on risk assessment for existing substances[11] have been used to estimate the local emissions. The nominal capacity of the production site was assumed to be 1,000 tonnes/year for HPV chemicals and 500 tonnes/year for LPV chemicals.

Production site releases:	2 per cent to waste water (LPV chemicals)
	0.3 per cent to waste water (HPV chemicals).

Formulation and use

For formulation and use in personal care products, the default methods from the TGD are used. This approach takes account of the maximum concentration of UV-filter that may be present in the final personal care product. The local release from the use of personal care products is taken to be a waste-water treatment plant serving a population of 10,000 people.

The relevant default emission factors to waste water are detailed below.

Formulation releases:	0.09 per cent to waste water (LPV and HPV chemicals)
Use by the general public:	80 per cent to waste water.

The default emission factor to air is dependent on the vapour pressure; this emission factor is generally very low for the substances considered in this report.

Polymer processing

For polymer processing, the release from a local polymer processing site has been estimated using the Emission Scenario Document (ESD) for plastics additives (OECD 2004) for a site processing polypropylene in a partially open process. A UV-stabiliser content of 0.5 per cent of the final polymer is assumed. Part of the emission estimation method requires knowledge of the particle size for solid additives. For this exercise, a particle size of >40 μm has been assumed in all cases based on the information in OECD 2004, but it should be noted that finer particles could also occur.

According to OECD 2004, the default amount of polypropylene processed at a local site is 8,880 tonnes/year. Assuming processing occurs on 300 days/year, this equates to around 30 tonnes of polypropylene processed per day. Assuming the UV-stabiliser content is 0.5 per cent, the amount of UV-stabiliser used at the default local site each day is 0.15 tonnes/day. This amount is used as the basis for the emission estimate for all UV-stabilisers.

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[11] Available from http://ecb.jrc.it/tgd/

Based on OECD 2004, the following emissions can be expected during manufacture of plastic products containing UV-stabilisers.

Raw materials' handling:	0.21 per cent to solid waste/water.
Compounding:	0.035 per cent to water
(assuming high volatility group)	0.025 per cent to air.
Conversion:	0.075 per cent to water
(assuming partially open process and high volatility group)	0.075 per cent to air.

Adding these together for the simplistic approach used here, the resulting local emission of each UV-stabiliser from a plastic processing (compounding and conversion) site is taken to be 0.47 kg/day to waste water and 0.15 kg/day to air.

For use in paints and coatings, a similar default calculation for a site employing an industrial paint was made using the default methods in the TGD.

2.3.4 Predicted environmental concentration calculations

Predicted environmental concentrations (PECs) were calculated in all cases using the EUSES 2.0.3 program.[12] The property data used for each chemical are summarised in Chapter 3. To simplify the calculations, regional emissions were estimated from the releases during production and during the formulation and use of sunscreens. Emissions resulting from use as a UV-stabiliser in plastics or other products were only considered at the local scale.

2.3.5 Risk characterisation ratios

An estimate of potential risk can be made by comparing the PEC with the predicted no effect concentration (PNEC), which is derived by applying an assessment factor to the lowest (most sensitive) result from the available ecotoxicity data set (further details are provided in the TGD). In general, the PNECs for this report have been derived by applying an assessment factor of 10 to the lowest of three chronic no-observed effect concentrations (NOECs), whether measured or calculated. This means that the PNECs have some level of comparability between substances, although the use of predicted data adds considerable uncertainty. In addition, it is likely that some effects (such as those associated with endocrine systems) are not addressed by conventional predictive methods. This is considered further in Chapter 4.

The PEC/PNEC ratio is also known as the risk characterisation ratio (RCR), and the worst case RCR for each substance has been used to allocate its priority for further work. Substances with potential risks (RCR > 1) derived from their use in sunscreens

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[12] Available from http://ecb.jrc.it/euses/

have been given a high priority (these substances will also have risks for production and formulation). Those with risks from production and formulation only have been assigned a medium priority (as this implies that wider pollution is not a serious problem). Substances showing a risk for production only or no risk have been given a low priority (production sites tend to be well controlled under European legislation).

For some types of chemical, it might be inappropriate to assess risks based on a threshold approach. For example, substances that are considered to be persistent, bioaccumulative and toxic (PBT) or very persistent and very bioaccumulative (vPvB) have the potential to cause effects in remote areas that may be difficult to reverse. The policy goal for such substances is to stop emissions. The substances were therefore also screened for their PBT/vPvB profile, using the criteria in the TGD.

Note: Due to the number of assumptions that have been made, the RCRs should not be interpreted as meaning that a substance truly presents a risk to the environment – RCRs simply comprise a screening approach.

3 Results

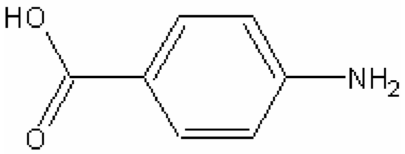
3.1 UV-filters permitted in cosmetic products in the EU

The substances considered in this section are listed in Annex VII of Directive 76/768/EEC as being permitted for use in sunscreens in the EU up to a specified maximum concentration.

It should be noted that the use of UV-filters is no longer restricted to sunscreens; they are now also being used in products for daily facial and body care. The names used in this report are generally those used by the INCI, but the Annex VII name is also included where different (in some cases it is not clear which chemical structure is being described).

3.1.1 PABA (CAS No 150-13-0)

The Annex VII name for this substance is 4-aminobenzoic acid. The structure of the substance is shown below.



Production and use

PABA is an LPV chemical in the ESIS database and there are two listed producers or importers in the EU (Bayer AG, Germany, and Nordic Synthesis AB, Sweden).

PABA is produced from *p*-nitrobenzoic acid by nitro reduction, and its main use is as a UV-absorber (Ashford 1994). The presence of this substance in commercial sunscreens has been confirmed by reverse-phase liquid chromatography (RP-LC) with UV detection (Schakel *et al.* 2004). A search of the Merck website[13] indicates that PABA is also used as an analytical reagent and a laboratory chemical, as well as in the pharmaceutical industry.

Directive 76/768/EEC indicates that the maximum authorised concentration of this substance in cosmetic products is 5 per cent.

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[13] www.merck.de

Property data

The available properties of PABA are summarised in Table 1.

Table 1 Properties of PABA

Property	**Value**		**Source**	**meas/calc**
Physico-chemical				
Molecular weight	137 g/mole		-	-
Melting point	188.5°C		EPIWIN v3.12 database	measured
Boiling point	307.7°C		EPIWIN v3.12	calculated
Vapour pressure	2.78×10^{-4} mmHg at 25°C		SRC Physico-chemical property Database	unclear
Water solubility	6,110 mg/l at 30°C		EPIWIN v3.12 database	measured
Partition coefficient (log K_{ow})	0.83 0.96		EPIWIN v3.12 database EPIWIN v3.12	measured calculated
Environmental fate and behaviour				
Photodegradation	Atmospheric OH rate constant 4.0×10^{-11} cm^3/molecule-sec at 25°C (half-life = 0.265 days; 12 hour day, 1.5×10^6 OH/cm^3)		EPIWIN v3.12	calculated
Biodegradation	Readily biodegradable 98 per cent dissolved organic carbon (DOC) removal (OECD coupled units) 96 per cent DOC removal after 3 days (Zahn-Wellens)		EPIWIN v3.12 Gerike and Fischer (1979) Gerike and Fischer (1979)	predicted measured measured
Bioaccumulation	3.2 (log BCF 0.5)		EPIWIN v3.12	calculated
Ecotoxicity				
Organism	Endpoint	Predicted value		
Neutral Organic Structure Activity Relationship (SAR) – Fish (Baseline toxicity)	14-d LC_{50} (mg/l)	1,483	EPIWIN v3.12	calculated
Fish toxicity	96-h LC_{50} (mg/l) 14-d LC_{50} (mg/l) Chv (mg/l)	2,419 1617 10.5	EPIWIN v3.12	calculated
Invertebrate toxicity	48-h LC_{50} (mg/l) Chv (mg/l)	17.5 0.47	EPIWIN v3.12	calculated
Algal toxicity	Chv (mg/l)	145	EPIWIN v3.12	calculated

Assessment of priority

The worst case RCRs obtained using EUSES are summarised in Table 2.

Table 2 Worst case RCRs for PABA

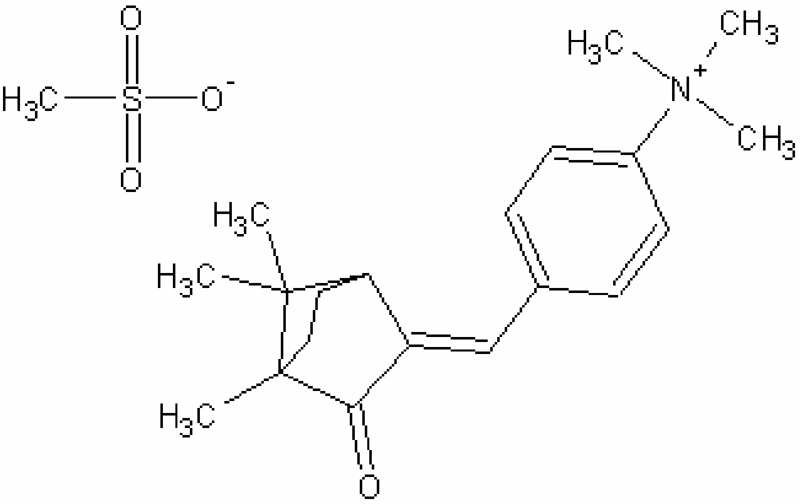
Life-cycle stage	**Predicted concentrations**			**RCRs**		
	Surface water (mg/l)	**Sediment (mg/kg wet wt.)**	**Soil (mg/kg wet wt.)**	**Surface water**	**Sediment**	**Soil**
Production	0.32	0.44	0.17	**6.7**	**6.7**	**6.0**
Formulation of sunscreens	5.5×10^{-4}	7.7×10^{-4}	2.1×10^{-4}	0.01	0.01	7×10^{-3}
Use of sunscreens	1.5×10^{-3}	2.2×10^{-3}	7.5×10^{-4}	0.03	0.03	0.03
Regional sources	1.7×10^{-4}	2.1×10^{-4}	1.4×10^{-6}	4×10^{-3}	3×10^{-3}	5×10^{-5}

The worst case calculations indicate a low risk from the formulation and use of this substance in sunscreens, although there may be a possible risk from production. PABA does not meet the EU PBT or vPvB criteria on the basis of the available data – it has a low log K_{ow} value, appears to be readily biodegradable and has a long-term NOEC for aquatic species well above 0.01 mg/l.

Based on this analysis, PABA is a low priority for further work.

3.1.2 Camphor benzalkonium methosulfate (CAS No 52793-97-2)

The Annex VII name for this substance is *N,N,N*-trimethyl-4-(2-oxoborn-3-ylidene-methyl) anilinium methyl sulphate. The substance is also known as 4-((2-oxo-3-bornylidene)methyl)phenyltrimethylammonium methylsulfate and its structure is outlined below.



Production and use

This is an LPV chemical on ESIS, with one listed producer or importer (Chimex, France).

No information is available on production methods. It is used as a UV-filter, with Directive 76/768/EEC indicating that the maximum authorised concentration in cosmetic products is 6 per cent.

Property data

The predicted properties of the substance are summarised in

Table 3.

Table 3 Properties of Camphor benzalkonium methosulfate

Property	Value		Source	meas/calc
Physico-chemical				
Molecular weight	393.55 g/mole		-	-
Melting point	277°C		EPIWIN v3.12	calculated
Boiling point	638°C		EPIWIN v3.12	calculated
Vapour pressure	1.21×10^{-14} mmHg at 25°C		EPIWIN v3.12	calculated
Water solubility	7.4 mg/l at 25°C		EPIWIN v3.12	calculated
Partition coefficient (log K_{ow})	3.11		EPIWIN v3.12	calculated
Environmental fate and behaviour				
Photodegradation	Atmospheric OH rate constant 88.4×10^{-12} cm^3/molecule-sec at 25°C (half-life = 0.121 days; 12 hour day, 1.5×10^6 OH/cm^3)		EPIWIN v3.12	calculated
Biodegradation	Not readily biodegradable		EPIWIN v3.12	predicted
Bioaccumulation	BCF 3.2 (log BCF 0.5)		EPIWIN v3.12	calculated
Ecotoxicity				
	Endpoint	Predicted value		
Neutral Organic SAR (Baseline toxicity)	14-d LC_{50} (mg/l)	57[a]	EPIWIN v3.12	calculated
Fish toxicity	96-h LC_{50} (mg/l) Chv (mg/l)	50[a] 2.7	EPIWIN v3.12	calculated
Invertebrate toxicity	48-h LC_{50} (mg/l) Chv (mg/l)	23[a] 3.1	EPIWIN v3.12	calculated
Algal toxicity	96-h EC_{50} (mg/l) Chv (mg/l)	11[a] 5.0	EPIWIN v3.12	calculated

Note: a) Above the expected water solubility of the substance.

Assessment of priority

The worst case RCRs obtained using EUSES are summarised in

Table 4.

Table 4 Worst case RCRs for camphor benzalkonium methosulfate

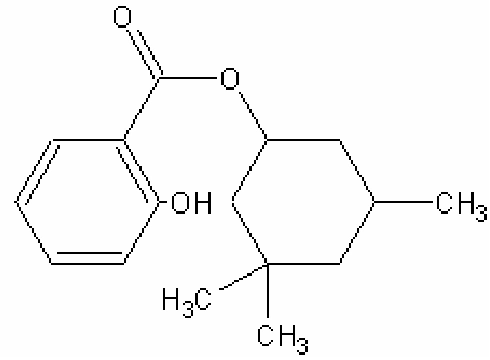
Life-cycle stage	Predicted concentrations			RCRs		
	Surface water (mg/l)	Sediment (mg/kg wet wt.)	Soil (mg/kg wet wt.)	Surface water	Sediment	Soil
Production	2.4	24	36	**8.8**	**8.8**	**17**
Formulation of sunscreens	7.1×10^{-3}	0.073	0.079	0.03	0.03	0.04
Use of sunscreens	0.012	0.13	0.16	0.05	0.05	0.07
Regional sources	2.0×10^{-3}	0.025	1.9×10^{-3}	7×10^{-3}	9×10^{-3}	9×10^{-4}

The worst case calculations indicate a low risk from the formulation and use of this substance in sunscreens. A possible risk from production is indicated. Camphor benzalkonium methosulfate does not meet the EU PBT or vPvB criteria based on the available data. Although predicted not to be readily biodegradable (and so potentially meeting the screening criteria for a persistent or very persistent substance), it does not appear to meet the screening criteria for a bioaccumulative or very bioaccumulative substance (log K_{ow} of 3.11) or a toxic substance (long-term NOEC for aquatic species >>0.01 mg/l).

Based on this analysis, camphor benzalkonium methosulfate is a low priority for further work.

3.1.3 Homosalate (HS) (CAS No 118-56-9)

The Annex VII name for this substance is also homosalate. Alternate names include benzoic acid, 2-hydroxy-, 3,3,5-trimethylcyclohexyl ester and 3,3,5-trimethylcyclohexyl salicylate. The structure of homosalate is shown below.



Production and use

Homosalate is an LPV chemical according to ESIS and the database lists one producer or importer in the EU (Merck KGAA, Germany).

It is produced by the esterification of trimethylcyclohexanol and salicyclic acid (Ashford 1994). This substance is widely used as a UV-filter in cosmetics. The presence of homosalate in various kinds of commercial suncare products has been confirmed by RP-LC with UV detection (Schakel *et al.* 2004).

A search of the Merck website revealed that homosalate is part of the Eusolex® product range of organic filters. Homosalate (Eusolex® HMS) is an oil-soluble liquid UVB filter with ‘excellent dissolving properties for solid organic UV-filters’.

Directive 76/768/EEC indicates that the maximum authorised concentration of this substance in cosmetic products is 10 per cent.

Property data

The available properties of homosalate are summarised in

Table 5.

Table 5 Properties of homosalate

Property	Value			Source	meas/calc
Physico-chemical					
Molecular weight	262.36 g/mole			-	-
Melting point	121°C			EPIWIN v3.12	calculated
Boiling point	163°C at 4 mmHg 356°C			EPIWIN v3.12 database EPIWIN v3.12	measured calculated
Vapour pressure	2.79×10^{-6} mmHg at 25°C			EPIWIN v3.12	calculated
Water solubility	Insoluble 0.42 mg/l at 25°C			Ashford (1994) EPIWIN v3.12	 calculated
Partition coefficient (log K_{ow})	6.16			EPIWIN v3.12	calculated
Environmental fate and behaviour					
Photodegradation	Atmospheric OH rate constant 4.3×10^{-11} cm^3/molecule-sec at 25°C (half-life = 0.25 days; 12 hour day, 1.5×10^6 OH/cm^3)			EPIWIN v3.12	calculated
Biodegradation	Not readily biodegradable			EPIWIN v3.12	predicted
Bioaccumulation	11,080 (log BCF 4.045)			EPIWIN v3.12	calculated
Ecotoxicity					
Organism	Endpoint	Esters[a]	Phenols[b]		
Neutral Organic SAR (Baseline toxicity)	14-d LC_{50} (mg/l)	0.084		EPIWIN v3.12	calculated
Fish toxicity	96-h LC_{50} (mg/l) Chv (mg/l)	0.24 0.005	0.11 0.015	EPIWIN v3.12	calculated
Invertebrate toxicity	48-h LC_{50} (mg/l) 21d-Chv (mg/l)	0.034 -	0.28 0.012	EPIWIN v3.12	calculated
Algal toxicity	96-h EC_{50} (mg/l) Chv (mg/l)	0.022 0.019	0.027 0.030	EPIWIN v3.12	calculated

Note: a) Estimates obtained using a method appropriate for esters.
b) Estimates obtained using a method appropriate for phenols.

Assessment of priority

The worst case RCRs obtained using EUSES are summarised in Table 6.

Table 6 Worst case RCRs for homosalate

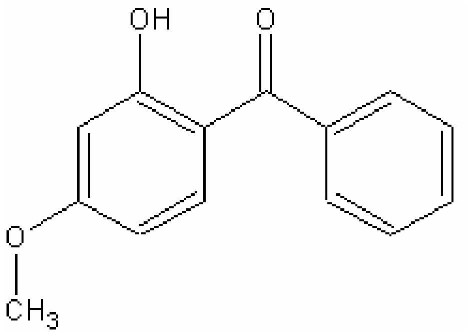
Life-cycle stage	**Predicted concentrations**			**RCRs**		
	Surface water (mg/l)	**Sediment (mg/kg wet wt.)**	**Soil (mg/kg wet wt.)**	**Surface water**	**Sediment**	**Soil**
Production	0.88	319	589	**1.8×10^3**	**1.8×10^4**	**4.0×10^4**
Formulation of sunscreens	4.0×10^{-3}	1.5	2.1	**8.0**	**80**	**144**
Use of sunscreens	4.7×10^{-3}	1.7	2.6	**9.3**	**93**	**174**
Regional sources	8.5×10^{-4}	0.59	0.45	**1.7**	**33**	**30**

The worst case calculations indicate a possible risk from production sites and from the formulation and use of sunscreens. Homosalate meets the screening criteria for a PBT/vPvB substance on the basis of the available data: it is predicted not to be readily biodegradable, with a high log K_{ow} (predicted to be 6.16) and a predicted NOEC for long-term toxicity of around 0.005 mg/l.

Based on this analysis, homosalate is a high priority for further work.

3.1.4 Benzophenone-3 (CAS No 131-57-7)

The Annex VII name for this substance is oxybenzone; other names include 2-hydroxy-4-methoxybenzophenone. The structure of the substance is shown below.



Production and use

Benzophenone-3 is an LPV chemical, and the ESIS database lists two producers or importers in the EU (Ciba Specialty Chemicals SPA, Italy, and Great Lakes Chemical, France).

It is produced by reaction of 2,4-dihydroxybenzophenone and dimethyl sulphate (ether formation), and a derivative of this substance is 2-hydroxy-4-methoxybenzophenone-5-sulphonic acid (Ashford 1994).

A search of the Ciba Speciality Chemicals website revealed that benzophenone-3 is used as a UV-filter in personal care products; it is also used as a light stabiliser in plastics (Ashford 1994). According to the Merck ChemDat[14] website, benzophenone-3 is part of the Eusolex® product range of organic UV-filters and is described as: ‘the UV-filter of choice for cosmetic product protection. Benzophenone-3 (Eusolex® 4360) is an oil soluble powder, which is suitable for broad-spectrum protection in a wide range of products.’

Directive 76/768/EEC indicates that the maximum authorised concentration of benzophenone-3 in cosmetic products is 10 per cent. This substance is also used as a UV-stabiliser in polymer applications (further details are provided in the Confidential Appendix).

Property data

The properties of benzophenone-3 are summarised in

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[14] www.chemdat.de

Table 7.

Table 7 Properties of benzophenone-3

Property	**Value**		**Source**	**meas/calc**
Physico-chemical				
Molecular weight	228.25 g/mole		-	-
Melting point	65.5°C 130°C		EPIWIN v3.12 database EPIWIN v3.12	measured calculated
Boiling point	155°C at 5 mmHg 363°C		EPIWIN v3.12 database EPIWIN v3.12	measured calculated
Vapour pressure	1.42×10^{-6} mmHg at 25°C		EPIWIN v3.12	calculated
Water solubility	68.6 mg/l at 25°C		EPIWIN v3.12	calculated
Partition coefficient (log K_{ow})	3.79 3.52		EPIWIN v3.12 database EPIWIN v3.12	measured calculated
Environmental fate and behaviour				
Photodegradation	Atmospheric OH rate constant 2.0×10^{-10} cm^3/molecule-sec at 25°C (half-life = 0.053 days; 12 hour day, 1.5×10^6 OH/cm^3)		EPIWIN v3.12	calculated
Biodegradation	>60 per cent MITI test (readily biodegradable)		Merck SDS (2006)	measured
Bioaccumulation	24 (log BCF 1.378)		EPIWIN v3.12	calculated
Ecotoxicity				
Organism	Endpoint	Value		
Neutral Organic SAR – Fish (Baseline toxicity)	14-d LC_{50} (mg/l)	14.538	EPIWIN v3.12	calculated
Fish toxicity	96-h LC_{50} (mg/l) *L. idus* 96-h LC_{50} (mg/l) 30d-Chv (mg/l)	100–220[a] 3.8 0.57	Merck SDS (2006) EPIWIN v3.12 EPIWIN v3.12	measured calculated calculated
Invertebrate toxicity	48-h LC_{50} (mg/l) 21d-Chv (mg/l)	2.9 0.42	EPIWIN v3.12	calculated
Algal toxicity	96-h EC_{50} (mg/l) 96-h Chv (mg/l)	5.1 1.2	EPIWIN v3.12	calculated

Note: a) Above the expected water solubility of the substance.

