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Programma di ricerca scientifica per una laguna "regolata"

Linea 2.3

Contaminanti emergenti in laguna, esposizione ed effetti

D2.3.1

Analisi della letteratura relativa alla chimica, all'ecotossicologia ed al rischio dei contaminanti emergenti

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Sommario

1   Introduction

The occurrence of priority substances in the lagoon environmental matrixes (water, biota and sediment) is frequently controlled by dedicated periodic monitoring, required by law (e.g. according to the requirements of the Water Framework Directive, DIR 2000/60/CE, and related directives, and their implementation at the national level). In this moment it is crucial to extend the current knowledge about the lagoon contamination to the "contaminants of emerging concerns" or simply the so-called "emerging contaminants", because the risk they pose to human health and the environment is not yet fully understood.

Contaminants of Emerging Concern (CECs) are defined as any synthetic or naturally occurring chemical that is not commonly monitored in the environment, though having the potential to enter soil and aquatic ecosystems and cause adverse effects in humans, wildlife, and the environment. CECs include synthesized and commercialized chemicals that have just gained entry into the environment and a range of chemicals that have been produced and released into the environment for long, for which new concerns (occurrence, fate, adverse effects on human health and the environment) have recently raised.

They include herbicides, pesticides (i.e. glyphosate, piretroids, neonicotinoids), pharmaceuticals and cosmetics, perfluorinated alkylated substances (PFAS), bisphenol A, microplastics. The contribution to the environmental status of water, sediments and biota of some classes of these contaminants could be even higher with respect to the contribution of priority pollutants. Recent Italian regulations added some emerging contaminants to the list of the priority pollutants (D. Lgs. 172/2015), such as some flame-retardants and pesticides.

It is important to underline that emerging pollutants are not necessary newly formulated chemical compounds; they could have been used for decades and have created concern in the last years, due to their environmental diffusion and their possible toxic effect to humans and other organisms. The hazard of these substances is mainly linked to the ability to generate long-term effects, individually and in mixture. To date, a census of the emerging contaminants in the Venice lagoon has never been conducted.

The line 2.3 has the specific objectives to deepen the knowledge regarding the contamination of water, sediments and biota in the Venice lagoon, due to the presence of emerging contaminants and to investigate the distribution and fate of these contaminants in the water environment of the lagoon, experimentally and using models. With this aim, the classes of substance that should be included in future monitoring activities will be identified by the assessment of the ecotoxicological effects and environmental risk associated with these contaminants.

For these reasons, the present document is crucial and prior to all the subsequent activities of the line 2.3, because it is the outcome of a careful and scrupulous bibliographic research carried out to identify the classes of emerging pollutants to be investigated, their main sources, the diffusion pathways and targets. It therefore constitutes the background of all planned activities.

The report is subdivided into chapters, one chapter for each class of contaminants: Pharmaceuticals, Plant Protection Products, Neonicotinoid insecticides, Industrial chemicals (it comprehends various emerging contaminants produced for different applications/uses and with different chemical characteristics), Fragrances, PFASs and Microplastics. The chapters are in turn subdivided into sections, one section for each individual chemical of the class that has been studied and will be analysed.

For each individual chemical, general properties, methods of analysis in the different environmental matrices, information about the emissions in the environment, the environmental concentration found in literature, the ecotoxicological effects and the biochemical and genetic responses are reported. All this information is organized in tables, with the aim of making the consultation of the document easier and finding easily the information of interest.

2   Pharmaceuticals

Pharmaceutical compounds cover all classes of chemicals used primarily to prevent or treat human and animal diseases. The main representative therapeutic groups are antibiotics, analgesics and painkillers, cardiovascular drugs and blood lipid regulators and antidepressants. Pharmaceuticals are generally excreted and emitted into the sewerage system following use and can then be released into surface water bodies or enter terrestrial systems. Moreover, this chemical class includes veterinary pharmaceuticals, used in intensive farming and aquaculture to increase livestock production. They are often released directly in surface waters or indirectly during the land application of manure and slurry from live-stock facilities.

The capability of pharmaceutical ingredients to be absorbed and to interact with living organisms makes them a potential hazard for the whole ecosystem. Pharmaceuticals are specifically designed to be biologically active substances (also at low doses) and to target certain metabolic, enzymatic or cell-signaling mechanisms. Thus, when released into the environment, their biological activity may interact with non-target organisms and impair the ecosystem health. Highly lipid-soluble medicinal products may also have the ability to accumulate in the fat tissues of animals and can be thus introduced into the food chain.

A major concern raised by the presence of pharmaceuticals in the environment is their ability to act as endocrine disruptors, i.e. interfere with the endocrine system to produce undesired effects/disruption of homeostasis. This applies for example to hormones.

Among other pharmaceuticals, the presence of antibiotics (antimicrobial compounds specifically targeting bacteria or fungi in human and animal hosts) in the environment causes significant concern due to the possibility of increasing multi-resistant bacteria.

2.1   Emissions of pharmaceuticals
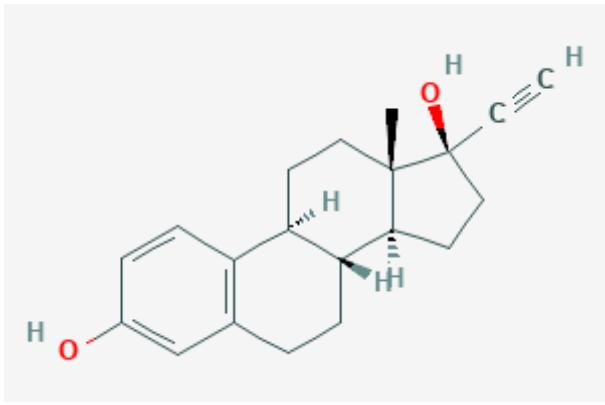
The use of active ingredients in pharmaceuticals authorised in Europe is monitored by the European Medicines Agency, and information are available through an online database (European Medicines Agency, 2016), where for each ingredient the list of pharmaceutical products accessible in the EC can be identified in their reports. Estimates of pharmaceutical products consumed is monitored by each member state; in Italy the Italian Agency for Pharmaceutical products (AIFA) hosts the national Observatory on the use of Pharmaceuticals (OsMED) which is releasing annual estimates of pharmaceuticals consumption with a focus at the regional scale (AIFA, 2014).

2.2   17-alpha-ethinylestradiol (EE2)

17-alpha-ethinyl estradiol (EE2) is a synthetic feminine sexual hormone, metabolite of mestranol, the estrogen used in contraceptives (mestranol is the prodrug that is activated in the body to improve ADME) (Human metabolome HBMD, n.d.).

Tab. 1. Substance identity.

Parameters	
Name	17-alpha-ethinylestradiol
IUPAC name	(8R,9S,13S,14S,17R)-17-ethynyl-13-methyl-7,8,9,11,12,14,15,16-octahydro-6H-cyclopenta[a]phenanthrene-3,17-diol
CAS number	57-63-6

Molecular formula	C20H24O2
Molecular weight	296.41 g/mol
Structure	
SMILES	C[C@]12CC[C@H]3[C@H]([C@@H]1CC[C@]2(C#C)O)CCC4=C3C=CC(=C4)O

Tab. 2. Physico-chemical properties.

Endpoint	Value	Source
Vapour pressure (Pa)	1.95×10^{-9} mm Hg at 25 deg C (est)	(PubChem, 2019e)
Water solubility (mg/L)	11.3 mg/L at 27 deg C	(PubChem, 2019e)
Log K_{ow}	3.67	(PubChem, 2019e)

Tab. 3. Environmental fate.

Endpoint	Value	Source
Sorption potential K_{OC}	510 (SRC)	(PubChem, 2019e)
Biodegradability	NRB	(PubChem, 2019e)
Bioconcentration (BCF)	110(SRC)	(PubChem, 2019e)

Tab. 4. Analytical methods.

Method	LOD (µg/L)	Description	Reference
SPE concentration and UPLC-MS analysis Qtrap	0.07	SPE Oasis HLB eluted with MeOH, evaporated to dryness and reconstituted with 0.1 ml of 9:1 H_2O:AcCN. Hypersil GOLD 1,9 µm 50 x 2.1 NH_4OH/AcCN	(Tavazzi et al., 2016)

Method	LOD (µg/L)	Description	Reference
SPE concentration and LC-MS analysis MSD and Trap (Venice Lagoon, water, sediment, biota)	2- 0.1	SPE Envi-C18 eluted with AcCN, MeOH, and Acidified water, concentrated and reconstructed to 400 µL in AcCN/H$_2$O (1:1).	(Pojana et al., 2007, 2004)
SPE concentration and GC MS/MS	40	SPE Oasis HLB eluted with EtOH, evaporated to dryness and reconstituted with 0.25 ml of EtOH. Derivatization with MSTFA and analysed by GC-MS, Zebron (30 m x 0.25mm)	(Sousa et al., 2019)
	1-0.012	Derivatization-direct injection	(Loos et al., 2018)
ASE and LC-MS/MS	0.5 ng/g (biota)	ASE extraction (AcCN:MeOH), concentration and analysis by LC-MS/MS	(Wang et al., 2014)
ASE and LC-MS/MS	0.5 ng/g (sediment)	ASE extraction (Acetone:MeOH), concentration and analysis by LC-MS/MS	(Wang et al., 2014)

2.2.1 Environmental exposure assessment

The oral contraceptives are the 3rd most sold pharmaceutical category in Italy, with higher consumption in the north of Italy compared to the south. EE2 is a synthetic hormone and is in the top-10 of the active ingredients consumed and sold at the national level according to AIFA (AIFA, 2018b).

Tab. 5. Environmental Emissions.

	Description/value
Use(s)	Synthetic hormone used as contraceptive and for the hormonal therapy during menopause
Total production or total emissions (tonnes/year)	Concentrations of ethinylestradiol in coastal/estuarine water and rivers of The Netherlands (11 locations) ranged from <0.1 to 4.3 ng/L (<0.1 ng/L median) (PubChem, 2019e)
Information on emissions in Veneto	This hormone is not indicated in the analysis for the Veneto region; the consumption information may be derived by the national estimate (AIFA, 2018b)
Possible contacts for relevant information	AIFA

Tab. 6. Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source

	Value	Matrix	Region/area	Source
Measured concentration in water MEC$_w$ (μg/L)	<0.8 – 28	Transitional water, (seasonal sampling Oct 2001-Oct 2002)	LV (Lagoon of Venice)-Industrial area - Tresse)	(Pojana et al., 2007)
	<0.8 – 25	Transitional water, (seasonal sampling Oct 2001-Oct 2002)	LV-Urban areas – (Celestia, S. Nicolò)	(Pojana et al., 2007)
	<0.8-34	Transitional water, (seasonal sampling Oct 2001-Oct 2002)	LV-Background site – (S. Erasmo)	(Pojana et al., 2007)
	<2-112	Transitional water, (seasonal sampling Dec 2001-May 2002)	LV-Osellino mouth	(Pojana et al., 2004)
	<2-37	Transitional water, (seasonal sampling Dec 2001-May 2002)	LV-Fusina	(Pojana et al., 2004)
	<2-6.3	Transitional water, (seasonal sampling Dec 2001-May 2002)	LV-Lido	(Pojana et al., 2004)
	<2-68	Transitional water, (seasonal sampling Dec 2001-May 2002)	LV-City of Venice-external sites	(Pojana et al., 2004)
	<2-75	Transitional water, (seasonal sampling Dec 2001-May 2002)	LV-City of Venice-inner canals	(Pojana et al., 2004)
Measured concentration in sediment MEC$_{sed}$ (μg/kg dw)	<2.0	Transitional water, (July 2001, July 2002)	LV-Industrial area - Tresse)	(Pojana et al., 2007)
	<2.0-41	Transitional water, (July 2001, July 2002)	LV-Urban areas – (Celestia, S. Nicolò)	(Pojana et al., 2007)
	<2.0-35	Transitional water, (July 2001, July 2002)	LV-Bkg site – (S. Erasmo)	(Pojana et al., 2007)
Measured concentration in biota MEC$_{biota}$ (ng/g)	<3.0	*Mytilus galloprovincialis*, (July 2001, July 2002)	LV-Industrial area - Tresse)	(Pojana et al., 2007)

	Value	Matrix	Region/area	Source
	<7.2-38	*Mytilus galloprovincialis*, (July 2001, July 2002)	LV-Urban areas – (Celestia, S. Nicolò)	(Pojana et al., 2007)
	<7.2-20	*Mytilus galloprovincialis*, (July 2001, July 2002)	LV-Bkg site – (S. Erasmo)	(Pojana et al., 2007)

Tab. 7. Predicted Environmental Concentrations.

	Value/Description	Region/area	Model or method used for the prediction	Source
Predicted concentrations in water PEC$_w$ (µg/L)	0.0063 - 0.0064 (median) 0.010 - 0.054 (median)	Europe	PhATE GREAT-ER	(Hannah et al., 2009)

Tab. 8. Ecotoxicological data.

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
Crustacea				
Acartia tonsa	48-h	Mortality	LC$_{50}$ = 1.100	Andersen et al., 1999
	5-d	Larval development	EC$_{50}$ = 88	
Nitocra spinipes	96-h	Mortality	LC$_{50}$ = 510	Breitholtz and Bengtsson, 2001
Tisbe battagliai	10-d	Mortality	NOEC > 100	Hutchinson et al., 1999
			LOEC > 100	
			LC$_{50}$ > 100	
	21-d	Mortality	NOEC > 100	
			LOEC > 100	
			LC$_{50}$ > 100	
		Fertility	NOEC > 100	
			LOEC > 100	

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
Neomysis integer	96-h	Mortality	LC_{50} = 1.200	Verslycke et al., 2004
Ampelisca brevicornis	10-d	Mortality	[A]NOEC > 100 ng/g	
Mollusca				
Saccostrea glomerata	4-d	Sex-ratio	NOEC = 0.05	Andrew et al., 2010
	21-d		NOEC = 0.05	
	49-d		NOEC = 0.05	
Mytilus galloprovincialis	1-h	Fertilization	NOEC = 0.05	Capolupo et al., 2018
			LOEC = 0.5	
	48-h	Larval development	NOEC < 0.05	
Echinoida				
Strongylocentrotus purpuratus	96-h	Larval development	EC_{50} = 30.3	Roepke et al., 2005
Paracentrotus lividus	1-h	Fertilization	NOEC < 0.005	Capolupo et al., 2018
	48-h	Larval development	NOEC = 0.005	
			LOEC = 0.05	
Fishes				
Fundulus heteroclitus	336-d	Sex-ratio	NOEC = 0.01	Peters et al., 2010
			LOEC = 0.1	
	364-d	Sex-ratio	NOEC = 0.01	
			LOEC = 0.1	
		Gamete production	NOEC = 0.01	
	427-d	Sex-ratio	NOEC = 0.01	
			LOEC = 0.1	
	28-d	Gamete production	NOEC = 0.1	Peters et al., 2007
		Spawning frequency	NOEC = 0.01	
			LOEC = 0.1	

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
		Mean female spawning	NOEC = 0.01	
			LOEC = 0.1	
	25-d	Mortality	NOEC = 1	Boudreau et al., 2004
			LOEC = 10	
	60-d	Survival	NOEC = 1	
			LOEC = 10	
		Development	NOEC = 0.01	
			LOEC = 1	
		Deformation	LOEC = 10	
		Deformation (spine)	LOEC = 1	
Gasterosteus aculeatus	76-h	Behavioural changes	NOEC = 0.015	Dzieweczynski, 2011
		Reproductive impairment	NOEC = 0.015	
		Swimming	LOEC = 0.015	
Pomatoschistus minutus	8-d	Sexual development	NOEC = 0.011	Saaristo et al., 2010
	13-d			
	18-d			
	23-d			
	28-d			
Sparus aurata	96-h	Survival	NOEC = 0.005	Capolupo et al., 2018
			LOEC = 0.05	
Syngnathus abaster	7-d	Swimming behaviour	NOEC = 0.003	Sárria et al., 2011
			LOEC = 0.009	
Syngnathus scovelli	10-d	Colour development	NOEC = 0.001	Partridge et al., 2010
			LOEC = 0.1	

[A] Sediment test

LC$_{50}$/EC$_{50}$ = Lethal/Effective Concentration 50

D2.3.1-Analisi della letteratura relativa alla chimica, all'ecotossicologia ed al rischio dei contaminanti emergenti

LOEC/LOEL = Lowest Observed Effect Concentration/Level
NOEC/NOEL = Non Observed Effect Concentration/Level

Tab. 9. Biochemical and genetic responses.
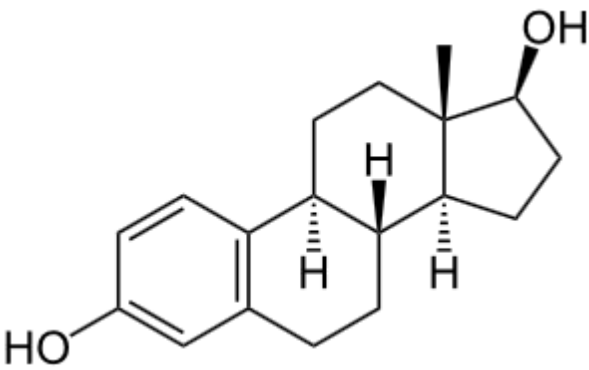
Species	Concentrations	Days of exposure	Biochemical/molecular effects	Reference
Mussels *Mytilus trossulus*	50 and 500 ng/dL	10 days	Evidence of gonadal pathologies: in females, increase of the frequency of atresia and retarded gonadal development; in males, increase of the frequency of melanised haemocyte aggregates into seminiferous tubules.	Smolarz et al., 2017.
Freshwater mussels *Lampsilis fasciola*	5 and 1000 ng/L	12 days	Alteration of the extracellular matrix of gill tissue; significant alterations in metabolites involved in signal transduction, immune response and neuromodulation. In males: reduction of siphoning and mantle display behaviour of females. In females: reduction of energy reserves (indicated by the decreases in glycogen metabolism end products, glucose, and several essential fatty acids).	Leonard et al., 2014.

Mussels *Mytilus edulis*	5 and 50 ng/L	10 days	Effects at different stages of gametogenesis process: significant increase in estrogen receptor 2 (ER2) and vitellogenin (VTG) mRNA expression at the early stage of gametogenesis; no statistically significant change in the VTG and ER2 mRNA expression in mature mussels. No significant change in VTG and ER2 expressions in both mature and immature mussels exposed to the higher dose (200 ng/l).	Ciocan et al., 2010.
Mussels *Mytilus edulis*	5 and 50 ng/l	10 days	Increase of 5-HT receptor mRNA expression level at the early gametogenesis stages; no significant effect in cyclooxygenases (COX) mRNA expression level.	Cubero-Leon et al., 2010.
Oyster *Crassostrea gigas* (embryos exposure)	0.02 –1.7 nM	16 h 20 h	No genotoxic effect on larvae was observed. No embryotoxic effect was observed.	Wessel et al., 2007.
Mussels *Scrobicularia plana*	1 µg/L in vitro	40 min	Genotoxic effect on exposed haemocytes.	Petridis et al., 2009.
Freshwater mussels *Elliptio complanata*	5 ng/L	28 days 180 days	Conglutinates contained few glochidia and more eggs. Increase of Vtg level in haemolymph.	Leonard et al., 2017.
Mussels *Mytilus galloprovincialis*	In vitro nM-µM 0.1-5µM 25-100 µM	30 min	Effect on immune parameters: alteration of lysosomal membrane stability; stimulation of phagocytosis; inhibition of phagocytosis.	Canesi et al, 2007b. Aquat.

2.3 17-beta-estradiol (E2)

17-beta- estradiol (E2) is a natural feminine sexual hormone and it is produced especially during the fertile period, and its production decreases at low levels during menopause. It is present also in men at a lower extent and also in other animal species. It is also used as an estrogen especially in the menopausal hormone therapy.

Tab. 10. Substance identity.

Parameters	
Name	17-Beta-estradiol
IUPAC name	(8R,9S,13S,14S,17S)-13-methyl-6,7,8,9,11,12,14,15,16,17-decahydrocyclopenta[a]phenanthrene-3,17-diol
CAS number	50-28-2
Molecular formula	272.388 g/mol
Molecular weight	C18H24O2
Structure	
SMILES	C[C@]12CC[C@H]3[C@H]([C@@H]1CC[C@@H]2O)CCC4=C3C=CC(=C4)O

Tab. 11. Physico-chemical properties.

Endpoint	Value	Source
Vapour pressure (Pa)	6.38 x 10-9 mm Hg at 25 deg C (est) 2.3 x 10-10 mmHg	(PubChem, 2019f) (Balzamo et al., 2017; Chowdhury, 2010)
Water solubility (mg/L)	3.90 mg/L at 27 deg C 13 mg/L	(PubChem, 2019f) (Balzamo et al., 2017; Chowdhury, 2010)
Log K_{ow}	4.01 3.94	(PubChem, 2019f) (Balzamo et al., 2017; Chowdhury, 2010)

Tab. 12. Environmental fate.

Endpoint	Value	Source
Sorption potential K_{OC}	30.000	(PubChem, 2019f)
Biodegradability	NRB	(PubChem, 2019f)
Bioconcentration (BCF)	200(SRC)	(PubChem, 2019f)

Tab. 13. Analytical methods.

Method	LOD (µg/L)	Description	Reference
SPE concentration and UPLC-MS analysis Qtrap	0.09	SPE Oasis HLB eluted with MeOH, evaporated to dryness and reconstituted with 0.1 ml of 9:1 H_2O:AcCN. Hypersil GOLD 1,9 µm 50 x 2.1 NH_4OH/AcCN	(Tavazzi et al., 2016)
SPE concentration and LC-MS analysis MSD and Trap (Venice Lagoon, water, sediment, biota)	2- 0.1	SPE Envi-C18 eluted with AcCN, MeOH, and Acidified water, concentrated and reconstructed to 400 µL in AcCN/H_2O (1:1).	(Pojana et al., 2007, 2004)
SPE concentration and GC MS/MS	40	SPE Oasis HLB eluted with EtOH, evaporated to dryness and reconstituted with 0.25 ml of EtOH. Derivatization with MSTFA and analysed by GC-MS, Zebron (30 m x 0.25mm)	(Sousa et al., 2019)
	1-0.053	Derivatization-direct injection	(Loos et al., 2018)
ASE and LC-MS/MS	0.5 ng/g (biota)	ASE extraction (AcCN:MeOH), concentration and analysis by LC-MS/MS	(Wang et al., 2014)
ASE and LC-MS/MS	0.5 ng/g (sediment)	ASE extraction (Acetone:MeOH), concentration and analysis by LC-MS/MS	(Wang et al., 2014)

2.3.1 Environmental exposure assessment

E2 is indicated as a drug consumed in Italy in combination with dienogest and nomegestrol at lower levels compared to EE2 (AIFA, 2018b).

Tab. 14. Environmental Emissions.

	Description/value
Use(s)	Synthetic hormone used in hormonal therapy during menopause

	Description/value
Banned use(s)	Banned for non-therapeutic uses in veterinary medicine (Balzamo et al., 2017)
Total production or total emissions (tonnes/year)	NA
Information on emissions in Veneto	This hormone is not indicated in the analysis for the Veneto region; the consumption information may be derived by the national estimate (AIFA, 2018b)
Possible contacts for relevant information	AIFA

Tab. 15. Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source
Measured concentration in water MEC$_w$ (µg/L)	<1.0 - 15	Transitional water, (seasonal sampling Oct 2001-Oct 2002)	LV (Lagoon of Venice)-Industrial area - Tresse)	(Pojana et al., 2007)
	<1.0 - 175	Transitional water, (seasonal sampling Oct 2001-Oct 2002)	LV-Urban areas – (Celestia, S. Nicolò)	(Pojana et al., 2007)
	<1.0 - 36	Transitional water, (seasonal sampling Oct 2001-Oct 2002)	LV-Background site – (S. Erasmo)	(Pojana et al., 2007)
	1.7 - 3.9	Transitional water, (seasonal sampling Dec 2001-May 2002)	LV-Osellino mouth	(Pojana et al., 2004)
	1.5 - 50	Transitional water, (seasonal sampling Dec 2001-May 2002)	LV-Fusina	(Pojana et al., 2004)
	1.5 - 42	Transitional water, (seasonal sampling Dec 2001-May 2002)	LV-Lido	(Pojana et al., 2004)
	<1.0 - 2.7	Transitional water, (seasonal sampling Dec 2001-May 2002)	LV-City of Venice-external sites	(Pojana et al., 2004)
	<1.0 - 51	Transitional water, (seasonal sampling Dec 2001-May 2002)	LV-City of Venice-inner canals	(Pojana et al., 2004)

	Value	Matrix	Region/area	Source
Measured concentration in sediment MEC_{sed} (µg/kg dw)	Non detected	Transitional water, (July 2001, July 2002)	LV- (Tresse, Celestia, S. Nicolò, S. Erasmo)	(Pojana et al., 2007)
Measured concentration in biota MEC_{biota} (ng/g)	Non detected	Transitional water, (July 2001, July 2002)	LV- (Tresse, Celestia, S. Nicolò, S. Erasmo)	(Pojana et al., 2007)

Tab. 8. Ecotoxicological data.

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
Crustacea				
Acartia tonsa	5-d	Larval development	$EC_{50} = 720$	Andersen et al., 1999
Nitocra spinipes	96-h	Mortality	$LC_{50} = 1.600$	Breitholtz and Bengtsson, 2001
	6.5-d	Larval development	NOEC = 50	
	18-d	Mortality	NOEC = 50	
		Reproduction	NOEC = 50	
Tigriopus japonicus	2-d	Mortality	$LC_{50} = 3.350$	Marcial et al., 2003
		Immobilization	NOEC = 1.000	
	13-d	Sexual maturity	NOEC = 10	
	21-d	Mortality	NOEC = 10	
		Reproduction	NOEC = 10	
	42-d	Mortality	NOEC = 10	
		Reproduction	NOEC = 10	
Tisbe battagliai	10-d	Mortality	NOEC > 100	Hutchinson et al., 1999
			LOEC > 100	
			$LC_{50} > 100$	
	21-d	Mortality	NOEC > 100	
			LOEC > 100	

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
			$LC_{50} > 100$	
		Fertility	$NOEC > 100$	
			$LOEC > 100$	
Americamysis bahia	48-h	Mortality	$LC_{50} = 1.690$	Hirano et al., 2004
	96-h		$LC_{50} = 890$	
Elminius modestus	6-d	Larval development	$LOEC = 10$	Billinghurst et al., 2001
	7-d		$LOEC = 10$	
	8-d		$NOEC = 10$	
	365-d	Maturity	$NOEC = 10$	
Mollusca				
Mytilus galloprovincialis	48-h	Larval development	$NOEC = 0.01$	Balbi et al., 2016
			$LOEC = 0.1$	
Echinoida				
Dendraster excentricus	1-h	Fertilization	$NOEC = 1.000$	Rempel et al., 2009
			$LOEC = 10.000$	
	48-h	Larval development	$NOEC = 1.000$	
			$LOEC = 10.000$	
Strongylocentrotus purpuratus	1-h	Cell cleavage	$LOEC = 500$	Mwatibo and Green, 1998
	2-h		$LOEC = 500$	
	48-h	Larval development	$LOEC = 0.5$	Roepke et al., 2005
	96-h	Larval development	$LOEC = 0.5$	
			$EC_{50} = 14,2$	
Fishes				
Fundulus heteroclitus	48-h	Larval mortality	$LC_{50} = 11.195$	Kelly and Giulio, 2000
	96-h		$LC_{50} = 5.094$	

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
Pomatoschistus minutus	60-d	Sexual development	NOEC = 0,669	Robinson et al., 2007
	90-d	Sexual development	NOEC = 0,097	
			LOEC = 0,669	
	152-d	Sexual development	NOEC = 0,016	
			LOEC = 0,097	
	243-d	Sexual development	NOEC = 0,097	
			LOEC = 0,669	
Kryptolebias marmoratus	96-h	Adult mortality	LC_{50} = 4.260	Rhee et al., 2011
	24-h	Juvenile mortality	LC_{50} = 1.290	
	96-h	Embryo mortality	LC_{50} = 620	

LC_{50}/EC_{50} = Lethal/Effective Concentration 50
LOEC/LOEL = Lowest Observed Effect Concentration/Level
NOEC/NOEL = Non Observed Effect Concentration/Level

Tab. 9. Biochemical and genetic responses.

Species	Concentrations	Days of exposure	Biochemical/molecular effects	Reference
Tapes philippinarum	5, 25, 50, 100 and 1000 ng/L	7 days 14 days	Resting phase, haemolymph: significant increase of Vg-like proteins level with increasing E2 concentrations; digestive gland: no significant variations were observed. Pre-spawning, haemolymph: in females, decrease of Vg-like proteins level at 50, 100 and 1000 ng/L, while in males no variations were observed. Resting phase, haemolymph: significant increase of Vg-like proteins level at 1000 ng/L; digestive gland: significant increase of Vg-like proteins level at 5 ng/L. Pre-spawning, haemolymph: significant increase of Vg-like proteins level at 50 and 100 ng/L in females and males, respectively; digestive gland: in females, increase of Vg-like proteins level at 5, 100 and 1000 ng/L, while in males no significant differences were observed.	Matozzo & Marin, 2008.
Clams *Ruditapes decussatus*	400 ng/L	30 days	Absence of negative effects on health; marked increase in gametogenesis both in females and males. Effects on reproductive cycle, after 4 months of transplantation in the field, in a sex-specific way: males showed a normal development and maturation of the gonads, while females showed lower health status and ovaries with atretic oocytes .	Mezghani-Chaari et al., 2017.

