4-Nonylphenols

Key References:

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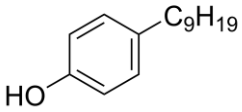
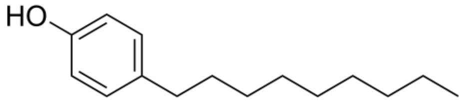
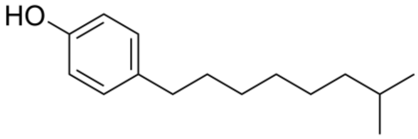
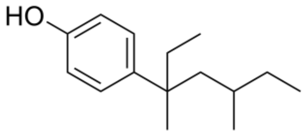
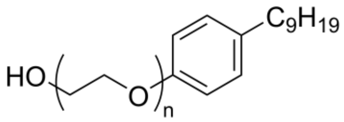
- European Chemicals Agency, ECHA SVHC Support Document for 4-Nonylphenol, branched and linear, 2012. https://echa.europa.eu/documents/10162/3024c102-20c9-4973-8f4e-7fc1dd361e7d
- European Chemicals Agency, ECHA SVHC Support Document for 4-Nonylphenol, branched and linear, ethoxylated, 2013. https://echa.europa.eu/documents/10162/9af34d5f-cd2f-4e63-859c-529bb39da7ae

Chemical Identification			
Name	**Abbreviation**	**CAS Numbers**	**Structure**
4-Nonylphenol, branched and linear	4NPs	84852-15-3; 26543-97-5; 104-40-5; 17404-66-9; 30784-30-6; 52427-13-1; 186825-36-5; 142731-63-3; 90481-04-2; 25154-52-3; others not identified	 CAS#: 84852-15-3  CAS#: 104-40-5  CAS#: 26543-97-5  CAS#: 186825-36-5
4-Nonylphenol, branched and linear, ethoxylated	4NPnEOs (where *n* is the grade of ethoxylation)	104-35-8; 7311-27-5; 14409-72-4; 20427- 84-3; 26027-38-3; 27942-27-4; 34166-38- 6; 37205-87-1; 127087-87-0; 156609-10-8; 68412-54-4; 9016-45-9; others not identified	

Completed assessments as the basis for inclusion: EU REACH SVHC

Notes: Nonylphenols are a group of chemicals that exist as many isomers having a nine carbon side chain which can be attached at various points on a phenol ring. 4-nonylphenols (4NPs) are nonylphenol isomers that exist in both branched and linear forms. For the inclusion as Substances of Very High Concern (SVHCs) within the European chemicals regulation, REACH [1], 4NPs are defined as “substances with a linear and/or branched alkyl chain with a carbon number of 9 covalently bound in position 4 to phenol, covering also UVCB* and well-defined substances which include any of the individual isomers or a combination thereof.”
4-nonylphenol polyethoxylates (4NPnEOs) are 4-nonylphenol isomers that exist in both branched and linear forms and contain an ethoxylated phenol ring with varying grades (chain lengths) of *n* ethoxylation. Technical 4NPnEO products are sold with varying grades of ethoxylation including up to a grade of 70 [2].

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* UVCB: Substances of unknown or variable composition, complex reaction products or biological materials.

Physical and Physicochemical Properties

Property	**4NPs** CAS#: 84852-15-3	**4NP (linear)** CAS#: 104-40-5	**4NP (minimally branched)** CAS#: 26543-97-5	**4NP (highly branched)** CAS#: 186825-36-5	**4NPnEOs** NP2EO[*] CAS#: 20427-84-3, NP10EO[*] CAS#: 29716-54-9
Molecular formula	$C_{15}H_{24}O$	$C_{15}H_{24}O$	$C_{15}H_{24}O$	$C_{15}H_{24}O$	$(C_2H_4O)_n\ C_{15}H_{24}O$
Molecular weight [g/mol]	220.4	220.4	220.4	220.4	308.5 (4NP2EO) to 660.9 (4NP10EO)
Physical state at 20°C	Liquid (see note below)	solid	solid	solid	solid
Melting point [°C]	-8 [3]	42 [4]	90 [†]	87 [†]	140 (4NP2EO) [†], 300 (4NP10EO) [†]
Density [g/cm^3]	0.95 [3]	NR	NR	NR	NR
Vapor pressure [mmHg]	$7.5*10^{-3}$ at 38 °C [3]; $2.25*10^{-3}$ at 25 °C [5]	$8.2*10^{-4}$ at 25 °C [5]	$6*10^{-5}$ at 25 °C[†]	$1.8*10^{-4}$ at 25 °C[†]	$1.33*10^{-7}$ (4NP2EO)[†] to $2.11*10^{-19}$ (4NP10EO)[†] at 25 °C
Water solubility at 25°C [mg/L]	5.7 [3]	7.0 [5]	1.2[†]	1.4[†]	1.05 (4NP2EO)[†] to 0.46 (4NP10EO)[†]
Octanol/water partition coefficient (log K_{OW})	5.4 [3]	5.76 [5]	5.92[†]	5.80[†]	5.30 (4NP2EO)[†] to 3.11 (4NP10EO)[†]
Organic carbon/water partition coefficient (log K_{OC})	4.41 (MCI Method)[†]; 4.28 (Kow Method)[†]	4.58 (MCI Method)[†]; 4.28 (Kow Method)[†]	4.51 (MCI Method)[†]; 4.37 (Kow Method)[†]	4.42 (MCI Method)[†]; 4.30 (Kow Method)[†]	3.394 (MCI Method)[†], 3.41 (Kow Method)[†] (4NP2EO) to 4.42 (MCI Method)[†]; 1.66 (Kow Method)[†] (4NP10EO)
Air/water partition coefficient (log K_{AW})	-3.61[†]	-2.86[†]	-3.61[†]	-3.61[†]	-6.98 (4NP2EO)[†] to -21.45 (4NP10EO)[†]
Dissociation constant (p*K*a)	Approx. 10 (or higher) [5]	NR	NR	NR	NR

Note: The physical state of 4NP (CAS# 104-40-5) is reported in the EU SVHC support document as being liquid, and the document does not provide a value for the melting point [5]. However, the reported melting point of 42 °C from another source suggests that it would be solid at 20 °C [4].

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[*] Derived from linear 4NP

[†] Estimated value using models in EPI Suite v4.11 [8].

NR = not reported

Degradation Pathways and Kinetics

Mechanism	Expected to occur?			Technosphere	Environment	Reference
	Yes	**No**	**Not reported**			
Hydrolysis		X				[5,6]
Photolysis	X				Shallow waters	[5–7]
OH-radical reactions	X				Atmosphere	[6,8]
Biodegradation	X			WWTP	Water, Sediments, Soil	[5,6]

Kinetics

Mechanism	Reported values	Reference
Photolysis	In clear shallow waters, half-lives of 10-15 h (4NPs)	[7]
OH-radical reactions	In atmosphere, half-lives of 2.48 h (4NPs) and 2.66 h (4NP1EO) to 0.88 h (4NP8EO)	[6,8]
Biodegradation (in water)	4NPs: Open flask (allowing volatilization): half-life = 2.5 d Closed flask: half-life = 16 d 4NPnEOs: Aerobic fresh water: >99 % degraded after 100 h, no change in 4NP concentration (mixture of 4NP2EO through 4NP15EO) Aerobic estuarine water: 100 % degraded after 4–24 d (adaption time of 0 –12 d, no 4NPs detected) (mixture of 4NP7EO through 4NP24EO, average NP18EO)	[8–11]
Biodegradation (in soil)	4NPs: Initially half-life = 4.5 to 16.7 d, then later >40 d (biphasic) 2.1 to 10.3 d (branched isomers), 1.4 d (linear isomer) 4NPnEOs: Dissipation half-life initially 7 d, then later 150 d, then >360 d (triphasic) (4NP1EO) Dissipation half-life initially 8 d, then later 110 d, then >360 d (triphasic) (4NP2EO) Dissipation half-life initially 0.3–5.2 d, then later 11.4–48 d (biphasic) (4NP12EO)	[8,12–15]
Biodegradation (in sediment)	4NPs: Freshwater sediments: half-life = 13.6–99 d (aerobic), 46.2 to >154 d (anaerobic) Marine sediments: half-life = 5.8 d to >70 d (aerobic or methanogenic) 4NPnEOs: Aerobic: half-life = 69–115 d (4NP1EO) Anaerobic: half-life = 49–77 d (4NP1EO)	[8,16–19]
Biodegradation (in WWTP sewage sludge)	4NPs: Aerobic: half-life = 7.5 d (at 20 °C) and 3.1–4.7 d (at 30 °C) (4NPs) Anaerobic: half-life = 38.5 d (at 20 °C) and 36.5 d (at 30 °C) (4NPs) 4NPnEOs: Anaerobic: 57% transformed into 4NP after 150 d (4NP2EO)	[8,19–21]

Notes: Degradation has generally been found to occur more quickly across environmental media under aerobic conditions than those under anaerobic conditions, with some studies finding little to no degradation under anaerobic conditions. The higher the branching degree of the alkyl chain, the lower the resulting biodegradability. Biodegradation is enhanced by increasing temperature, and microorganisms were found in some studies to need a period to adapt to an environment containing the nonylphenol before biodegradation could begin [6].

The ethylene oxide groups on highly-ethoxylated 4NPnEOs can break down and yield shorter-chain 4NPnEOs. The degradation rates of longer-chain 4NPnEOs were found to be similar or higher than those of shorter-chain 4NPnEOs [6]. Studies found that 4NPnEOs degrade into 4NPs at varying rates in wastewater treatment plant sludges, depending on the sludge composition [6].

Intentional Uses and Production Levels

Uses

4NPs

- Most commercialized forms of nonylphenols [22].
- Primarily used for the production of nonylphenol polyethoxylates (4NPnEOs) and also in lubricant additives, formaldehyde resins, epoxy resins, and polymeric stabilizers [22].

4NPnEOs

- Primarily used in industrial, commercial, and household products as surfactants [23].
- Also used in emulsion polymerization, textile and leather auxiliaries, paints, pesticides, metal processing, and film development [23].

Production Levels

4NPs

- First produced in 1940 with almost exponential increase in production and use in the years following [24].
- Reported and estimated annual production levels: 154 200 tonnes in the United States 2001 [24], 16 500 tonnes in Japan in the year 2000 [25], 16 000 tonnes in China in 2004 [24], and near 73 500 tonnes in the EU in 1997 [23].
- Increased restrictions in the EU are estimated to have caused a decrease in production there by 50 % since the year 2005 [26].
- Switzerland has banned the use of both nonylphenol and nonylphenol ethoxylates [27].
- Production has been noted in developing countries and countries with economies in transition including China, India, and across South America with no known phase-out schedules in place, and annual production is estimated to be increasing in some of these markets [28].

4NPnEOs

- Estimated worldwide production: 520 000 tonnes in 1995 [29].
- Annual production in the EU: 118 000 tonnes in 1997 [23].
- Annual production in Japan: 34 600 tonnes in 1998 [25].
- Estimated production in China: 50 000 tonnes per year in 2006 [30].
- Replacement by alternative surfactants (often alcohol ethoxylates) in many of the European, Canadian, and Japanese markets [24].

Emission Sources into the Environment

- Limited information found on ongoing uses and release sources.
- Most releases occur during the use and disposal of products containing 4NPs and 4NPnEOs [28].

4NPs

	Emission Sources
Production	Likely released; e.g., estimated releases in Canada in 1996 with about 0.5 % by mass of total Canadian production [31].
Use	Diffuse emissions expected from degradation of nonylphenol ethoxylates; higher concentrations in the environment are found in closer proximity to urban or industrialized areas and storm water releases [28].
Disposal	• Degradation of nonylphenol ethoxylates, especially in wastewater treatment plant (WWTP) processes, are a source of release of NPs into the environment [32]. • One study identified that 60–65 % of nonylphenolic compounds entering a WWTP were released into the environment with much of the released nonylphenol found in the effluent sludge [33]. • Treated wastewaters released to nearby natural water bodies and contaminated sludge applied to open lands are important sources of environmental contamination [24].
Other sources	Not produced naturally [28].

4NPnEOs

	Emission Sources
Production	Not reported
Use	Continental releases into the environment estimated for Europe in 2002 from multiple sectors including releases of about 12 tonnes per day in the agricultural industry, 18 tonnes per day from textile processing, and 51 tonnes per day in the public domain as industrial and institutional cleaning products [23].
Disposal	The degradation of nonylphenol ethoxylates, especially in wastewater treatment plant (WWTP) processes, are a source of release of NPs into the environment [32].
Other sources	Not produced naturally [28].

Distribution in the Abiotic Environment and Biota

Estimated Environmental Distribution

Based on the identified uses and emission sources for these chemicals as surfactants, a plausible emission pattern was assumed to estimate the resulting distribution in the natural environment using the Level III fugacity model in EPI Suite [8]. The assumed emission pattern and the resulting environmental distribution from the model are presented in the table below for each chemical.

	Assumed Emission Pattern			Modelled Distribution Results			
	Air	**Water**	**Soil**	**Air**	**Water**	**Soil**	**Sediment**
4NP linear	0 %	90 %	10 %	0 %	41 %	16 %	43 %
4NP min. branched	0 %	90 %	10 %	0 %	30 %	18 %	52 %
4NP highly branched	0 %	90 %	10 %	0 %	33 %	19 %	48 %
4NP2EO	0 %	90 %	10 %	0 %	71 %	24 %	5 %
4NP10EO	0 %	90 %	10 %	0 %	27 %	20 %	53 %

Bioaccumulation Potential

	Bioconcentration factor (BCF)	Organism	Reference
4NPs	740	fish	[3]
	124 (estimate for linear isomer, CAS# 140-40-5)	fish	[8]
	3138 (estimate for branched isomer, CAS# 186825-36-5)	fish	[8]
4NP2EO	34 (estimate)	fish	[8]
4NP10EO	29 (estimate)	fish	[8]

Measured Environmental Concentrations

Measured concentrations for these chemicals have been reported in numerous environmental media. A non-exhaustive set of reported concentrations is included below, and further measurements can be found in published literature including in the following:

- Careghini, A.; Mastorgio, A. F.; Saponaro, S.; Sezenna, E. Bisphenol A, nonylphenols, benzophenones, and benzotriazoles in soils, groundwater, surface water, sediments, and food: a review. Environ. Sci. Pollut. Res. 2015, 22 (8), 5711–5741.

Concentrations are provided in varying units depending on the media. Mass per mass dry weight (dw) and wet weight (ww) are sometimes used. ND = not detected, i.e., below the limit of detection (LOD). NQ = not quantified, i.e., below the limit of quantification (LOQ). NR = not reported.

Measured compartment	**Sampling location**	**Sampling Year**	**Number of samples**	**Concentration range**	**Median concentration**	**Samples > LOD**	**Refer-ence**
4-Nonylphenols (4NPs)							
River water (low-flow season)	China	2005/2006	8	0.036 – –33.23 µg/L	2.52 µg/L	100 % (LOD = 0.1 ng/L)	[35]
River water (high-flow season)	China	2005/2006	10	0.48 – –30.55 µg/L	1.28 µg/L	100 %	[35]
River water (Mississippi River)	United States	1999	6	ND	<0.05 µg/L	NR	[36]
River water (Cuyahoga River)	United States	2000	4	0.07 – –0.20 µg/L	0.14 µg/L	NR	[36]
River water (Texacoco River)	Mexico	2001	15	0.93 – –7.6 µg/L	NR	NR	[37]
Wastewater influent (Chicago)	United States	2005/2006	7	3.4 – –150 µg/L	79 µg/L	NR	[36]
4NP1EO							
River water (Mississippi River)	United States	1999	6	ND	<0.05 µg/L	NR	[36]
River water (Cuyahoga River)	United States	2000	4	0.05 – –0.14 µg/L	0.05 µg/L	NR	[36]
River water (Texacoco River)	Mexico	2001	15	ND – –6.1 µg/L	NR	NR	[37]

Measured compartment	**Sampling location**	**Sampling Year**	**Number of samples**	**Concentration range**	**Median concentration**	**Samples > LOD**	**Refer-ence**
Wastewater influent (Chicago)	United States	2005/2006	7	2.9 – –58 µg/L	15 µg/L	NR	[36]
4NP4EO							
River water (Mississippi River)	United States	1999	6	ND	<0.05 µg/L	NR	[36]
River water (Cuyahoga River)	United States	2000	4	ND – –0.05 µg/L	<0.05 µg/L	NR	[36]
Wastewater influent (Chicago)	United States	2005/2006	7	ND – –3.1 µg/L	1.4 µg/L	NR	[36]

Scientific Evidence of Adverse Endocrine-Related Environmental Effects

Reported scientific evidence of adverse endocrine-related environmental effects from exposure to 4NPs and 4NPnEOs exist for different organisms and across different study levels. A comprehensive but non-exhaustive set of reported observations is included below, and further observations can be found in published literature reviews including in the following:

- A. Soares, B. Guieysse, B. Jefferson, E. Cartmell, J.N. Lester, Nonylphenol in the environment: A critical review on occurrence, fate, toxicity and treatment in wastewaters, Environ. Int. 34 (2008) 1033–1049. doi:10.1016/j.envint.2008.01.004
- European Chemicals Agency, ECHA SVHC Support Document for 4-Nonylphenol, branched and linear, 2012. https://echa.europa.eu/documents/10162/3024c102-20c9-4973-8f4e-7fc1dd361e7d

Population level / field studies

No reported studies investigating this level were identified during the preparation of this fact sheet.

In vivo level

Substance	**Organism**	**Observation**	**Reference**
4NP; 4NPnEO	frog, medaka	Increased vitellogenin level in males (feminization)	[38–41]
4NP; 4NPnEO	carp, medaka, rainbow trout	Histological alterations in gonads (testis, ovaries)	[41–43]
4NP	rainbow trout, oyster	Impaired reproduction (fecundity, fertility, spermatogenesis inhibition)	[44–46]
4NP; 4NPnEO	medaka, oyster	Altered sex ratio (skewed to females)	[47–49]
4NP	amphibians	Thyroid axis related developmental effects	[50,51]
4NP	crassostrea gigas larvae	Growth and abnormal developments of individuals	[52]
4NP	fish (various species)	Altered spawning behaviour	[53,54]

In vitro level

Substance	Cell line	Observation	Reference
4NP	MCF-7	Induced cell proliferation and adipocyte formation	[55–57]
4NP	MCF-7, yeast (Sphingobium xenophagum Bayram)	Estrogen receptor (ER) activation (including binding and transcription processes)	[56,58]
4NP; 4NPnEO	rainbow trout hepatocytes, male African clawed frog hepatocytes	Vitellogenin* mRNA or protein expression	[59–61]
4NP	yeast two-hybrid system, stickleback kidney cell	Androgen receptor (AR) blockage (receptor inhibition or suppression of androgen production)	[62,63]
4NP	blood plasma from bear cubs, thyroid hormone transport protein transthyretin from several species	Weak potency to bind to thyroid hormone transport proteins	[64,65]

Notes:
The exact chemicals (including CAS numbers) used in the studies are often not reported, and instead mixtures are commonly reported to have been used.
Based on available information, it can be expected that in-vivo data for branched nonylphenols describe the adverse effects for linear nonylphenols as well [5].
Nonylphenol ethoxylates are expected to have similar effects to nonylphenols, and toxicity to aquatic organisms tends to decrease with increasing degree of ethoxylation [66].

* Vitellogenin is a precursor protein normally synthesized by females during oocyte maturation.

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4-tert-Octylphenols

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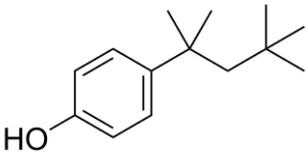
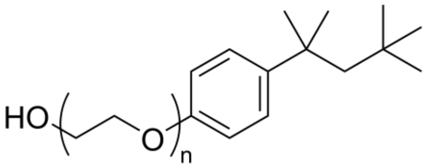
- European I Chemicals Agency, SVHC Support Document: 4-(1,1,3,3-Tetramethylbutyl)phenol, ethoxylated, 2012. https://echa.europa.eu/candidate-list-table/-/dislist/details/0b0236e1807db570.
- C.A. Staples, G.M. Klecka, C.G. Naylor, B.S. Losey, C8- and C9-Alkylphenols and Ethoxylates: I. Identity, Physical Characterization, and Biodegradation Pathways Analysis, Hum. Ecol. Risk Assess. An Int. J. 14 (2008) 1007–1024. doi:10.1080/10807030802387705.

Chemical Identification			
Name(s)	**Abbreviation**	**CAS Number**	**Structure**
4-tert-Octylphenol; 4-(1,1,3,3-tetramethylbutyl)phenol	4tOP	140-66-9	
4-tert-Octylphenol, ethoxylated; 4-(1,1,3,3-tetramethylbutyl)phenol, ethoxylated	4tOPnEO (where *n* is the grade of ethoxylation)	2315-67-5; 2315-61-9; 2497-59-8; 9002-93-1; others not identified	
Completed assessments as the basis for inclusion: EU REACH SVHC			

Physical and Physicochemical Properties			
Property	**4tOP**	**4tOP1EO** CAS#: 2315-67-5	**4tOP10EO** CAS#: 9002-93-1
Molecular formula	$C_{14}H_{22}O$	$(C_2H_4O)_1C_{14}H_{22}O$	$(C_2H_4O)_{10}C_{14}H_{22}O$
Molecular weight [g/mol]	206.32	250.38	646.86
Physical state at 20°C	solid	solid	solid
Melting point [°C]	84 - 85 [1]; 79 - 82 [2]	102†	309†
Density [g/cm^3]	0.89 at 90°C [1]; 0.95 [2]	NR	NR
Vapor pressure at 25°C [mmHg]	$1.575*10^{-3}$ [3]; $7.5*10^{-3}$ [2]	6.99†	$4.42*10^{-18}$ †
Water solubility [mg/L]	19 at 22 °C [2]; 12.6 at 20.5 °C [4]	8.0 at 20.5 °C [4]; 5.4†	2.3†
Octanol/water partition coefficient (log K_{OW})	4.1 [5]; 3.7 [6]	4.86†	2.39†
Organic carbon/water partition coefficient (log K_{OC})	4.0 (MCI method)†; 4.0 (Kow method)†	2.9 (MCI method)†; 3.3 (Kow method)†	3.8 (MCI method)†; 1.3 (Kow method)†
Air/water partition coefficient (log K_{AW})	-3.7†	-5.3†	-21.6†
Dissociation constant (pKa)	10.33 at 25 °C (estimated) [2]	NR	NR

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† Estimated value using models in EPI Suite v4.11 [9].
NR = not reported

Degradation Pathways and Kinetics

Mechanism	Expected to occur?			Technosphere	Environment	Reference
	Yes	No	Not reported			
Hydrolysis		4tOP; 4tOPnEO				[3,7]
Photolysis	4tOP; 4tOPnEO				Surface water	[8]
OH-radical reactions	4tOP; 4tOPnEO				Atmosphere	[9]
Biodegradation	4tOP; 4tOPnEO (inherently, see notes)			WWTP	River water	[3]

Kinetics – 4-tert-Octylphenol (4tOP)

Mechanism	Reported values	Reference
OH-radical reactions	Half-life = 0.25 d	[8]
Photolysis in water	Half-life = 6.9–13.9 h	[3,8]
Biodegradation (mixed population of non-adapted micro-organisms from activated sewage sludge)	No degradation after 28 d	[3]
Biodegradation (non-adapted aerobic micro-organisms from activated sludge)	20 % degraded after 28 d	[3]
Biodegradation (domestic activated sludge)	69.9 % degraded after 35 d	[3]
Biodegradation (bacterial community isolated from activated sludge, aerobic conditions)	> 90 % degraded after 32 h	[10]
Biodegradation (bacterial community isolated from activated sludge, anaerobic conditions)	20 % degraded after 36 h	[10]
Biodegradation (river water)	Half-life = 7–50 d	[3]

Kinetics – 4-tert-Octylphenol, ethoxylated (4tOPnEO)

Mechanism	Reported values	Reference
Biodegradation (bacterial community isolated from activated sludge, aerobic conditions)	>90 % degraded (Triton X-100 & Triton X-15) within 36 h	[10]
Biodegradation (bacterial community isolated from activated sludge, anaerobic conditions)	>90 % degraded (Triton X-100) within 36 h; 35 % degraded (Triton X-15) within 36 h	[10]

Notes:
Due to the similar structures of octylphenol and nonylphenol and that octylphenol can be a significant impurity in nonylphenol, it can be expected that some degree of general acclimation of microbial populations has occurred. Therefore, 4tOP is considered to be inherently biodegradable. [3]

Triton is a commercially available mixture of ethoxylated 4tOP of different ethoxylation degrees. The average ethoxylation degree of Triton X-100 is 9.5 and that of Triton X-15 is 1.5 [11,12].

Intentional Uses and Production Levels

Uses

4tOP

- Use in the EU: 1050 tonnes in 2001, primarily for the production of phenolic resins (98 % of total use), mostly for the manufacture of tire rubber and also electrical insulation coatings, adhesives, paints and printing inks [13–15].
- 2 % of the total use in the EU in 2001 for the production of octylphenol ethoxylates and subsequent derivatives [15].
- Switzerland and Norway have largely prohibited the use of octylphenol [15,16].

4tOPnEOs

- Used mostly used in the EU for emulsion polymerization (52 %) in 2001 [14].
- Additional uses: textile and leather finishing (14 % of uses in the EU in 2001), pesticide formulations as emulsifiers (4 % of uses in the EU in 2001), and minor uses in water-based paints and veterinary medicines [15].
- Use largely prohibited in Switzerland and Norway [15,16].

Production Levels

4tOP

- Production in the EU: 22 663 tonnes in 2001 [14].

Emission Sources into the Environment

- Limited information was found for ongoing uses and release sources of 4tOP and 4tOPnEOs.
- Similarly to nonylphenols, some direct releases from production, use of containing products, and disposal and treatment of wastes are likely to occur.

4tOP

	Emission Sources
Production	• Potential release as impurity during the production of nonylphenols [15]. • 240 kg released from one facility in the UK to controlled waters in 2003 [15]. • Estimated to be similar to emissions from nonylphenol production due to almost identical production processes [15].
Use	Primarily from abrasion of tires, marine paint application, and production of resins [15].
Disposal	No information found on specific releases during disposal. However, based on the products they are used in, releases may occur from disposal of products containing them (such as marine paints and improper disposal of tires).
Other sources	Not reported

4tOPnEOs

	Emission Sources
Production	200 kg released from one facility in the UK to controlled waters in 2003 [15].
Use	Primarily from washing of imported textiles [10] and from use of pesticides [15].
Disposal	Not reported
Other sources	Not reported

Distribution in the Abiotic Environment and Biota

Estimated Environmental Distribution

Inadequate data regarding the emission patterns for these chemicals across their wide range of uses have been identified, hindering a representative understanding of their environmental distribution. Additional efforts are needed to better understand the emission patterns, and environmental models (e.g., the Level III fugacity model in EPI Suite [9]) could then be used to estimate the distribution of these chemicals across the different environmental compartments.

Bioaccumulation Potential

	Bioconcentration factor (BCF)	Organism	Reference
4tOP	12-470	fish (several species)	[17]
4tOP1EO	417 (estimate)	fish	[9]
4tOP10EO	10 (estimate)	fish	[9]

Measured Environmental Concentrations

Measured concentrations for these chemicals have been reported in numerous environmental media. A non-exhaustive set of reported concentrations is included below, and further measurements can be found in published literature including in the following:

- G. Klečka, J. Zabik, K. Woodburn, C. Naylor, C. Staples, B. Huntsman, Exposure Analysis of C8- and C9-Alkylphenols, Alkylphenol Ethoxylates, and Their Metabolites in Surface Water Systems within the United States, Hum. Ecol. Risk Assess. An Int. J. 13 (2007) 792–822. doi:10.1080/10807030701456726.

Concentrations are provided in varying units depending on the media. Mass per mass dry weight (dw) and wet weight (ww) are sometimes used. ND = not detected, i.e., below the limit of detection (LOD). NQ = not quantified, i.e., below the limit of quantification (LOQ)). NR = not reported.

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concentration**	**Samples > LOD**	**Reference**
4-tert-Octylphenol (4tOP)							
River water	China	2015	4	1.20–3.99 ng/L	1.38 ng/L	100 % (LOD = 0.13 ng/L)	[18]
River water	Vietnam	2013	36	ND–35 ng/L	NR	NR (LOD = 2.0 ng/L)	[19]
River water	China	2009	26	1.54–45.8 ng/L	4.12 ng/L	100 % (LOD = NR)	[20]
River water	China	2008	30	2.4–14.5 ng/L	4.3 ng/L	100 % (LOD = NR)	[21]
River water	UK	2005	8	NR–37.6 ng/L	NR	100 % (LOD = 0.1 ng/L)	[22]
River water	Germany	2000	15	ND–5 ng/L	2.5 ng/L	93 % (LOD = NR)	[23]
River water	Canada	1999	5	ND–48 ng/L	ND	40 % (LOD = 1 ng/L)	[24]
River water	Germany	1998/1999	19	0.4–6.0 ng/L	1.0 ng/L	100 % (LOD = NR)	[25]
Sea water (surface microlayer)	Poland	2011/2012	54	ND–177.9 ng/L	19.4 ng/L	NR	[26]
Sea water (sub-surface water, river outlet)	Poland	2011/2012	24	ND–834.8 ng/L	6.0 ng/L	NR	[26]
Sea water (sub-surface water, coastal sea)	Poland	2011/2012	36	ND–63.0 ng/L	5.8 ng/L	NR	[26]

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concen-tration**	**Samples > LOD**	**Refer-ence**
Sea water (open water <4 m depth)	Poland	2011/ 2012	30	ND–65.9 ng/L	2.3 ng/L	NR	[26]
Sea water (near bottom)	Poland	2011/ 2012	30	ND–56.4 ng/L	0.1 ng/L	NR	[15]
Sea water	Portugal	2010	36	4.3–41 ng/L (mean values)	NR	NR	[27]
Sea water	Greece	2005/ 2006	22	1.7–18.2 ng/L	NR	NR	[28]
Sea water	USA	1999	21	1.56–8.34 ng/L	2.76 ng/L	100 % (LOD = 0.08 ng/L)	[29]
Sea water	Germany	1998/ 1999	19	0.02–18 ng/L	3.6 ng/L	100 % (LOD = NR)	[25]
River sediment	China	2015	4	ND	ND	0 % (LOD = 0.17 ng/g dw)	[18]
River sediment	China	2009	25	0.14–1.7 ng/g dw	0.52 ng/g dw	100 % (LOD = NR)	[20]
River sediment	China	2008	29	ND–2.6 ng/L	ND	38 % (LOD = NR)	[21]
River sediment	UK	2005	8	4.7–31.3 ng/g	NR	100 % (LOD = 0.14 ng/g)	[22]
River sediment	Germany	1998/ 1999	11	21–86 ng/g dw	39 ng/g dw	100 % (LOD = NR)	[25]
Sea Sediment	Greece	2005/ 2006	20	6.0–25.0 ng/g dw	NR	NR	[28]
Sea sediment	China	2010/ 2011	66	0.7–11.1 ng/g dw	5.1 ng/g dw	100 % (LOD = NR)	[30]
Sea sediment	India	2014	30	107.35–268.89 ng/g dw	184.07 ng/g dw	(LOD = 0.1 ng/g dw)	[31]
Sea sediment	USA	1999	10	ND–45.0 ng/g	ND	50 % (LOD = NR)	[29]
Suspended particulate matter (sea)	Greece	2005/ 2006	22	61–196 ng/g dw	NR	NR	[28]
4tOP1EO							
River water	Germany	1998/ 1999	19	0.8–6.3 ng/L	1.5 ng/L	100 % (LOD = NR)	[25]
Sea water	Portugal	2010	36	6.9–36 ng/L (mean values)	NR	NR	[27]
Sea water	Greece	2005/ 2006	22	ND–9.5 ng/L	NR	NR (LOD = 4 ng/L)	[28]

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concen-tration**	**Samples > LOD**	**Refer-ence**
Sea water	USA	1999	21	2.27–26 ng/L	7.75 ng/L	100 % (LOD = 0.08 ng/L)	[29]
Sea water	Germany	1998/ 1999	19	0.1–12 ng/L	1.3 ng/L	100 % (LOD = NR)	[25]
River sediment	Germany	1998/ 1999	11	30–113 ng/g dw	91 ng/g dw	100 % (LOD = NR)	[25]
Sea sediment	Greece	2005/ 2006	20	ND– 14.3 ng/g dw	NR	NR (LOD = 5 ng/g dw)	[28]
Sea sediment	USA	1999	10	ND–45.0 ng/g	ND	50 % (LOD = NR)	[29]
Suspended particulate matter (sea)	Greece	2005/ 2006	22	9.3– 443 ng/g dw	NR	100 % (LOD = NR)	[28]
4tOP2EO							
River water	Vietnam	2013	36	ND–37.1 ng/L	NR	NR (LOD = 2.7 ng/L)	[19]
River water	Germany	1998/ 1999	19	0.6–6.8 ng/L	1.3 ng/L	100 % (LOD = NR)	[25]
Sea water	Greece	2005/ 2006	22	ND–11.7 ng/L	NR	NR (LOD = 4 ng/L)	[28]
Sea water	Portugal	2010	36	46–182 ng/L (mean values)	NR	NR	[27]
Sea water	USA	1999	21	1.7–15.6 ng/L	4.53 ng/L	100 % (LOD = 0.08 ng/L)	[29]
Sea water	Germany	1998/ 1999	19	0.1–21 ng/L	6.4 ng/L	100 % (LOD = NR)	[25]
Suspended particulate matter (sea)	Greece	2005/ 2006	22	71–429 ng/g dw	NR	100 % (LOD = NR)	[28]
Sea sediment	Greece	2005/ 2006	20	ND–66 ng/g dw	NR	NR (LOD = 5 ng/g dw)	[28]
Sea sediment	USA	1999	10	ND–46.6 ng/g	ND	50 % (LOD = NR)	[29]
River sediment	Germany	1998/ 1999	11	45–140 ng/g dw	110 ng/g dw	100 % (LOD = NR)	[25]
4tOP3EO							
River water	Vietnam	2013	36	ND–36 ng/L	NR	NR (LOD = 1.6 ng/L)	[19]
Sea water	USA	1999	21	0.31–10.3 ng/L	1.67 ng/L	100 % (LOD = 0.08 ng/L)	[29]
Sea sediment	USA	1999	10	ND–14.1 ng/g	ND	50 % (LOD = NR)	[29]

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concen-tration**	**Samples > LOD**	**Refer-ence**
4tOPnEO (unspecified mixture)							
River water	Germany	2000	15	ND–9.6 ng/L	2.2 ng/L	93 % (LOD = NR)	[23]

Scientific Evidence of Adverse Endocrine-Related Environmental Effects

Reported scientific evidence of adverse endocrine-related environmental effects from exposure to 4tOP exist for different organisms and across different study levels. A comprehensive but non-exhaustive set of reported observations is included below, and further observations can be found in published literature reviews including in the following:

- L.J. Mills, C. Chichester, Review of evidence: Are endocrine-disrupting chemicals in the aquatic environment impacting fish populations?, Sci. Total Environ. 343 (2005) 1–34. doi:10.1016/j.scitotenv.2004.12.070.
- European Chemicals Agency, SVHC support document 4-(1,1,3,3-tetramethylbutyl)phenol, (2011). https://echa.europa.eu/documents/10162/4c6cccfd-d366-4a00-87e5-65aa77181fb6.