Assessment of priority

The worst case RCRs obtained using EUSES are summarised in Table 8.

Table 8 Worst case RCRs for benzophenone-3

Life-cycle stage	**Predicted concentrations**			**RCRs**		
	Surface water (mg/l)	**Sediment (mg/kg wet wt.)**	**Soil (mg/kg wet wt.)**	**Surface water**	**Sediment**	**Soil**
Production	0.29	6.5	5.5	**7.0**	**7.0**	**7.5**
Formulation of sunscreens	1.2×10^{-3}	0.027	0.020	0.03	0.03	0.03
Use of sunscreens	1.4×10^{-3}	0.032	0.024	0.03	0.03	0.03
Polymer processing	2.9×10^{-3}	0.064	0.052	0.07	0.07	0.07
Regional sources	1.6×10^{-4}	3.6×10^{-3}	4.7×10^{-5}	4×10^{-3}	4×10^{-3}	6×10^{-5}

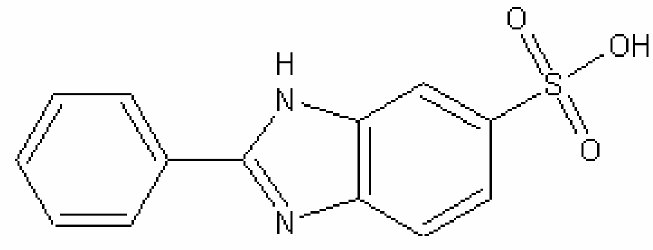
The worst case calculations indicate a low risk from the formulation and use of this substance in sunscreens, and also from its use in polymers. A possible risk from production sites is indicated. It would not be expected for this substance to meet the

EU PBT or vPvB criteria based on the available information (it appears to be readily biodegradable, has a log K_{ow} value of 3.79 and has a long-term NOEC for aquatic species far in excess of 0.01 mg/l).

Based on this analysis, benzophenone-3 is a low priority for further work.

3.1.5 Phenylbenzimidazole sulfonic acid (CAS No 27503-81-7) and its potassium (CAS No unknown), sodium (CAS No 5997-53-5) and triethanolamine salts (CAS No 73705-00-7)

The Annex VII name for the acid is 2-phenylbenzimidazole-5-sulphonic acid. Other names include 2-phenyl-1H-benzimidazole-5-sulphonic acid or PBSA and ensulizole. The triethanolamine salt is also known as 1H-benzimidazolesulfonic acid, 2-phenyl-, sodium salt, compd. with 2,2',2''-nitrilotris(ethanol). The structure of the acid is shown below.



Production and use

PBSA is listed as an LPV chemical in the ESIS database, with two producers or importers in the EU (Bayer AG and Merck KGAA, both in Germany). ESIS was also checked for CAS No 5997-53-5 (sodium salt) and 73705-00-7 (triethanolamine salts). Neither is listed as an existing substance[15] and so they are either new substances or are not supplied to the EU market in significant amounts.

PBSA is a common sunscreen constituent. A search of the Merck website revealed that it is used as a cosmetic raw material in sunscreens. It is 'a UVB filter for the water phase and has excellent protection properties after neutralisation with triethanolamine or sodium hydroxide'. It is part of the Eusolex® product range of organic UV-filters supplied by Merck (Eusolex® 232).

Directive 76/768/EEC indicates that the maximum authorised concentration of this substance in cosmetic products is 8 per cent (expressed as the acid).

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[15] On the European INventory of Existing Commercial chemical Substances (EINECS).

Property data

The available properties of PBSA are summarised in Table 9.

Table 9 Properties of PBSA

Property	**Value**		**Source**	**meas/calc**
Physico-chemical				
Molecular weight	274.3 g/mole		-	-
Melting point	243°C		EPIWIN v3.12	calculated
Boiling point	566°C		EPIWIN v3.12	calculated
Vapour pressure	7.32x10^{-15} mmHg at 25°C		EPIWIN v3.12	calculated
Water solubility	12 mg/l at 25°C[a] 24 g/l at 25°C[a]		Merck SDS (2006) EPIWIN v3.12	measured calculated
Partition coefficient (log K_{ow})	-1.0 -0.16 (used to estimated water sol.)		Merck SDS (2006) EPIWIN v3.12	measured calculated
Environmental fate and behaviour				
Photodegradation	Atmospheric OH rate constant 12x10^{-12} cm^3/molecule-sec at 25°C (half-life = 0.884 days; 12 hour day, 1.5x10^6 OH/cm^3)		EPIWIN v3.12	calculated
Biodegradation	Not readily biodegradable Biological oxygen demand (BOD) 4 per cent over 5 days (closed bottle) Biodegradation 36 per cent in 28 days (closed bottle test)		EPIWIN v3.12 Merck SDS (2006) Merck SDS (2006)	predicted measured measured
Bioaccumulation	3.2 (log BCF 0.5)		EPIWIN v3.12	calculated
Ecotoxicity				
Organism	Endpoint	Value		
Neutral Organic SAR (Baseline toxicity)	14-d LC$_{50}$ (mg/l)	28,027[b]	EPIWIN v3.12	calculated
Fish toxicity	48-h LC$_{50}$ (mg/l) *L.idus* 96-h LC$_{50}$ (mg/l)	4,250[b] 18,223[b]	Merck SDS (2006) EPIWIN v3.12	measured calculated
Invertebrate toxicity	EC$_{50}$ (mg/l) *D. magna* 48-h LC$_{50}$ (mg/l)	>10,000[b] 1,018[b]	Merck SDS (2006) EPIWIN v3.12	measured calculated
Algal toxicity	96-h EC$_{50}$ (mg/l) 96-h Chv (mg/l)	911[b] 124[b]	EPIWIN v3.12	calculated

Note: a) There appears to be some discrepancy over the water solubility for this substance. If the 12 mg/l value is correct, then the predicted and experimental toxicity data are all well above the water solubility. However, the very low log K_{ow} value is suggestive of a high water solubility.

b) Potentially above the expected water solubility of the substances.

Note that these properties have been estimated for the neutral form of the molecule. The sulphonic acid group will be ionised under environmental conditions, which would lead to a lower predicted log K_{ow} value of -1.95. This is reflected in the measured value of -1.0.

Assessment of priority

The worst case RCRs obtained using EUSES are summarised in

Table 10.

Table 10 Worst case RCRs for PBSA

Life-cycle stage	Predicted concentrations			RCRs		
	Surface water (mg/l)	Sediment (mg/kg wet wt.)	Soil (mg/kg wet wt.)	Surface water	Sediment	Soil
Production	2.5	2.1	0.035	**2.8**	**2.8**	0.22
Formulation of sunscreens	9.2×10^{-3}	7.9×10^{-3}	1.6×10^{-4}	0.01	0.01	1×10^{-3}
Use of sunscreens	0.013	0.011	1.5×10^{-4}	0.01	0.01	1×10^{-3}
Regional sources	2.0×10^{-3}	1.5×10^{-3}	5.1×10^{-7}	2×10^{-3}	2×10^{-3}	3×10^{-6}

The worst case calculations indicate a low risk from the formulation and use of this substance in sunscreens. A possible risk from production sites is suggested. PBSA and its salts would not be expected to meet the EU PBT or vPvB criteria. Although predicted not to be readily biodegradable (and so potentially meeting the screening criteria for a persistent or very persistent substance), it does not meet the screening criteria for a bioaccumulative or very bioaccumulative substance (log K_{ow} of -1.0) or a toxic substance (long-term NOEC for aquatic species much higher than 0.01 mg/l).

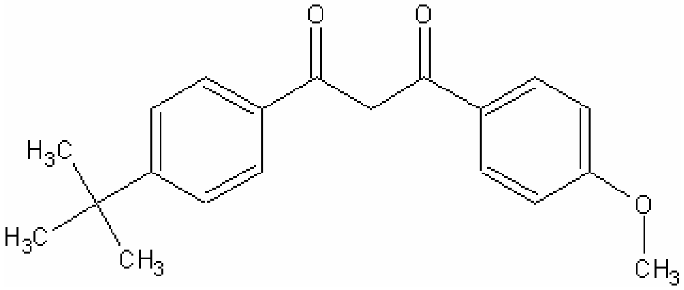
Based on this analysis, PBSA and its salts are a low priority for further work.

3.1.6 Terephthalylidene dicamphor sulphonic acid (CAS No 90457-82-2 or 92761-26-7) and its salts

The Annex VII name for this substance is 3,3'-(1,4-phenylenedimethylene) bis (7,7-dimethyl-2-oxobicyclo-[2.2.1]hept-1-yl-methanesulfonic acid). The acid is also known as ecamsule in North America. This is a new substance, and has already been assessed under the relevant procedures. It is therefore not considered further in this part of the report, although data relating to this substance are included in the Confidential Annex.

3.1.7 Butylmethoxydibenzoylmethane (BMDBM) (CAS No 70356-09-1)

The Annex VII name for this substance is 1-(4-*tert*-butylphenyl)-3-(4-methoxyphenyl) propane-1,3-dione. The substance is more commonly known as avobenzone and its structure is shown below.



Production and use

BMDBM is an LPV chemical in the ESIS database and there are three listed producers or importers in the EU (Givaudan Roure in the UK, Italy and Spain).

A search of the internet revealed that this substance is used as a UV-filter in a range of cosmetic products (topical lotions and creams) and is part of the Eusolex® product range supplied by Merck (Eusolex® 9020). BMDBM is a: 'UVA filter with high efficacy even at low concentrations. Moreover, BMDBM is the only UVA filter with worldwide approval and is therefore the most prevalent filter for UVA protection in cosmetics.' However, it is known to undergo serious photo-fragmentation and requires the addition of photo-stabilizers to help retain its UVA protection potential. This substance may therefore be used in conjunction with other UV-filters.

Directive 76/768/EEC indicates that the maximum authorised concentration of this substance in cosmetic products is 5 per cent.

Property data

The available properties of BMDBM are summarised in Table 11.

Table 11 Properties of BMDBM

Property	**Value**		**Source**	**meas/calc**
Physico-chemical				
Molecular weight	310.40 g/mole		-	-
Melting point	83.5°C 155°C		EPIWIN v3.12 database EPIWIN v3.12	measured calculated
Boiling point	409°C		EPIWIN v3.12	calculated
Vapour pressure	1.36×10^{-6} mmHg at 25°C		EPIWIN v3.12	calculated
Water solubility	1.5 mg/l at 25°C		EPIWIN v3.12	calculated
Partition coefficient (log K_{ow})	4.51		EPIWIN v3.12	calculated
Environmental fate and behaviour				
Photodegradation[16]	Atmospheric OH rate constant 2.5×10^{-11} cm^3/molecule-sec at 25°C (half-life = 0.422 days; 12 hour day, 1.5×10^6 OH/cm^3)		EPIWIN v3.12	calculated
Biodegradation	6 per cent after 20 days (test type unknown) Not readily biodegradable		Merck SDS (2006) EPIWIN v3.12	measured predicted
Bioaccumulation	85 (log BCF 1.929)		EPIWIN v3.12	calculated
Ecotoxicity				
Organism	Endpoint	Predicted value		
Neutral Organic SAR (Baseline toxicity)	14-d LC_{50} (mg/l)	2.7[a]	EPIWIN v3.12	calculated
Fish toxicity	96-h LC_{50} (mg/l)	2.4[a]	EPIWIN v3.12	calculated
Invertebrate toxicity	48-h LC_{50} (mg/l) Chv (mg/l)	0.83 0.030	EPIWIN v3.12	calculated
Algal toxicity	Chv (mg/l)	0.067	EPIWIN v3.12	calculated

Note: a) Above the expected water solubility of the substance.

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[16] The photostability and photoreactivity of BMDBM has been investigated by Schwack & Rudolph 1996. This paper has not been reviewed for this assessment.

Assessment of priority

The worst case RCRs obtained using EUSES are summarised in Table 12.

Table 12 Worst case RCRs for BMDBM

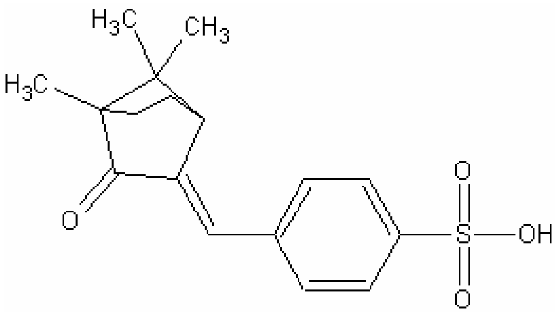
Life-cycle stage	**Predicted concentrations**			**RCRs**		
	Surface water (mg/l)	**Sediment (mg/kg wet wt.)**	**Soil (mg/kg wet wt.)**	**Surface water**	**Sediment**	**Soil**
Production	1.9	99	193	**3.2×10^3**	**3.2×10^3**	**7.8×10^3**
Formulation of sunscreens	4.1×10^{-3}	0.21	0.23	**6.8**	**6.8**	**9.5**
Use of sunscreens	0.010	0.52	0.84	**17**	**17**	**34**
Regional sources	1.7×10^{-3}	0.14	0.035	**2.9**	**4.7**	**1.4**

The worst case calculations indicate a possible risk from production sites and from the formulation and use of sunscreens. Based on the available data, the substance would not be expected to meet the EU PBT or vPvB criteria. Although predicted not to be readily biodegradable (and so potentially meeting the persistent or very persistent screening criteria), the estimated log K_{ow} of 4.51 is borderline for the bioaccumulative screening criterion and the substance does not appear to meet the toxic criterion based on the long-term aquatic toxicity (NOEC is >0.01 mg/l). There is no harmonised classification for human health effects according to ESIS, so there is no suggestion of chronic mammalian toxicity.

Based on this assessment BMDBM is a high priority for further work.

3.1.8 Benzylidene camphor sulfonic acid (CAS No 56039-58-8) and its salts

The Annex VII name for the acid is alpha-(2-oxoborn-3-ylidene)-toluene-4-sulphonic acid. An alternative name is 4-[(4,7,7-trimethyl-3-oxo-norbornan-2-ylidene)methyl] benzenesulfonic acid. The structure of the substance is given below.



Production and use

This substance is not listed in ESIS or the European Inventory of Existing Commercial Chemical Substances (EINECS), and does not appear to have been notified as a new chemical. Therefore, it appears not to be supplied in significant amounts in the EU. The substance is, however, listed in Directive 76/768/EEC and this indicates that the maximum authorised concentration of this substance in cosmetic products is 6 per cent (as the acid).

Property data

The properties of benzylidene camphor sulfonic acid are summarised in Table 13.

Table 13 Properties of benzylidene camphor sulfonic acid

Property	**Value**		**Source**	**meas/calc**
Physico-chemical				
Molecular weight	320 g/mole		-	-
Melting point	200°C		EPIWIN v3.12	calculated
Boiling point	472°C		EPIWIN v3.12	calculated
Vapour pressure	1.9×10^{-11} mmHg at 25°C		EPIWIN v3.12	calculated
Water solubility	120 mg/l at 25°C		EPIWIN v3.12	calculated
Partition coefficient (log K_{ow})	2.22		EPIWIN v3.12	calculated
Environmental fate and behaviour				
Photodegradation	Atmospheric OH rate constant 84×10^{-12} cm^3/molecule-sec at 25°C (half-life = 0.13 days; 12 hour day, 1.5×10^6 OH/cm^3)		EPIWIN v3.12	calculated
Biodegradation	Not readily biodegradable		EPIWIN v3.12	predicted
Bioaccumulation	BCF 3.2 (log BCF 0.5)		EPIWIN v3.12	calculated
Ecotoxicity				
Organism	Endpoint	Predicted value		
Neutral Organic SAR (Baseline toxicity)	14-d LC_{50} (mg/l)	277[a]	EPIWIN v3.12	calculated
Fish toxicity	96-h LC_{50} (mg/l) Chv (mg/l)	1,516[a] 117	EPIWIN v3.12 EPIWIN v3.12	calculated calculated
Invertebrate toxicity	48-h LC_{50} (mg/l) Chv (mg/l)	903[a] 112	EPIWIN v3.12 EPIWIN v3.12	calculated calculated
Algal toxicity	96-h LC_{50} (mg/l) Chv (mg/l)	446 157	EPIWIN v3.12 EPIWIN v3.12	calculated calculated

Note: a) Above the expected water solubility of the substance.

Note that these properties have been estimated for the neutral form of the molecule. The sulphonic acid group will be ionised under environmental conditions, leading to a lower log K_{ow} value (the predicted log K_{ow} value for the sodium salt is 0.43). The predicted toxicity values would also be higher (in other words the substance would be less toxic).

Assessment of priority

The worst case RCRs obtained using EUSES are summarised in Table 14.

Table 14 Worst case RCRs for benzylidene camphor sulfonic acid

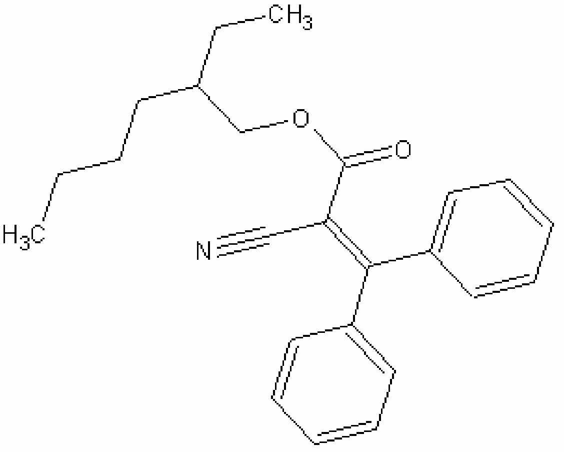
Life-cycle stage	Predicted concentrations			RCRs		
	Surface water (mg/l)	Sediment (mg/kg wet wt.)	Soil (mg/kg wet wt.)	Surface water	Sediment	Soil
Production	2.5	9.9	8.4	0.2	0.2	0.3
Formulation of sunscreens	7.3×10^{-3}	0.030	0.019	7×10^{-4}	7×10^{-4}	6×10^{-4}
Use of sunscreens	0.013	0.051	0.036	1×10^{-3}	1×10^{-3}	1×10^{-4}
Regional sources	2.0×10^{-3}	8.6×10^{-3}	2.4×10^{-4}	2×10^{-4}	2×10^{-4}	8×10^{-6}

The worst case calculations indicate a low risk from the production, formulation and use of this substance. Based on the available data, it does not meet the EU PBT or vPvB criteria. Although the substance is predicted not to be readily biodegradable (and so potentially meets the screening criteria for a persistent or very persistent substance), it does not meet the screening criteria for a bioaccumulative or very bioaccumulative substance (log K_{ow} of 2.22) or for a toxic substance (NOEC far in excess of 0.01mg/l).

Hence, benzylidene camphor sulfonic acid and its salts are a low priority for further work.

3.1.9 Octocrylene (CAS No 6197-30-4)

The Annex VII name for this substance is 2-cyano-3,3-diphenyl acrylic acid, 2-ethylhexyl ester. Alternative names include octocriliene and 2-propenoic acid, 2-cyano-3,3-diphenyl-, 2-ethylhexyl ester. The chemical structure is shown below.



Production and use

Octocrylene is listed as an LPV chemical in the ESIS database and there appears to be just one producer or importer in the EU (Haarmann & Reimer GmbH, Germany).

A search of the internet revealed that octocrylene is used as a UV-filter in a range of cosmetic products. Merck supply this product as part of the Eusolex® product range.

According to the Merck website, octocrylene is: ‘an oil soluble liquid UVB filter with very good protection potential. It has excellent dissolving properties for solid sunscreens and is also a photo-stabiliser.’

Directive 76/768/EEC indicates that the maximum authorised concentration of this substance in cosmetic products is 10 per cent.

Property data

The available properties of octocrylene are summarised in Table 15.

Table 15 Properties of octocrylene

Property	**Value**		**Source**	**meas/calc**
Physico-chemical				
Molecular weight	361.50 g/mole		-	-
Melting point	181°C		EPIWIN v3.12	calculated
Boiling point	473°C		EPIWIN v3.12	calculated
Vapour pressure	3.2×10^{-9} mmHg at 25°C		EPIWIN v3.12	calculated
Water solubility[a]	1.3 mg/l at 20°C		Merck SDS (2006)	measured
	0.0038 mg/l at 25°C		EPIWIN v3.12	calculated
Partition coefficient (log K$_{ow}$)	6.88		EPIWIN v3.12	calculated
Environmental fate and behaviour				
Photodegradation	Atmospheric OH rate constant 21×10^{-12} cm^3/molecule-sec at 25°C (half-life = 0.516 days; 12 hour day, 1.5×10^6 OH/cm^3)		EPIWIN v3.12	calculated
Biodegradation	Not readily biodegradable		EPIWIN v3.12	predicted
	<20 per cent biodegradation in a MITI test		Merck SDS (2006)	measured
Bioaccumulation	39,700 (log BCF 4.599)		EPIWIN v3.12	calculated
Ecotoxicity				
Organism	Endpoint	Value		
Neutral Organic SAR (Baseline toxicity)	14-d LC$_{50}$ (mg/l)	0.027	EPIWIN v3.12	calculated
Fish toxicity	96-h LC$_{50}$ (mg/l) *L.idus*	>10,000[b]	Merck SDS (2006)	measured
	96-h LC$_{50}$ (mg/l) (Acrylates)	0.72[b]	EPIWIN v3.12	calculated
	32d-Chv (mg/l) (Acrylates)	0.00089	EPIWIN v3.12	
	96-h LC$_{50}$ (mg/l) (Allylic/vinyl nitrates)	0.33[b]	EPIWIN v3.12	
Invertebrate toxicity	48-h EC$_{50}$ (mg/l) *D. magna*	100[b]	Merck SDS (2006)	calculated
	48-h LC$_{50}$ (mg/l) (Acrylates)	0.11[b]	EPIWIN v3.12	
Algal toxicity	96-h EC$_{50}$ (mg/l)	0.015[b]	EPIWIN v3.12	calculated

Note: a) There appears to be some discrepancy over the water solubility for this substance.
b) Potentially above the expected water solubility of the substance.