Mussels *Mytilus galloprovincialis*	5, 25 and 50 nM *in vitro*	30 min	Effects on immune processes: increase adhesion of haemocytes to ECM proteins (laminin-1, collagen IV and oxidized collagen IV) and increase of α₂ integrin subunit levels.	Koutsogiannaki & Kaloyianni, 2011.
Mussels *Mytilus edulis*	5 and 50 ng/l	10 days	Effects at different stages of gametogenesis process: significant increase in *estrogen receptor 2 (ER2)* and *vitellogenin (VTG)* mRNA expression at the early stage of gametogenesis; no statistically significant change in the *VTG* and *ER2* mRNA expression in mature mussels.	Ciocan et al., 2010.
Mussels *Mytilus edulis*	5 and 50 ng/L	10 days	Significant alteration of *5-HTreceptor* and *cyclooxygenases (COX)* mRNA expression level at different stages of gametogenesis process: in mature mussels, decrease of *5-HT* expression; increase of *5-HT* expression at the early gametogenesis stages. Decrease of *COX* expression level at both stages.	Cubero-Leon et al., 2010.
Mussels *Mytilus edulis*	50 ng/l	10 days	The presence of several differentially regulated genes from mussel testis was evidenced, including testis-specific kinases, vitelline lysine and envelope sequences.	Ciocan et al., 2011.
Mussels *Mytilus galloprovincialis*	25 nM *in vitro*	30 min	Modulation of redox status in haemocytes by affecting oxidative parameters and antioxidant gene expression.	Koutsogiannaki et al., 2014.

Mussels *Mytilus galloprovincialis*	50 nM	1, 3 and 7 days	Induction of oxidative stress by increasing ROS levels and apoptosis through the suppression of antioxidant enzymes expression levels, leading to the increase of prooxidant level.	Koutsogiannaki et al., 2015.
Mussels *Scrobicularia plana*	100 ng/L *in vitro* 1 µg/L *in vivo*	40 min 6 days	Genotoxic effect on exposed haemocytes.	Petridis et al., 2009.
Mussels Mytilus galloprovincialis	*in vitro* 1-10 nM 0.1-5 µM 25-100 µM	30 min	Effects on immune parameters: alteration of lysosomal membrane stability; stimulation of phagocytosis; inhibition of phagocytosis.	Canesi et al, 2007b.
Mussels Mytilus galloprovincialis	5 and 25 nM *in vitro* 50 nM *in vitro* 5, 25 and 100 pmol *in vivo*	6 and 24 h	Effects on immune parameters: stimulation of phagocytosis and oxyradical production; inhibition of phagocytosis. Alteration of haemocyte lysosomal membrane stability and phagocytosis.	Canesi et al., 2006.

Tab. 18. Derivation of PNEC values.

PNEC	Endpoint	Endpoint value (µg/L)	AF	Source
0.0004 (µg/L)				(Loos Robert et al., 2018)
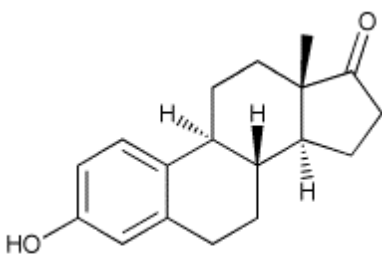
Tab. 109. Risk Quotient (MEC or PEC/PNEC).

MEC o PEC/PNEC			Source
RQ (P95)	3.3	Sc1	(Loos Robert et al., 2018)
RQ (P95)	3.8	Sc2	(Loos Robert et al., 2018)
RQ (P95)	1.3	Sc3	(Loos Robert et al., 2018)

2.4 Estrone (E1)

Estrone (E1) is a natural feminine sexual hormone; it is less active compared to EE2 and it can be converted into estradiol. It is also used as an estrogen especially in the menopausal hormone therapy.

Tab. 20. Substance identity.

Parameters	
Name	Estrone (E1)
Other names	Oestrone; E1; 3-Hydroxyestra-1,3,5(10)-trien-17-one
IUPAC name	(8R,9S,13S,14S)-3-hydroxy-13-methyl-7,8,9,11,12,14,15,16-octahydro-6H-cyclopenta[a]phenanthren-17-one
CAS number	53-16-7
Molecular formula	C18H22O2
Molecular weight	270.366 g/mol
Structure	
SMILES	CC12CCC3C(C1CCC2=O)CCC4=C3C=CC(=C4)O

Tab. 21. Physico-chemical properties.

Endpoint	Value	Source
Vapour pressure (Pa)	2.49 x 10-10 mm Hg at 25 deg C (est) 2.3 x 10-10 mmHg	(PubChem, 2019g) (Balzamo et al., 2017; Chowdhury, 2010)
Water solubility (mg/L)	0.03 mg/mL 13 mg/L	(PubChem, 2019g) (Balzamo et al., 2017; Chowdhury, 2010)
Log K_{ow}	3.13 3.43	(PubChem, 2019g) (Balzamo et al., 2017; Chowdhury, 2010)

Tab. 22. Environmental fate.

Endpoint	Value	Source
Sorption potential K_{OC}	457-18,000	(PubChem, 2019g)
Biodegradability	NRB	(PubChem, 2019g)
Bioconcentration (BCF)	54 (SRC)	(PubChem, 2019g)

Tab. 23. Analytical methods.

Method	LOD (μg/L)	Description	Reference
SPE concentration and UPLC-MS analysis Qtrap	0.1	SPE Oasis HLB eluted with MeOH, evaporated to dryness and reconstituted with 0.1 ml of 9:1 H_2O:AcCN. Hypersil GOLD 1.9 μm 50 x 2.1 NH_4OH/AcCN	(Tavazzi et al., 2016)
SPE concentration and LC-MS analysis MSD and Trap (Venice Lagoon, water, sediment, biota)	2- 0.1	SPE Envi-C18 eluted with AcCN, MeOH, and Acidified water, concentrated and reconstructed to 400 **μ**L in AcCN/H_2O (1:1).	(Pojana et al., 2007, 2004)
SPE concentration and GC MS/MS	40	SPE Oasis HLB eluted with EtOH, evaporated to dryness and reconstituted with 0.25 ml of EtOH. Derivatization with MSTFA and analysed by means GC-MS, Zebron (30 m x 0.25mm)	(Sousa et al., 2019)
ASE and LC-MS/MS	0.5 ng/g (biota)	ASE extraction (AcCN:MeOH), concentration and analysis by LC-MS/MS	(Wang et al., 2014)
ASE and LC-MS/MS	0.5 ng/g (sediment)	ASE extraction (Acetone:MeOH), concentration and analysis by LC-MS/MS	(Wang et al., 2014)

2.4.1 Environmental exposure assessment

E1 is not indicated as a drug consumed in Italy (AIFA, 2018b).

Tab. 24. Environmental Emissions.

	Description/value
Use(s)	Synthetic hormone used in hormonal therapy during menopause
Total production or total emissions (tonnes/year)	NA
Information on emissions in Veneto	This hormone is not indicated in the analysis for the Veneto region
Possible contacts for relevant information	AIFA

Tab. 25. Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source
Measured concentration in water	<1.2 - 3.2	Transitional water, (seasonal sampling Oct 2001-Oct 2002)	LV (Lagoon of Venice)-Industrial area - Tresse)	(Pojana et al., 2007)

	Value	Matrix	Region/area	Source
MEC$_w$ (µg/L)	<1.2 – 6.7	Transitional water, (seasonal sampling Oct 2001-Oct 2002)	LV-Urban areas – (Celestia, S. Nicolò)	(Pojana et al., 2007)
	<1.2 – 10	Transitional water, (seasonal sampling Oct 2001-Oct 2002)	LV-Background site – (S. Erasmo)	(Pojana et al., 2007)
	<2-2.3	Transitional water, (seasonal sampling Dec 2001-May 2002)	LV-Osellino mouth	(Pojana et al., 2004)
	<2-4.2	Transitional water, (seasonal sampling Dec 2001-May 2002)	LV-Fusina	(Pojana et al., 2004)
	<2	Transitional water, (seasonal sampling Dec 2001-May 2002)	LV-Lido	(Pojana et al., 2004)
	<2-16	Transitional water, (seasonal sampling Dec 2001-May 2002)	LV-City of Venice-external sites	(Pojana et al., 2004)
	<2-85	Transitional water, (seasonal sampling Dec 2001-May 2002)	LV-City of Venice-inner canals	(Pojana et al., 2004)
Measured concentration in sediment MEC$_{sed}$ (µg/kg dw)	Non detected	Transitional water, (July 2001, July 2002)	LV- (Tresse, Celestia, S. Nicolò, S. Erasmo)	(Pojana et al., 2007)
Measured concentration in biota MEC$_{biota}$ (ng/g)	Non detected	Transitional water, (July 2001, July 2002)	LV- (Tresse, Celestia, S. Nicolò, S. Erasmo)	(Pojana et al., 2007)

Tab. 26. P, B, T, C, M, R, ED properties

	YES/NO	Source
Toxic (T)	YES	(PubChem, 2019g)

Tab. 11. Ecotoxicological data.

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
Crustacea				
Acartia tonsa	5-d	Larval development	EC_{50} = 410	Andersen et al., 1999
Tisbe battagliai	10-d	Mortality	NOEC > 100	Hutchinson et al., 1999
			LOEC > 100	
			LC_{50} > 100	
	21-d	Mortality	NOEC > 100	
			LOEC > 100	
			LC_{50} > 100	
		Fertility	NOEC > 100	
			LOEC > 100	
Echioida				
Strongylocentrotus purpuratus	96-h	Larval development	EC_{50} = 604	Roepke et al., 2005

LC_{50}/EC_{50} = Lethal/Effective Concentration 50
LOEC/LOEL = Lowest Observed Effect Concentration/Level
NOEC/NOEL = Non Observed Effect Concentration/Level

Tab. 28. Biochemical and genetic responses.

Species	Concentrations	Days of exposure	Biochemical/molecular effects	Reference
Freshwater mussel *Unio tumidus*	100 ng/l	14 days	Prooxidative changes; increase of lysosomal membranes permeability and oxyradicals formation; signs of genotoxicity.	Fal'fushinskaya et al., 2015.

Tab. 29. Derivation of PNEC values.

PNEC	Endpoint	Endpoint value (µg/L)	AF	Source
0.0036 (µg/L)				(Loos Robert et al., 2018)

Tab. 30. Risk Quotient (MEC or PEC/PNEC).
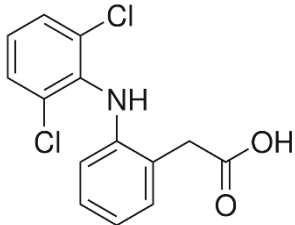
MEC o PEC/PNEC			Source

MEC o PEC/PNEC			Source
RQ (P95)	1.39	Sc1	(Loos Robert et al., 2018)
RQ (P95)	1.39	Sc2	(Loos Robert et al., 2018)
RQ (P95)	0.97	Sc3	(Loos Robert et al., 2018)

2.5 Diclofenac

Diclofenac is a nonsteroidal anti-inflammatory drug used to treat pain and inflammatory diseases. At the national level it ranks second after azelastine, an antihistaminic, with regard to national spending on pharmaceuticals for self-medication, and it follows an increasing trend compared to 2016 (AIFA, 2018a).

Tab. 31. Substance identity.

Parameters	
Name	Diclofenac
Other names	Feloran, Novapirina, Orthofen, Voltaren
IUPAC name	[2-(2,6-Dichloroanilino)phenyl]acetic acid
CAS number	15307-79-6
Molecular formula	C14H11Cl2NO2
Molecular weight	296.1481
Structure	
SMILES	C1=CC=C(C(=C1)CC(=O)O)NC2=C(C=CC=C2Cl)Cl

Tab. 32. Physico-chemical properties.

Endpoint	Value	Source
Vapour pressure (Pa)	6.14×10^{-8} mm Hg at 25 deg C	(PubChem, 2019a)
Water solubility (mg/L)	2.37 mg/L	(PubChem, 2019a)
Log K_{ow}	4.51	(PubChem, 2019a)

Tab. 33. Analytical methods.

Method	LOD (µg/L)	Description	Reference

Method	LOD (µg/L)	Description	Reference
SPE concentration and UPLC-MS analysis Qtrap	2,6	SPE Oasis HLB eluted with MeOH, evaporated to dryness and reconstituted with 0.1 ml of 9:1 H_2O:AcCN. Hypersil GOLD 1.9 µm 50 x 2.1 NH_4Ac/MeOH	(Tavazzi et al., 2016)
SPE concentration and UPLC-MS/MS analysis Qtrap	0.9	SPE Oasis HLB eluted with EtOH, evaporated to dryness and reconstituted with 0.25 ml of EtOH. XB-C18 Kinetex 1,7 µm 100 x 2.1 MeOH/H_2O	(Sousa et al., 2019)
SPE concentration, derivatization and GC-MS analysis	3	SPE by means 15 ml disk filtered (H_2O-Philic DVB Speedisk) eluted 30 ml of MeOH. Derivatization with N,O-Bis(trimethylsilyl)trifluoroacetamide and analysis by means GC-MS RTX-5 (30m, 0.25mm, film thickness 0.25 µm). Water and biota	(Świacka et al., 2019)
ASE, SPE and derivatization for GC-MS analysis	20 ng/L (biota)	ASE extraction (MeOH:H_2O), SPE (Strata X) eluted with MeOH(5% Aq):Ex 1:1. Derivatization for GC-MS analysis	(Świacka et al., 2019)
ASE, SPE and LC-MS/MS	3.7 ng/g (sediment)	ASE. SPE clean up was performed using a combination of SAX cartridge and Oasis HLB	(Segarra et al., 2009)

2.5.1 Environmental exposure assessment

Tab. 34. Environmental Emissions.

	Description/value
Use(s)	Treatment of pain and inflammatory diseases
Total production or total emissions (tonnes/year)	NA
Information on emissions in Veneto	Considering the expenditure registered in the Veneto region, Diclofenac is listed as an active principle for the muscle-skeletal and for the dermal apparatus (AIFA, 2017a)
Possible contacts for relevant information	AIFA for an estimate on the total consumption or prescription

Tab. 35. Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source
Measured concentration in water MEC_w (µg/L)	60-695	Surface water (freshwater)	River Lambro basin - Lombardia	(Castiglioni et al., 2018)

Tab. 36. Ecotoxicological data.

Species	Time-scale	Endpoint		Toxicity (µg/L)	Source
Bacteria					
Vibrio fischeri	30-min	Bioluminescence inhibition		EC_{50} = 27.800	Schmidt et al., 2011
Algae					
Dunaliella tertiolecta	96-h	Cell density		EC_{50} = 185.690	DeLorenzo and Fleming, 2008
Skeletonema costatum	96-h	Growth rate		IC_{50} = 5.000	Schmidt et al., 2011
Polychaeta					
Arenicola marina	1-h	Sperm motility		LOEC = 1	Mohd Zanuri et al., 2017
				EC_{50} = 107	
		Fertilization (incubation of sperm)		LOEC = 10	
				EC_{50} = 566	
		Fertilization (incubation of eggs)		LOEC = 10	
				EC_{50} = 552	
		Fertilization (incubation of all gametes)		LOEC = 0,01	
				EC_{50} = 113	
Crustacea					
Artemia salina	48-h	Immobilization		EC_{50} > 100	Minguez et al., 2016
Tisbe battagliai	48-h	Mortality		EC_{50} = 15.800	Schmidt et al., 2011
Mollusca					
Perna perna	1-h	Fertilization		LOEC = 31.250	Fontes et al., 2018
				EC_{50} = 389.000	
	48-h	Larval development		NOEC = 10.000	
				LOEC = 100.000	
				EC_{50} = 18.000	

Asteroidea

Asterias rubens	1-h	Sperm motility	LOEC = 1	Mohd Zanuri et al., 2017
			EC$_{50}$ = 2336	
		Fertilization (incubation of sperm)	LOEC = 1	
			EC$_{50}$ = 2610	
		Fertilization (incubation of eggs)	LOEC = 10	
			EC$_{50}$ = 1680	
		Fertilization (incubation of all gametes)	LOEC = 0,01	
			EC$_{50}$ = 616	

Echinoidea

Psammechinus miliaris	1-h	Sperm motility	LOEC = 0.1	Mohd Zanuri et al., 2017
			EC$_{50}$ = 378	
		Fertilization (incubation of sperm)	LOEC = 0.1	
			EC$_{50}$ = 298	
		Fertilization (incubation of eggs)	LOEC = 10	
			EC$_{50}$ = 429	
		Fertilization (incubation of all gametes)	LOEC = 0.01	
			EC$_{50}$ = 247	

Fishes

Oryzias latipes	96-h	Mortality	LC50 = 10.100	Bonnefille et al., 2018

LOEC/LOEL = Lowest Observed Effect Concentration/Level
NOEC/NOEL = Non Observed Effect Concentration/Level
LC$_{50}$/EC$_{50}$ = Lethal/Effective Concentration 50
IC$_{50}$ = Inhibition Concentration 50

Tab. 37. Biochemical and genetic responses.

Species	Concentrations	Days of exposure	Biochemical/molecular effects	Reference

Mussels *Mytilus galloprovincialis*	250 ng/L	15 days	Oxidative stress, supported by the significant induction of superoxide dismutase (SOD) and glutathione reductase (GR) activities in the gills; high catalase (CAT) activity and lipid peroxidation (LPO) levels in the digestive gland; glutathione-S-transferase (GST) remained unaltered. In females, up-regulation of acetilcolinesterase (AChE) activity and vitellogenin-like (Vtg) protein levels.	Gonzalez-Rey & Bebianno, 2014.
Mussels *Mytilus galloprovincialis*	2.5 µg/L	60 days	Alterations of immunological parameters, genotoxic effects, modulation of lipid metabolism and changes in cellular turn-over.	Mezzelani et al., 2018.
Mussels *Mytilus galloprovincialis*	0.5 µg/L	14 days	Alteration of immunological responses, lipid metabolism and DNA integrity, supported by the modulation of a large number of genes involved in the arachidonic acid and lipid metabolism, immune responses, cell cycle and DNA repair.	Mezzelani et al., 2016.
Mussels *Mytilus galloprovincialis*	25 µg/L	14 days	Alteration of immunological parameters and lipid metabolism; oxidative, genotoxic and neurotoxic effects.	Mezzelani et al., 2016.

Mussels *Mytilus edulis trossulus*	100, 1000 and 5000 µg/L 1, 100 and 10000 µg/L	14 and 19 days 8 and 21 days	Decrease of scope of growth. Decrease of byssus strength and byssus threads, resulting in reduced ability to attach to the substrate.	Ericson et al., 2010.
Mytilus spp.	1 and 1000 µg/L *Injection*	96 h	Tissue damage (digestive gland) supported by the induction of lipid peroxidation (LPO).	Schmidt et al., 2011.
Freshwater mussel *Dreissena polymorpha*	1 and 1000 µg/L	24 and 96 h	Modulation of oxidation pathways with significant destabilization of the lysosomal membrane.	Quinn et al., 2011.
Freshwater mussel *Dreissena polymorpha*	0.001, 0.01, 0.1, 1 and 10 mg/L	24, 48 and 96 h	The exposure to increasing concentrations significantly decrease the viability of haemocytes, gill and digestive gland cells.	Parolini et al., 2011.
Freshwater mussel *Dreissena polymorpha*	2 nM	96 h	Slight decrease of lysosomal membrane stability.	Parolini et al., 2011.
Mussels *Mytilus galloprovincialis*	100 µg/L	3 days	Decrease of prostaglandin E2 (PGE2) synthesis.	Courant et al., 2018.

Mussel *Perna perna*	31.25, 62.5, 125, 250, 500 and 1000 mg/L	24 h	Inhibition of fertilization rate.	Fontes et al., 2018.
	100 mg/L	48 h	Significant inhibition of embryo-larval development.	
	20, 200 and 2000 ng/L	48 h	Decrease of haemocytes lysosomal membrane stability. In digestive gland:	
	2000 ng/L	48 h	decrease of DNA damage; increase of ChE activity;	
	200 ng/L	96 h	decrease of lipid peroxidation; increase of COX activity. In gill:	
	20, 200 and 2000 ng/L 200 and 2000 ng/L	48 h and 96 h 48 h and 96 h	decrease of COX activity; decrease of GPX activity;	
	200 and 2000 ng/L	48 h	decrease of DNA damage; increase of lipid peroxidation;	
	20 and 200 ng/L	96 h	decrease of lipid peroxidation;	
Mussels *Mytilus galloprovincialis*	100 µg/L	7 days	Modulation of tyrosine and tryptophan metabolism, suggesting potential effects on osmoregulation and reproduction.	Bonnefille et al., 2018.
Mussels *Mytilus galloprovincialis*	0.01, 0.1, 1, 10, and 100 µg/L	48 h	Alteration of larval development (shell deformation).	Fabbri et al., 2014.

| Mussels *Mytilus galloprovincialis* | From 10 ng/L to 20 µg/L *in vitro* | 1 h | Genotoxic effects on exposed haemocytes. | Toufexi et al., 2016. |

Tab. 38. Derivation of PNEC values.

PNEC	Endpoint	Endpoint value (µg/L)	AF	Source
0.1 (µg/l) (watch list 2015)				(Loos Robert et al., 2018)
0.05 (µg/l) (watch list 2018)				(Loos Robert et al., 2018)
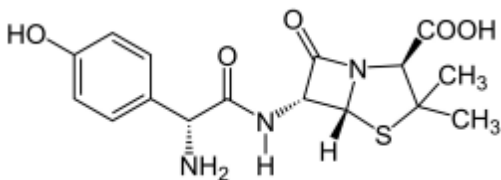
Tab. 39. Risk Quotient (MEC or PEC/PNEC).

MEC o PEC/PNEC	Source
5,3-6,8 (PNEC of 0.05 µg/l)	(Loos Robert et al., 2018)

2.6 Amoxicillin

The antimicrobial pharmaceutical amoxicillin ranks first in terms of national expenditure in the category of antibiotics of systemic application (AIFA, 2018b).

Tab. 40. Substance identity.

Parameters	
Name	Amoxicillin
IUPAC name	(2S,5R,6R)-6-{[(2R)-2-Amino-2-(4-hydroxyphenyl)acetyl]amino}-3,3-dimethyl-7-oxo-4-thia-1-azabicyclo[3.2.0]heptane-2-carboxylic acid
CAS number	26787-78-0
Molecular formula	C16H19N3O5S
Molecular weight	365.4 g/mol
Structure	
SMILES	O=C(O)[C@@H]2N3C(=O)[C@@H](NC(=O)[C@@H](c1ccc(O)cc1)N)[C@H]3SC2(C)C

Tab. 41. Physico-chemical properties.

Endpoint	Value	Source
Water solubility (mg/L)	3430	(Loos Robert et al., 2018)

Endpoint	Value	Source
Log K_{ow}	0.87	(Moarefian et al., 2014)

Tab. 42. Environmental fate.

Endpoint	Value	Source
Biodegradability	Amoxicillin has a hydrolysis half-life in water at pH 7 of ca. 20 days.	(Braschi et al., 2013)

Tab. 43. Analytical methods.

Method	LOD (µg/L)	Description	Reference
SPE concentration and UPLC-MS analysis	100-8	direct injection (LC-MS)- SPE	(Loos et al., 2018)
SPE-LC-MS/MS	0.2-1.3	pH 3 EDTA, Oasis HLB (MeOH:H_2O) concentration	(Hu et al., 2018)
SPE-LC-MS/MS	0.1-0.5 ng/g (sediment)	Solid extracted with MeOH and citrate buffer. The solid was centrifugated and diluted with H_2O SPE	(Hu et al., 2018)

2.6.1 *Environmental exposure assessment*

Tab. 44. Environmental Emissions.

	Description/value
Use(s)	Treatment of bacterial infections (Beta-lactam antibiotic)
Total production or total emissions (tonnes/year)	0.006-0.011 (Denmark) (Loos Robert et al., 2018)
Information on emissions in Veneto	Amoxicillin ranks first in the list of antimicrobials sold in Veneto and followed an increasing trend in 2016-2017 (AIFA, 2017b). Use in fish farms in 2012-2016 (Denmark). Widely used in the UK for both human and animal health. Available data note it is one of the most commonly used antibiotics for human health used in the UK. Various products approved for veterinary use on a range of animals including cats, dogs, sheep, pigs, chickens, turkeys, ducks and cattle.(Loos Robert et al., 2018)
Possible contacts for relevant information	AIFA

Tab. 45. Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source
Measured concentration in water MEC_w (µg/L)	2.0-25.3	Surface water (freshwater)	River Lambro Basis, Italy	(Castiglioni et al., 2018)
	<2.08	Surface water (freshwater)	River Po, Italy	(Zuccato et al., 2010)
	5.7 (3.57-9.91)	Surface water (freshwater)	River Arno, Italy	(Zuccato et al., 2010)
	15 – 120	WWTP effluents	Italy	(Castiglioni et al., 2005)
	<1.8 – 120	Different WWTP effluents	Italy	(Andreozzi et al., 2004)

Tab. 46. Predicted Environmental Concentrations.

	Value/Description	Model or method used for the prediction	Source
Predicted concentrations in water PEC_w (µg/L)	0.0068		(Besse and Garric, 2008)

Amoxicillin has a hydrolysis half-life in water at pH 7 of ca. 20 days (Braschi et al., 2013).

In water, amoxicillin is rapidly degraded by biotic and abiotic factors, yielding different intermediate products; these are suspected of being more resistant to degradation, and potentially more toxic, than the parent compound. Amoxicillin may bioaccumulate in fish muscle tissues, with the possibility of the occurrence of these drugs in food, leading to a passive consumption of this antibiotic resulting in undesirable effects on consumer health such as immunoallergic responses. However, the main problem related with the presence of this antimicrobial compounds in fish tissues is the possibility of inducing bacterial resistance gene. (Elizalde-Velázquez et al., 2016).

Tab. 47. Ecotoxicological data.

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
Algae				
Phaeodactylum tricornutum	96-h	Growth	NOEC = 250.000	de Orte et al., 2013
Isochrysis galbana	96-h	Growth	NOEC = 250.000	
Rhodomonas salina	72-h	Growth	NOEC = 318.000	Lützhøft et al., 1999
Echinoida				
Arbacia lixula	72-h	Larval development	LOEC = 100.000	Carballeira et al., 2012

Paracentrotus lividus	48-h	Larval development	LOEC = 100.000	

LOEC/LOEL = Lowest Observed Effect Concentration/Level
NOEC/NOEL = Non Observed Effect Concentration/Level

Tab. 48. Biochemical and genetic responses.

Species	Concentrations	Day of exposure	Biochemical/molecular effects	Ref.
Mytilus galloprovincialis + Ruditapes philippinarum	100, 200 and 400 µg/L	1, 3 and 7 days	Alterations of haemocyte parameters	Matozzo et al., 2016.
Mytilus galloprovincialis + Ruditapes philippinarum	100, 200 and 400 µg/L	1, 3 and 7 days	Slight alterations of antioxidant enzyme activities	Matozzo et al., 2016.

Tab. 49. Derivation of PNEC values.

PNEC	Endpoint	Endpoint value (µg/L)	AF	Source
0.078	96 h, cell proliferation *Synechococcus leopolensis*	0.78	10	(Loos Robert et al., 2018)

Tab. 50. Risk Quotient (MEC or PEC/PNEC).
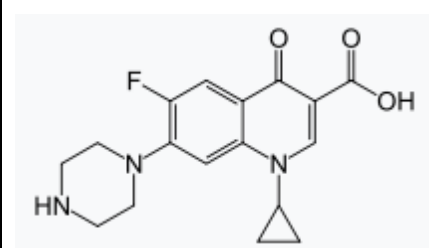
MEC o PEC/PNEC	Source
RQ_{fw} = 1.28 (MEC(P(95))/PNEC)	(Loos Robert et al., 2018)

2.7 Ciprofloxacin

Ciprofloxacin is an antibiotic. It is at the third place in terms of antimicrobial agents consumption after amoxicillin and ceftriaxone at the national level, and the trend in consumption has been slightly decreasing in the period 2016-2017 (-3.9%) (AIFA, 2018b).

Tab. 51. Substance identity.

Parameters	
Name	Ciprofloxacin
IUPAC name	1-cyclopropyl-6-fluoro-4-oxo-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid
CAS number	85721-33-1
Molecular formula	C17H18FN3O3

Molecular weight	331.3 g/mol
Structure	
SMILES	c1c2c(cc(c1F)N3CCNCC3)n(cc(c2=O)C(=O)O)C4CC4

Tab. 52. Physico-chemical properties.

Endpoint	Value	Source
Vapour pressure (Pa)	2.85E-13	(PubChem, 2019b)
Water solubility (mg/L)	30000	(PubChem, 2019b)
Log K_{ow}	0.28	(PubChem, 2019b)

Tab. 53. Environmental fate.

Endpoint	Value	Source
Sorption potential K_{OC}	Possible FQ removal mechanisms during wastewater treatment are biodegradation and sorption on activated sludge. 4.3–4.9 l/kg (SPM). 4.8 l/kg (soil)	(Van Doorslaer et al., 2014). (Cardoza et al., 2005) (Nowara et al., 1997)
Partition coefficient solid-water in sediment Kp_{sed} (L/kg)		
Biodegradability	Half-life time in surface water: 2 h - 10.6 days	(Cardoza et al., 2005); (Van Doorslaer et al., 2014)
Bioconcentration (BCF)	3.2 L/kg	(Schwab et al., 2005)
Biomagnification (BMF)	1	(EC, 2011)

Tab. 54. Analytical methods.