Population level / field studies

No reported studies investigating this level were identified during the preparation of this fact sheet.

In vivo level

Substance	**Organism**	**Observation**	**Reference**
4tOP	frogs	No change in plasma steroid levels	[32]
4tOP	killfish, eelpout, atlantic salmon and frogs	Increased plasma or liver vitellogenin* level	[32–35]
4tOP	medaka and clams	Intersex gonads	[36,37]
4tOP	guppies	Histological alterations in gonads (testis, ovaries)	[38]
4tOP	rainbow trout	Delayed / reduced gonad development	[39]
4tOP	zebrafish, medaka and eelpout	Impaired reproduction (fecundity, fertility, spermatogenesis inhibition, impaired oocyte development, decreased egg production or egg fertility)	[34,36,40]
4tOP	guppies, medaka and frogs	Decreased / altered sexual behaviour in males	[36,41,42]
4tOP	guppies and frogs	No effect on sex ratio	[32,38]

In vitro level

Substance	**Cell line**	**Observation**	**Reference**
4tOP	rainbow trout cells	Weak estrogenic potential (to induce vitellogenin synthesis in primary hepatocytes)	[40,43]
4tOP	frogs	Vitellogenin* mRNA or protein expression	[44]
4tOP	carp and frogs	Competitive binding to the estrogen receptor (displacing 17β-estradiol) in liver cytosol of carp and frog estrogen receptor	[40,45]
4tOP	arctic charr	Competitive binding to sex steroid-binding protein in plasma	[46]

Notes: *Vitellogenin is a precursor protein normally synthesized by females to be incorporated in eggs.

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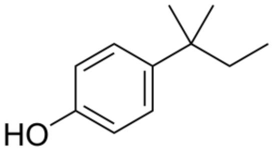
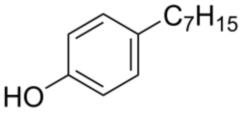
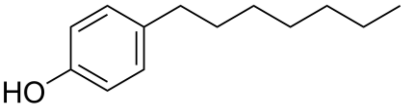
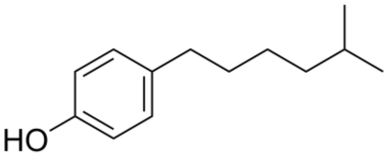
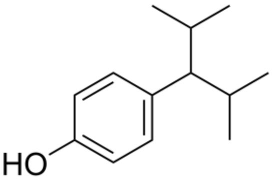
4-tert-pentylphenol & 4-heptylphenol, branched and linear

Key References:

- European Chemicals Agency, ECHA SVHC Support Document for 4-Heptylphenol, branched and linear, 2016. https://echa.europa.eu/documents/10162/f3dba6ab-8dd8-2457-4213-2f390b0539f1.
- European Chemicals Agency, ECHA SVHC Support Document for p-(1,1-dimethylpropyl)phenol, 2016. https://echa.europa.eu/documents/10162/3cbffe6e-fc78-0884-e5cd-a519eccf6a02.

Chemical Identification

Name(s)	Abbreviation	CAS Number(s)	Structure(s)
4-tert-pentylphenol; p-(1,1-dimethylpropyl) phenol; p-tert-amylphenol	4tPP	80-46-6	
4-heptylphenol, branched and linear	4HPbl	6465-71-0; 6465-74-3; 6863-24-7; 1987-50-4; 72624-02-3; 1824346-00-0; 1139800-98-8; 911371-07-8; 911371-06-7; 911370-98-4; 861011-60-1; 861010-65-3; 857629-71-1; 854904-93-1; 854904-92-0; 102570-52-5; 100532-36-3; 72861-06-4; 71945-81-8; 37872-24-5; 33104-11-9; 30784-32-8; 30784-31-7; 30784-27-1	 *CAS#: 72624-02-3*  *CAS#: 1987-50-4*  *CAS#: 100532-36-3*  *CAS#: 1824346-00-0*

Completed assessments as the basis for inclusion: EU REACH SVHC

Note: 4-Heptylphenols are a group of chemicals that exist as many isomers having an either linear or branched seven carbon side chain in the para-position relative to the OH-group. For inclusion as Substances of Very High Concern (SVHCs) within the European chemicals regulation (REACH) [1], 4-Heptylphenols are defined as "substances with a linear and/or branched alkyl chain with a carbon number of 7 covalently bound predominantly in position 4 to phenol, covering also UVCB- and well-defined substances which include any of the individual isomers or a combination thereof."

Physical and Physicochemical Properties					
Property	**4tPP**	**4HPbl** (CAS#: 72624-02-3)	**4HPbl, linear** (CAS#: 1987-50-4)	**4HPbl, minimally branched** (CAS#: 100532-36-3)	**4HPbl, highly branched** (CAS#: 1824346-00-0)
Molecular formula	$C_{11}H_{16}O$	$C_{13}H_{20}O$	$C_{13}H_{20}O$	$C_{13}H_{20}O$	$C_{13}H_{20}O$
Molecular weight [g/mol]	164.25	192.3	192.3	192.3	192.3
Physical state at 20°C	solid	liquid	solid	solid	solid
Melting point [°C]	94.7 [2]	-9°C (pour point) [3]	80.4[†]	70.2[†]	49.6[†]
Density [g/ cm^3]	0.962 at 20°C [4]	0.965 at 15.6 °C [3]	NR	NR	NR
Vapor pressure at 25°C [mmHg]	$2.00*10^{-3}$ [5]	$1.95*10^{-3}$ [3]	$2.8*10^{-4}$ [†]	$5.1*10^{-4}$ [†]	$2.4*10^{-3}$ [†]
Water solubility at 25°C [mg/L]	193 at 21°C[2]; 168 at 25°C [6]	42 at 20°C [3]	9.6[†]	11.1[†]	14.9[†]
Octanol/water partition coefficient (log K_{OW})	3.6 at 22 °C[2] ; 4.03 [7]	NR	5.01[†]	4.93[†]	4.79[†]
Organic carbon/water partition coefficient (log K_{OC})	3.40 (MCI method)[†], 3.25 (Kow method)[†]	NR	(4.06 MCI method)[†], (3.86 Kow method)[†]	(3.99 MCI method)[†], (3.82 Kow method)[†]	(3.90 MCI method)[†], (3.74 Kow method)[†]
Air/water partition coefficient (log K_{AW})	-4.11[†]	NR	-3.86[†]	-3.86[†]	-3.86[†]
Dissociation constant (p*K*a)	10.43 [7]	10.25 [3]	NR	NR	NR

[†] Estimated value using models in EPI Suite v4.11 [9].
NR = not reported

Degradation Pathways and Kinetics

Mechanism	**Expected to occur?**			**Technosphere**	**Environment**	**Reference**
	Yes	**No**	**Not reported**			
Hydrolysis		4tPP; 4HPbl				[2,3]
Photolysis			4tPP; 4HPbl			
OH-radical reactions	4tPP; 4HPbl				Atmosphere	[2]
Biodegradation	4tPP; 4HPbl			WWTP		[2,3]

Kinetics – 4-tert-Pentylphenol (4tPP)

Mechanism	**Reported values**	**Reference**
OH-radical reactions	Half-life = 3 h (estimated)†	[2]
Biodegradation (domestic non-adapted activated sludge)	73 % degraded after 28 d	[8]
Biodegradation (activated sludge, adaptation not specified)	0 % degraded after 28 d	[8]

Kinetics – 4-Heptylphenol, branched & linear (4HPbl)

Mechanism	**Reported values**	**Reference**
OH-radical reactions	Half-life = 2.6 h (estimated)†	[9]
Biodegradation (closed bottle test)	1.6 % degraded after 28 d	[1]
Biodegradation (mixed culture inoculum derived from activated sewage sludge/soil)	25.4 % degraded after 29 d	[1]

Intentional Uses and Production Levels

Uses

4tPP

- Used as a monomer in the production of phenolic resins (novolaks and resols) which are used in paints, varnishes and as printing ink resins; ethoxylated novolaks are used as oil field demulsifiers [10].
- Used as a germicide in cleaning solutions [10].
- The disulphide derivative is used as a vulcanizing agent for the curing of rubber [10].

4HPbl

- No information available on uses; however, it is probable that they are used in applications similar to other alkylphenols including 4tPP and 4-nonylphenols.

Production Levels

4tPP and 4HPbl

- Both currently registered in the EU with 100–1000 tonnes per year of production or import [2].

Emission Sources into the Environment

4tPP

	Emission Sources
Production	Not reported
Use	Not reported. However, based on the reported uses (including in resins, cleaning solutions, and rubber) and its low air/water partition coefficients, releases from products could occur during use and enter the environment through wastewater treatment effluent or rainwater runoff.
Disposal	Not reported. However, depending on the treatment method of disposed products, releases into the environment could potentially occur through wastewater treatment plant effluents or leachate runoff from landfills.
Other sources	Not reported

4HPbl

	Emission Sources
Production	Not reported
Use	Not reported. However, based on their expected uses as well as their low air/water partition coefficients, releases from products could occur during use and enter the environment through wastewater treatment effluent or rainwater runoff.
Disposal	Not reported. However, depending on the treatment method of disposed products, releases into the environment could potentially occur through wastewater treatment plant effluents or leachate runoff from landfills.
Other sources	Not reported

Distribution in the Abiotic Environment and Biota

Expected Partitioning

Inadequate data regarding the emission patterns for these chemicals across their wide range of uses have been identified, hindering a representative understanding of their environmental distribution. Additional efforts are needed to better understand the emission patterns, and environmental models (e.g., the Level III fugacity model in EPI Suite [9]) could then be used to estimate the distribution of these chemicals across the different environmental compartments.

Bioaccumulation Potential

	Bioconcentration factor (BCF)	**Organism**	**Reference**
4tPP	177 (estimate)	fish	[9]
4HPbl	555 (steady state) – 578 (kinetic)	fish	[3]

Measured Environmental Concentrations

Measured concentrations for these chemicals have been reported in numerous environmental media. A non-exhaustive set of reported concentrations is included below.

Concentrations are provided in varying units depending on the media. Mass per mass dry weight (dw) and wet weight (ww) are sometimes used. ND = not detected, i.e., below the limit of detection (LOD). NQ = not quantified, i.e., below the limit of quantification (LOQ). NR = not reported.

Measured compartment	**Sampling location**	**Sampling Year**	**Number of samples**	**Concentration range**	**Median concen-tration**	**Samples > LOD**	**Refer-ence**
4-tert-Pentylphenol (4tPP)							
River water	Germany	2000	15	ND–5.9 ng/L	1.7 ng/L	53 % (LOD = NR)	[11]
River water	Germany	1998	13	0.1–0.7 ng/L	0.4 ng/L	100 % (LOD = NR)	[12]
River water	Germany	1998	6	ND–0.02 ng/L	ND	17 % (LOD = NR)	[12]
Sea water	Germany	1999	11	ND–7.7 ng/L	3.8 ng/L	82 % (LOD = NR)	[12]
Sea water	Germany	1998	8	ND–0.3 ng/L	ND	25 % (LOD = NR)	[12]
River sediment	Germany	2000	12	ND–1.9 ng/g dw	ND	17 % (LOD = NR)	[11]
River sediment	Germany	1998	11	ND–77 ng/g dw	31 ng/g dw	91 % (LOD = NR)	[12]
Industrial effluent	NR (Belgium)	NR (2004)	1	17.3 ng/L	17.3 ng/L	100 % (LOD = 5.0 ng/L)	[13]
4-Heptylphenol, branched & linear (4HPbl)							
River water	South Korea	2008	6	ND–10 ng/L	ND	17 % (LOD = NR)	[14]
River water	Japan	NR (2004)	1	ND	ND	0 % (LOD = NR)	[15]
River water	South Korea	2003	5	ND–166.4 µg/L	159.2 µng/L	80 % (LOD = 10 µg/L)	[16]
River water	South Korea	2002	5	ND–399 µg/L	362.7 µg/L	80 % (LOD = 10 µg/L)	[16]
River water	Japan	NR (2000)	1	80 ng/L	80 ng/L	100 % (LOD = 20 ng/L)	[17]
WWTP effluent	South Korea	2003	6	ND–180.6 µg/L	122 µg/L	83 % (LOD = 10 µg/L)	[16]
WWTP effluent	South Korea	2002	6	ND–384.1 µg/L	339.3 µg/L	67 % (LOD = 10 µg/L)	[16]

Note: Additional information regarding the sampling location and year is sometimes provided after values that are not reported (NR) in parentheses. This represents an estimated value for this not reported information based on the general details provided in the study.

Scientific Evidence of Adverse Endocrine-Related Environmental Effects

Reported scientific evidence of adverse endocrine-related environmental effects from exposure to 4HPbl or 4tPP exist for different organisms and across different study levels. A comprehensive but non-exhaustive set of reported observations is included below, and further observations can be found in published literature reviews including in the following:

- L.J. Mills, C. Chichester, Review of evidence: Are endocrine-disrupting chemicals in the aquatic environment impacting fish populations?, Sci. Total Environ. 343 (2005) 1–34. doi:10.1016/j.scitotenv.2004.12.070.

Population level / field studies

No reported studies investigating this level were identified during the preparation of this fact sheet.

In vivo level

Substance	Organism	Observation	Reference
4HPbl	atlantic cod	Changed plasma steroid levels	[18]
4HPbl	common carp, medaka and atlantic cod	Increased plasma, hepatic vitellogenin* levels	[18–22]
4HPbl	atlantic cod	Delayed gonad development	[23]
4HPbl	common carp and atlantic cod	Histological alterations in gonads (testis, ovaries)	[18,19]
4HPbl	common carp, medaka, atlantic cod and fathead minnow	Impaired reproduction (fecundity, fertility, spermatogenesis inhibition, impaired oocyte development, decreased egg production)	[18–22]
4HPbl	atlantic cod	Altered spawning behavior	[18]
4tPP	common carp and medaka	Exposure duration dependent altered sexual differentiation	[21,24]

In vitro level

Substance	Cell line	Observation	Reference
4tPP	rainbow trout cells	Estrogen receptor (ER) activation	[25]

Notes:
*Vitellogenin is a precursor protein normally synthesized by females to be incorporated in eggs.

References

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[2] European Chemicals Agency, Substance Registration Dossier for p-(1,1-dimethylpropyl)phenol, (2017). https://echa.europa.eu/de/registration-dossier/-/registered-dossier/14435/3/ (accessed March 6, 2017).

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Phthalates (EU SVHCs)

Key References:

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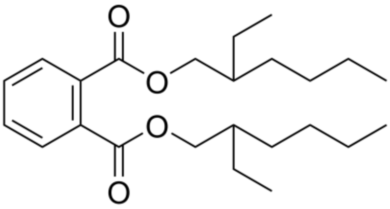
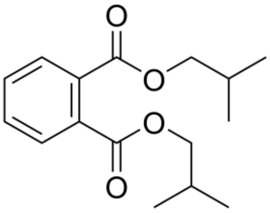
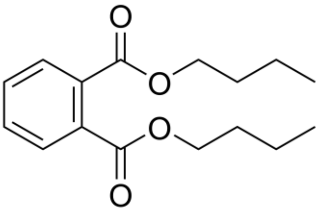
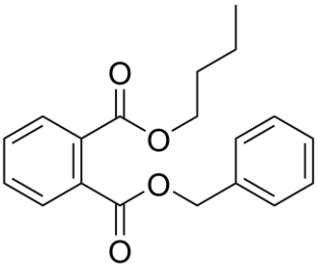
- C.A. Staples, D.R. Peterson, T.F. Parkerton, W.J. Adams, The Environmental Fate of Phthalate Esters: A Literature Review, Chemosphere. 35 (1997) 667–749.

Chemical Identification			
Name(s)	**Abbreviation**	**CAS Number**	**Structure**
Diethylhexyl phthalate; bis(2-ethylhexyl) phthalate	DEHP	117-81-7	
Diisobutyl phthalate	DIBP	84-69-5	
Dibutyl phthalate	DBP	84-74-2	
Benzylbutyl phthalate	BBP	85-68-7	

Completed assessments as the basis for inclusion: EU REACH SVHC

Notes: These phthalates are all used as plasticizers, with DEHP being the most common and limited information available for the others. These four phthalates are classified as Substances of Very High Concern (SVHCs) within the European Union.

Physical and Physicochemical Properties				
Property	**DEHP**	**DIBP**	**DBP**	**BBP**
Molecular formula	$C_{24}H_{38}O_4$	$C_{16}H_{22}O_4$	$C_{16}H_{22}O_4$	$C_{19}H_{20}O_4$
Molecular weight [g/mol]	390.6	278.3	278.3	312.4
Physical state at 20°C	liquid	liquid	liquid	liquid
Melting point [°C]	-55 [1]; -46 [2]	-64 [3]	-35 [1] [2]	-35 [2]
Density [g/cm^3]	0.981 at 25 °C [1]; 0.986 [2]	1.049 at 15 °C [1]	1.0465 at 20 °C [4]; 1.0459[4]; 1.0465 [2]	1.119 at 25 °C [1]; 1.1 [2]
Vapor pressure at 25°C [mmHg]	$1.42*10^{-7}$ [5]; $6.2*10^{-6}$ [2]	$4.76*10^{-5}$ [6]	$2*10^{-5}$ at 25 °C [7]; $1.4*10^{-5}$ at 20°C [2]	$8*10^{-7}$ [2]
Water solubility at 25°C [mg/L]	0.25 [8]; 0.34 [2]	6.2 at 24 °C [9]	11.2 at 20 °C [10]; 13 at 20 °C [2]	2.69 at 20 °C [2]
Octanol/water partition coefficient (log K_{OW})	7.45 [11]	4.46†; 4.11 (QSAR estimate) [12]	4.50 [13]	4.73 [13]
Organic carbon/water partition coefficient (log K_{OC})	5.08 (MCI method)†; 5.00 (Kow method)†	2.91 (MCI method)†; 3.07 (Kow method)†	3.06 (MCI method)†; 3.28 (Kow method)†	3.85 (MCI method)†; 3.41 (Kow method)†
Air/water partition coefficient (log K_{AW})	-4.96†	-4.30†	-4.13†	-4.29†
Dissociation constant (pKa)	Not applicable	Not applicable	Not applicable	Not applicable

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[†] Estimated value using models in EPI Suite v4.11 [16].
NR = not reported

Degradation Pathways and Kinetics

Mechanism	Expected to occur?			Technosphere	Environment	Reference
	Yes	No	Not reported			
Hydrolysis		DEHP; DIBP; DBP; BBP (all negligible)				[14]
Photolysis	DBP; BBP	DEHP (negligible)	DIBP		Surface water	[15]
OH-radical reactions	DEHP; DIBP; DBP; BBP				Atmosphere	[16,17]
Biodegradation	DEHP; DIBP; DBP; BBP			WWTP	Surface water	[17–20]

Kinetics – Diethylhexyl phthalate (DEHP)

Mechanism	Reported values	Reference
OH-radical reactions	Half-life = 1 d	[17]
Hydrolysis	Half-life = 2000 yr	[14]
Hydrolysis and photolysis (artificial river water, in sunlight)	Half-life = 1600 d (pH = 7)	[15]
Biodegradation (surface water)	Half-life = 50 d	[17]
Biodegradation (aerobic sediment)	Half-life = 300 d	[17]
Biodegradation (semi-continuous activated sludge)	81.5 % degraded after 24 h	[18]
Biodegradation (acclimated shake flask, inoculum prepared from soil and sewage microorganisms)	73–92 % degraded after 28 d, Half-life = 4.6–6.8 d	[19]

Kinetics – Diisobutyl phthalate (DIBP)

Mechanism	Reported values	Reference
OH-radical reactions	Half-life = 14 h (estimated)†	[16]
Biodegradation (aqueous solutions in flask, inoculum prepared from activated sludge)	Half-lives = 15–23.3 h	[21]

Kinetics – Dibutyl phthalate (DBP)

Mechanism	Reported values	Reference
OH-radical reactions	Half-life = 14 h (estimated)†	[16]
Hydrolysis	Half-life = 22 yr	[14]
Hydrolysis (artificial river water, in the dark)	Half-life = 1300 d (pH = 7)	[15]
Hydrolysis and photolysis (artificial river water, in sunlight)	Half-life = 360 d (pH = 7)	[15]
Biodegradation (semi-continuous activated sludge)	>95 % degraded after 24 h	[18]
Biodegradation (acclimated shake flask, inoculum prepared from soil and sewage microorganisms)	57 % degraded after 28 d, Half-life = 15.4 d	[19]

Kinetics – Benzylbutyl phthalate (BBP)

Mechanism	Reported values	Reference
OH-radical reactions	12 h (estimated)†	[16]
Hydrolysis	<5 % degraded after 28 d, half-life ≥ 100 d	[20]
Photolysis	<5 % degraded after 28 d, half-life ≥ 100 d	[20]
Hydrolysis (artificial river water, in the dark)	Half-life = 1500 d (pH = 7)	[15]
Hydrolysis and photolysis (artificial river water, in sunlight)	Half-life = 480 d (pH = 7)	[15]
Biodegradation (activated sludge)	93–99 % degraded after 1d (aerobic), <10 % degraded after 28 d (anaerobic)	[20]
Biodegradation (river water)	100 % degraded after 9 d, half-life = 2 d	[20]
Biodegradation (lake water microcosm)	>95 % degraded after 7 d, half-life ≤ 4 d; 51–65 % degraded after 28 d	[20]
Biodegradation (activated sludge)	93 % degraded after 48 h	[18]
Biodegradation (acclimated shake flask, inoculum prepared from soil and sewage microorganisms)	43–88 % degraded after 28 d, half-life = 19.4–15.3 d	[19]

Intentional Uses and Production Levels

Uses

DEHP

- Mainly used as a plasticizer in polymer products (>95 % of its total use in the EU), mostly in flexible PVC products [17].
- The content of DEHP in flexible polymer materials is typically around 30 % (w/w) [17].
- Applications of flexible PVC are widespread and include wiring and cable, film and sheeting, flooring, tubing, and other miscellaneous products such as shoe soles and gloves [17,22].

Other phthalates

- DBP and BBP are fast-fusing plasticizers for PVC and are mostly used in combination with DEHP [22].

Production Levels

DEHP

- Global production estimates: 2.12 million tonnes per year in 1988, with Eastern Asia and Western Europe producing the largest regional amounts (490 000 and 465 000 tonnes per year, respectively) [22].
- Production volume in Western Europe: 595 000 tonnes per year in 1997; 221 000 tonnes per year in 2004 [17].

Other phthalates

- Total use volumes of DEHP, DBP, DIBP and BBP together: approximately 63 000 tonnes in article manufacturing in the EU in 2014 [23].
- No other recent data on DEHP and no production levels for DIBP, DBP, and BBP were found.

Emission Sources into the Environment

- The use and disposal of polymer products containing phthalates are estimated to be the main release sources into the environment [17].

DEHP

	Emission Sources
Production	Contributes a small fraction (5 %) to the total emissions during the product lifecycle [17].
Use	Not reported
Disposal	• Released from municipal landfills through leachates [17]; thus, landfills may serve as long-term emission sources. • Potential local emission sources include the incineration of DEHP containing products, de-inking process of paper recycling, and car shredding [17].
Other sources	Not reported

Phthalates in general

The table below provides general information relevant for all phthalates including DEHP. As no specific information was found for DIBP, DBP, or BBP, the information below is meant to provide an overview of potential emission sources of phthalates in general; for some specific information on other phthalates, see the fact sheets “Phthalates (non-EU REACH SVHCs) 1” and “Phthalates (non-EU REACH SVHCs) 2”.

	Emission Sources
Production	Likely released during production [24,25,17].
Use	• Main source of releases to the atmosphere is through evaporation during the processing with PVC. The extent of such losses may vary from 0.02 % for injection molding to up to 1 % for coating processes [26]. • Phthalates can migrate slowly out of polymer products throughout their entire lifetime, since plasticizers are not chemically bound to the polymer matrix [17].
Disposal	• Different levels of emissions may occur depending on the treatment applied. • 86 % of the plastics disposed of in the US in 2008 (approximately 34 million tons) have ended up in landfills [27]. • Releases (e.g. through landfill leachate) can be expected, as phthalates are not covalently bound in plastic products that may later be disposed of. [28]
Other sources	Not reported

Distribution in the Abiotic Environment and Biota

Estimated Environmental Distribution

Based on the identified uses and emission sources for these chemicals as plastic additives and the emission scenario information generated by the OECD [29], a plausible emission pattern was assumed to estimate the resulting distribution in the environment using the Level III fugacity model in EPI Suite [16]. The assumed emission pattern and the resulting environmental distribution from the model are presented in the table below for each chemical.

	Assumed Emission Pattern			Modelled Distribution Results			
	Air	**Water**	**Soil**	**Air**	**Water**	**Soil**	**Sediment**
DEHP	50 %	50 %	0 %	2 %	39 %	15 %	44 %
DIBP	50 %	50 %	0 %	5 %	73 %	20 %	2 %
DBP	50 %	50 %	0 %	9 %	81 %	8 %	2 %
BBP	50 %	50 %	0 %	5 %	69 %	11 %	15 %

Bioaccumulation Potential

	Bioconcentration factor (BCF)	Organism	Reference
DEHP	40–900	fish	[14]
	38–2627	various aquatic species	[14]
DIBP	239 (estimated)†	fish	[16]
DBP	2068–2125	fish	[14]
	185–1485	various aquatic species	[14]
BBP	29 – 662	fish	[14]
	100	fresh water snails (*Physa*)	[14]

DEHP is reported as persistent (but not very persistent), toxic, and not bioaccumulative under REACH [30,31].

Measured Environmental Concentrations

Measured concentrations for these chemicals have been reported in numerous environmental media. A non-exhaustive set of reported concentrations is included below.

Concentrations are provided in varying units depending on the media. Mass per mass dry weight (dw) and wet weight (ww) are sometimes used. ND = not detected, i.e., below the limit of detection (LOD). NQ = not quantified, i.e., below the limit of quantification (LOQ). NR = not reported.

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concentration**	**Samples > LOD**	**Reference**
Diethylhexyl phthalate (DEHP)							
River water	Spain	2012	7	ND	ND	0 % (LOD = 460 ng/L)	[32]
Surface water (rivers, lakes, channels)	Germany	1997	116	0.33–97.8 µg/L	2.27 µg/L	100 %	[33]
Sea water	Arctic	2004	16	ND–3326 pg/L	210.5 pg/L	94 % (LOD = 24 pg/L)	[34]
River sediment	China	2014	7	18.5–355 µg/g dw	180 µg/g dw (mean)	NR	[35]
River sediment	China	2014	9	2.33–44.5 µg/g dw	12.2 µg/g dw (mean)	NR	[35]
Surface water sediment	Germany	1997	35	0.21–8.44 mg/kg dw	0.7 mg/kg dw	100 %	[33]
Atmosphere	Arctic	2004	6	375–1129 pg/m^3	724.5 pg/m^3	100 %	[34]
Diisobutyl phthalate (DIBP)							
Sea water	Arctic	2004	16	ND–204 pg/L	6 pg/L	56 % (LOD = 5 pg/L)	[34]
River sediment	China	2014	7	0.414–4.35 µg/g dw	2.02 µg/g dw (mean)	NR	[35]
River sediment	China	2014	9	0.131–0.404 µg/g dw	0.303 µg/g dw (mean)	NR	[35]
Atmosphere	Arctic	2004	6	132–617 pg/m^3	187.5 pg/m^3	100 %	[34]
Dibutyl phthalate (DBP)							
River water	Spain	2012	7	ND–1759 ng/L	604 ng/L	86 % (LOD = 230 ng/L)	[32]
Surface water (rivers, lakes, channels)	Germany	1997	116	0.12–8.80 µg/L	0.5 µg/L	100 %	[33]
River sediment	China	2014	7	0.469–2.43 µg/g dw	1.28 µg/g dw (mean)	NR	[35]
River sediment	China	2014	9	0.158–0.304 µg/g dw	0.246 µg/g dw (mean)	NR	[35]

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concen-tration**	**Samples > LOD**	**Refer-ence**
Surface water sediment	Germany	1997	35	0.06–2.08 mg/kg dw	0.45 mg/kg dw	100 %	[33]
Benzylbutyl phthalate (BBP)							
River water	Spain	2012	7	ND	ND	0 % (LOD = 190 ng/L)	[32]
Surface water (rivers, lakes, channels)	Germany	1997	116	ND–2.95 µg/L	NR	22 % (LOD = 0.02 µg/L)	[33]
Sea water	Arctic	2004	16	ND–48 pg/L	5.5 pg/L	94 % (LOD = 0.2 pg/L)	[34]
Surface water sediment	Germany	1997	35	ND–0.19 mg/kg dw	NR	11 % (LOD = 0.02 µg/L)	[33]
Atmosphere	Arctic	2004	6	42 - 124 pg/m^3	74 pg/m^3	100 %	[34]

Scientific Evidence of Adverse Endocrine-Related Environmental Effects

Reported scientific evidence of adverse endocrine-related environmental effects from exposure to benzophenones exists for different organisms and across different study levels. A comprehensive but non-exhaustive set of reported observations is included below, and further observations can be found in published literature reviews including in the following:

- European Chemicals Agency, ECHA SVHC Support Document for Bis (2-ethylhexyl) phthalate (DEHP), (2014). https://echa.europa.eu/documents/10162/fa429d23-21e7-4764-b223-6c8c98f8a01c.
- C.R. Tyler, S. Jobling, J.P. Sumpter, Endocrine Disruption in Wildlife: A Critical Review of the Evidence, Crit. Rev. Toxicol. 28 (1998) 319–361. doi:10.1080/10408449891344236.

Population level / field studies

No reported studies investigating this level were identified during preparation of the fact sheet.