Assessment of priority

The worst case RCRs obtained using EUSES are summarised in Table 16.

Table 16 Worst case RCRs for octocrylene

Life-cycle stage	Predicted concentrations			RCRs		
	Surface water (mg/l)	Sediment (mg/kg wet wt.)	Soil (mg/kg wet wt.)	Surface water	Sediment	Soil
Production	0.53	454	720	**5.9×10^4**	**5.9×10^5**	**1.2×10^6**
Formulation of sunscreens	2.9×10^{-3}	2.5	2.6	**320**	**3.2×10^3**	**4.2×10^3**
Use of sunscreens	3.2×10^{-3}	2.8	3.1	**364**	**3.6×10^3**	**5.0×10^3**
Regional sources	9.5×10^{-4}	1.6	2.0	**107**	**2.1×10^3**	**3.2×10^3**

The worst case calculations indicate a potential risk from the production, formulation and use of this substance. The substance appears potentially to meet the EU screening criteria for PBT and vPvB. It is predicted not to be readily biodegradable, has a predicted log K_{ow} value of 6.88 and has a predicted long-term NOEC for aquatic organisms of 8.9×10^{-4} mg/l (although there is a conflict between the measured and predicted acute toxicity data, which suggests that the prediction method could be misleading).

Based on this assessment the substance is a high priority for further work.

3.1.10 Polyacrylamidomethylbenzylidene camphor (CAS No 113783-61-2)

The Annex VII name for this substance is ‘polymer of N-{(2 and 4)-[(2-oxoborn-3-ylidene)methyl]benzyl} acrylamide’.

Production and use

The substance is listed in Directive 76/768/EEC, which indicates that the maximum authorised concentration of this substance in cosmetic products is 6 per cent. As a polymer it is not listed in EINECS or included on ESIS.

Property data

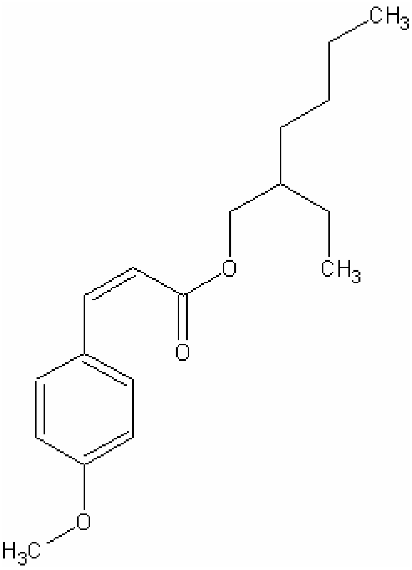
No information on the properties of this substance has been found, and it is not possible to predict reliably its properties due to its polymeric nature.

Assessment of priority

No calculations have been carried out for this substance owing to the lack of data. On this basis, it is a priority for further work. Issues for further investigation could include the breakdown potential of the polymer chain and possible impurities.

3.1.11 Ethylhexyl methoxycinnamate (CAS No 5466-77-3)

The Annex VII name for this substance is octyl methoxycinnamate; alternative names include 2-ethylhexyl 4-methoxycinnamate. The structure of the substance is:



Production and use

Ethylhexyl methoxycinnamate is listed as an HPV chemical in the ESIS database, which lists eight producers or importers in the EU:

- ISP Europe, UK
- Givaudan Roure Ltd, UK
- Givaudan Roure SpA, Italy
- Givaudan Roure SA, Spain
- Givaudan Roure SA, France
- Amway Europe, Belgium
- Haarmann & Reimer GmbH, Germany
- Mallinckrodt Chemical GmbH, Germany.

Ethylhexyl methoxycinnamate is produced by the reaction of *p*-anisaldehyde with sodium acetate and 2-ethylhexanol (Perkin condensation/ esterification; Ashford 2004).

It is used as a light stabiliser in plastics (Ashford 1994), and as a UV-filter in a wide variety of cosmetic products including sun-care, skin-care and hair-care products (Household Products Database).[17] It is one of the most tested and widely used UVB filters, and is part of the Eusolex® product range supplied by Merck (Eusolex® 2292). It is a liquid UVB filter and is oil soluble with 'very good protection potential and excellent dissolving properties for solid organic UV-filters'. Merck also supplies

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[17] http://hpd.nlm.nih.gov/

encapsulated ethylhexyl methoxycinnamate in aqueous suspension (Eusolex® UV-Pearls™ OMC) for use as a cosmetic raw material. This suspension is composed of ethylhexyl methoxycinnamate, silica, PVP (presumably polyvinyl pyrrolidone), chlorphenesin and butylated hydroxytoluene (BHT).

DSM[18] also supplies ethylhexyl methoxycinnamate (as PARSOL®MXC), formulating sun-care preparations containing 2–10 per cent of the substance and everyday cosmetics containing 2–6 per cent (in association with an effective UVA filter).

An internet search revealed that BASF produces the substance under the trade name Univul MC 80. Its plant in Ludwigshafen, Germany, has a capacity of 4,500 tonnes/year, equivalent to half a billion 300ml bottles of sun cream. BASF now supplies all the main manufacturers of sun-protection products.

Directive 76/768/EEC indicates that the maximum authorised concentration of this substance in cosmetic products is 10 per cent.

Property data

The available properties of ethylhexyl methoxycinnamate are summarised in

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[18] http://www.dsm.com/en_US/html/dnpus/pe_uv_filters.htm?source=search

Table 17.

Table 17 Properties of ethylhexyl methoxycinnamate

Property	**Value**		**Source**	**meas/calc**
Physico-chemical				
Molecular weight	290.41 g/mole			
Melting point	100°C		EPIWIN v3.12	calculated
Boiling point	160°C at 1 hPa 361°C		Merck SDS (2006) EPIWIN v3.12	measured calculated
Vapour pressure	1.38×10^{-5} mmHg at 25°C		EPIWIN v3.12	calculated
Water solubility	0.2 mg/l at 20°C 0.155 mg/l at 25°C		Merck SDS (2006) EPIWIN v3.12	measured calculated
Partition coefficient (log K_{ow})	6.1 5.8		Merck SDS (2006) EPIWIN v3.12	measured calculated
Environmental fate and behaviour				
Photodegradation	Atmospheric OH rate constant 5.2×10^{-11} cm^3/molecule-sec at 25°C (half-life = 2.5 days; 12 hour day, 1.5×10^6 OH/cm^3; cis-isomer) OH rate constant 5.4×10^{-11} cm^3/ molecule-sec at 25°C (half-life = 2.4 days; trans-isomer)		EPIWIN v3.12	calculated
Biodegradation	Readily biodegradable		EPIWIN v3.12	predicted
Bioaccumulation	5,856 (log BCF 3.768)		EPIWIN v3.12	calculated
Ecotoxicity				
Organism	Endpoint	Value		
Neutral Organic SAR (Baseline toxicity)	14-d LC_{50} (mg/l)	0.191	EPIWIN v3.12	calculated
Fish toxicity	96-h LC_{50} (mg/l) *B. rerio* 96-h LC_{50} (mg/l) 32d-Chv (mg/l)	>10,000[a] 0.91 0.003	Merck SDS (2006) EPIWIN v3.12 EPIWIN v3.12	measured calculated calculated
Invertebrate toxicity	48-h EC_0 (mg/l) *D. magna* 48-h LC_{50} (mg/l)	1 0.32	Merck SDS (2006) EPIWIN v3.12	measured calculated
Algal toxicity	96-h EC_{50} (mg/l)	0.040	EPIWIN v3.12	calculated

Note: a) Above the expected water solubility of the substance.

Assessment of priority

The worst case RCRs obtained using EUSES are summarised in Table 18.

Table 18 Worst case RCRs for ethylhexyl methoxycinnamate

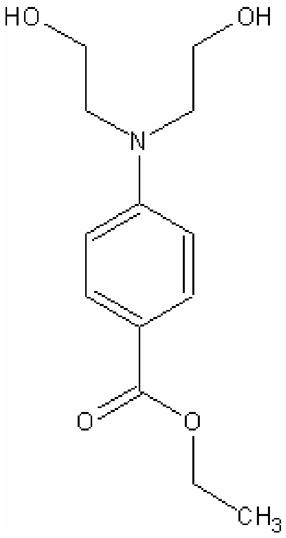
Life-cycle stage	**Predicted concentrations**			**RCRs**		
	Surface water (mg/l)	**Sediment (mg/kg wet wt.)**	**Soil (mg/kg wet wt.)**	**Surface water**	**Sediment**	**Soil**
Production	0.040	13	15	**629**	**6.3×10^3**	**9.3×10^3**
Formulation of sunscreens	9.0×10^{-3}	3.0	3.2	**149**	**1.5×10^3**	**2.0×10^3**
Use of sunscreens	5.3×10^{-3}	1.8	1.7	**88**	**877**	**1.0×10^3**
Regional sources	1.3×10^{-3}	0.78	0.042	**22**	**386**	**25**

The worst case calculations indicate a potential risk from the production, formulation and use of this substance. It is unlikely to meet the EU PBT or vPvB criteria since it is predicted to be readily biodegradable. It should be noted, however, that the substance appears to meet the bioaccumulative, very bioaccumulative and toxic screening criteria (based on predicted data) and so this conclusion crucially depends on the assumption that the substance will degrade rapidly in the environment. Since it is a HPV substance, it is likely that at least one of the suppliers will hold test data on ready biodegradability.

Based on this analysis, ethylhexyl methoxycinnamate is a high priority for further work.

3.1.12 PEG-25 PABA (CAS No 116242-27-4)

The Annex VII name for this substance is ethoxylated ethyl-4-aminobenzoate with CAS Nos 116242-27-4 and 15716-30-0. Alternative names include polyoxyethylene ethyl-4-aminobenzoate (25 mol ethoxylate (EO) average molar ratio). This substance is a polymer, with CAS No 15716-30-0 appearing to relate to the hydroxyethyl derivative (ethyl 4-[bis(2-hydroxyethyl)amino]benzoate). The structure of this latter substance is shown below.



This substance has some structural similarities with PABA (see Section 3.1.1).

Production and use

Neither of the two CAS numbers from Annex VII appear to be listed in the ESIS database or in EINECS, although this is not surprising for CAS No 116242-27-4 as it is a polymer. The other CAS number may be a degradation product, which would explain its omission. There is no information on the amounts that may be produced or imported into the EU and it is not listed as a new substance.

An internet search revealed that this substance is used as a UV-filter in cosmetic products in the EU to a maximum concentration of 10 per cent, but it is not approved as a sunscreen agent in the US or Japan.[19]

Directive 76/768/EEC indicates that the maximum authorised concentration of this substance in cosmetic products is 10 per cent.

Property data

The predicted properties of PEG-25 PABA are summarised in

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[19] www.portalfarma.com

Table 19. The properties have been estimated using the structure detailed above, but it should be noted that the commercial substance has extended ethoxy chains. This will increase the solubility and reduce the octanol-water partition coefficient (and hence potentially reduce the predicted toxicities, although the surfactant nature of this chain would also need to be taken into account).

Table 19 Properties of ethyl 4-[bis(2-hydroxyethyl)amino]benzoate

Property	Value		Source	meas/calc
Physico-chemical				
Molecular weight	253.30 g/mole			
Melting point	136°C		EPIWIN v3.12	calculated
Boiling point	392°C		EPIWIN v3.12	calculated
Vapour pressure	1.04×10^{-8} mmHg at 25°C		EPIWIN v3.12	calculated
Water solubility	1,591 mg/l at 25°C		EPIWIN v3.12	calculated
Partition coefficient (log K_{ow})	1.35		EPIWIN v3.12	calculated
Environmental fate and behaviour				
Photodegradation	Atmospheric OH rate constant 79×10^{-12} cm^3/molecule-sec at 25°C (half-life = 0.14 days; 12 hour day, 1.5 x 10^6 OH/cm^3)		EPIWIN v3.12	calculated
Biodegradation	Readily biodegradable		EPIWIN v3.12	predicted
Bioaccumulation	BCF 0.49 (log BCF -0.310)		EPIWIN v3.12	calculated
Ecotoxicity				
Organism	Endpoint	Predicted value		
Neutral Organic SAR (Baseline toxicity)	14-d LC_{50} (mg/l)	1,253	EPIWIN v3.12	calculated
Fish toxicity	96-h LC_{50} (mg/l) Chv (mg/l)	85 51	EPIWIN v3.12	calculated
Invertebrate toxicity	48-h LC_{50} (mg/l)	785	EPIWIN v3.12	calculated
Algal toxicity	96-h EC_{50} (mg/l) 96-h Chv (mg/l)	6.6 5.1	EPIWIN v3.12	calculated

Assessment of priority

The worst case RCRs obtained using EUSES are summarised in Table 20.

Table 20 Worst case RCRs for ethyl 4-[bis(2-hydroxyethyl)amino]benzoate

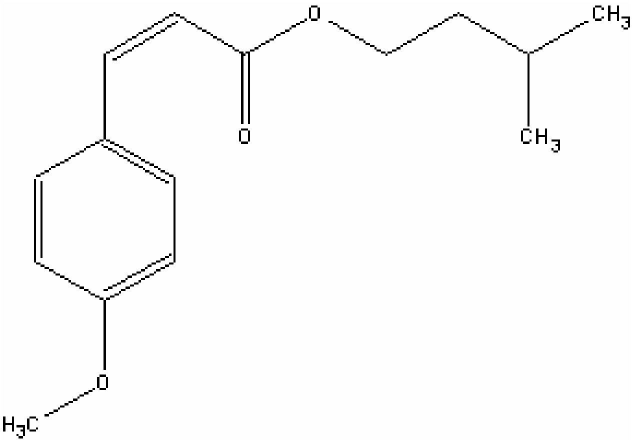
Life-cycle stage	Predicted concentrations			RCRs		
	Surface water (mg/l)	Sediment (mg/kg wet wt.)	Soil (mg/kg wet wt.)	Surface water	Sediment	Soil
Production	0.32	0.61	0.33	**3.1**	**3.1**	**3.1**
Formulation of sunscreens	1.3×10^{-3}	2.5×10^{-3}	1.2×10^{-3}	0.01	0.01	0.01
Use of sunscreens	1.5×10^{-3}	3.0×10^{-3}	1.4×10^{-3}	0.02	0.02	0.01
Regional sources	1.7×10^{-4}	3.0×10^{-4}	2.7×10^{-6}	2×10^{-3}	2×10^{-3}	3×10^{-5}

The worst case calculations indicate a low risk from the formulation and use of this substance in sunscreens, although a possible risk from production sites is indicated. The substance is unlikely to meet the EU PBT or vPvB criteria: it is predicted to be readily biodegradable, with a low log K_{ow} value and a long term NOEC for aquatic organisms far greater than 0.01 mg/l.

Based on this assessment, and the fact that the toxicity of the commercial substance is likely to be lower due to the longer ethoxylate chains, this substance is considered a low priority for further work.

3.1.13 Isoamyl-p-methoxycinnamate (CAS No 71617-10-2)

The Annex VII name for this substance is isopentyl-4-methoxycinnamate; alternative names include amiloxate. The structure of the substance is shown below.



Production and use

Isoamyl-p-methoxycinnamate is listed as an LPV chemical in the ESIS database, which lists a single producer/importer in the EU (Haarmann & Reimer GmbH, Germany).

An internet search indicates that this substance is used as a UV-absorber in sunscreens; it is also classified as a drug and therapeutic agent. Directive 76/768/EEC indicates that the maximum authorised concentration of this substance in cosmetic products is 10 per cent.

Property data

The predicted properties of isoamyl-p-methoxycinnamate are summarised in Table 21.

Table 21 Properties of isopentyl-4-methoxycinnamate

Property	Value		Source	meas/calc
Physico-chemical				
Molecular weight	248.32 g/mole			
Melting point	72°C		EPIWIN v3.12	calculated
Boiling point	324°C		EPIWIN v3.12	calculated
Vapour pressure	1.88×10^{-4} mmHg at 25°C		EPIWIN v3.12	calculated
Water solubility	4.9 mg/l at 25°C		EPIWIN v3.12	calculated
Partition coefficient (log K_{ow})	4.33		EPIWIN v3.12	calculated
Environmental fate and behaviour				
Photodegradation	Atmospheric OH rate constant 47×10^{-12} cm^3/molecule-sec at 25°C (half-life = 2.7 days; 12 hour day, 1.5×10^6 OH/cm^3; cis-isomer). OH rate constant 49×10^{-12} cm^3/molecule-sec at 25°C (half-life = 2.6 days; trans-isomer)		EPIWIN v3.12	calculated
Biodegradation	Not readily biodegradable		EPIWIN v3.12	predicted
Bioaccumulation	430 (log BCF 2.633)		EPIWIN v3.12	calculated
Ecotoxicity				
Organism	Endpoint	Predicted value		
Neutral Organic SAR (Baseline toxicity)	14-d LC_{50} (mg/l)	3.1	EPIWIN v3.12	calculated
Fish toxicity	96-h LC_{50} (mg/l) 32d-Chv (mg/l)	1.4 0.013	EPIWIN v3.12	calculated
Invertebrate toxicity	48-h LC_{50} (mg/l)	1.5	EPIWIN v3.12	calculated
Algal toxicity	96-h EC_{50} (mg/l)	0.18	EPIWIN v3.12	calculated

Assessment of priority

The worst case RCRs obtained using EUSES are summarised in Table 22.

Table 22 Worst case RCRs for isopentyl-4-methoxycinnamate

Life-cycle stage	**Predicted concentrations**			**RCRs**		
	Surface water (mg/l)	**Sediment (mg/kg wet wt.)**	**Soil (mg/kg wet wt.)**	**Surface water**	**Sediment**	**Soil**
Production	2.0	82	154	**1.5×10^4**	**1.5×10^4**	**3.6×10^4**
Formulation of sunscreens	7.9×10^{-3}	0.33	0.56	**61**	**61**	**129**
Use of sunscreens	9.4×10^{-3}	0.39	0.67	**72**	**72**	**156**
Regional sources	7.6×10^{-4}	0.050	0.019	**5.9**	**9.3**	**4.4**

The worst case calculations indicate a potential risk from the production, formulation and use of this substance, but it is not expected to meet the EU PBT or vPvB criteria. Although predicted not to be readily biodegradable (and so potentially meeting the screening criteria for a persistent or very persistent substance), the substance does not appear to meet the screening criteria for bioaccumulative or very bioaccumulative (log K_{ow} of 4.33) or toxicity (NOEC around 0.013 mg/l).

However, it should be noted that the log K_{ow} and NOEC are both estimated values and are close to the bioaccumulation and toxicity criteria cut-off values of 4.5 mg/l and 0.01 mg/l respectively. Based on this assessment the substance is a high priority for further work.

3.1.14 Ethylhexyl triazone (CAS No 88122-99-0)

The Annex VII name for this substance is 2,4,6-trianilino-(p-carbo-2'-ethylhexyl-1'oxy)-1,3,5,-triazine. Other names include octyl triazone and benzoic acid, 4,4',4''-(1,3,5-triazine-2,4,6-triyltriimino)tris-,tris(2-ethylhexyl) ester. This is a new substance and has been assessed under the relevant procedures; therefore, it is not considered further in this part of the report. Data relating to this substance are included in the Confidential Annex.

3.1.15 Drometrizole trisiloxane (CAS No 155633-54-8)

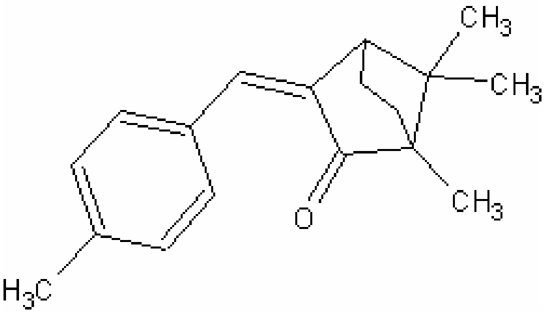
The Annex VII name for this substance is phenol, 2-(2H-benzotriazol-2-yl)-4-methyl-6-(2-methyl-3-(1,3,3,3-tetramethyl-I-(trimethylsilyl)oxy)-disiloxanyl)propyl). This is a new substance and has been assessed under the relevant procedures; therefore, it is not considered further in this part of the report. Data relating to this substance are included in the Confidential Annex.

3.1.16 Diethylhexyl butamidotriazone (CAS No 154702-15-5)

The Annex VII name for this substance is benzoic acid, 4,4-((6-(((1,1-dimethylethyl)-amino)carbonyl)phenyl) amino) 1,3,4-triazine-2,4-diyl)diimino)bis-,bis-(2-ethylhexyl)-ester). This is a new substance and has been assessed under the relevant procedures; therefore, it is not considered further in this part of the report. Data relating to this substance are included in the Confidential Annex.

3.1.17 4-Methylbenzylidene camphor (CAS No 36861-47-9 or 38102-62-4)

The Annex VII name for this substance is 3-(4'-methylbenzylidene)-d-1 camphor. Other names include (±) 1,7,7-trimethyl-3-[(4-methylphenyl) methylene]bicyclo[2.2.1]heptan-2-one, enzacamene and 4-MBC. The structure of the substance is shown below.



Production and use

4-MBC is listed on the ESIS database as an LPV chemical. There are two listed producers/importers in the EU (Haarmann & Reimer GmbH, Germany, and Rohner AG, Switzerland).

An internet search revealed that this substance is part of the Eusolex® product range supplied by Merck (Eusolex® 6300). It is an oil soluble UVB filter and 'provides a perfect combination of high efficacy and photostability'. 4-MBC also acts as a photostabiliser for avobenzone (see Section 3.1.7).

DSM also supplies the substance for formulation in sun care products (as Parsol® 5000). It is used in association with other UVB filters (up to 4 per cent) to raise sun protection factor (SPF) values. This substance is not listed in Japan and is an unapproved new drug in the US.

Directive 76/768/EEC indicates that the maximum authorised concentration of this substance in cosmetic products is 4 per cent.

Property data

The available properties of 4-MBC are summarised in

Table 23.