Method	LOD (µg/L)	Description	Reference
SPE concentration and UPLC-MS analysis	200-4.5	direct injection (LC-MS)- SPE	(Loos et al., 2018)

Method	LOD (µg/L)	Description	Reference
SPE concentration and UPLC-MS/MS analysis		SPE Oasis HLB eluted with MeOH, evaporated to dryness and reconstituted with 0.2 ml of H$_2$O:MeOH 9:1. Acquacity (100 mm x 2.1 mm x 1.8 µm) NH$_4$Ac/MeOH. Method tested in Antarctica for salty water and Waste Water	(Hernández et al., 2019)
SPE concentration and UPLC-MS/MS analysis (Qtrap)	5-2	SPE Oasis HLB eluted with MeOH, evaporated to dryness and reconstituted with 0.5 ml of MeOH: H$_2$O 1:1. Zorbax eclipse XBD-C18 (100 mm x 4.6 mm x 3,5 µm MeOH/H$_2$O +formic acid	(Mirzaei et al., 2017)
ASE and LC-MS/MS	6.18 ng/g (sediment)	ASE and LC-MS/MS	(Kerrigan et al., 2018)
ASE, SPE and LC-MS/MS	11 ng/g (sediment)	ASE. SPE cleaned up was performed using a combination of SAX cartridge and Oasis HLB	(Segarra et al., 2009)

2.7.1 Environmental exposure assessment

Tab. 55. Environmental Emissions.

	Description/value
Use(s)	Antibiotic (it inhibits the bacterial cell division)
Total production or total emissions (tonnes/year)	NA
Information on emissions in Veneto	Ciprofloxacin ranks second in terms of national pharmaceutical expenditure after amoxicillin (AIFA, 2017b)
Possible contacts for relevant information	AIFA

Tab. 56. Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source
Measured concentration in water MEC$_w$ (µg/L)	6.7-60	Surface water	River Lambro basin, Italy	(Castiglioni et al., 2018)
	8.8 (1.32-16)	Surface water	River Po Italy	(Zuccato et al., 2010)
	19 (<1.8-37.5)	Surface water	River Arno Italy	(Zuccato et al., 2010)
	40-70	WWTP effluents	Italy	(Andreozzi et al., 2003)

	Value	Matrix	Region/area	Source
	20 (median)	Surface water	Po and Lambro River, Italy	(Calamari et al., 2003)
Measured concentration in sediment MEC_{sed} (µg/kg dw)	3.78			(Carvalho et al., 2015)
Measured concentration in biota MEC_{biota} (ng/g)	0.004			(Carvalho et al., 2015)

Tab. 57. Predicted Environmental Concentrations.

	Value/Description	Model or method used for the prediction	Source
Predicted concentrations in water PEC_w (µg/L)	0.000538	Human consumption, (Eq. G) (Besse et al., 2008)	(Carvalho et al., 2015)
	0.139		(Besse and Garric, 2008)
	7.5		(Källqvist et al., 2006)
	The predicted annual-average antibiotic concentrations ranged between 0 and 10 ng/l for 90% by length of surface waters.		(Johnson et al., 2015)
	0.00124	MEC95 (SE – NORMAN DB)	(Carvalho et al., 2015)
Predicted concentrations in sediment PEC_{sed} (mg/kg dw)	1.6418	Human consumption, (Eq. G) (Besse et al., 2008)	(Carvalho et al., 2015)
	3.78	MEC95 (SE – NORMAN DB)	(Carvalho et al., 2015)
Predicted concentrations in biota PEC_{biota} (mg/kg)	0.0017	$PEC_{biota} = PEC_{fw} \times BCF \times BMF$, Human consumption (Eq. G) (Besse et al., 2008)	(Carvalho et al., 2015)
	0.004	$PEC_{biota} = PEC_{fw} \times BCF \times BMF$ MEC95 (SE – NORMAN DB)	(Carvalho et al., 2015)

Tab. 12. P, B, T, C, M, R, ED properties

	YES/NO	Source
Toxic (T)	YES	(Loos Robert et al., 2018)
Endocrine Disruptive (ED)	Not investigated	(Loos Robert et al., 2018)

Eight in vitro mutagenicity tests have been conducted with Ciprofloxacin, 2 of the 8 tests were positive, but results of the further 3 in vivo test systems gave negative results. Long-term carcinogenicity studies in rats and mice resulted in no carcinogenic or tumorigenic effects. Fertility studies performed in rats at oral doses of Ciprofloxacin up to 100 mg/kg (approximately 0.7-times the highest recommended therapeutic dose based upon mg/m2) revealed no evidence of impairment. An estimated BCF of 3 (SRC), from its log K_{ow} of 0.28, suggests the potential for bioconcentration in aquatic organisms is low (SRC). Using the OECD closed bottle biodegradation study, 0% degradation 150 over a 40-day incubation period was observed indicating that biodegradation is not an important environmental fate process in water (Carvalho et al., 2015).

The half-life time of fluoroquinolone antibiotics in surface water is approximately 10.6 days (Andreozzi et al., 2004; Van Doorslaer et al., 2014).

Tab. 59. Ecotoxicological data.

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
Bacteria				
Vibrio fischeri	5-min	Bioluminescence inhibition	$EC_{50} > 5.900$	Hernando et al., 2007
	15-min		$EC_{50} > 5.900$	
	30-min		$EC_{50} > 5.900$	
Algae				
Cylindrotheca closterium	up to 5-d	Growth	$EC_{50} = 55.430$	Hagenbuch and Pinckney, 2012
Navicula ramosissima			$EC_{50} = 72.120$	

LC_{50}/EC_{50} = Lethal/Effective Concentration 50

Tab. 60. Biochemical and genetic responses.

Species	Concentrations	Day of exposure	Biochemical/molecular effects	Ref.
Freshwater mussel *Elliptio complanata*	20, 100, 500 and 2500 ng/L	24h in vitro exposure	Alterations of haemocyte parameters (ROS production, phagocytosis, lysozyme activity)	Gust et al., 2012.

Tab. 61. Derivation of PNEC values.

PNEC	Endpoint	Endpoint value (µg/L)	AF	Source

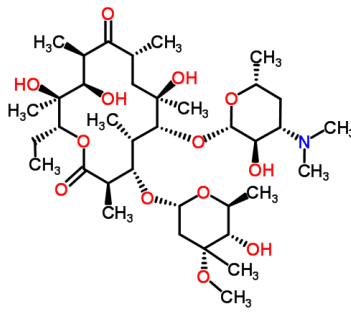| PNEC	Endpoint	Endpoint value (µg/L)	AF	Source
$PNEC_{fw}$ = 8.9E-05 mg/L	*Anabaena flos-aquae*, 72 h, EC	0.00447 mg/L	50	(Carvalho et al., 2015)
$PNEC_{sed}$ = 0.272 mg/kg dw				(Carvalho et al., 2015)
$PNEC_{dw}$, hh = 0.006 mg/L	ADI	0.0016 mg/kg day		(Carvalho et al., 2015)

Tab. 62. Risk Quotient (MEC or PEC/PNEC).

MEC o PEC/PNEC	Human consumption (Besse et al., 2008)	MEC o PEC/PNEC	Human consumption (Besse et al., 2008)
RQ_{fw}	6.045	13.93	(Carvalho et al., 2015)
RQ_{fw} = 84.2 (PEC/PNEC)			(Loos Robert et al., 2018)
RQ_{sed}	6.045	13.93	(Carvalho et al., 2015)
$RQ_{biota, \ sec \ pois}$	N.R.	N.R.	(Carvalho et al., 2015)
$RQ_{biota, \ hh}$	N.R.	N.R.	(Carvalho et al., 2015)
$RQ_{dw, \ hh}$	0.10	0.22	(Carvalho et al., 2015)

2.8 Erythromycin

Erythromycin is a macrolide antibiotic and is commercialized in Italy, but it is not appearing in the main ranking on pharmaceuticals consumption and expenditure in the national report from AIFA (AIFA, 2018b).

Tab. 63. Substance identity.

Parameters	
Name	Erythromycin
IUPAC name	(3R,4S,5S,6R,7R,9R,11R,12R,13S,14R)-6-{[(2S,3R,4S,6R)-4-(dimethylamino)-3-hydroxy-6-methyloxan-2-yl]oxy}-14-ethyl-7,12,13-trihydroxy-4-{[(2R,4R,5S,6S)-5-hydroxy-4-methoxy-4,6-dimethyloxan-2-yl]oxy}-3,5,7,9,11,13-hexamethyl-1-oxacyclotetradecane-2,10-dione
CAS number	114-07-8
Molecular formula	C37H67NO13
Molecular weight	733.94

Parameters	
Name	Erythromycin
IUPAC name	(3R,4S,5S,6R,7R,9R,11R,12R,13S,14R)-6-{[(2S,3R,4S,6R)-4-(dimethylamino)-3-hydroxy-6-methyloxan-2-yl]oxy}-14-ethyl-7,12,13-trihydroxy-4-{[(2R,4R,5S,6S)-5-hydroxy-4-methoxy-4,6-dimethyloxan-2-yl]oxy}-3,5,7,9,11,13-hexamethyl-1-oxacyclotetradecane-2,10-dione
Structure	
SMILES	CC[C@@H]1[C@@]([C@@H]([C@H](C(=O)[C@@H](C[C@@]([C@@H]([C@H]([C@@H]([C@H](C(=O)O1)C)O[C@H]2C[C@@]([C@H]([C@@H](O2)C)O)(C)OC)C)O[C@H]3[C@@H]([C@H](C[C@H](O3)C)N(C)C)O)(C)O)C)C)O)(C)O

Tab. 64. Physico-chemical properties.

Endpoint	Value	Source
Vapour pressure (Pa)	3.04E-25	(Carvalho et al., 2015)
Water solubility (mg/L)	2000	(Carvalho et al., 2015)
Log K_{ow}	3.06	(Carvalho et al., 2015)

Tab. 65. Environmental fate.

Endpoint	Value	Source
Sorption potential K_{OC}	570	(PubChem, 2019c)
Biodegradability	NRB	(NORMAN-DB, 2014)
Bioconcentration (BCF)	48.5	(NORMAN-DB, 2014)
Biomagnification (BMF)	1 (Default value)	(EC, 2011)

Tab. 66. Analytical methods.

Method	LOD (µg/L)	Description	Reference
SPE concentration and UPLC-MS analysis Qtrap		SPE Oasis HLB eluted with MeOH, evaporated to dryness and reconstituted with 0.1 ml of 9:1 H_2O:AcCN. Hypersil GOLD 1.9 µm 50 x 2.1 NH_4Ac/MeOH	(Tavazzi et al., 2016)

Method	LOD (µg/L)	Description	Reference
SPE concentration and UPLC-MS/MS analysis	0.51	SPE Oasis HLB eluted with EtOH, evaporated to dryness and reconstituted with 0.25 ml of EtOH. XB-C18 Kinetex (100 mm x 2.1 mm x 1.7 µm MeOH/H_2O	(Sousa et al., 2019)
SPE concentration and UPLC-MS/MS analysis		SPE Oasis HLB eluted with MeOH, evaporated to dryness and reconstituted with 0.2 ml of H_2O:MeOH 9:1. Acquacity (100 mm x 2.1 mm x 1.8 µm) NH_4Ac/MeOH. Method tested in Antarctica for salty water and Waste Water	(Hernández et al., 2019)
UPLC-MS/MS (direct injection) and online SPE and LC-MS/MS	0.8	UPLC column Acquacity Acquacity (100 mm x 2.1 mm x 1.7 µm) NH_4Ac/MeOH. Method tested in surface water and WW	(Boix et al., 2015)
SPE concentration and UPLC-MS/MS analysis (Qtrap)	5-2	SPE Oasis HLB eluted with MeOH, evaporated to dryness and reconstituted with 0.5 ml of MeOH: H_2O 1:1. Zorbax eclipse XBD-C18 (100 mm x 4.6 mm x 3,5 µm MeOH/H_2O +formic acid	(Mirzaei et al., 2017)
ASE and LC-MS/MS	1.36 ng/g (sediment)	ASE and LC-MS/MS	(Kerrigan et al., 2018)

2.8.1 Environmental exposure assessment

Tab. 67. Environmental Emission.

	Description/value
Use(s)	Macrolide antibiotic
Total production or total emissions (tonnes/year)	NA
Information on emissions in Veneto	It is not mentioned in the regional pharmaceutical inventory (AIFA, 2017b)
Possible contacts for relevant information	AIFA

Tab. 68. Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source
Measured concentration in water	2.9 (0.78-4.62)	Surface water	River Po, Italy	Zuccato et al., 2010
	5.4 (2.88-8.12)	Surface water	River Arno, Italy	Zuccato et al., 2010

	Value	Matrix	Region/area	Source
MEC$_w$ (µg/L)	< LOQ		(CH, NL)	(Carvalho et al., 2015; NORMAN-DB, 2014)
Measured concentration in sediment MEC$_{sed}$ (µg/kg dw)	< LOQ		(CH, NL)	(Carvalho et al., 2015; NORMAN-DB, 2014)
Measured concentration in biota MEC$_{biota}$ (ng/g)	< LOQ		(CH, NL)	(Carvalho et al., 2015; NORMAN-DB, 2014)

Tab. 69. Predicted Environmental Concentrations.

	Value/Description	Model or method used for the prediction	Source
Predicted concentrations in water PEC$_w$ (µg/L)	0.00526	ECETOC	(Carvalho et al., 2015)
	0.0002	Human consumption, (Eq. G) (Besse et al., 2008)	(Carvalho et al., 2015)
	0.000613	MEC95 (SE) (NORMAN-DB, 2014)	(Carvalho et al., 2015)
Predicted concentrations in sediment PEC$_{sed}$ (mg/kg dw)	0.3185	ECETOC	(Carvalho et al., 2015)
	0.006	Human consumption, (Eq. G) (Besse et al., 2008)	(Carvalho et al., 2015)
	0.0185	MEC95 (SE) (NORMAN-DB, 2014)	(Carvalho et al., 2015)
Predicted concentrations in biota PEC$_{biota}$ (mg/kg)	0.255	PEC$_{biota}$ = PEC$_{fw}$ X BCF X BMF, ECETOC	(Carvalho et al., 2015)
	0.010	PEC$_{biota}$ = PEC$_{fw}$ X BCF X BMF, Human consumption, (Eq. G) (Besse et al., 2008)	(Carvalho et al., 2015)
	0.030	PEC$_{biota}$ = PEC$_{fw}$ X BCF X BMF, MEC95 (SE) (NORMAN-DB, 2014)	(Carvalho et al., 2015)

Utilizing the Closed Bottle Test, -3% of the theoretical BOD was reported in 4 weeks, indicating that biodegradation is not an important environmental fate process in water (P) (PubChem, 2019c). A pKa of 8.9 indicates erythromycin will exist almost entirely in the cation form at pH values of 5 to 9 and therefore volatilization from water surfaces is not expected to be an important fate process. An estimated BCF of 49 suggests the potential for bioconcentration in aquatic organisms is moderate (Not B) (PubChem, 2019c).

(Carvalho et al., 2015)

Tab. 70. Ecotoxicological data.

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
Bacteria				
Vibrio fischeri	5-min	Bioluminescence inhibition	$EC_{50} > 100.000$	Hernando et al., 2007
	15-min		$EC_{50} > 100.000$	
	30-min		$EC_{50} > 100.000$	
Algae				
Dunaliella tertiolecta	96-h	Growth	$EC_{50} = 5.750$	Machado and Soares, 2019
Tetrasuelmis suecica	72-h	Growth	$EC_{50} = 10$	Sendra et al., 2018
		Quantum yield	$EC_{50} = 140$	
Dunaliella salina	72-h	Quantum yield	$EC_{50} = 8.790$	
Phaeodactylum tricornutum	72-h	Quantum yield	$EC_{50} = 3.590$	
Cylindrotheca closterium	72-h	Quantum yield	$EC_{50} = 750$	
Chaetoceros gracilis	72-h	Quantum yield	$EC_{50} = 270$	
Crustacea				
Artemia salina	5-d	Mortality	$EC_{50} > 480.000$	Migliore et al., 1997
Litopenaeus vannamei	24-h	Immobilization	NOEC = 25.000	Williams et al., 1992
			LOEC = 50.000	
			$EC_{50} = 29.200$	
		Mortality	$LC_{50} = 30.800$	
	48-h	Immobilization	NOEC > 4.900	
			LOEC > 15.100	
			$EC_{50} > 22.700$	
		Mortality	$LC_{50} > 50.000$	

LC_{50}/EC_{50} = Lethal/Effective Concentration 50

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LOEC/LOEL = Lowest Observed Effect Concentration/Level
NOEC/NOEL = Non Observed Effect Concentration/Level

Tab. 71. Biochemical and genetic responses.

Species	Concentrations	Days of exposure	Biochemical/molecular effects	Reference
Mussels *Mytilus edulis*	100mg/L 20 and 100 mg/L	21 h	Detrimental effects on haemocytes either via immunotoxicity and genotoxicity: DNA damage; decrease of intracellular ROS production, which was correlated with a decrease in phagocytosis.	Lacaze et. al 2015.
Freshwater mussel *Elliptio complanata*	10, 50, 250 and 1250 ng/L in vitro	24 h	Modulation of haemocytes immune response (increase of phagocytosis, decrease of lysozyme activity, decrease of intracellular thiol levels).	Gust et al., 2012.

Tab. 72. Derivation of PNEC values.

PNEC	Endpoint	Endpoint value (µg/L)	AF	Source
PNEC$_{fw}$ = 0.0002 mg/l	*Synechococcus leopoldensis* IAM-M6, 144 h, NOEC	0.002 mg/L	10	(Carvalho et al., 2015)
PNEC$_{biota, hh}$ = 0.043 mg/kg, food	ADI	0.0007 mg/kg bw/day		(Carvalho et al., 2015)
PNEC$_{dw, hh}$	ADI	0.0007 mg/kg bw/day		(Carvalho et al., 2015)

Tab. 73. Risk Quotient (MEC or PEC/PNEC).

MEC o PEC/PNEC	ECETOC	Human consumption (Eq. G) (Besse et al., 2008)	MEC95 (SE) (NORMAN-DB, 2014)	Source
RQ$_{fw}$	26.3	1.00	3.07	(Carvalho et al., 2015)
RQ$_{sed}$	52.9	1.00	3.07	(Carvalho et al., 2015)
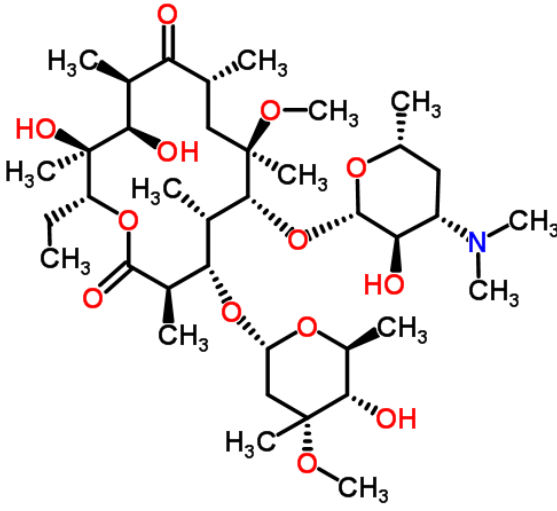
MEC o PEC/PNEC	ECETOC	Human consumption (Eq. G) (Besse et al., 2008)	MEC95 (SE) (NORMAN-DB, 2014)	Source
RQ$_{biota, sec pois}$	No info	No info	No info	(Carvalho et al., 2015)
RQ$_{biota, hh}$	5.99	0.23	0.7	(Carvalho et al., 2015)
RQ$_{dw, hh}$	2.15	0.08	0.25	(Carvalho et al., 2015)

2.9 Clarithromycin

Clarythromycin is a macrolide antibiotic and is prescribed in Italy, although it is not the most widespread. A decrease in medical prescriptions and consumption of 5.6% in 2017 compared to 2016 is reported (AIFA, 2018b).

Tab. 74. Substance identity.

Parameters	
Name	Clarithromycin
IUPAC name	2R,3R,4S,5R,8R,9S,10S,11R,12R,14R)-11-[(2S,3R,4S,6R)-4-(dimethylamino)-3-hydroxy-6-methyloxan-2-yl]oxy-5-ethyl-3,4-dihydroxy-9-[(2R,4R,5S,6S)-5-hydroxy-4-methoxy-4, 6-dimethyloxan-2-yl]oxy-12-methoxy-2,4,8,10,12,14-hexamethyl-6-oxacyclotetradecan-1,7-dione
CAS number	81103-11-9
Molecular formula	C38H69NO13
Molecular weight	747.95
Structure	
SMILES	CC[C@@H]1[C@@]([C@@H]([C@H](C(=O)[C@@H](C[C@@]([C@@H]([C@H]([C@@H]([C@H](C(=O)O1)C)O[C@H]2C[C@@]([C@H]([C@@H](O2)C)O)(C)OC)C)O[C@H]3[C@@H]([C@H](C[C@H](O3)C)N(C)C)O)(C)OC)C)O)(C)O

Tab. 75. Physico-chemical properties.

Endpoint	Value	Source
Vapour pressure (Pa)	2.32E-25	(Carvalho et al., 2015; PubChem, 2019d)
Water solubility (mg/L)	0.33	(Carvalho et al., 2015; Drugbank, 2014)
Log K_{ow}	3.16	(Carvalho et al., 2015; Drugbank, 2014)

Tab. 76. Environmental fate.

Endpoint	Value	Source
Sorption potential K_{OC}	150	(Carvalho et al., 2015; PubChem, 2019d)
Biodegradability	NRB	(Carvalho et al., 2015; PubChem, 2019d)
Bioconcentration (BCF)	56.49 (estimated)	(Carvalho et al., 2015; PubChem, 2019d)
Biomagnification (BMF)	1 (Default value)	(Carvalho et al., 2015; EC, 2011)

Tab. 77. Analytical methods.

Method	LOD (µg/L)	Description	Reference
SPE concentration and UPLC-MS analysis Qtrap	4.6	SPE Oasis HLB eluted with MeOH, evaporated to dryness and reconstituted with 0.1 ml of 9:1 H_2O:AcCN. Hypersil GOLD 1.9 µm 50 x 2.1 NH_4Ac/MeOH	(Tavazzi et al., 2016)
SPE concentration and UPLC-MS/MS analysis	0.03	SPE Oasis HLB eluted with EtOH, evaporated to dryness and reconstituted with 0.25 ml of EtOH. XB-C18 Kinetex (100 mm x 2.1 mm x 1,7 µm MeOH/H_2O	(Sousa et al., 2019)
SPE concentration and UPLC-MS/MS analysis		SPE Oasis HLB eluted with MeOH, evaporated to dryness and reconstituted with 0.2 ml of H_2O:MeOH 9:1. Acquaticy (100 mm x 2.1 mm x 1.8 µm) NH_4Ac/MeOH. Method tested in Antarctica for salty water and Waste Water	(Hernández et al., 2019)
UPLC-MS/MS (direct injection) and online SPE and LC-MS/MS	2.9	UPLC column Acquaticy (100 mm x 2.1 mm x 1.7 µm) NH_4Ac/MeOH. Method tested in surface water and WW	(Boix et al., 2015)

2.9.1 Environmental exposure assessment

Tab. 78. Environmental Emissions.

	Description/value
Use(s)	Macrolide antibiotic

	Description/value
Total production or total emissions (tonnes/year)	NA
Information on emissions in Veneto	Clarythromycin is prescribed and consumed in Veneto and the trend in the period 2016-2017 follows the national decrease (up to 4.6% decrease in consumption in 2017 compared to 2016) (AIFA, 2017b)
Possible contacts for relevant information	AIFA

Tab. 79. Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source
Measured concentration in water MEC_w (µg/L)	119-326	Surface water	River Lambro basin	Castiglioni 2018
	1.7 (0.89-2.19)	Surface water	River Po. Italy	Zuccato 2010
	25.4 (6.70-44.76)	Surface water	River Arno, Italy	Zuccato 2010

Tab. 80. Predicted Environmental Concentrations.

	Value/Description	Model or method used for the prediction	Source
Predicted concentrations in water PEC_w (µg/L)	0.000438	Human consumption, (Eq. G) (Besse et al., 2008)	(Carvalho et al., 2015)
	0.000645	MEC95 (SE) (NORMAN-DB, 2014)	(Carvalho et al., 2015)
Predicted concentrations in sediment PEC_{sed} (mg/kg dw)	0.0040	Human consumption, (Eq. G) (Besse et al., 2008)	(Carvalho et al., 2015)
	0.0059	MEC95 (SE) (NORMAN-DB, 2014)	(Carvalho et al., 2015)
Predicted concentrations in biota PEC_{biota} (mg/kg)	0.025	$PEC_{biota} = PEC_{fw}$ X BCF X BMF, Human consumption, (Eq. G) (Besse et al., 2008)	(Carvalho et al., 2015)
	0.036	$PEC_{biota} = PEC_{fw}$ X BCF X BMF, MEC95 (SE) (NORMAN-DB, 2014)	(Carvalho et al., 2015)

Tab. 81. P, B, T, C, M, R, ED properties

	YES/NO	Source

	YES/NO	Source
Persistent (P) Bioaccumulative (B)	YES NO	
Mutagenic (M)	YES	

Clarithromycin failed to exhibit mutagenic potential in several in vitro tests, including the Salmonella mammalian microsome test, bacterial induced mutation frequency test, rat hepatocyte DNA synthesis assay, mouse lymphoma assay, mouse dominant lethal test, and mouse micronucleus test. P: Very persistent (DT50 sediment = 379 days) (NORMAN-DB, 2014). B: Not Bioaccumulative (BCF estimated = 56.49) (NORMAN-DB, 2014). (Carvalho et al., 2015).

Tab. 82. Ecotoxicological data.

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
Bacteria				
Vibrio fischeri	15-min	Bioluminescence inhibition	$EC_{50} > 8.200$	Yamashita et al., 2006

LC_{50}/EC_{50} = Lethal/Effective Concentration 50

Tab. 83. Derivation of PNEC values.

PNEC	Endpoint	Endpoint value (µg/L)	AF	Source
PNECfw = 0.13 µg/L	Anabaena flos-aquae, 72h, EC10	2.6 µg/L	10*2	(Carvalho et al., 2015)
PNECsed = 0.0012 mg/kg dw				(Carvalho et al., 2015)
PNECbiota,sec pois				
PNECbiota, hh = 0.012 mg/kg food	ADI	0.0002 mg/kg bw/day		(Carvalho et al., 2015)
PNECdw, hh = 0.001 mg/L	ADI	0.0002 mg/kg bw/day		(Carvalho et al., 2015)

Tab. 84. Risk Quotient (MEC or PEC/PNEC).
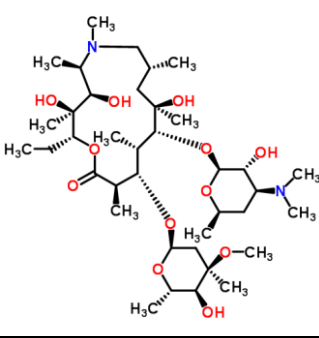
MEC o PEC/PNEC	Human consumption, (Eq. G) (Besse et al., 2008)	MEC95 (SE) (NORMAN-DB, 2014)	Source
RQ_{fw}	3.37	4.96	(Carvalho et al., 2015)
RQ_{sed}	3.37	4.96	(Carvalho et al., 2015)
$RQ_{biota, sec\ pois}$	No info	No info	(Carvalho et al., 2015)

MEC o PEC/PNEC	Human consumption, (Eq. G) (Besse et al., 2008)	MEC95 (SE) (NORMAN-DB, 2014)	Source
$RQ_{biota, hh}$	2.03	2.99	(Carvalho et al., 2015)
$RQ_{dw, hh}$	0.63	0.92	(Carvalho et al., 2015)

2.10 Azithromycin

Azythromycin is an antibiotic and, according to AIFA (AIFA, 2018b), it is more prescribed than clarithromycyn at the national level.

Tab. 85. Substance identity.

Parameters	
Name	Azithromycin
IUPAC name	(2R,3S,4R,5R,8R,10R,11R,13S,14R)-11-[(2S,3R,4S,6R)-4-dimethylamino-3-hydroxy-6-methyloxan-2-yl]oxy-2-ethyl-3,4,10-trihydroxy-13-[(2R,4R,5S,6S)-5-hydroxy-4-methoxy-4,6-dimethyloxan-2-yl]oxy-3,5,6,8,10,12,14-heptamethyl-1-oxa-6-azacyclopentadecan-15-one
CAS number	83905-01-5
Molecular formula	C38H72N2O12
Molecular weight	748.98
Structure	
SMILES	CC[C@@H]1[C@@]([C@@H]([C@H](N(C[C@@H](C[C@@]([C@@H]([C@H]([C@@H]([C@H](C(=O)O1)C)O[C@H]2C[C@@]([C@H]([C@@H](O2)C)O)(C)OC)C)O[C@H]3[C@@H]([C@H](C[C@H](O3)C)N(C)C)O)(C)O)C)C)O)(C)O

Tab. 86. Physico-chemical properties.