In vivo level

Substance	Organism	Observation	Reference
DEHP; DIBP	marine (rare) medaka, Chinese rare minnow, mouse	Changed plasma steroid (testosterone and 17b-estradiol) levels	[36–38]
DEHP; DBP	*Xenopus leavis* (DBP), zebrafish (DEHP)	Changed expression profiling of key genes involved in various thyroid hormone pathways	[39,40]
DIBP	rat	Changed expression profiling of key genes involved in steroidogenesis	[41,42]
DEHP	marine (rare) medaka	Increased plasma or liver vitellogenin* level; no effect found for DBP	[36,43]
DEHP; DIBP	marine (rare) medaka, Chinese rare minnow, rat, mouse	Impaired reproduction (reduced egg production, inhibited oocyte maturation in females and retarded spermiation in males, anogenital distance and nipple development in males, decreased sperm count and motility)	[36–38,44,45]
DEHP	Chinese rare minnow	Decreased egg protein content in offspring (F1)	[37]
DEHP; DIBP	marine medaka, rat, mouse	Changed testicular testosterone levels and histological alterations in gonads (testis, ovaries)	[33,35,38, 43,44,39]
DEHP; DBP	abalone	Growth and abnormal developments of individuals	[48]
DEHP; DBP	abalone	Altered hatching rates; no effect found for BBP in rainbow trout	[48,49]
DEHP; BBP, DBP	*Daphnia magna*	No effects on reproduction found	[49,50]
DEHP; DBP	fathead minnow, goldfish	No effects on expression of mRNA of the ER alpha or beta or androgen receptor found	[44,51]

In vitro level

Substance	Cell line	Observation	Reference
DBP; BBP	fathead minnow	Competitive binding to the estrogen receptor (displacing 17β-estradiol) in in vitro assay; no effect found for DEHP	[52]
DEHP	marine (rare) medaka, Chinese rare minnow	Altered gene transcription in gonads (testis, ovaries)	[36,37]
DEHP	Chinese rare minnow	Altered transcription profiles of genes involved in steroidogenesis and plasma sex hormone levels	[53]
DEHP	Chinese rare minnow	Vitellogenin* mRNA or protein expression	[37]
DEHP; DBP	fathead minnow	Affected sex steroid hormone synthesis	[51]

Notes:
*Vitellogenin is a precursor protein normally synthesized by females to be incorporated in eggs.

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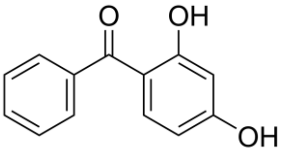
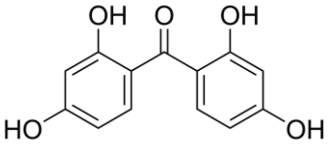
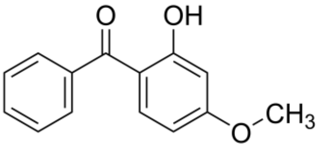
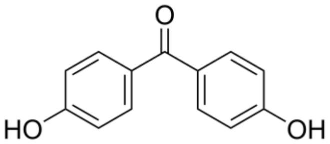
Benzophenones

Key References:

- A. Careghini, A.F. Mastorgio, S. Saponaro, E. Sezenna, Bisphenol A, nonylphenols, benzophenones, and benzotriazoles in soils, groundwater, surface water, sediments, and food: a review, Environ. Sci. Pollut. Res. 22 (2015) 5711–5741. doi:10.1007/s11356-014-3974-5.
- S. Kim, K. Choi, Occurrences, toxicities, and ecological risks of benzophenone-3, a common component of organic sunscreen products: A mini-review, Environ. Int. 70 (2014) 143–157. doi:10.1016/j.envint.2014.05.015.
- D. Sánchez-Quiles, A. Tovar-Sánchez, Are sunscreens a new environmental risk associated with coastal tourism?, Environ. Int. 83 (2015) 158–170. doi:10.1016/j.envint.2015.06.007.

Chemical Identification			
Name(s)	**Abbreviation**	**CAS Number**	**Structure**
Benzophenone-1; 2,4-Dihydroxybenzophenone	BP-1	131-56-6	
Benzophenone-2; 2,2',4,4'-tetrahydroxybenzophenone	BP-2	131-55-5	
Benzophenone-3; Oxybenzone	BP-3	131-57-7	
4,4'-Dihydroxybenzophenone	4,4'-DHB	611-99-4	
Completed assessments as the basis for inclusion: SIN List (BP-1; BP-2; BP-3; 4,4'-DHB), Danish Criteria (BP-1; BP-2; BP-3; 4,4'-DHB)			

Physical and Physicochemical Properties

Property	**BP-1**	**BP-2**	**BP-3**	**4,4’-DHB**
Molecular formula	$C_{13}H_{10}O_3$	$C_{13}H_{10}O_5$	$C_{14}H_{12}O_3$	$C_{13}H_{10}O_3$
Molecular weight [g/mol]	214.2	246.2	228.2	214.2
Physical state at 20°C	solid	solid	solid	solid
Melting point [°C]	142 [1]	186 [†]	65 [2]; 62.9 [3]	142 [†]
Density [g/ cm^3]	1.27 [4]	1.22 [5]	1.43 [3]	NR
Vapor pressure at 25°C [mmHg]	$1.41*10^{-7}$ [†]	$3.44*10^{-10}$ [†]	$7.5*10^{-6}$ [3]	$2.46*10^{-8}$ [†]
Water solubility at 25°C [mg/L]	413.4 [†]	398.5 [†]	6 [3]	1905 [†]
Octanol/water partition coefficient (log K_{OW})	2.96 [†]	2.78 [†]	3.79 [6]; 3.6 [3]	2.19 [†]
Organic carbon/water partition coefficient (log K_{OC})	3.28 (MCI method)[†]; 3.09 (Kow method)[†]	3.51 (MCI method)[†]; 3.33 (Kow method)[†]	2.98 (MCI method)[†]; 3.44 (Kow method)[†]	3.27 (MCI method)[†]; 2.67 (Kow method)[†]
Air/water partition coefficient (log K_{AW})	-8.97 [†]	-13.83 [†]	-6.21 [†]	-12.07 [†]
Dissociation constant (p*K*a)	NR	NR	NR	NR

[†] Estimated value using models in EPI Suite v4.11 [14].
NR = not reported

Degradation Pathways and Kinetics

Mechanism	Expected to occur?			Technosphere	Environment	Reference
	Yes	**No**	**Not reported**			
Hydrolysis	BP-3		BP-1; BP-2; 4,4'-DHB		Water	[3]
Photolysis		BP-1; BP-2; BP-3; 4,4'-DHB				[7]
OH-radical reactions	BP-3		BP-1; BP-2; 4,4'-DHB		Atmosphere	[7]
Biodegradation	BP-1; BP-3; 4,4'-DHB		BP-2	WWTP	Sediments	[8–10]

Kinetics – Benzophenone-3 (BP3)

Mechanism	Reported values	Reference
Hydrolysis	Half-life = 41.9 d (pH 7 and 25 °C)	[3]
Biodegradation (activated sludge)	Half-life = 10.7 d (aerobic conditions)	[8]
Biodegradation (digested sludge)	Half-life = 8.7 d (nitrate-reducing conditions) Half-life = 5.1 d (Fe(III)-reducing conditions) Half-life = 4.3 d (sulfate-reducing conditions) Half-life = 4.2 d (non-amended conditions)	[8]

Notes: Information on half-lives were found to be only available for BP-3. The major product of biodegradation of BP-3 is BP-1 [10].

Production Levels and Uses

Uses

Benzophenones in general are used as:

- UV-filters in cosmetic products including sunscreens, skin care products, hairsprays and shampoos [7].
- UV-filters in plastic packaging including in food packaging [7].
- Photo-initiators for inks and varnishes that are cured with UV-light [7].

Intentional Production Levels

- Little information is available on the current and historical production levels of benzophenones.
- BP-3 was listed as High-Production Volume (HPV) chemical in the US in 1990 [11] and is currently registered in the EU with 100–1000 tonnes per year of production or import [3].

Emission Sources into the Environment

- Primary releases occur during use and disposal of products containing benzophenones [7,10,12].
- BP-3 can transform into BP-1 in both the environment and during treatment processes [8].

Releases From:

Production – No information on emissions during production of benzophenones was found.

Use – Benzophenones can be released directly into the aquatic environment during recreational activities (e.g. applied products washing off) [7,10].

Disposal – Removal of benzophenones in wastewater treatment plants is often incomplete*, and they are consequently released into the aquatic environment via effluents [7,10,13].

*Exact removal efficiencies of many benzophenones in wastewater treatment processes are still unclear. Removal efficiencies of BP-1 and BP-3 during primary sedimentation of wastewater treatment in Hong Kong are low (7–28%). In the same treatment plant, biological treatment and chlorination of wastewater both led to a moderate removal efficiency for BP-1 of up to 70 %, whereas sand filtration only removed up to 43 % of BP-1 and BP-3 in wastewater. The most efficient treatment for the removal of BP-1 and BP-3 is reverse osmosis (removal efficiency >99 %) [10].

Distribution in the Abiotic Environment and Biota

Expected Distribution

Based on the identified uses and emission sources for these chemicals as additives in personal care products, a plausible emission pattern was assumed to estimate the resulting partitioning in the environment using the Level III fugacity model in EPI Suite [14]. The assumed emission pattern and the resulting environmental partitioning from the model are presented in the table below for each chemical.

	Assumed Emission Pattern			**Modeled Distribution Results**			
	Air	**Water**	**Soil**	**Air**	**Water**	**Soil**	**Sediment**
BP-1	0 %	90 %	10 %	0 %	71 %	24 %	5 %
BP-2	0 %	90 %	10 %	0 %	70 %	23 %	7 %
BP-3	0 %	90 %	10 %	0 %	65 %	32 %	3 %
4,4’-DHB	0 %	90 %	10 %	0 %	72 %	24 %	4 %

Bioaccumulation Potential

	Bioconcentration factor (BCF)	**Organism**	**Reference**
BP-1	11 (estimated)†	fish	[14]
BP-2	8 (estimated)†	fish	[14]
BP-3	36–158 (estimated)	fish	[3]
4,4’-DHB	3 (estimated)†	fish	[14]

The potential for BP-3 to bioaccumulate in aquatic organisms is reported as being moderate to high [7]. However, there are only a few cases of BP-3 detection in aquatic wildlife from Swiss lakes and Spanish rivers [7].

Measured Environmental Concentrations

Measured concentrations for these chemicals have been reported in numerous environmental media. A non-exhaustive set of reported concentrations is included below, and further measurements can be found in published literature including in the following:

- A. Careghini, A.F. Mastorgio, S. Saponaro, E. Sezenna, Bisphenol A, nonylphenols, benzophenones, and benzotriazoles in soils, groundwater, surface water, sediments, and food: a review, Environ. Sci. Pollut. Res. 22 (2015) 5711–5741. doi:10.1007/s11356-014-3974-5.
- S. Kim, K. Choi, Occurrences, toxicities, and ecological risks of benzophenone-3, a common component of organic sunscreen products: A mini-review, Environ. Int. 70 (2014) 143–157. doi:10.1016/j.envint.2014.05.015.
- D. Sánchez-Quiles, A. Tovar-Sánchez, Are sunscreens a new environmental risk associated with coastal tourism?, Environ. Int. 83 (2015) 158–170. doi:10.1016/j.envint.2015.06.007.

Concentrations are provided in varying units depending on the media. Mass per mass dry weight (dw) and wet weight (ww) are sometimes used. ND = not detected, i.e., below the limit of detection (LOD). NQ = not quantified, i.e., below the limit of quantification (LOQ). NR = not reported.

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concen-tration**	**Samples > LOD**	**Refer-ence**
Benzophenone-1 (BP-1)							
River water	Spain	2011	5	ND–7.54 ng/L	ND	40 % (LOD = 1.0 ng/L)	[15]
River water	Korea	2003	25	ND–47 ng/L	ND	4 % (LOD = 25 ng/g dw)	[16]
Lake water	Korea	2003	6	ND	ND	0 % (LOD = 5 ng/L)	[16]
Sea water	Spain	2009	3	ND–280 ng/L	ND	30 % (LOD = 32 ng/L)	[17]
River sediment	China	2009	6	ND	ND	0 % (LOD = 0.041 ng/g dw)	[18]
River sediment	Chile	2009	6	ND	ND	0 % (LOD = 4.6 ng/g dw)	[19]
River sediment	Korea	2003	15	ND	ND	0 % (LOD = 0.1 ng/g dw)	[16]
Coastal sea sediment	Chile	2009	4	ND	ND	0 % (LOD = 4.6 ng/g dw)	[19]
WWTP effluent	Spain	2011	5	ND–31.1 ng/L	2.98 ng/L	60 % (LOD = 2.5 ng/L)	[15]
WWTP influent	Spain	2011	5	152.4–722 ng/L	283.2 ng/L	100 % (LOD = 8.0 ng/L)	[15]
WWTP sludge	China	2009	5	4.41–91.6 ng/g dw	NR	100 % (LOD = 0.41 ng/g dw)	[18]

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concen-tration**	**Samples > LOD**	**Refer-ence**
Benzophenone-2 (BP-2)							
River water	Spain	2011	5	ND	ND	0 % (LOD = 1.2 ng/L)	[15]
Urban groundwater	Spain	2011	5	ND	ND	0 % (LOD = 1 ng/L)	[15]
River sediment	China	2009	6	ND	ND	0 % (LOD = 0.067 ng/g dw)	[18]
WWTP effluent	Spain	2011	5	ND	ND	0 % (LOD = 3 ng/L)	[15]
Benzophenone-3 (BP-3)							
River water	Japan	2008	2	16–41 ng/L	36.5 ng/L	100 % (LOD = NR)	[20]
River water	Spain	2011	5	ND–37.8 ng/L	ND	40 % (LOD = 0.7 ng/L)	[15]
Lake water	Korea	2003	6	ND	ND	0 % (LOD = 5 ng/L)	[16]
Lake water	Switzer-land	2005	11	ND–30 ng/L	20 ng/L	82 % (LOD = 2 ng/L)	[13]
Lake water	Czech Republic	2011	6	21–550 ng/L	NR	NR	[21]
Urban groundwater	Spain	2011	5	ND–34 ng/L	ND	40 % (LOD = 0.5 ng/L)	[15]
River sediment	Korea	2003	15	ND	ND	0 % (LOD = 0.1 ng/g dw)	[16]
River sediment	China	2009	6	0.272–0.545 ng/g dw	NR	100 % (LOD = 0.067 ng/g dw)	[18]
River sediment	Colombia	2010	6	ND–5.38 ng/g dw	NR	NR (LOD = 0.4 ng/g dw)	[19]
WWTP effluent	Spain	2011	5	7.71–34 ng/L	15.6 ng/L	100 % (LOD = 1.5 ng/L)	[15]
WWTP effluent	Switzer-land	2002/ 2003	13	ND–600 ng/L	85 ng/L	92 % (LOD = 10 ng/L)	[13]
Lake fish	Switzer-land	2002	10	ND–123 ng/L	102 ng/L	60 % (LOD = 15 ng/L)	[13]
Aquaculture fish	China	2015	19	ND–3.1 ng/g dw	ND	26 % (LOD = 0.9 ng/g dw)	[22]
Wild mussels & clams	China	2015	6	ND–12.4 ng/g dw	<LOQ	50 % (LOD = 0.9 ng/g dw, LOQ = 2.9 ng/g dw)	[22]

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concen-tration**	**Samples > LOD**	**Refer-ence**
4,4’-Dihydroxybenzophenone (4,4’-DHB)							
River water	Spain	2011	5	ND	ND	0 % (LOD = 1.8 ng/g dw)	[15]
Urban groundwater	Spain	2010	31	ND–4.1 ng/L	NR	6 % (LOD = NR)	[23]
Urban groundwater	Spain	2011	5	ND	ND	0 % (LOD = 1.5 ng/L)	[15]
River sediment	Chile	2009	6	ND	ND	0 % (LOD = 0.8 ng/g dw)	[19]
River sediment	Colombia	2009	6	ND	ND	0 % (LOD = 0.8 ng/g dw)	[19]
WWTP effluent	Spain	2011	5	ND	ND	0 % (LOD = 3.5 ng/L)	[15]

Scientific Evidence of Adverse Endocrine-Related Environmental Effects

Reported scientific evidence of adverse endocrine-related environmental effects from exposure to benzophenones exist for different organisms and across different study levels. A comprehensive but non-exhaustive set of reported observations is included below, and further observations can be found in published literature reviews including in the following:

- P.Y. Kunz, K. Fent, Multiple hormonal activities of UV filters and comparison of in vivo and in vitro estrogenic activity of ethyl-4-aminobenzoate in fish, Aquat. Toxicol. 79 (2006) 305–324. doi:10.1016/j.aquatox.2006.06.016.
- M. Krause, A. Klit, M. Blomberg Jensen, T. Søeborg, H. Frederiksen, M. Schlumpf, W. Lichtensteiger, N.E. Skakkebaek, K.T. Drzewiecki, Sunscreens: Are they beneficial for health? An overview of endocrine disrupting properties of UV-filters, Int. J. Androl. 35 (2012) 424–436. doi:10.1111/j.1365-2605.2012.01280.x.
- J. Wang, L. Pan, S. Wu, L. Lu, Y. Xu, Y. Zhu, M. Guo, S. Zhuang, Recent Advances on Endocrine Disrupting Effects of UV Filters, Int. J. Environ. Res. Public Health. 13 (2016) 782. doi:10.3390/ijerph13080782.

Population level / field studies

No reported studies investigating this level were identified during the preparation of this fact sheet.

In vivo level

Substance	Organism	Observation	Reference
BP-1; BP-2	fathead minnow	Increased vitellogenin* level in females	[24]
BP-3; 4,4’-DHB	fathead minnow	No effect found on vitellogenin* level in females	[24]

In vitro level

Substance	Cell line	Observation	Reference
BP-1; BP-2	human, fish	Competitive binding to the estrogen receptor (displacing 17β-estradiol)	[25]
BP-1; BP-2; BP-3; 4,4’-DHB	yeast, with rainbow trout estrogen receptor	Reporter gene expression – estrogenicity	[24]
BP-1; BP-2	human, with rainbow trout estrogen receptor	Reporter gene expression – estrogenicity; no effect found for BP-3	[25]
BP-1; BP-2	human, fish	Induced vitellogenin* synthesis / vitellogenin* mRNA or protein expression; no effect found for BP-3	[25]

Notes:
*Vitellogenin is a precursor protein normally synthesized by females to be incorporated in eggs.

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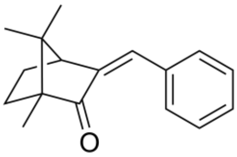
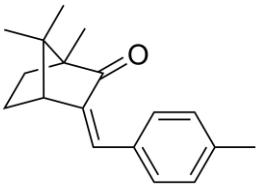
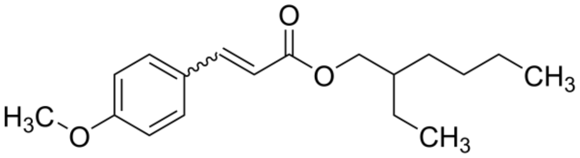
3-BC, 4-MBC, EHMC

Key References:

- D. Sánchez-Quiles, A. Tovar-Sánchez, Are sunscreens a new environmental risk associated with coastal tourism?, Environ. Int. 83 (2015) 158–170. doi:10.1016/j.envint.2015.06.007.
- S. Ramos, V. Homem, A. Alves, L. Santos, Advances in analytical methods and occurrence of organic UV-filters in the environment — A review, Sci. Total Environ. 526 (2015) 278–311. doi:10.1016/j.scitotenv.2015.04.055.
- M.M.P. Tsui, H.W. Leung, T.-C. Wai, N. Yamashita, S. Taniyasu, W. Liu, P.K.S. Lam, M.B. Murphy, Occurrence, distribution and ecological risk assessment of multiple classes of UV filters in surface waters from different countries, Water Res. 67 (2014) 55–65. doi:10.1016/j.watres.2014.09.013.

Chemical Identification			
Name(s)	**Abbreviation**	**CAS Number**	**Structure**
3-Benzylidene camphor; 1,7,7-trimethyl-3-(phenylmethylene)bicyclo[2.2.1] heptan-2-one	3-BC	15087-24-8	
4-Methylbenzylidene camphor; Enzacamene; 1,7,7,-trimethyl-3-[(4-methylphenyl) methylene]bicycle[2.2.1] heptan-2-one	4-MBC	36861-47-9	
2-ethylhexyl 4-methoxycinnamate; octyl methoxycinnamate; Octinoxate	EHMC	5466-77-3; 83834-59-7	
Completed assessments as the basis for inclusion: SIN List (3-BC; 4-MBC; EHMC), Danish Criteria (3-BC; 4-MBC; EHMC)			

Physical and Physicochemical Properties			
Property	**3-BC**	**4-MBC**	**EHMC**
Molecular formula	$C_{17}H_{20}O$	$C_{18}H_{22}O$	$C_{18}H_{26}O_3$
Molecular weight [g/mol]	240.4	254.4	290.4
Physical state at 20°C	solid	solid	liquid
Melting point [°C]	77.4 [1]	66–69 [2]	-68.3 [3]
Density [g/ cm^3]	NR	NR	NR
Vapor pressure at 25°C [mmHg]	$2.59*10^{-4}$ [1]†	$1.52*10^{-5}$ †	$1.38*10^{-5}$ †
Water solubility at 25°C [mg/L]	9.9 [4]	1.3 at 20 °C [2]; 5.1 [4]	150 [4]
Octanol/water partition coefficient (log K_{OW})	4.49 [4]	5.14 [2]; 4.95 [4]	5.8 [4]
Organic carbon/water partition coefficient (log K_{OC})	3.88 (MCI method)†; 4.09 (Kow method)†	4.09 (MCI method)†; 4.40 (Kow method)†	3.94 (MCI method)†; 4.12 (Kow method)†
Air/water partition coefficient (log K_{AW})	-11.10 †	-4.06†	-4.14†
Dissociation constant (pKa)	Not applicable	Not applicable	Not applicable

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[1] Estimated value using models in EPI Suite v4.11 [6].
NR = not reported

Degradation Pathways and Kinetics

Mechanism	Expected to occur?			Technosphere	Environment	Reference
	Yes	No	Not reported			
Hydrolysis			3-BC; 4-MBC; EHMC			
Photolysis	EHMC		3-BC			[5]
OH-radical reactions	3-BC; 4-MBC; EHMC				Atmosphere	[6]
Biodegradation	EHMC; 4-MBC		3-BC	WWTP	Sediment	[7–9]

Kinetics – 3-Benzylidene camphor (3-BC)

Mechanism	Reported values	Reference
OH-radical reactions	Half-life = 1.5 h (estimated)[1]	[6]

Kinetics – 4-Methylbenzylidene camphor (4-MBC)

Mechanism	Reported values	Reference
OH-radical reactions	Half-life = 1.4 h (estimated)[1]	[6]
Biodegradation (marine sediment, aerobic)	2–23 % degraded after 130 d 29–68 % degraded after 420 d	[7]
Biodegradation (marine sediment, anaerobic)	8–24 % degraded after 130 d 36–47 % degraded after 420 d	[7]
Biodegradation (WWTP water phase primary and biological treatments)	Approximately 75 % degraded during WWTP process	[8]
Biodegradation (WWTP water phase primary and biological treatments)	13–23 % degraded during WWTP process	[9]

Kinetics – 2-Ethylhexyl 4-methoxycinnamate (EHMC)

Mechanism	Reported values	Reference
OH-radical reactions	Half-life = 2.4 h (estimated)[1]	[6]
Biodegradation (WWTP water phase primary and biological treatments)	Approximately 90 % degraded during WWTP process	[8]
Biodegradation (WWTP water phase primary and biological treatments)	86–97 % degraded during WWTP process	[9]
Photolysis (natural sunlight)	Half-life = 0.8 h	[5]
Photolysis	Half-life = 21 h	[10]

Intentional Production Levels and Uses

Uses

- 3-BC and 4-MBC are used as UV filters in cosmetic products, especially sunscreens [1,2,12].
- EHMC is also used as a UV filter in cosmetics, as well as in adhesives and sealants, coating products, fillers, putties, plaster, biocides, cleaning products and several other applications [13].
- The use of these chemicals as UV filters is regulated within the EU and other countries [12]:
    - In 2015, the use of 3-BC as a UV filter and absorber in cosmetics in the EU was revoked [14].
    - China, India, South Africa, and countries that are members of ASEAN and Mercosur authorize use of 3-BC as a UV filter in sunscreen with a maximum concentration of 2 % (as of 2015) [15].
    - 4-MBC is used as a UV-filter in sunscreen and other cosmetics with a maximum concentration of 4 % in the EU [2].
- Use of 4-MBC in cosmetics is prohibited in Japan and the USA [13].

Production Levels

- No information was found on the current and historical production levels of 3-BC and 4-MBC.
- EHMC is registered in the EU with 1000–10 000 tonnes per year of production or import [3].

Emission Sources into the Environment

- Little information regarding 3-BC, 4-MBC and EHMC emissions into the environment found to be available.
- However, they are all used as UV filters, a class of chemicals for which releases into the environment are well known [4,12,16].
- Release into the aquatic environment via recreational activities and wastewater effluent is the primary pathway of UV filters into the environment [16].

Releases From:

Production – UV filters are released into wastewater during manufacturing of products containing them, such as cosmetics and products used for protection of UV-light sensitive materials [13,16].

Use – UV filters are released directly into the aquatic environment by washing off the skin during bathing activities and by discharge of untreated wastewater from plants manufacturing sunscreen products [16]. Additionally, they can also be released from the many other products (e.g. paper or plastic-based products, adhesives and sealants, cleaning products) [13].

Disposal – Removal of 4-MBC and EHMC in wastewater treatment plants is often incomplete, and they are consequently released into the aquatic environment via effluents [18,19]. Residues of UV-filters in packaging of personal care products are reported to be released in landfills [16]

Distribution in the Abiotic Environment and Biota

Expected Distribution

Based on the identified uses and emission sources for these chemicals as additives in personal care products, a plausible emission pattern was assumed to estimate the resulting distribution in the environment using the Level III fugacity model in EPI Suite [6]. The assumed emission pattern and the resulting environmental distribution from the model are presented in the table below for each chemical.

	Assumed Emission Pattern			**Modeled Distribution Results**			
	Air	**Water**	**Soil**	**Air**	**Water**	**Soil**	**Sediment**
3-BC	0 %	90 %	10 %	0 %	44 %	31 %	25 %
4-MBC	0 %	90 %	10 %	0 %	38 %	28 %	34 %
EHMC	0 %	90 %	10 %	0 %	62 %	22 %	16 %

Bioaccumulation Potential

	Bioconcentration factor (BCF)	**Organism**	**Reference**
3-BC	313	fish (fathead minnow)	[20]
4-MBC	251–1955	fish (zebrafish embryos)	[21]
EHMC	167–1500	fish	[22]

Measured Environmental Concentrations

Measured concentrations for these chemicals have been reported in numerous environmental media. A non-exhaustive set of reported concentrations is included below, and further measurements can be found in published literature including in the following:

- D. Sánchez-Quiles, A. Tovar-Sánchez, Are sunscreens a new environmental risk associated with coastal tourism?, Environ. Int. 83 (2015) 158–170. doi:10.1016/j.envint.2015.06.007.
- S. Ramos, V. Homem, A. Alves, L. Santos, Advances in analytical methods and occurrence of organic UV-filters in the environment — A review, Sci. Total Environ. 526 (2015) 278–311. doi:10.1016/j.scitotenv.2015.04.055.
- Y. Kameda, K. Kimura, M. Miyazaki, Occurrence and profiles of organic sun-blocking agents in surface waters and sediments in Japanese rivers and lakes, Environ. Pollut. 159 (2011) 1570–1576. doi:10.1016/j.envpol.2011.02.055.

Concentrations are provided in varying units depending on the media. Mass per mass dry weight (dw) and wet weight (ww) are sometimes used. ND = not detected, i.e., below the limit of detection (LOD). NQ = not quantified, i.e., below the limit of quantification (LOQ). NR = not reported.

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concentration**	**Samples > LOD**	**Reference**
3-Benzylidene camphor (3-BC)							
Seawater surface microlayer	South Pacific ocean	2006	2	9–13 ng/L	10.5 ng/L	100 % (LOD = NR)	[23]
Lake fish	Switzerland	2006	NR	ND	ND	0 % (LOD = 29 ng/g lipids)	[24]
Aquaculture fish	China	2015	19	ND	ND	0 % (LOD = 1.8 ng/g dw)	[25]
Wild mussels & clams	China	2015	6	ND	ND	0 % (LOD = 1.8 ng/g dw)	[25]
4-Methylbenzylidene camphor (4-MBC)							
Lake water	China	2013/ 2014	60	ND–89.1 ng/L	1.0 ng/L	65 % (LOD = NR)	[26]
Lake water	Switzerland	2002	11	ND–28 ng/L	7 ng/L	82 % (LOD = NR)	[19]
River water	Spain	2011	5	ND–12.6 ng/L	ND	20 % (LOD = 3.5 ng/L	[27]
Groundwater	Poland	2012/ 2013	16	ND–3.625 µg/L	0.262 µg/L	NR (LOD = 0.014 µg/L)	[28]
Groundwater	Spain	2011	5	ND–<10 ng/L (LOQ)	ND	0 % (LOD = 3 ng/L)	[27]
Seawater	Arctic	2012/ 2013	14	ND	ND	0 % (LOD = 0.28 ng/L)	[17]
Seawater	Thailand	2012/ 2013	2	ND	ND	0 % (LOD = 0.28 ng/L)	[17]

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concentration**	**Samples > LOD**	**Refer-ence**
Seawater	China	2012/ 2013	7	ND	ND	0 % (LOD = 0.28 ng/L)	[17]
Seawater	USA	2012/ 2013	10	ND	ND	0 % (LOD = 0.28 ng/L)	[17]
Seawater	Japan	2012/ 2013	8	ND	ND	0 % (LOD = 0.28 ng/L)	[17]
Seawater	Hong Kong	2012/ 2013	60	ND–379 ng/L	NR	12 % (LOD = 0.28 ng/L)	[17]
Seawater	China	2013	61	20.39–74.5 ng/L	31.3 ng/L	100 % (LOD = NR)	[25]
Seawater (surface microlayer)	Majorca Island	2011	3	25.7–109.6 ng/L	59.8 ng/L	100 % (LOD = NR)	[29]
Seawater (surface microlayer)	Majorca Island	2011	5	26.6–65.0 ng/L	51.4 ng/L	100 % (LOD = NR)	[29]
Beach water	Canary Islands	2011	108	ND–1043.4 ng/L	ND–46.1 ng/L*	70 % (LOD = 0.9 ng/L)	[30]
Seawater (near beaches)	Norway	NR (2007)	2	ND	ND	0 % (LOD = NR)	[31]
Seawater (near beaches)	Norway	NR (2007)	4	13.4–439.9 ng/L	56.5 ng/L	100 % (LOD = NR)	[31]
Seawater (Fjord)	Norway	NR (2007)	9	ND–2.6 ng/L	ND	33 % (LOD = NR)	[31]
Seawater (Fjord)	Norway	NR (2007)	10	ND–38.2 ng/L	13.5 ng/L	70 % (LOD =NR)	[31]
River sediment	Spain	2009	20	ND	ND	0 % (LOD = 8 ng/g dw)	[32]
Lake sediment (recreational)	Germany	2007	3	ND	ND	0 % (LOD = 6 ng/g)	[33]
Lake sediment	China	2013/ 2014	15	ND–13.9 ng/g dw	5.64 ng/g dw	93 % (LOD = NR)	[26]
Estuarine sediment	Chile	2009	2	ND	ND	0 % (LOD = 1.1 ng/g dw)	[34]
River sediment	Chile	2009	6	ND	ND	0 % (LOD = 1.1 ng/g dw)	[34]
Estuarine sediment (swamp)	Colombia	2010	3	ND–17.2 ng/g dw	NR	NR (LOD = 1.1 ng/g dw)	[34]
Estuarine sediment (river)	Colombia	2010	6	ND	ND	0 % (LOD = 1.1 ng/g dw)	[34]

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concentration**	**Samples > LOD**	**Refer-ence**
Marine sediment	Hong Kong	2012 (August)	13	ND	ND	0 % (LOD = 7.33 ng/g dw)	[35]
Marine sediment	Hong Kong	2013 (Feb.)	13	ND	ND	0 % (LOD = 7.33 ng/g dw)	[35]
Marine sediment	Hong Kong	2013 (June)	13	ND	ND	0 % (LOD = 7.33 ng/g dw)	[35]
Marine sediment (Tokyo bay)	Japan	2013 (July)	8	ND	ND	0 % (LOD = 7.33 ng/g dw)	[35]
Coastal sediment	Chile	2009	11	ND	ND	0 % (LOD = 1.1 ng/g dw)	[34]
Coastal sediment	Colombia	2010	4	ND –7.9 ng/g dw	NR	NR (LOD = 1.1 ng/g dw)	[34]
Mussels and clam	China	2015	6	ND–<6 ng/L (LOQ)	ND	17 % (LOD = 1.8 ng/g dw)	[25]
Fish	China	2015	19	ND	ND	0 % (LOD = 1.8 ng/g dw)	[25]
WWTP effluent (24-hour composite samples)	Spain	2011	5	ND–23.8 ng/L	ND	20 % (LOD = 4 ng/L)	[27]
WWTP influent (24-hour composite samples)	Spain	2011	5	<33.3 (LOQ) - 48.3 ng/L	<33.3 ng/L (LOQ)	20 % (LOD = 10 ng/L)	[27]
Landfill leachate	Poland	2012/ 2013	9	1.22–16.64 µg/L	3.77 µg/L	NR (LOD = 0.056 µg/L)	[28]
2-Ethylhexyl 4-methoxycinnamate (EHMC)							
Lake water	Switzer-land	2002	11	ND–7 ng/L	ND	36 % (LOD = 2 ng/L)	[19]
Seawater	China	2013	61	34.15–191.67 ng/L	131.73 ng/L	100 % (LOD = NR)	[25]
Beach water	Canary Islands	2011	108	ND–756.4 ng/L	ND–71 ng/L*	77 % (LOD = 1.6 ng/L)	[30]
Seawater	Arctic	2012/ 2013	14	ND–66 ng/L	25 ng/L	71 % (LOD = 0.41 ng/L)	[17]
Seawater	Thailand	2012/ 2013	2	NR–95 ng/L	88 ng/L	100 % (LOD = 0.41 ng/L)	[17]
Seawater	China	2012/ 2013	7	ND–79 ng/L	NR	57 % (LOD = 0.41 ng/L)	[17]
Seawater	USA	2012/ 2013	10	ND–150 ng/L	NR	100 % (LOD = 0.41 ng/L)	[17]

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concentration**	**Samples > LOD**	**Refer-ence**
Seawater	Japan	2012/ 2013	8	ND–95 ng/L	46 ng/L	63 % (LOD = 0.41 ng/L)	[17]
Seawater	Hong Kong	2012/ 2013	60	ND–4043 ng/L	89 ng/L	93 % (LOD = 0.41 ng/L)	[17]
River sediment	Chile	2009	6	ND	ND	0 % (LOD = 4.1 ng/g dw)	[34]
River sediment	Spain	2009	20	ND–42 ng/g dw	ND	35 % (LOQ = 1.6 ng/g dw)	[32]
Lake sediment (recreational)	Germany	2007	3	14–34 ng/g	21 ng/g	100 % (LOD = 5 ng/g)	[33]
Estuarine sediment	Chile	2009	2	ND	ND	0 % (LOD = 4.1 ng/g dw)	[34]
Estuarine sediment (swamp)	Colombia	2010	3	ND–39 ng/g dw	NR	NR (LOD = 4.1 ng/g dw)	[34]
Estuarine sediment (river)	Colombia	2010	6	ND–47.1 ng/g dw	ND	NR (LOD = 4.1 ng/g dw)	[34]
Marine sediment	Hong Kong	2012 (August)	13	ND–447 ng/g dw	8.3 ng/g dw (of samples >LOD)	85 % (LOD = 0.51 ng/g dw)	[35]
Marine sediment	Hong Kong	2013 (Feb.)	13	ND–291 ng/g dw	6.5 ng/g dw (of samples >LOD)	69 % (LOD = 0.51 ng/g dw)	[35]
Marine sediment	Hong Kong	2013 (June)	13	ND–119 ng/g dw	5.1 ng/g dw (of samples >LOD)	92 % (LOD = 0.51 ng/g dw)	[35]
Marine sediment (Tokyo bay)	Japan	2013 (July)	8	0.3–54.5 ng/g dw	10.3 ng/g dw	100 % (LOD = 0.51 ng/g dw)	[35]
Coastal sediment	Chile	2009	11	ND	ND	0 % (LOD = 4.1 ng/g dw)	[34]
Coastal sediment	Colombia	2010	4	ND –17.8 ng/g dw	NR	NR (LOD = 4.1 ng/g dw)	[34]
Fish	China	2015	19	ND–12.7 ng/L	<4.0 ng/L (LOQ)	73.7 % (LOD = 1.2 ng/g dw)	[25]
Mussels and clam	China	2015	6	<4.0 (LOQ)–51.3 ng/L	21.05 ng/L	100 % (LOD = 1.2 ng/g dw)	[25]

Notes:
Additional information regarding the sampling location and year is sometimes provided after values that are not reported (NR) in parentheses. This represents an estimated value for this non-reported information based on the general details provided in the study.