Table 23 Properties of 4-MBC

Property	Value		Source	meas/calc
Physico-chemical				
Molecular weight	254.37 g/mole			
Melting point	121°C		EPIWIN v3.12	calculated
Boiling point	349°C		EPIWIN v3.12	calculated
Vapour pressure	1.52×10^{-5} mmHg at 25°C		EPIWIN v3.12	calculated
Water solubility	0.20 mg/l at 25°C		EPIWIN v3.12	calculated
Partition coefficient (log K_{ow})	5.92		EPIWIN v3.12	calculated
Environmental fate and behaviour				
Photodegradation	Atmospheric OH rate constant 89×10^{-12} cm^3/molecule-sec at 25°C (half-life = 0.120 days; 12 hour day, 1.5×10^6 OH/cm^3)		EPIWIN v3.12	calculated
Biodegradation	Not readily biodegradable		Merck SDS (2006) EPIWIN v3.12	predicted
Bioaccumulation	7,224 (log BCF 3.859)		EPIWIN v3.12	calculated
Ecotoxicity				
Organism	Endpoint	Value		
Neutral Organic SAR (Baseline toxicity)	14-d LC_{50} (mg/l)	0.13	EPIWIN v3.12	calculated
Fish toxicity	96-h LC_{50} (mg/l) Chv (mg/l)	0.51^a 0.008	EPIWIN v3.12 EPIWIN v3.12	calculated calculated
Invertebrate toxicity	48-h EC_{50} (mg/l) 48-h LC_{50} (mg/l) Chv (mg/l)	$<0.8^a$ 0.11 0.047	Merck SDS (2006) EPIWIN v3.12 EPIWIN v3.12	measured calculated calculated
Algal toxicity	96-h EC_{50} (mg/l) Chv (mg/l)	0.048 0.017	EPIWIN v3.12 EPIWIN v3.12	calculated calculated

Note: a) Above the expected water solubility of the substance.

Nagtegaal *et al*. 1997 estimated a fish BCF of 5,400 (wet weight basis) using monitoring data from water and fish samples taken from a German lake. When expressed on a lipid basis, the BCF was 240,000. This information is taken from Geyer *et al*. 2000 (the original reference is in German), although few details were provided (e.g. actual concentrations in fish are not cited).

Assessment of priority

The worst case RCRs obtained using EUSES are summarised in Table 24.

Table 24 Worst case RCRs for 4-MBC

Life-cycle stage	Predicted concentrations			RCRs		
	Surface water (mg/l)	Sediment (mg/kg wet wt.)	Soil (mg/kg wet wt.)	Surface water	Sediment	Soil
Production	1.0	272	524	**1.2×10^3**	**1.2×10^4**	**3.0×10^4**
Formulation of sunscreens	1.6×10^{-3}	0.43	0.63	**2.0**	**20**	**36**

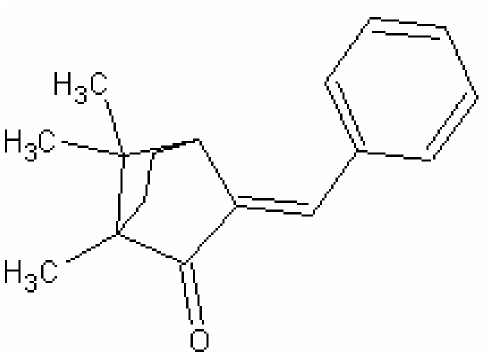
Use of sunscreens	4.7×10^{-3}	1.3	2.3	**5.9**	**59**	**129**
Regional sources	3.9×10^{-4}	0.20	0.30	0.49	**9.3**	**17**

The worst case calculations indicate a potential risk from the production, formulation and use of this substance, and it may meet the EU PBT and vPvB screening criteria. The substance is predicted not to be readily biodegradable, has a predicted log K_{ow} value of 5.92 and a predicted long-term NOEC of 0.008 mg/l for fish.

Based on this analysis, 4-MBC is a high priority for further work.

3.1.18 3-Benzylidene camphor (CAS No 15087-24-8)

The Annex VII name for this substance is also 3-benzylidene camphor; other names include 1,7,7-trimethyl-3-(phenylmethylene)bicyclo[2.2.1]heptan-2-one. The structure of the substance is shown below.



This substance is closely related to 4-MBC (see Section 3.1.17).

Production and use

3-Benzylidene camphor is listed as an LPV chemical on the ESIS database. One producer/importer is listed (Chimex, France).

The substance is used as a UV-filter in cosmetics products. Directive 76/768/EEC indicates that the maximum authorised concentration of this substance in cosmetic products is 2 per cent.

Property data

The predicted properties of 3-benzylidene camphor are summarised in

Table 25.

Table 25 Properties of 3-benzylidene camphor

Property	**Value**		**Source**	**meas/calc**
Physico-chemical				
Molecular weight	240.35 g/mole			
Melting point	110°C		EPIWIN v3.12	calculated
Boiling point	338°C		EPIWIN v3.12	calculated
Vapour pressure	3.8×10^{-5} mmHg at 25°C		EPIWIN v3.12	calculated
Water solubility	0.69 mg/l at 25°C		EPIWIN v3.12	calculated
Partition coefficient (log K_{ow})	5.37		EPIWIN v3.12	calculated
Environmental fate and behaviour				
Photodegradation	Atmospheric OH rate constant 86×10^{-12} cm^3/molecule-sec at 25°C (half-life = 0.13 days; 12 hour day, 1.5×10^6 OH/cm^3)		EPIWIN v3.12	calculated
Biodegradation	Not readily biodegradable		EPIWIN v3.12	predicted
Bioaccumulation	2,738 (log BCF 3.437)		EPIWIN v3.12	calculated
Ecotoxicity				
Organism	Endpoint	Predicted		
Neutral Organic SAR (Baseline toxicity)	14-d LC_{50} (mg/l)	0.38	EPIWIN v3.12	calculated
Fish toxicity	96-h LC_{50} (mg/l) Chv (mg/l)	1.09[a] 0.022	EPIWIN v3.12	calculated
Invertebrate toxicity	48-h LC_{50} (mg/l) Chv (mg/l)	0.28 0.041	EPIWIN v3.12	calculated
Algal toxicity	96-h EC_{50} (mg/l) Chv (mg/l)	0.12 0.10	EPIWIN v3.12	calculated

Note: a) Above the expected water solubility of the substance.

Assessment of priority

The worst case RCRs obtained using EUSES are summarised in

Table 26.

Table 26 Worst case RCRs for 3-benzylidene camphor

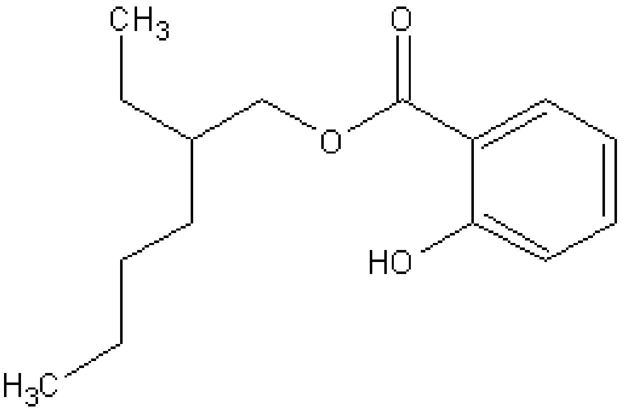
Life-cycle stage	Predicted concentrations			RCRs		
	Surface water (mg/l)	Sediment (mg/kg wet wt.)	Soil (mg/kg wet wt.)	Surface water	Sediment	Soil
Production	1.4	194	385	**622**	**6.2×10^{3}**	**1.5×10^{4}**
Formulation of sunscreens	2.2×10^{-3}	0.31	0.46	0.99	**9.9**	**18**
Use of sunscreens	6.5×10^{-3}	0.92	1.67	**3.0**	**30**	**66**
Regional sources	5.4×10^{-4}	0.14	0.13	0.25	**4.5**	**5.3**

The worst case calculations indicate a potential risk from the production, formulation and use of this substance. It meets the EU screening criteria for a vPvB substance, since it is predicted not to be readily biodegradable and has an estimated log K_{ow} value of 5.37. The lowest predicted long-term NOEC in aquatic species is around 0.022 mg/l and so the substance does not meet the toxicity criterion.

Based on this assessment, 3-benzylidene camphor is a high priority for further work.

3.1.19 Ethylhexyl salicylate (CAS No 118-60-5)

The Annex VII name for this substance is 2-ethylhexyl salicylate, and it is also known as octyl salicylate. The structure is shown below.



Production and use

Ethylhexyl salicylate is listed as an LPV chemical in the ESIS database, with a single EU producer/importer (Haarmann & Reimer GmbH, Germany).

Ethylhexyl salicylate is produced by the esterification of 2-ethylhexanol and salicyclic acid (Ashford 1994). An internet search indicates that this substance is used as a

UV-filter in a variety of sunscreen and cosmetic products (Household products database).

It is also used as a fragrance ingredient (Ashford 1994). Merck supplies ethylhexyl salicylate (as part of the Eusolex® product range) as an oil soluble UVB filter 'with excellent dissolving properties for solid organic UV-filters'.

Directive 76/768/EEC indicates that the maximum authorised concentration of this substance in cosmetic products is 5 per cent.

Property data

The available properties of ethylhexyl salicylate are summarised in

Table 27.

Table 27 Properties of ethylhexyl salicylate

Property	**Value**			**Source**	**meas/calc**
Physico-chemical					
Molecular weight	250.34 g/mole				
Melting point	109°C			EPIWIN v3.12	calculated
Boiling point	189–190°C at 28 hPa			Merck SDS (2006)	measured
	345°C			EPIWIN v3.12	calculated
Vapour pressure	3.17×10^{-6} mmHg at 25°C			EPIWIN v3.12	calculated
Water solubility	0.5 mg/l at 20			Merck SDS (2006)	measured
	0.72 mg/l at 20°C			EPIWIN v3.12	calculated
Partition coefficient (log K_{ow})	5.97			EPIWIN v3.12	calculated
Environmental fate and behaviour					
Photodegradation	Atmospheric OH rate constant 22×10^{-12} cm^3/molecule-sec at 25°C (half-life = 0.49 days; 12 hour day, 1.5×10^6 OH/cm^3)			EPIWIN v3.12	calculated
Biodegradation	Readily biodegradable			EPIWIN v3.12	predicted
Bioaccumulation	7,856 (log BCF 3.895)			EPIWIN v3.12	calculated
Ecotoxicity					
Organism	Endpoint	Esters[b]	Phenols[c]		
Neutral Organic SAR (Baseline toxicity)	14-d LC_{50} (mg/l)	0.117		EPIWIN v3.12	calculated
Fish toxicity	LC_{50} (mg/l) *B.rerio*	613[a]	-	Merck SDS (2006)	measured
	96-h LC_{50} (mg/l)	0.29	0.13	EPIWIN v3.12	calculated
	Chv (mg/l)	0.008	0.018	EPIWIN v3.12	calculated
Invertebrate toxicity	EC_{50} (mg/l) *D.magna*	10[a]	-	Merck SDS (2006)	measured
	48-h LC_{50} (mg/l)	0.049	0.32	EPIWIN v3.12	calculated
	21-d Chv (mg/l)	-	0.014	EPIWIN v3.12	calculated
Algal toxicity	96-h EC_{50} (mg/l)	0.026	0.038	EPIWIN v3.12	calculated
	Chv (mg/l)	0.022	0.038	EPIWIN v3.12	calculated

Note: a) Above the expected water solubility of the substance.
b) Estimate based on the substance behaving like an ester.
c) Estimate based on the substance behaving like a phenol.

Assessment of priority

The worst case RCRs obtained using EUSES are summarised in

Table 28.

Table 28 Worst case RCRs for ethylhexyl salicylate

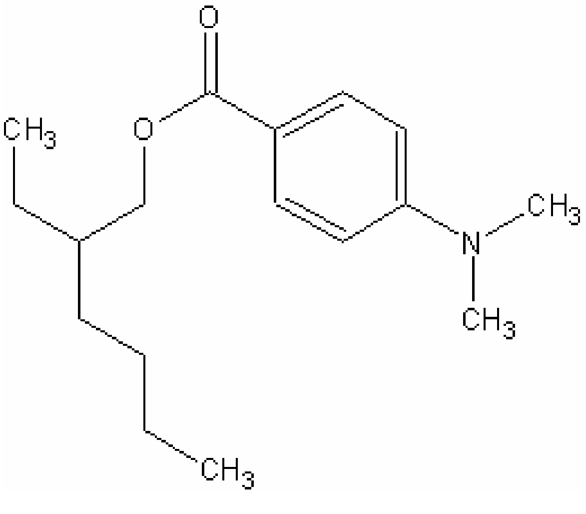
Life-cycle stage	Predicted concentrations			RCRs		
	Surface water (mg/l)	Sediment (mg/kg wet wt.)	Soil (mg/kg wet wt.)	Surface water	Sediment	Soil
Production	0.19	56	73	**240**	**2.4×10^3**	**3.9×10^3**
Formulation of sunscreens	3.6×10^{-4}	0.10	0.087	0.45	**4.5**	**4.6**
Use of sunscreens	9.6×10^{-4}	0.28	0.32	**1.2**	**12**	**17**
Regional sources	1.3×10^{-4}	0.065	2.6×10^{-3}	0.16	**2.8**	0.14

The worst case calculations indicate a potential risk from the production, formulation and use of this substance. It is unlikely to meet the EU PBT or vPvB screening criteria as it is predicted to be readily biodegradable, although it does meet the bioaccumulative/very bioaccumulative and toxic screening criteria (again based on predicted data). This assessment therefore hinges around the assumption that the substance will degrade rapidly in the environment; the presence of ester and hydroxyl groups suggests that this will be the case.

Based on this assessment, the substance is a high priority for further work.

3.1.20 Ethylhexyl dimethyl PABA (CAS No 21245-02-3)

The Annex VII name for this substance is '4-dimethyl-amino-benzoate of ethyl-2-hexyl'. Other names include octyl dimethyl PABA, 2-ethylhexyl 4-dimethylaminobenzoate and Padimate O. The structure of the substance is shown below.



Production and use

The substance is listed in the ESIS database as an LPV chemical with three producers/importers (ISP Europe, UK; Mallinckrodt Chemical GmbH, Germany; Nordic Synthesis AB, Sweden).

An internet search revealed that this substance is used as a UV-filter in sunscreens and cosmetic products. It is part of the Eusolex® product range supplied by Merck (Eusolex® 6007). It is an oil soluble liquid UVB filter with ‘very good protection potential and good dissolving properties for solid organic UV-filters’.

Directive 76/768/EEC indicates that the maximum authorised concentration of this substance in cosmetic products is 8 per cent.

A breakdown product of this substance is also known (see Section 3.2.11).

Property data

The properties of ethylhexyl dimethyl PABA are summarised in Table 29.

Table 29 Properties of ethylhexyl dimethyl PABA

Property	**Value**		**Source**	**meas/calc**
Physico-chemical				
Molecular weight	277.41 g/mole			
Melting point	97°C		EPIWIN v3.12	calculated
Boiling point	345°C		EPIWIN v3.12	calculated
Vapour pressure	3.54×10^{-5} mmHg at 25°C		EPIWIN v3.12	calculated
Water solubility	0.20 mg/l at 25°C		EPIWIN v3.12	calculated
Partition coefficient (log K_{ow})	5.77		EPIWIN v3.12	calculated
Environmental fate and behaviour				
Photodegradation	Atmospheric OH rate constant 133×10^{-12} cm^3/molecule-sec at 25°C (half-life = 0.08 days; 12 hour day, 1.5 x 10^6 OH/cm^3)		EPIWIN v3.12	calculated
Biodegradation	Not readily biodegradable		EPIWIN v3.12	calculated
Bioaccumulation	BCF 5,486 (log BCF 3.739)		EPIWIN v3.12	calculated
Ecotoxicity				
Organism	Endpoint	Value		
Neutral Organic SAR (Baseline toxicity)	14-d LC_{50} (mg/l)	0.19	EPIWIN v3.12	calculated
Fish toxicity	96-h LC_{50} (mg/l) Chv (mg/l)	0.40[a] 0.012	EPIWIN v3.12	calculated
Invertebrate toxicity	48-h LC_{50} (mg/l)	0.082	EPIWIN v3.12	calculated
Algal toxicity	96-h EC_{50} (mg/l) Chv (mg/l)	0.037 0.031	EPIWIN v3.12	calculated

Note: a) Above the expected water solubility of the substance.

Assessment of priority

The worst case RCRs obtained using EUSES are summarised in Table 30.

Table 30 Worst case RCRs for ethylhexyl dimethyl PABA

Life-cycle stage	**Predicted concentrations**			**RCRs**		
	Surface water (mg/l)	**Sediment (mg/kg wet wt.)**	**Soil (mg/kg wet wt.)**	**Surface water**	**Sediment**	**Soil**
Production	1.0	238	472	**4200**	**4200**	**1.1×10^5**
Formulation of sunscreens	3.3×10^{-3}	0.75	1.4	**14**	**136**	**305**
Use of sunscreens	4.8×10^{-3}	1.1	2.1	**20**	**200**	**462**
Regional sources	2.8×10^{-4}	0.12	0.24	**1.2**	**22**	**54**

The worst case calculations indicate a potential risk from the production, formulation and use of ethylhexyl dimethyl PABA. The substance potentially meets the EU screening criteria for a vPvB substance: it is predicted not to be readily biodegradable and has an estimated log K_{ow} value of 5.77. The lowest predicted long-term NOEC in aquatic species is around 0.012 mg/l, which is very close to the toxic criterion cut-off. Therefore, the possibility that the substance also meets the EU screening criteria for a PBT substance cannot be ruled out at this stage.

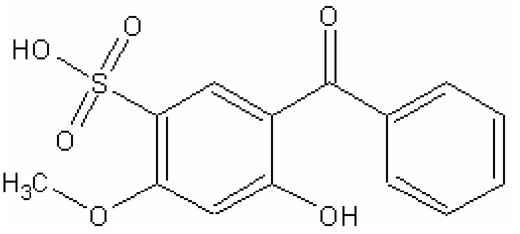
Based on this assessment, ethylhexyl dimethyl PABA is a high priority for further work.

3.1.21 Benzophenone-4 (CAS No 4065-45-6) and its sodium salt (CAS No 6628-37-1)

The Annex VII name for the acid is 2-hydroxy-4-methoxybenzophenone-5-sulfonic acid. Other names include sulisobenzone and 5-benzoyl-4-hydroxy-2-methoxybenzenesulfonic acid.

The INCI name for the sodium salt is benzophenone-5. Other names include benzenesulfonic acid, 5-benzoyl-4-hydroxy-2-methoxy-monosodium salt.

The structure of the acid is shown below.



Production and use

Benzophenone-4 (CAS No 4065-45-6) is listed as an LPV chemical in the ESIS database with one producer/importer in the EU (Great Lakes Chemical, France).

The sodium salt does not appear to be listed in either the ESIS database or EINECS.

Benzophenone-4 is produced by reaction of 2,4-dihydroxybenzophenone and dimethyl sulphate (ether formation) (Ashford 1994).

An internet search revealed that benzophenone-4 is used as a UV-filter in sunscreens. It is classified as a sunscreening agent and a UV screen. It is used in a wide range of cosmetic and personal care products, such as sunscreens, shampoos, hair sprays and hair dyes. The substance also appears to be used in coatings, and in photographic films and lithographic plates.

Directive 76/768/EEC indicates that the maximum authorised concentration of this substance in cosmetic products is 5 per cent (expressed as the acid).

Property data

The available properties of benzophenone-4 are summarised in Table 31.

Table 31 Properties of benzophenone-4

Property	**Value**		**Source**	**meas/calc**
Physico-chemical				
Molecular weight	308.31 g/mole			
Melting point	212°C		EPIWIN v3.12	calculated
Boiling point	498°C		EPIWIN v3.12	calculated
Vapour pressure	1.34×10^{-11} mmHg at 25°C		EPIWIN v3.12	calculated
Water solubility	250 g/l 20 g/l at 25°C		Merck (1989) EPIWIN v3.12	measured calculated
Partition coefficient (log K_{ow})	0.37		EPIWIN v3.12	calculated
Environmental fate and behaviour				
Photodegradation	Atmospheric OH rate constant 75×10^{-12} cm^3/molecule-sec at 25°C (half-life = 0.14 days; 12 hour day, 1.5×10^6 OH/cm^3)		EPIWIN v3.12	calculated
Biodegradation	Not readily biodegradable		EPIWIN v3.12	predicted
Bioaccumulation	BCF 3.2 (log BCF 0.5)		EPIWIN v3.12	calculated
Ecotoxicity				
Organism	Endpoint	Value		
Neutral Organic SAR (Baseline toxicity)	14d-LC$_{50}$ (mg/l)	10,882	EPIWIN v3.12	calculated
Fish toxicity	96-h LC$_{50}$ (mg/l) 30d-Chv (mg/l)	4,572 719	EPIWIN v3.12	calculated
Invertebrate toxicity	48-h LC$_{50}$ (mg/l) 21d-Chv (mg/l)	770 488	EPIWIN v3.12	calculated
Algal toxicity	96-h EC$_{50}$ (mg/l) 96-h Chv (mg/l)	42,416 1654	EPIWIN v3.12	calculated

Note that these properties have been estimated for the neutral form of the molecule. The sulphonic acid group will be ionised under environmental conditions, leading to a lower log K_{ow} value (the log K_{ow} value predicted for the sodium salt is -1.42). The predicted toxicity values already include an adjustment for the acid group (ECOSAR increases the values by a factor of 10).

Assessment of priority

The worst case RCRs obtained using EUSES are summarised in Table 32.