Endpoint	Value	Source
Vapour pressure (Pa)	2.65E-24	(Carvalho et al., 2015; PubChem, 2014)
Water solubility (mg/L)	2.37	(Carvalho et al., 2015; PubChem, 2014)
Log K_{ow}	4.02	(Carvalho et al., 2015; PubChem, 2014)

Tab. 87. Environmental fate.

Endpoint	Value	Source
Sorption potential K_{OC}	3100	(Carvalho et al., 2015; PubChem, 2014)
Biodegradability	NRB	(Carvalho et al., 2015; NORMAN-DB, 2014)
Bioconcentration (BCF)	200 (estimated)	(Carvalho et al., 2015; PubChem, 2014)
Biomagnification (BMF)	1 (Default value)	(Carvalho et al., 2015; EC, 2011)

Tab. 88. Analytical methods.

Method	LOD (µg/L)	Description	Reference
SPE concentration and UPLC-MS analysis Qtrap	2.6	SPE Oasis HLB eluted with MeOH, evaporated to dryness and reconstituted with 0.1 ml of 9:1 H_2O:AcCN. Hypersil GOLD 1.9 µm 50 x 2.1 NH_4Ac/MeOH	(Tavazzi et al., 2016)
SPE concentration and UPLC-MS analysis	90-3.6	SPE- direct injection (LC-MS)	(Loos et al., 2018a)
SPE concentration and UPLC-MS/MS analysis	0.37	SPE Oasis HLB eluted with EtOH, evaporated to dryness and reconstituted with 0.25 ml of EtOH. XB-C18 Kinetex (100 mm x 2.1 mm x 1.7 µm MeOH/H_2O	(Sousa et al., 2019)
SPE concentration and UPLC-MS/MS analysis		SPE Oasis HLB eluted with MeOH, evaporated to dryness and reconstituted with 0.2 ml of H_2O:MeOH 9:1. Acquacity (100 mm x 2.1 mm x 1.8 µm) NH_4Ac/MeOH. Method tested in Antarctica for salty water and Waste Water	(Hernández et al., 2019)
SPE concentration and UPLC-MS/MS analysis (Qtrap)	2.5	SPE Oasis HLB eluted with MeOH, evaporated to dryness and reconstituted with 0.5 ml of MeOH: H_2O 1:1. Zorbax eclipse XBD-C18 (100 mm x 4.6 mm x 3.5 µm MeOH/H_2O +formic acid	(Mirzaei et al., 2017)

2.10.1 Environmental exposure assessment

Tab. 89. Environmental Emissions.

	Description/value
Use(s)	Macrolide antibiotic
Total production or total emissions (tonnes/year)	NA

	Description/value
Information on emissions in Veneto	Azythromycin is consumed in Veneto, with a slight increase in the period 2016-2017 (2.8%) (AIFA, 2017b)
Possible contacts for relevant information	AIFA

Tab. 90. Measured Environmental Concentrations.

	Value	Region/area	Source
Measured concentration in water MEC_w (µg/L)	whole: <LOQ dissolved: 0.583 µg/L 0.645 µg/L	(NL) (PT) (SE)	(Carvalho et al., 2015; NORMAN-DB, 2014) (Carvalho et al., 2015; Munthe et al., 2011)

Tab. 91. Predicted Environmental Concentrations.

	Value/Description	Model or method used for the prediction	Source
Predicted concentrations in water PEC_w (µg/L)	0.000128	Human consumption, (Eq. G) (Besse et al., 2008)	(Carvalho et al., 2015)
	0.000583	MEC95 (SE) (NORMAN-DB, 2014)	(Carvalho et al., 2015)
Predicted concentrations in sediment PEC_{sed} (mg/kg dw)	0.0200	Human consumption, (Eq. G) (Besse et al., 2008)	(Carvalho et al., 2015)
	0.0913	MEC95 (SE) (NORMAN-DB, 2014)	(Carvalho et al., 2015)
Predicted concentrations in biota PEC_{biota} (mg/kg)	0.026	$PEC_{biota} = PEC_{fw}$ X BCF X BMF, Human consumption, (Eq. G) (Besse et al., 2008)	(Carvalho et al., 2015)
	0.117	$PEC_{biota} = PEC_{fw}$ X BCF X BMF, MEC95 (SE) (NORMAN-DB, 2014)	(Carvalho et al., 2015)

Azithromycin does not cause gene mutations in microbial or mammalian cells, or chromosomal aberrations in cultured human lymphocytes or in mouse bone marrow in vivo. A BCF value of 200 L/kg was reported in PubChem (PubChem, 2014). P: Very persistent (DT50 water > 3 years) (NORMAN-DB, 2014). (Carvalho et al., 2015).

Tab. 92. Derivation of PNEC values.

PNEC	Endpoint	Endpoint value (µg/L)	AF	Source
$PNEC_{fw}$ = 9.00E-05 mg/L	*Ceriodaphnia dubia*, 7 d, NOEC	0.0044 mg/L	50	(Carvalho et al., 2015)

PNEC	Endpoint	Endpoint value (µg/L)	AF	Source
PNEC$_{sed}$ = 0.014 mg/kg dw				(Carvalho et al., 2015)
PNEC$_{biota}$ hh=0.103 mg/kg food	ADI	0.0017 mg/kg day		(Carvalho et al., 2015)
PNEC$_{dw}$, hh = 0.006 mg/L	ADI	0.0017 mg/kg day		(Carvalho et al., 2015)

Tab. 93. Risk Quotient (MEC or PEC/PNEC).

MEC o PEC/PNEC	Human consumption (Eq. G) (Besse et al., 2008)	MEC95 (SE) (NORMAN-DB, 2014	Source
RQ$_{fw}$	1.422	6.48	(Carvalho et al., 2015)
RQ$_{sed}$	1.422	6.48	(Carvalho et al., 2015)
RQ$_{biota,sec\ pois}$	No info	No info	(Carvalho et al., 2015)
RQ$_{biota,\ hh}$	0.25	1.13	(Carvalho et al., 2015)
RQ$_{dw,\ hh}$	0.02	0.10	(Carvalho et al., 2015)

2.11 Analytical methods employed

The literature review on analytical methods showed that usually, for water analysis, samples are pre-concentrated on SPE and analysed with LC-MS/MS. The JRC report presents an exhaustive guide for the analysis of Watch List substances, by describing also the conservation modalities of samples and the effects of adsorption phenomena of these substances on the suspended particulate matter. Only few papers report the analysis of marine water, however the analytical conditions for sample treatment are the same used for the freshwater analysis. For this reason, methods proposed in the JRC reports are considered to be a good starting point for the lagoon water analysis. The literature on analytical approaches for sediments and biota is poor, especially because the compounds of interest can degrade very quickly, and commonly have a low K$_{OW}$. However, it is also reported that some substances can adsorb on suspended particulate matter depending on their chemical characteristics. Several methods will be tested in order to reach the lowest LOQ.

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3 Plant Protection Products

Plant protection products (PPP) are pesticides that are mainly used to keep crops (or other useful or desirable plants) healthy and prevent them and their products from being destroyed by disease and infestation. They include herbicides, fungicides, insecticides, acaricides, molluscicides, plant growth regulators and repellents (while "pesticides" are a wider class which includes also biocides, intended for non-plant use) (EC, 2019). They are primarily used in the agricultural sector but also in forestry, horticulture, amenity areas and in home gardens. Each formulation consists of one or more active substances, responsible for the properties of the plant protection product and substances called co-formulants.

A large body of EU legislation regulates the marketing and use of PPPs and companies have to produce a large dossier of information to the regulatory authorities before a PPP can be placed on the market. A dual system is in place, under which the European Food Safety Agency (EFSA) evaluates active substances used in PPPs and Member States evaluate and authorise the products at national level. Plant protection products are principally regulated by framework Regulation (EC) No 1107/2009.

Several tools are available for estimating PPP emissions, for instance FOCUS (Forum for the co-ordination of pesticide fate models and their use) model and other tools for LCA, like AGRIBALYSE agricultural database (life cycle inventory) (Koch, 2016).

Source of information come from the quantity of sold products: data for the quantity sold in Veneto is provided by ARPAV (ARPAV, 2017a), and the composition of each product is available as a database at the Ministry of the Environment (Il Ministero dell'Ambiente, 2017). By crossing the two sources it is possible to identify which PPP is actually sold as PPP in Veneto.

Source of information may be also the EU database on PPP (EU, n.d.).

Furthermore, information on PPP concentrations in river water is provided by ARPAV (ARPAV, 2017b). Detection of a PPP in the list is also a check for the use of the PPP under study.

3.1 Methiocarb
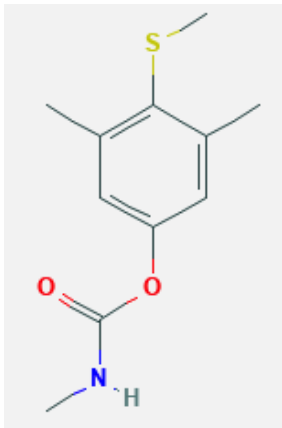
Methiocarb is used as an insecticide and bird repellent for maize crops. EFSA re-evaluated the risk assessment in 2018 (Arena et al., 2018).

For the Veneto region, Methiocarb is not taken into consideration in the lists available from ARPAV as shown in the following table.

Its use as a molluscicide was banned (EC, 2014).

Tab. 94. Substance identity.

Parameters	
Name	Methiocarb
IUPAC name	Mercaptodimethur/3,5-Dimethyl-4-methylthiophenyl N-methylcarbamate
CAS number	2032-65-7
Molecular formula	C11H15NO2S
Molecular weight	225.3

Structure	
SMILES	CNC(=O)Oc1cc(C)c(SC)c(C)c1

Tab. 95. Physico-chemical properties.

Endpoint	Value	Source
Vapour pressure (Pa)	1.5E-05	(EFSA, 2006)
Water solubility (mg/L)	27	(EFSA, 2006)
Log K_{ow}	3.18	(EFSA, 2006)

Tab. 96. Environmental fate.

Endpoint	Value	Source
Sorption potential K_{OC}	Highest value: 1000 Mean value: 660 (used for PEC calculation Step 2)	(EFSA, 2006)
Biodegradability	NRB	(EFSA, 2006)
Bioconcentration (BCF)	75.86	Experimental value retrieved from VegaNIC vers. 1.0.8 (Negrao de Carvalho et al., 2015)
Biomagnification (BMF)	1	(EC, 2011)

Tab. 97. Analytical methods.

Method	LOD (ng/L)	Description	Reference
SPE concentration and UPLC-MS analysis	0.02	SPE Oasis HLB eluted with MeOH, evaporated to dryness and reconstituted with 0.1 ml of 9:1 H_2O:AcCN. Hypersil GOLD 1.9 μm 50 x 2.1 NH_4Ac/MeOH	(Tavazzi et al., 2016)
	40-0.69	Derivatization & GC-MS, - direct injection (LC-MS)	(Loos et al., 2018a)

Method	LOD (ng/L)	Description	Reference
SPE concentration and UPLC-MS/MS analysis Qtrap	0.54	SPE Oasis HLB eluted with EtOH, evaporated to dryness and reconstituted with 0.25 ml of EtOH. XB-C18 Kinetex 1.7 µm 100 x 2.1 MeOH/H$_2$O	(Sousa et al., 2019)
QuEchERS LC-MS/MS	1.69 (ng/g) sediment	QuEchERS concentration and analysis	(Campo et al., 2013; Masiá et al., 2013)
QuEchERS LC-MS/MS	0.75 (ng/g) sediment	QuEchERS concentration and analysis	(Campo et al., 2013; Masiá et al., 2013)

3.1.1 Environmental exposure assessment

Tab. 98. Environmental Emissions.

	Description/value
Use(s)	Insecticide and bird repellent for maize crops (Arena et al., 2018)
Total production or total emissions (tonnes/year)	NA
Information on emissions in Veneto	Methiocarb is sold in Veneto as Mesurol, Nimrod, Provado, Sepran, Kollant as insecticide; these trade names are identified for the active ingredient methiocarb in the Ministerial database on PPP (Il Ministero dell'Ambiente, 2017) and appear as sold products in the Regional database (ARPAV, 2017)
Possible contacts for relevant information	ARPAV for the quantities per area (spatial distribution)

Tab. 99. Measured Environmental Concentrations.

	Value	Source
Measured concentration in water MEC$_w$ (µg/L)	1)0.0585 µg/L; 2) 0.095 µg/L; 3) <LOQ µg/L; 4) 0.02 µg/L.	1) NORMAN DB, 2014; 2)IPCheM; 3) SE pesticide monitoring programme; 4) IT monitoring programme; (Negrao de Carvalho et al., 2015)

Tab. 100. Predicted Environmental Concentrations.

	Value/Description	Model or method used for the prediction	Source

	Value/Description	Model or method used for the prediction	Source
Predicted concentrations in water PEC_w (µg/L)	0.00395	FOCUS Step 2 (TOXSWA, 2001)	(Negrao de Carvalho et al., 2015)
Predicted concentrations in sediment PEC_{sed} (mg/kg dw)	0.026	FOCUS Step 2 (TOXSWA, 2001)	(Negrao de Carvalho et al., 2015)
Predicted concentrations in biota PEC_{biota} (mg/kg)		$PEC_{biota} = PEC_{fw} \times BCF \times BMF$	(ECHA, 2012)

Tab. 101. P, B, T, C, M, R, ED properties

	YES/NO	Source
Persistent (P) Bioaccumulative (B) Toxic (T)	YES NO NO	(Negrao de Carvalho et al., 2015)
Carcinogenic (C) Mutagenic (M) Reproduction toxicity (R)	NO YES YES	

Tab. 102. Ecotoxicological data.

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
Algae				
Skeletonema costatum	96-h	Growth (biomass)	$EC_{50} = 630$	Wildlife International Inc.[1]
Crustacea				
Americamysis bahia	96-h	Mortality	$EC_{50} = 12,4$	Wildlife International Inc.[1]
	28-d	Growth	$EC_{50} = 3,32$	Wildlife International Inc.[1]
Palaeomonetes pugio	4-d	Mortality	NOEC = 18	Brunson et al., 1985
			LOEC = 49	
			$LC_{50} = 51 - 65$	
Penaeus duorarum	48-h	Mortality	$LC_{50} = 32$	EPA Research Labs[1]
Mollusca				

Crassostrea virginica	96-h	Shell development	NOEC = 560	Brunson et al., 1985
			LOEC = 1.000	
			EC$_{50}$ = 1.000	
Fishes				
Menidia menidia	96-h	Mortality	LC$_{50}$ = 53,5	EA Engineering, Science and Technology[1]
			NOEC = 40	Brunson et al., 1985
			LOEC = 100	
			LC$_{50}$ = 51 - 57	
Cyprinodon variegatus	96-h	Mortality	LC$_{50}$ = 3.010	Wildlife International Inc.[1]
	33-d	Growth	LOEC = 15	Wildlife International Inc.[1]

1 Data available at USEPA OPP Pesticide Ecotoxicity Database, http://www.ipmcenters.org/Ecotox/DataAccess.cfm
LOEC = Lowest Observed Effect Concentration
LC50/EC50 = Lethal/Effective Concentration 50

Tab. 103. Derivation of PNEC values.

PNEC	Endpoint	Endpoint value (µg/L)	AF	Source
1.00E-05 mg/L	Daphnia magna, 21 d, NOEC	0.0001 mg/L	10	(Negrao de Carvalho et al., 2015)
0.001 mg/kg dw				(Negrao de Carvalho et al., 2015)
0.591 mg/kg food	Dog, 90 d, conversion factor 40, NOAEL	1.33 mg/kg bw/day	90	(Negrao de Carvalho et al., 2015)
0.046 mg/L	ADI	0.013 mg/kg bw/day		(Negrao de Carvalho et al., 2015)

Tab. 104. Risk Quotient (MEC or PEC/PNEC).
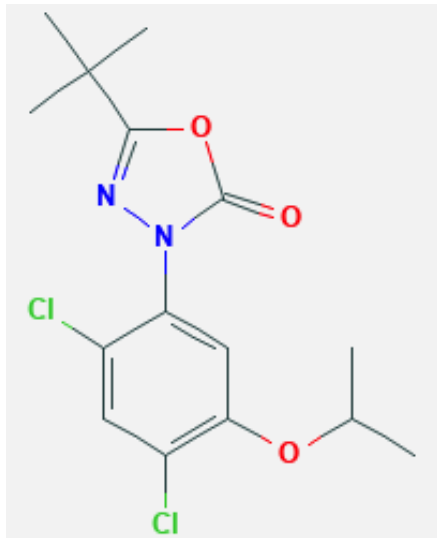
MEC o PEC/PNEC	Source
395	(Negrao de Carvalho et al., 2015)
50.39	(Negrao de Carvalho et al., 2015)
0.51	(Negrao de Carvalho et al., 2015)
0.38	(Negrao de Carvalho et al., 2015)

MEC o PEC/PNEC	Source
0.09	(Negrao de Carvalho et al., 2015)

3.2 Oxadiazon

Oxadiazon is a herbicide.

Tab. 105. Substance identity.

Parameters	
Name	Oxadiazon
IUPAC name	3-[2,4-dichloro-5-(1-methylethoxy)phenyl]-5-(1,1-dimethylethyl)-1,3,4-oxadiazol-2(3H)-one
CAS number	19666-30-9
Molecular formula	C15H18Cl2N2O3
Molecular weight	345.22
Structure	
SMILES	CC(C)Oc1cc(c(cc1Cl)Cl)n2c(=O)oc(n2)C(C)(C)C

Tab. 106. Physico-chemical properties.

Endpoint	Value	Source
Vapour pressure (Pa)	0.1035	(EFSA, 2010)
Water solubility (mg/L)	0.57	(EFSA, 2010)
Log K_{ow}	5.33	(EFSA, 2010)

Tab. 107. Environmental fate.

Endpoint	Value	Source
Sorption potential K_{OC}	1294	(EFSA, 2010)
Biodegradability	NRB	(EFSA, 2010)
Bioconcentration (BCF)	243	(EFSA, 2010)
Biomagnification (BMF)	1	(EC, 2011)

Tab. 108. Analytical methods.

Method	LOD (ng/L)	Description	Reference
SPE concentration and UPLC-MS analysis Qtrap	1	SPE Oasis HLB eluted with MeOH, evaporated to dryness and reconstituted with 0.1 ml of 9:1 H_2O:AcCN. Hypersil GOLD 1.9 µm 50 x 2.1 NH_4Ac/MeOH	(Tavazzi et al., 2016)
SPE concentration, derivatization and GC-MS analysis	52	SPE Oasis HLB eluted with EtOH, evaporated to dryness and reconstituted with 0.25 ml of EtOH. Derivatization with MSTFA and analysed by means GC-MS, Zebron (30 m x 0.25mm)	(Sousa et al., 2019)

3.2.1 Environmental exposure assessment

Tab. 109. Environmental Emissions.

	Description/value
Use(s)	Herbicide
Total production or total emissions (tonnes/year)	NA
Information on emissions in Veneto	Oxadiazon is sold in Veneto (trade name Potclean) (ARPAV, 2017; Il Ministero dell'Ambiente, 2017)
Possible contacts for relevant information	ARPAV for the quantities per area (spatial distribution)

Tab. 110. Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source
Measured concentration in water	0.03-0.10 (May) <0.01 (Feb, Jul, Oct)	Freshwater	Lagoon of Venice-Drainage basin	ARPAV-Open data-2017 Seasonal monitoring

	Value	Matrix	Region/area	Source
MEC$_w$ (µg/L)	0.13-0.18 (May) 0.02 (Aug) <0.01 (Feb, Oct)	Transitional water	Po Delta (Veneto)	ARPAV-Open data-2017 Seasonal monitoring
	0.14 (Nov) <0.01 (other seasons)	Coastal water	Veneto Region-Isola Verde	ARPAV-Open data-2017 Seasonal monitoring
	<0.01	Coastal water	Veneto Region-other sites	ARPAV-Open data-2017 Seasonal monitoring
	0.02 (Jun) <0.01 (other seasons)	Coastal water	Veneto Region-Porto Tolle	ARPAV-Open data-2016 Seasonal monitoring
	<0.01	Coastal water	Veneto region-other sites	ARPAV-Open data-2016 Seasonal monitoring

Tab. 111. Predicted Environmental Concentrations.

	Value/Description	Model or method used for the prediction	Source
Predicted concentrations in water PEC$_w$ (µg/L)	0.039	FOCUS Step 2 (TOXSWA, 2001)	(Negrao de Carvalho et al., 2015)
Predicted concentrations in sediment PEC$_{sed}$ (mg/kg dw)	0.496	FOCUS Step 2 (TOXSWA, 2001)	(Negrao de Carvalho et al., 2015)
Predicted concentrations in biota PEC$_{biota}$ (mg/kg)	9477	PEC$_{biota}$ = PEC$_{fw}$ X BCF X BMF	(ECHA, 2012)

Tab. 112. P, B, T, C, M, R, ED properties

	YES/NO	Source
Persistent (P) Bioaccumulative (B) Toxic (T)	YES YES YES	(Negrao de Carvalho et al., 2015)
Carcinogenic (C) Mutagenic (M))	YES YES	(Negrao de Carvalho et al., 2015)

Tab. 113. Ecotoxicological data.

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source

Algae				
Skeletonema costatum	120-h	Growth (biomass)	$EC_{50} = 5,2$	Springborn Laboratory Inc.[1]
Crustacea				
Americamysis bahia	96-h	Mortality	$EC_{50} = 270$	Springborn Laboratory Inc.[1]
	28-d	Growth	$EC_{50} = 88$	Springborn Laboratory Inc.[1]
Fishes				
Cyprinodon variegatus	96-h	Mortality	$LC_{50} = 1.500$	Springborn Laboratory Inc.[1]

[1] Data available at USEPA OPP Pesticide Ecotoxicity Database, http://www.ipmcenters.org/Ecotox/DataAccess.cfm
LC_{50}/EC_{50} = Lethal/Effective Concentration 50

Tab. 114. Biochemical and genetic responses.

Species	Concentrations	Days of exposure	Biochemical/molecular effects	Reference
Mussels *Anodonta woodiana*	0.001, 0.005, 0.05, 0.5, 5 mg/L 0.5 mg/L	30 min 6 h	No notable changes in the pattern of valve movements.	Giari et al., 2017. WATER SA. 43, 200-208.

Tab. 115. Derivation of PNEC values.

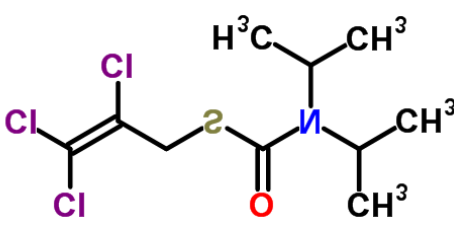| PNEC	Endpoint	Endpoint value (µg/L)	AF	Source
0.000088 mg/L	*Oncorhynchus mykiss*, 60 d, ELS NOEC	0.00088 mg/L	10	(Negrao de Carvalho et al., 2015)
0.05 mg/L	*Chironomus riparius*, 28 d, NOEC	5 mg/L	100	(Negrao de Carvalho et al., 2015)
0.24 mg/kg	Rat, 2 years, NOAEL	0.36 mg/kg bw/day	30	(Negrao de Carvalho et al., 2015)
0.0126	ADI	0.0036 mg/kg bw/day		(Negrao de Carvalho et al., 2015)

Tab. 116. Risk Quotient (MEC or PEC/PNEC).

MEC o PEC/PNEC	Human consumption (Besse et al., 2008)
443.18	(Negrao de Carvalho et al., 2015)

MEC o PEC/PNEC	Human consumption (Besse et al., 2008)
9.92	(Negrao de Carvalho et al., 2015)
39.49	(Negrao de Carvalho et al., 2015)
43.25	(Negrao de Carvalho et al., 2015)
3.10	(Negrao de Carvalho et al., 2015)

3.3 Triallate

Triallate (S-2,3,3-trichloroallyl di-isopropyl thiocarbamate) is a carbamothioate herbicide widely used to control annual and perennial grasses in wheat, barley, legumes and a number of other crops. Its use, in the last decades, has exceeded 500 tons per year in some European countries (Barbosa et al., 2016). Triallate is highly hydrophobic, therefore it adsorbs to loam and clay soils and is not readily dissolved in water, suggesting that this herbicide is not likely to move through the soil, even though it has a long soil half-life (82 days). Nevertheless, it may be desorbed if there is significant moisture and/or low levels of organic matter in the soil. Leaching and consequent groundwater contamination would be possible in such situations (Barbosa et al., 2016). A lack of knowledge exists about its occurrence and removal in the aquatic environment due to its chemical nature.

Tab. 117. Substance identity.

Parameters	
Name	S-2,3,3-trichloroallyl diisopropylthiocarbamate
Other names	S-2,3,3-trichloroallyl diisopropylthiocarbamate
IUPAC name	S-2,3,3-trichloroallyl diisopropylthiocarbamate
CAS number	2303-17-5
Molecular formula	C10H16Cl3NOS
Molecular weight	304.7
Structure	
SMILES	CC(C)N(C(C)C)C(=O)SCC(=C(Cl)Cl)Cl
Metabolites (or other related substances)	2,3,3-trichloroprop-2-ene-sulfonic acid (TCPSA)

Tab. 118. Physico-chemical properties.

Endpoint	Value	Source

Endpoint	Value	Source
Vapour pressure (Pa)	0.012	(Negrao de Carvalho et al., 2015)
Water solubility (mg/L)	4.1	(Negrao de Carvalho et al., 2015)
Log K_{ow}	4.06	(Negrao de Carvalho et al., 2015)

Tab. 119. Environmental fate.

Endpoint	Value	Source
Sorption potential K_{OC}	4301.4	(Negrao de Carvalho et al., 2015)
Biodegradability	NRB	(Negrao de Carvalho et al., 2015)
Bioconcentration (BCF)	1400	(Negrao de Carvalho et al., 2015)
Biomagnification (BMF)	1	(Negrao de Carvalho et al., 2015)

Tab. 120. Analytical methods.

Method	LOD (µg/L)	Description	Reference
Water: SPE + GC-MS	0.017	Watchlist.	(Sousa et al., 2019)
Water: GFF&PUF. ASE + GC-MS	Instrumental 0.1 pg/µL	Battery operated sampling	(Wu et al., 2017)
Water: SPE + HPLC-MS/MS	0.0003	Automated on-line SPE-LC-ESI-(QqLIT) MS/MS	(Rubirola et al., 2017)
Water: HPLC-MS/MS	0.010	Direct injection	(Reemtsma et al., 2013)
Water: POCIS + HPLC-MS/MS	0.0006	Passive sampling	(Billon et al., 2017)
Soil: ultrasonic + GC-ECD	0.005 mg kg^{-1}	Ultrasonic + horizontal shaker + SPE	(Wang et al., 1998)
Biota: QuEChERS + LC-MS/MS	0.00293 mg kg^{-1}	QuEChERS + LC-MS/MS	(Barbieri et al., 2019)
Biota: QuEChERS + GC-MS/MS	0.002 mg kg^{-1}	Multi-walled carbon nanotubes (MWCNTs) as reversed-dispersive solid-phase (r-DSPE) extraction materials	(Han et al., 2016)

3.3.1 Environmental exposure assessment

Tab. 121. Environmental Emissions.

	Description/value
Use(s)	Herbicide
Total production or total emissions (tonnes/year)	NA
Information on emissions in Veneto	Trade names included in the regional registry include Avadex factor, Avadex factor combi, Avadex in a mixture (ARPAV, 2017a; Il Ministero dell'Ambiente, 2017)
Possible contacts for relevant information	ARPAV for the quantities per area (spatial distribution)

Tab. 122. Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source
Measured concentration in water MEC_w (µg/L)	0.177 – 0.513	River	Portugal	(Sousa et al., 2019)
	0.00000018 – 0.000350	Glacier fed lake (preconcentration of 700-1200 L)	New Zealand	(Wu et al., 2017)
	<LOQ – 0.0017	River	France, Marque River, Lille	(Billon et al., 2017)
Measured concentration in biota MEC_{biota} (µg/kg)	nd	Fish muscle tissue	Adige River basin	(Barbieri et al., 2019)

NB: the concentration ranges reported above should be intended as referred only to the values resulting higher than the quantification limits reported in the publications.

Tab. 123. Ecotoxicological data.

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
Algae				
Isochrysis galbana	48-h	Algal growth	$EC_{50} = 390$	EPA Research Lab[1]
Pavlova girans	48-h	Algal growth	$EC_{50} = 530$	EPA Research Lab[1]
Pavlova lutheri	48-h	Algal growth	$EC_{50} = 790$	EPA Research Lab[1]
Skeletonema costatum	96-h	Algal growth	$EC_{50} = 330$	EPA Research Lab[1]
Dunaliella tertiolecta	48-h	Algal growth	$EC_{50} = 1400$	EPA Research Lab[1]
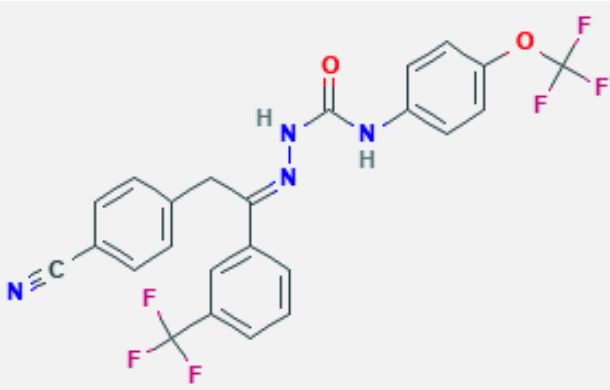
LC_{50}/EC_{50} = Lethal/Effective Concentration 50

3.4 Metaflumizone

Metaflumizone is an active substance applied as an insecticide; EFSA reviewed this PPP for risk assessment under request by BASF in 2013.