*Range of medians from six beaches

Scientific Evidence of Adverse Endocrine-Related Environmental Effects

Reported scientific evidence of adverse endocrine-related environmental effects from exposure exist for different organisms and across different study levels. A comprehensive but non-exhaustive set of reported observations is included below, and further observations can be found in published literature reviews including in the following:

- P.Y. Kunz, K. Fent, Multiple hormonal activities of UV filters and comparison of in vivo and in vitro estrogenic activity of ethyl-4-aminobenzoate in fish, Aquat. Toxicol. 79 (2006) 305–324. doi:10.1016/j.aquatox.2006.06.016.
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- J. Wang, L. Pan, S. Wu, L. Lu, Y. Xu, Y. Zhu, M. Guo, S. Zhuang, Recent Advances on Endocrine Disrupting Effects of UV Filters, Int. J. Environ. Res. Public Health. 13 (2016) 782. doi:10.3390/ijerph13080782.

Population level / field studies

No reported studies investigating this level were identified during the preparation of this fact sheet.

In vivo level

Substance	Organism	Observation	Reference
3-BC; 4-MBC	zebrafish	No estrogenicity observed	[36]
3-BC; 4-MBC; EHMC	fathead minnows, rainbow trout, medaka	Increased vitellogenin* level in females	[37–39]
3-BC	aquatic species	Histological alterations in gonads (testis, ovaries)	[20]
3-BC	aquatic species	Impaired reproduction (inhibited oocyte and spermatocyte development)	[20]
3-BC; 4-MBC	frog	No effect on sex ratio or alterations in gonads observed	[40]

In vitro level

Substance	Cell line	Observation	Reference
3-BC	yeast, with rainbow trout estrogen receptor	Reporter gene expression - estrogenicity	[37]
4-MBC; EHMC	yeast, with rainbow trout estrogen receptor	No effect on reporter gene expression - estrogenicity	[37]
4-MBC; EHMC	medaka	Induced vitellogenin* synthesis / vitellogenin* mRNA or protein expression	[39]

Notes:
*Vitellogenin is a precursor protein normally synthesized by females to be incorporated in eggs.

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Bisphenol F and S

Key References:

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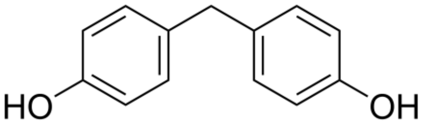
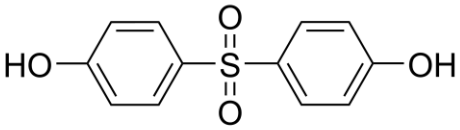
Chemical Identification			
Name(s)	**Abbreviation**	**CAS Number**	**Structure**
Bisphenol F	BPF	620-92-8	
Bisphenol S	BPS	80-09-1	
Completed assessments as the basis for inclusion: SIN List (BPF; BPS)			

Physical and Physicochemical Properties		
Property	**BPF**	**BPS**
Molecular formula	$C_{13}H_{12}O_2$	$C_{12}H_{10}O_4S$
Molecular weight [g/mol]	200.23	250.27
Physical state at 20°C	solid	solid
Melting point [°C]	162.5 [1]	240.5 [1]
Density [g/cm^3]	NR	1.37 at 15 °C [1]
Vapor pressure at 25°C [mmHg]	$3.72*10^{-7}$ †	$4.72*10^{-10}$ †
Water solubility at 25°C [mg/L]	542.8†	1100 [2]; 3518†
Octanol/water partition coefficient (log K_{OW})	3.06†	1.2 [3]; 1.65†
Organic carbon/water partition coefficient (log K_{OC})	4.18 (MCI method)†; 2.87 (Kow method)†	3.26 (MCI method)†; 2.20 (Kow method)†
Air/water partition coefficient (log K_{AW})	-9.67†	-12.96†
Dissociation constant (p*K*a)	pKa1 = 7.55, pKa2 = 10.80 at 25 °C [4]	pKa1 = 8 [3]; 8.2 [5]

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† Estimated value using models in EPI Suite v4.11 [7].

NR = not reported

Degradation Pathways and Kinetics

Mechanism	Expected to occur?			Technosphere	Environment	Reference
	Yes	No	Not reported			
Hydrolysis		BPF; BPS				[2]
Photolysis	BPF; BPS					[2,6]
OH-radical reactions	BPF; BPS				Atmosphere	[7]
Biodegradation	BPF; BPS (sediment)	BPS (water, activated sludge)		WWTP	Sea, River	[3,8,9]

Kinetics – Bisphenol S (BPS)

Mechanism	Reported values	Reference
OH-radical reactions	Half-life = 1.6 h (estimated)†	[7]
Photolysis	Half-life = 91 min	[6]
Biodegradation (activated sludge)	No degradation after 4 weeks	[2]
Biodegradation (seawater)	No degradation after 30 d (modified TOC-Handai method); No degradation after 30 d (sea die-away method)	[2,8]
Biodegradation (river water, aerobic)	No degradation after 3 weeks in 24 of 24 cases	[9]
Biodegradation (pond sediment, anaerobic)	Approximately 60 % degraded after 80 d	[9]

Kinetics – Bisphenol F (BPF)

Mechanism	Reported values	Reference
OH-radical reactions	Half-life = 8.8 h (estimated)†	[7]
Biodegradation (river water, aerobic)	Complete degradation after 2 weeks in 21 of 24 cases	[9]
Biodegradation (pond sediment, anaerobic)	Approximately 80 % degraded after 80 d	[9]
Biodegradation (activated sludge)	1 % degraded after 4 weeks	[2]
Biodegradation (seawater)	8–58 % degraded after 30 d (modified TOC-Handai method); 75–100 % degraded after 30 d (sea die-away method)	[2,8]

Intentional Production Levels and Uses

Uses

- Bisphenols S and F are used as substitutes for bisphenol A (BPA) as monomers in the production of polycarbonate plastics and epoxy resins [10].
    - Polycarbonate plastics are used primarily in the building and construction, optical media, electronics, and the automotive sectors [11].
    - Epoxy resins are mainly used for protective coatings (>50 %), printed circuit board laminates, semiconductor encapsulates, tooling, molding, flooring, and adhesives [12].
- Bisphenol S is widely used as a developer in thermal paper, which is used for receipts, tickets, etc. [13]

Production Levels

Bisphenol S

- Currently registered in the EU with 1000–10 000 tonnes per year of production or import [3].
- Imported by 8 companies in the US with four of those companies reporting a total import volume of 2107 tonnes in the year 2011, while the remaining four companies listed their import volumes as classified business information [14].

Bisphenol F

- Produced by one company in the US with a production volume of 161 tonnes in the year 2011 [14].

Emission Sources into the Environment

- As bisphenols F and S are used as direct substitutes for bisphenol A, it can be expected that the primary sources of releases into the environment are similar to bisphenol A.
- This may include releases during production and processing, releases from polycarbonate and epoxy resin products, disposal of thermal paper, and landfill leachates.
- The table below shows known emissions of bisphenol A as a reference.

Bisphenol A

	Emission Sources
Production	• 148 kg per year into water in the EU [11]. • 418 kg per year into air in the EU [11].
Use	Release from polycarbonate and epoxy resins products, and thermal paper during use [15].
Disposal	• Inappropriate disposal of thermal paper can lead to emissions into the environment or enter the paper recycling process [13]. • Disposal of products containing bisphenols either as an additive or monomer (e.g. polycarbonate plastics) in landfills can lead to contamination of the environment via leachates [11].
Other sources	Occurs in a type of orchid [16] and in mustard made from one type of mustard seeds [17].

Distribution in the Abiotic Environment and Biota

Expected Partitioning

Inadequate data regarding the emission patterns for these chemicals across their wide range of uses have been identified, hindering a representative understanding of their environmental distribution. Additional efforts are needed to better understand the emission patterns, and environmental models (e.g., the Level III fugacity model in EPI Suite [7]) could then be used to estimate the distribution of these chemicals across the different environmental compartments.

Bioaccumulation Potential

	Bioconcentration factor (BCF)	**Organism**	**Reference**
Bisphenol F	6.6–11	fish	[3]
Bisphenol S	<0.2–<2.2	fish	[3]

Measured Environmental Concentrations

Measured concentrations for these chemicals have been reported in numerous environmental media. A non-exhaustive set of reported concentrations is included below.

Concentrations are provided in varying units depending on the media. Mass per mass dry weight (dw) and wet weight (ww) are sometimes used. ND = not detected, i.e., below the limit of detection (LOD). NQ = not quantified, i.e., below the limit of quantification (LOQ). NR = not reported.

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concen-tration**	**Samples > LOD**	**Refer-ence**
Bisphenol F (BPF)							
River water	Korea	2014	10	ND–1301 ng/L	ND	40 % (LOD = NR)	[18]
River water	Japan	2013/ 2014	8	76.2–2846 ng/L	287.5 ng/L	100 % (LOD = NR)	[18]
River water	China	2013	13	ND–ND	ND	0 % (LOD = 0.059 ng/L)	[19]
River water	China	2013	10	ND–ND	ND	0 % (LOD = 0.059 ng/L)	[19]
River water	China	2012	5	ND–3.47 ng/L	ND	40 % (LOD = 0.45 ng/L)	[20]
River/Canal water	India	2014	12	ND–289 ng/L	ND	33 % (LOD = NR)	[18]
Lake water	China	2013	23	ND–5.6 ng/L	0.5 ng/L	87 % (LOD = 0.059 ng/L)	[19]
Surface water (rivers, lakes, channels)	Germany	1997	30	ND–180 ng/L	NR	77 % (LOD = 0.1 ng/L)	[21]
Seawater	Japan	2013/ 2014	10	ND–1474 ng/L	167 ng/L	90 % (LOD = NR)	[18]
River sediment	China	2013	12	ND–0.41 ng/g dw	ND	8 % (LOD = 0.053 ng/g dw)	[19]
River sediment	China	2013	7	ND–3.8 ng/g dw	ND	43 % (LOD = 0.053 ng/g dw)	[19]
River sediment	China	2012	5	ND–30.16 ng/g dw	6.24 ng/g dw	60 % (LOD = 0.2 ng/g dw)	[20]
River sediment	USA	1998 to 2012	82	ND–27.5 ng/g dw	1.44 ng/g dw	59 % (LOD = NR)	[22]
Lake sediment	China	2013	23	ND–1.2 ng/g dw	0.47 ng/g dw	91 % (LOD = 0.053 ng/g dw)	[19]
Surface water sediment	Germany	1997	7	ND–7.3 µg/kg dw	NR	58 % (LOD = 1 µg/kg dw)	[21]
Sewage sludge	USA	2006/ 2007	76	ND–242 ng/g dw	8.16 ng/g dw	68 % (LOD = 1.79 ng/g dw)	[23]

Bisphenol S (BPS)							
River water	Korea	2014	10	ND–42 ng/L	ND	20 % (LOD = NR)	[18]
River water	Japan	2013/ 2014	8	1.5–8.7 ng/L	3.35 ng/L	100 % (LOD = NR)	[18]
River water	China	2013	13	0.22–52 ng/L	8.9 ng/L	100 % (LOD = 0.047 ng/L)	[19]
River water	China	2013	10	0.61–46 ng/L	8.4 ng/L	100 % (LOD = 0.047 ng/L)	[19]
River water	China	2012	5	0.29–18.99 ng/L	0.51 ng/L	100 % (LOD = 0.04 ng/L)	[20]
River/canal water	India	2014	12	ND–7204 ng/L	44 ng/L	83 % (LOD = NR)	[18]
Lake water	China	2013	23	0.28–67 ng/L	2.0 ng/L	100 % (LOD = 0.047 ng/L)	[19]
Seawater	Japan	2013/ 2014	10	ND–15 ng/L	ND	40 % (LOD = NR)	[18]
Lake sediment	China	2013	23	ND–0.76 ng/g dw	0.071	57 % (LOD = 0.043 ng/g dw)	[19]
River sediment	China	2013	12	ND–1.1 ng/g dw	ND	8 % (LOD = 0.043 ng/g dw)	[19]
River sediment	China	2013	7	ND–0.051 ng/g dw	ND	14 % (LOD = 0.043 ng/g dw)	[19]
River sediment	China	2012	5	ND–0.22 ng/g dw	0.07 ng/g dw	60 % (LOD = 0.03 ng/g dw)	[20]
River sediment	USA	1998 to 2012	82	ND–4.65 ng/g dw	ND	16 % (LOD = NR)	[22]
Sewage sludge	USA	2006/ 2007	76	ND–1480 ng/g dw	5.8 ng/g dw	84 % (LOD = 1.79 ng/g dw)	[23]

Scientific Evidence of Adverse Endocrine-Related Environmental Effects

Reported scientific evidence of adverse endocrine-related environmental effects from exposure to bisphenols F and S exist for different organisms and across different study levels. A comprehensive but non-exhaustive set of reported observations is included below, and further observations can be found in published literature reviews including in the following:

- M. Naderi, M.Y.L. Wong, F. Gholami, Developmental exposure of zebrafish (Danio rerio) to bisphenol-S impairs subsequent reproduction potential and hormonal balance in adults, Aquat. Toxicol. 148 (2014) 195–203. doi:10.1016/j.aquatox.2014.01.009.

Population level / field studies

No reported studies investigating this level were identified during the preparation of this fact sheet.

In vivo level

Substance	**Organism**	**Observation**	**Reference**
BPS	zebrafish embryo	Increased vitellogenin* level in males (feminization)	[24]
BPS	zebrafish	Changed plasma steroid and thyroid levels	[24–26]
BPS	zebrafish	Impaired reproduction (decreased egg production)	[24]
BPS	zebrafish	Altered sex ratio (skewed to females)	[24]
BPS; BPF	zebrafish	Altered spawning behavior and hatching rates	[24,25,27]

In vitro level

Substance	**Cell line**	**Observation**	**Reference**
BPS	zebrafish transcriptomics	Altered gene transcription hypothalamic-pituitary-gonad (HPG) axis, especially indirectly affected gonadotropin hormones production that play important role in reproduction	[25]
BPF	zebrafish transcriptomics	Altered expression of genes involved in various thyroid hormone pathways (e.g. signalling, synthesis and transport)	[26]
BPS	zebrafish	Altered reproductive neuroendocrine-related gene expression	[28]

Notes:
*Vitellogenin is a precursor protein normally synthesized by females to be incorporated in eggs.

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BHT and BHA

Key References:

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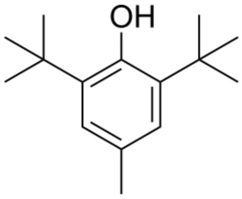
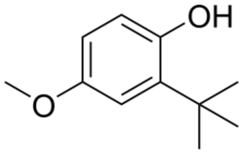
Chemical Identification			
Name(s)	**Abbreviation**	**CAS Number**	**Structure**
Butylated hydroxytoluene	BHT	128-37-0	
Butylated hydroxyanisole; tert-Butylhydroxyanisole; tert-Butyl-4-methoxyphenol	BHA	25013-16-5	
Completed assessments as the basis for inclusion: SIN List (BHT; BHA), Danish Criteria (BHA) **Note**: BHA often refers to a mixture of two isomers 2-tert-butyl-4-methoxyphenol and 3-tert-butyl-4-methoxyphenol [1].			

Physical and Physicochemical Properties		
Property	**BHT**	**BHA**
Molecular formula	$C_{15}H_{24}O$	$C_{11}H_{16}O_2$
Molecular weight [g/mol]	220.36	180.24
Physical state at 20°C	solid	solid
Melting point [°C]	70 [2]	51 [2]
Density [g/cm^3]	1.048 at 20 °C [3]	0.666 at 27 °C [4]
Vapor pressure at 25°C [mmHg]	$5.16*10^{-3}$ [5]	$2.34*10^{-3}$ [†]
Water solubility at 25°C [mg/L]	0.6 [6]; 0.4 at 20 °C [7]	insoluble [2]; 610 at 29 °C, pH=1.28 [4]
Octanol/water partition coefficient (logK_{OW})	5.10 [8]	3.29 [9]; 3.5[†]
Organic carbon/water partition coefficient (log K_{OC})	4.17 (MCI method)[†], 3.91 (Kow method)[†]	2.92 (MCI method)[†] , 3.08 (Kow method)[†]
Air/water partition coefficient (log K_{AW})	-3.77[†]	-5.46[†]
Dissociation constant (pKa)	12.2 [8]	$1.67*10^{-4}$ [4] (see note)
Note: The included pKa value for BHA as reported in the REACH dossier may be a typo.		

[†] Estimated value using models in EPI Suite v4.11 [13].
NR = not reported

Degradation Pathways and Kinetics

Mechanisms	Expected to occur?			Technosphere	Environment	Reference
	Yes	No	Not reported			
Hydrolysis	BHT	BHA				[10,11]
Photolysis	BHT; BHA					[10,11]
OH-radical reactions			BHT; BHA			
Biodegradation	BHT	BHA		WWTP	Soil, water	[4,6,11,12]

Kinetics – Butylated Hydroxytoluene (BHT)

Mechanism	Reported values	Reference
OH-radical reactions	Half-life = 7 h (estimated) †	[13]
Photolysis	20 % of BHT remains after 240 h of UV irradiation	[14]
Photolysis + Hydrolysis (water with sunlight)	74.8 % degraded after 8 d	[10]
Hydrolysis (water in the dark)	40.4 % degraded after 8 d	[10]
Biodegradation (soil)	77–86.7 % degraded after 1 d, 82.4–93.7 % degraded after 24 d	[12]
Biodegradation (activated sludge)	50.1–79.4 % degraded after 7d, 79.2–95 % degraded after 28 d, 94.1–99.2 % degraded after 56 d	[6]

Kinetics – Butylated Hydroxyanisole (BHA)

Mechanism	Reported values	Reference
OH-radical reactions	Half-life = 4 h (estimated) †	[13]
Photolysis	65 % of BHA remains after 240 h UV irradiation	[14]

Intentional Uses and Production Levels

Uses

BHT and BHA

- Widely used as antioxidants and preservatives [15,16].
- Permitted as food additives in the US with certain limitations [17].
- Also used as antioxidants in pesticide formulations [11].

BHT

- Used as an antioxidant in food products, animal feed, cosmetics, packaging material, petroleum products, synthetic rubbers, plastics, elastomers, oils, waxes, soaps, paints, and inks [18,19].
- Global use profile in 2000:
    - 27 % rubber,
    - 27 % plastics,
    - 17 % mineral oils/fuels,
    - 12 % foodstuff/pharmaceuticals/cosmetics,
    - 11 % animal feed/pet food,
    - 6 % printing inks/miscellaneous [19].

BHA

- Mainly used in food, food packaging, animal feed, cosmetics, and in rubber and petroleum products [4,15].

Production Levels

BHT

- Global production volume: approximately 62 000 tonnes in 2000 [19].
- This included:
    - US – 7000 tonnes,
    - Japan – 15 000 tonnes,
    - Western Europe – 25 000 tonnes,
    - Russia – 5000 tonnes,
    - India – 1000 tonnes,
    - China – 9000 tonnes [19].
- Currently registered in the EU with 10 000–100 000 tonnes per year of production or import [4].
- 757 tonnes reported for production or import in the US by 11 producers in 2011; another 12 producers are listed, but have declared their annual production volumes as classified business information [20].

BHA

- Currently registered in the EU with 100–1000 tonnes per year of production or import [4].

Emission Sources into the Environment

- Little information on emission sources of BHT and no information on emission source of BHA has been found.

BHT

	Emission Sources
Production	Released into the environment during processing of plastics containing BHT, due to its volatility at processing temperatures [18].
Use	• Released from polyolefin plastics (e.g. LDPE films) [21] and polylactic acid [16]. • This can occur throughout the use phase of relevant plastic products.
Disposal	• Not reported • Releases from plastics during disposal could be expected due to its known potential to leach from those plastics.
Other sources	Not reported

BHA

	Emission Sources
Production	Not reported
Use	Not reported
Disposal	Not reported
Other sources	Not reported

Distribution in the Natural Environment

Expected Distribution

Based on the identified uses and emission sources for these chemicals as plastic additives and the emission scenario information generated by the OECD [22], a plausible emission pattern was assumed to estimate the resulting distribution in the natural environment using the Level III fugacity model in EPI Suite [13]. The assumed emission pattern and the resulting environmental distribution from the model are presented in the table below for each chemical.

	Assumed Emission Pattern			Modeled Partitioning Results			
	Air	**Water**	**Soil**	**Air**	**Water**	**Soil**	**Sediment**
BHT	50 %	50 %	0 %	2 %	51 %	3 %	44 %
BHA	50 %	50 %	0 %	1 %	87 %	8 %	4 %

Bioaccumulation Potential

	Bioconcentration factor (BCF)	Organism	Reference
BHT	646 (estimated)[†]	fish	[13]
BHA	57 (estimated)[†]	fish	[13]

Measured Environmental Concentrations

Measured concentrations for BHT and BHA have been reported in numerous environmental media. A non-exhaustive set of reported concentrations is included below.

Concentrations are provided in varying units depending on the media. Mass per mass dry weight (dw) and wet weight (ww) are sometimes used. ND = not detected, i.e., below the limit of detection (LOD). NQ = not quantified, i.e., below the limit of quantification (LOQ). NR = not reported.

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concen-tration**	**Samples > LOD**	**Refer-ence**
Butylated Hydroxytoluene (BHT)							
River water	Germany	2000/ 2001	9	25–365 ng/L	172 ng/L	100 % (LOD = 5 ng/L)	[23]
River water (upstream of WWTP)	Sweden	2002	1	0.62 µg/L	0.62 µg/L	100 % (LOD = NR)	[24]
River water (downstream of WWTP)	Sweden	2002	3	0.1–0.47 µg/L	0.16 µg/L	100 % (LOD = NR)	[24]
Ground water	Germany	2000/ 2001	78	ND–2156 ng/L	126 ng/L	78 % (LOD = 5 ng/L)	[23]
WWTP influent	Germany	2001	4	263–478 ng/L	349 ng/L	100 % (LOD = 5 ng/L)	[23]
WWTP influent	Sweden	2002	1	2.53 µg/L	2.53 µg/L	100 % (LOD = NR)	[24]
WWTP effluent	Germany	2001	4	22–258 ng/L	105 ng/L	100 % (LOD = 5 ng/L)	[23]
WWTP effluent	Sweden	2002	4	0.32–0.61 µg/L	0.505 µg/L	100 % (LOD = NR)	[24]
Wastewater	USA	1999/ 2000	85	NR–0.2 µg/L	0.1 µg/L (estimated)	2.4 % (LOD = 0.12 µg/L)	[25]
Sewage sludge	China	2010/ 2011	56	51.7–30 300 ng/g dw	2350 ng/g dw	100 % (MQL = 1.2 ng/g dw)	[26]
DWTP source water	USA	2006/ 2007	19	ND–49 ng/L	ND	5 % (LOD = 25 ng/L)	[27]
DWTP finished water	USA	2006/ 2007	18	ND–26 ng/L	ND	6 % (LOD = 25 ng/L)	[27]
DWTP distribution water (tap water)	USA	2006/ 2007	15	ND	ND	0 % (LOD = 25 ng/L)	[27]

Butylated Hydroxyanisole (BHA)

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concen-tration**	**Samples > LOD**	**Refer-ence**
River water	South Korea	2008	6	ND	ND	0 % (LOD = 1 ng/L)	[28]
Creek water (effluent-dominated)	South Korea	2008	4	ND–4.5 ng/L	ND	25 % (LOD = 1 ng/L)	[28]
Wastewater	USA	1999/ 2000	85	NR–0.1 µg/L	0.1 µg/L (estimated)	2.4 % (LOD = 0.08 µg/L)	[25]
Sewage sludge	China	2010/ 2011	56	ND–17.4 ng/g dw	2.44 ng/g dw	66.1 % (MQL = 15 ng/g dw)	[26]
DWTP source water	USA	2006/ 2007	19	ND	ND	0 % (LOD = NR)	[27]
DWTP finished water	USA	2006/ 2007	18	ND	ND	0 % (LOD = NR)	[27]
DWTP distribution water (tap water)	USA	2006/ 2007	15	ND	ND	0 % (LOD = NR)	[27]

Scientific Evidence of Adverse Endocrine-Related Environmental Effects

Reported scientific evidence of adverse endocrine-related environmental effects from exposure exist for different organisms and across different study levels. A comprehensive but non-exhaustive set of reported observations is included below.

Population level / field studies

No reported studies investigating this level were identified during the preparation of this fact sheet.

In vivo level

Substance	**Organism**	**Observation**	**Reference**
BHT	rat	Increased iodine uptake (iodine is crucial for thyroid hormone synthesis)	[29]
BHA	rat	Altered thyroid and sex hormone levels in serum	[30]
BHA	rat	Altered reproduction (decreased sperm quality, disrupted recurring period of sexual receptivity and fertility)	[30]
BHT; BHA	rat	Altered sex organ weights in females	[30–32]

In vitro level

Substance	**Cell line**	**Observation**	**Reference**
BHA	U2OS human cells with ERa and ERb receptors	Estrogen receptor (ER) activation (including binding and transcription processes)	[33]
BHA	rainbow trout	Competitive binding to the estrogen receptor (displacing 17β-estradiol)	[34]
BHT	rainbow trout	No competitive binding to the estrogen receptor (displacing 17β-estradiol)	[34]
BHA	human	Induced cell proliferation (estrogenic activity) in proliferation assay	[35]
BHT	human	No induced cell proliferation (estrogenic activity) in proliferation assay	[35]
BHT; BHA	human breast cancer cell line	Androgen receptor (AR) blockage (receptor inhibition or transcription process alteration)	[36]

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Carbon disulphide

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Chemical Identification			
Name	**Abbreviation**	**CAS Number**	**Structure**
Carbon disulphide	CS2	75-15-0	S=C=S
Completed assessments as the basis for inclusion: SIN List			

Physical and Physicochemical Properties	
Property	**Carbon disulphide**
Molecular formula	CS_2
Molecular weight [g/mol]	76.14
Physical state at 20°C	liquid
Melting point [°C]	-112.1 [1]; -111.6 [2]
Density [g/cm^3]	1.2632 at 20 °C [1]
Vapor pressure at 25°C [mmHg]	359 [3]; 206 [4]
Water solubility at 25°C [mg/L]	2160 [5], 2900 at 20 °C and pH of 5.9 [6]
Octanol/water partition coefficient (log K_{OW})	1.94 (QSAR estimate) [7]; 2.7 [8]
Organic carbon/water partition coefficient (log K_{OC})	1.34 (MCI method)[†], 1.68 (Kow method)[†]
Air/water partition coefficient (log K_{AW})	-0.23[†]
Dissociation constant (p*K*a)	Not applicable

[†] Estimated value using models in EPI Suite v4.11 [11].

NR = not reported

Degradation Pathways and Kinetics

Mechanisms	Expected to occur?			Technosphere	Environment	Reference
	Yes	No	Not reported			
Hydrolysis		X (negligible)			Water	[9]
Photolysis	X					[9]
OH-radical reactions	X				Atmosphere	[9]
Biodegradation	X			WWTP		[6]

Kinetics – Carbon disulphide (CS2)

Mechanism	Reported values	Reference
OH-radical reactions	Half-life = 5.5–15 d	[9]
Photolysis	Half-life = 7.7 d (calculated)	[9]
Biodegradation (activated sludge, non-adapted, aerobic)	>80 % degraded after 7 d	[6]

Intentional Uses and Production Levels

Uses

- Mainly used for the production of regenerated cellulose (viscose rayon and cellophane) and carbon tetrachloride (via chlorination) [2,10].
- Minor uses include other applications such as in the rubber industry, as a flotation agent, in pesticides, and in other miscellaneous chemical reagents [2].

Production Levels

- Registered in the EU with a volume of 100 000 to 1 000 000 tonnes per year of production or import [6].
- Approximately 900 000 tonnes produced globally in 1990 [2].

Emission Sources into the Environment

- Mainly released into the atmosphere due to its high volatility [9].
- Can also occur naturally, either by bacterial processes, volcanic activity or weathering of sulfide minerals [9,10].CS2 can also occur naturally, either by bacterial processes, volcanic activity or weathering of sulphide minerals. While estimates in Canada suggest that up to 35 000 tonnes CS2 may be added to the Canadian environment annually from these natural sources alone, other reports state that the natural emissions of carbon disulphide are thought to be small compared to anthropogenic sources [9,10].

	Emission Sources
Production	Approximately 16 000 tonnes released into the environment from manufacturing and processing facilities in the USA in 1999 [9].
Use	Can be released into the environment from viscose fibers and cellophane films since it is not bound to the end product [9,10].
Disposal	Not reported
Other sources	• Estimates in Canada suggest that up to 35 000 tonnes may be added to the Canadian environment annually from natural sources [9,10]. • Other reports state that the natural emissions of carbon disulfide are small compared to anthropogenic sources [9,10].

Distribution in the Natural Environment

Expected Distribution

Based on the identified primary emissions of carbon disulphide to air [9], a plausible emission pattern was assumed to estimate the resulting distribution in the environment using the Level III fugacity model in EPI Suite [11]. The assumed emission pattern as well as the resulting environmental distribution from the model are presented in the table below.