Table 32 Worst case RCRs for benzophenone-4

Life-cycle stage	Predicted concentrations			RCRs		
	Surface water (mg/l)	Sediment (mg/kg wet wt.)	Soil (mg/kg wet wt.)	Surface water	Sediment	Soil
Production	2.5	2.8	0.25	0.051	0.051	0.013
Formulation of sunscreens	9.2×10^{-3}	0.011	8.6×10^{-4}	1.9×10^{-4}	1.9×10^{-4}	4.3×10^{-5}
Use of sunscreens	0.013	0.015	1.1×10^{-3}	2.6×10^{-4}	2.6×10^{-4}	5.5×10^{-5}
Use of coatings	6.2×10^{-3}	7.1×10^{-3}	4.2×10^{-4}	1.3×10^{-4}	1.3×10^{-4}	2.1×10^{-5}
Regional sources	2.1×10^{-3}	2.1×10^{-3}	4.4×10^{-6}	4.2×10^{-5}	3.8×10^{-5}	2.2×10^{-7}

The worst case calculations indicate a low risk from all life cycle stages. In addition, benzophenone-4 does not meet the EU PBT or vPvB screening criteria. Although predicted not to be readily biodegradable (and so potentially meeting the persistent/very persistent screening criteria), it does not meet the screening criteria for a bioaccumulative/very bioaccumulative (log K_{ow} of 0.37) or toxic substance (NOEC >>0.01 mg/l).

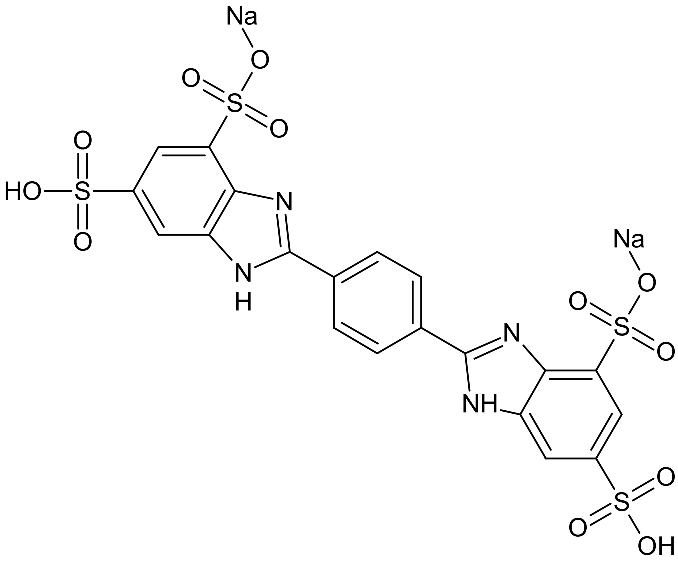
On this basis, benzophenone-4 is a low priority for further work.

3.1.22 2,2'-Methylene-bis-6-(2H-benzotriazol-2yl)-4-(tetramethylbutyl)-1,1,3,3-phenol (CAS No 103597-45-1)

This substance – a derivative of octrizole (see Section 3.2.14) – is listed in INCI as methylene bis-benzotriazolyl tetramethylbutylphenol. It is also known as bisoctrizole and by the trade name Tinosorb® M. It is a new substance and has been assessed under the relevant procedures; therefore, it is not considered further in this part of the report. Data relating to this substance are included in the Confidential Annex.

3.1.23 Monosodium salt of 2-2'-bis-(1,4-phenylene)1H-benzimidazole-4,6-disulphonic acid) (CAS No 180898-37-7)

This substance is also known as bisymidazylate and bisdisulizole disodium. It is listed in INCI as disodium phenyl dibenzimidazole tetrasulfonate. The structure derived from the name of the substance is shown below.



Production and use

This substance is not listed on the ESIS website – it is therefore either a new substance (though a record has not been identified) or is not currently supplied in any significant quantity.

Directive 76/768/EEC indicates that the maximum authorised concentration of this substance in cosmetic products is 10 per cent (expressed as the acid). No other information on its use in the UK or EU has been located.

Property data

The properties of the substance are summarised in

Table 33.

Table 33 Properties of monosodium salt of 2,2’-bis-(1,4-phenylene)1H-benzimidazole-4,6-disulphonic acid

Property	Value		Source	meas/calc
Physico-chemical				
Molecular weight	674.56 g/mole			
Melting point	350°C		EPIWIN v3.12	calculated
Boiling point	1297°C		EPIWIN v3.12	calculated
Vapour pressure	2.35×10^{-42} mmHg at 25°C		EPIWIN v3.12	calculated
Water solubility	1.23×10^{5} mg/l at 25°C		EPIWIN v3.12	calculated
Partition coefficient (log K_{ow})	-6.79		EPIWIN v3.12	calculated
Environmental fate and behaviour				
Photodegradation	Atmospheric OH rate constant 6.36×10^{-12} cm^3/molecule-sec at 25°C (half life = 1.68 days; 12 hour day, 1.5×10^{6} OH/cm^3)		EPIWIN v3.12	calculated
Biodegradation	Not readily biodegradable		EPIWIN v3.12	predicted
Bioaccumulation	BCF 3.2 (log BCF 0.5)		EPIWIN v3.12	calculated
Ecotoxicity				
Organism	Endpoint	Value		
Neutral organic SAR (baseline toxicity)	14-d LC_{50} (mg/l)	4.1×10^{10}	EPIWIN v3.12	calculated
Fish toxicity	96-h LC_{50} (mg/l)	7.85×10^{8}	EPIWIN v3.12	calculated
Invertebrate toxicity	48-h LC_{50} (mg/l)	1.86×10^{7}	EPIWIN v3.12	calculated
Algal toxicity	96-h EC_{50} (mg/l) Chv (mg/l)	1.69×10^{6} 4.99×10^{4}	EPIWIN v3.12 EPIWIN v3.12	calculated calculated

Assessment of priority

The worst case RCRs obtained using EUSES are summarised in Table 34.

Table 34 Worst case RCRs for 2,2’-bis-(1,4-phenylene)1H-benzimidazole-4,6-disulphonic acid

Life-cycle stage	Predicted concentrations			RCRs		
	Surface water (mg/l)	Sediment (mg/kg wet wt.)	Soil (mg/kg wet wt.)	Surface water	Sediment	Soil
Production	2.5	1.96	5.6×10^{-5}	1.5×10^{-3}	1.5×10^{-3}	2.8×10^{-7}
Formulation of sunscreens	0.011	8.6×10^{-3}	4.0×10^{-5}	6.5×10^{-6}	6.5×10^{-6}	2.0×10^{-7}
Use of sunscreens	0.013	0.01	1.6×10^{-7}	7.6×10^{-5}	7.6×10^{-5}	8.1×10^{-10}
Regional sources	$2. \times 10^{-3}$	1.4×10^{-3}	2.9×10^{-8}	1.2×10^{-5}	1.1×10^{-6}	1.4×10^{-10}

The worst case calculations indicate a low risk from all life cycle stages. Based on its predicted properties, the substance does not appear to meet the EU PBT or vPvB screening criteria (although not readily biodegradable, the low log K_{ow} value suggests that the substance will not be bioaccumulative).

On this basis, the substance is a low priority for further work.

3.1.24 (1,3,5)-Triazine-2,4-bis((4-(2-ethyl-hexyloxy)-2-hydroxy)-phenyl)-6-(4-methoxyphenyl) (CAS No 187393-00-6)

This substance is listed in INCI as bis-ethylhexyloxyphenol methoxyphenyl triazine An alternative name is bemotrizinol; it is also known by the trade name Tinosorb® S. It is a new substance and has been assessed under the relevant procedures; therefore it is not considered further in this part of the report. Data relating to this substance are included in the Confidential Annex.

3.1.25 Dimethicodiethylbenzalmalonate (CAS No 207574-74-1)

This substance is listed in INCI as polysilicone-15. No structural information has been located, though the substance appears to be a polymer.

Production and use

The substance does not appear to be listed in either the ESIS database or EINECS, although polymers are not included in these sources.

Directive 76/768/EEC indicates that the maximum authorised concentration of this substance in cosmetic products is 10 per cent.

Property data

No data have been located on the properties of this substance and no estimates have been made (properties cannot be calculated for polymers).

Assessment of priority

No calculations have been carried out owing to the lack of property data. On this basis, the substance is a priority for further work. The first step would be to establish the chemical structure.

3.1.26 Benzoic acid, 2-[-4-(diethylamino)-2-hydroxybenzoyl]-, hexyl ester (CAS No 302776-68-7)

This substance is listed in INCI as diethylamino hydroxybenzoyl hexyl benzoate. It is a new substance and has been assessed under the relevant procedures; therefore, it is not considered further in this part of the report. Data relating to this substance are included in the Confidential Annex.

3.1.27 Titanium dioxide (CAS No 13463-67-7)

The INCI name is titanium dioxide. The structure is shown below.

O=Ti=O

Production and use

Titanium dioxide is listed as an HPV chemical on the ESIS database, and the total amount of titanium dioxide produced or imported into the EU is >1,000,000 tonnes/year (ECB 2000). ECB 2000 lists 59 producers and/or importers of the substance in the EU. Five of these are based in the UK:

3M United Kingdom Plc
Brenntag (UK) Ltd
SCM Chemicals Europe
SCM Chemicals Ltd
Tioxide Europe Ltd.

Reisch 2005 mentions that a UK company, Oxonica, had introduced an ultrafine titanium dioxide sunscreen doped with 0.7% manganese. The manganese changes the pigment's electronic structure, and it is claimed that this eliminates the substance’s potential to generate free radicals.

The main uses of titanium dioxide are as a white filler or pigment in a large number of products including paper coatings, plastics, rubber, sealants, caulks, paints, printing inks, polishes, ceramics, vitreous enamels and food (Ashford 1994). It is also used to manufacture other titanium products.

Within cosmetics, titanium dioxide is used as a UV-absorber/opacifying agent. Directive 76/768/EEC indicates that the maximum authorised concentration of this substance in cosmetic products is 25 per cent. The actual quantity of titanium dioxide currently used in cosmetics is not clear, but it is likely that cosmetics use accounts for only a relatively small proportion of the total use of titanium dioxide.

Property data

The properties of titanium dioxide are summarised in

Table 35. These data refer to the typical commercial form of titanium dioxide; however, its use as a UV-absorber requires a nano-particulate form and data have not been sought for this. The property data might therefore not reflect the behaviour of this form of the substance.

Table 35 Properties of titanium dioxide

Property	**Value**		**Source**	**meas/calc**
Physico-chemical				
Molecular weight	79.90 g/mole			
Melting point	1,855°C		Ashford 1994	measured
Boiling point	Not available			
Vapour pressure	Not available – expected to be very low			
Water solubility	Of very low solubility		ECB 2000	
Partition coefficient (log K_{ow})	Not applicable – inorganic substance		ECB 2000	
Environmental fate and behaviour				
Photodegradation	Stable or inert		ECB 2000	
Biodegradation	Not applicable – inorganic substance The substance is stable and inert		ECB 2000	
Bioaccumulation	No information available		ECB 2000	
Ecotoxicity				
Organism	Endpoint	Value		
Fish toxicity	30-d LC_o (mg/l)	>3 mg/l[a]	ECB 2000	measured
Invertebrate toxicity	30-EC_o (mg/l)	>3 mg/l[a]	ECB 2000	measured
Algal toxicity	No data available.		ECB 2000	measured

Note: a) The substance has a very low water solubility. The reported data are likely to be well above the actual solubility for this substance.

Assessment of priority

No calculations have been carried out for titanium dioxide as cosmetics use is likely to account for only a very small proportion of the total use of this substance. In addition, the risk assessment of metal compounds is a complex process and a number of factors need to be taken into account (such as bio-availability) that are beyond the scope of the simplistic approach used in this study.

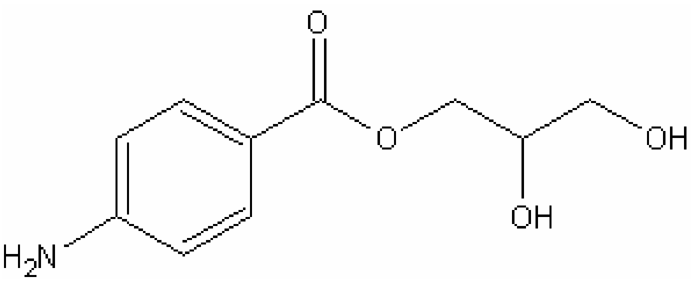
Titanium dioxide is an inorganic chemical and so it is inappropriate to apply the PBT/vPvB criteria. Nevertheless, more information is needed on the properties of the nano-particulate form of the substance and so it is a priority for further work.

3.2 Other substances used as UV-filters in sunscreens outside the EU

This section lists other substances that appear to be used as UV-filters in sunscreens, based on an internet search. They are not listed in Annex VII of Directive 76/768/EEC and so are unlikely to be used in sunscreens produced in the EU. As a result, no calculations have been carried out.

3.2.1 1-(4-Aminobenzoate)-1,2,3-propanetriol (CAS No 136-44-7)

This substance does not appear to be listed on INCI. The structure is shown below.



Production and use

This CAS number is registered in EINECS, but the substance has not been registered by EU industry as an HPV or LPV chemical. This substance is classified in the ChemIDplus database[20] as a sunscreen and a sunscreen agent.

Property data

The properties of 1-(4-aminobenzoate)-1,2,3-propanetriol are summarised in Table 36.

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[20] http://chem.sis.nlm.nih.gov/chemidplus/

Table 36 Properties of 1-(4-aminobenzoate)-1,2,3-propanetriol

Property	Value	Source	meas/calc
Physico-chemical			
Molecular weight	250.30 g/mole		
Melting point	130°C	EPIWIN v3.12	calculated
Boiling point	378°C	EPIWIN v3.12	calculated
Vapour pressure	3.24x10^{-8} mmHg at 25°C	EPIWIN v3.12	calculated
Water solubility	70 g/l	EPIWIN v3.12	calculated
Partition coefficient (log K_{ow})	-0.31	EPIWIN v3.12	calculated
Environmental fate and behaviour			
Photodegradation	Atmospheric OH rate constant 51x10^{-12} cm^3/molecule-sec at 25°C (half-life = 0.21 days; 12 hour day, 1.5x10^6 OH/cm^3).	EPIWIN v3.12	calculated
Biodegradation	Readily biodegradable	EPIWIN v3.12	calculated
Bioaccumulation	BCF 3.162 (log BCF 0.5)	EPIWIN v3.12	calculated

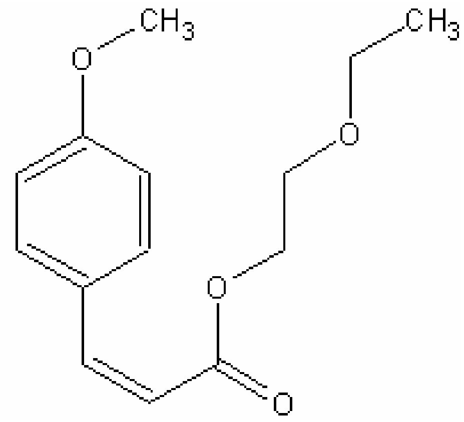
Property	Value			Source	meas/calc
Ecotoxicity					
Organism	Endpoint	Amines[a]	Esters[b]		
Neutral Organic SAR (Baseline toxicity)	14-d LC_{50} (mg/l)	29,157		EPIWIN v3.12	calculated
Fish toxicity	96-h LC_{50} (mg/l) Chv (mg/l)	3,234 10	550 1,006	EPIWIN v3.12	calculated
Invertebrate toxicity	48-h LC_{50} (mg/l) Chv (mg/l)	6 0.21	21,224 -	EPIWIN v3.12	calculated
Algal toxicity	96-h EC_{50} (mg/l) Chv (mg/l)	- 125	40 30	EPIWIN v3.12	calculated

Note: a) Estimates using a quantitative structure-activity relationship (QSAR) appropriate for aromatic amines.
b) Estimates using a QSAR appropriate for esters.

Based on the above information, the substance would not be expected to meet the EU PBT or vPvB criteria. The substance is predicted to be readily biodegradable, has a low predicted log K_{ow} and the predicted long-term NOEC for aquatic species is >>0.01 mg/l.

3.2.2 Cinoxate (CAS No 104-28-9)

The INCI name for this substance is cinoxate; other names include 2-propenoic acid, 3-(4-methoxyphenyl)-, 2-ethoxyethyl ester and 2-ethoxyethyl p-methoxycinnamate. The structure is outlined below.



Production and use

Cinoxate is listed in the ESIS database and the CAS number is in EINECS, but it is not an HPV or LPV chemical.

Cinoxate is produced by the reaction of p-anisaldehyde with acetic anhydride and ethylene glycol monoethyl ether (Perkin condensation/ esterification; Ashford 1994). The substance is soluble in oxygenated solvents and is used as a sunscreening agent.

Property data

The properties of cinoxate are summarised in Table 37.

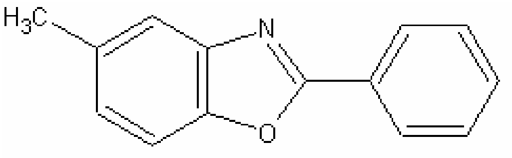
Table 37 Properties of cinoxate

<table>
<tr><th>Property</th><th colspan="2">Value</th><th>Source</th><th>meas/calc</th></tr>
<tr><td colspan="5">Physico-chemical</td></tr>
<tr><td>Molecular weight</td><td colspan="2">250.30 g/mole</td><td></td><td></td></tr>
<tr><td>Melting point</td><td colspan="2">88°C</td><td>EPIWIN v3.12</td><td>calculated</td></tr>
<tr><td>Boiling point</td><td colspan="2">185.5 at 2 mmHg
333°C</td><td>EPIWIN v3.12 database
EPIWIN v3.12</td><td>measured
calculated</td></tr>
<tr><td>Vapour pressure</td><td colspan="2">$3.4x10^{-4}$ mmHg at 25°C</td><td>EPIWIN v3.12</td><td>calculated</td></tr>
<tr><td>Water solubility</td><td colspan="2">500 mg/l
127 mg/l</td><td>Merck (1989)
EPIWIN v3.12</td><td>measured
calculated</td></tr>
<tr><td>Partition coefficient (log K_{ow})</td><td colspan="2">2.65</td><td>EPIWIN v3.12</td><td>calculated</td></tr>
<tr><td colspan="5">Environmental fate and behaviour</td></tr>
<tr><td>Photodegradation</td><td colspan="2">Atmospheric OH rate constant $56x10^{-12}$ cm^3/molecule-sec at 25°C (half-life = 2.3 days; 12 hour day, $1.5x10^6$ OH/cm^3; cis-isomer). OH rate constant $58x10^{-12}$ cm^3/molecule-sec at 25°C, half-life = 2.2 days; trans-isomer)</td><td>EPIWIN v3.12</td><td>calculated</td></tr>
<tr><td>Biodegradation</td><td colspan="2">Not readily biodegradable</td><td>EPIWIN v3.12</td><td>calculated</td></tr>
<tr><td>Bioaccumulation</td><td colspan="2">BCF 22 (log BCF 1.344)</td><td>EPIWIN v3.12</td><td>calculated</td></tr>
<tr><td colspan="5">Ecotoxicity</td></tr>
<tr><td>Organism</td><td>Endpoint</td><td>Predicted</td><td></td><td></td></tr>
<tr><td>Neutral Organic SAR (Baseline toxicity)</td><td>14-d LC_{50} (mg/l)</td><td>91</td><td>EPIWIN v3.12</td><td>calculated</td></tr>
<tr><td>Fish toxicity</td><td>96-h LC_{50} (mg/l)
32d-Chv (mg/l)</td><td>2.9
0.10</td><td>EPIWIN v3.12</td><td>calculated</td></tr>
<tr><td>Invertebrate toxicity</td><td>48-h LC_{50} (mg/l)</td><td>11</td><td>EPIWIN v3.12</td><td>calculated</td></tr>
<tr><td>Algal toxicity</td><td>96-h EC_{50} (mg/l)</td><td>1.2</td><td>EPIWIN v3.12</td><td>calculated</td></tr>
</table>

Based on these data, the substance is unlikely to meet the EU screening criteria for a PBT or vPvB substance. Although the substance is predicted not to be readily biodegradable (and so potentially meets the screening criteria for persistent/very persistent), the predicted log K_{ow} is 2.65 and the predicted long-term NOEC is >0.01 mg/l.

3.2.3 5-Methyl-2-phenylbenzoxazole (CAS No 7420-86-2)

This substance is not listed on INCI; alternative names include Witisol. The structure is shown below.



Production and use

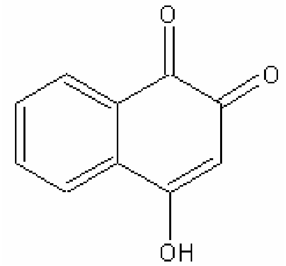
5-Methyl-2-phenylbenzoxazole is listed in the ESIS database and in EINECS, but is not an LPV or HPV chemical. According to the ChemIDplus database, 5-methyl-2-phenylbenzoxazole is classified as a sunscreening agent, but it also appears to have been linked with contact dermatitis and therefore may no longer be used in sunscreens and cosmetic products.

Property data

This substance appears no longer to be used in cosmetic products and so the properties of the substance have not been estimated here.

3.2.4 2-Hydroxy-1,4-napthalenedione (CAS No. 83-72-7)

The INCI name for this substance is HENNA; alternative names include lawsone and 2-hydroxy-1,4-naphthoquinone. The structure is shown below.



Production and use

2-Hydroxy-1,4-napthalenedione is listed in the ESIS database and in EINECS, but it is not a HPV or LPV chemical. This substance is listed in INCI as being used in cosmetics as a hair dyeing agent, bulking agent and conditioning agent. There are reports on the internet that the substance may also be used as a topical sunscreening agent. The substance appears to be derived from the leaves of the Henna plant, *Lawsonia inermis* (Lythraceae).

Property data

The properties of 2-hydroxy-1,4-napthalenedione are summarised in Table 38.