For the Veneto region, metaflumizone is included in the lists available from ARPAV as shown in Table 128.

Tab. 124. Substance identity.

Parameters	
Name	Metaflumizone
Other names	Promeris, Alverde
CAS number	139968-49-3
Molecular formula	C24H16F6N4O2
Molecular weight	506.40 g/mol
Structure	

Tab. 125. Physico-chemical properties.

Endpoint	Value	Source
Water solubility (mg/L)	0.00179	(EFSA, 2013)
Log K_{ow}	4.2-4.9	(EFSA, 2013)

Tab. 126. Environmental fate.

Endpoint	Value	Source
Sorption potential K_{OC}	30714 mL/g	(EFSA, 2013)
Biodegradability	NRB	(EFSA, 2013)
Bioconcentration (BCF)	7800 - 8100	(EFSA, 2013)

Tab. 127. Analytical methods.

Method	LOD (µg/L)	Description	Reference
LC-MS/MS	0.025	Metaflumizone E-isomer and Z-isomer can be monitored in drinking water and surface water by LC-MS/MS. The validation was performed using the 2nd mass transition 507>178 m/z as well as primary mass transition 507>287 m/z for quantitation	(EFSA, 2013)
LC-MS/MS	0.05	LLE from 50 ml water with dichloromethane; LC-MS/MS transitions: 507> 287, 178 m/z	(Loos et al., 2018b)
EN ISO 1136925 modif.	0.01/0.02	Slovenia, (SPE – solid-phase extraction)	
LC-MS	0.005	Water sample preconcentration by SPE followed by Ultra-High-Definition (UHD) Accurate-Mass Quadrupole Time-of-Flight (Q-TOF) MS. England	
UPLC-MS/MS		Centrifugation and direct injection, Acquity BEH C18 (100mm x 2.1 x 1.7 µm) H_2O/AcCN. Degradation study in water, soil and rice	(Li et al., 2012)
LC-MS/MS	50-10	SPE- direct injection (LC-MS)	JRC analytical methods for substances in the watch list under the water framework directive workshop 2018

3.4.1 Environmental exposure assessment

Tab. 128. Environmental Emissions.

	Description/value
Use(s)	Active substance as insecticide
Total production or total emissions (tonnes/year)	0.054 in 2015 (Loos et al., 2018b)
Information on emissions in Veneto	Metaflumizone is applied in Veneto (brand name Alverde) (ARPAV, 2017)
Possible contacts for relevant information	ARPAV for the quantities per area (spatial distribution)

Tab. 129. Measured Environmental Concentrations.

	Value	Region/area	Source
Measured concentration in water MEC$_w$ (µg/L)	Only detected once out of the approx. 1700 samples taken at these sites (0.14 µg/l).	Monitored as part of national catchment sensitive farming (CSF) (2 samples per week) & watch list programmes through LC-MS samples at approx. 80 sites	(Loos et al., 2018b)

Tab. 130. P, B, T, C, M, R, ED properties

	YES/NO	Source
Persistent (P) Bioaccumulative (B) Toxic (T)	YES YES YES	(Loos et al., 2018b)

Tab. 131. Ecotoxicological data.

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
Mollusca				
Crassostrea virginica	96-h	Spat immobilization	NOEL = 3,5	Analytical Biochemical Laboratory[1]
			EC$_{50}$ = 136	
Crustacea				
Americamysis bahia	96-h	Mortality	NOEL = 289	Analytical Biochemical Laboratory[1]
			LC$_{50}$ > 289	
Leptocheirus plumulosus	10-d	Mortality	[A]LC$_{50}$ = 935 mg kg^{-1}	Analytical Biochemical Laboratory[1]
Fishes				
Cyprinodon variegatus	96-h	Mortality	NOEL = 12,7	BASF Corporation[1]
			LC$_{50}$ =257	

[1] Data available at USEPA OPP Pesticide Ecotoxicity Database, http://www.ipmcenters.org/Ecotox/DataAccess.cfm
[A] Sediment test
NOEC/NOEL = Non Observed Effect Concentration/Level
LC$_{50}$/EC$_{50}$ = Lethal/Effective Concentration 50

Tab. 132. Derivation of PNEC values.

PNEC	Endpoint	Endpoint value (µg/L)	AF	Source

PNEC	Endpoint	Endpoint value (µg/L)	AF	Source
0.0654	28-d NOEC (Reproduction/survival for *A. bahia*)	0.654	10	(Loos et al., 2018b)
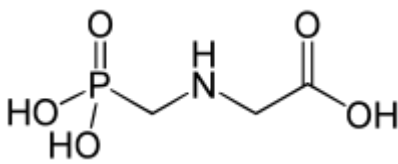
Tab. 133. Risk Quotient (MEC or PEC/PNEC).

MEC o PEC/PNEC	Source
RQ_{fw} (PEC/PNEC; PEC=0.3 µg/l)= 4.6	(Loos et al., 2018b)

3.5 Glyphosate

Glyphosate is an active substance that is widely used in pesticides. Glyphosate-based pesticides – i.e. formulations containing glyphosate and other chemicals – are used in agriculture and horticulture primarily to combat weeds that compete with cultivated crops. They are typically applied before crops are sown and as a pre-harvest desiccating treatment, accelerating and evening the ripening process. In March 2019 the European Commission announced a plan to set up a group of Member States to act as co-rapporteurs for the next assessment of glyphosate. If the plan is approved, the Assessment Group on Glyphosate (AGG) will assess the application dossier and prepare a draft renewal assessment report to be reviewed by EFSA in 2021.

Tab. 134. Substance identity.

Parameters	
Name	Glyphosate
IUPAC name	*N*-(phosphonomethyl)glycine
CAS number	1071-83-6
Molecular formula	$C_3H_8NO_5P$
Molecular weight	169.07
Structure	
SMILES	C(C(:O)O)NCP(:O)(O)O
Metabolites (or other related substances)	AMPA

Tab. 135. Physico-chemical properties.

Endpoint	Value	Source
Vapour pressure (Pa)	At 20 °C: negligible	https://pubchem.ncbi.nlm.nih.gov/compound/glyphosate

Endpoint	Value	Source
Water solubility (mg/L)	10.5 g/L in water at pH 1.9 and 20 deg C	https://pubchem.ncbi.nlm.nih.gov/compound/glyphosate
Log K_{ow}	-3.40	https://pubchem.ncbi.nlm.nih.gov/compound/glyphosate

Tab. 136. Environmental fate.

Endpoint	Value	Source
Sorption potential K_{OC}	15844 (arithmetic mean)	EFSA, 2015
Biodegradability	RB	
Bioconcentration (BCF)	BCF fish : 0.38 – 0.63 (bluegill fish); 0.52 (whole body); 0.38 (edible portion); 0.63 (non-edible portion). Bioconcentration of glyphosate in aquatic organisms is low. In carp (*Cyprinus carpio*) and tilapia (*Oreochromis mossambicus*) BCFs ranged from 10.0 to 42.3 and 12.0 to 65.5, respectively depending on the period of exposure. Maximum accumulation was achieved after 5 to 7 days. These estimates of bioconcentration were based on total radioactivity and not on the identification of glyphosate residues. (UK Environmental agency draft dossier on glyphosate)	(Wang et al., 1994)

Tab. 137. Analytical methods.

Method	LOD (µg/L)	Description	Reference
HPLC/MS/MS	0.1 ng/mL	Matrix: water matrices (drinking, surface and groundwater). No derivatization	(Guo et al., 2016)
LC-SPE-ESI-MS/MS	0.0002 ng/mL	Matrix: general water	(Ibanez et al. 2006)
LC-MS/MS	1.2 ng/mL	Matrix : water	(Hao et al. , 2011)
LC-FLD+MS/MS	0.058 ng/mL	Matrix: water canals Derivatization reagent: (FMOC-Cl)	(Ramirez et al., 2014)
GC/FPD	8.1 ng/mL	Matrix: river water. Derivatization reagent: N-isopropoxycarbonylmethyl	(Kataoka et al, 1996)
GC/MS	0.1 ng/mL	Matrix: groundwater. Derivatization reagent: TFAA and TFE	(Kudzin et al. 2002)

Method	LOD (µg/L)	Description	Reference
IC-ICP/MS	0.7 ng/mL	Matrix: water	(Guo et al., 2005)
HPLC-FLD	0.02 ng/mL	Matrix: surface and ground-waters. Treatment: online SPE. Derivatization reagent: OPA-MCE	(Patsia et al., 2001)
HPLC-UV	MQL : 0.25 mg/Kg	Matrix: sediment. Sample size : 15 g. Sample treatment: with extraction with KH2PO4 0.1 M in agitation; centrifugation and filtration. Derivatization reagent: (FMOC-Cl).	(Peruzzo et al., 2008)
LC-MS/MS	0.027 ng/mL	Matrix: seawater	(Mercurio et al., 2014)
LC-MS/MS	<0.1 ng/mL	Matrix: seawater. Treatment: SPE	(Skeff et al., 2015)
LC-MS/MS	<0.0005 ng/mL	Matrix: ground, surface, river waters. Treatment: SPE	(Hanke et al., 2008)
LC-MS/MS	0.005 ng/mL	Matrix: water. Treatment: online SPE	(Ibanez et al., 2005)
LC-SPE-ESI-MS/MS	0.03 ng/mL	Matrix: surface, drinkable and waste water. Derivatization reagent: FMOC-Cl	(Vreeken et al., 1998)
LC-FLD	0.1 ng/mL	Matrix: natural waters Treatment: anion-exchange resin	(Corbera et al., 2005)
LC-FLD	0.04 ng/mL	Matrix: natural waters	(Le Fur et al, 2000)
LC-LC- FLD	0.007 ng/mL	Matrix: natural waters Treatment: anion-exchange resin	(Hidalgo et al, 2004)
LC-FLD	0.24 ng/mL	Matrix: different fresh waters	(Wang et al., 2016)

3.5.1 Environmental exposure assessment

Glyphosate is a broad-spectrum systemic herbicide. Its brand names are Rodeo and Roundup, and it appears under this name in the PPPs sold in Veneto as shown in the following table.

Tab. 138. Environmental Emissions.

	Description/value

	Description/value
Use(s)	Active substance as herbicide
Total production or total emissions (tonnes/year)	NA
Information on emissions in Veneto	Glyphosate is sold in Veneto (trade name Roundup, Buggy, Glifosan, Fandango, Rasikal, Touchdown, Gliphogan, Glister, Fast, pantox, Glyfos, Silglif, Efesto, Glifene, Diserbon, Mastiff, Glifosate, Glifo, Glisene, Gliphogan top, Klaro,Hopper, Myrtos, Premium, etc.) (ARPAV, 2017b; Il Ministero dell'Ambiente, 2017)
Possible contacts for relevant information	ARPAV for the quantities per area (spatial distribution)

Tab. 139. Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source
Measured concentration in water MEC_w (µg/L)	Mean value 0.7 period 2015-2016	Fresh water	Veneto, Musoncello River	(ARPAV report, 2015-2016)
	Mean value 0.4 period 2015-2016	Fresh water	Veneto, Cagnola Canal	(ARPAV report, 2015-2016)
	Mean value 0.3 period 2015-2016	Fresh water	Veneto, Brenta River	(ARPAV report, 2015-2016)
	Mean value 0.4 period 2015-2016	Fresh water	Veneto, Nuovo Adagetto	(ARPAV report, 2015-2016)
	Mean value 0.5 period 2015-2016	Fresh water	Veneto, Livenza River	(ARPAV report, 2015-2016)
	Mean value 0.5 period 2015-2016	Fresh water	Veneto, Cervada River	(ARPAV report, 2015-2016)
	Mean value 0.2	Fresh water	Veneto, Piave River	(ARPAV report, 2015-2016)
	Mean value 0.3 period 2015-2016	Fresh water	Veneto, Scolo Bigonzo	(ARPAV report, 2015-2016)

	Value	Matrix	Region/area	Source
	BE : <0.1 - <10 µg/L FR : <0.1 − 50 µg/L DE : <0.1 − 4.7 µg/L IE : <0.1 − 1.8 µg/L IT : <0.1 − 11 µg/L SK : <0.1 − 3.6 µg/L SP : <0.1 − 15.3 µg/L SW : <0.1 − 13 µg/L UK : <0.1 − 8.8 µg/L	Fresh waters	Each country is specify in the value column	(Horth, et al 2009)
Measured concentration in sediment MEC_{sed} (µg/kg dw)	MQL (0.25 mg/kg)-1.38 mg/Kg	Sediment	sediments associated with direct sowing soybean cultivation in north pampasic region of Argentina	(Peruzzo et al., 2008)

Tab. 140. Ecotoxicological data.

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
Protozoa				
Perkinsus olseni	3-d 3-d	Growth	IC_{50} = 574.850 IC_{50} = 93.556	Elandalloussi et al., 2008
Bacteria				
Vibrio fischeri	5-min 15-min 30-min	Bioluminescence inhibition	EC_{50} = 43.000 EC_{50} = 43.800 EC_{50} = 44.200	Hernando et al., 2007
Algae				
Skeletonema costatum	5-d 5-d	Growth	EC_{50} = 12.000 EC_{50} = 33.400	Environmental Fate and Effects Division,

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
	5-d		NOEL = 1.800	U.S.EPA[1]
	5-d		NOEL = 21.000	
	7-d		EC_{50} = 770	
	7-d		NOEL < 240	
	96-h	Growth	NOEL = 57	U.S. EPA Ecotox database
			EC_{50} = 340	
Thalassiosira weissfolgi	48-h	Growth	NOEC = 2000	U.S.EPA Ecotox database
Vascular plants				
Zostera marina	3-d	Chlorophyll A/B content	NOEC = 16.907	Nielsen and Dahllöf, 2007
		Growth rate	NOEC = 16.907	
Coelenterata				
Hydra attenuata	4-d	Mortality	LC_{50} = 18.200	Demetrio et al., 2012
			LC_{50} = 21.800	
Crustacea				
Americamysis bahia	96-h	Mortality	LC_{50} = 79.000	Environmental Fate and Effects Division, U.S.EPA[1]
			LC_{50} = > 190.800	
			LC_{50} = 40.000	
			LC_{50} = 29.000	
			NOEL = 32.000	
			NOEL = 190.800	
			NOEL = 16.000	
Callinectes sapidus	24-h	Mortality (megalopae)	LC_{50} = 6.279	Osterberg et al., 2012
		Mortality (juveniles)	LC_{50} = 316.000	

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
	64-h	Larval development	LOEC = 5.500	
		Larval mortality	LOEC = 5.500	
		Larval development	NOEC = 5.500	
Palaemonetes vulgaris	96-h	Mortality	NOEL = 210.000	Environmental Fate and Effects Division, U.S.EPA[1]
			LC$_{50}$ = 281.000	
Uca pugilator	96-h	Mortality	NOEL = 650.000	Environmental Fate and Effects Division, U.S.EPA[1]
Neohelice granulata	10-d	Progeny	LOEC = 2.200	Avigliano et al., 2014
		Hatch	NOEC = 2.200	
		Growth	NOEC = 2.200	
	32-d	Mortality	NOEC = 2.200	
		Resorbed embryos	NOEC = 2.200	
		Oocytes development	NOEC = 2.200	
Mollusca				
Crassostrea gigas	48-h	Larval development	EC$_{50}$ = 82.000	Brixham Laboratory[1]
	24-h	Larval development	EC$_{50}$ > 100.000	Mottier et al., 2013
		Larval mortality	EC$_{50}$ = 7.934	
		Metamorphosis	EC$_{50}$ = 6.060	
	48-h	Larval development	EC$_{50}$ = 27.175	
		Embryo development	EC$_{50}$ = 1.672	
Ruditapes decussatus	96-h	Mortality	LC$_{50}$ = 10.000	Elandalloussi et al., 2008

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
Crassostrea virginica	30-min	Sperm-cell viability	NOEC = 16.000	Favret and Lynn, 2010
		Membrane potential	NOEC = 16.000	
Septifer bilocularis	2-h	Oxygen consumption	LOEL = 720.000	Lasut and Angmalisang, 1997
			NOEL = 480.000	
Echinoida				
Lytechinus variegatus	24-h	Development	EC$_{50}$ = 31.946	U.S.EPA Ecotox database
			EC$_{50}$ = 34.332	
Fishes				
Cyprinodon variegatus	96-h	Mortality	LC$_{50}$ = 240.000	Environmental Fate and Effects Division, U.S.EPA[1]
			LC$_{50}$ > 180.200	
			LC$_{50}$ > 320.000	
			NOEL = 320.000	
			NOEL = 100.000	
			NOEL = 180.200	
Gasterosteus aculeatus	42-d	Growth (condition index)	NOEC = 100	Le Mer et al., 2013
			NOEC = 78	
Alburnus alburnus	96-h	Mortality	LC$_{50}$ = 16.000	Linden et al., 1979
Dicentrarchus labrax	96-h	Mortality	LC$_{50}$ = 610.000	Richard et al., 2014

[1] Data available at USEPA OPP Pesticide Ecotoxicity Database, http://www.ipmcenters.org/Ecotox/DataAccess.cfm
LOEC/LOEL = Lowest Observed Effect Concentration/Level
NOEC/NOEL = Non Observed Effect Concentration/Level
LC$_{50}$/EC$_{50}$ = Lethal/Effective Concentration 50
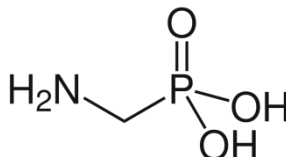IC$_{50}$ = Inhibition Concentration 50

Tab. 141. Biochemical and genetic rsponses

Species	Concentrations	Days of exposure	Biochemical/molecular effects	Ref.
Mussels *Mytilus galloprovincialis*	10, 100 and 1000 µg/L	7, 14 and 21 days	Alterations of haemocyte parameters (e.g., THC, cell volume, haemolymph pH, lysozyme and acid phosphatase activities) and acetylcholinesterase (AChE) activity	Matozzo et al., 2018.
Mussels *Limnoperna fortunei*	1, 3 and 6 mg/L	26 days	Significant increases in glutathione-s-transferase (GST) and alkaline phosphatase (ALP) activities and lipid peroxidation. Levels; significant decrease in superoxide dismutase (SOD) and carboxylesterases activities	Iummato et al., 2013.
Clams *Ruditapes decussatus*	0.2 and 1 g/L	24 and 72 h	Negative effects on energy metabolism and metabolic biomarkers, such as alanine, succinate, acetate and propionate.	Hanana et al., 2012. Talanta 97, 425-431
Juvenile oysters *Crassostrea gigas*	0.1, 1 and 100 mg/L	56 days	Influence on growth, condition index, sexual maturity, tissue alterations, enzymatic activities, lipid peroxidation and expression of reference genes	Mottier et al., 2015.
Mussels *Mytilus galloprovincialis*	10, 100 and 1000 µg/L	21 days	Effects on digestive gland transcriptional profiles. Disruption of several key biological processes, such as energy metabolism and Ca2+ homeostasis, cell signalling, and endoplasmic reticulum stress response.	Milan et al., 2018.
Mussels *Limnoperna fortunei*	Mussels were fed with the green algae *Scenedesmus vacuolatus* previously	4 weeks	Significant increases in the GST activity and significant decreases in the carboxylesterases activity were observed. Alkaline phosphatase activity was significantly increased at 21	Iummato et al., 2018.

	exposed to glyphosate (6 mg/L active principle)		and 28 days of dietary exposure. No oxidative damage to lipids and proteins was found.	

3.6   AMPA

The primary metabolite of glyphosate is aminomethylphosphonic acid (AMPA). Degradation of AMPA is generally slower than that of glyphosate possibly because AMPA may adsorb onto soil particles more strongly than glyphosate and/or because it may be less likely to permeate the cell walls or membranes of soil microorganisms. AMPA is not ecotoxicologically relevant for water, sediment and groundwater compartments. For precautionary reasons AMPA is proposed as relevant residue due to the frequent detections in surface waters and groundwater and the widespread intended uses of glyphosate in almost all crops. (EFSA Journal 2015;13(11):4302).

Tab. 142. Substance identity.

Parameters	
Name	AMPA
Other names	Aminomethanephosphonic acid
IUPAC name	(Aminomethyl)phosphonic acid
CAS number	1066-51-9
Molecular formula	CH6NO3P
Molecular weight	111.037
Structure	
SMILES	O:P(O)(O)CN

Tab. 143 Physico-chemical properties.

Endpoint	Value	Source
Vapour pressure (Pa)	No data – estimated $7.68 \cdot 10^{-3}$ Pa at 25°C	Estimated with EPIWIN
Water solubility (mg/L)	50 mg/mL	https://www.chemicalbook.com/ChemicalProductProperty_EN_CB5139354.htm
Log K_{ow}	No data - estimated: -2.17 - 2.36 (estimated ClogP)	Estimated with EPIWIN

Tab. 144. Environmental fate.

Endpoint	Value	Source
Biodegradability	NRB	EC, 2002
Bioconcentration (BCF)	Given the extremely low Log K_{ow} value, the bioaccumulation in fish is not relevant. No measured data	EC, 2002

Tab. 145. Analytical methods.

Method	LOD (µg/L)	Description	Reference
LC-MS/MS	0.031 ng/mL	Matrix: seawater	(Mercurio et al., 2014)
LC-MS/MS	<0.1 ng/mL	Matrix: seawater. Treatment: SPE	(Skeff et al., 2015)
LC-MS/MS	<0.0004 ng/mL	Matrix: ground, surface, river waters. Treatment: SPE	(Hanke et al., 2008)
LC-MS/MS	0.05 ng/mL	Matrix: water. Treatment: online SPE	(Ibanez et al., 2005)
LC-FLD	0.03 ng/mL	Matrix: surface, drinkable and waste water. Derivatization reagent :FMOC-Cl	(Vreeken et al., 1998)
LC-FLD	0.3 ng/mL	Matrix: natural waters Treatment: anion-exchange resin	(Corbera et al., 2005)
LC-FLD	0.01 ng/mL	Matrix: natural waters	(Le Fur et al, 2000)
LC-LC- FLD	0.03 ng/mL	Matrix: natural waters. Treatment: anion-exchange resin	(Hidalgo et al, 2004)
LC-FLD	0.06 ng/mL	Matrix: different fresh waters	(Wang et al., 2016)
LC-FLD	0.30 ng/mL	Matrix: seawater	(Wang et al., 2016)

3.6.1 Environmental exposure assessment

Tab. 146. Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source
Measured concentration in water MEC_w (µg/L)	Mean value 0.2 period 2015-2016	Fresh water	Veneto, Adige River	(ARPAV report, 2015-2016)
	Mean value 0.2 period 2015-2016	Fresh water	Veneto, Zero River	(ARPAV report, 2015-2016)

	Value	Matrix	Region/area	Source
	Mean value 0.5 period 2015-2016	Fresh water	Veneto, Musoncello River	(ARPAV report, 2015-2016)
	Mean value 0.4 period 2015-2016	Fresh water	Veneto, Cagnola Canal	(ARPAV report, 2015-2016)
	Mean value 0.4 period 2015-2016	Fresh water	Veneto, Nuovo Adagetto	(ARPAV report, 2015-2016)
	Mean value 0.6 period 2015-2016	Fresh water	Veneto, Livenza River	(ARPAV report, 2015-2016)
	Mean value 0.4 period 2015-2016	Fresh water	Veneto, Monticano River	(ARPAV report, 2015-2016)
	Mean value 0.3 period 2015-2016	Fresh water	Veneto, Cervada River	(ARPAV report, 2015-2016)
	Mean value 0.3 period 2015-2016	Fresh water	Veneto, Piave River	(ARPAV report, 2015-2016)
	Mean value 0.2 period 2015-2016	Fresh water	Veneto, Po di Venezia	(ARPAV report, 2015-2016)
	Mean value 0.2 period 2015-2016	Fresh water	Veneto, Scolo Bigonzo	(ARPAV report, 2015-2016)
	BE : <0.1 - <10 µg/L FR : <0.1 – 49 µg/L DE : <0.1 – 3.6 µg/L SW : <0.1 – 4 µg/L	Fresh waters	Each country is specify in the value column	(Horth et al 2009)

Tab. 147. Ecotoxicological data.

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
Crustacea				
Crassostrea gigas	24-h	Larval mortality	$EC_{50} > 100.000$	Mottier et al., 2013
		Larval development	NOEC = 100.000	
			$EC_{50} > 100.000$	
	48-h	Larval development	NOEC = 10.000	

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
			LOEC = 20.000	
			EC_{50} = 46.105	

LOEC/LOEL = Lowest Observed Effect Concentration/Level
NOEC/NOEL = Non Observed Effect Concentration/Level
LC_{50}/EC_{50} = Lethal/Effective Concentration 50

Tab. 148. Biochemical and genetic responses.

Species	Concentrations	Day of exposure	Biochemical/molecular effects	Ref.
Mussels *Mytilus galloprovincialis*	1, 10 and 100 µg/L	7, 14 and 21 days	Alterations of haemocyte parameters (e.g., THC, cell diameter and volume, haemolymph pH, haemocyte proliferation, lactate dehydrogenase (LDH) activity	Matozzo et al., 2018.

3.7 Analytical methods employed

The results of the extensive bibliographical review indicate that the most widely used preanalytical procedures for the determination of Triallate (and also for BHT, EHMC, and the Fragrances, as reported in the following chapters) in water samples use SPE extraction with Oasis HLB cartridges. These analytes are also effectively analysed by GC-MS, or GC-MS/MS, generally achieving lower detection limits. These techniques suggest a comprehensive multi-analyte method for their determination in water samples. Similarly the preparation of samples of solid matrices (sediments, biota) will be performed following a common procedure for BHT, EHMC, Triallate and Fragrances, using Accelerated Solvent Extraction (ASE).

Previous studies mainly reported quantification of glyphosate and AMPA in surface, drinking and ground waters. The determination of these compounds in sediment samples is very rare. We reported only one paper where glyphosate was determined using HPLC-UV. The analytical technique mainly used is liquid chromatography coupled with a lot of detection systems (i.e. UV, FLD, MD), although some studies reported also GC-MS methods. Both chromatographic techniques need a derivatization step with a purification step using SPE cartridges. To minimize the preanalytical steps and considering the instrument available in our laboratories, an innovative method is being developed using ion chromatography coupled mass spectrometer. The method consists in a direct injection of 250 µL of seawater in a non-line pre-concentration cartridges. Chromatographic separation is carried out using an anion exchange stationary phase while glyphosate and AMPA are detected using a mass spectrometer. Sediment samples will be extracted using ultrapure water and directly analysed using the same method.

3.8 References

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Web site:

European Chemicals Agency (ECHA): echa.europa.eu

4   Neonicotinoid insecticides

In July 2009, a group of entomologists met at Notre Dame de Londres (France), following an international survey which revealed the dramatic decrease in insects and arthropods throughout Europe since the 1950s (van Lexmond et al., 2015) Among the various causes of the problem they identified intensive agriculture and the use of pesticides and herbicides. They also noticed an abrupt decline of insects in the decade 1990-2000, with consequent decline of insectivorous bird species as well. On the basis of the available studies, the investigations in the field and overwhelming evidence suggested the hypothesis that the new generation of systemic neonicotinoid pesticides, characterized by persistence and neurotoxicity together with fipronil, another insecticide, was responsible at least in part for this decline (van Lexmond et al., 2015).

Neonicotinoid insecticides were discovered in the late 1980s and this class, includes: imidacloprid, thiamethoxam, clothianidin, acetamiprid and thiacloprid. They are currently the most widely used insecticides in the world. It is estimated that together with fipronil they represent one third of the world market of insecticides and that in 2010 at the global level imidacloprid, the most representative compound, was produced in about 20,000 tons (Simon-Delso et al., 2015). They are used on a large scale for the protection of plants (crops, vegetables, fruit), as veterinary products, biocides to invertebrate pest control in fish farming. Neonicotinoid compounds act as neurotoxins as they destroy the neuronal transmission of the nervous system of invertebrates. In fact, they mimic the action of neurotransmitters and by continuously stimulating neurons lead to the death of target organisms. However, they can have a lethal or sub-lethal impact even on non-target organisms such as predator insects and vertebrate animals. Considering their wide commercial expansion, mode of action, the systemic properties in plants, persistence and environmental fate, coupled with limited information about the toxicity profiles of these compounds and their metabolites, neonicotinoids may entail significant risks to the environment.(Simon-Delso et al., 2015).

Environmental contamination occurs via a number of routes including dust generated during drilling of dressed seeds, contamination and accumulation in arable soils and soil water, runoff into waterways, and uptake of pesticides by no-target plants via their roots or dust deposition on leaves. Persistence in soils, waterways, and no-target plants is variable but can be prolonged; for example, the half-lives of neonicotinoids in soils can exceed 1,000 days, so they can accumulate when used repeatedly. Similarly, they can persist in woody plants for periods exceeding 1 year (Bonmatin et al., 2015).

A range of concerns has emerged about the impacts of neonicotinoids on the environment: other than soil persistence and accumulation, their impact on soil invertebrates. Being water soluble, neonicotinoids leach into ponds, ditches and streams and contaminate groundwater. Contamination of marine environments has been observed but as yet has not been monitored systematically (van Lexmond et al., 2015). Dust created during drilling of treated seeds is lethal to flying insects and has caused large-scale acute losses of honeybee colonies. Although vertebrates are less susceptible than arthropods, consumption of small numbers of dressed seeds offers a potential route for direct mortality in granivorous birds and mammals, for such birds need to eat only a few spilt seeds to receive a lethal dose (van Lexmond et al., 2015). Breakdown results in toxic metabolites that can themselves be toxic (Simon-Delso et al., 2015), though concentrations of these in the environment are rarely measured (Bonmatin et al., 2015).