	Assumed Emission Pattern			**Modelled Distribution Results**			
	Air	**Water**	**Soil**	**Air**	**Water**	**Soil**	**Sediment**
MTBE	100 %	0 %	0 %	100 %	0 %	0 %	0 %

Bioaccumulation Potential

	Bioconcentration factor (BCF)	**Organism**	**Reference**
Carbon disulphide	<60	fish	[6]

Measured Environmental Concentrations

Measured concentrations for carbon disulphide have been reported in numerous environmental media. A non-exhaustive set of reported concentrations is included below.

Concentrations are provided in varying units depending on the media. Mass per mass dry weight (dw) and wet weight (ww) are sometimes used. ND = not detected, i.e., below the limit of detection (LOD). NQ = not quantified, i.e., below the limit of quantification (LOQ). NR = not reported.

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concen-tration**	**Samples > LOD**	**Refer-ence**
Carbon disulphide (CS2)							
Seawater	Pacific Ocean, Indian Ocean, Southern Ocean	1996	NR	ND	ND	0% (LOD = 0.04 nM)	[12]
Air (above river water surface)	China	2006	8	0.1–14.8 µg/m^3	6.4 µg/m^3	100 % (LOD = 0.048 µg/m^3)	[13]
Air (above riverbank)	China	2006	8	ND–0.71 µg/m^3	0.16 µg/m^3	NR (LOD = (0.048 µg/m^3)	[13]
Ambient air (near landfills)	Spain	2014	51	0.09–0.44 mg/m^3	0.13 mg/m^3	NR (LOD = 0.8 pg/m^3)	[14]
Air (rural/ coastal areas)	China	2002	19	5–896 pptv	35 pptv*	100 % (LOD = 0.5 pptv)	[15]
Ambient air (industrial area)	Korea	2004/ 2005	60	ND–2.23 ppbv	0.82 ppbv*	98 % (LOD = 0.01 ppbv)	[16]
Ambient air (rural area)	Senegal	2006	NR	0.1 ppbv (mean)	NR	NR	[17]
Atmosphere (above ocean surface)	Pacific Ocean, Indian Ocean, Southern Ocean	1996	NR	ND–13.5 pptv	5.6 pptv*	NR (LOD = 1 pptv)	[12]

Note: *pptv = parts per trillion volume / ppbv = parts per billion volume

Scientific Evidence of Adverse Endocrine-Related Environmental Effects

Reported scientific evidence of adverse endocrine-related environmental effects from exposure to carbon disulphide exist for different organisms at the in vivo level. A comprehensive but non-exhaustive set of reported observations is included below.

Population level / field studies

No reported studies investigating this level were identified during the preparation of this fact sheet.

In vivo level

Substance	Organsim	Observation	Reference
CS2	rat	Changed sex hormone levels (plasma and/or whole body) / affected sex hormone secretion	[18,19]
CS2	rat	Impaired reproduction (decreased sperm counts and activity, increased teratospermia)	[18]
CS2	mouse	Loss of the early embryo (due to damaged endometrial cells)	[20]

In vitro level

No reported studies investigating this level were identified during the preparation of this fact sheet.

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Dithiocarbamates

Key References:

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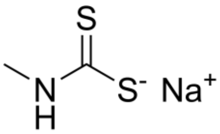
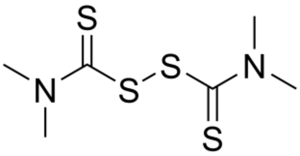
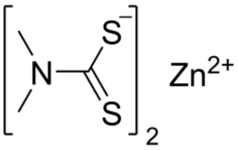
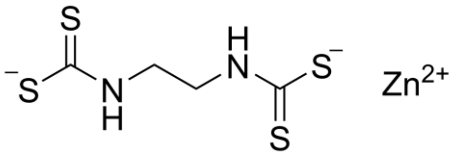
Chemical Identification			
Name(s)	**Abbreviation**	**CAS Number**	**Structure**
Metam-sodium; Sodium methyldithiocarbamate	MS	137-42-8	
Thiram; Tetramethylthiuram disulphide	TM	137-26-8	
Ziram	ZM	137-30-4	
Zineb	ZB	12122-67-7	
Completed assessments as the basis for inclusion: SIN List (MS; TM; ZM; ZB), Danish Criteria (MS; TM; ZB)			

Physical and Physicochemical Properties				
Property	**Metam-sodium**	**Thiram**	**Ziram**	**Zineb**
Molecular formula	$C_2H_4NS_2Na$	$C_6H_{12}N_2S_4$	$C_6H_{12}N_2S_4Zn$	$(C_4H_6N_2S_4Zn)_n$
Molecular weight [g/mol]	129.2	240.4	305.8	275.8
Physical state at 20°C	solid	solid	solid	solid
Melting point [°C]	86.5–90.5 [1]; decomposes upon melting [2]	155–156 [3]; 144–146 [4]	246 [5]; 251–252.5 [6]	157 (decomposes) [7]
Density [g/cm^3]	1.44 [1]	1.3 at 25 °C [8]; 1.36 at 20 °C [4]	1.71 at 20 °C [6]	1.74 at 20 °C [9]
Vapor pressure at 25°C [mmHg]	$4.31*10^{-4}$ [1]	$1.72*10^{-5}$ [10]	$7.5*10^{-9}$ at 0 °C [11]	$<7.5*10^{-8}$ at 20 °C [10]
Water solubility at 25°C [mg/L]	$7.22*10^5$ [12]	30 [13]; 17 [4]	1 [6]	10 [10]
Octanol/water partition coefficient (log K_{OW})	-2.9 [1]	1.73 [10] ; 2.1 [4]	1.23 [11] ; 1.65 [6]	1.30 [10]
Organic carbon/water partition coefficient (log K_{OC})	1.77 (MCI method)†, 0.73 (Kow method)†	2.79 (MCI method)†, 3.07 (Kow method)†	3.05 (MCI method)†, 2.79 (Kow method)†	3.13 (MCI method)†, 2.88 (Kow method)†
Air/water partition coefficient (log K_{AW})	NR	-5.13†	-7.60†	-8.19†
Dissociation constant (p*K*a)	pKa1 = 2.99, pKa2 = 11.06 [1]	NR	NR	NR

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† Estimated value using models in EPI Suite v4.11 [16].
NR = not reported

Degradation Pathways and Kinetics

Mechanism	Expected to occur?			Technosphere	Environment	Reference
	Yes	No	Not Reported			
Hydrolysis	MS; TM; ZM; ZB					[1,14]
Photolysis	MS; TM; ZM		ZB			[15]
OH-radical reactions	MS; TM; ZM; ZB					[1,16]
Biodegradation	MS; TM; ZM; ZB					[1]

Kinetics – Metam-sodium (MS)

Mechanism	Reported values	Reference
OH-radical reactions	Half-life = 2 h (estimate)	[16]
Photochemical degradation	Half-life = 1.6 h	[1]
Photolysis (in shallow water)	Half-life = 28–44 min	[14,15]
Hydrolysis	Half-life = 2–7.5 d	[14]
Biodegradation (soil)	Half-life = 23 min–4 d	[1]

Kinetics – Thiram (TM)

Mechanism	Reported values	Reference
OH-radical reactions	Half-life = 21 min (estimate)	[16]
Photolysis (in water)	Half-life = 24–28 min	[17]
Hydrolysis	Half-life = 3.5 d	[1]
Hydrolysis	Half-life = 7.8 d (20 °C, pH 6.3)	[18]
Biodegradation (soil)	Half-life = 1–105 d	[1]
Biodegradation (soil)	Half-life = 2.6–9.9 d	[19]
Biodegradation (soil)	Half-life = 4.6–7.7 d	[18]

Kinetics – Ziram (ZM)

Mechanism	Reported values	Reference
OH-radical reactions	Half-life = 0.9 h (estimate)	[16]
Photolysis	Half-life = 0.3 d	[1]
Hydrolysis	Half-life = 0.7 d	[1]
Biodegradation (soil)	Half-life = 30 d	[1]
Biodegradation (soil)	Half-life = 5.7–11.4 d	[20]

Kinetics – Zineb (ZB)

Mechanism	Reported values	Reference
OH-radical reactions	Half-life = 0.9 h (estimate)	[16]
Hydrolysis	Half-life = 8.6 d	[1]
Hydrolysis (natural seawater)	Half-life = 4 d	[21]
Biodegradation (soil)	Half-life = 23 d	[22]
Biodegradation (soil)	Half-life = 30 d	[1]

Emission Sources into the Environment

Metam-sodiumMetam-sodium

	Emission Sources
Production	Not reported
Use	Breaks down into several volatile compounds upon application in soils [14,32,33].
Disposal	Not reported
Other sources	Not reported

Thiram

	Emission Sources
Production	Not reported
Use	Not reported. However, based on its use as a fungicide it can be expected that it mostly releases to soil during use.
Disposal	Not reported
Other sources	Not reported

Ziram

	Emission Sources
Production	Not reported
Use	Not reported. However, based on its use as a fungicide it can be expected that it mostly releases to soil during use.
Disposal	Not reported
Other sources	Not reported

Zineb

	Emission Sources
Production	Not reported
Use	Expected to be released to surface waters due to its use in antifouling paints [26,27].
Disposal	Not reported
Other sources	Not reported

Uses and Production Levels

Uses

Metam-sodium
- Used as a broad-spectrum non-systemic soil fungicide with nematicidal, herbicidal, bactericidal, and insecticidal activities.
- Decomposes rapidly in moist soil to its active form methyl isocyanate, which acts as a soil fumigant and is used on a large number of crops [1].

Thiram
- Used as a fungicide, mainly as a broad-spectrum seed treatment for many crops [1].
- Also applied to foliage on grapes, vegetables, ornamentals, fruits, and used to control scab and storage diseases on apples, pears, etc. [1].
- Used in higher concentrations as a deer, rodent, bird and insect repellent [23–25].
- Another large use is as an accelerator and vulcanizing agent in rubber processing [25].
- Other uses include slime control in paper production and use as a bacteriostat in soap and antiseptic sprays [25].

Ziram
- Used as a fungicide for fruits, nuts, vines, vegetables and ornamentals [1].
- Also used as a repellent against birds and rodents [1].

Zineb
- Used to control a number of plant diseases in different crops and approved for use in antifouling paints in many countries [1,26,27].
- Its fungicidal activity is due to its degradation products, mainly ethylenethiuram monosulfide [1].

Production Levels

Metam-sodium
- Annual use in agriculture in the US: 23 000–25 000 tonnes in 2007 [28].
- Annual use in agriculture in California, US: 5125 tonnes in 2001 [29].

Thiram
- Registered in the EU with a volume of 1000–10 000 tonnes per year of production or import [4].
- Use in the US: 286 tonnes in 2004 [30].

Ziram
- Registered in the EU with a volume of 100–1000 tonnes per year of production or import [6].
- Use in the US: 862 tonnes in 2004 [31].

Zineb
- No information on production or use levels was found.

Distribution in the Natural Environment

Estimated Environmental Distribution

Based on the identified uses and emission sources for these chemicals as fungicides, a plausible emission pattern was assumed to estimate the resulting distribution in the environment using the Level III fugacity model in EPI Suite [16]. The assumed emission pattern is based on the estimated foliar interception and retention values [34]. The assumed emission pattern and the resulting environmental distribution from the model are presented in the table below for each chemical.

	Assumed Emission Pattern			Modelled Distribution Results			
	Air	**Water**	**Soil**	**Air**	**Water**	**Soil**	**Sediment**
Metam-S.	10 %	0 %	90 %	0 %	5 %	95 %	0 %
Thiram	10 %	0 %	90 %	0 %	1 %	99 %	0 %
Ziram	10 %	0 %	90 %	0 %	1 %	99 %	0 %
Zineb	10 %	0 %	90 %	0 %	1 %	99 %	0 %

Bioaccumulation Potential

Thiram and zineb are reported to be not bioaccumulative [21].

	Bioconcentration factor (BCF)	Organism	Reference
Metam-Sodium	3.2 (estimate)	fish	[16]
Thiram	6.4 (estimate)	fish	[16]
Ziram	3.0 (estimate)	fish	[16]
Zineb	3.3 (estimate)	fish	[16]

Measured Environmental Concentrations

Only few measured environmental concentrations were identified for these chemicals. A non-exhaustive set of the reported measurements that have been found are included below. No measurements were found for metam-sodium.

Concentrations are provided in varying units depending on the media. Mass per mass dry weight (dw) and wet weight (ww) are sometimes used. ND = not detected, i.e., below the limit of detection (LOD). NQ = not quantified, i.e., below the limit of quantification (LOQ). NR = not reported.

Measured compartment/ medium	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concentration**	**Samples > LOD**	**Reference**
Thiram (TM)							
River water	Spain	NR (1996)	1	ND	ND	0 % (LOD = 36 µg/L)	[35]
Groundwater and surface water	USA	NR (1987–1996)	NR	ND	ND	0 % (LOD = NR)	[36]
Sea sediment	Republic of Korea	2010/ 2011	39	22.3–62.2 ng/g dw	39.8 ng/g dw (mean)	100 % (LOD = NR)	[37]
Agriculture waste water	India	NR (1998)	2	18.2–18.4 µg/L	18.3 µg/L	100 % (LOD = NR)	[38]
Ziram (ZM)							
Fog water (near treated crops)	India	2001/ 2002	8	ND–404 µg/L	164 µg/L	75 % (LOD = 20 µg/L)	[39]
Sea sediment	Republic of Korea	2010/ 2011	39	ND	ND	0 % (LOD = NR)	[37]
Air over treated almond orchard (before application)	USA	1994	5	ND	ND	0 % (LOD = 14– 23 ng/m^3)	[40]
Air over treated almond orchard (after application)	USA	1994	2.26 µg/m^3	ND	ND	55 % (LOD = 14–23 ng/m^3)	[40]
Agriculture waste water	India	NR (1998)	1	26 µg/L	26 µg/L	100 % (LOD = NR)	[38]
Zineb (ZB)							
Fog water (near treated crops)	India	2001/ 2002	8	ND–231 µg/L	140 µg/L	75 % (LOD = 21 µg/L)	[39]
Sea sediment	Republic of Korea	2010/ 2011	39	1.29–107 ng/g dw	37.1 ng/g dw	100 % (LOD = NR)	[37]

Measured compartment/ medium	Sampling location	Sampling year	Number of samples	Concentration range	Median concentration	Samples > LOD	Reference
Agriculture waste water	India	NR (1998)	2	24.8–30 µg/L	27.4 µg/L	100 % (LOD = NR)	[38]

Note: Additional information regarding the sampling location and year is sometimes provided after values that are not reported (NR) in parentheses. This represents an estimated value for this non-reported information based on the general details provided in the study.

Scientific Evidence of Adverse Endocrine-Related Environmental Effects

Reported scientific evidence of adverse endocrine-related environmental effects from exposure exist for different organisms and across different study levels. A comprehensive but non-exhaustive set of reported observations is included below.

Population level / field studies

No reported studies investigating this level were identified during preparation of the fact sheet.

In vivo level

Substance	Organism	Observation	Reference
ZM	rat	Antithyroid effect (reduced iodine uptake and/or iodine protein bound required for thyroid hormone synthesis)	[41]
TM; MS	rat	Blocked ovulation (time dependent for certain compounds)	[42,43]
ZM; TM	mouse	Induced sperm shape abnormalities	[44]
ZM; TM	chicken	Antifertility effects (decreased ovarian weight, reduced egg production) in laying hens	[45,46]
ZB	chicken	No fertility effects in laying hens	[45,46]
TM	rat	Altered reproduction (ovulation delay, decreased fertilized oocytes, increased supernumerary sperm, ovulated oocyte numbers), no such effect found for MS	[47,48]

In vitro level

Substance	Cell line	Observation	Reference
ZB	hamster cells with human TPO enzymes	Inhibition of thyroid peroxidase (TPO) enzyme leads to decreased thyroidal synthesis of thyroid hormones	[49]
ZM; TM	hamster cells with human TPO enzymes	No inhibition of thyroid peroxidase (TPO) enzyme	[49]
ZM; ZB	hamster cells with human TPO enzymes	Altered gene expression involved in thyroid signaling pathway (TPO iodinating activity)	[49]

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Methyl tert-butyl ether

Key References:

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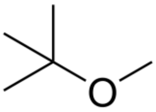
Chemical Identification			
Name(s)	**Abbreviation**	**CAS Number**	**Structure**
Methyl tert-butyl ether; 2-methoxy-2-methylpropane	MTBE	1634-04-4	
Completed assessments as the basis for inclusion: SIN List, Danish Criteria			

Physical and Physicochemical Properties	
Property	**MTBE**
Molecular formula	$C_5H_{12}O$
Molecular weight [g/mol]	88.15
Physical state at 20°C	liquid
Melting point [°C]	-108.6 [1]
Density [g/cm^3]	0.7353 [1]
Vapor pressure at 25°C [mmHg]	250 [2]
Water solubility at 25°C [mg/L]	$4.8*10^4$ [3]
Octanol/water partition coefficient (log K_{OW})	1.06 [4]
Organic carbon/water partition coefficient (log K_{OC})	1.06 (MCI method)†, 1.35 (Kow method)†
Air/water partition coefficient (log K_{AW})	-1.62†
Dissociation constant (pKa)	Not applicable

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† Estimated value using models in EPI Suite v4.11 [9].
NR = not reported

Degradation Pathways and Kinetics

Mechanisms	Expected to occur?			Technosphere	Environment	Reference
	Yes	No	Not reported			
Hydrolysis			X			
Photolysis			X			
OH-radical reactions	X				Atmosphere	[4]
Biodegradation		X		WWTP	Soil	[4]

Kinetics – MTBE

Mechanism	Reported values	Reference
OH-radical reactions	Half-life = 3–6 d	[4]
Biodegradation (activated sludge, domestic, non-adapted, aerobic)	0 % degraded after 28 d	[4]
Biodegradation (soil, aerobic)	Half-life = 80–102 d	[4]
Biodegradation (soil, anaerobic)	0 % degraded after 250 d	[5]

Intentional Uses and Production Levels

Uses

- Mainly (98 % of total quantity produced) used as an additive in petrol, where it acts as an octane enhancer [6,7].
- To a lesser extent also used in the production of high purity isobutylene, as reaction solvent, extractant, and chromatographic eluent [6,7].

Production Levels

- Currently registered in the EU with 1 000 000–10 000 000 tonnes per year of production or import [4].
- In 1997, the production volume in the EU was 3 000 000 tonnes [6].
- Since 2001 the production and use has been declining due to legislative efforts in the US to phase out MTBE and replace it with ethanol [8].

Emission Sources into the Environment

- Environmental emissions result mainly from storage, distribution and use of petrol [6].
- Other uses contribute only negligibly to the total emissions, partly because of the low amounts used and partly because of the uses themselves, where fewer amounts are released into the environment [6].

	Emission Sources
Production	Not reported
Use	• Automobile exhaust gases are a major source of emissions in ambient air [6]. • Releases to the aquatic environment from disposal of tank bottom water either directly or via WWTPs to surface water (during storage of petrol in storage tanks, water is condensed at the bottom of the tanks, and due to the high water solubility of MTBE this water may have a high concentration of MTBE) [6].
Disposal	Not reported
Other sources	Not reported

Distribution in the Natural Environment

Estimated Environmental Distribution

Based on the identified uses and emission sources for MTBE as a fuel additive, a plausible emission pattern was assumed to estimate the resulting partitioning in the environment using the Level III fugacity model in EPI Suite [9]. The assumed emission pattern as well as the resulting environmental distribution from the model are presented in the table below.

	Assumed Emission Pattern			**Modelled Distribution Results**			
	Air	**Water**	**Soil**	**Air**	**Water**	**Soil**	**Sediment**
MTBE	50 %	50 %	0 %	26 %	74 %	0 %	0 %

Bioaccumulation Potential

	Bioconcentration factor (BCF)	**Organism**	**Reference**
MTBE	1.5	fish	[6]

Measured Environmental Concentrations

Measured concentrations for MTBE have been reported in numerous environmental media. A non-exhaustive set of reported concentrations is included below, and further measurements can be found in published literature including in the following:

- C. Sablayrolles, A. Breton, C. Vialle, C. Vignoles, M. Montréjaud-Vignoles, Priority organic pollutants in the urban water cycle (Toulouse, France), Water Sci. Technol. 64 (2011) 541. doi:10.2166/wst.2011.580.

Concentrations are provided in varying units depending on the media. Mass per mass dry weight (dw) and wet weight (ww) are sometimes used. ND = not detected, i.e., below the limit of detection (LOD). NQ = not quantified, i.e., below the limit of quantification (LOQ). NR = not reported.

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concentration**	**Samples > LOD**	**Reference**
MTBE							
River water	Japan	2002/ 2003	72	ND–0.46 µg/L	NR	68 % (LOD = 0.003 µg/L)	[10]
Ground water	Korea	NR (2009)	110	ND–0.45 µg/L	NR	57.3 % (LOD = 0.01 µg/L)	[11]
Ground water	France	2006-2009	4	<LOQ	<LOQ	0 % (LOQ = 1 µg/L)	[12]
Ground water	Japan	2002/ 2003	66	ND–5.9 µg/L	NR	33 % (LOD = 0.003 µg/L)	[10]
Ground water	Denmark	1993-2001	218	ND–1.4 µg/L	ND	0.5 % (LOD = NR)	[13]
Ground water	USA	1993/ 1994	211	ND–23 000 µg/L	NR	26.5 % (LOD = 0.2 µg/L)	[14]
Rainwater	France	2006-2009	4	<LOQ	<LOQ	0 % (LOQ = 1 µg/L)	[12]
Run-off water	France	2006-2009	10	<LOQ–1.9 µg/L	<LOQ	NR (LOQ = 1 µg/L)	[12]
Estuary water	UK	2002	17	ND–194 ng/L	16 ng/L	88 % (LOD = 6 ng/L)	[15]
Roof collected water	France	2006-2009	4	<LOQ	<LOQ	0 % (LOQ = 1 µg/L)	[12]
Raw wastewater	France	2006-2009	8	<LOQ	<LOQ	0 % (LOQ = 1 µg/L)	[12]
Treated wastewater	France	2006-2009	8	<LOQ	<LOQ	0 % (LOQ = 1 µg/L)	[12]

Note: Additional information regarding the sampling location and year is sometimes provided after values that are not reported (NR) in parentheses. This represents an estimated value for this non-reported information based on the general details provided in the study.

Scientific Evidence of Adverse Endocrine-Related Environmental Effects

Reported scientific evidence of adverse endocrine-related environmental effects from exposure to MTBE exist for different organisms and across different study levels. A comprehensive but non-exhaustive set of reported observations is included below.

Population level / field studies

No reported studies investigating this level were identified during the preparation of this fact sheet.

In vivo level

Substance	Organism	Observation	Reference
MTBE	zebrafish, fathead minnow	No effect on reproduction (fecundity) observed	[16]
MTBE	rat	Changed sex- and thyroid hormone levels (in serum)	[17,18]
MTBE	rat	Enzyme induction involved in testosterone metabolism	[19]
MTBE	rat	Impaired reproduction (altered sperm count and quality)	[18]
MTBE	rat	No effects on reproduction (altered oocyte count and fragility) found	[20]

In vitro level

Substance	Cell line	Observation	Reference
MTBE	rat	Altered spermatogenic cell morphology and decreased number of spermatogenic cells	[21]
MTBE	rat	Altered testosterone production	[22]
MTBE	rat prostate, human adrenal corticocarcinoma	No androgen receptor binding affinity observed	[23]
MTBE	rat prostate, human adrenal corticocarcinoma	No altered production of testosterone and estradiol (steroidogenic pathways) observed	[23]

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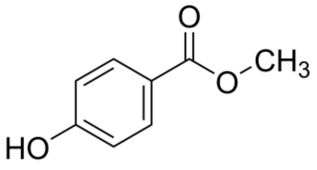
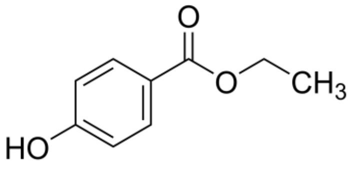
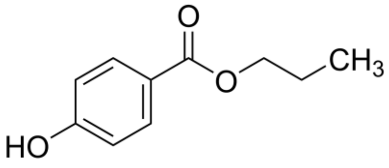
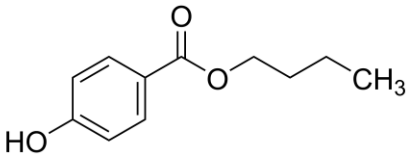
Parabens

Key References:

- D. Błędzka, J. Gromadzińska, W. Wąsowicz, Parabens. From environmental studies to human health., Environ. Int. 67 (2014) 27–42. doi:10.1016/j.envint.2014.02.007.

Chemical Identification			
Name(s)	**Abbreviation**	**CAS Number**	**Structure**
Methylparaben	MP	99-76-3	
Ethylparaben	EP	120-47-8	
Propylparaben	PP	94-13-3	
Butylparaben	BP	94-26-8	
Completed assessments as the basis for inclusion: SIN List (PP; BP), Danish Criteria (MP; EP; PP; BP)			

Physical and Physicochemical Properties				
Property	**MP**	**EP**	**PP**	**BP**
Molecular formula	$C_8H_8O_3$	$C_9H_{10}O_3$	$C_{10}H_{12}O_3$	$C_{11}H_{14}O_3$
Molecular weight [g/mol]	152.1	166.2	180.2	194.2
Physical state at 20°C	solid	solid	solid	solid
Melting point [°C]	131 [1]	116 [1]	96 [1]	68 [2]
Density [g/cm^3]	NR	NR	1.06 [3]	NR
Vapor pressure at 25°C [mmHg] [†]	$8.55*10^{-4}$ [†]	$9.29*10^{-5}$ [†]	$3.07*10^{-4}$ [†]	$2.51*10^{-4}$ [†]
Water solubility at 25°C [mg/L] [†]	2 500 [4]	1 894[†]	500 [5]	207 [5]
Octanol/water partition coefficient (log K_{OW})	1.96 [6]	2.47 [6]	3.04 [6]	3.57 [6]
Organic carbon/water partition coefficient (log K_{OC}) [†]	1.94 (MCI method)[†]; 2.11 (Kow method)[†]	2.07 to 2.32 [7]	2.46 (MCI method)[†]; 2.71 (Kow method) [†]	2.72 (MCI method)[†]; 3.00 (Kow method)[†]
Air/water partition coefficient (log K_{AW}) [†]	-6.83 [†]	-6.71 [†]	-6.58 [†]	-6.46 [†]
Dissociation constant (p*K*a)	8.4 [8]	NR	NR	8.47 [9]

[†] Estimated value using models in EPI Suite v4.11. [29]
NR = not reported

Degradation Pathways and Kinetics

Mechanism	Expected to occur?			Technosphere	Environment	Reference
	Yes	No	Not reported			
Hydrolysis		MP; EP; PP; BP (all negligible)				[10]
Photolysis		MP; EP; PP; BP (all negligible)				[11–13]
OH-radical reactions	MP; EP; PP; BP				Natural waters	[14]
Biodegradation	MP; EP; PP; BP			WWTP		[15–17]

Kinetics – Methylparaben (MP)

Mechanism	Reported values	Reference
Biodegradation (activated sludge)	99 % degraded within 5 d Half-life = ≤3 d	[16,17]

Kinetics – Ethylparaben (EP)

Mechanism	Reported values	Reference
Biodegradation (activated sludge)	99 % degraded within 5 d Half-life = ≤3	[16,17]

Kinetics – Propylparaben (PP)

Mechanism	Reported values	Reference
Biodegradation (activated sludge)	99 % degraded within 5 d Half-life = ≤3 d	[16,17]

Kinetics – Butylparaben (BP)

Mechanism	Reported values	Reference
Photolysis	Half-life = 410 h in air	[11]
Biodegradation (activated sludge)	99 % degraded within 5 d Half-life = ≤3 d	[16,17]

Intentional Uses and Production Levels

Uses

- Widely used as preservatives in cosmetics, pharmaceuticals, food commodities, and industrial products [18].
- First used in 1920s as preservatives in drug products [19]. Used as preservatives in more than 60 % of personal care products in 2006 [20]. Other estimates from 2005 place MP and/or PP as present in 48 % of cosmetics and personal care products and BP in 13 % [21].
- Approved by the US Food and Drug Administration for use in foods as a preservative following specific regulations; MP and PP generally recognized as safe (GRAS) for use in foods when adhering to the use limits of 0.1 % [10].
- Following the studies published in the early 2000s suggesting PB to have estrogenic activity and potential to be a carcinogen, some manufacturers began replacing parabens with other preservatives. Content of parabens in cosmetics significantly decreased between 1981 and 1995 (from upwards of 25 % down to <1 %) [18,22].

Production Levels

Methylparaben
- Registered for production or import in the EU with a range of 1000–10 000 tonnes per year [23].
- In the US in 2011: had active manufacturers and/or importers; however, the actual production/import levels are marked as confidential business information [26].

Ethylparaben
- Registered for production or import in the EU with a range of 100–1000 tonnes per year [24,25].

Propylparaben
- Registered for production or import in the EU with a range of 100–1000 tonnes per year [24,25].
- In the US in 2011: had active manufacturers and/or importers; however, the actual production/import levels are marked as confidential business information [26].

Butylparaben
- No information on production volumes found.
- Not registered for production or import in the EU.

Emission Sources into the Environment

- Use of parabens worldwide in products leads to their ubiquitous occurrence in the environment [18].
- Releases often end up in surface waters mainly through wastewater treatment plant effluents, runoffs, and deposition of particles from the air [18].

Releases From:

Production – No information found on emissions during the production of parabens. It is therefore not clear whether emissions occur or not.

Use – Parabens can be released from products in which they are present. This is apparent from their widespread presence in wastewater treatment plants [18] (e.g. washing off cosmetics, etc.).

Disposal – The observed average efficiency of paraben removal from wastewater treatment plants is high (96.1 to 99.9 %) [17,27]; however, they have still been detected in most WWTP effluents at concentrations up to 4000 ng/L [18]. Effluents from wastewater treatment processes considered as major point sources into the environment (0–1.6 % of the influent mass released in final effluents [28]).

Distribution in the Abiotic Environment and Biota

Estimated Environmental Distribution

Based on the identified uses and emission sources for these chemicals as additives in personal care products, a plausible emission pattern was assumed to estimate the resulting distribution in the environment using the Level III fugacity model in EPI Suite [29]. The assumed emission pattern and the resulting environmental distribution from the model are presented in the table below for each chemical.

	Assumed Emission Pattern			Modelled Distribution Results			
	Air	**Water**	**Soil**	**Air**	**Water**	**Soil**	**Sediment**
MP	0 %	90 %	10 %	0 %	77 %	23 %	0 %
EP	0 %	90 %	10 %	0 %	76 %	24 %	0 %
PP	0 %	90 %	10 %	0 %	75 %	24 %	1 %
BP	0 %	90 %	10 %	0 %	77 %	22 %	1 %

Bioaccumulation Potential

	Bioconcentration factor (BCF)	Organism	Reference
Methylparaben	9 (estimated)†	fish	[29]
Ethylparaben	20 (estimated)†	fish	[29]
Propylparaben	47 (estimated)†	fish	[29]
Butylparaben	105 (estimated)†	fish	[29]

Measured Environmental Concentrations

Measured concentrations for these chemicals have been reported in numerous environmental media. A non-exhaustive set of reported concentrations is included below, and further measurements can be found in published literature including in the following:

- Będzka, D., Gromadzińska, J., Wąsowicz, W., 2014. Parabens. From environmental studies to human health. Environ. Int. 67, 27–42. doi:10.1016/j.envint.2014.02.007

Concentrations are provided in varying units depending on the media. Mass per mass dry weight (dw) and wet weight (ww) are sometimes used. ND = not detected, i.e., below the limit of detection (LOD). NQ = not quantified, i.e., below the limit of quantification (LOQ). NR = not reported.