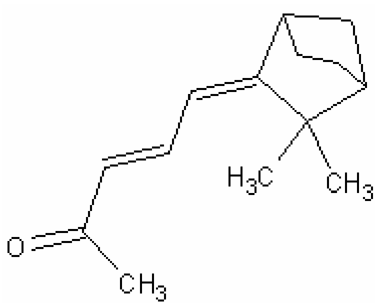
Table 38 Properties of 2-hydroxy-1,4-napthalenedione

Property	**Value**		**Source**	**meas/calc**
Physico-chemical				
Molecular weight	174.2 g/mole			
Melting point	195.5°C		EPIWIN v3.12 database	measured
Boiling point	357°C		EPIWIN v3.12	calculated
Vapour pressure	5.2×10^{-8} mmHg at 25°C		EPIWIN v3.12	calculated
Water solubility	339 mg/l		EPIWIN v3.12	calculated
Partition coefficient (log K_{ow})	0.78		EPIWIN v3.12	calculated
Environmental fate and behaviour				
Photodegradation	Atmospheric OH rate constant 12×10^{-12} cm^3/molecule-sec at 25°C (half-life = 0.93 days; 12 hour day, 1.5×10^6 OH/cm^3)		EPIWIN v3.12	calculated
Biodegradation	Readily biodegradable		EPIWIN v3.12	calculated
Bioaccumulation	BCF 0.33 (log BCF -0.48)		EPIWIN v3.12	calculated
Ecotoxicity				
Organism	Endpoint	Predicted		
Neutral Organic SAR (Baseline toxicity)	14-d LC_{50} (mg/l)	2,701	EPIWIN v3.12	calculated
Fish toxicity	96-h LC_{50} (mg/l) 32d-Chv (mg/l)	0.15 0.054	EPIWIN v3.12	calculated
Invertebrate toxicity	48-h LC_{50} (mg/l)	0.24	EPIWIN v3.12	calculated
Algal toxicity	96-h EC_{50} (mg/l)	0.57	EPIWIN v3.12	calculated

2-Hydroxy-1,4-napthalenedione is unlikely to meet the screening criteria for a PBT or vPvB substance. It is predicted to be readily biodegradable, has a low predicted log K_{ow} value and the predicted long-term NOEC for aquatic organisms is >0.01mg/l.

3.2.5 Bornelone (CAS No 2226-11-1)

The substance is listed in INCI; alternative names include 3-penten-2-one, 5-(3,3-dimethylbicyclo[2.2.1]hept-2-ylidene)-. The structure is shown below.



Production and use

This CAS number is found in EINECS, but this substance is not an LPV or HPV chemical. According to the ChemIDplus database, this substance is classified as a sunscreening agent and an ultraviolet screen.

Property data

The properties of bornelone are summarised in Table 39.

Table 39 Properties of bornelone

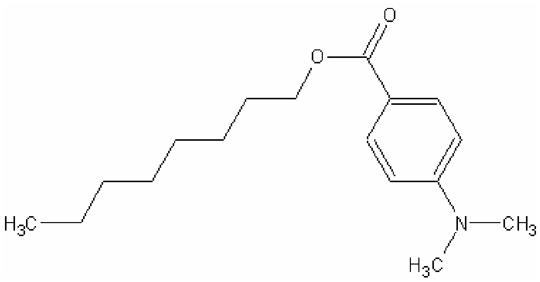
Property	Value		Source	meas/calc
Physico-chemical				
Molecular weight	204.31 g/mole			
Melting point	65°C		EPIWIN v3.12	calculated
Boiling point	277°C		EPIWIN v3.12	calculated
Vapour pressure	4.8×10^{-3} mmHg at 25°C		EPIWIN v3.12	calculated
Water solubility	4.2 mg/l		EPIWIN v3.12	calculated
Partition coefficient (log K_{ow})	4.26		EPIWIN v3.12	calculated
Environmental fate and behaviour				
Photodegradation	Atmospheric OH rate constant 177×10^{-12} cm^3/molecule-sec at 25°C (half-life = 0.061 days; 12 hour day, 1.5×10^6 OH/cm^3)		EPIWIN v3.12	calculated
Biodegradation	Not readily biodegradable		EPIWIN v3.12	calculated
Bioaccumulation	BCF 378 (log BCF 2.58)		EPIWIN v3.12	calculated
Ecotoxicity				
Organism	Endpoint	Predicted		
Neutral Organic SAR (Baseline toxicity)	14-d LC_{50} (mg/l)	3.0	EPIWIN v3.12	calculated
Fish toxicity	96-h LC_{50} (mg/l) 32d-Chv (mg/l)	4.8[a] 0.16	EPIWIN v3.12	calculated
Invertebrate toxicity	48-h LC_{50} (mg/l) Chv (mg/l)	1.6 0.23	EPIWIN v3.12	calculated
Algal toxicity	96-h EC_{50} (mg/l) Chv (mg/l)	0.74 0.46	EPIWIN v3.12	calculated

Note: a) Value close to the predicted water solubility of the substance.

Bornelone is unlikely to meet the screening criteria for a PBT or vPvB substance. Although it is predicted not to be readily biodegradable (and so potentially meets the persistent/very persistent screening criteria), the predicted log K_{ow} value is 4.26 and the predicted long-term NOEC for aquatic organisms is >>0.01mg/l.

3.2.6 Octyl dimethyl 4-aminobenzoic acid (CAS No 58817-05-3)

The substance is not listed in INCI. The structure is shown below.



Production and use

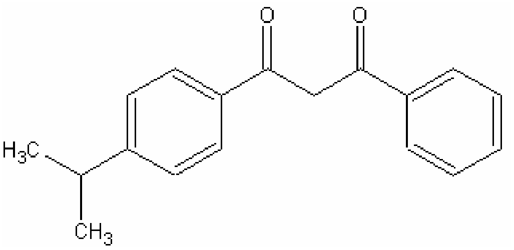
The CAS number for this substance was not found in the ESIS database. It is listed as a sunscreening agent in the ChemIDplus database, but it is also classified as a skin/eye irritant so it is possible that it is no longer used in cosmetics products.

Property data

As this substance no longer appears to be used in cosmetics products, the properties have not been estimated as part of this study.

3.2.7 1-[4-(1-Methylethyl)phenyl]-3-phenylpropane-1,3-dione (CAS No 63250-25-9)

The INCI name for this substance is isopropyl dibenzoylmethane; alternative names/ trade names include Eusolex® 8021. The structure of the substance is shown below.



Production and use

1-[4-(1-Methylethyl)phenyl]-3-phenylpropane-1,3-dione is listed in EINECS, but it is not an HPV or LPV chemical. An internet search revealed that it is used as a UVA filter for sunscreens, but causes allergic or photoallergic contact dermatitis. Eusolex® 8021 is presumably a Merck trade name; however, this substance does not appear on the Merck website as part of the current Eusolex® product range and it is possible that it is no longer used in cosmetics and sunscreens. The substance is, however, still listed in INCI as a UV-filter.

Property data

The predicted properties of 1-[4-(1-methylethyl)phenyl]-3-phenylpropane-1,3-dione are summarised in

Table 40.

Table 40 Properties of 1-[4-(1-methylethyl)phenyl]-3-phenylpropane-1,3-dione

Property	Value		Source	meas/calc
Physico-chemical				
Molecular weight	266.34 g/mole			
Melting point	128 6°C		EPIWIN v3.12	calculated
Boiling point	379°C		EPIWIN v3.12	calculated
Vapour pressure	2.6×10^{-6} mmHg at 25°C		EPIWIN v3.12	calculated
Water solubility	7.8 mg/l at 25°C		EPIWIN v3.12	calculated
Partition coefficient (log K_{ow})	3.97		EPIWIN v3.12	calculated
Environmental fate and behaviour				
Photodegradation[21]	Atmospheric OH rate constant 8.8×10^{-12} cm^3/molecule-sec at 25°C (half-life = 1.22 days; 12 hour day, 1.5×10^6 OH/cm^3)		EPIWIN v3.12	calculated
Biodegradation	Not readily biodegradable		EPIWIN v3.12	predicted
Bioaccumulation	BCF 33 (log BCF 1.517)		EPIWIN v3.12	calculated
Ecotoxicity				
Organism	Endpoint	Predicted		
Neutral Organic SAR (Baseline toxicity)	14-d LC_{50} (mg/l)	6.9	EPIWIN v3.12	calculated
Fish toxicity	96-h LC_{50} (mg/l)	3.6	EPIWIN v3.12	calculated
Invertebrate toxicity	48-h LC_{50} (mg/l) Chv (mg/l)	1.3 0.047	EPIWIN v3.12	calculated
Algal toxicity	Chv (mg/l)	0.096	EPIWIN v3.12	calculated

Based on these data, it is unlikely that the substance would meet the PBT or vPvB screening criteria. Although it is predicted not to be readily biodegradable (and so potentially meets the persistent/very persistent screening criteria), the predicted log K_{ow} value is 3.97 and the predicted long-term NOEC for aquatic organisms is >0.01 mg/l.

3.2.8 2-Propenoic acid, 3-(4-methoxyphenyl)-, 2-ethoxyethyl ester, mixture with 2-methyl-5-(1-methylethyl)cyclohexyl 2-aminobenzoate (CAS No 78065-42-6)

This substance is not listed in INCI; alternative names/trade names include maxafil. No structure is available for this substance.

Production and use

This substance is not listed in the ESIS database and very little information is available on the internet. Maxafil is listed as a sunscreening agent on the ChemIDplus website and appears to be a combination of the sunscreening agent cinoxate (see Section 3.2.2) and methyl anthranilate.

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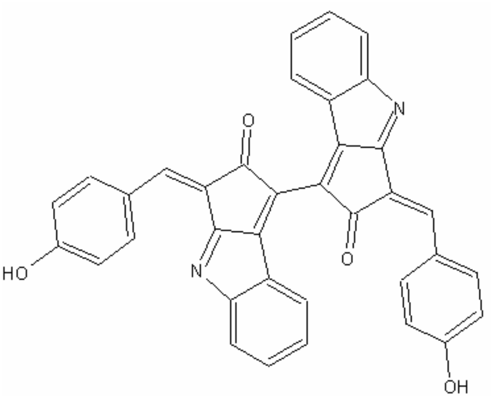
[21] The photostability and photoreactivity of this substance has been investigated by Schwack & Rudolph 1996. This paper has not been reviewed for this assessment.

Property data

No estimates can be made for the properties of this substance as it is a mixture of unspecified composition. The properties of cinoxate are summarised in Section 3.2.2.

3.2.9 Scytonemin (CAS No 152075-98-4)

This substance is not listed in INCI; alternative names include 1,1’-bicyclopent(b)indole-2,2’(3H,3’H)-dione, 3,3’bis((4-hydroxyphenyl)methylene. The structure is shown below.



Production and use

Scytonemin is a naturally-occurring ultraviolet sunscreen pigment, derived from the sheaths of cyanobacteria. This substance is not listed in the ESIS database or on EINECS, but it is classified as a sunscreening agent on the ChemIDplus database.

Property data

The predicted properties of scytonemin are summarised in Table 41.

Table 41 Properties of scytonemin

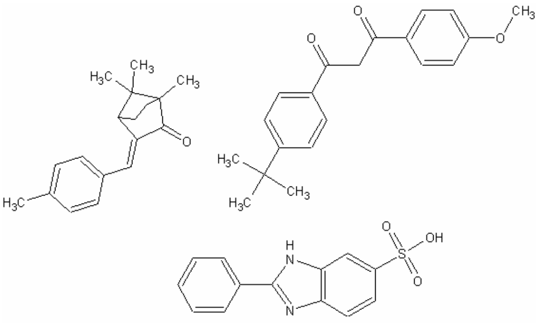
Property	**Value**		**Source**	**meas/calc**
Physico-chemical				
Molecular weight	544.57 g/mole			
Melting point	342°C		EPIWIN v3.12	calculated
Boiling point	776°C		EPIWIN v3.12	calculated
Vapour pressure	$5.4x10^{-22}$ mmHg at 25°C		EPIWIN v3.12	calculated
Water solubility	7.4×10^{-5} mg/l at 25°C		EPIWIN v3.12	calculated
Partition coefficient (log K_{ow})	6.28		EPIWIN v3.12	calculated
Environmental fate and behaviour				
Photodegradation	Atmospheric OH rate constant $104x10^{-12}$ cm^3/molecule-sec at 25°C (half-life = 0.063 days; 12 hour day, $1.5x10^6$ OH/cm^3)		EPIWIN v3.12	calculated
Biodegradation	Not readily biodegradable		EPIWIN v3.12	predicted
Bioaccumulation	BCF 13,660 (log BCF 4.14)		EPIWIN v3.12	calculated
Ecotoxicity				
Organism	Endpoint	Predicted		
Neutral Organic SAR (Baseline toxicity)	14-d LC_{50} (mg/l)	0.14[a]	EPIWIN v3.12	calculated
Fish toxicity	96-h LC_{50} (mg/l) Chv (mg/l)	0.64[a] 0.009[a]	EPIWIN v3.12	calculated
Invertebrate toxicity	48-h LC_{50} (mg/l) Chv (mg/l)	0.13[a] 0.020[a]	EPIWIN v3.12	calculated
Algal toxicity	96-h EC_{50} (mg/l) Chv (mg/l)	0.054[a] 0.058[a]	EPIWIN v3.12	calculated

Note: a) The predicted toxicity data are all above the predicted water solubility of this substance.

The substance would appear to meet the screening criteria for a PBT or vPvB substance. It is predicted not to be readily biodegradable, has a predicted log K_{ow} of 6.28 and the lowest predicted NOEC for aquatic organisms is 0.009 mg/l (the ability of the prediction software to cater for this type of structure is unclear). It should be noted that the substance is also predicted to have a very low water solubility and so there are uncertainties as to whether this substance has the potential to cause toxic effects in aquatic species.

3.2.10 1H-Benzimidazole-5-sulfonic acid, 2-phenyl-, mixture with 1-(4-(1,1-dimethylethyl-phenyl)-3-(4-methoxyphenyl)-1,3-propanedione and (+-)-1,7,7-trimethyl-3-((4-methylphenyl)methylene)bicyclo(2.2.1)heptan-2-one (CAS No 156586-95-7)

This substance is not listed in INCI; alternative names/trade names include contralume ultra. The structure is shown below (the substance is a mixture of three components).



Production and use

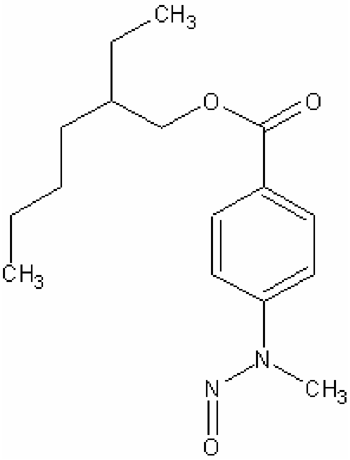
This substance is not listed in INCI, the ESIS database or EINECS. The CAS number appears to relate to a mixture of avobenzone (see Section 3.1.7), Eusolex® 6300 (4-methylbenzylidene camphor, see Section 3.1.17) and Eusolex® 232 (phenylbenzimidazole sulfonic acid, see Section 3.1.5). Eusolex® 6300 and 232 are UVB filters supplied by Merck.

Property data

See the property data for the main components in Section 3.1.5, Section 3.1.7 and Section 3.1.17.

3.2.11 2-Ethylhexyl 4-(N-methyl-N-nitrosamino) benzoate (CAS No 122021-01-6)

2-Ethylhexyl 4-(N-methyl-N-nitrosamino) benzoate is a breakdown product of 2-ethylhexyl 4-dimethylaminobenzoate (Padimate O; see Section 3.1.20) found in sunscreens. The structure of the substance is shown below.



Production and use

The substance is not listed in the ESIS database or EINECS, but it is listed as a sunscreening agent in the ChemIDplus database. It is not clear whether this listing relates to the use of the substance itself or its presence as an impurity in, or breakdown product of, another chemical.

Property data

The predicted properties of the substance are summarised in Table 42.

Table 42 Properties of 2-ethylhexyl 4-(N-methyl-N-nitrosamino) benzoate

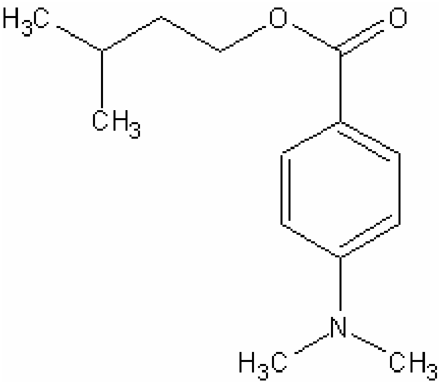
Property	**Value**		**Source**	**meas/calc**
Physico-chemical				
Molecular weight	292.38 g/mole			
Melting point	140°C		EPIWIN v3.12	calculated
Boiling point	410°C		EPIWIN v3.12	calculated
Vapour pressure	7.9×10^{-7} mmHg at 25°C		EPIWIN v3.12	calculated
Water solubility	0.53 mg/l at 25°C		EPIWIN v3.12	calculated
Partition coefficient (log Kow)	5.09		EPIWIN v3.12	calculated
Environmental fate and behaviour				
Photodegradation	Atmospheric OH rate constant 12×10^{-12} cm^3/molecule-sec at 25°C (half-life = 0.66 days; 12 hour day, 1.5×10^6 OH/cm^3)		EPIWIN v3.12	calculated
Biodegradation	Not readily biodegradable		EPIWIN v3.12	predicted
Bioaccumulation	BCF 1,651 (log BCF 3.22)		EPIWIN v3.12	calculated
Ecotoxicity				
Organism	Endpoint	Predicted		
Neutral Organic SAR (Baseline toxicity)	14-d LC_{50} (mg/l)	0.80[a]	EPIWIN v3.12	calculated
Fish toxicity	96-h LC_{50} (mg/l) Chv (mg/l)	0.98[a] 0.047	EPIWIN v3.12	calculated
Invertebrate toxicity	48-h LC_{50} (mg/l)	0.36	EPIWIN v3.12	calculated
Algal toxicity	96-h EC_{50} (mg/l) Chv (mg/l)	0.088 0.072	EPIWIN v3.12	calculated

Note: a) The predicted toxicity data are above the predicted water solubility of this substance.

Based on these data, the substance would appear to meet the screening criteria for a vPvB substance. It is predicted not to be readily biodegradable and has a predicted log K_{ow} of 5.09. The predicted long-term NOEC data for aquatic organisms are above 0.01 mg/l.

3.2.12 Benzoic acid, 4-(dimethylamino)-, 3-methylbutyl ester (CAS No 21245-01-2)

This substance is not listed in INCI; alternative names/trade names include Padimate and Spectraban. The structure of the substance is shown below.



Production and use

The substance is not an LPV or HPV chemical in the EU. It may be combined with the structurally similar Padimate O (see Section 3.1.20) in Spectraban 15 lotion (ChemIDplus database).

The predicted properties of this substance are summarised in Table 43.

Table 43 Properties of benzoic acid, 4-(dimethylamino)-, 3-methylbutyl ester

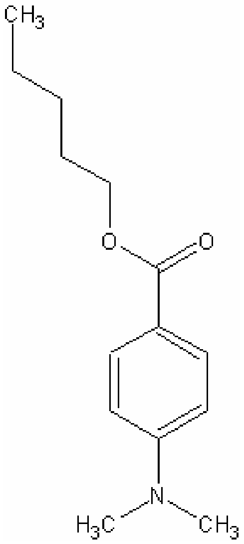
Property	Value	Source	meas/calc
Physico-chemical			
Molecular weight	235.33 g/mole		
Melting point	69°C	EPIWIN v3.12	calculated
Boiling point	306°C	EPIWIN v3.12	calculated
Vapour pressure	5.6×10^{-4} mmHg at 25°C	EPIWIN v3.12	calculated
Water solubility	6.2 mg/l at 25°C	EPIWIN v3.12	calculated
Partition coefficient (log Kow)	4.29	EPIWIN v3.12	calculated
Environmental fate and behaviour			
Photodegradation	Atmospheric OH rate constant 128×10^{-12} cm^3/molecule-sec at 25°C (half-life = 0.084 days; 12 hour day, 1.5×10^6 OH/cm^3)	EPIWIN v3.12	calculated
Biodegradation	Not readily biodegradable	EPIWIN v3.12	calculated
Bioaccumulation	BCF 403 (log BCF 2.605)	EPIWIN v3.12	calculated

Property	**Value**		**Source**	**meas/calc**
Ecotoxicity				
Organism	Endpoint	Value		
Neutral Organic SAR (Baseline toxicity)	14-d LC_{50} (mg/l)	3.2	EPIWIN v3.12	calculated
Fish toxicity	96-h LC_{50} (mg/l) Chv (mg/l)	2.1 0.17	EPIWIN v3.12	calculated
Invertebrate toxicity	48-h LC_{50} (mg/l)	1.5	EPIWIN v3.12	calculated
Algal toxicity	96-h EC_{50} (mg/l) Chv (mg/l)	0.18 0.15	EPIWIN v3.12	calculated

The substance is unlikely to meet the PBT or vPvB screening criteria. Although predicted not to be readily biodegradable, it has a predicted log K_{ow} value of 4.29 and the long-term NOEC with aquatic organisms is predicted to be >0.01 mg/l.

3.2.13 Pentyl 4-(dimethylamino) benzoate (CAS No. 14779-78-3)

This substance is not listed on INCI; alternative names/trade names include Padimate A. The structure of the substance is shown below.



Production and use

Pentyl 4-(dimethylamino) benzoate is structurally related to benzoic acid, 4-(dimethylamino)-, 3-methylbutyl ester (see Section 3.2.12) and is listed as an LPV chemical in the ESIS database, with one producer/importer (Mallinckrodt Chemical GmbH, Germany).

This substance is listed as a sunscreening agent in the ChemIDplus database, but it is also classified as a skin/eye irritant. It does not appear to be included in Directive 76/768/EEC and so it is unlikely to be used in sunscreens in the EU.

Property data

The predicted properties of pentyl 4-(dimethylamino) benzoate (Padimate A) are summarised in

Table 44.

Table 44 Properties of pentyl 4-(dimethylamino) benzoate

Property	**Value**		**Source**	**meas/calc**
Physico-chemical				
Molecular weight	235.33 g/mole			
Melting point	73°C		EPIWIN v3.12	calculated
Boiling point	314°C		EPIWIN v3.12	calculated
Vapour pressure	2.8×10^{-4} mmHg at 25°C		EPIWIN v3.12	calculated
Water solubility	5.3 mg/l at 25°C		EPIWIN v3.12	calculated
Partition coefficient (log Kow)	4.37		EPIWIN v3.12	calculated
Environmental fate and behaviour				
Photodegradation	Atmospheric OH rate constant 128×10^{-12} cm^3/molecule-sec at 25°C (half-life = 0.084 days; 12 hour day, 1.5×10^6 OH/cm^3)		EPIWIN v3.12	calculated
Biodegradation	Not readily biodegradable		EPIWIN v3.12	calculated
Bioaccumulation	BCF 459 (log BCF 2.661)		EPIWIN v3.12	calculated
Ecotoxicity				
Organism	Endpoint	Value		
Neutral Organic SAR (Baseline toxicity)	14-d LC_{50} (mg/l)	2.7	EPIWIN v3.12	calculated
Fish toxicity	96-h LC_{50} (mg/l) Chv (mg/l)	1.9 0.15	EPIWIN v3.12	calculated
Invertebrate toxicity	48-h LC_{50} (mg/l)	1.3	EPIWIN v3.12	calculated
Algal toxicity	96-h EC_{50} (mg/l) Chv (mg/l)	0.17 0.14	EPIWIN v3.12	calculated

The substance is unlikely to meet the PBT or vPvB screening criteria. Although predicted not to be readily biodegradable, it has a predicted log K_{ow} value of 4.37 and all predicted long-term NOECs are above 0.01 mg/l.