Due to the chemical and toxicological characteristics, the spread use in Europe, the possibility of contamination of water, these substances are suspected of posing a significant risk to, or via, the aquatic environment. So there is reliable evidence of hazard and of a possible exposure to aquatic organisms and mammals (JRC, technical report). For these reasons neonicotinoid insecticides (imidacloprid, thiamethoxam, clothianidin, acetamiprid and thiacloprid) were inserted in a watch list of substances (COMMISSION IMPLEMENTING DECISION (EU) 2015/495 of 20 March 2015 establishing a watch list of substances for Union-wide monitoring. the field of water policy pursuant to Directive 2008/105/EC of the

European Parliament and of the Council). The monitoring data are to be gathered for the purpose of supporting future prioritisation exercises.

4.1 Measured concentration in environmental matrices

Neonicotinoid insecticides are usually determined in surface water and in groundwater. The European legislation (Directive 2008/105/EC) sets the Environmental Quality Standard (EQS) for a limited number of priority substances (including few pesticides) in surface waters. Moreover the Italian legislation (D.lgs. 172/2015) sets EQS for some other pesticides and fixes for all the other pesticides (including metabolites), not explicitly regulated, the limit of 100 ng/L and, for the sum of pesticides, the limit of 1000 ng/L. The Directive 2006/118/EC on the protection of groundwater sets standards of environmental quality, defined as the concentrations which should be exceeded in order to protect the human health and the environment. In particular for the pesticides and their degradation products the limits are equal to those for drinking water, equal to 100 ng/L and 500 ng/L, respectively for the single substance and for the sum of the substances (ISPRA, Rapporti 282/2018).

Regarding neonicotinoid insecticides in the Veneto Region (Italy) to the best of our knowledge there is only a publication (De Liguoro et al., 2014), reporting levels of contamination in waters used for field irrigation and livestock watering. Among this class of compounds Imidacloprid was in livestock watering ranging from 3 to 14 ng/L. Clothianidin and acetamiprid were only in one sample both at a concentration of 3 ng/L. The regional agency ARPAV performs a regular monitoring of pesticides in surficial and ground waters (Arpav 2017, Stato delle Acque superficiali del Veneto – Anno 2017) (Arpav 2017, Qualità delle acque sotteranee 2017). Imidacloprid is included in the list of pesticides analysed. In surficial waters imidacloprid was observed sporadically at levels above the quantification limit in a range from 10-250 ng/L. In ground waters imidacloprid was quantified at concentrations of < 50 ng/L in eleven stations mainly in the Treviso province.
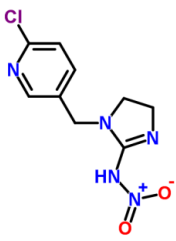
Recently ISPRA (ISPRA, Rapporti 289/2018) published the results of a pesticide monitoring performed in 2016 in Italy. Regarding the neonicotinoid insecticides, the document reported that the occurrence of the insecticide imidacloprid both in surface and groundwater is relatively recent. Imidacloprid is the insecticide most frequently found in groundwater. The rate of investigation is significantly increasing over the years, but is still largely incomplete, considering that the substance is used throughout Italy and determines the highest number of exceedances of the EQSs. In Italy, the highest imidacloprid concentrations measured in 2016 were of 690 ng/L in surface water and 1670 ng/L in groundwater.

Neonicotinoid insecticides are compounds used all around the world. The most frequently observed in surficial and ground waters and in river sediments are imidacloprid and thiamethoxam. Imidacloprid, thiamethoxam, clothianidin have in general higher concentration, especially in surface waters: they have been quantified in concentration from BDL to hundreds ng/L (see corresponding tables). The highest concentration of imidacloprid (range from below detection limit, BDL to 480 ng/L) and chlotinanidin (BDL-159 ng/L) in surface water were registered in Portugal (Sousa et al, 2019). Acetamiprid and thiacloprid were in lower concentration, both were observed in Pearl River, China: acetamiprid at a mean concentration of 52.2±32.5 ng/L in Pearl River Guangzhou, China (Xiong et al., 2019) and thiacloprid in a range 0.40-0.90 ng/L (Zhang et al., 2019). In river sediment neonicotinoid were quantified in concentration in general below 1 ng/g dw.

4.2 Imidacloprid

Imidacropid is a neonicotinoid insecticide. The uses as seed treatment and soil treatment of plant protection products containing Imidacloprid, should be prohibited for crops attractive to bees and for cereals except for uses in greenhouses and for winter cereals. Foliar treatments with plant protection products containing Imidacloprid, should be prohibited for crops attractive to bees and for cereals with the exception of uses in greenhouses and uses after flowering (EC, 2013).

Tab. 149. Substance identity.

Parameters	
Name	Imidacloprid
Other names	1-(2-Chloro-pyridinylmethyl-5-yl)-2-nitroamino-imidazoline; 1-[(6-Chloro-3-pyridinyl)methyl]-N-nitro-4,5-dihydro-1H-imidazol-2-amine, 'Confidor', 'Gaucho'
IUPAC name	1-[(6-Chloro-3-pyridinyl)methyl]-N-nitro-4,5-dihydro-1H-imidazol-2-amine
CAS number	105827-78-9/138261-41-3
Molecular formula	C9H10ClN5O2
Molecular weight	255.7
Structure	
SMILES	c1cc(ncc1CN2CCN:C2N[N+](:O)[O-])Cl
Metabolites (or other related substances)	6-CNA, 6-chloronicotinic acid in soil (Simon-Delso et al., 2015) M01; M02; M06; M07 NTN33893-nitrosimine; M09 NTN33893-desnitro; M12 NTN33893-urea; M14 6-chloronicotinic acid; M16 NTN33893-AMCP NTN33893-6-CNA; M23 NTN33893-desnitroolefine.

Tab. 150. Physico-chemical properties.

Endpoint	Value	Source
Vapour pressure (Pa)	4E-10	EFSA conclusion, 2008,
Water solubility (mg/L)	610	EFSA conclusion, 2008, (Bonmatin et al., 2015)
Log K_{ow}	0.57	EFSA conclusion, 2008, (Bonmatin et al., 2015)

Tab. 151. Environmental fate.

Endpoint	Value	Source
Sorption potential K_{OC}	225 (mean)	EFSA conclusion, 2008
Biodegradability	NRB	EFSA conclusion, 2008
Bioconcentration (BCF)	0.61	EFSA conclusion, 2008

Tab. 152. Analytical methods.

Method	LOD (µg/L)	Description	Reference
UHPLC-MS/MS	MDL 2.00 ng/L MQL 6.06 ng/L	Surface water: SPE preconcentration of 500mL on Oasis HLB	(Sousa et al. 2019)
LC-TOFMS	LOQ 14.4 ng/L	Surface or wastewater: SPE preconcentration of 200mL on Oasis HLB	(Robles-Molina et al., 2014)
HPLC-MS/MS	MDL 4.9 ng/L	Water: SPE preconcentration of 1 L on Oasis HLB	(Hladik et al. 2012) In JRC report
HPLC-MS/MS	MDL 2 ng/L	Surface water: SPE preconcentration of 100 mL on Oasis HLB e Strata X	(Hao et al., 2015)
HPLC-MS/MS	LOD 0.25 ng/L	Surface Water: passive sampler POCIS equipped with a prototype newly synthesized SPE	(Xiong et al., 2019)
HPLC-MS/MS	LOD 0.04 ng/L LOQ 0.2 ng/L	Surface water: SPE preconcentration of 200 mL on Oasis HLB	(Masia et al., 2013b)
UHPLC-MS/MS	LOD 35 ng/L	Surface water: SPE preconcentration of 100 mL on Oasis HLB	(Marin et al., 2009)
HPLC-MS/MS	MDL 0.3 ng/L	Surface water: SPE preconcentration of 10 mL using On –line SPE. SPE cartridge Hyspere 18HD	(Rubirola et al., 2017)
HPLC-MS/MS	Groundwater LOD 4.1 ng/L, LOQ 13.5 ng/L Surface water LOD 5.0 ng/L, LOQ 16.5 ng/L	Water: SPE preconcentration of 1 L on Oasis HLB	(Dujakovic et al., 2010)
HPLC-MS/MS	LOD 2.5 ng/L	Surface water: SPE preconcentration of 1 L on Oasis HLB	(De Liguoro et al., 2014)
HPLC-APPI-MS/MS	MDL 0.88 ng/L	Surface water: SPE preconcentration of 500 mL on Oasis HLB	(Yamamoto et al., 2012)
HPLC-MS/MS	LOQ 1.1 ng/L	Water: SPE preconcentration of 500 mL on Oasis HLB	(Main et al., 2014)In JRC report
HPLC-MS/MS	LOQ <0.05 ng/L	Water: SPE preconcentration of 500 mL on PolySery HLB	(Zhang et al., 2019)
HPLC-MS/MS	LOQ <0.005 ng/g	Sediment: 5g freeze-dried sediment was extracted using the dispersive	

Method	LOD (µg/L)	Description	Reference
HPLC-MS/MS	LOQ 0.1 ng/g	Sediment: 1g lyophilized sediment was extracted using QuEChERS. This procedure was employed in fish analysis	Masia et al., 2015) (Masia et al., 2013a) (Ccanccapa et al., 2016)
HPLC-MS/MS	LOQ 1 ng/g	Bees: 2 gr of matrix extracted using QuEChERS.	(Niell et al., 2015)
HPLC-MS/MS	LOQ 10 ng/g	Odonate Nymphs: 0.5-0.2 gr of matrix extracted using QuEChERS.	(Jesus et al., 2018)

4.2.1 Environmental exposure assessment

Tab. 153. Environmental Emissions.

	Description/value
Use(s)	Active substance as insecticide
Total production or total emissions (tonnes/year)	NA
Information on emissions in Veneto	Imidacropid is sold Veneto (trade name Confidor, provado Pin, Kohinor, Nemacur, Warrant, Corsarium, Nuprid, Suscon, Siattol, Decis Energy, Imidasect, Toreador, Imidachem, Imprint, Afidane, Aphids, Nuprid, Mediator, Lotus, Aflor, Mido, Intercept, Tobago) (ARPAV, 2017; Il Ministero dell'Ambiente, 2017)
Possible contacts for relevant information	ARPAV for the quantities per area (spatial distribution)

Tab. 154. Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source
Banned use(s)	Range 3-8 ng/L	Ground waters	Veneto, Italy	(De Liguoro et al., 2014)
Banned use(s)	BDL-480 ng/L	River waters	Veneto, Italy	Arpav 2017, Stato delle Acque superficiali del Veneto, Pesticidi open data
Banned use(s)	< 50 ng/L	Ground waters	Veneto, Italy	QualitaAcqueSotterranee2017, Arpav 2017
Banned use(s)	BDL-480 ng/L BDL-213 ng/L	Ave River Water Sousa River Water	Portugal	(Sousa et al., 2019)

	Value	Matrix	Region/area	Source
Banned use(s)	BDL-35.3 ng/L BDL-10.1 ng/L	Sope Creek (Georgia, USA) Chattahochee River	Georgia, USA	(Hladik et al. 2012) In JRC report
Banned use(s)	81.1±49.5 ng/L	urban waterways	Waters collected near the Pearl River Guangzhou, China	(Xiong et al., 2019)
Banned use(s)	Range 1.1-6.1 ng/L	Surface waters	Waters taken from Jucar, Ebro, Llobregat and Guadalquivir rivers, Spain	(Masia et al., 2013b)
Banned use(s)	Range 8.0-258 ng/L	Surface waters	Waters taken from Llobregat rivers, Spain	(Rubirola et al., 2017)
Banned use(s)	Geometric mean 2.5 and 8.6 ng/L August 2009 and May 2010	Surface waters	Rivers of Osaka, Japan	(Yamamoto et al., 2012)
Banned use(s)	Range 1.4-15.9 ng/L	Surface waters	Water from Prairie wetlands, Canada	(Main et al., 2014) In JRC report
Banned use(s)	Range 2.2-10.3 ng/L	River water	Great Lakes tributaries, USA	(Hladik et al., 2018)
Banned use(s)	Range 28-102 ng/L	Surface waters	Water from the major rivers (Aspropotamos, Kompsatos, Lissos, Kosynthos) of the Lake Vistonis basin	(Papadakis et al., 2015)
Banned use(s)	Range of mean values 24.9-36.5 ng/L	Surface waters	Water of the Pearl Rivers, South China	(Zhang et al., 2019)

	Value	Matrix	Region/area	Source
Banned use(s)	Range 1.4-15.9 ng/L	Surface waters	Water from Prairie wetlands, Canada	(Main et al., 2014) In JRC report
Banned use(s)	Range 2.2-10.3 ng/L	River water	Great Lakes tributaries, USA	(Hladik et al., 2018)
Measured concentration in sediment MEC_{sed} (µg/kg dw)	Range of mean values 0.04-1.33 ng/g dw	Sediment	sediment of the Pearl Rivers, South China	(Zhang et al., 2019)

Tab. 155. Predicted Environmental Concentrations.

	Value/Description	Matrix	Region/area	Model or method used for the prediction	Source
Predicted concentrations in water PEC_w (µg/L)	0.008	freshwater	Germany	FOCUS Step 2 (TOXSWA, 2001)	(EFSA, 2008)
Predicted concentrations in sediment PEC_{sed} (mg/kg dw)	0.018	freshwater	Germany	FOCUS Step 2 (TOXSWA, 2001)	(EFSA, 2008)
Predicted concentrations in biota PEC_{biota} (mg/kg)	0.005			$PEC_{biota} = PEC_{fw} \times BCF \times BMF$	(EFSA, 2008)

Tab. 156. P, B, T, C, M, R, ED properties

	YES/NO	Source
Persistent (P) Bioaccumulative (B) Toxic (T)	YES NO NO	(EFSA, 2008)
Carcinogenic (C) Mutagenic (M) Reproduction toxicity (R)	NO NO NO	(EFSA, 2008)
Endocrine Disruptive (ED)	NO	(EFSA, 2008)

Tab. 157. Ecotoxicological data.

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
Crustacea				
Mysidopsis bahia	96-h	Mortality	EC_{50} = 34.1	Pisa et al., 2015
		Mortality	NOEC = 13,3	
		Mortality[1]	NOEC = 21	
Artemia spp.	48-h	Mortality	LC_{50} = 361.000	Song et al., 1997
Paeneus monodon	48-h	Mortality	LC_{50} = 175	Hook et al., 2018
Callinectes sapidus	24-h	Mortality of megalopae	LC_{50} = 10	Osterberg et al., 2012
		Mortality of juveniles	LC_{50} = 1,1	
Insecta				
Aedes taeniorhynchus	72-h	Mortality	LC_{50} = 21	Song et al., 1997

[1] Data referred to a commercial mixture (ADMIRE).
NOEC = Non-Observed Effect Concentration
LC_{50}/EC_{50} = Lethal/Effective Concentration 50

Tab. 158. Biochemical and genetic responses.

Species	Concentrations	Days of exposure	Biochemical/molecular effects	Reference
Mussels *Mytilus galloprovincialis*	0.1, 1, and 10 mg/L	4 days	Decrease in lysosomal membrane stability of gonad tissue; reduction of AChE activity (100 and 1000 µg/L).	Dondero et al., 2010.
Freshwater mussels *Lampsilis fasciola*	1000 µg/L	48h	Reduction in the viability of glochidia (<10 %).	Prosser et al., 2016.
Freshwater mussels *Dreissena bugensis*	1 and 10 mg/L	12-14days	Enhancement of the multixenobiotic resistance (MXR) activity (chemostimulation).	Vehovszky et al., 2018.

Freshwater mussels *Lampsilis siliquoidea (juvenile)* and *Villosa iris (glochidia)*	9121 µg/L 16800 µg/L	28days 24h	No effect in survival was observed. Reduction in the viability of glochidia (<7%).	Salerno et al., 2018.

Tab. 13. Derivation of PNEC values.

PNEC	Endpoint	Endpoint value (µg/L)	AF	Source
0.009 µg/L	HC5	0.027 µg/L	3	(EFSA, 2014)
0.210 mg/L	ADI	0.06 mg/kg bw/day		(EFSA, 2008)
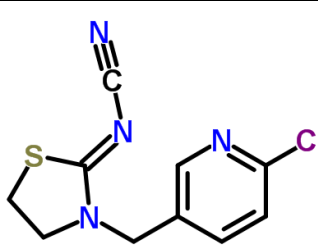
Tab. 159. Risk Quotient (MEC or PEC/PNEC).

MEC o PEC/PNEC	Source
888.9 (PEC/PNEC)	(Negrao de Carvalho et al., 2015)
0.04 (PEC/PNEC)	(Negrao de Carvalho et al., 2015)

4.3 Thiacloprid

Thiacloprid is a neonicotinoid insecticide, targeted chiefly to control aphid pest species in orchards and vegetables.

Tab. 160. Substance identity.

Parameters	
Name	Thiacloprid
Other names	(Z)-3-(6-chloro-3-pyridylmethyl)-1,3-thiazolidin-2-ylidenecyanamide, calypso
IUPAC name	[3-[(6-chloropyridin-3-yl)methyl]-1,3-thiazolidin-2-ylidene]cyanamide
CAS number	111988-49-9
Molecular formula	C10H9ClN4S
Molecular weight	252.7
Structure	

SMILES	C1CSC(:NC#N)N1CC2:CN:C(C:C2)Cl
Metabolites (or other related substances)	THI-NH, M29, thiacloprid thiazolidinimine, 3-[(6-Chloro-3-pyridinyl)methyl]-2-thiazolidinimine, descyano derivative, THI-4-OH, 4-hydroxy-thiacloprid, {3-[(6-chloro-3-pyridinyl)methyl]-4-hydroxy-2-thiazolidinylidene}cyanamide, Thiacloprid-amide, THI-NCONH2, 3-[(6-chloro-3-pyridinyl)methyl]-2-thiazolidinylidene}urea, M02, THI-SO3-H-NCONH2, Thiacloprid sulfonic acid, M30 (Simon-Delso et al., 2015)

Tab. 161. Physico-chemical properties.

Endpoint	Value	Source
Vapour pressure (Pa)	3 x 10-10	EU List of Endpoints (LoE), 2002
Water solubility (mg/L)	184	EU List of Endpoints (LoE), 2002
Log K_{ow}	1.26	EU List of Endpoints (LoE), 2002

Tab. 162. Environmental fate.

Endpoint	Value	Source
Sorption potential K_{OC}	27	EU List of Endpoints (LoE), 2002
Partition coefficient solid-water in sediment Kpsed (L/kg)	615	EU List of Endpoints (LoE), 2002
Bioaccumulation (BAF)	NRB	
Biomagnification (BMF)	3.15	EPI Suite, BCFBAF vers. 3.01

Tab. 163. Analytical methods.

Method	LOD (µg/L)	Description	Reference
SPE-UHPLC-MS/MS	MDL 0.03 ng/L MQL 0.08 ng/L	Water: SPE preconcentration of 500mL on Oasis HLB	(Sousa et al. 2019)
LC-TOFMS	LOQ 4.3 ng/L	Surface or wastewater: SPE preconcentration of 200mL on Oasis HLB	(Robles-Molina et al., 2014)
HPLC-MS/MS	MDL 3.8 ng/L	Water: SPE preconcentration of 1 L on Oasis HLB	(Hladik et al. 2012) In JRC report
HPLC-MS/MS	MDL 1 ng/L	Surface water: SPE preconcentration of 100 mL on Oasis HLB e Strata X	(Hao et al., 2015)
HPLC-MS/MS	LOD 0.10 ng/L	Surface Water: passive sampler POCIS equipped with a prototype newly synthesized SPE	(Xiong et al., 2019)

Method	LOD (µg/L)	Description	Reference
HPLC-MS/MS	MDL 0.1 ng/L	Surface water: SPE preconcentration of 10 mL using On –line SPE. SPE cartridge Hyspere 18HD	(Rubirola et al., 2017)
HPLC-MS/MS	LOD 2.5 ng/L	Surface water: SPE preconcentration of 1 L on Oasis HLB	(De Liguoro et al., 2014)
HPLC-MS/MS	LOQ <0.05 ng/L	Water: SPE preconcentration of 500 mL on PolySery HLB	(Zhang et al., 2019)
HPLC-MS/MS	LOQ <0.005 ng/g	Sediment: 5g freeze-dried sediment was extracted using the dispersive liquideliquid microextraction.	(Zhang et al., 2019)
HPLC-MS/MS	LOQ 10 ng/g	Bees: 2 gr of matrix extracted using QuEChERS.	(Niell et al., 2015)
HPLC-MS/MS	LOQ 1 ng/g	Odonate Nymphs: 0.5-0.2 gr of matrix extracted using QuEChERS.	(Jesus et al., 2018)

4.3.1 Environmental exposure assessment

Tab. 164. Environmental Emissions.

	Description/value
Use(s)	Active substance as insecticide
Total production or total emissions (tonnes/year)	NA
Information on emissions in Veneto	Thiacloprid is sold Veneto (trade name Calypso) (ARPAV, 2017; Il Ministero dell'Ambiente, 2017)
Possible contacts for relevant information	ARPAV for the quantities per area (spatial distribution)

Tab. 165. Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source
Measured concentration in	Range of mean values 0.40-0.90 ng/L	Surface waters	Water of the Pearl Rivers, South China	(Zhang et al., 2019)

	Value	Matrix	Region/area	Source
water MEC_w (µg/L)	1) <LOQ; 2) 0.116 µg/L; 3) 0.03 µg/L; 4) 0.14 µg/L (NL);			1)WATERBASE, 2014; 2) SE pesticide monitoring programme; 3) IT monitoring programme; 4) NORMAN DB, 2014; (Negrao de Carvalho et al., 2015)
Measured concentration in sediment MEC_{sed} (µg/kg dw)	Range of mean values 0.01-0.11 ng/g dw	Sediment	Water of the Pearl Rivers, South China	(Zhang et al., 2019)

Tab. 166. Predicted Environmental Concentrations.

	Value/Description	Model or method used for the prediction	Source
Predicted concentrations in water PEC_w (µg/L)	0.0109	FOCUS Step 2 (TOXSWA, 2001)	(Negrao de Carvalho et al., 2015)
Predicted concentrations in sediment PEC_{sed} (mg/kg dw)	0.042	FOCUS Step 2 (TOXSWA, 2001)	(Negrao de Carvalho et al., 2015)
Predicted concentrations in biota PEC_{biota} (mg/kg)	0.034	$PEC_{biota} = PEC_{fw} \times BCF \times BMF$	(ECHA, 2012)

Tab. 167. P, B, T, C, M, R, ED properties

	YES/NO	Source
Persistent (P) Bioaccumulative (B) Toxic (T)	NO NO YES	(EC, 2008a)
Carcinogenic (C) Mutagenic (M)	YES NO	(EC, 2008a)+*

Tab. 168. Ecotoxicological data.

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
Crustacea				

Americamysis bahia	96-h	Mortality	EC$_{50}$ = 31-50	Morrissey et al., 2015 Wildlife International Inc.[1]
	32-d	Growth	LOEC = 2,2	Wildlife International Inc.[1]
Fishes				
Cyprinodon variegatus	96-h	Mortality	LC$_{50}$ = 19.700	Bayer Co., Agricultural Division, U.S.[1]

[1] Data available at USEPA OPP Pesticide Ecotoxicity Database,
http://www.ipmcenters.org/Ecotox/DataAccess.cfm
LOEC = Lowest Observed Effect Concentration
LC$_{50}$/EC$_{50}$ = Lethal/Effective Concentration 50

Tab. 169. Biochemical and genetic responses.

Species	Concentrations	Days of exposure	Biochemical/molecular effects	Reference
Freshwater mussels *Lampsilis fasciola*	1000 µg/L	48h	Reduction in the viability of glochidia (<10 %),	Prosser et al., 2016.
Mussels *Mytilus galloprovincialis*	0.1, 1, and 10 mg/L	4 days	Decrease in lysosomal membrane stability of gonad tissue; increase of AChE activity only at 1000 µg/L.	Dondero et al., 2010.

Tab. 170. Derivation of PNEC values.

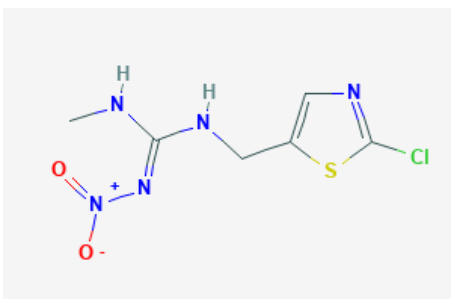| PNEC	Endpoint	Endpoint value (µg/L)	AF	Source
5E-05 mg/L	Chironomus riparius, 28 d, NOEC , number and time of emergence	0.0005 mg/L	10	(EC, 2008a)
0.035 mg/L	ADI	0.01 mg/kg bw/day		(Negrao de Carvalho et al., 2015) ADI value, retrieved from (EC, 2004b)

Tab. 171. Risk Quotient (MEC or PEC/PNEC).

MEC o PEC/PNEC	Source
218.00 (PEC/PNEC)	(Negrao de Carvalho et al., 2015)
0.31 (PEC/PNEC)	(Negrao de Carvalho et al., 2015)

4.4 Clothianidin

Clothianidin is a neonicotinoid, systemic insecticide acting as acute contact and stomach poison. Clothianidin belongs to the chemical class of insecticides known as neonicotinoid and is classified by the Insecticide Resistance Action Committee (IRAC) as "nicotinic Acetylcholine receptor agonist/antagonist". Clothianidin has a broad spectrum of activity, particularly against sucking insects such as aphids, leaf hoppers, thrips and white flies. Furthermore, various species of beetles (e.g. Atomaria spp., Agriotes lineatus, Diabrotica spp.) and some species of flies (e.g. Oscinella frit and Pegomyia spp.) and cut worm (e.g. Agrotis spp.) are effectively controlled. Clothianidin shows no efficacy against spider mites and nematodes. Products containing clothianidin are used as foliar and soil applications as well as seed treatments (FAO, 2011).

The uses as seed treatment and soil treatment of plant protection products containing clothianidin should be prohibited for crops attractive to bees and for cereals except for uses in greenhouses and for winter cereals. Foliar treatments with plant protection products containing clothianidin, should be prohibited for crops attractive to bees and for cereals with the exception of uses in greenhouses and uses after flowering (EC, 2013).

Tab. 172. Substance identity.

Parameters	Clothianidin
Name	Celero
Other names	1-[(2-chloro-1,3-thiazol-5-yl)methyl]-3-methyl-2-nitroguanidine
IUPAC name	210880-92-5
CAS number	C6H8Cl N5O2S
Molecular formula	249.7
Molecular weight	Clothianidin
Structure	
SMILES	CN/C(:N\N(:O)[O-])/NCc1cnc(s1)Cl

Metabolites (or other related substances)	CTM-i, cACT, 2-chlorothiazol-5-Ylmethylamine, MG, NG-F, Methylguanidine, CTNU, N-(2-chlorothiazol-5-ylmethyl)-N'-nitrourea, MIO, 4-hydroxy-2-methylamino-2-imidazolin-5-one, MIT, 7-methylamino-4H-imidazo[5,1-b][1,2,5]thiadiazin-4-one, Formamide, Methylurea in water TZNG, CLO-dm N-(2-chlorothiazol-5- ylmethyl)-N'-Nitroguanidine, CLO-NH, TMG, N-(2-chlorothiazol-5-ylmethyl)-N'-methylguanidine, CLO-Urea, TZMU, N-(2-chlorothiazol-5-ylmethyl)-N-methylurea, CLO-dm-Urea, TZU, 2-chloro-1, 3-thiazole-5-ylmethylurea, MNG, NG-E, N-methyl-N-nitroguanidine, NG-G, NTG, nitroguanidine, DIN-Urea, UF, 1-Methyl-3-(tetrahydro-3-furylmethyl)urea, these methabolites are produced in soil (Simon-Delso et al., 2015)

Tab. 173. Physico-chemical properties.

Endpoint	Value	Source
Vapour pressure (Pa)	1.3E-10	Biocide Assessment Report, 2007
Water solubility (mg/L)	327	Biocide Assessment Report, 2007
Log K_{ow}	0.7	Biocide Assessment Report, 2007

Tab. 174. Environmental fate.

Endpoint	Value	Source
Sorption potential K_{OC}	160	EU Review Report, 2005
Biodegradability	NRB	Biocide Assessment Report, 2007
Bioconcentration (BCF)	a) BCFfish 0.78 b) BCF 3.16 (estimated)	a) Biocide Assessment Report, 2007 b) EPI Suite, BCFBAF V3.01

Tab. 175. Analytical methods.