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concentration**	**Samples > LOD or LOQ**	**Reference**
Methylparaben (MP)							
River water	Australia	2014	32	ND– 12 510 ng/L	2810 ng/L	50 % (LOD = 1000 ng/L)	[30]
River water (low-flow)	China	2005	8	NQ–1062 ng/L	82 ng/L	75 % (LOD = 0.5 ng/L)	[31]
River water (high-flow)	China	2005	10	NQ–213 ng/L	12 ng/L	90 % (LOD = 0.5 ng/L)	[31]
River water	Spain	NR (2011)	9	ND–42 ng/L	NR	NR (LOD = 0.3 ng/L)	[32]
Storm water	Australia	2014	34	ND– 13 780 ng/L	6570 ng/L	82 % (LOD = 1000 ng/L)	[30]
Sediment	Spain	NR (2008)	2	0.84–6.35 ng/g	1.8 ng/g	100 % (LOQ = 0.49 ng/g)	[33]
Sediment (high-flow)	China	2013	23	1.82–15.1 ng/g	4.73 ng/g	100 % (LOD = 0.01 ng/g)	[34]
Sediment (low-flow)	China	2013	23	1.43–11.1 ng/g	4.14 ng/g	100 % (LOD = 0.01 ng/g)	[34]
Ethylparaben (EP)							
River water	Australia	2014	32	ND– 35 170 ng/L	5260 ng/L	94 % (LOD = 2000 ng/L)	[30]
Storm water	Australia	2014	34	ND– 305 550 ng/L	5155 ng/L	94 % (LOD = 2000 ng/L)	[30]
River water	Spain	NR (2011)	9	ND–1.1 ng/L	NR	NR (LOD = 0.17 ng/L)	[32]
Sediment	Spain	NR (2008)	2	0.54–5.10 ng/g	0.82 ng/g	100 % (LOQ = 0.49 ng/g)	[33]
Sediment (high-flow)	China	2013	23	ND–0.63 ng/g	0.14 ng/g	96 % (LOD = 0.01 ng/g)	[34]
Sediment (low-flow)	China	2013	23	0.13–0.32 ng/g	0.23 ng/g	100 % (LOD = 0.01 ng/g)	[34]

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concentration**	**Samples > LOD or LOQ**	**Refer-ence**
Propylparaben (PP)							
River water	Australia	2014	32	ND–8290 ng/L	2870 ng/L	81 % (LOD = 1000 ng/L)	[30]
Storm water	Australia	2014	34	ND–6220 ng/L	2790 ng/L	79 % (LOD = 1000 ng/L)	[30]
River water (low-flow)	China	2005	8	8–2142 ng/L	631 ng/L	100 % (LOD = 0.1 ng/L)	[31]
River water (high-flow)	China	2005	10	NQ–480 ng/L	34 ng/L	90 % (LOD = 0.1 ng/L)	[31]
River water	Spain	NR (2011)	9	ND–2.5 ng/L	NR	NR (LOD = 0.2 ng/L)	[32]
Sediment	Spain	NR (2008)	3	0.59–4.03 ng/g	1.47 ng/g	100 % (LOQ = 0.28 ng/g)	[33]
Sediment (high-flow)	China	2013	23	ND–0.19 ng/g	0.06 ng/g	65 % (LOD = 0.01 ng/g)	[34]
Sediment (low-flow)	China	2013	23	0.2–2.40 ng/g	0.58 ng/g	100 % (LOD = 0.01 ng/g)	[34]
Butylparaben (BP)							
River water	Australia	2014	32	ND–8470 ng/L	4335 ng/L	94 % (LOD = 1000 ng/L)	[30]
Storm water	Australia	2014	34	ND–5530 ng/L	4375 ng/L	97 % (LOD = 1000 ng/L)	[30]
River water (low-flow)	China	2005	8	ND	ND	0 % (LOD = 0.1 ng/L)	[31]
River water (high-flow)	China	2005	10	ND	ND	0 % (LOD = 0.1 ng/L)	[31]
River water	Spain	NR (2011)	9	ND	NR	0 % (LOD = 0.03 ng/L)	[32]
Sediment	Spain	NR (2008)	3	0.28–0.71 ng/g	0.39 ng/g	100 % (LOQ = 0.21 ng/g)	[33]
Sediment (high-flow)	China	2013	23	ND	ND	0 % (LOD = 0.01 ng/g)	[34]
Sediment (low-flow)	China	2013	23	ND	ND	0 % (LOD = 0.01 ng/g)	[34]

Scientific Evidence of Adverse Endocrine-Related Environmental Effects

Reported scientific evidence of adverse endocrine-related environmental effects from exposure to parabens exist for different organisms and across different study levels. A comprehensive but non-exhaustive set of reported observations is included below.

Population level / Field studies

No reported studies investigating this level were identified during the preparation of this fact sheet.

In vivo level

Substance	Organism	Observation	Reference
PP	zebrafish	Anti-estrogenicity	[35]
MP; PP	rainbow trout, zebrafish and medaka	Increased vitellogenin* level in males (feminization)	[35–37]
EP; PP; BP	rainbow trout	Impaired reproduction (decreased egg production)	[38]
PP	zebrafish	Altered sex ratio (skewed to females)	[39]

In vitro level

Substance	Cell line	Observation	Reference
MP	medaka	Vitellogenin* mRNA or protein expression	[37]
MP	zebrafish	Altered gene transcription – anti-estrogenicity	[40]

Notes:
*Vitellogenin is a precursor protein normally synthesized by females to be incorporated in eggs.

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Key References:

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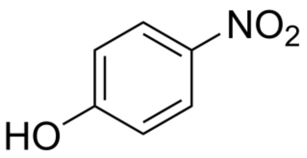
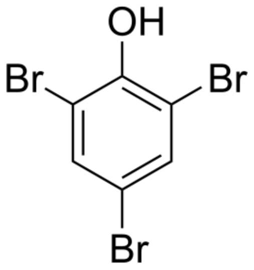
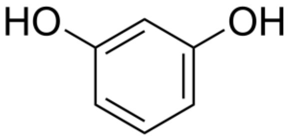
Chemical Identification			
Name(s)	**Abbreviation**	**CAS Number**	**Structure**
4-Nitrophenol	4NiP	100-02-7	
2,4,6-Tribromophenol	TBP; Tribromophenol	118-79-6	
Resorcinol; 3-Hydroxyphenol; 1,3-Dihydroxybenzene; 1,3-Benzenediol	RS	108-46-3	
Completed assessments as the basis for inclusion: SIN List (4NiP; TBP; RS), Danish Criteria (4NiP; RS)			

Physical and Physicochemical Properties			
Property	**4NiP**	**TBP**	**Resorcinol**
Molecular formula	$C_6H_5NO_3$	$C_6H_3Br_3O$	$C_6H_6O_2$
Molecular weight [g/mol]	139.1	330.8	110.1
Physical state at 20°C	solid	solid	solid
Melting point [°C]	113–114 [1]	94–96 [1]; 95.5 [2]	109.8 [3]
Density [g/cm^3]	1.479 [2]	2.55 [4]	1.278 [3]
Vapor pressure at 25°C [mmHg]	$9.79*10^{-5}$ at 20 °C [5]	$3.15*10^{-4}$ [2]	$4.89*10^{-4}$ [6]
Water solubility at 25°C [mg/L]	15.6 [7]	70 at 15 °C [8]	$7.17*10^5$ [7]; $1.41*10^6$ [9]
Octanol/water partition coefficient (log K_{OW})	1.91 (QSAR estimate) [10]	4.13 (QSAR estimate) [10]	0.80 (QSAR estimate) [10]
Organic carbon/water partition coefficient (log K_{OC})	2.46 (MCI method)†, 2.37 (Kow method)†	2.91 (MCI method)†, 3.38 (Kow method)†	2.38 (MCI method)†, 1.70 (Kow method)†
Air/water partition coefficient (log K_{AW})	-7.77†	-5.84†	-8.39†
Dissociation constant (pKa)	7.15 [11]; 7.08 [5]	6.80 [11]	pKa1 = 9.30, pKa2 = 11.06 [11]; pKa1 = 9.4, pKa2 = 11.4 [9]

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† Estimated value using models in EPI Suite v4.11 [24].
NR = not reported

Degradation Pathways and Kinetics

Mechanism	Expected to occur?			Technosphere	Environment	Reference
	Yes	No	Not reported			
Hydrolysis		TBP; RS	4NiP			[12,13]
Photolysis	4NiP; TBP; RS			In aqueous solution: pH $\geqslant$ 9	Atmosphere	[13–15]
OH-radical reactions	4NiP		TBP; RS		Atmosphere	[14]
Biodegradation	4NiP; TBP; RS			WWTP	Soil	[9,13,16–20]

Kinetics – 4-Nitrophenol (4NiP)

Mechanism	Reported values	Reference
Photolysis	Half-life = 1.3 d (calculated as sunny summer day equivalents)	[14]
OH-radical reactions	Half-life = 2.5 h (calculated as sunny summer day equivalents)	[14]
Biodegradation (topsoil, 10°C, 15% water, aerobic)	Half-life = 0.7–1.2 d	[17]
Biodegradation (topsoil, 10°C, 3% water, aerobic)	Half-life = 1.2 d	[17]
Biodegradation (topsoil, 10°C, 15% water, anaerobic)	Half-life = 14 d	[17]
Biodegradation (subsoil, 10°C, anaerobic)	Half-life = 40 d	[17]
Biodegradation (soil; 10 µg 4NiP /g soil)	Mineralization rate constant = 0.152 mg/(L*d)	[21]
Biodegradation (soil; 100 µg 4NiP /g soil)	Mineralization rate constant = 0.75 mg/(L*d)	[21]
Biodegradation (soil)	Depletion of 30–40 % of 4NiP after one month	[22]
Biodegradation (sterile river water with river water biofilms)	Half-life = ND–5.63 days (upstream of WWTP); 8.2–16.1 d (WWTP effluent); ND–5.7 d (downstream of WWTP)	[23]

Kinetics – 2,4,6-Tribromophenol (TBP)

Mechanism	Reported values	Reference
OH-radical reactions	Half-life = 22.5 d (estimated)†	[24]
Photolysis (simulated sunlight)	Half-lives = 110–116 (river water), 144 min (seawater), 223 min (ultrapure water)	[25]

Kinetics – Resorcinol (RS)

Mechanism	Reported values	Reference
OH-radical reactions	Half-life = 0.6 h (estimated)†	[24]
Biodegradation (activated sludge, non-adapted, aerobic)	66.7 % degraded after 14 d	[12]
Biodegradation (activated sludge, adapted, aerobic)	97 % degraded after 4 d	[12]

Intentional Uses and Production Levels

Uses

4-Nitrophenol

- Registered in the EU as an intermediate chemical only and in unreported quantities [26].
- Used in the production of pharmaceuticals, dyes, insecticides and herbicides [27,28].

Tribromophenol

- Used as a wood preservative and flame retardant [29].
- Registered in the EU as being used in polymers for the manufacture of plastic products [13].

Resorcinol

- Used as an industrial intermediate. The primary use (>50 %) is in the production of reinforced rubber products (e.g. tires, conveyor belts), followed by (circa 25 %) high-quality wood adhesives (e.g. for the manufacture of laminated wooden beams). Other uses include production of dyes, pharmaceuticals, and light stabilizers. [9]

Production Levels

4-Nitrophenol

- No recent production volumes found [26].
- Consumption and export in the US: about 10 000 tonnes in 1987 [30].

Tribromophenol

- Global annual production volume: approximately 9500 tonnes in 2001 [31].
- Annual production volume in Japan: approximately 2500 tonnes [31].
- Registered in the EU with 0–10 tonnes per year of production or import [13].

Resorcinol

- Global annual production capacity: approximately 50 000 tonnes in 2010 [9].
- Currently registered in the EU with 10 000–100 000 tonnes per year of production or import [12].

Emission Sources into the Environment

4-Nitrophenol

	Emission Sources
Production	Not reported
Use	• Used as an intermediate chemical only [26]. • Likely being released into the environment through its industrial use [26].
Disposal	Incineration as waste from chemical production sites may lead to release of small quantities into the atmosphere [30].
Other sources	• Released as a secondary pollutant by phenol nitration in the atmosphere (in both the liquid and gas phases) [14,32] and in surface waters [33]. • Also released by hydrolysis of pesticides (e.g. parathion) [34]. • Released into the atmosphere to a smaller extent as primary pollutant from gasoline and diesel engines [35]. Car exhausts are the main source of atmospheric concentrations [36].

Tribromophenol

	Emission Sources
Production	Not reported
Use	Emissions when used as a flame retardant or wood preservative [31,37].
Disposal	Not reported
Other sources	• Bromination of organic substrates by marine algae [38]. • Produced by a class of worms (polychaete) [39]. • Formed in water treatment systems by chlorination of water containing bromide ions [37] for production of drinking water [40], and cooling water for nuclear power plants [41,42]. • May also be formed as a by-product of tetrabromobisphenol A, which is used as a flame retardant [43].

Resorcinol

	Emission Sources
Production	• Approximately 22.4 tonnes (estimated) annually and globally released during production in the early 2000s [15]. • During the production of tires in Europe the early 2000s, approximately 5 tonnes (estimated) annually released to WWTPs and approximately 1.5 tonnes to the atmosphere [44]. • Production of dyes and hair dyes releases 3 and 1.5 tonnes (estimated), respectively, to WWTPs per year in Europe in the early 2000s [44].
Use	Approximately 170 tonnes per year released to WWTPs during use of hair dyes and pharmaceutical products (e.g. topical ointments) in Europe in the early 2000s [44].
Disposal	Expected to occur with landfilling of discarded pharmaceutical products [44].
Other sources	Not reported

Distribution in the Natural Environment

Estimated Environmental Distribution

Inadequate data regarding the emission patterns for these chemicals across their wide range of uses have been identified, hindering a representative understanding of their environmental distribution. Additional efforts are needed to better understand the emission patterns, and environmental models (e.g., the Level III fugacity model in EPI Suite [24]) could then be used to estimate the distribution of these chemicals across the different environmental compartments.

Bioaccumulation Potential

	Bioconcentration factor (BCF)	**Organism**	**Reference**
4-Nitrophenol	57	fish (golden orfe)	[45]
	80	fish (fathead minnow)	[46]
	11	algae (*Chlorella fusca*)	[45]
Tribromophenol	513	fish (zebrafish)	[47]
Resorcinol	3 (estimate)†	fish	[24]

Measured Environmental Concentrations

Measured concentrations for these chemicals have been reported in numerous environmental media. A non-exhaustive set of reported concentrations is included below.

Concentrations are provided in varying units depending on the media. Mass per mass dry weight (dw) and wet weight (ww) are sometimes used. ND = not detected, i.e., below the limit of detection (LOD). NQ = not quantified, i.e., below the limit of quantification (LOQ). NR = not reported.

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concen-tration range**	**Median concen-tration**	**Samples > LOD**	**Refer-ence**
4-Nitrophenol (4NiP)							
Surface water	Germany	1999	30	ND–0.60 µg/L	NQ (LOQ = 0.04 µg/L)	40 % (LOD = 0.01 µg/L)	[48]
Lake water	Ant-arctica	1998/ 1999	9	11–70 ng/L	28 ng/L	100 %	[49]
Ground water (low depth, on site of former ammunition plant)	Germany	NR (1995)	1	15 µg/L	15 µg/L	100 %	[50]
Ground water (high depth, on site of former ammunition plant)	Germany	NR (1999)	1	88 µg/L	88 µg/L	100 %	[50]
Rain water	France	1991	8	1.11–757 µg/L	1.69 µg/L	100 %	[51]
Rain water	Germany	1989/ 1999	20	1.2–19.5 µg/L	5.7 µg/L (mean)	100 %	[52]
Cloud water	Germany	1994	6	6.4–46 µg/L	21 µg/L	100 %	[53]
Cloud water	United Kingdom	1993	6	0.05–4.94 µg/L	2.03 µg/L	100 %	[36]
Cloud water	France	1991	7	1.66–16.27 µg/L	3.76 µg/L	100 %	[51]
Mountain fog	Germany	1988	10	8.1–40.2 µg/L	17.7 µg/L	100 %	[54]
Urban radiation fog	Germany	1988	4	13.9–23.0 µg/L	20.2 µg/L	100 %	[54]
Lake suspended matter	Antarctica	1998/ 1999	3	ND–42 735 ng/kg	ND	33 % (LOD = NR)	[49]
Snow	Antarctica	1996/ 1997	6	8–13 ng/L	10 ng/L	67 % (LOD = 5 ng/L)	[49]
Snow	Russia	2011	7	0.22–1.65 µg/L	0.27 µg/L	100 %	[55]
Soil (surburban area)	China	NR (2011)	1	800 mg/kg	800 mg/kg	100 %	[56]

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concentration**	**Samples > LOD**	**Reference**
Air particle phase	Japan	1982	5	5.1–42 µg/g	8 µg/g	100 %	[35]
Air (mountain summit, liquid and gas phases)	United Kingdom	1993	10	1.23–39.0 ng/m^3	13.42 ng/m^3	100 %	[36]
Urban air	Italy	1998	1	0.3 µg/m^3	0.3 µg/m^3	100 %	[57]
2,4,6-Tribromophenol (TBP)							
River water	Republic of Korea	2006	13	ND–3.34 ng/L	0.685 ng/L	69 % (LOD = 0.21 ng/L)	[41]
River water	China	2014	1	ND	ND	0 % (LOD = 2.8 ng/L)	[58]
River water	China	2014	15	ND–810 pg/L	250 pg/L	80 % (LOD = 30 pg/L)	[43]
River water (e-waste recycling area, control site negative)	China	2013	14	ND–320 ng/L	110 ng/L (mean)	NR (LOD = NR)	[59]
Seawater	China	2014	2	26.2–68.4 ng/L	47.3 ng/L	100 %	[58]
Seawater (close to nuclear power plant, surface)	Republic of Korea	2006 (Spring)	15	1.11–16.2 ng/L	2.87 ng/L	87 % (LOD = 0.21 ng/L)	[41]
Seawater (close to nuclear power plant, bottom)	Republic of Korea	2006 (Spring)	15	1.73–6.14 ng/L	2.96 ng/L	80 % (LOD = 0.21 ng/L)	[41]
Seawater (close to nuclear power plant, surface)	Republic of Korea	2006 (Summer)	15	0.378 - 7.23 ng/L	0.655 ng/L	100 %	[41]
Seawater (close to nuclear power plant, bottom)	Republic of Korea	2006 (Summer)	15	0.718 - 3.42 ng/L	1.58 ng/L	100 %	[41]
Seawater (close to nuclear power plant, surface)	Republic of Korea	2006 (Fall)	15	0.793 - 20.2 ng/L	14.0 ng/L	20 %	[41]
Seawater (close to nuclear power plant, bottom)	Republic of Korea	2006 (Fall)	15	0.810–2.78 ng/L	1.17 ng/L	100 %	[41]
Seawater (close to nuclear power plant, surface)	Republic of Korea	2007 (Winter)	15	0.515–3.50 ng/L	1.51 ng/L	80 % (LOD = 0.21 ng/L)	[41]
Seawater (close to nuclear power plant, bottom)	Republic of Korea	2007 (Winter)	15	0.580–2.64 ng/L	1.45 ng/L	73 % (LOD = 0.21 ng/L)	[41]

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concen-tration range**	**Median concen-tration**	**Samples > LOD**	**Refer-ence**
Snow	China	NR (2014)	1	ND	ND	0 % (LOD = NR)	[60]
River sediment	China	2014	13	ND–410 pg/g dw	20 pg/g dw	54 % (LOD = 3 pg/g dw)	[43]
River sediment	Republic of Korea	2006	4	ND–1.10 ng/g dw	0.757 ng/g dw	75 % (LOD = 0.11 ng/g dw)	[41]
River sediment (e-waste recycling area, control site negative)	China	2013	14	ND–47 ng/g	21 ng/g (mean)	NR (LOD = NR)	[59]
Marine sediment (close to nuclear power plant)	Republic of Korea	2006 (Spring)	15	1.56–6.31 ng/g dw	3.94 ng/g dw	100 %	[41]
Marine sediment (close to nuclear power plant)	Republic of Korea	2006 (Summer)	15	1.80–12.3 ng/g dw	2.90 ng/g dw	100 %	[41]
Marine sediment (close to nuclear power plant)	Republic of Korea	2006 (Fall)	15	1.25–3.57 ng/g dw	2.55 ng/g dw	100 %	[41]
Marine sediment (close to nuclear power plant)	Republic of Korea	2007 (Winter)	15	0.560–3.78 ng/g dw	2.38 ng/g dw	100 %	[41]
Air	Norway	2003	49	ND - >LOD	NR	35 % (LOD = NR)	[61]
Resorcinol (RS)							
River water	Japan	2010/2011	24	1.2–1150 ng/L	20.8 ng/L	100 %	[62]
River water	China	NR (2005)	5	0.26 µg/L (mean)	NR	NR	[63]
Lake water (near WWTP)	Denmark	2006	2	ND	ND	0 % (LOD = 0.0056 µg/L)	[64]
Seawater (background)	Denmark	2006	1	ND	ND	0 % (LOD = 0.0056 µg/L)	[64]
Surface water (near pulp industry)	Sweden	2006	3	ND	ND	0 % (LOD = 0.0056 µg/L)	[64]
Seawater (near WWTP)	Denmark	2005	2	ND	ND	0 % (LOD = 0.0056 µg/L)	[64]
Seawater (harbor)	Faroe Islands	2005	1	0.0857 µg/L	0.0857 µg/L	100 %	[64]
Surface water (near industrial site)	Norway	2005	2	ND–0.354 µg/L	NR	50 % (LOD = 0.1 µg/L)	[64]

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concen-tration range**	**Median concen-tration**	**Samples > LOD**	**Refer-ence**
Coastal seawater (near landfill)	Iceland	2006	1	0.0018 µg/L	0.0018 µg/L	100 %	[64]
Seawater (near WWTP)	Norway	2005	2	ND	ND	0 % (LOD = 0.1 µg/L)	[64]
Runoff water (near factory hall)	Faroe Islands	2005	1	ND	ND	0 % (LOD = 0.0056 µg/L)	[64]
Air (near pulp industry)	Sweden	2006	3	ND	ND	0 % (LOD = 0.1 ng/m^3)	[64]
River sediment	Finland	2005	1	ND	ND	0 % (LOD = 1–10 ng/g dw)	[64]
Lake sediment	Norway	2005	2	ND–17 ng/g dw	NR	50 % (LOD = 2 ng/g dw)	[64]
Lake sediment	Sweden	2006	3	ND	ND	0 % (LOD = 2–4 ng/g dw)	[64]
Lake sediment	Finland	2005	1	ND	ND	0 % (LOD = 1–10 ng/g dw)	[64]
Lake sediment (near WWTP)	Denmark	2005	2	ND–1.0 ng/g dw	NR	50 % (LOD = 1–10 ng/g dw)	[64]
Marine sediment	Norway	2005	1	ND	ND	0 % (LOD = 1–10 ng/g dw)	[64]
Marine sediment (near WWTP)	Denmark	2005	2	ND	ND	0 % (LOD = 2 ng/g dw)	[64]
WWTP effluent	Faroe Islands	2005	1	ND	ND	0 % (LOD = 0.1 µg/L)	[64]
WWTP effluent	Denmark	2005/ 2006	2	ND–0.24 µg/L	NR	50 % (LOD = 0.0054 µg/L)	[64]
WWTP effluent	Norway	2006	3	ND	ND	0 % (LOD = 0.1 µg/L)	[64]
WWTP effluent	Sweden	2005	9	ND–0.008 µg/L	ND	22 % (LOD = 0.0055–0.0057 µg/L)	[64]
WWTP effluent	Finland	2005	6	ND–0.011 µg/L	ND	17 % (LOD = 0.0056–0.0058 µg/L)	[64]
Pulp and paper industry effluent	Finland	2005	2	ND	ND	0 % (LOD = 0.0054–0.0057 µg/L)	[64]

Note: Additional information regarding the sampling location and year is sometimes provided after values that are not reported (NR) in parentheses. This represents an estimated value for this not reported information based on the general details provided in the study.

Scientific Evidence of Adverse Endocrine-Related Environmental Effects

Reported scientific evidence of adverse endocrine-related environmental effects from exposure to benzophenones exists for different organisms and across different study levels. A comprehensive but non-exhaustive set of reported observations is included below, and further observations can be found in published literature reviews including in the following:

- B.S. Lynch, E.S. Delzell, D.H. Bechtel, Toxicology Review and Risk Assessment of Resorcinol: Thyroid Effects, Regul. Toxicol. Pharmacol. 36 (2002) 198–210. doi:10.1006/rtph.2002.1585.

Population level / field studies

No reported studies investigating this level were identified during the preparation of this fact sheet.

In vivo level

Substance	Organism	Observation	Reference
TBP; 4NiP	zebrafish, rat	Changed plasma steroid levels	[65–67]
RS	rat	Disrupted iodine uptake (iodine is crucial for thyroid hormone synthesis)	[68]
RS	zebrafish	Thyroid gland function disrupting activity	[69]
4NiP	rat	Altered sex organ weight	[70]
TBP	zebrafish	Disturbed the gonad morphology	[71]
TBP	zebrafish	Reduced fertilization success	[71]
TBP	zebrafish	Altered sex ratio (skewed to females)	[65]

In vitro level

Substance	Cell line	Observation	Reference
TBP	zebrafish	Vitellogenin* mRNA or protein expression	[65]
4NiP	yeast cells with human ER and AR receptors	Estrogenic and anti-androgenic effect (receptor transactivation assay)	[72]
TBP	zebrafish	Altered transcription profiles of steroidogenic genes in gonads (testes and ovary)	[65]
4NiP	cells from chicken embryo	Decrease in testicular cell viability and spermatogonial cell number	[73]
RS	enzyme assay, thyroid endpoint	Inhibition of thyroid peroxidase (TPO) enzyme leads to decreased thyroidal synthesis of thyroid hormones	[74]
TBP	seabream	Weak potency to bind to thyroid hormone transport proteins and displace the thyroid hormone	[75]

Notes:
*Vitellogenin is a precursor protein normally synthesized by females to be incorporated in eggs.

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PCP, Tebuconazole, and Triclosan

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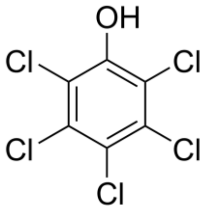
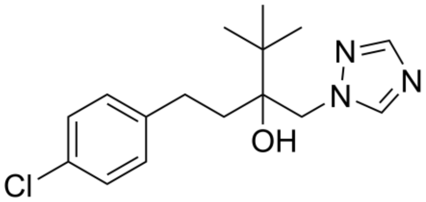
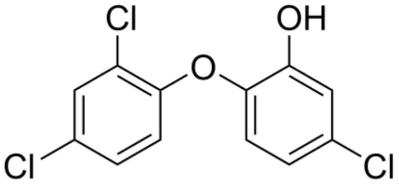
Chemical Identification			
Name(s)	**Abbreviation**	**CAS Number(s)**	**Structure**
Pentachlorophenol	PCP	87-86-5	
Tebuconazole	TCZ	107534-96-3; 80443-41-0	
Triclosan; 5-chloro-2-(2,4-dichlorophenoxy)phenol	TCS	3380-34-5	
Completed assessments as the basis for inclusion: SIN List (PCP), Danish Criteria (PCP; TCZ; TCS)			

Physical and Physicochemical Properties			
Property	**Pentachlorophenol**	**Tebuconazole**	**Triclosan**
Molecular formula	C_6HOCl_5	$C_{16}H_{22}ON_3Cl$	$C_{12}H_7Cl_3O_2$
Molecular weight [g/mol]	266.34	307.81	289.54
Physical state at 20°C	solid	solid	solid
Melting point [°C]	174 [1]; 191 [2]	104.7 [2]; 105 [3]	54–57.3 [4]; 56–57 [5]
Density [g/cm^3]	1.978 [4]; 1.99 [2]	1.25 at 26 °C [2]	1.55 at 22 °C [5]
Vapor pressure at 25°C [mmHg]	0.12 [2]; 1.1*10^{-4} [6]	2.9*10^{-8} [2]; 1.3*10^{-8} [7]	4.65*10^{-6} †
Water solubility at 25°C [mg/L]	14 at 20 °C [8]; 14 at 25 °C [9]	36 at 20 °C [7]	10 at 20 °C [10]
Octanol/water partition coefficient (logK_{OW})	3.82 [2]	3.7 [2]	4.76 [5]
Organic carbon/water partition coefficient (logK_{OC})	3.70 (MCI method)†, 4.07 (Kow method)†	3.19 (MCI method)†, 2.63 (Kow method)†	4.37 (MCI method)†, 3.93 (Kow method)†
Air/water partition coefficient (logK_{AW})	-6.00†	-8.23†	-6.69†
Dissociation constant (pKa)	4.70 [11]; 4.73 [2]	NR	7.9 [4]; 8.14 [5]

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† Estimated value using models in EPI Suite v4.11 [14].
NR = not reported

Degradation Pathways and Kinetics

Mechanism	Expected to occur?			Technosphere	Environment	Reference
	Yes	No	Not reported			
Hydrolysis			PCP; TCS; TCZ			
Photolysis	PCP	TCS	TCZ			[2,12,13]
OH-radical reactions	PCP; TCS; TCZ				Atmosphere	[14]
Biodegradation	PCP; TCS; TCZ			WWTP	Soil, Sediment	[2,5,15–19]

Kinetics – Pentachlorophenol

Mechanism	Reported values	Reference
OH-radical reactions	Half-life = 19.4 d (estimate)	[14]
Photolysis (in water under natural sunlight)	Half-life = 48 d	[12]
Biodegradation (soil)	Half-life = 63 d	[2]
Biodegradation (soil, flooded conditions)	Half-life = 10–70 d	[17]
Biodegradation (soil, upland conditions)	Half-life = 20–120 d	[17]

Kinetics – Tebuconazole

Mechanism	Reported values	Reference
OH-radical reactions	Half-life = 11 h (estimate)	[14]
Biodegradation (soil)	Half-life = 62 d	[2]
Biodegradation (soil)	Half-life = 365 d	[16]
Biodegradation (sediment)	Half-life = 305 d	[2]
Biodegradation (water)	Half-life = >30 d	[16]
Biodegradation (water)	20 % degraded after 28 d	[15]

Kinetics – Triclosan

Mechanism	Reported values	Reference
OH-radical reactions	Half-life = 8 h (estimate)	[14]
Photolysis (in water)	Half-life = 4 d (freshwater) – 8 d (seawater)	[20]
Biodegradation (activated sludge)	50.1 %, 71.2% and 99.4% degraded after 1 d, 7 d, and 14 d, respectively	[5]
Biodegradation (soil)	Half-life = 17.4–35.2 d	[5]
Biodegradation (soil)	Half-life = 104 d (TCS), 443 d (MeTCS, primary metabolite)	[18]
Biodegradation (activated sludge)	Half-life = 54–86 h	[19]

Intentional Uses and Production Levels

Uses

Pentachlorophenol

- Mainly used as a wood preservative to protect utility poles, cross-arms, and building materials [21,22].
- Also used as a pre-harvest defoliant on selected crops [2], although it is presumably no longer used for agricultural purposes [22].
- Regulated in the US as a restricted-use pesticide since 1984, meaning its use is limited to certified applications [23].
- Its use is forbidden in the EU in the excess of 0.1 % by weight in mixtures [24].
- It is listed under Annex A of the Stockholm Convention, which aims to eliminate production and use for ratifying members. A specific exemption is in place for use in utility poles and cross arms. [25]

Tebuconazole

- Used as a fungicide and formulated as an oil-in-water emulsifier, as a foliar spray, and as a concentrate for seed treatment [2].
- Also used as a wood preservative [26].

Triclosan

- Used as a broad spectrum antimicrobial in clinical settings and consumer products, including antimicrobial soaps, antiseptics, antimicrobial detergents, skin care products, and oral care products [27].
- It is also incorporated on the surface of plastics and textile products for antimicrobial treatment [13].

Production Levels

Pentachlorophenol

- Production and imports in the US: 450–4500 tonnes in 2012 [23].

Tebuconazole

- Worldwide consumption: 15 000–16 000 tonnes in 2015 [28].
- Agricultural use in the US: 177 tonnes in 2006 [16].

Triclosan

- Worldwide annual production: 1500 tonnes in 1998, of which 350 tonnes were used in Europe and 450 tonnes in the US [29].
- Use in the EU: about 450 tonnes in 2006 [29].

Emission Sources into the Environment

Pentachlorophenol

	Emission Sources
Production	About 18 kg are estimated to be released to air from the production of around 2000 tonnes annually in countries that are members of the UN Economic Commission for Europe [22].
Use	Released during its use as wood preservative: can occur via different pathways during the treatment process itself and can also migrate from wood that has been treated with it [22,30,31].
Disposal	• Can be released by disposal of pre-treated wood in landfills [22,30]. • Leachate of the landfills containing pre-treated wood products and hazardous waste is reported as the main release pathway in the US [22].
Other sources	Not reported.

Tebuconazole

	Emission Sources
Production	Not reported.
Use	Not reported. However, based on its use as agricultural biocide, it can be expected that it is mostly released to soil during its use.
Disposal	Not reported.
Other sources	Not reported.

Triclosan

	Emission Sources
Production	Not reported.
Use	Emissions mostly from personal care products ending up in domestic wastewater. Incomplete removal from wastewater treatment plants, and especially the spreading of biosolids onto soils, releases it into the environment [13,29].
Disposal	Not reported.
Other sources	Not reported.

Distribution in the Natural Environment

Expected Distribution

Based on the identified uses and emission sources for these chemicals, a plausible emission pattern was applied to estimate the resulting distribution in the environment using the Level III fugacity model in EPI Suite [14]. The assumed emission pattern for tebuconazole is based on the estimated foliar interception and retention values [32], and the one for triclosan is based on its use as an additive in personal care products. The assumed emission pattern and the resulting environmental distribution from the model for these two chemicals are presented in the table below.