3.2.14 Other UV-filters listed in INCI

Several other UV-stabilisers are listed in INCI (see Table 46). No specific searches were undertaken for these substances, but little or no readily available information was found on their uses as UV-filters in sunscreens in the UK or EU as part of the other searches performed. It is unlikely that these substances are used in large quantities for this application in the EU or UK. However, many of these substances (or similar substances) appear to be used as UV-stabilisers for polymer applications (see Section 3.3).

Table 45 Other UV-stabilisers listed in INCI

CAS Number	INCI Name	Other names
4207-42-5	Allantoin PABA	Urea, (2,5-dioxo-4-imidazolydinyl)-, compound with 4-aminobenzoic acid (1:1)
575-61-1	Benzalphthalide	3-Benzylidenephthalide
119-61-9	Benzophenone	
131-56-6	Benzophenone-1	2,4-Dihydroxybenzophenone
131-55-5	Benzophenone-2	2,2',4,4'-Tetrahydroxy benzophenone
131-54-4	Benzophenone-6	2,2'-Dihydroxy-4,4'-dimethoxybenzophenone
85-19-8	Benzophenone-7	5-chloro-2-hydroxybenzophenone
131-53-3	Benzophenone-8	2,2'-Dihydroxy-4-methoxybenzophenone
76656-36-5	Benzophenone-9	Disodium 3,3'-carbonylbis[4-hydroxy-6-methoxybenzene sulphonate]
1641-17-4	Benzophenone-10	2-Hydroxy-4-methoxy-4'-methylbenzophenone
1341-54-4	Benzophenone-11	Bis(2,4-dihydroxyphenyl)methanone and bis(2-hydroxy-4-methoxyphenyl)methanone
1843-05-6	Benzophenone-12	2-Hydroxy-4-octyloxybenzophenone
118-58-1	Benzyl salicylate	
3896-11-5 (729-33-5 in INCI)	Bumetrizole	Phenol, 2-(5-chloro-2H-benzotriazol-2-yl)-6-(1,1-dimethylethyl)-4-methyl
243133-71-3	Ceria/silica	Carbonic acid, cerium (3+) salt, calcination products with silica
243133-70-2	Ceria/silica talc	Carbonic acid, cerium (3+) salt, calcination products with silica and talc ($Mg_3Al_2(SiO_3)_4$)
56265-46-4	Deamthoxycinnamate	p-Methoxycinnamic acid, compound with 2,2'-iminodiethanol (1:1)
5089-22-5	Dibenzoxazoyl naphthalene	2,2'-(Naphthalene-1,4-diyl)bis(benzoxazole)
32580-71-5	Diisopropylmethyl cinnamate	2-Propenoic acid, 3-[2,4-bis(1-methylethyl)phenyl]-, methyl ester
Not known	Dimethyl PABA ethylcetearyl dimomium tosylate	Quaternary ammonium compounds, N-C16-C18-alkyl-N-[2-(4-dimethylaminobenzoyloxy)-ethyl]-N,N-dimethyl-, salt with 4-methylbenzenesulfonic acid
169682-22-8	Diphenyl carbomethoxy acetoxy naphthopyran	2-H-Naphtho[1,2-b]pyran-5-carboxylic acid, 6-(acetoxy)-2,2-diphenyl-, methyl ester
65215-54-5	Diphenylmethyl piperazinylbenzimidazole	2H-benzimidazole, 1-[3-[4-(diphenylmethyl)-1-piperazinyl] propyl]-
Not known	Di-t-butyl hydroxybenzylidene camphor	Bicyclo[2.2.1]heptan-2-one, 1,7,7-trimethyl-bis(1,1-dimethylethyl) phenyl) methylene]-
2440-22-4	Drometrizole	2-(2H-Benzotriazol-2-yl)-p-cresol
103-36-6	Ethyl cinnamate	

CAS Number	**INCI Name**	**Other names**
58882-17-0	Ethyl dihydroxypropyl PABA	Ethyl 4-[bis(2-hydroxypropyl) amino]benzoate
32580-72-6	Ethyl diisopropyl cinnamate	Ethyl 3-[2,4-bis(1-methylethyl) phenyl]acrylate
99880-64-5	Ethyl methoxycinnamate	Ethyl p-methoxycinnamate
5232-99-5	Etocrylene	2-Propenoic acid, 2-cyano-3,3-diphenyl-, ethyl ester
Not known	Glyceryl ethylhexanoate dimethoxycinnamate	2-Propenoic acid, 3-(4-methoxyphenyl)-, diester dihydroxy-2-(2-ethyl-1-oxohexyl)oxypropane
87-28-5	Glycol salicylate	2-Hydroxyethyl salicylate
5466-76-2	Isopropylmethoxy cinnamate	Isopropyl p-methoxycinnamate.
94134-93-7	Isopropylbenzyl salicylate	[4-(1-methylethyl)phenyl]methyl salicylate
134-09-8	Menthyl anthranilate	
89-46-3	Menthyl salicylate	
2788-74-1	N-Ethyl-3-nitro PABA	4-Ethylamino-3-nitrobenzoic acid
3147-75-9	Octrizole	2-(2H-benzotriazol-2-yl)-4-(1,1,3,3-tetramethylbutyl)phenol
86636-96-6	Potassium methoxycinnamate	2-Propenoic acid, 3-(4-methoxyphenyl)-, potassium salt
Not known	TriPABA pantenol	Benzoic acid, 4-amino-, triester with 2,4-dihydroxy-N-(3-hydroxypropyl)-3,3-dimethylbutanamide
1314-13-2	Zinc oxide	Zinc oxide (CI 77947)

3.3 UV-stabilisers

In addition to sunscreens, additives that provide UV light protection are used in a number of other applications, notably polymers, coatings and paints. These are generally known as UV-stabilisers or light stabilisers, and the term UV-stabiliser is used here to distinguish this use from the UV-filters used in sunscreens. The function of the UV-stabiliser is to prevent degradation and weathering of treated articles when exposed to UV light.

There are two broad types of UV-stabilisers:

- UV-absorbers that absorb light in the 290–380 nm wavelength range; and
- radical scavengers that intercept the free radicals formed during polymer degradation.

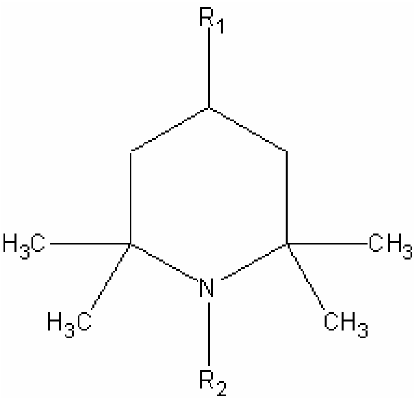
In some cases, a combination of both types of UV-stabiliser is used.

Following a search of the websites of several major European suppliers of plastics and coatings additives, we found that the UV-absorbers supplied within the EU fall within the following general chemical types.

- (Hydroxy)Benzophenone derivatives (such as 2-hydroxy benzophenones)
- Benzotriazole derivatives (such as 2-(2-hydroxyphenyl) benzotriazoles)
- Triazine derivatives (such as hydroxyphenyltriazines)
- Benzylidene malonate derivatives
- Oxalanilide derivatives
- Carbon black.

Of these, the benzophenone derivatives, benzotriazole derivatives and benzylidene malonate derivatives have structural similarities with some of the UV-filters used in sunscreens. For example, the (hydroxy)benzophenone derivatives are structurally similar to oxybenzone (see Section 3.1.4) and 2-hydroxy-4-methoxybenzophene-5-sulfonic acid (see Section 3.1.21). The benzotriazole derivatives have some structural similarities with 2-phenylbenzimidazole-5-sulphonic acid (see Section 3.1.5) and also possibly 2,2'-methylene-bis-6-(2H-benzotriazol-2yl)-4-(tetramethyl-butyl)-1,1,3,3-phenol (see Section 3.1.22). The benzylidene malonate derivatives have some structural similarity with 3,3'-(1,4-phenylenedimethylene) bis (7,7,-dimethyl-2-oxobicyclo-[2.2.1]hept-1-yl-methanesulfonic acid) (see Section 3.1.6), alpha-(2-oxoborn-3-ylidene)-toluene-4-sulphonic acid (see Section 3.1.8), octocrylene (see Section 3.1.9), octyl methoxycinnamate (see Section 3.2.11), isopentyl-4-methoxycinnamate (see Section 3.1.13), 3-(4'-methylbenzylidene)-d-1 camphor (see Section 3.1.17) and 3-benzylidene camphor (see Section 3.1.18). In addition, the triazine derivatives may be structurally related to the UV-filters 2,3,6-trianilino-(*p*-carbo-2'-ethylhexyl-1'-oxy)-1,3,5-triazine (see Section 0) and (1,3,5)-triazine-2,4-bis((4-(2-ethyl-hexyloxy)-2-hydroxy)-phenyl)-6-(4-methoxyphenyl) (see Section 3.1.24), although in this case the complex structures make it difficult to compare the similarities directly.

The most common types of radical scavengers are known as hindered amine light stabilisers (HALS). A wide range of HALS appears to be available, from relatively low molecular weight substances to oligomeric substances. HALS are almost exclusively derivatives of 2,2,6,6-tetramethylpiperidine.[22] The general structure of this substance is shown below.



Owing to their mechanism of action, it is unlikely that radical scavengers of this type will be used as UV-filters in sunscreens.

Although information on UV-stabiliser products supplied in Europe can be found on the internet, websites often do not explicitly name the active ingredients involved. These can be identified in other ways, such as the CAS numbers given in the associated Safety Data Sheets. However, since the suppliers have chosen not to explicitly identify the substances in their commercial products, this information has not been summarised for this report.

For clear coatings, the recommended UV-absorber concentration is 1–3 per cent (based on the solid binder content) for a dry film thickness of about 40µm.[23] For thinner films a higher concentration of the UV-absorber is needed. The recommended concentration of HALS used for clear coatings is 0.5–2.0 per cent (based on the solid binder content);[23] the concentration needed is independent of film thickness. When used in combination, a concentration of 1.5–2.0 per cent UV-absorber and 1 per cent HALS is generally used.

For pigmented coatings, the recommended concentration of HALS is 1–3 per cent (based on the solid binder content) for monocoats, while the concentration of UV-absorber is usually around 0–2 per cent depending on the pigmentation of the coating.[23]

Polyolefins are subject to light-induced degradation and so UV-stabilisers are often used, particularly in fibre applications (Wust Jr and Landoll 1993). The most effective light stabilisers for polyolefin fibres are radical scavengers such as HALS. The high molecular weight and polymeric amines show a low mobility and a low tendency to migrate to the surface of the fibre and are therefore usually the preferred choice.

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[22] See http://www.cibasc.com/index/ind-index/ind-pla.htm and associated webpages.

[23] See http://www.cibasc.com/index/ind-index/ind-paints_and_coatings.htm and associated webpages.

The preferred UV-stabilisers for high density polyethylene are carbon black (2–4 per cent) or salicylic acid esters/derivatives of benzotriazole or benzophenone (0.1–0.5 per cent) for colourless articles (Kissin 1996). UV-stabilisers commonly used for styrenic plastics include benzotriazoles (at around 0.25 per cent by weight) and benzophenones (Priddy 1997).

4 Information on endocrine disrupting potential

In recent years, there has been a growing interest within the scientific community in the endocrine disrupting potential of UV-filters in mammals, amphibia and fish. In particular, several papers have arisen from work performed in Switzerland under the auspices of their National Research Programme on endocrine disrupters,[24] and a recent overview paper provides some additional references that are not included below (Fent *et al*. 2008).

An initial literature search was conducted in 2006, shortly after this project began, to provide a snapshot. Given the growth in research it was not the intention to keep up with all publications after that date (but a brief search *was* conducted before the finalisation of the report). Studies were identified by carrying out an on-line search of the PubMed database for ‘endocrine’ + ‘UV-filters’ and ‘endocrine’ + ‘sun screen’. In addition, a wider search for ‘UV-filters’ alone was also carried out. However, this wider search resulted in a large number of ‘hits’ (over 500), many of which were not relevant to this project. Therefore these results were only scanned briefly to check for any other relevant information. The available data are summarised briefly in Table 46. It should be noted that, owing to resource limitations, none of these data have been reviewed or validated in detail for this project – most of the values are taken from abstracts.

It should also be noted that many different chemical names are used for the various substances. The names used in Table 46 are the names used in the papers, with the INCI names (if different) added where possible for clarity.

It is also possible that some metabolites of these substances may be relevant in this context. For example, Geyer *et al*. 2000 indicate that the demethylated and hydroxylated metabolites of BP-3 may be weakly oestrogenic.

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[24] http://www.nrp50.ch/projects.html

Table 46 Brief summary of readily available data on the endocrine disruption potential of UV-filters

Species	Brief summary of result	Reference
Fathead minnow (*Pimephales promelas*)	The estrogenic, anti-estrogenic, androgenic, and anti-androgenic activity of 18 UV-filters and one metabolite were systematically analysed *in vitro* at non-cytotoxic concentrations with recombinant yeast systems carrying either a human estrogen (hERα) or androgen receptor (hAR). All 19 compounds elicited hormonal activities; surprisingly, most of them had multiple activities. Ethyl 4-aminobenzoate (Et-PABA) was then investigated *in vivo* in fish. Et-PABA induced vitellogenin after 14 days of exposure in juvenile fathead minnows at 4394 µg/l.	Kunz and Fent 2006
Fathead minnow (*Pimephales promelas*)	Following the determination of estrogenic activity of 23 UV-filters and one metabolite using a recombinant yeast carrying the rainbow trout estrogen receptor (ERα) and another yeast carrying the human ERα receptor, eight substances were tested for vitellogenin induction potential in fathead minnows over 14 days of aqueous exposure. Three compounds were active *in vivo*: 3-benzylidene camphor induced vitellogenin at lower concentrations (435 µg/l) than benzophenone-1 (4919 µg/l) and benzophenone-2 (8,783 µg/l).	Kunz *et al*. 2006a
Fathead minnow (*Pimephales promelas*)	After a pre-exposure period of 21 days, reproductively mature fathead minnows were exposed to increasing concentrations of 3-benzylidene camphor (3BC) for 21 days in a static-renewal procedure. Actual 3BC concentrations decreased to 23 per cent of initial levels and median concentrations were 0.5 µg/l, 3 µg/l, 33 µg/l, 74 µg/l and 285 µg/l. 3BC affected reproduction in a dose-dependent manner with weak effects on fecundity at 3 µg/l, a significant decrease at 74 µg/l, and a cessation of reproduction at 285 µg/l. 3BC was accumulated in fish with an average bioconcentration factor of 313 ± 151. Dose-dependent demasculinization in secondary sex characteristics of male fish and dose-dependent induction of plasma vitellogenin occurred, which was significant at 74 µg/l and higher. 3BC had a profound and dose-dependent effect on the histology of gonads of male and female fish at 3 µg/l and higher. At 74 µg/l and 285 µg/l, oocyte and spermatocyte development was inhibited in male and female gonads. Testes of exposed males had much fewer spermatogenic cysts, and ovaries of exposed females had much fewer mature, but more atretic, follicles.	Kunz *et al.* 2006b
Fathead minnow (*Pimephales promelas*)	After a pre-exposure period of 19 days, reproductively mature fathead minnows were exposed to 0.002 mg/l, 0.1 mg/l, 1.2 mg/l, 5.0 mg/l and 9.7 mg/l of benzophenone-2 (BP-2) for 15 days. BP-2 was accumulated in fish up to 3.1 µg/g body weight. In males, a dose-dependent vitellogenin induction and decrease in the number of nuptial tubercles occurred. Moreover, significant dose-related effects on gonads of male and female fish were observed. At concentrations of 1.2 mg/l and higher, spermatocyte and oocyte development was significantly inhibited in male and female fish, respectively. Testes of exposed males had much fewer spermatocytes and ovaries of exposed females had much fewer mature, but more atretic, follicles. Reproduction was negatively affected in a dose-dependent manner with a decrease in egg production at 5.0 mg/l and a complete cessation of spawning activity at 9.7 mg/l BP-2.	Weisbrod *et al*. 2007

Species	**Brief summary of result**	**Reference**
Rainbow trout (*Oncorhynchus mykiss*)	The capability of 3-benzylidene camphor to cause vitellogenin induction was investigated in an *in vivo* assay with juvenile rainbow trout (enzyme linked immunosorbent assay; ELISA). The fish were exposed by direct injection, and a clear dose-response relationship was found in the concentration of plasma vitellogenin (10^5 times induction at a dose of 68 mg/kg). The ED_{50} was determined to be 16 mg/kg (for two injections over six days).	Holbech *et al.* 2002
Rainbow trout (*Oncorhynchus mykiss*) and Japanese medaka (*Oryzias latipes*)	Oxybenzone and benzophenone were evaluated for estrogenic activity using a juvenile rainbow trout assay. Three 14-day static-renewal exposures were carried out: one with oxybenzone, one with benzophenone and the other with a commercial sunscreen containing oxybenzone as the active ingredient. At the end of the 14-day exposure, the fish were sacrificed and vitellogenin expression was measured in the plasma by ELISA. Results showed that estrogenic activity at 1000 ng/l is approximately 100 times greater than concentrations observed in previous wastewater effluent. Intraperitoneal injection of oxybenzone up to 1000 ng/g body weight failed to show a similar relationship to that found in previous studies of sediment extracts from the outfalls off the coast of California, US. To evaluate the reproductive effects of each agent, Japanese medaka were exposed to aqueous concentrations of oxybenzone and benzophenone that had elicited vitellogenin induction in the previous study. Fecundity and hatchability showed a similar trend with that of vitellogenin induction, but no significant differences were observed relative to control with both agents. These data indicate that oxybenzone and benzophenone do not alter endocrine or reproduction endpoints in two fish species at concentrations measured in the environment.	Coronado *et al*. 2006
Zebrafish (*Danio rerio*) and mammalian cell lines	Octyl methoxycinnamate (ethylhexyl methoxycinnamate), octyl dimethyl-*p*-aminobenzoic acid (ethylhexyl dimethyl PABA), homosalate, benzophenone-3, 4-methylbenzylidene camphor and butyl methoxydibenzoylmethane were assessed for estrogenicity using both an *in vitro* reporter gene assay using human embryonal kidney 293 cells and *in vivo* using the transgenic zebrafish assay. All six compounds were found to activate the alpha estrogen receptor ER_α in a dose-dependent manner in the reporter gene assay and four out of the six induced transcriptional activity of ER_β. In the transgenic zebrafish assay, none of the compounds induced transcriptional activation (maximum concentrations tested were generally 10 µM).	Schreurs *et al.* 2002
South African clawed frog (*Xenopus laevis*)	3-(4-Methylbenzylidene)-camphor (4-MBC) was tested for its potential to bind to and activate endogenous estrogen receptors (ER). At a concentration of 100 µM, 4-MBC weakly binds to the ER, but is not able to completely replace estradiol from the receptor. The results of a gene induction assay indicate that 4-MBC has the potential to change physiological and developmental processes mediated by ER signalling mechanisms, and therefore may be harmful for water dwelling animals when present at micromolar concentrations.	Klann *et al.* 2005

Species	**Brief summary of result**	**Reference**
Rat	Groups of two-month-old female Sprague-Dawley rats were treated by gavage with five concentrations of 4-MBC over a period of five days on a background of a soy-free diet two weeks after bilateral ovariectomy. Thyroid stimulating hormone (TSH) serum levels were significantly elevated from concentrations of 33 mg/kg b.w., while T4 serum levels were slightly decreased and T3 levels almost unchanged. This serum data are typical for the early stages of hypothyroidism, when the peripheral organs maintain T3 serum levels during the initial phase of the disease. In the pituitary, TSHα and TSHβ were markedly increased from concentrations of 33 mg/kg b.w. (≥ 2 fold change). Additionally, the weight of the thyroid glands was remarkably increased after five days of treatment at concentrations exceeding 33 mg/kg b.w. These results indicate that 4-MBC is a potent inhibitor of the pituitary-thyroid-axis.	Hamann *et al*. 2006
Rat	Multiple organ ED activity of BP2 (benzophenone-2) was investigated by measuring expression of marker genes in the uterus, liver, vagina and pituitary after five days oral application in adult ovariectomized rats. An effect on lipid metabolism was assessed by determination of cholesterol, high- and low-density lipoproteins (HDL and LDL) in the blood. A dose dependent estradiol (E2)-agonistic activity was observed in the uterus (increased weight), vagina (increased IGF1 expression), pituitary (reduced luteinising hormone (LH) synthesis), liver (increased IGF1 expression) and lipid parameters (reduction). A non-E2-like action of BP2 was observed on T4- and T3-levels, which were significantly reduced. Except for the action on thyroid hormone levels where it may inhibit thyroid peroxidase, BP2 exerts clear E2-agonistic actions.	Jarry *et al*. 2004
Rat	A dose-response study was carried out on the estrogenic activity of benzophenone-2 on various endpoints in the serum, pituitary and uterus of female rats. Administration of BP-2 at dosages of 10–1000 mg/kg bodyweight led to changes of these parameters.	Schlecht *et al.* 2006
Rat	Octyl methoxycinnamate (ethylhexyl methoxycinnamate; OMC) and 4-methylbenzylidene camphor (4-MBC) were shown to exert endocrine disrupting effects including estrogenic effects in a study carried out on rats. It was concluded that these substances have effects on several metabolic parameters such as fat and lipid homeostasis as well as on thyroid hormone production.	Seidlova-Wuttke *et al.* 2005
Rat	Octyl methoxycinnamate (OMC) was found to have multi-organ estrogenic properties in an experiment carried out with adult ovariectomized rats. Effects on metabolic parameters were assessed by determination of the serum concentrations of leptin, cholesterol, high and low density lipoproteins, glucose and triglycerides. It was concluded that in addition to estrogenic actions of OMC, non-estrogenic effects were found for this chemical.	Klammer *et al.* 2005