Method	LOD (µg/L)	Description	Reference
SPE-UHPLC-MS/MS	MDL 0.24 ng/L MQL 0.73 ng/L	Water: SPE preconcentration of 500mL on Oasis HLB	(Sousa et al., 2019)
LC-TOFMS	LOQ 58.7 ng/L	Surface or wastewater: SPE preconcentration of 200mL on Oasis HLB	(Robles-Molina et al., 2014)
HPLC-MS/MS	MDL 6.2 ng/L	Water: SPE preconcentration of 1 L on Oasis HLB	(Hladik et al., 2012) In JRC report
LC-MS/MS	LOD 17 ng/L	Water: 10mL QuEChERS	(Schaafsma et al., 2015)
HPLC-MS/MS	MDL 2 ng/L	Surface water: SPE preconcentration of 100 mL on Oasis HLB e Strata X	(Hao et al., 2015)

Method	LOD (μg/L)	Description	Reference
HPLC-MS/MS	LOD 0.5 ng/L	Surface Water: passive sampler POCIS equipped with a prototype newly synthesized SPE	(Xiong et al., 2019)
HPLC-MS/MS	MDL 0.3 ng/L	Surface water: SPE preconcentration of 10 mL using On –line SPE. SPE cartridge Hyspere 18HD	(Rubirola et al., 2017)
HPLC-MS/MS	LOD 2.5 ng/L	Surface water: SPE preconcentration of 1 L on Oasis HLB	(De Liguoro et al., 2014)
HPLC-APPI-MS/MS	MDL 0.62ng/L	Surface water: SPE preconcentration of 500 mL on Oasis HLB	(Yamamoto et al., 2012)
HPLC-MS/MS	LOQ 1.2 ng/L	Water: SPE preconcentration of 500 mL on Oasis HLB	(Main et al., 2014)
HPLC-MS/MS	LOQ <0.05 ng/L	Water: SPE preconcentration of 500 mL on PolySery HLB	(Zhang et al., 2019)
LC-MS/MS	LOD 23 ng/l	Soil: 10g using QuEChERS	(Schaafsma et al., 2015)
HPLC-MS/M	MDL 23 ng/L	Soil: exytraction of 10 g with QuEChERS	(Schaafsma et al., 2015)
HPLC-MS/MS	LOQ <0.005 ng/g	Sediment: 5g freeze-dried sediment was extracted using the dispersive; liquideliquid microextraction.	(Zhang et al., 2019)
HPLC-MS/MS	LOQ 1 ng/g	Bees: 2 gr of matrix extracted using QuEChERS.	(Niell et al., 2015)
HPLC-MS/MS	LOQ 1 ng/g	Odonate Nymphs: 0.5-0.2 gr of matrix extracted using QuEChERS.	(Jesus et al., 2018)

4.4.1 Environmental exposure assessment

Tab. 176. Environmental Emissions.

	Description/value
Use(s)	Active substance as insecticide
Total production or total emissions (tonnes/year)	NA
Information on emissions in Veneto	Clothianidin is sold Veneto (trade name Dantop) (ARPAV, 2017; Il Ministero dell'Ambiente, 2017)

	Description/value
Possible contacts for relevant information	ARPAV for the quantities per area (spatial distribution)

Tab. 177. Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source
Measured concentration in water MEC$_w$ (µg/L)	3 ng/L	Ground waters	Veneto, Italy	(De Liguoro et al., 2014)
	BDL-51.7 ng/L BDL-159 ng/L	Ave River Water Sousa River Water	Portugal	(Sousa et al., 2019)
	25.6±8.90 ng/L	Urban waterways	Waters collected near the Pearl River Guangzhou, China	(Xiong et al., 2019)
	Geometric mean 3.5 and 2.9 ng/L August 2009 and May 2010	Surface waters	Rivers of Osaka, Japan	(Yamamoto et al., 2012)
	Range 1.1-57.8 ng/L	Surface waters	Water from Prairie wetlands, Canada	(Main et al., 2014) In JRC report
	Range 2.0-27.0 ng/L	River water	Great Lakes tributaries, USA	(Hladik et al., 2018)
	Range of mean values 13.9-49.7 ng/L	Surface waters	Water of the Pearl Rivers, South China	(Zhang et al., 2019)
Measured concentration in sediment MEC$_{sed}$ (µg/kg dw)	Range of mean values 0.17-0.31 ng/g dw	Sediment	sediment of the Pearl Rivers, South China	(Zhang et al., 2019)

Tab. 178. Predicted Environmental Concentrations.

	Value/Description	Matrix	Model or method used for the prediction	Source
Predicted concentrations in water PEC$_w$ (µg/L)	0.008	freshwater	FOCUS Step 2 (TOXSWA, 2001)	
Predicted concentrations in sediment PEC$_{sed}$ (mg/kg dw)	0.014		FOCUS Step 2 (TOXSWA, 2001)	

	Value/Description	Matrix	Model or method used for the prediction	Source
Predicted concentrations in biota PEC$_{biota}$ (mg/kg)	0.025		PEC$_{biota}$ = PEC$_{fw}$ X BCF X BMF	(ECHA, 2012)

Tab. 179. P, B, T, C, M, R, ED properties

	YES/NO	Source
Persistent (P) Bioaccumulative (B) Toxic (T)	NO NO YES	(Negrao de Carvalho et al., 2015)
Carcinogenic (C) Mutagenic (M) Reproduction toxicity (R)	NO NO NO	(Negrao de Carvalho et al., 2015)
Endocrine Disruptive (ED)	NO	(Negrao de Carvalho et al., 2015)

Tab. 180. Ecotoxicological data.

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
Algae				
Skeletonema costatum	96-h	Growth (biomass)	EC$_{50}$ = 17.600	Bayer Co., Agricultural Division, U.S.[1]
Crustacea				
Americamysis bahia	96-h	Mortality	LC$_{50}$ = 51	Wildlife International Inc.[1]
	39-d	Eggs hatchability	LOEC = 9,7	Wildlife International Inc.[1]
Leptocheirus plumulosus	10-d	Mortality	LC$_{50}$ = 3,23 (OW) LC$_{50}$ = 20,4 (PW)	Wildlife International Inc.[1]
Mollusca				
Crassostrea virginica	96-h		EC$_{50}$ = 129.140	Dr. V. Noack Lab for Applied Biology, Sarstedt, Germany[1]
Fishes				

| *Cyprinodon variegatus* | 96-h | Survival | LC$_{50}$ = 93.600 | Dr. V. Noack Lab for Applied Biology, Sarstedt, Germany[1] |

[1] Data available at USEPA OPP Pesticide Ecotoxicity Database,
http://www.ipmcenters.org/Ecotox/DataAccess.cfm
OW = overlying water; PW = porewater
LOEC = Lowest Observed Effect Concentration
LC$_{50}$/EC$_{50}$ = Lethal/Effective Concentration 50

Tab. 181. Biochemical and genetic responses.

Species	Concentrations	Days of exposure	Biochemical/molecular effects	Reference
Freshwater mussel *Dreissena bugensis*	1 and 10 mg/L	12 and 14 days	Enhancement of the multi-xenobiotic resistance (MXR) activity (chemo stimulation).	Vehovszky et al., 2018.
Freshwater mussel *Lampsilis fasciola*	1000 µg/L	48h	Reduction in the viability of glochidia (<10 %).	Prosser et al., 2016.
Freshwater mussels *Lampsilis siliquoidea* And *Villosa iris (glochidia)*	9033 µg/L 13800 µg/L	28 days 24 h	Reduction of juvenile viability (<22%), while in adults no effect in survival was observed. Reduction in the viability of glochidia (<8,2 %).	Salerno et al., 2018.

Tab. 182. Derivation of PNEC values.

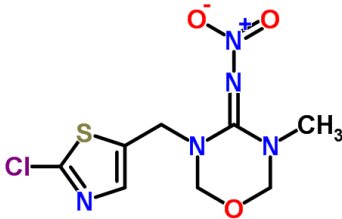| PNEC	Endpoint	Endpoint value (µg/L)	AF	Source
1.3E-04 mg/L	Chironomus riparius, 28d, EC10	0.00065 mg/L	5	(Negrao de Carvalho et al., 2015)
0.340 mg/L	ADI	0.097 mg/kg bw/day		(Negrao de Carvalho et al., 2015)

Tab. 183. Risk Quotient (MEC or PEC/PNEC).

MEC o PEC/PNEC	Source
61.54	(Negrao de Carvalho et al., 2015)
0.02	(Negrao de Carvalho et al., 2015)

4.5 Thiamethoxam

Thiamethoxam is a neonicotinoid insecticide with a broad spectrum of activity against many types of insects.

Tab. 184. Substance identity.

Parameters	
Name	Thiamethoxam
Other names	CHEBI:39185
IUPAC name	3-[(2-Chloro-1,3-thiazol-5-yl)methyl]-5-methyl-N-nitro-1,3,5-oxadiazinan-4-imine
CAS number	153719-23-4
Molecular formula	C8H10ClN5O3S
Molecular weight	291.71
Structure	
SMILES	CN1COCN(C1:N[N+](:O)[O-])Cc2cnc(s2)Cl
Metabolites (or other related substances)	Clothianidin in soil5-methyl-2(3H)-thiazolone, oxazine derivative, acrylonitrile derivative, carbonyl sulfide and isocyanic acid, CTM-i, cACT, 2-chlorothiazol-5-Ylmethylamine, MG, NG-F, Methylguanidine, CTNU, N-(2-chlorothiazol-5-ylmethyl)-N'-nitrourea, MIO, 4-hydroxy-2-methylamino-2-imidazolin-5-one, MIT, 7-methylamino-4H-imidazo [5,1-b][1,2,5]thiadiazin-4-one, Formamide, Methylurea in water TZNG, CLO-dm, N-(2-chlorothiazol-5- ylmethyl)-N'-Nitroguanidine, CLO-NH, TMG, N-(2-chlorothiazol-5-ylmethyl)-N'-methylguanidine, CLO-Urea, TZMU, N-(2-chlorothiazol-5-ylmethyl)-N-methylurea, CLO-dm-Urea, TZU, 2-chloro-1, 3-thiazole-5-ylmethylurea, MNG, NG-E, N-methyl-N-nitroguanidine, NG-G, NTG, nitroguanidine, DIN-Urea, UF, 1-Methyl-3-(tetrahydro-3-furylmethyl)urea, these methabolites are produced in soil (Simon-Delso et al., 2015)

Tab. 185. Physico-chemical properties.

Endpoint	Value	Source
Vapour pressure (Pa)	6.6 E-09	Biocide Assessment Report
Water solubility (mg/L)	4100	Biocide Assessment Report

Endpoint	Value	Source
Log K_{ow}	-0.13	Biocide Assessment Report

Tab. 186. Environmental fate.

Endpoint	Value	Source
Sorption potential K_{OC}	56.2	Biocide Assessment Report
Biodegradability	NRB	Biocide Assessment Report
Bioconcentration (BCF)	3.16 (estimanted)	EPI Suite BCFBAF, v.3.01
Biomagnification (BMF)	1	Default value, TG n. 27 - CIS WFD

Tab. 187. Analytical methods.

Method	LOD (µg/L)	Description	Reference
SPE-UHPLC-MS/MS	MDL 1.22 ng/L MQL 3.71 ng/L	Water: SPE preconcentration of 500mL of water on Oasis HLB	(Sousa et al., 2019)
LC-TOFMS	LOQ 42.6 ng/L	Surface or wastewater: SPE preconcentration of 200mL of water on Oasis HLB	(Robles-Molina et al., 2014)
HPLC-MS/MS	MDL 3.9 ng/L	Water: SPE preconcentration of 1 L of water on Oasis HLB	(Hladik et al., 2012) In JRC report
LC-MS/MS	LOD 4 ng/L	Water: 10mL QuEChERS	(Schaafsma et al., 2015)
HPLC-MS/MS	MDL 2 ng/L	Surface water: SPE preconcentration of 100 mL of water on Oasis HLB e Strata X	(Hao et al., 2015)
HPLC-MS/MS	LOD 0.25 ng/L	Surface Water: passive sampler POCIS equipped with a prototype newly synthesized SPE	(Xiong et al., 2019)
HPLC-MS/MS	LOQ < 1.5 ng/L	Coastal seawater: SPE preconcentration of 1 L of water on Oasis HLB	(Xie et al., 2019)
HPLC-MS/MS	MDL 0.5 ng/L	Surface water: SPE preconcentration of 10 mL using On –line SPE. SPE cartridge Hyspere 18HD	(Rubirola et al., 2017)
HPLC-MS/MS	LOD 2.5 ng/L	Surface water: SPE preconcentration of 1 L on Oasis HLB	(De Liguoro et al., 2014)

Method	LOD (µg/L)	Description	Reference
HPLC-APPI-MS/MS	MDL 0.63 ng/L	Surface water: SPE preconcentration of 500 mL on Oasis HLB	(Yamamoto et al., 2012)
HPLC-MS/MS	LOQ <0.05 ng/L	Water: SPE preconcentration of 500 mL on PolySery HLB	(Zhang et al., 2019)
HPLC-MS/MS	LOQ 1.8 ng/L	Water: SPE preconcentration of 500 mL on Oasis HLB	(Main et al., 2014) In JRC report
LC-MS/MS	LOD 17 ng/l	Soil: 10g using QuEChERS	(Schaafsma et al., 2015)
HPLC-MS/M	MDL 17 ng/L	Soil: exytraction of 10 g with QuEChERS	(Schaafsma et al., 2015)
HPLC-MS/MS	LOQ <0.005 ng/g	Sediment: 5g freeze-dried sediment was extracted using the dispersive; liquideliquid microextraction.	(Zhang et al., 2019)
HPLC-MS/MS	LOQ 10 ng/g	Bees: 2 gr of matrix extracted using QuEChERS.	(Niell et al., 2015)
HPLC-MS/MS	LOQ 10 ng/g	Odonate Nymphs: 0.5-0.2 gr of matrix extracted using QuEChERS.	(Jesus et al., 2018)

4.5.1 Environmental exposure assessment

Tab. 14. Environmental Emissions.

	Description/value
Use(s)	Active substance as insecticide
Total production or total emissions (tonnes/year)	NA
Information on emissions in Veneto	Thiamethoxan is sold Veneto (trade name Cruiser, Actara, Luzindo) (ARPAV, 2017; Il Ministero dell'Ambiente, 2017)
Possible contacts for relevant information	ARPAV for the quantities per area (spatial distribution)

Tab. 189. Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source
Measured concentration in	BDL-154 ng/L BDL-17.8 ng/L	Ave River Water Sousa River Water	Portugal	(Sousa et al., 2019)

	Value	Matrix	Region/area	Source
water MEC_w (µg/L)	10.9±13.2 ng/L	Urban waterways	Waters collected near the Pearl River Guangzhou, China	(Xiong et al., 2019)
	Range ND-2.8 ng/L Mean 2.7 ng/L	Coastal sea waters	coastal waters around the Liaodong Peninsula, China	(Xie et al., 2019)
	Geometric mean 1.5 and 3.8 ng/L August 2009 and May 2010	Surface waters	Rivers of Osaka, Japan	(Yamamoto et al., 2012)
	Range 1.3-41.9 ng/L	Surface waters	Water from Prairie Wetlands, Canada	(Main et al., 2014) In JRC report
	Range 3.7-4.2 ng/L	River water	Great Lakes tributaries, USA	(Hladik et al., 2018)
	630 ng/L	Surface waters	Mekong River delta, Vietnam	(Chau et al., 2015)
	Range of mean values 29.4-79.5 ng/L	Surface waters	Water of the Pearl Rivers, South China	(Zhang et al., 2019)
Measured concentration in sediment MEC_{sed} (µg/kg dw)	Range of mean values 0.08-0.18 ng/g dw	Sediment	sediment of the Pearl Rivers, South China	(Zhang et al., 2019)

Tab. 15. Predicted Environmental Concentrations.

	Value/Description	Model or method used for the prediction	Source
Predicted concentrations in water PEC_w (µg/L)	0.011	FOCUS Step 2 (TOXSWA, 2001)	(Negrao de Carvalho et al., 2015)
Predicted concentrations in sediment PEC_{sed} (mg/kg dw)	0.0074	FOCUS Step 2 (TOXSWA, 2001)	(Negrao de Carvalho et al., 2015)

	Value/Description	Model or method used for the prediction	Source
Predicted concentrations in biota PEC$_{biota}$ (mg/kg)	0.035	PEC$_{biota}$ = PEC$_{fw}$ X BCF X BMF	(ECHA, 2012)

Tab. 16. P, B, T, C, M, R, ED properties

	YES/NO	Source
Persistent (P) Bioaccumulative (B)	YES NO	(EC, 2008b); (FAO/WHO, 2010)
Carcinogenic (C) Mutagenic (M)	NO YES	(EC, 2008b); (FAO/WHO, 2010)

Tab. 17. Ecotoxicological data.

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
Algae				
Skeletonema costatum	72-h and 96-h	Growth rate	NOEC > 99.000	Finnegan et al., 2017
		Biomass	NOEC = 48.000	
		Yield	NOEC > 99.000	
Mollusca				
Crassostrea virginica	96-h	Growth inhibition	NOEC = 119.000	Finnegan et al., 2017
			EC$_{50}$ > 119.000	
Crustacea				
Americamysis bahia	96-h	Mortality	EC$_{50}$ = 6.900	Finnegan et al., 2017
Americamysis bahia	28-d	Postpairing survival	NOEC = 1.100	Finnegan et al., 2017
		Overall survival	NOEC = 560	
		F1 survival	NOEC = 2.000	
		Offspring production	NOEC = 2.000	
		Length	NOEC = 3.900	
		Weight	NOEC = 3.900	

Fishes

Cyprinodon variegatus	96-h	Mortality	EC_{50} > 111.000	Finnegan et al., 2017
Cyprinodon variegatus	33-d	Hatching success	NOEC = 9.900	Finnegan et al., 2017
		Normal hatch	NOEC = 9.900	
		Larval survival	NOEC = 9.900	
		Larval length	NOEC = 1.700	
		Wet weigth	NOEC = 9.900	

NOEC = Non Observed Effect Concentration
EC50 = Effective Concentration 50

Tab. 18. Biochemical and genetic responses.

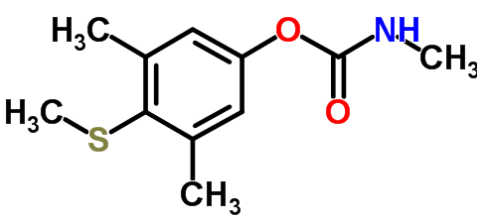| Species	Concentrations	Days of exposure	Biochemical/molecular effects	Reference
Freshwater mussels *Dreissena bugensis*	1 and 10 mg/L	12-14days	Enhancement of the multi-xenobiotic resistance (MXR) activity (chemo stimulation).	Vehovszky et al., 2018.
Freshwater mussels *Lampsilis fasciola*	1000 µg/L	48h	Reduction in the viability of glochidia (<10 %).	Prosser et al., 2016.
Freshwater mussels *Villosa iris (glochidia)*	17400 µg/L	24 h	Slight reduction in the viability of glochidia (<1.1%).	Salerno et al., 2018.

Tab. 19. Derivation of PNEC values.

PNEC	Endpoint	Endpoint value (µg/L)	AF	Source
0.00014 mg/L	Cleon sp. (Ephemeroptera), 48 h, EC50	0.014 mg/L	100	(EC, 2008b)
0.091 mg/L	ADI	0.026 mg/kg bw/day		(Negrao de Carvalho et al., 2015)ADI from EU LoE, 2006 (EFSA, 2013)

Tab. 20. Risk Quotient (MEC or PEC/PNEC).

MEC o PEC/PNEC	Source
78.57 (PEC/PNEC)	(Negrao de Carvalho et al., 2015)

4.6   Acetamiprid

Tab. 196. Substance identity.

Parameters	
Name	Acetamiprid
Other names	Mospilan, Intruder; Stonkat
IUPAC name	N-[(6-chloropyridin-3-yl)methyl]-N'-cyano-N-methylethanimidamide
CAS number	135410-20-7/160430-64-8
Molecular formula	C10H11ClN4
Molecular weight	222.67
Structure	H₃C, O, NH, CH₃, H₃C, S, CH₃
SMILES	C/C(:N\C#N)/N(C)Cc1ccc(nc1)Cl
Metabolites (or other related substances)	IM-1-3, N-[(6-chloro-3-pyridyl)methyl]-N-methylacetamide, ACE-acet, ACE-urea in soil and water Acetamiprid-D-desmethyl, N-desmethyl acetamiprid, IM-2-1, ACE-dm, N-(6-Chloro-3-pyridylmethyl)-N'-cyanoacetamidine, IM-1-2, N2-carbamoyl-N1- [(6-chloro-3-pyridyl)methyl]-N1-methylacetamidine, ACE-NCONH2, IM-1-4, N-methyl(6-chloro-3-pyridyl)methylamine, Nmethylpyridinylmethylamine, ACE-NH, descyano derivative, N-methylpyridinylmethylamine, (E)-1-ethylideneurea in soil (Simon-Delso et al., 2015)

Tab. 21. Physico-chemical properties.

Endpoint	Value	Source
Vapour pressure (Pa)	1E-06Pa (25°C)	EU Review Report, 2004
Water solubility (mg/L)	2950 (pH 7, 25°C)	EU Review Report, 2004
Log K_{ow}	0.8 (25°C)	EU Review Report, 2004

Tab. 2298. Environmental fate.

Endpoint	Value	Source
Sorption potential K_{OC}	106.5	EU Review Report, 2004
Biodegradability	NRB	EU Review Report, 2004
Bioconcentration (BCF)	3.16 (estimated)	EPisuite, BCFBAF v3.01

Tab. 2399. Analytical methods.

Method	LOD (µg/L)	Description	Reference
SPE-UHPLC-MS/MS	MDL 0.32 ng/L MQL 0.98 ng/L	Water: SPE preconcentration of 500mL on Oasis HLB	(Sousa et al., 2019)
LC-TOFMS	LOQ 12.9 ng/l	Surface or wastewater: SPE preconcentration of 200mL on Oasis HLB	(Robles-Molina et al., 2014)
HPLC-MS/MS	MDL 3.6 ng/l	Water: SPE preconcentration of 1 L on Oasis HLB	(Hladik et al., 2012) In JRC report
HPLC-MS/MS	MDL 2 ng/l	Surface water: SPE preconcentration of 100 mL on Oasis HLB e Strata X	(Hao et al., 2015)
HPLC-MS/MS	LOD 0.1 ng/L	Surface Water: passive sampler POCIS equipped with a prototype newly synthesized SPE	(Xiong et al., 2019)
UHPLC-MS/MS	LOD 5 ng/L	Surface water: SPE preconcentration of 100 mL on Oasis HLB	(Marin et al., 2009)
HPLC-MS/MS	MDL 0.2ng/L	Surface water: SPE preconcentration of 10 mL using On –line SPE. SPE cartridge Hyspere 18HD	(Rubirola et al., 2017)
HPLC-MS/MS	Groundwater LOD 3.5 ng/L Surface water LOD 3.2 ng/L	Water: SPE preconcentration of 1 L on Oasis HLB	(Dujakovic et al., 2010)
HPLC-MS/MS	LOD 2.5 ng/L	Surface water: SPE preconcentration of 1 L on Oasis HLB	(De Liguoro et al., 2014)
HPLC-APPI-MS/MS	MDL 0.82 ng/L	Surface water: SPE preconcentration of 500 mL on Oasis HLB	(Yamamoto et al., 2012)
HPLC-MS/MS	LOQ 0.5 ng/L	Water: SPE preconcentration of 500 mL on Oasis HLB	(Main et al., 2014) In JRC report

Method	LOD (µg/L)	Description	Reference
HPLC-MS/MS	LOQ <0.05 ng/L	Water: SPE preconcentration of 500 mL on PolySery HLB	(Zhang et al., 2019)
HPLC-MS/MS	LOQ <0.005 ng/g	Sediment: 5g freeze-dried sediment was extracted using the dispersive; liquideliquid microextraction.	(Zhang et al., 2019)
HPLC-MS/MS	LOQ 1 ng/g	Bees: 2 gr of matrix extracted using QuEChERS.	(Niell et al., 2015)
HPLC-MS/MS	LOQ 10 ng/g	Odonate Nymphs: 0.5-0.2 gr of matrix extracted using QuEChERS.	(Jesus et al., 2018)

4.6.1 Environmental exposure assessment

Tab. 200 Environmental Emissions.

	Description/value
Use(s)	Active substance as insecticide
Total production or total emissions (tonnes/year)	NA
Information on emissions in Veneto	Acetamiprid is sold Veneto (trade name Chopco, Epik, Polysect) (ARPAV, 2017; Il Ministero dell'Ambiente, 2017)
Possible contacts for relevant information	ARPAV for the quantities per area (spatial distribution)

Tab. 201 Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source
Measured concentration in water MEC$_w$ (µg/L)	3 ng/L	Ground waters	Veneto, Italy	(De Liguoro et al., 2014)
	51.2±32.5 ng/L	Urban waterways	Waters collected near the Pearl River Guangzhou, China	(Xiong et al., 2019)
	Geometric mean 1.4 ng/L, May 2010	Surface waters	Rivers of Osaka, Japan	(Yamamoto et al., 2012)
	Range 0.4-4.2 ng/L	Surface waters	Water from Prairie wetlands, Canada	(Main et al., 2014)

	Value	Matrix	Region/area	Source
	Range of mean values 9.42-24.7 ng/L	Surface waters	Water of the Pearl Rivers, South China	(Zhang et al., 2019)
Measured concentration in sediment MEC_{sed} (µg/kg dw)	Range of mean values 0.06-0.29 ng/g dw	Sediment	Sediment of the Pearl Rivers, South China	(Zhang et al., 2019)

Tab. 202. Predicted Environmental Concentrations.

	Value/Description	Matrix	Model or method used for the prediction	Source
Predicted concentrations in water PEC_w (µg/L)	0.005	freshwater	FOCUS Step 2 (TOXSWA, 2001)	
Predicted concentrations in sediment PEC_{sed} (mg/kg dw)	0.0045		FOCUS Step 2 (TOXSWA, 2001)	
Predicted concentrations in biota PEC_{biota} (mg/kg)	0.016		$PEC_{biota} = PEC_{fw} \times BCF \times BMF$	(ECHA, 2012)

Tab. 203. P, B, T, C, M, R, ED properties

	YES/NO	Source
Persistent (P) Bioaccumulative (B) Toxic (T)	NO NO NO	(EC, 2004a)
Carcinogenic (C) Mutagenic (M) Reproduction toxicity (R)	NO NO YES	(EC, 2004a)
Endocrine Disruptive (ED)	NO	(EC, 2004a)

Tab. 204. Ecotoxicological data.

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
Algae				
Skeletonema costatum	120-h	Growth	EC_{50} = 1.000	Springborn Laboratory Inc., Wareham[1]

Crustacea				
Americamysis bahia	96-h	Mortality	$EC_{50} = 66$	Morrissey et al., 2015
Americamysis bahia	28-d	Growth	$EC_{50} = 4,7$	Springborn Laboratory Inc., Wareham[1]
Fishes				
Cyprinodon variegatus	96-h	Mortality	$LC_{50} = 100.000$	Springborn Laboratory Inc., Wareham[1]

[1] Data available at USEPA OPP Pesticide Ecotoxicity Database,
http://www.ipmcenters.org/Ecotox/DataAccess.cfm
LC_{50}/EC_{50} = Lethal/Effective Concentration 50

Tab. 205. Biochemical and genetic responses.

Species	Concentrations	Days of exposure	Biochemical/molecular effects	Reference
Freshwater mussel *Lampsilis fasciola*	1000 µg/L	48h	Reduction in the viability of glochidia (<10 %)	Prosser et al., 2016.

Tab. 206. Derivation of PNEC values.

PNEC	Endpoint	Endpoint value (µg/L)	AF	Source
5.00E-04 mg/L	*Chironomus riparius*, 28d, emergence and developmental rate, NOEC	0.005 mg/L	10	(EC, 2004a)
0.245 mg/L	ADI	0.07mg/kg bw/day	-	(EC, 2004a)

Tab. 207. Risk Quotient (MEC or PEC/PNEC).

MEC o PEC/PNEC	Source
10	(Negrao de Carvalho et al., 2015)
0.02	(Negrao de Carvalho et al., 2015)

4.7 Analytical methods employed

The revision of literature available shows that the majority of studies were performed in surface and ground waters. Only one study deals with the quantification of thiamethoxam in marine coastal waters of China (Xie et al., 2019). The analytical technique mostly employed is LC-MS/MS, which guarantees sensitivity and selectivity, in order to obtain the low limit of detection required of 9 ng/L (DECISION (EU) 2015/495). It a choice of the author of paper expresses the sensitivity of an analytical method as: instrumental detection limit (LOD), instrumental quantification limit (LOQ) or method detection limit (MDL) or quantification limit (MQL) or a combination of these parameters. In table we report the information

available. In general published methods reports LOQ or MDL lower than 9 ng/L. Neonicotinoid compounds are generally extracted from water samples (volumes from 100mL to 1L) using SPE Oasis HLB cartridges. The analytes are eluted with methanol or mixture of methanol and dichloromethane or methanol and acetone. The extract is then concentrated to dryness and reconstituted with a solvent compatible with those used during HPLC analysis. Chromatographic separation is performed using reverse phase C18 stationary phase, using a mobile phase of water and methanol of water acetonitrile. Sometimes modifiers such as formic acid or acetic acid are employed. Due to the availability in our laboratory of a liquid chromatograph coupled to a triple quadrupole MS we chose as analytical technique the HPLC-MS/MS for the quantification of neonicotinoids. The sample preparation procedure reported in a great number of publications seems well established and we will extract target compound using the methodology previously described.

Different is the case of marine sediment of biota (mussels). Publications on these topics to the best of our knowledge are lacking. Some papers treat the analysis of these compounds in soil, river sediment, sludge, insects and fish. For the analysis of these matrices frequently a QuEChERS approach is chosen. The extract is then analysed using HPLC-MS/MS. Because this approach is very often used for solid matrixes we will employ it for the sample preparation procedure.