	Assumed Emission Pattern			**Modelled Distribution Results**			
	Air	**Water**	**Soil**	**Air**	**Water**	**Soil**	**Sediment**
TCZ	10 %	0 %	90 %	0 %	1 %	99 %	0 %
TCS	0 %	90 %	10 %	0 %	28 %	21 %	51 %

Insufficient data was found to be available for pentachlorophenol in order to determine its emission pattern. Additional efforts are needed to better estimate the emission pattern, and environmental modeling could then be used to estimate the partitioning across the different environmental compartments.

Bioaccumulation Potential

	Bioconcentration factor (BCF)	**Organism**	**Reference**
Pentachlorophenol	3.5–188.5	lake salmon (eggs)	[33]
	7.9–64	killifish (*Fundulus similus*)	[34]
Tebuconazole	9.79–16.25	zebrafish	[35]
Triclosan	646	mussels	[36]
	74	daphnia (eggs)	[37]
	2.7–90	aquatic species	[29]

Measured Environmental Concentrations

Measured concentrations for these chemicals have been reported in numerous environmental. A non-exhaustive set of reported concentrations is included below, and further measurements can be found in published literature including in the following:

- G. Bedoux, B. Roig, O. Thomas, V. Dupont, B. Le Bot, Occurrence and toxicity of antimicrobial triclosan and by-products in the environment, Environ. Sci. Pollut. Res. 19 (2012) 1044–1065. doi:10.1007/s11356-011-0632-z.
- A.L. Perez, M.A. De Sylor, A.J. Slocombe, M.G. Lew, K.M. Unice, E.P. Donovan, Triclosan occurrence in freshwater systems in the United States (1999-2012): A meta-analysis, Environ. Toxicol. Chem. 32 (2013) 1479–1487. doi:10.1002/etc.2217.

Concentrations are provided in varying units depending on the media. Mass per mass dry weight (dw) and wet weight (ww) are sometimes used. ND = not detected, i.e., below the limit of detection (LOD). NQ = not quantified, i.e., below the limit of quantification (LOQ). NR = not reported. RL = reporting level.

Measured compartment	Sampling location	Sampling year	Number of samples	Concentration range	Median concentration	Samples > LOD	Reference
Pentachlorophenol							
River water	China	2014	62	0.09–8.65 µg/L	0.12 µg/L	100 %	[38]
River water	USA	2001	76	ND–51 ng/L	ND	2.6 % (LOD = NR)	[39]
Lake water	China	2014	37	0.03–9.57 µg/L	0.38 µg/L	100 %	[38]
Lake water	China	1998	8	ND–103.7 µg/L	3.76 µg/L	87.5 % (LOD = 0.005 µg/L)	[40]
Fresh water	USA	2001	73	ND–<RL (2 µg/L)	ND	5.4 % (LOD = NR)	[41]
River and pond sediments	China	2000/ 2001	44	0.56–163 ng/g dw	NR	NR (LOD = NR)	[42]
Lake sediment	China	1998	8	0.18–48.3 µg/g dw	15.85 µg/g dw	100 %	[40]
Estuary sediment	Poland	2012/ 2013	4	ND–12.4 ng/g dw	3.47 ng/g dw	75 % (LOD = 0.85 ng/g dw)	[43]
Lake fish (bile)	China	1998	15	ND–0.63 ng/mg	ND	40 % (LOD = 0.01 ng/mg)	[40]
Tebuconazole							
River water	China	2010/ 2011	41	ND–7.1 ng/L	1.6 ng/L	98 % (LOQ = 0.6 ng/L)	[44]
River water	China	NR (2009)	1	3 ng/L	3 ng/L	100 %	[45]
River water	USA	2005/ 2006	103	ND–115 ng/L	ND	6 % (RL = 10 ng/L)	[16]
Seawater	Europe (North Sea)	2014	12	ND–1.02 ng/L	0.285 ng/L	58 % (LOD = 0.14 ng/L)	[46]
River sediment	China	NR (2009)	NR	ND	ND	NR	[45]

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concen-tration**	**Samples > LOD**	**Refer-ence**
River sediment	China	2010/ 2011	14	ND–2.5 ng/g dw	0.15 ng/g dw	86 % (LOQ = 0.4 ng/g dw)	[44]
Estuary sediment	China	NR (2009)	NR	ND	ND	NR	[45]
Agricultural soil (30 d after treatment)	India	2011	2	<LOQ	<LOQ	0 % (LOQ = 50 ng/g)	[47]
Treated wastewater	China	NR (2009)	3	2 ng/L (mean)	2 ng/L (mean)	NR (MQL = 3 ng/L)	[45]
Untreated wastewater	China	NR (2009)	NR	<MQL	<MQL	NR (MQL = 3 ng/L)	[45]
Sewage sludge	China	NR (2009)	NR	ND	ND	NR (MQL = 5 ng/L)	[45]
Sewage sludge	China	NR (2009)	NR	<MQL	<MQL	NR (MQL = 5 ng/L)	[45]
Triclosan							
River water	Spain	2012	22	ND–16 ng/L	ND	9 % (LOD = NR)	[48]
River water	Brazil	2010/2011	71	ND–66 ng/L	ND	48 % (LOD = 0.7 ng/L)	[49]
River water	India	2009	26	approx. 10–139 ng/L	40.7 ng/L	NR (LOD = 3.0 ng/L)	[50]
River water	India	2009	22	approx. 10–5160 ng/L	142 ng/L	NR (LOD = 3.0 ng/L)	[50]
River/estuary water	India	2009	8	NR	8.95 ng/L	NR (LOD = 3.0 ng/L)	[50]
River water (low-flow season)	China	2005/2006	8	48–1023 ng/L	405 ng/L	100 %	[51]
River water (low-flow season)	China	2005/2006	10	35–217 ng/L	77 ng/L	100 %	[51]
River water (upstream of WWTP)	Australia	2004	NR	9–47 ng/L	NR	100 %	[52]
River water (downstream of WWTP)	Australia	2004	NR	21–43 ng/L	NR	100 %	[52]
River water	Germany	NR (2002)	NR	ND–10 ng/L	NR	NR (LOD = 3 ng/L)	[53]
River water	USA	2001	76	ND–140 ng/L	ND	4 % (LOD = NR)	[39]

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concen-tration**	**Samples > LOD**	**Refer-ence**
Surface and ground water	USA	2001	73	<100 ng/L	ND	8.1 % (LOD = NR)	[41]
Still water	Spain	2012	11	ND–13 ng/L	ND	36 % (LOD = NR)	[48]
Domestic well	USA	2000	1	ND	ND	0 % (LOD = 1 µg/L)	[54]
Wells downgradient from landfill	USA	2000/ 2002	4	ND	ND	0 % (LOD = 1 µg/L)	[54]
Estuary / river water	Spain	NR (2014)	11	27–310 ng/L	120 ng/L	100 %	[55]
Estuary / river sediment	Spain	NR (2014)	13	0.3–9.6 ng/g dw	3.8 ng/g dw	100 %	[55]
Mangrove water	India	2009	2	ND–approx. 26 ng/L	ND	NR (LOD = 3.0 ng/L)	[50]
River sediment	Spain	2012	18	ND–8 ng/g dw	7 ng/g dw	94 % (LOD = NR)	[48]
River sediment	India	2009	39	approx. 4–85.3 ng/g dw	11.0 ng/g dw	NR (LOD = 1.5 ng/g dw)	[50]
River sediment	India	2009	33	approx. 8.5–46.87 ng/g dw	14.0 ng/g dw	NR (LOD = 1.5 ng/g dw)	[50]
River sediment	India	2009	12	approx. 6.8–32.1 ng/g dw	22.5 ng/g dw	NR (LOD = 1.5 ng/g dw)	[50]
River sediment	India	2009	3	ND–approx. 11 ng/g dw	ND	NR (LOD = 1.5 ng/g dw)	[50]
Soil	USA	2006	26	ND–66.6 ng/g dw (range of means from all sites)	8.2 ng/g dw (median of means)	92 % (LOD = 1.0 ng/g dw)	[56]
Agricultural soil	Spain	NR (2010)	6	ND–3.8 ng/g	NR	NR (LOD = 0.08 ng/g)	[57]
WWTP sludge (dewatered)	Canada	2009	1	10 900 ng/g dw	10 900 ng/g dw	100 %	[58]
Drinking water	Spain	2012	8	ND	ND	0 % (LOD = NR)	[48]
WWTP influent	Spain	2012	21	ND–18.4 ng/L	5.4 ng/L	57 % (LOD = NR)	[48]
WWTP effluent	Spain	2012	21	9.2–71.3 ng/L	45.1 ng/L	100 %	[48]

Note: Additional information regarding the sampling location and year is sometimes provided after values that are not reported (NR) in parentheses. This represents an estimated value for this non-reported information based on the general details provided in the study.

Scientific Evidence of Adverse Endocrine-Related Environmental Effects

Reported scientific evidence of adverse endocrine-related environmental effects from exposure exist for different organisms and across different study levels. A comprehensive but non-exhaustive set of reported observations is included below.

Population level / field studies

No reported studies investigating this level were identified during the preparation of this fact sheet.

In vivo level

Substance	Organism	Observation	Reference
TCZ; PCP	zebrafish	Changed thyroid levels (plasma and/or whole body)	[59–61]
TCZ	carp and frog	Changed steroid levels (plasma and/or whole body)	[62,63]
TCZ	zebrafish	Increased vitellogenin* level (whole body)	[64]
PCP	zebrafish	Abnormal individual developments	[61]
TCS	male fathead minnows	No effect on plasma vitellogenin* levels	[65,66]
TCS	medaka	Increased hepatic vitellogenin* levels	[67]
TCS	rat	Altered thyroid hormone (TH) homeostasis (changed serum TH levels)	[68–70]
TCS	frog	No effect on thyroid hormone (TH) homeostasis	[71]
TCS	rat	Increased uterine weight	[72]
TCS	mosquitofish	Impaired reproduction (decreased sperm counts)	[73]
TCS	medaka	No effect on reproduction (hatching, egg production)	[67]
TCS	frog	Interference with the thyroid axis, altered development	[74]
TCS	fathead minnow	No effect on gonad development	[66]
TCS	rat	Altered sex ratio (skewed to females)	[70]
TCS	japanese medaka	No effect on sex ratio (skewed to females)	[75]

In vitro level

Substance	Cell line	Observation	Reference
TCZ; PCP	rat pituitary GH3 cells	Altered transcription profiles of genes involved in various thyroid pathways in zebrafish larvae and rats	[59,60]
PCP	biological material from multiple species	Weak potency to bind to thyroid hormone transport proteins (and replace the thyroid hormone) in salmon, frog and seabream	[76,77]
TCS	frog tadpole tail fin cells and rat pituitary GH3 cells	No effect on thyroid hormone-associated gene expression (but effect from metabolite, methyl TCS)	[71]
TCS	frog (*Xenopus laevis*) XTC-2 cells	Altered thyroid hormone-associated gene expression	[78]
TCS	mosquitofish	Altered vitellogenin* mRNA expression in	[73]
TCS	rat uteri and GH3 cells	Altered estrogen-sensitive gene expression in rats	[72]

Notes:
*Vitellogenin is a precursor protein normally synthesized by females to be incorporated in eggs.

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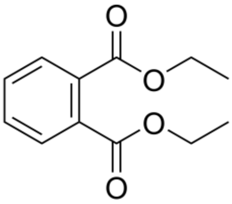
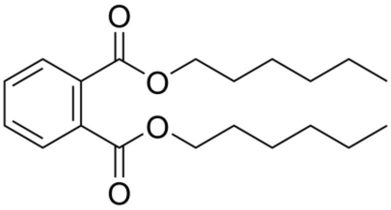
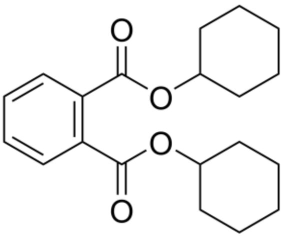
Phthalates (non-EU REACH SVHCs) 1

Key References:

- C.A. Staples, D.R. Peterson, T.F. Parkerton, W.J. Adams, The Environmental Fate of Phthalate Esters: A Literature Review, Chemosphere. 35 (1997) 667–749.

Chemical Identification			
Name(s)	**Abbreviation**	**CAS Number**	**Structure**
Diethyl phthalate; Palatinol A	DEP	84-66-2	
Dihexyl phthalate	DHP	84-75-3	
Dicyclohexyl phthalate	DCHP	84-61-7	
Completed assessments as the basis for inclusion: SIN List (DEP; DHP; DCHP), Danish Criteria (DEP; DHP; DCHP)			

Physical and Physicochemical Properties

Property	**DEP**	**DHP**	**DCHP**
Molecular formula	$C_{12}H_{14}O_4$	$C_{20}H_{30}O_4$	$C_{20}H_{26}O_4$
Molecular weight [g/mol]	222.24	334.45	330.42
Physical state at 20°C	liquid	liquid	solid
Melting point [°C]	-40.5 °C [1]; -60 °C [2]	-58 °C [3]	66 [4]
Density [g/cm^3]	1.120 at 25 °C [5]; 1.118 at 20 °C [2];	1.010–1.016 at 20 °C [5]	1.383 at 20 °C [4]
Vapor pressure at 25°C [mmHg]	$1.65*10^{-3}$ [6]; $2.1*10^{-3}$ [7]; $4*10^{-4}$ [3]	$5*10^{-6}$ [8]; $1.4*10^{-5}$ [6]	$8.69*10^{-7}$ [9]
Water solubility at 25°C [mg/L]	1080 [6]; 932 at 20 °C [2]; 896 at 20 °C [3]	0.05 [10]	4 [11]
Octanol/water partition coefficient (log K_{OW})	2.24 [6]; 2.42 [10]; 2.38 [8]	6.82 [12]; 6.30 [8]	6.20[†]
Organic carbon/water partition coefficient (log K_{OC})	2.02 (MCI method)[†], 2.13 (Kow method)[†]	4.10 (MCI method)[†], 4.57 (Kow method)[†]	4.12 (MCI method)[†], 4.22 (Kow method)[†]
Air/water partition coefficient (log K_{AW})	-5.4 (QSAR estimate) [13]; -4.6[†]	-3.53 (QSAR estimate) [13]; -2.98[†]	-5.39[†]
Dissociation constant (p*K*a)	Not applicable	Not applicable	Not applicable

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[†] Estimated value using models in EPI Suite v4.11 [36].
NR = not reported

Degradation Pathways and Kinetics

Mechanism	Expected to occur?			Technosphere	Environment	Reference
	Yes	No	Not reported			
Hydrolysis		DEP; DHP; DCHP (all negligible)				[14]
Photolysis			DEP; DHP; DCHP			
OH-radical reactions	DEP; DHP		DCHP		Atmosphere	[14]
Biodegradation	DEP; DHP; DCHP			WWTP	River water, river sediment	[14–20]

Kinetics – Diethyl phthalate (DEP)

Mechanism	Reported values	Reference
OH-radical reactions	Half-life = 57 h (estimated)†	[14]
Biodegradation (semi-continuous activated sludge)	>94.8 % degraded after 24 h	[16]
Biodegradation (acclimated shake flask, inoculum prepared from soil and sewage microorganisms)	99 % degraded after 28 d, half-life = 2.2 d	[15]
Biodegradation (aerobic, RDA, shaken)	Half-life = 0.4 d	[14]
Biodegradation (aerobic, MITI inoculum)	Half-life = 4.3 d	[14]
Biodegradation (sludge, anaerobic)	100 % degraded after 2 weeks, half-life = <2.3 d	[14,17]
Biodegradation (sewage sludge, anaerobic)	100 % degraded after 8 d	[18]
Biodegradation (soil)	100 % degraded after 25 d	[19]
Biodegradation (sludge, anaerobic)	Half-life = 5 d	[14]
Biodegradation (six river sediment samples, aerobic)	Half-life = 0.5–8.8 d	[20]
Biodegradation (six river sediment samples, anaerobic)	Half-life = 24.7–49.3 d	[20]

Kinetics – Dihexyl phthalate (DHP)

Mechanism	Reported values	Reference
OH-radical reactions	Half-life = 13 h (estimated)†	[14]
Biodegradation (semi-continuous activated sludge)	>92.8 % degraded after 24 h	[16]
Biodegradation (acclimated shake flask, inoculum prepared from soil and sewage microorganisms)	>99 % degraded after 28d. Half-life = 2.9 d.	[15]
Biodegradation (six river sediment samples, aerobic)	Half-life = 3.1–19.6 d	[20]
Biodegradation (six river sediment samples, anaerobic)	Half-life = 19.1–30.2 d	[20]

Kinetics – Dicyclohexyl phthalate (DCHP)

MechanismCompartment	Reported values	Reference
Biodegradation (six river sediment samples, aerobic)	Half-life range = 2.3–37.4 d	[20]
Biodegradation (six river sediment samples, anaerobic)	Half-life range = 24.9–28.8 d	[20]

Intentional Uses and Production Levels

Uses

DEP

- Primarily used as a plasticizer in cellulose acetate polymers (e.g. plastic films and sheets, molded and extruded articles such as toothbrushes and tool handles) and as a solvent in cosmetics (e.g. perfume, hair spray, soaps and nail polish) [3,21,22].
- Used as a vehicle for fragrances in perfumes and other personal care products [23].
- Used as an alcohol denaturant in certain cosmetic products detergents and insecticides, and can be found in non-polymer products such as dye application agents, adhesives and sealants [23].

DHP

- Used as a plasticizer in cellulose and vinyl plastics [3].

DCHP

- Used in PVC products, in sealants, textile printing, plastisol products, coating products and many more [24,25].

Production Levels

DEP

- Currently registered in the EU with 1000–10 000 tonnes per year of import or production [2].
- Production level in the US: 4500 tonnes in 2008 [21].

DHP

- No information on the production levels of DHP was found.
- Pre-registered under EU REACH on November 30th 2010, but no registrations have been submitted as of May 2017 [26].
- Could be assumed that it is not produced or imported in quantities equal to or larger than 100 tonnes per year in the EU [27].

DCHP

- Currently registered in the EU with 100–1000 tonnes per year of import or production [28].
- Approximately 27 tonnes produced in the Nordic countries in 2013 [25].

Emission Sources into the Environment

DEP

	Emission Sources
Production	Released during production [29].
Use	May leach out or volatilize from products it is incorporated in [22].
Disposal	May leach out of landfills into water or soil, and can also enter the atmosphere through the combustion of plastics [22].
Other sources	Not reported

Phthalates in general

The table below provides general information relevant for all phthalates including DEHP. As no specific information was found for DIBP, DBP, or BBP, the information below is meant to provide an overview of potential emission sources of phthalates in general; for some specific information on other phthalates, see the fact sheets "Phthalates (EU REACH SVHCs)" and "Phthalates (non-EU REACH SVHCs) 2".

	Emission Sources
Production	Likely released during production [29–31].
Use	• Main source of the releases to the atmosphere is through evaporation during processing with PVC. The extent of such losses may vary from 0.02 % for injection molding to up to 1 % for coating processes [32]. • Phthalates can migrate slowly out of polymer products throughout their entire lifetime, since plasticizers are not chemically bound to the polymer matrix [31].
Disposal	• Different levels of emissions may occur depending on the treatment applied. • 86 % of the plastics disposed of in the US in 2008 (approximately 34 million tons) ended up in landfills [33]. • Releases (e.g. through landfill leachate) can be expected, as phthalates are not covalently bound in disposed plastic products. [34]
Other sources	Not reported

Distribution in the Natural Environment

Estimated Environmental Distribution

Based on the identified uses and emissions for these chemicals as plastic additives and the emission scenario information generated by the OECD [35], a plausible emission pattern was assumed to estimate the resulting distribution in the environment using Level III fugacity modeling in EPI Suite [36]. The assumed emission pattern and the resulting environmental distribution from the model are presented in the table below for each chemical.

	Assumed Emission Pattern			**Modelled Distribution Results**			
	Air	**Water**	**Soil**	**Air**	**Water**	**Soil**	**Sediment**
DEP	50 %	50 %	0 %	8 %	64 %	28 %	0 %
DHP	50 %	50 %	0 %	7 %	76 %	3 %	14 %
DCHP	50 %	50 %	0 %	1 %	36 %	38 %	25 %

Bioaccumulation Potential

	Bioconcentration factor (BCF)	**Organism**	**Reference**
DEP	118	fish (bluegill sunfish)	[37]
DHP	1066–3254	*Daphnia magna*	[38]
DCHP	1600	fish	[39]

Measured Environmental Concentrations

Measured concentrations for these chemicals have been reported in numerous environmental media. A non-exhaustive set of reported concentrations is included below, and further measurements can be found in published literature including in the following:

- A. Bergé, M. Cladière, J. Gasperi, A. Coursimault, B. Tassin, R. Moilleron, Meta-analysis of environmental contamination by phthalates, Environ. Sci. Pollut. Res. 20 (2013) 8057–8076. doi:10.1007/s11356-013-1982-5.

Concentrations are provided in varying units depending on the media. Mass per mass dry weight (dw) and wet weight (ww) are sometimes used. ND = not detected, i.e., below the limit of detection (LOD). NQ = not quantified, i.e., below the limit of quantification (LOQ)). NR = not reported.

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concen-tration**	**Samples > LOD**	**Refer-ence**
Diethyl phthalate (DEP)							
River water	Spain	NR (2014)	7	ND–ND	ND	0 % (LOD = 330 ng/L)	[40]
River water	France	2008/ 2009	29	ND–528 ng/L (range of means)	NR	NR (LOD = 29 pg/L)	[41]
River water	China	2004/ 2005	15	ND–0.288 µg/L	NR	60 % (LOD = 0.01 µg/L)	[42]
River water	Taiwan	2000	14	ND–2.5 µg/L	0.5 µg/L (mean)	NR	[20]
Rainwater	Nether-lands	1999	3	240–430 ng/L	340 ng/L	100 %	[43]
Surface water	Nether-lands	1999	87	ND–2300 ng/L	430 ng/L (of values >LOD)	28 % (LOD = 70 ng/L)	[43]
Urban lake water	China	2005	15	15–320 ng/L	31 ng/L	100 %	[44]
Sea water (dissolved)	Arctic	2004	11	0.03–4 ng/L	0.35 ng/L	100 %	[45]
Sea water (total suspended matter)	Arctic	2004	11	ND–4.1 ng/L	0.09 ng/L	78 % (LOD = NR)	[45]
Sea water	Arctic	2004	NR	ND–795 pg/L	40 pg/L	71 % (LOD = 8 pg/L)	[46]
River bed sediment	France	2008/ 2009	10	1–239 ng/g dw	NR (33 ng/g dw)	NR (LOD = 1.6 ng/g dw)	[41]
Sediment	Nether-lands	1999	16	ND–1200 ng/g dw	133 ng/g dw	94 % (LOD = 65 ng/g dw)	[43]

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concentration**	**Samples > LOD**	**Reference**
Diethyl phthalate (DEP)							
Sediment	Taiwan	2000	6	ND–1.9 µg/g dw	0.2 µg/g dw (mean)	NR	[20]
Marine sediment	Spain	2007	5	ND	ND	0 % (LOD = 50 ng/g)	[47]
Urban lake sediment	China	2005	15	0.028–1.05 µg/g dw	0.13 µg/g dw	100 %	[44]
Suspended matter	Netherlands	1999	50	ND–2692 ng/g dw	NR	64 % (LOD = 46 ng/g dw)	[43]
Soil	China	NR (2003)	23	ND–2.61 µg/g	0.18 µg/g	78 % (LOD = 4.43 ng/g)	[48]
Atmosphere (vapour)	Arctic	2004	3	0.64–3.4 ng/m^3	0.75 ng/m^3	100 %	[45]
Atmosphere (particle)	Arctic	2004	3	ND–0.18 ng/m^3	0.01 ng/m^3	67 % (LOD = NR)	[45]
Atmosphere (gas phase)	Arctic	2004	NR	177–895 pg/m^3	320 pg/m^3	NR	[46]
Atmosphere (particle phase)	Arctic	2004	NR	5–41 pg/m^3	18 pg/m^3	NR	[46]
Tap water	Spain	NR (2014)	7	ND–381 ng/L	ND	14 % (LOD = 330 ng/L)	[40]
WWTP influent	NR (Austria)	NR (2010)	15	0.77–9.2 ng/L	3.9 ng/L	100 %	[49]
WWTP effluent	NR (Austria)	NR (2010)	15	ND–1.1 ng/L	0.15 ng/L	80 % (LOD = 0.065-0.11 ng/L)	[49]
Untreated municipal wastewater	Netherlands	1999	12	4.1–44 000 ng/L	13 000 ng/L	100 %	[43]
WWTP effluent	Netherlands	1999	9	ND–930 ng/L	840 ng/L	67 % (LOD = 300 ng/L)	[43]
Industrial wastewater	Netherlands	1999	10	ND–5200 ng/L	4200 ng/L	50 % (LOD = 350 ng/L)	[43]
Dihexyl phthalate (DHP)							
Surface water (lakes, rivers and reservoirs), wet season	China	2013	19	ND	ND	0 % (LOD = 0.03 µg/L)	[50]
Surface water (lakes, rivers and reservoirs), dry season	China	2013	19	ND	ND	0 % (LOD = 0.03 µg/L)	[50]

Measured compartment	Sampling location	Sampling year	Number of samples	Concentration range	Median concen-tration	Samples > LOD	Refer-ence
Diethyl phthalate (DEP)							
River water, surface (0.5 m deep)	China	2012	9	ND–1.12 µg/L	ND	11 % (LOD = NR)	[51]
River water, deep (5 m deep)	China	2012	9	ND	ND	0 % (LOD = NR)	[51]
River water	Taiwan	2000	14	ND	ND	NR	[20]
River water	United States	1984	4	ND–8 ng/L	ND	25 % (LOD NR)	[52]
Urban lake water	China	2005	15	ND	ND	0 % (LOD = NR)	[44]
Surface snow	Antarctic	1993/ 1994	7	ND–20 ng/L	2 ng/L	57 % (LOD = 0.7 ng/L)	[53]
Buried snow	Antarctic	1993/ 1994	6	ND–67 ng/L	31 ng/L	67 % (LOD = 0.7 ng/L)	[53]
Urban lake sediment	China	2005	15	ND– 0.34 µg/g dw	0.046 µg/g dw	87 % (LOD = NR)	[44]
Sediment	Taiwan	2000	6	0.1–1.1 µg/g dw	0.2 µg/g dw (mean)	NR	[20]
Sediment 0-10 cm depth	United States	1979	1	5.6 ng/g dw	5.6 ng/g dw	100%	[54]
Filtered tap water	China	NR (2012)	1	ND	ND	0 % (LOD = 29 ng/L)	[55]
Dicyclohexyl phthalate (DCHP)							
River water, level period (spring)	China	2010	23	ND–3.609 µg/L	0.664 µg/L (mean)	61 % (LOD = NR)	[56]
River water, wet season	China	2010	23	ND–1.411 µg/L	0.120 µg/L (mean)	65 % (LOD = NR)	[56]
River water, level period (autumn)	China	2010	23	ND–1.937	0.197 µg/L (mean)	83 % (LOD = NR)	[56]
River water, dry season	China	2009	23	0.057–1.434 µg/L	0.297 µg/L (mean)	100 %	[56]
River water	Taiwan	2000	14	ND	ND	NR	[20]
Surface water (lakes, rivers and reservoirs), wet season	China	2013	19	0.08–1.65 µg/L	0.31 µg/L	100 %	[50]

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concentration**	**Samples > LOD**	**Reference**
Diethyl phthalate (DEP)							
Surface water (lakes, rivers and reservoirs), dry season	China	2013	19	ND	ND	0 % (LOD = 0.03 µg/L)	[50]
Surface water	China	NR (2016)	4	ND	ND	0 % (LOD = 0.45 µg/L)	[57]
Surface water	Netherlands	1999	87	ND–60 ng/L	ND	33 % (LOD = 3 ng/L)	[43]
Urban lake water	China	2005	15	ND–76 ng/L	ND	7 % (LOD = NR)	[44]
Rain water	Netherlands	1999	3	ND	ND	0 % (LOD = 8 ng/L)	[43]
Suspended matter	Netherlands	1999	51	ND–1300 ng/g dw	ND	47 % (LOD = 2 ng/g dw)	[43]
Sediment	Netherlands	1999	21	ND–11 ng/g dw	ND	19 % (LOD = 2 ng/g dw)	[43]
Sediment	Taiwan	2000	6	ND–1.9 µg/g dw	0.2 µg/g dw (mean)	NR	[20]
Urban lake sediment	China	2005	15	ND–0.22 µg/g dw	0.066 µg/g dw	53 % (LOD = NR)	[44]
WWTP effluent	Netherlands	1999	9	2–20 ng/L	ND	22 % (LOD = NR)	[43]
Untreated municipal wastewater	Netherlands	1999	12	ND–210 ng/L	150 ng/L	50 % (LOD = 11 ng/L)	[43]
Industrial wastewater	Netherlands	1999	10	ND–16 000 ng/L	370 ng/L	80 % (LOD = 5 ng/L)	[43]
WWTP sludge	China	2010	25	0.1–0.19 µg/g dw	0.11 µg/g dw	100 %	[58]
Note: Additional information regarding the sampling location and year is sometimes provided after values that are not reported (NR) in parentheses. This represents an estimated value for this non-reported information based on the general details provided in the study.							

Scientific Evidence of Adverse Endocrine-Related Environmental Effects

Reported scientific evidence of adverse endocrine-related environmental effects from exposure to phthalates exists for different organisms and across different study levels. A comprehensive but non-exhaustive set of reported observation is included below.

Population level / field studies

No reported studies investigating this level were identified during the preparation of this fact sheet.

In vivo level

Substance	Organism	Observation	Reference
DEP	zebrafish	Disrupted sex hormone balances through modulating key steroidogenic genes	[59]
DEP	carp	Dose-dependent vitellogenin induction	[60]
DEP	abalone	Growth and abnormal developments of individuals	[61]
DCHP	rat	Increased thyroid	[62]
DEP	abalone	Altered hatching rates	[61]
DHP	rainbow trout	No effect on hatching rates and reproduction observed	[63]
DCHP	rat	Impaired reproduction (decreased sperm count and motility, disrupted recurring period of sexual receptivity and fertility, altered nippel development, decreased testicular germ cells)	[62–67]
DEP, DHP	*Daphnia magna*, Japanese medaka	No impaired reproduction (decreased sperm count and motility, disrupted recurring period of sexual receptivity and fertility, altered nippel development, decreased testicular germ cells) observed	[62–67]

In vitro level

Substance	Cell line	Observation	Reference
DCHP	human, mouse	Induced cell proliferation (estrogenic activity)	[68,69]
DCHP	mouse	Glucocorticoid receptor activation	[68]
DCHP	mouse	No PPAR-gamma receptor activation observed	[68]

Notes:
*Vitellogenin is a precursor protein normally synthesized by females to be incorporated in eggs.

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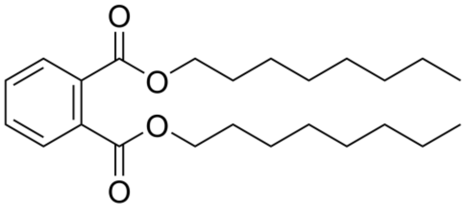
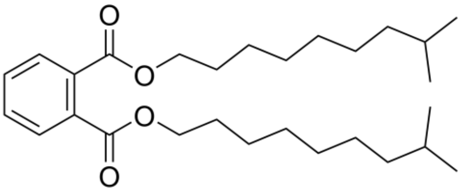
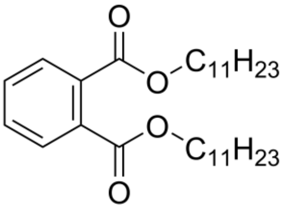
Chemical Identification			
Name(s)	**Abbreviation**	**CAS Number**	**Structure**
Dioctyl phthalate	DOP	117-84-0	
Diisodecyl phthalate	DIDP	26761-40-0; 89-16-7; 68515-49-1 (mixture)	
Diundecyl phthalate, branched and linear	DUP	3648-20-2 (linear); 85507-79-5 (diisoundecyl phthalate)	

Completed assessments as the basis for inclusion: SIN List (DOP; DIDP; DUP)

Note: DIDP CAS number 68515-49-1 is a mixture of di-C9–C11-branched alkyl esters, C10-rich.