Species	Brief summary of result	Reference
Rat	An *in vivo* study was conducted with ovariectomised rats treated for five days with different doses of octyl methoxycinnamate (ethylhexyl methoxycinnamate; OMC) to investigate effects on the hypothalamo-pituitary-thyroid (HPT) axis. Determined parameters comprised serum levels of TSH, T4 and T3, hypothalamic TRH mRNA expression, protein-expression of the sodium-iodide-symporter (NIS) and the TSH receptor, and the activities of thyroid peroxidase (TPO) in the thyroid and the T3-responsive hepatic type I 5'deiodinase (Dio1) in the liver. OMC caused a dose-dependent decrease of serum concentrations of all of these hormones. TRH expression remained unaffected, while in the thyroid expression of the TSH receptor but not of NIS was stimulated by OMC. TPO activity was unaltered but Dio1 activity was reduced by OMC. These results demonstrate a non-estrogenic interference of OMC within the rodent HPT axis with inadequate feedback response to impaired thyroid hormone status, indicated by decreased serum thyroid hormone and hepatic Dio1 levels.	Klammer *et al*. 2007
Rat	Estrogen target gene expression in the uterus of Long Evans rats exposed to 4-methylbenzylidene camphor (4-MBC) was studied. 4-MBC was found to alter steady-state levels of mRNAs encoding for ERα, ERβ, progesterone receptor, IGF-I, androgen receptor. Data from the study indicate that developmental exposure to 4-MBC affects the regulation of estrogen target genes and the expression of nuclear receptor coregulators in the uterus at mRNA and protein levels.	Durrer *et al.* 2005
Rat	Benzophenone (BP-1, BP-2, BP-3), 3-benzylidene camphor (3-BC), 4-methylbenzylidene camphor (4-MBC) and octylmethoxycinnamate (ethylhexyl methoxycinnamate; OMC) increased uterine weight in a study with immature Long Evans rats. 3-BC and 4-MBC displaced estradiol from the human estrogen receptor, ERβ. Weight gain of pregnant rats was reduced by 3-BC. Early postnatal survival rates, thymus weight and male puberty was reduced by 3-BC and 4-MBC. Reproductive organ weights of adult male and female F1 offspring were affected by 3-BC and 4-MBC. Thyroid weight was increased by 4-MBC. Tissue-specific changes in mRNA levels of estrogen-related genes in prostate, uterus and brain regions were observed. Lowest effective doses were 0.24 mg/kg/day for 3-BC and 7 mg/kg/day for 4-MBC.	Schlumpf *et al.* 2004 (similar results appear in Schlumpf *et al.* 2002, 2008a & 2008b – the later references include some further details)
Rat	Rats receiving 33 mg/kg body weight 4-MBC for five days showed a 15 per cent increase in thyroid-stimulating hormone, which prompts the thyroid to produce metabolism-regulating hormones. Those that received 600 mg/kg body weight per day had double the normal amount of thyroid stimulating hormone. Rats receiving a daily dose (over five days) of 100 mg/kg body weight 4-MBC showed a 20 per cent increase in thyroid size.	Khamsi 2006
Rat	The authors of this paper screened for the effects of benzophenone-2 (BP-2) on thyroid hormone biosynthesis and serum levels. Adult female ovariectomized rats were treated via gavage for five days with 10 mg/kg, 33 mg/kg, 100 mg/kg, 333 mg/kg and 1000 mg/kg body weight BP2. Data indicated that BP-2 interferes with thyroid hormone biosynthesis, thereby disturbing thyroid hormone homeostasis. The differences were significant for 333 mg/kg and 1000 mg/kg body weight BP2.	Schmutzler *et al.* 2006
Rat	3-(4-Methylbenzylidine) camphor (4-MBC) was found to be uterotrophic in immature rats when administered by either subcutaneous injection or oral gavage. There were also indications that 4-MBC binds to isolated rat uterine estrogen receptors and shows activity in a human estrogen receptor yeast transactivation assay. However, the authors considered both of these latter effects to be equivocal.	Tinwell *et al.* 2002

Species	Brief summary of result	Reference
Rat	The effects of 4-methylbenzylidene camphor (4-MBC) and 3-benzylidene camphor (3-BC) were investigated on the developing prostate of the fetal rat. Pregnant Long Evans rats were fed diets containing doses of 4-MBC and 3-BC that resulted in average daily intakes of these chemicals corresponding to the lowest observed adverse effects level (LOAEL) and the no observed adverse effects level (NOAEL) doses in prior developmental toxicity studies. Using digital photographs of serial sections from postnatal day one animals, the total volume for specific regions of the developing prostate was calculated from three-dimensional, surface-rendered models. Fetal exposure to 4-MBC (7.0 mg/kg body weight/day) resulted in a significant increase ($p < 0.05$) in tissue volume in the prostate and accessory sex glands. Treated males exhibited a 62 per cent increase in the number of ducts in the caudal dorsal prostate. 4-MBC exposure during development of the male reproductive accessory sex glands exhibited classical growth effects associated with estrogenic endocrine disruptors.	Hofkamp *et al*. 2008
Rat and human cells	Studies using 4-methylbenzylidene camphor (4-MBC). The direct interaction of 4-MBC with estrogen receptor (ER) α and ERβ was studied in a series of assays including receptor binding, ER transactivation and functional tests in human and rat cells. The study showed that 4-MBC is able to induce ERα and ERβ activity at relatively high doses (more than 1 µM).	Mueller *et al.* 2003
Mammalian (human?) cell lines	Tests for (anti-)estrogenic activity using 293HEK cells *in vitro* were carried out. Benzophenone-3, 3-benzylidene camphor, homosalate and 4-methylbenzylidene camphor were found to be antagonists towards the androgen receptor (AR) and the progesterone receptor (PR). Octyl dimethyl p-aminobenzoic acid (ethylhexyl dimethyl PABA) showed ER alpha antagonism. Octyl methoxy cinnamate (ethylhexyl methoxycinnamate) showed weak ER antagonism, but potent PR antagonism. Butyl methoxydibenzoylmethane showed weak ER alpha antagonism and weak AR antagonism. Most effects were observed at relatively high concentrations (above 1µM).	Schreurs *et al.* 2005
Japanese quail (*Coturnix japonica*)	The effects of 3-benzylidene camphor (3BC), 4-methyl benzylidene camphor (4MBC), benzophenone (BP), 1,2- and 3,4-hydroxybenzophenone (4-HB), 4-dihydroxybenzophenone (4DHB), benzyl salicylate (BS) and ethyl 4-aminobenzoate (Et-PABA) on the developing brain and gonads of bird embryos were studied. Exposure to 3BC or 4MBC caused ovotestis formation and malformations of the Müllerian ducts in Japanese quail embryos. The estrogenic effects were increased by co-exposure to the PCB mixture Clophen A50 (a well-known inducer of biotransformation enzymes).	Axelsson 2008

Other studies are available that have used human cell lines or *in vitro* yeast bioassays. These include Ashby *et al*. 2001, Schlumpf *et al*. 2001, Miller *et al.* 2001 and Ma *et al.* 2003. These studies have not been reviewed as part of this work. At the moment, it is not possible to relate effects seen in *in vitro* tests to effects in whole organisms (due to the influence of factors such as toxicokinetics).

From the available information, the substances listed in Table 47 appear capable of affecting the endocrine system in aquatic species and mammals.

Table 47 Endocrine active UV-filters

Substance	**Comment**
Homosalate	See Section 3.1.3
Benzophenone-1	Not listed in Directive 76/768/EEC – see Section 3.2
Benzophenone-2	Not listed in Directive 76/768/EEC – see Section 3.2
Benzophenone-3	Also known as oxybenzone – see Section 3.1.4
Butyl methoxydibenzoylmethane	Also known as 1-(4-tert-butylphenyl)-3-(4-methoxyphenyl) propane-1,3-dione or avobenzone – see Section 3.1.7
Ethylhexyl methoxycinnamate	Also known as octyl methoxycinnamate – see Section 3.1.11
4-Methylbenzylidene camphor	Also known as 3-(4'-Methylbenzylidene)-d-1 camphor or 3-(4-methylbenzylidene)camphor – see Section 3.1.17
3-Benzylidene camphor	See Section 3.1.18
Ethylhexyl dimethyl PABA	Also known as octyl dimethyl p-aminobenzoic acid and 4-dimethyl-amino-benzoate of ethyl-2-hexyl – see Section 3.1.20

These substances are considered to be a priority for further work based on their potential for affecting endocrine systems.[25] All except butyl methoxydibenzoylmethane have been considered under the European Commission's strategy for endocrine disrupters.[26] In all cases, they were categorised as 'substances with no or insufficient data gathered' (BKH 2002; DHI 2007). Currently, there is no co-ordinated European activity on testing; instead, substances may be nominated as priorities under existing regulatory schemes.

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[25] As benzophenone-1 and -2 are not listed in Annex VII of Directive 76/768/EEC, they are not approved for use in sunscreens in the EU and are not included in the conclusion (Chapter 6) for this reason.

[26] Further information is available at http://ec.europa.eu/environment/endocrine/strategy/short_en.htm

5 Environmental occurrence of UV-filters

The search for 'UV-filters' detailed in Chapter 4 also revealed a relatively large number of papers related to the levels of UV-filters found in water (surface water, groundwater and drinking water), as well as other environmental media in a few instances. The vast majority of the reported information relates to Switzerland – little or no monitoring data was found for the UK or for the rest of Europe in this search. The available data are briefly summarised in Table 48. Again, it should be noted that the search was not meant to be exhaustive and none of these data have been reviewed or validated in detail for this project – most of the values are taken from the abstract. The names used are as they appear in the papers, with the INCI name added if appropriate. Abbreviations are also used in the table following the first appearance of a substance.

A survey of analytical methods for a range of substances used in cosmetics, including UV filters, has been performed by the Danish Environmental Protection Agency (Vinzents & Pors 2007). The report is in Danish and only a very brief English summary is provided.

Table 48 Brief summary of readily available monitoring data for UV-filters

Location	Media monitored	Findings	Reference
Switzerland	Fish from rivers with inputs from waste water treatment plants (WWTPs)	4-Methylbenzylidene camphor (4-MBC) and octocrylene (OC) were determined in the muscle tissue of fish from seven small Swiss rivers, all receiving inputs from WWTPs. Lipid-weight based concentrations of up to 1,800 ng/g (4-MBC) and 2,400 ng/g (OC) were found. It was concluded that there is a higher availability of OC and 4-MBC for fish in rivers than in lakes and WWTPs are a major source for UV-filters in the aquatic environment.	Buser *et al.* 2006
Switzerland	Wastewater, surface waters and lake fish	4-MBC, OC, benzophenone-3 (BP-3) and ethylhexyl methoxy cinnamate (EHMC) were present in untreated wastewater (WWTP influent) (max. 19 μg/l for EHMC with influent loads increasing in the warmer season). Concentrations were considerably lower in WWTP effluent (max. 2.7 μg/l 4-MBC). The UV-filters were also detected in Swiss midland lakes and the River Limmat, all of which receive inputs from WWTPs (2–35 ng/l). Data also suggested the potential for these substances to accumulate in biota, with white fish, roach and perch taken from these lakes containing low but detectable concentrations of UV-filters (4-MBC 166 ng/g lipid basis).	Balmer *et al.* 2005

Location	**Media monitored**	**Findings**	**Reference**
Switzerland	Sewage sludge	Four widely used UV-filters originating mainly from private households (additional sources are surface runoff and industries) were found in sewage sludge originating from a monitoring network in Switzerland. Mean concentrations in stabilised sludge from 14 WWTPs were 1780 μg/kg, 110 μg/kg, 4840 μg/kg and 5510 μg/kg dry matter for 4-MBC, OMC, OC and octyl triazone respectively.	Plagellat *et al.* 2006
Switzerland	Surface water	PECs for EHMC were extrapolated from substance specific environmental fate monitoring data and by applying two environmental models. The worst case summer PEC is 70.8–81.3 ng/l and for the remaining eight months of the year the PEC is 13.1–15.1 ng/l	Straub 2002
Switzerland	Lakes	Concentrations of EHMC, OC, 4-MBC, butyl methoxydibenzoylmethane (BMDBM) and BP-3 in two Swiss lakes were found to be higher in summer compared to the rest of the year. In Lake Zurich, concentrations of individual UV-filters were low, ranging from the detection limit of <2 ng/l to 29 ng/l, but higher in Lake Huttnersee (a small bathing lake), at <2–125 ng/l.	Poiger *et al.* 2004
Germany	Human breast milk	BP-3 and octyl methoxycinnamate (presumably the same as EHMC) were determined in human breast milk samples at a concentration of 16 – 417 μg/kg (on a fat basis).	Hany and Nagel 1995 as reported in Geyer *et al*. 2000
Switzerland	Human breast milk	A monitoring study was conducted on human milk with three series of mother-child pairs (2004, 2005, 2006). Methods for UV-filter analysis followed the principles of European standardised methods for pesticide residue analysis (EN 15289). In cohorts 2004 and 2005, 78.8 per cent of women reported use of product(s) containing cosmetic UV-filters in a questionnaire, and 76.5 per cent of milk samples contained these filters. Use of UV-filters and their concentration in human milk were significantly correlated. The results agree with the idea of transdermal passage of UV filters. [The identity of the substances is not mentioned in the abstract, though it does mention 4-MBC and 3-benzylidene camphor in terms of toxicity results.]	Schlumpf *et al*. 2008b
Norway	Sea and WWTP discharge points	BP-3, EHMC, OC and 4-MBC were all ubiquitously detected in Oslo fjord near bathing areas and WWTP discharge points during summer 2006 as part of a pilot screening study. Trace levels of all targeted substances were also detected in winter suggesting that these seasonally-used chemicals are relatively persistent. The report also mentions a previous study that monitored BMDBM but it was not detected in any matrices. No further details are given.	SFT 2008

Geyer *et al*. 2000 report that several UV filters (4-MBC, BMDBM, BP-3, homosalate, EHMC and *p*-dimethylaminobenzoic isooctyl ester (assumed to be the same as ethylhexyl dimethyl PABA)) were detected in fish in Germany during the early 1990s, citing German references (particularly Nagtegaal *et al*. 1997). Concentrations are not given. A further overview (including some data from Norway, Germany and Slovenia) is provided by Fent *et al*. (2008).

The available monitoring data show that the investigated substances (generally the same substances as those investigated for effects on the endocrine system – see Chapter 4) have been found in waste water, surface water, sewage sludge and fish close to sources. These data confirm the presence of UV-filters in the environment from consumer use of the substances in sunscreen products. They also show that at least some of the substances can be taken up into biota, as may be expected from the relatively high log K_{ow} values predicted for many of these substances (detection in human tissues may arise as a direct consequence of skin application, so such data do not necessarily provide an indication of bioaccumulation potential). The measured concentrations in river water are between 10 and 1,000 times lower than the surface water PECs estimated in Chapter 3, which might reflect the conservative nature of the calculations. However, it is very difficult to make a direct comparison, given the limited data set.

6 Conclusions

Worst case calculations show that almost all of the UV-filters considered in this study give PEC/PNEC ratios above 1 (a potential risk) for production sites. This most probably reflects the highly conservative nature of the approach taken rather than any actual risk at such sites, and so any substance that flags as a concern for production only is not considered a priority for further investigation.

Several of the substances also give PEC/PNEC ratios above 1 for use in sunscreens (and some other applications where relevant). Although the approach is conservative, it is possible that these substances may present a risk to the environment. Meeting the EU screening PBT/vPvB criteria, or having apparent endocrine disrupting properties, are additional factors that raise the overall priority ranking. Finally, the supply tonnage is also relevant – regulatory resources are usually best targeted at those substances that are on the market in the highest amounts. The resulting priority list based on these factors is presented in Table 49.

In considering substances for further work, it may be relevant to use a grouping approach, such as similarity of chemical structures, to facilitate read-across of data. Although this can be a complicated approach, based on the discussion in Section 3.3 a tentative grouping approach might be as follows:

Group A – benzophenone-type derivatives;
Group B – benzotriazole-type derivatives;[27]
Group C – benzylidene malonate-type derivatives;
Group D – triazine derivatives; and
Group E – others.

These are mentioned in Table 49. It should be noted that other groupings may also be relevant (such as by including UV-stabilisers) and it might be possible to read across data from those UV-filters that have been notified as new substances (see Chapter 3 and the Confidential Annex for further details), since these should already have a reliable data set. In addition, further examples of Group A, B and C structures could possibly be used as UV-filters in sunscreens outside the EU, and these might also have data that could be useful in any grouping approach.

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[27] Based on the analysis in this report, the risk to the environment from use of this type of UV-filter in sunscreens generally appears to be low (see Section 3.1.5).

Table 49 Priority list for further work

Group	CAS No	Name	Possible risk in use	PBT/vPvB candidate	Potential endocrine effect	Supply tonnage[a]
A	131-57-8	Benzophenone-3	-	-	✓	LPV
A/E	118-56-9	Homosalate	✓	✓	✓	LPV
	118-60-5	Ethylhexyl salicylate	✓	-	-	LPV
	21245-02-3	Ethylhexyl dimethyl PABA	✓	✓	✓	LPV
C	5466-77-3	Ethylhexyl methoxycinnamate	✓	-	✓	HPV
	6197-30-5	Octocrylene	✓	✓	-	LPV
	15087-24-8	3-Benzylidene camphor	✓	✓	✓	LPV
	36861-47-9/ 38102-62-4	4-Methylbenzylidene camphor	✓	✓	✓	LPV
	71617-10-2	Isoamyl-p-methoxycinnamate	✓	-	-	LPV
E	70356-09-1	Butylmethoxydibenzoyl methane	✓	-	✓	LPV

Note: a) HPV = high production volume substance (EU supply > 1,000 tonnes/year); LPV = low production volume substance (EU supply 10–1,000 tonnes/year).

The highest priority substances for further investigation are those that have a tick in every column: **homosalate**; **4-methylbenzylidene camphor**; **3-benzylidene camphor**; and **ethylhexyl dimethyl PABA** (although these are all supplied at relatively low volumes). Due to its supply level, **ethylhexyl methoxycinnamate** is also a high priority.

It is important to remember that this report is only concerned with priority setting – the listed substances do not necessarily pose any real danger for the environment. This can only be determined by more thorough assessment, and several actions could now be taken:

- An in-depth risk assessment could be performed, taking account of measured property data (if available) and the actual use pattern of the substances.

- The PBT properties of these substances will need to be investigated further, in accordance with the test strategy laid out in the relevant REACH guidance documents.

- For those substances that flag as potential endocrine disruptors, further testing may be needed to establish reliable NOECs for appropriate species and life cycle stages (the need for these data would depend on the outcome of the PBT testing).

Further progress can only be made in co-operation with the suppliers and their downstream users (Appendix 1 gives a list of relevant trade associations). In Europe, the REACH Regulation will compel industry to assess its products to ensure that they are safe. This will require registration, data collection and a risk assessment for any substance that is classified as hazardous. The timing of this process will depend on the supply level as well as the hazard classification. Regulatory authorities in the UK or other EU member states may wish to nominate some or all of these substances for evaluation under REACH at the appropriate time. This will ensure that any risk management measures proposed by industry are sufficiently rigorous to protect the environment.

The main focus of this work has been on the UV-filters listed in Schedule 7 of the Cosmetic Products (Safety) Regulations 2008 and Annex VII of Directive 76/768/EEC. Neither of these two sources list CAS numbers for the UV-filters, and it has not been possible to make an estimate of potential risks for those substances for which a chemical structure could not be established. These substances are therefore also priorities for further investigation, and the starting point would be to establish the chemical structures (and impurity profile and degradation products, where relevant). Such substances include:

> Polyacrylamidomethylbenzylidene camphor (CAS No 113783-61-2)
> Dimethicodiethylbenzalmalonate (CAS No 207574-74-1).

Finally, more information is needed on the properties of the nano-particulate form of titanium dioxide (CAS No 13463-67-7). This issue should be kept under review as more data become available under the REACH Regulation over the next few years.

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Abbreviations

Chv	Chronic toxicity value
EINECS	European Inventory of Existing Commercial Chemical Substances
ELISA	Enzyme-linked immunosorbent assay
ESD	Emission Scenario Document
ESIS	European chemical Substances Information System
EU	European Union
IUCLID	International Uniform Chemical Database
HALS	Hindered amine light stabilisers
HPV	High Production Volume
INCI	International Nomenclature of Cosmetics Ingredients
LOEC	Lowest observed effect concentration
LPV	Low Production Volume
NOEC	No observed effect concentration
PBT	Persistent, bioaccumulative and toxic
PEC	Predicted environmental concentration
PNEC	Predicted no effect concentration
QSAR	Quantitative structure-activity relationship
RCR	Risk characterisation ratio
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
RP-LC	Reverse-phase liquid chromatography
SPF	Sun protection factor
TGD	Technical Guidance Document
UV	Ultra-violet
vPvB	Very persistent and very bioaccumulative

Appendix 1 Trade Associations

Three relevant trade associations exist within the UK and EU. These are listed below.

CTPA (UK Cosmetic, Toiletry and Perfumery Association)
Josaron House, 5-7 John Princes Street
London WIG OJN
UK
http://www.ctpa.org.uk/home.asp

COLIPA (European Cosmetic, Toiletry and Perfumery Association)
Avenue Herrmann Debroux 15A
B-1160 Auderghem – Brussels
Belgium
http://www.colipa.com

ELiSANA (European Light Stabiliser and Antioxidant Association)
CEFIC
Avenue E. van Nieuwenhuyse 4
B-1160 Brussels
Belgium
http://www.cefic.be/Templates/shwAssocDetails.asp?NID=473&HID=26&ID=183

Other potentially useful trade associations include the following:

Physical sunscreen manufacturers association (PSMA)
http://www.cefic.org/Templates/shwAssocDetails.asp?NID=473&HID=27&ID=68

European Stabiliser Producers Association (ESPA)
http://www.stabilisers.org/

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