Physical and Physicochemical Properties

Property	**DIDP**	**DUP (mix)** CAS#: 85507-79-5	**DUP (linear)** CAS#: 3648-20-2	**DOP**
Molecular formula	$C_{28}H_{46}O_4$	$C_{30}H_{50}O_4$	$C_{30}H_{50}O_4$	$C_{24}H_{38}O_4$
Molecular weight [g/mol]	446.66	474.72	474.72	390.56
Physical state at 20°C	liquid	liquid	unclear	unclear
Melting point [°C]	-50 [1]	-40 (pour point) [2]	35.5 [3]; -9 [4]	25 [1]; -25 [4]
Density [g/ cm^3]	0.966 at 20 °C [1]	0.9527 at 20 °C [2]	0.955 at 20 °C [5]	0.978 at 20 °C [6]
Vapor pressure at 25°C [mmHg]	$5.28*10^{-7}$ [7]	<5.25 [2]	$1.2*10^{-9\,\dagger}$	$1*10^{-7}$ [4]
Water solubility at 25°C [mg/L]	0.28 [8]	$7*10^{-8\,\dagger}$	1.11 at 20 °C [9]	0.022 [10]; $5*10^{-4}$ [11]
Octanol/water partition coefficient (log K_{OW})	$10.36^{\dagger}$	$11.83^{\dagger}$	$11.49^{\dagger}$	8.10 [12] ; 8.06 [4] ; 8.2 [11]
Organic carbon/water partition coefficient (log K_{OC})	6.04 (MCI method)†, 6.52 (Kow method)†	6.91 (MCI method)†, 7.34 (Kow method)†	6.71 (MCI method)†, 7.15 (Kow method)†	5.15 (MCI method)†, 5.27 (Kow method)†
Air/water partition coefficient (log K_{AW})	$-4.34^{\dagger}$	$-2.46^{\dagger}$	$-2.58^{\dagger}$	-2.8 (QSAR estimate) [13]; $-3.98^{\dagger}$
Dissociation constant (p*K*a)	Not applicable	Not applicable	Not applicable	Not applicable

Note: The reported melting points of DUP and DOP show substantial inconsistencies.

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† Estimated value using models in EPI Suite v4.11 [21].
NR = not reported

Degradation Pathways and Kinetics

Mechanism	Expected to occur?			Technosphere	Environment	Reference
	Yes	No	Not reported			
Hydrolysis		DOP; DIDP; DUP (all negligible)				[14]
Photolysis			DOP; DIDP; DUP			
OH-radical reactions	DOP		DIDP; DUP		Atmosphere	[14]
Biodegradation	DOP; DIDP; DUP			WWTP	River water	[14–20]

Kinetics – Dioctyl phthalate (DOP)

Mechanism	Reported values	Reference
OH-radical reactions	Half-life = 10 h (estimated)†	[14]
Biodegradation (semi-continuous activated sludge)	84.5 % degraded after 24 h (for diisooctyl, a branched isomer of DUP)	[16]
Biodegradation (aerobic, RDA, shaken)	Half-life = 1 d	[14]
Biodegradation (acclimated shake flask, inoculum prepared from soil and sewage microorganisms)	>99 % degraded after 28 d. Half-life = 8.8 d (for diisooctyl, a branched isomer of DUP)	[15]
Biodegradation (sludge, anaerobic)	Approximately 25 % degraded after 70 d. Half-life = 115 d	[14,17]
Biodegradation (sewage sludge, anaerobic)	No degradation after 32 d	[18]
Biodegradation (sludge, anaerobic)	Half-life = 20.6 d	[14]

Kinetics – Diisodecyl phthalate (DIDP)

Mechanism	Reported values	Reference
OH-radical reactions	Half-life = 4.9 h (estimated)†	[21]
Biodegradation (laboratory scale landfill reactor)	0 % degradation	[19]
Biodegradation (semicontinuous activated sludge)	68 % degraded after 24 h	[16]
Biodegradation (acclimated shake flask, inoculum prepared from soil and sewage microorganisms)	>99 % degraded after 28 d. Half-life = 9.6 d.	[15]

Kinetics – Diundecyl phthalate (DUP)

Mechanism	Reported values	Reference
OH-radical reactions	Half-life = 4.0–4.4 h (estimated)†	[21]
Biodegradation (semicontinuous activated sludge)	29–45 % degraded after 24 h	[20]
Biodegradation (acclimated shake flask, inoculum prepared from soil and sewage microorganisms)	>99 % degraded after 28 d. Half-life = 6.2 d	[15]

Uses and Production Levels

Uses

DOP

- Used as a plasticizer in plastics and cellulose acetate resins [22].
- Exists primarily as a component of mixed phthalate products, such as C6–C10-phthalate. DOP comprises approximately 20% of such mixed phthalate products, and very little pure DOP is commercially manufactured. [22]

DIDP

- Primarily used as plasticizer in polyvinyl chloride (PVC), with a typical content of 25 to 50% in flexible PVC products [23].
- End products include cable sheaths, films and sheets, flooring, and coating [23].
- Also used in adhesives, sealants, paints and automotive applications [24].

DUP

- Primarily used as a plasticizer in PVC [22].
- End products include wiring, cable jacketing and insulation, furniture, automobile upholstery, floor mats and seat covers, flooring, wall coverings, coil coatings, pool liners, water stops, roofing membranes, and coated fabrics [25].
- Also used in thermoplastics (i.e. flame retardant nylon), rubbers, paints and adhesives [25].

Production Levels

DOP

- Global consumption: 3.24 million tonnes in 2014 [26].
- Pre-registered under EU REACH by several hundred legal entities [27]; however, quantities of use or production are not yet reported in the registration process.

DIDP

- Production in the EU: approximately 280 000 tonnes per year in 1994 [23].
- Consumption in the EU: approximately 191 000 tonnes for PVC uses and about 9000 tonnes per year for non-PVC uses [23] in 1994. Remained roughly the same in 2010 [28].
- Consumption in the US: 533 000 tonnes per year for PVC uses and 85 000 tonnes for non-PVC uses in the mid 1990s [23].
- Canada: 10–100 tonnes produced in 2012, with a net import of 900–9000 tonnes [24].

DUP

- Production of DUP in the US: reported as 18 000 tonnes in 2008 [25].
- Production in Canada: more than 10 000 tonnes in 2012 with a net export of 900 to 9000 tonnes [24].

Emission Sources into the Environment

DOP

	Emission Sources
Production	Released to the atmosphere by plastic producers and transportation machinery producers, e.g., 250 kg released as such in Japan in 2008 [29].
Use	Not reported
Disposal	Not reported
Other sources	Not reported

Phthalates in general

The table below provides general information relevant for all phthalates including DOP. As no specific information was found for DIDP or DUP, the information below is meant to provide an overview of potential emission sources of phthalates in general; for some specific information on other phthalates, see the fact sheets "Phthalates (EU REACH SVHCs)" and "Phthalates (non-EU REACH SVHCs) 1".

	Emission Sources
Production	Likely released during production [29–31].
Use	• Main source of the releases to the atmosphere is through evaporation during processing with PVC. The extent of such losses may vary from 0.02 % for injection molding to up to 1 % for coating processes [32]. • Phthalates can migrate slowly out of polymer products throughout their entire lifetime, since plasticizers are not chemically bound to the polymer matrix [31].
Disposal	• Different levels of emissions may occur depending on the treatment applied. • 86 % of the plastics disposed of in the US in 2008 (approximately 34 million tons) ended up in landfills [33]. • Releases (e.g. through landfill leachate) can be expected, as phthalates are not covalently bound in plastic products disposed of. [34]
Other sources	Not reported

Distribution in the Natural Environment

Estimated Environmental Distribution

Based on the identified uses and emission sources for these chemicals as plastic additives and the emission scenario information generated by the OECD [35], a plausible emission pattern was assumed to estimate the resulting distribution in the environment using the Level III fugacity model in EPI Suite [21]. The assumed emission pattern and the resulting environmental distribution from the model are presented in the table below for each chemical.

	Assumed Emission Pattern			Modelled Distribution Results			
	Air	**Water**	**Soil**	**Air**	**Water**	**Soil**	**Sediment**
DOP	50 %	50 %	0 %	2 %	56 %	11 %	31 %
DIDP	50 %	50 %	0 %	1 %	61 %	34 %	34 %
DUP	50 %	50 %	0 %	1 %	59 %	39 %	1 %

Bioaccumulation Potential

	Bioconcentration factor (BCF)	Organism	Reference
DOP	974 (estimated)†	aquatic species	[21]
	660 (3-day magnification factor) 28 500 (33-day magnification factor)	algae	[36]
	9400 (3-day magnification factor), 2600 (33-day magnification factor)	*Daphnia magna*	[36]
	1.2 (3-day magnification factor), 9400 (33-day magnification factor)	fish	[36]
DIDP	3500	mussels	[37]
	116	*Daphnia magna*	[38]
DUP	640	fish	[39]

Measured Environmental Concentrations

Measured concentrations for these chemicals have been reported in numerous environmental media. A non-exhaustive set of reported concentrations is included below, and further measurements can be found in published literature including in the following:

- A. Bergé, M. Cladière, J. Gasperi, A. Coursimault, B. Tassin, R. Moilleron, Meta-analysis of environmental contamination by phthalates, Environ. Sci. Pollut. Res. 20 (2013) 8057–8076. doi:10.1007/s11356-013-1982-5.
- M. Remberger, L. Kaj, K. Hansson, H. Andersson, E. Brorström-Lundén, H. Lunder, M. Schlabach, Selected Plasticisers and Additional Sweeteners in the Nordic Environment, 2013. doi:10.6027/TN2013-505.

Concentrations are provided in varying units depending on the media. Mass per mass dry weight (dw) and wet weight (ww) are sometimes used. ND = not detected, i.e., below the limit of detection (LOD). NQ = not quantified, i.e., below the limit of quantification (LOQ). NR = not reported.

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concentration**	**Samples > LOD**	**Reference**
Dioctyl phthalate (DOP)							
River water	France	2012	11	ND	ND	0 % (LOQ = 0.01 µg/L)	[40]
River water	France	2012	2	ND	ND	0 % (LOQ = 0.01 µg/L)	[40]
River water	France	2008/ 2009	29	ND–26 ng/L (range of means)	NR	NR (LOD = 53 pg/L)	[41]
River water	China	2004/ 2005	15	ND–0.059 µg/L	ND	NR (LOD = 0.01 µg/L)	[42]
Surface water	Netherlands	1999	87	ND–78 ng/L	ND	28 % (LOD = 2 ng/L)	[43]
Urban lake water	China	2005	15	ND	ND	0 % (LOD = NR)	[44]
Urban lake sediment	China	2005	15	ND–0.629 µg/g dw	0.02 µg/g dw	80 % (LOD = NR)	[44]
Rainwater	Netherlands	1999	3	38–250 ng/L	41 ng/L	100 %	[43]
River bed sediment	France	2008/ 2009	2	65 ng/g dw (mean)	NR	NR (LOD = 16.2 ng/g dw)	[41]
Industrial wastewater	Netherlands	1999	10	12–2800 ng/L	150 ng/L	100 %	[43]
Suspended matter	Netherlands	1999	51	ND–47 ng/g dw	90 ng/g dw	73 % (LOD = 2 ng/g dw)	[43]
Sediment (type NR)	Netherlands	1999	21	ND–55 ng/g dw	11 ng/g dw	62 % (LOD = 2 ng/g dw)	[43]

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concentration**	**Samples > LOD**	**Reference**
Air urban area (gas and particle phases)	China	2005/ 2006	10	0.3–2.7 ng/m^3	1.2 ng/m^3	100 %	[45]
Air suburban area (particle phase only, gas phase ND)	China	2005/ 2006	10	0.01–0.7 ng/m^3	0.2 ng/m^3	100 %	[45]
Air (gas and particle phases)	North Sea	NR (2006)	10	ND	ND	0 % (MDL = 0.002 ng/m^3)	[46]
Air particle phase	Germany	NR (2006)	6	ND–0.013 ng/m^3	0.002 ng/m^3 (mean)	NR (MDL = 0.002 ng/m^3)	[46]
Air gas phase	Germany	NR (2006)	6	ND	ND	0 % (MDL = 0.002 ng/m^3)	[46]
Air vapor phase	France	2002/ 2003	20	0.0–1.1 ng/m^3	NR	NR (LOD = 25–75 pg/m^3)	[47]
Air particle phase	France	2002/ 2003	20	0–0.6 ng/m^3	NR	NR (LOD = 25–75 pg/m^3)	[47]
Untreated municipal wastewater	Netherlands	1999	12	260–2400 ng/L	660	100 %	[43]
WWTP effluent	Netherlands	1999	9	ND–19 ng/L	ND	44 % (LOD = 2 ng/L)	[43]
WWTP influent	Denmark	1999	7	220–790 ng/L	570 ng/L	100 % (LOD = NR)	[48]
WWTP effluent	Denmark	1999	7	0–30 ng/L	10 ng/L	40 % (LOD = NR)	[48]
WWTP influent	NR (Austria)	NR (2010)	15	ND–1.1 ng/L	0.54 ng/L	80 % (LOD = 0.13–0.26 ng/L)	[49]
WWTP effluent	NR (Austria)	NR (2010)	15	ND–0.26 ng/L	ND	7 % (LOD = 0.067–0.14 ng/L)	[49]
Diisodecyl phthalate (DIDP)							
River water	France	NR (1997)	6	ND–1.08 µg/L	ND	33% (LOD = 0.5 µg/L)	[50]
River water	England	1998	4	ND–0.4 µg/L	0.25 µg/L	75 % (LOD = 0.2 µg/L)	[51]
Urban storm water	Sweden	2006	13	ND–17 µg/L	0.77 µg/L	69 % (LOD = 0.1 µg/L)	[52]
Seawater	Canada	NR (2006)	9	NR	76.7 ng/L (mean)	83 % (LOD = 50 ng/L)	[53]
Rainwater	Netherlands	2003	50	ND–98 µg/L	ND	6 % (LOD = 10–100 ng/L)	[54]

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concen-tration**	**Samples > LOD**	**Refer-ence**
Raw drinking water	England	1998	1	ND	ND	0 % (LOD = 0.2 µg/L)	[51]
Road runoff water (motorway)	Austria	2008	4	ND–9.9 µg/L	ND	25 % (LOD = 0.01 µg/L)	[49]
Road runoff water (suburban area)	Austria	2008	4	ND–4.8 µg/L	ND	50 % (LOD = 0.01 µg/L)	[49]
Suspended matter river water	Germany	NR (2000)	3	6–10 mg/kg dw	9.2 mg/kg dw	100 %	[55]
Sediment (landfill)	Sweden	2006	1	290 µg/kg dw	290 µg/kg dw	100 %	[56]
Sediment (remote areas)	Sweden	2006	3	ND	ND	0 % (LOD = 100 µg/kg dw)	[56]
Sediment (urban area)	Sweden	2006	3	1.2–3.4 mg/kg dw	1.5 mg/kg dw	100 %	[56]
Sediment (industrial area)	Sweden	2006	6	ND–360 µg/kg dw	190 µg/kg dw	67 % (LOD = 100 µg/kg dw)	[56]
Bottom sediment	Canada	NR (2006)	12	NR	385 ng/g dw (mean)	92 % (mean LOD = 4.6 ng/g dw)	[53]
Suspended sediment	Canada	NR (2006)	9	NR	43 200 ng/g dw	92 % (mean LOD = 4.6 ng/g dw)	[53]
Sediment	Netherlands	NR (1999)	30	ND–1.11 mg/kg dw	ND	32 % (LOD = 15 µg/kg dw)	[57]
Sediment	Denmark	2010/ 2011	3	NQ–63 µg/kg dw	NQ	33 % (LOQ = 20 µg/kg dw)	[58]
Sediment	Finland	2011	3	510–940 µg/kg dw	660 µg/kg dw	100 %	[58]
Sediment	Faroe Islands	2011	4	0.11–36 mg/kg dw	10.1 mg/kg dw	100 %	[58]
Sediment	Iceland	2011	3	NQ–1.3 mg/kg dw	0.88 mg/kg dw	67 % (LOQ = 0.02 mg/kg dw)	[58]
Sediment	Norway	2002/ 2005	3	77–850 µg/kg dw	370 µg/kg dw	100 %	[58]
Sediment	Sweden	2011	3	25–510 µg/kg dw	55 µg/kg dw	100 %	[58]
Soil (forest)	France	2011	1	<LOQ	<LOQ	0 % (LOQ = 0.64–1.78 ng/g)	[59]
Soil (rural)	France	2011	1	13.5 ng/g dw	13.5 ng/g dw	100 %	[59]

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concen-tration**	**Samples > LOD**	**Refer-ence**
Soil (agriculture)	France	2011	1	40.2 ng/g dw	40.2 ng/g dw	100 %	[59]
Soil (urban)	France	2011	2	NR	65 ng/g dw	NR	[59]
Soil	Nether-lands	NR (1999)	35	ND	ND	0 % (LOD = 15 µg/kg dw)	[57]
Air (remote area)	Sweden	2006/ 2007	3	ND	ND	0 % (LOD = 0.25 ng/m^3)	[56]
Air (industrial areas)	Sweden	2006/ 2007	6	ND–2.4 ng/m^3	0.46 ng/m3	83 % (LOD = 0.25 ng/m^3)	[56]
Air (urban area)	Sweden	2006/ 2007	3	1.1–5.5 ng/m3	2.3 ng/m3	100 %	[56]
WWTP effluent	Denmark	2011	3	NQ	NQ	0 % (LOQ = 100 ng/L)	[58]
WWTP effluent	Faroe Islands	2011	2	1.4–4 µg/L	2.7 µg/L	100 %	[58]
WWTP influent	Faroe Islands	2011	1	1.5 µg/L	1.5 µg/L	100 %	[58]
WWTP effluent	Norway	2011	3	170–200 ng/L	180 ng/L	100 %	[58]
WWTP effluent	Sweden	2011	3	NQ–370 ng/L	200 ng/L	0 % (LOQ = 100 ng/L)	[58]
WWTP effluent	Finland	2011	3	NQ–220 ng/L	110 ng/L	67 % (LOQ = 100 ng/L)	[58]
WWTP Sludge	Sweden	2006/ 2007	16	16–51 mg/kg dw	20.5 mg/kg dw	100 %	[56]
WWTP Sludge	Denmark	2011	2	9.9–14 mg/kg dw	12 mg/kg dw	100 %	[58]
WWTP Sludge	Norway	2011	3	14–15 mg/kg dw	14 mg/kg dw	100 %	[58]
WWTP Sludge	Sweden	2011	3	19–42 mg/kg dw	20 mg/kg dw	100 %	[58]
WWTP Sludge	Faroe Islands	2011	2	1.8–8.6 mg/kg dw	5.2 mg/kg dw	100 %	[58]
WWTP Sludge	Finland	2011	3	4.9–32 mg/kg dw	25 mg/kg dw	100 %	[58]
WWTP Sludge	Iceland	2011	3	6.7–19 mg/kg dw	12 mg/kg dw	100 %	[58]
Drinking water	England	1998	2	ND	ND	0 % (LOD = 0.2 µg/L)	[51]

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concen-tration**	**Samples > LOD**	**Refer-ence**
Diundecyl phthalate (DUP)							
Sediment	Denmark	2010/ 2011	3	NQ	NQ	0 % (LOQ = 10 µg/kg dw)	[58]
Sediment	Finland	2011	3	NQ	NQ	0 % (LOQ = 10 µg/kg dw)	[58]
Sediment	Faroe Islands	2011	4	NQ	NQ	100 %	[58]
Sediment	Iceland	2011	3	NQ	NQ	0 % (LOQ = 10 µg/kg dw)	[58]
Sediment	Norway	2002/ 2005	3	NQ–58 µg/kg dw	NQ	33 % (LOQ = 10 µg/kg dw)	[58]
Sediment	Sweden	2011	3	NQ–21 µg/kg dw	NQ	33 % (LOQ = 10 µg/kg dw)	[58]
WWTP influent	Faroe Islands	2011	1	NQ	NQ	0 % (LOQ = 20 ng/L)	[58]
WWTP effluent	Denmark	2011	3	NQ	NQ	0 % (LOQ = 20 ng/L)	[58]
WWTP effluent	Finland	2011	3	NQ	NQ	0 % (LOQ = 20 ng/L)	[58]
WWTP effluent	Faroe Islands	2011	2	NQ	NQ	0 % (LOQ = 20 ng/L)	[58]
WWTP effluent	Norway	2011	3	NQ	NQ	0 % (LOQ = 20 ng/L)	[58]
WWTP effluent	Sweden	2011	3	NQ	NQ	0 % (LOQ = 20 ng/L)	[58]
WWTP Sludge	Denmark	2011	2	NQ	NQ	0 % (LOQ = 20 µg/kg dw)	[58]
WWTP Sludge	Finland	2011	3	NQ	NQ	0 % (LOQ = 20 µg/kg dw)	[58]
WWTP Sludge	Faroe Islands	2011	2	NQ	NQ	0 % (LOQ = 20 µg/kg dw)	[58]
WWTP Sludge	Iceland	2011	3	NQ–230 µg/kg dw	NQ	33 % (LOQ = 20 µg/kg dw)	[58]
WWTP Sludge	Norway	2011	3	1.2–1.4 mg/kg dw	1.4 mg/kg dw	100 %	[58]
WWTP Sludge	Sweden	2011	3	NQ–870 µg/kg dw	NQ	33 % (LOQ = 20 µg/kg dw)	[58]
Note: No reports of measurements of the occurrence of DUP in the natural environment were found during the preparation of this fact sheet. Therefore, only measurements of DUP concentrations in different WWTP compartments are presented. It remains unclear whether or not DUP exists in the natural environment at measurable concentrations.							

Scientific Evidence of Adverse Endocrine-Related Environmental Effects

Reported scientific evidence of adverse endocrine-related environmental effects from exposure to phthalates exists for different organisms and across different study levels. A comprehensive but non-exhaustive set of reported observations is included below.

Population level / field studies

No reported studies investigating this level were identified during the preparation of this fact sheet.

In vivo level

Substance	Organism	Observation	Reference
DOP	abalone	Effect on metamorphosis	[60]
DOP	rat	Decreased sperm count and motility, elevated alkaline phosphatase and calcium levels in serum	[61]
DIDP	Japanese medaka	No effect on sex ratio observed	[62]
DIDP	mouse	Increase in the incidence of non-neoplastic lesions, increase in brain, kidney, spleen adrenal and liver weights and decrease in body weight	[63]
DIDP	rat	Decreased testis weight, increased liver weight, increased serum levels of alkaline phosphatase, and decreased total cholesterol	[64]
DIDP; DUP	*Daphnia magna*, Japanese medaka	No effect on reproduction (egg production) observed	[62,65,66]
DUP	rainbow trout	No effect on hatching rates observed	[66]
DUP	rat	Decreased implantation sites, decreased relative anogenital distance in males, increased occurrence of lumbar ribs, increased number of ossification centers in caudal vertebral centra	[67]

In vitro level

Substance	Cell line	Observation	Reference
DOP	rat	Disrupted iodine uptake (iodine is crucial for thyroid hormone synthesis)	[68]
DOP	human, yeast, rat	Not competitively binding to uterine estrogen receptor	[69]
DIDP	human	Decreased the expression of genes involved in sulphonation	[70]

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Quadrosilan

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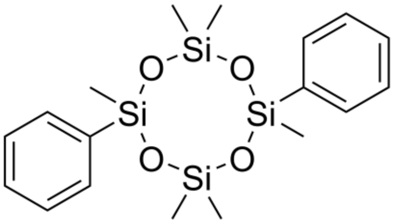
Chemical Identification			
Name(s)	**Abbreviation**	**CAS Number**	**Structure**
Quadrosilan; 2,6-cis-diphenyl-hexamethyl-cyclotetraosiloxane	QS	33204-76-1	
Completed assessments as the basis for inclusion: SIN List, Danish Criteria			

Physical and Physicochemical Properties	
Property	**Quadrosilan**
Molecular formula	$C_{18}H_{28}O_4Si_4$
Molecular weight [g/mol]	420.76
Physical state at 20°C	solid
Melting point [°C]	44.0 °C [1]
Density [g/cm^3]	NR
Vapor pressure at 25°C [mmHg]	$8.37*10^{-6}$ †
Water solubility at 25°C [mg/L]	$2.6*10^{-3}$ †
Octanol/water partition coefficient (log K_{OW})	9.22†
Organic carbon/water partition coefficient (log K_{OC})	6.88 (MCI method)†, 8.00 (Kow method)†
Air/water partition coefficient (log K_{AW})	-1.87†
Dissociation constant (pKa)	Not applicable

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† Estimated value using models in EPI Suite v4.11 [5].
NR = not reported

Degradation Pathways and Kinetics

Information on degradation pathways of quadrosilan was not found during the preparation of this fact sheet.

Intentional Uses and Production Levels

Uses

- May be used in breast implants and bearing grease [2], although other reports state that this use is not documented [3].
- May be used as a treatment for prostatic cancer under the trade name Cisobitan [4].

Production Levels

No information on production levels was found.

Emission Sources into the Environment

- 0.1 kg per year are released to air and 200 kg per year to wastewater [2].
- Specific information regarding emissions during the different phases of the life cycle was not found.

Distribution in the Natural Environment

Estimated Environmental Distribution

Inadequate data regarding the emission patterns for quadrosilan across its wide range of uses have been identified, hindering a representative understanding of its environmental distribution. Additional efforts are needed to better understand the emission patterns, and environmental models (e.g., the Level III fugacity model in EPI Suite [5]) could then be used to estimate the distribution of quadrosilan across the different environmental compartments.

Bioaccumulation Potential

	Bioconcentration factor (BCF)	**Organism**	**Reference**
Quadrosilan	1085 (estimated)†	fish	[5]

Measured Environmental Concentrations

No measured environmental concentrations were found during the preparation of this fact sheet. It is unclear whether or not the chemical exists in the environment at measurable concentrations.

Scientific Evidence of Adverse Endocrine-Related Environmental Effects

Reported scientific evidence of adverse endocrine-related environmental effects from exposure to quadrosilan exists for different organisms at the in vivo level. A comprehensive but non-exhaustive set of reported observations is included below.

Population level / field studies

No reported studies investigating this level were identified during the preparation of this fact sheet.

In vivo level

Substance	Organism	Observation	Reference
Quadrosilan	rat	Decreased testosterone levels in males	[6]
Quadrosilan	rabbit, dog, rat, mouse	Impaired reproduction (altered genital / reproductive organs, disrupted sperm / oocyte production, increased fragmentation)	[7–9]

In vitro level

No reported studies investigating this level were identified during the preparation of this fact sheet.

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Triphenyl phosphate

Key References:

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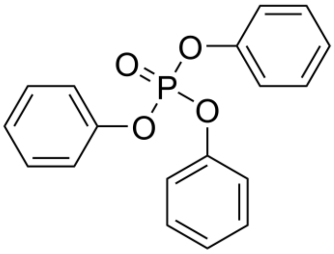
Chemical Identification			
Name	**Abbreviation**	**CAS Number**	**Structure**
Triphenyl phosphate	TPhP	115-86-6	
Completed assessments as the basis for inclusion: SIN List			

Physical and Physicochemical Properties	
Property	**TPhP**
Molecular formula	$C_{18}H_{15}O_4P$
Molecular weight [g/mol]	326.3
Physical state at 20°C	solid
Melting point [°C]	50.5 [1]
Density [g/cm^3]	1.2055 at 50 °C [1]
Vapor pressure at 25°C [mmHg]	$6.28*10^{-6}$ [2]
Water solubility at 25°C [mg/L]	1.9 [2]; $7.3*10^{-7}$ [3]
Octanol/water partition coefficient (log K_{OW})	4.59 (QSAR estimate) [4] ; 4.76 [2]
Organic carbon/water partition coefficient (log K_{OC})	4.03 (MCI method)[†], 3.24 (Kow method)[†]
Air/water partition coefficient (log K_{AW})	-3.87[†]
Dissociation constant (pKa)	Not applicable

[†] Estimated value using models in EPI Suite v4.11 [6].
NR = not reported

Degradation Pathways and Kinetics

Mechanisms	Expected to occur?			Technosphere	Environment	Reference
	Yes	No	Not reported			
Hydrolysis	X				Natural waters	[5]
Photolysis	X				Surface water	[5]
OH-radical reactions	X				Atmosphere	[6]
Biodegradation	X			WWTP	Soil, sediment	[5,7]

Kinetics – TPhP

Mechanism	Reported values	Reference
OH-radical reactions	Half-life = 12 h (estimated)†	[6]
Hydrolysis	Half-life = 7.5 d (pH 8.2)	[5]
Hydrolysis	Half-life = 19 d (pH 7)	[5]
Biodegradation (activated sludge, aerobic)	83–94 % degraded after 28 d	[7]
Biodegradation (river sediment, mostly anaerobic)	89.7 % degraded after 40 d	[7]
Biodegradation (activated sludge, domestic, aerobic)	93 % degraded after 49 d	[7]
Biodegradation (soil, aerobic)	Half-life = 37 d	[7]

Intentional Uses and Production Levels

Uses

- Mainly used as a flame retardant and plasticizer in plastics such as cellulose acetates, cellulose nitrates, vinyl polymers, and others. [5,8,9]
- Also used as an additive in hydraulic fluids and lubricants [5].
- Main areas of use in the EU in 2005 included printed circuit boards, thermoplastic/styrenic polymers, thermosets and epoxy resins, and photographic film [5].

Production Levels

- Currently registered in the EU with 1000–10 000 tonnes of production or import. [7]
- 4500–22 700 tonnes produced or used in the US in 2006 [8].

Emission Sources into the Environment

	Emission Sources
Production	Only a minor source of total environmental emissions [8].
Use	Hydraulic fluid leakages and leaching from plastics it is incorporated in [5,8].
Disposal	Leaching from disposed plastics [5].
Other sources	Not reported

Distribution in the Natural Environment

Estimated Environmental Distribution

Based on the identified uses and emission sources for triphenyl phosphate as a plastic additive and the emission scenario information generated by the OECD [10], a plausible emission pattern was assumed to estimate the resulting distribution in the environment using the Level III fugacity model in EPI Suite [6]. The assumed emission pattern and the resulting environmental distribution from the model are presented in the table below.

	Assumed Emission Pattern			**Modelled Distribution Results**			
	Air	**Water**	**Soil**	**Air**	**Water**	**Soil**	**Sediment**
DEP	50 %	50 %	0 %	2 %	39 %	35 %	24 %

Bioaccumulation Potential

	Bioconcentration factor (BCF)	**Organism**	**Reference**
Triphenyl phosphate	144	killifish	[7]
	113	fish	[8]

Measured Environmental Concentrations

Measured concentrations for TPhP have been reported in numerous environmental media. A non-exhaustive set of reported concentrations is included below.

Concentrations are provided in varying units depending on the media. Mass per mass dry weight (dw) and wet weight (ww) are sometimes used. ND = not detected, i.e., below the limit of detection (LOD). NQ = not quantified, i.e., below the limit of quantification (LOQ). NR = not reported.

Measured compartment	**Sampling location**	**Sampling year**	**Number of samples**	**Concentration range**	**Median concentration**	**Samples > LOD**	**Refer-ence**
Triphenyl phosphate (TPhP)							
River water	UK	2011	13	ND–21.7 ng/L	15.1 ng/L	87 % (LOD = 4.5 ng/L)	[11]
River water	Austria	2005	4	<MQL (=4.4 ng/L)–10 ng/L	NR	NR	[12]
River water	Germany	2002	10	<LOQ (10)–80 ng/L	15 ng/L	80 % (LOD = NR)	[13]
Surface and ground water	USA	2001	73	ND–<RL (= 0.5 µg/L)	NR	1.35 % (LOD = NR)	[14]
River sediment	Austria	2005	4	ND–160 µg/kg dw	NR	NR	[12]
WWTP effluent	Austria	2005	16	<MQL (=7.0 ng/L)–170 ng/L	NR	NR	[12]
WWTP sludge	China	NR (2013)	19	<LOQ (4.2) – – 656.7 µg/kg dw	46.7 µg/kg dw	95 % (LOD = 2.1 µg/kg dw	[15]
River water	UK	2011	13	ND – 21.7 ng/L	15.1 ng/L	87 % (LOD = 4.5 ng/L)	[11]
Marine herring	Sweden	NR (2009)	72	7.1 – –34 ng/g lipid	16 ng/g lipid	100 % (LOD = NR)	[9]

Note: Additional information regarding the sampling location and year is sometimes provided after values that are not reported (NR) in parentheses. This represents an estimated value for this non-reported information based on the general details provided in the study.

Scientific Evidence of Adverse Endocrine-Related Environmental Effects

Reported scientific evidence of adverse endocrine-related environmental effects from exposure to triphenyl phosphate exist for different organisms and across different study levels. A comprehensive but non-exhaustive set of reported observations is included below.

Population level / field studies

No reported studies investigating this level were identified during the preparation of this fact sheet.

In vivo level

Substance	Organism	Observation	Reference
TPhP	zebrafish	Changed sex hormone levels (plasma and/or whole body)	[16,17]
TPhP	zebrafish	Increased plasma vitellogenin* levels in males	[16]

In vitro level

Substance	Cell line	Observation	Reference
TPhP	human, zebrafish	Altered transcription profiles of genes involved in estrogen and thyroid hormone pathways	[16,18,19]
TPhP	zebrafish	Altered mRNA expression involved in various hormonal receptor centered gene networks	[17]

*Vitellogenin is a precursor protein normally synthesized by females to be incorporated in eggs.

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