4.8   References

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5 Industrial chemicals

Industrial chemicals produced and potentially released in European atmosphere and waters are monitored under the Task Force on Pollutant Release and Transfer Registers (PRTRs) of the Organisation for Economic Co-operation and Development (OECD), in cooperation with the United Nations Economic Commission for Europe (UNECE). The European Pollutant Release and Transfer Register (E-PRTR (European Pollutant Release and Transfer Register, n.d.) is in line with the EU Directive on industrial emissions (European Parliament and the Council, 2010) and is organized as a geographical database, containing data for each of the 30000 industrial facilities covering more than 65 economic activities in Europe. Information concerns amounts of pollutant releases to air, water and land as well as off-site transfers of waste and of pollutants. Pollutants include heavy metals, pesticides, greenhouse gases and dioxins for the period 2007 until 2016 (EC, 2006).

Search can be country based, on the level of river basin or on administrative regions, and by pollutants group. Organic chemicals are covered in the following pollutants classes: chlorinated organic substances, other organic substances. The full list of pollutants considered in E-PRTR is listed in Annex II of Directive 2010/75/EU (European Parliament and the Council, 2010).

None of the chemicals monitored under this species are explicitly considered in the registry, thus it is not possible to make an assumption on the emitted quantities.
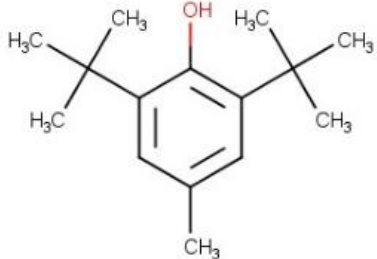
Cosmetics include a wide range of products, including hygiene-related products (soap, shampoo, toothpaste) and luxury products such as make up and perfumes. Europe is a leader in the global cosmetics and a dominant cosmetics exporter. EU regulation strengthen especially the safety of cosmetics, streamlines the framework for all operators in the sector (European Parliament and Council, 2009). The European Commission database for information on cosmetic substances and ingredients (CosIng) (EC, n.d.) contains all the chemicals applied in cosmetics, their INCHI, CASN, EC EINEC, and the regulation(s) under which the chemical is addressed, and when an opinion by the Scientific Committee on Consumer Safety (SCCS) is available. The European project Integrated In SilicoModels for the Prediction of Human Repeated Dose Toxicity of Cosmetics to Optimise Safety (COSMOS) also released a database on cosmetic ingredients where safety data are reported, and links to other institutional databases are highlighted (e.g. EFSA, ECHA) (Molecular Networks, n.d.). The use type of each chemical substance is reported in both COSMOS and CosIng. However, consumption data or production volumes are not indicated in the available databases, nor a link on the products containing the chemical substances identified in Venezia 2021. Thus, emissions estimates are not possible.

5.1 2,6-Di-tert-butyl-4-methylphenol (BHT)

2,6-di-tert-butyl-4-methylphenol (BHT) is an anti-oxidant commonly used since the 1950s to preserve and stabilize the freshness, nutritive value, flavour and colour of food and animal feed products. BHT is also used to improve the stability of pharmaceuticals and cosmetics and increase the durability of rubber and plastics (Barbosa et al., 2016). The use of BHT as a food additive is generally not considered to pose a public health risk and it has been detected in different aquatic environments (Barbosa et al., 2016). However, in the natural environment, BHT is degraded biologically to 3,5-di-tert-butyl-4-hydroxybenzaldehyde (BHT-CHO), which is reported to generate peroxides in mice and rats and induce cellular DNA damage (Barbosa et al., 2016). Additional data are needed to understand the human health and environmental risks associated with the exposure to this compound.

Tab. 208. Substance identity.

Parameters	

Name	2,6-ditert-butyl-4-methylphenol
Other names	Butylated Hydroxytoluene, 2,6-di-tert-butyl-p-cresol
IUPAC name	2,6-ditert-butyl-4-methylphenol
CAS number	128-37-0
Molecular formula	C15H24O
Molecular weight	220
Structure	
SMILES	CC1=CC(=C(O)C(=C1)C(C)(C)C)C(C)(C)C
Metabolites (or other related substances)	3,5-di-tert-butyl-4-hydroxybenzaldehyde (BHT-CHO)(Barbosa et al., 2016), BHT-CH2OH, BHT-CHO, BHT-COOH, BHT-Q, BHT-QM, DBP, BHT-OH, BHT-OOH, TBP, BHQ, BHT-OH(t), BHT-OH(t)QM, 2-BHT, and 2-BHT-QM (Nieva-Echevarría et al., 2015)

Tab. 209. Physico-chemical properties.

Endpoint	Value	Source

Vapour pressure (Pa)	0.39 Pa at 24.85 °C
	  1.1
		ECHA
		  (Negrao de Carvalho et al., 2015)

Water solubility (mg/L)	400 - 5748 µg/L at 20 - 30°C
	  0.76
		ECHA
		  (Negrao de Carvalho et al., 2015)

Log K_{ow}	4.17 - 5.1 at 37 °C
	  5.1
		ECHA
		  (Negrao de Carvalho et al., 2015)

Tab. 210. Environmental fate.

Endpoint	Value	Source

Sorption potential K_{OC}	23 030
	  8183
		ECHA
		  (Negrao de Carvalho et al., 2015)

Biodegradability	Under test conditions no biodegradation observed	ECHA
Bioconcentration (BCF)	598.4 L/kg ww	ECHA

Endpoint	Value	Source
Biomagnification (BMF)	2	(Negrao de Carvalho et al., 2015)

Tab. 211. Analytical methods.

Method	LOD (µg/L)	Description	Reference
Water: SPE + GC-MS	0.200	Watchlist.	(Sousa et al., 2019)
Water: SPE + GC-MS	-	RP-C18	(Bendz et al., 2005)
Water: SPE + GC-MS	0.005	Styrene divinyl benzene polymer	(Fries and Püttmann, 2004)
Sediment: ultrasonic extraction + GC-MS	0.00002 mg kg^{-1}	Extraction Hex:DCM 1:3, BSTFA derivatization	(Zhang et al., 2018)
Biota: ultrasonic extraction + GC-MS/MS	0.0014 mg kg^{-1}	Extraction Hex:DCM 1:3 + SPE purification	(Wang et al., 2018)

5.1.1 Environmental exposure assessment

Tab. 212. Environmental Emissions.

	Description/value	Reference
Use(s)	Industrial uses, use in plastics, rubber products, adhesives, coatings, dyes, fuel (biodiesel), use for the formulation of PPP, and biocides, use as laboratory reagent. Used as antioxidant in food. Uses in Europe (UK communication): Stabiliser for rubber (largely during polymerisation) (50%) Stabiliser for oils, lubricants and fuels (25%) Stabiliser for plastics (10%) Food additive/others (15%)	(Negrao de Carvalho et al., 2015)
Total production or total emissions (tonnes/year)	A confidential and recent tonnage value was used for calculation	(Negrao de Carvalho et al., 2015)

Tab. 213. Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source
Measured concentration in water MEC$_w$ (µg/L)	< MQL	River	Portugal	(Sousa et al., 2019)
	0.1 – 0.62	River	Sweden (Hoje River)	(Bendz et al., 2005)

	Value	Matrix	Region/area	Source
	0.025 -0.365	River	Germany (Frankfurt)	(Fries and Püttmann, 2004)
	0.026 – 0.049	Source drinking water	USA	(Benotti et al., 2009)
Measured concentration in sediment MEC$_{sed}$ (mg/kg dw)	0.09 –6.93	Lake sediment	China, Nanjing, Tai lake	(Zhang et al., 2018)
Measured concentration in biota MEC$_{biota}$ (mg/kg)	0.383 - 501	Mollusks	Chinese Bohai Sea	(Wang et al., 2018)

Tab. 214. Predicted Environmental Concentrations.

	Value/Description	Model or method used for the prediction	Source
Predicted concentrations in water PEC$_w$ (µg/L)	0.423	ECETOC	(Negrao de Carvalho et al., 2015)
Predicted concentrations in sediment PEC$_{sed}$ (mg/kg dw)	367.64	ECETOC	(Negrao de Carvalho et al., 2015)
Predicted concentrations in biota PEC$_{biota}$ (mg/kg)	2115	PEC$_{biota}$ = PEC$_{fw}$ X BCF X BMF	(ECHA, 2012)

Tab. 215. P, B, T, C, M, R, ED properties

	YES/NO	Source
Persistent (P)	YES	
Carcinogenic (C)	NO	

Tab. 216. Derivation of PNEC values.

PNEC	Endpoint	Endpoint value (µg/L)	AF	Source
3.16E-03 mg/L	*Daphnia magna*, 21 d, NOEC	0.316 mg/L	100	(Negrao de Carvalho et al., 2015)

PNEC	Endpoint	Endpoint value (µg/L)	AF	Source
1.290 mg/kg dw				(Negrao de Carvalho et al., 2015)
16.7 mg/kg food			30	(Negrao de Carvalho et al., 2015)
0.875 mg/L	DMEL	0.25 mg/kg bw/day		(Negrao de Carvalho et al., 2015)

Tab. 217. Risk Quotient (MEC or PEC/PNEC).

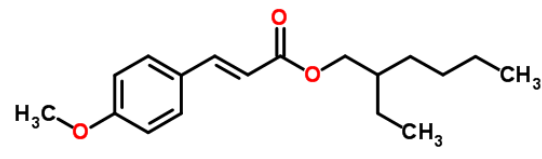| MEC o PEC/PNEC	Source
133.86	(Negrao de Carvalho et al., 2015)
283.24	(Negrao de Carvalho et al., 2015)
126.65	(Negrao de Carvalho et al., 2015)
138.99	(Negrao de Carvalho et al., 2015)
0.48	(Negrao de Carvalho et al., 2015)

5.2   EHMC

2-ethylhexyl-4-methoxycinnamate (EHMC) is an organic UV filter used in many personal care products. Its occurrence in the environment has been described in several papers that have been given a great attention to the aqueous matrices, entering in the environment by wash off from skin or through wastewater or swimming pool water and finally reaching the sediments ant the biota (Barbosa et al., 2016).

Organic UV filters have known estrogenic effects on biota and humans with recognized in vivo and in vitro estrogenic activity to fish and mammals, but also other non- estrogenic hormonal targets in such organisms. Little is known about the removal of EHMC in the aquatic environment, while in WWTPs it resulted refractory to ozonation, but could be removed by UV treatment (Barbosa et al., 2016).

Tab. 218. Substance identity.

Parameters	
Name	2-Ethylhexyl 4-methoxycinnamate
Other names	2-Ethylhexyl 4-methoxycinnamate
IUPAC name	2-Ethylhexyl 4-methoxycinnamate
CAS number	5466-77-3
Molecular formula	C18H26O3
Molecular weight	290.4

Parameters	
Name	2-Ethylhexyl 4-methoxycinnamate
Other names	2-Ethylhexyl 4-methoxycinnamate
IUPAC name	2-Ethylhexyl 4-methoxycinnamate
Structure	
SMILES	CCCCC(CC)COC(=O)/C=C/C1=CC=C(C=C1)OC

Tab. 219. Physico-chemical properties.

Endpoint	Value	Source
Vapour pressure (Pa)	30	(Negrao de Carvalho et al., 2015)
Water solubility (mg/L)	0.75	(Negrao de Carvalho et al., 2015)
Log K_{ow}	>6	(Negrao de Carvalho et al., 2015)

Tab. 220. Environmental fate.

Endpoint	Value	Source
Sorption potential K_{OC}	13290	(Negrao de Carvalho et al., 2015)
Biodegradability	Readily biodegradable	(Negrao de Carvalho et al., 2015)
Bioconcentration (BCF)	433	(Negrao de Carvalho et al., 2015)
Biomagnification (BMF)	1	(Negrao de Carvalho et al., 2015)

Tab. 221. Analytical methods.

Method	LOD (µg/L)	Description	Reference
Water: SPE + UHPLC-MS/MS	0.00267	Watchlist. ESI + Kinetex XB- C18.	(Sousa et al., 2019)
Water: USAEME + GC-MS/MS	0.00066	Ultrasound-assisted emulsification microextraction	(Vila et al., 2016)
Water: DLLME + GC-MS	0.014	Dispersive liquid–liquid microextraction	(Negreira et al., 2010)
Water: SPE + HPLC-MS/MS	0.001	Automated on-line SPE-LC-ESI-(QqLIT) MS/MS	(Rubirola et al., 2017)

Method	LOD (µg/L)	Description	Reference
Water: SPE + LC-MS/MS	0.001	Exactive Orbitrap HR-LC-MS	(Picot-Groz et al., 2018)
Water: SPE + GC-MS	0.0001 – 0.003*	DSC-18LT, DSC-PH eluted with DCM	(Kameda et al., 2011)
Sediment: ultrasonic extraction + GC-MS	0.002 mg kg^{-1}	Extraction with DCM and multiple column purification	(Kameda et al., 2011)
Sediment: ASE + GC-MS/MS	0.000003 - 0.00054 mg kg^{-1}*	In cell purification (alumina); extraction with DCM.	(Combi et al., 2016)
Sediment: PLE + GC-MS/MS	0.0003 mg kg^{-1}*	In cell purification (alumina); extraction with DCM.	(Pintado-Herrera et al., 2016)
Sediment: ASE + HPLC-MS/MS	0.0016 mg kg^{-1}*	In cell purification (alumina); extraction with MeOH.	(Mizukawa et al., 2017)
Sediment: Microwave + GC-MSn	0.0015 mg kg^{-1}*	Acetone-Heptane extraction. Ion trap analyser.	(Amine et al., 2012)
Biota: QuEChERS + DLLME + GC-MS	0.0005 - 0.015 mg kg^{-1}*	QuEChERS followed by dispersive liquid–liquid microextraction.	(Castro et al., 2018)
Biota: QuEChERS + GC-MS/MS	0.0005 mg kg^{-1}	QuEChERS + derivatization	(Cunha et al., 2018)
Biota: ASE + HPLC–MS/MS	0.005 mg kg^{-1}	Extraction with AcEt/DCM and in cell purification with florisil + Isolute C18	(Gago-Ferrero et al., 2015)
Biota: QuEChERS + GC-MS/MS	<0.010 mg kg^{-1}*	GC Ultra Trace TSQ Quantum GC XLS	(Picot-Groz et al., 2018)

* range of different analytes

5.2.1 Environmental exposure assessment

Tab. 222. Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source
Measured concentration in water MEC$_w$ (µg/L)	0.0054 - 7.552	River	Portugal	(Sousa et al., 2019)
	0.019 – 0.813	River	Spain	(Negreira et al., 2010)

	Value	Matrix	Region/area	Source
	0.010 – 0.059	River	Spain	(Vila et al., 2016)
	0.0089 0.640	River	Australia (Melbourne)	(Allinson et al., 2018)
	< 0.001 – 0.106	Seawater	France (Montpellier)	(Picot-Groz et al., 2018)
	0.012 – 1.4	River	Japan	(Kameda et al., 2011)
	0.0001 – 0.143	Seawater	Japan (Okinawa)	(Tashiro and Kameda, 2013
Measured concentration in sediment MEC_{sed} (µg/kg dw)	0.003 – 0.101	River sediment	Japan	(Kameda et al., 2011)
	0.0009 – 0.0104	Sea sediment	Adriatic (Italian coast)	(Combi et al., 2016)
	0.0032 – 0.0262	Sea sediment	Spain (Andalusia coast)	(Pintado-Herrera et al., 2016)
	0.0046 – 0.167	River sediment	Brazil (Iguazu watershed)	(Mizukawa et al., 2017)
	0.045 ± 0.006	Rivers sediments in coastal, transition and upstream zones.	Lebanon	(Amine et al., 2012)
Measured concentration in biota MEC_{biota} (µg/kg)	0.002 – 0.182	Mussels (*Mytilus galloprovincialis* and *Mytilus edulis*)	Portuguese coast	(Castro et al., 2018)
	0.0008 – 0.0654	Seafood (different species)	Europe (Belgium, Ireland, Italy, Portugal and Spain)	(Cunha et al., 2018)
	0.012 – 0.242	Different freshwater species	Spanish rivers	(Gago-Ferrero et al., 2015)
	< 0.001 – 0.032	*Mytilus galloprovincialis*	France (Montpellier)	(Picot-Groz et al., 2018)

Tab. 223. Ecotoxicological data.

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
Bacteria				
Aliivibrio fischeri	180-min	Bioluminescence inhibition	EC_{50} = 400	Gackowska et al. 2018
Algae				
Isochrysis galbana	72-h	Algal growth	EC_{50} = 74.7	Paredes et al., 2014
			NOEC = 15	
			LOEC = 30	
Mollusca				
Mytilus galloprovincialis	48-h	Larval development	EC_{50} = 3118	Paredes et al., 2014
			NOEC = 500	
			LOEC = 1000	
Crustacea				
Siriella armata	96-h	Larval development	EC_{50} = 199	Paredes et al., 2014
			NOEC = 62.5	
			LOEC = 125	
Echinoida				
Paracentrotus lividus	48-h	Larval development	EC_{50} = 284	Paredes et al., 2014
			NOEC = 600	
			LOEC = 800	

LOEC/LOEL = Lowest Observed Effect Concentration/Level
NOEC/NOEL = Non Observed Effect Concentration/Level
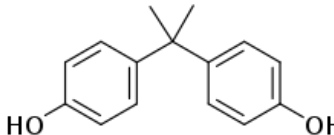LC_{50}/EC_{50} = Lethal/Effective Concentration 50

5.3   Bisphenol A

Bisphenol A (BPA) is a contaminant of emerging concern that has been already measured in many European environmental samples and belong to different classes of widely used emerging substances (plasticizers, surfactants, personal care products, and industrial chemicals). Bisphenol A (2,2-bis(4-hydroxyphenyl)propane) is an organic compound composed of two phenol molecules bonded by a methyl bridge and two methyl groups.

BPA is used as an intermediate (binding, plasticizing, and hardening) in plastics, paints/lacquers, binding

materials, and filling materials. Furthermore, it is used as an additive for flame-retardants, brake fluids, and thermal papers. About 95 % of BPA produced in industry is used to make plastics, in particular polycarbonate resins (71 %) and epoxy resins (29 %). Due to the increasing demand for polycarbonates and epoxy resins, BPA production has constantly grown in the last years: the global demand was 3.2, 3.9, and 5.0 million tons in 2003, 2006, and 2010, respectively.

Tab. 224. Substance identity.

Parameters	
Name	Bisphenol A
Other names	BPA, *p,p'*-Isopropylidenebisphenol, 2,2-Bis(4-hydroxyphenyl)propane
IUPAC name	4,4'-(propane-2,2-diyl)diphenol
CAS number	80-05-7
Molecular formula	C15H16O2
Molecular weight	228.291
Structure	
SMILES	Oc1ccc(cc1)C(c2ccc(O)cc2)(C)C CC(C)(c1ccc(cc1)O)c2ccc(cc2)O
Metabolites (or other related substances)	Not relevant for the identification of the substance as SVHC in accordance with Article 57 (f) REACH.

Tab. 225. Physico-chemical properties.

Endpoint	Value	Source
Melting point	155-158°C at p atm	https://echa.europa.eu/documents/10162/d35a98bb-d173-4f31-b578-c056f91c1270
Boiling point	About 360°C with decomposition at p atm	https://echa.europa.eu/documents/10162/d35a98bb-d173-4f31-b578-c056f91c1270
Relative density	1.1-1.2 kg/m^3 at 25°C	https://echa.europa.eu/documents/10162/d35a98bb-d173-4f31-b578-c056f91c1270
Vapour pressure (Pa)	5.3.10^{-9} kPa at 25°C	https://echa.europa.eu/documents/10162/d35a98bb-d173-4f31-b578-c056f91c1270
Water solubility (mg/L)	300 mg/L at ntp	https://echa.europa.eu/documents/10162/d35a98bb-d173-4f31-b578-c056f91c1270

Endpoint	Value	Source
Log K_{ow}	3.4	https://echa.europa.eu/documents/10162/d35a98bb-d173-4f31-b578-c056f91c1270
Flash point	About 532°C	https://echa.europa.eu/documents/10162/d35a98bb-d173-4f31-b578-c056f91c1270
Autoflammability	About 532°C	https://echa.europa.eu/documents/10162/d35a98bb-d173-4f31-b578-c056f91c1270
Oxidising proprieties	Not an oxidising agent	https://echa.europa.eu/documents/10162/d35a98bb-d173-4f31-b578-c056f91c1270

Tab. 226. Environmental fate.

Endpoint	Value	Source
Sorption potential K_{OC}	715 L/Kg	(Zielinska et al., 2018)
Partition coefficient solid-water in sediment Kp_{sed} (L/kg)	35.8 L/Kg	(Zielinska et al., 2018)
Biodegradability	NRB	https://echa.europa.eu/documents/10162/12d03565-e386-c6cd-0f5b-4851d2dd2767
Bioaccumulation (BAF)	Bisphenol A has a low potential for bioaccumulation in aquatic and terrestrial organisms (fish, earthworms).	https://echa.europa.eu/documents/10162/12d03565-e386-c6cd-0f5b-4851d2dd2767
Bioconcentration (BCF)	the bioconcentration factor for fish is estimated to be ≤ 73.4 and using QSAR methods a bioconcentration factor for earthworms was calculated to be 7.9 kg/kg.	https://echa.europa.eu/documents/10162/12d03565-e386-c6cd-0f5b-4851d2dd2767

Tab. 227. Analytical methods.

Method	LOD	Description	Reference
HPLC- QTRAP Triple quadrupole MS	LOD 8.5 ng/g	Matrix: sediment Sample size: 2 grams Sample treatment: extraction with QUECHERS followed by clean up using dispersive solid phase extraction using PSA/GCB	(Berlioz-Barbier et al., 2014)

Method	LOD	Description	Reference
HPLC-MS	5.7 ng/L dissolved phase 9.8 ng/g particle phase	Matrix: wastewater (dissolved and particulate phase) Sample volume: 250 mL (dissolved), 0.1~0.2 g (particulate) Sample treatment: SPE Sep PAK VAC C18 (dissolved); Extraction with Ultrasonic Assisted Extraction (particulate)	(Vega-Morales et al., 2010).
GC-MS	0.7 ng/L	Matrix: seawater Sample volume: 2 L Sample treatment: Clean up using cyanopropyl (CN) and 2,3-dihydoxypropoxypropyl (DIOL) followed by analyte enrichment using SPE OASIS HLB. Derivatization reagent: MTBSTFA with 1% TBDMSCI	(Guitart et al., 2010)
GC -MS	1.5 ng/L	Matrix: river water Sample volume: 1 L Sample treatment: Extraction using SPE cartridge (C18-E). Derivatization reagent: MSTFA	(Selvaraj et al, 2014)
GC-MS	1.0 ng/g	Matrix: river sediment Sample size: 5 grams Sample treatment: microwave assisted extraction followed by silica gel cleaned up Derivatization reagent: BSTFA + pyridine	(Liu et al., 20004),
LC- MSD-Trap SL	3.0 ng/g	Matrix: Mussel – *Mytilus galloprovincialis*; Sample size: 5 g Sample treatment: Extraction using sonication, cleaned up using activated Florisil.	(Pojana et al., 2007)
LC: QTRAP	0.01 ng/g	Matrix: fish (*Cyprinus carpio*) Sample size: 1 grams Sample treatment: Pressurised Liquid Extraction followed by QuECheRS (Agilent Technologies) clean up	(Jakimska et al., 2013)
GC–MS–MS	2.5 ng/L	Matrix: Sediment Sample treatment: SPE: C18-HF	(Hoai et al., 2003)

5.3.1 Environmental exposure assessment

Tab. 228. Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source
Measured concentration in water MEC$_w$ (µg/L)	0.07-4.0 Mean 1.0	River and coastal waters	Portugal	(Azevedo et al., 2001)
	0.0014-0.776 Mean 0.105	Elbe river and some of its tributaries	Germany	(Heemken et al., 2001)
	<0.002-2.47 Mean 0.40	Surface coastal water	Singapore	(Basheer et al., 2004)
	<0.005-0.08 Mean 0.40	Estuarine and marine waters	Okinawa and Ishigaki Islands, Japan	(Kawahata et al, 2004)
	<0.09-2.97 Mean 0.44	River water	Llobregat River basin, Spain	(Cespedes et al., 2005)
	<0.009-1.0 Median 0.0045	Fresh, marine and estuarine water	The Netherlands	(Vethaak et al., 2005)
	<0.03-0.14 Mean 0.07	River water	Tiber River, Italy	(Patrolecco et al, 2006)
	0.009-0.076	River water	Glatt River, Switzerland	(Vousta et al, 2006)
	0.0015-0.262	Estuarine and marine waters	Jiaozhou, China	(Fu et al., 2007)
	0.003-0.55 Mean 0.031	River water	Belgium	(Loos et al., 2007)
	<0.002-0.175 Mean 0.065	River water	Italy	(Loos et al., 2007)
	<0.005-0.007	Surface water	Mexico City, Mexico	(Felix-Canedo et al., 2013)
	0.006-0.126	River water	Spain	(Esteban et al., 2014)
	0.029-0.098	Range of concentrations in rivers	Portugal	(Michalowicz et al, 2014)
	4-92	River water	Elba River, Germany	(Michalowicz et al, 2014)

	Value	Matrix	Region/area	Source
	0.01-45	River water	16 major rivers, Taiwan	(Michalowicz et al, 2014)
Measured concentration in sediment MEC$_{sed}$ (µg/kg dw)	66–343 Mean 163	River sediment	Elba River and some of its tributaries, Germany	(Heemken et al., 2001)
	<0.5–13 Mean 3.2	Estuarine and marine sediments	Okinawa and Ishigaki Islands, Japan	(Kawahata et al., 2004)
	<1.1–43 Median 3.2	Fresh, marine, and estuarine sediments	The Netherlands	(Vethaak et al., 2005)
	0.7–27.3	Estuarine and marine sediments from	Jiaozhou Bay and surrounding rivers, China	(Fu et al., 2007)
	<2.0–118 Mean 36	Sediments	Venice Lagoon, Italy	(Pojana et al., 2007)
	1.4–140	Fresh sediments	USA	(USEPA, 2010)
	1.5–5.0	Marine sediments	USA	(USEPA, 2010)
	<0.24–100	River sediment	Ebro River basin, Spain	(Gorga et al., 2014)
	10–380	River sediment	Elba River sediments, Germany	(Michałowicz et al., 2014)
	0.37–492	River sediment	16 major rivers' sediments, Taiwan	(Michałowicz et al., 2014)
	<50–145 Mean 57	Estuarine sediments	Auckland, New Zealand	(Stewart et al. (2014)
	0.96–14.44 Mean 7.22	River sediment	Huangpu River and its tributaries, China	(Wu et al., 2013)
	<0.24–117	River sediment	Different rivers, Spain	(Gorga et al., 2015)
Measured concentration in biota	<MDL (3.0 ng/g)	Mussel - *Mytillus galloprovincialis*	Venice lagoon (Italy)	(Pojana et al., 2007)

MEC$_{biota}$ (µg/kg)	Value	Matrix	Region/area	Source
	224 ± 12 ng/g	Fish - *Cyprinus carpio*	Mediterranean sea	(Jakimska et al. 2013)
	13.3-213.1 Mean 82.5	Seafood from supermarkets	Singapore	(Basheer et al., 2004)
	1.1-13.7	Green mussel	India, Indonesia, Singapore, Malaysia, Thailand, Cambodia, Vietnam, Philippines	(Isobe et al., 2007)
	7.1-103	Fish	Worldwide	(Michalowicz et al., 2014)

Tab. 229. Ecotoxicological data.

	Time-scale	Endpoint	Toxicity (µg/L)	Source
Algae				
Skeletonema costatum	96-h	Growth inhibition	EC$_{50}$ = 1.000	Alexander et al., 1988
Crustacea				
Acartia tonsa	48-h	Mortality	EC$_{50}$ = 4.200	Andersen et al., 2001
	5-d	Larval development	EC$_{50}$ = 550	
Tigriopus japonicus	48-h	Mortality	NOEC = 3.500	Marcial et al., 2003
			EC$_{50}$ = 4.320	
	96-h	Mortality	NOEC = 100	Lee et al., 2007
			LC$_{10}$ = 110	
			LC$_{50}$ = 200	
	21-d	Mortality	NOEC = 10	Marcial et al., 2003
		Reproduction	NOEC = 10	
	42-d	Mortality	NOEC = 10	Marcial et al., 2003
		Reproduction	NOEC = 10	
Americamysis bahia	24-h	Mortality	LC$_{50}$ = 3.300	Alexander et al.,

	Time-scale	Endpoint	Toxicity (µg/L)	Source
	48-h		$LC_{50} = 1.600$	1988
	72-h		$LC_{50} = 1.200$	
	96-h		$LC_{50} = 1.100$	
	24-h	Mortality	$LC_{50} = 1.340$	Hirano et al., 2004
	48-h		$LC_{50} = 1.030$	
Artemia salina	24-h	Mortality	$LC_{50} = 56.200$	Kalčíková et al., 2012
	24-h	Mortality	$LC_{50} = 70$	
Artemia sinica	48-h	Mortality	$LC_{50} = 50$	Shaukat et al., 2014
	72-h	Mortality	$LC_{50} = 17$	
Charybdis japonica	24-h	Mortality	$LC_{50} = 2.350$	Park and Kwak, 2013
Homarus gammarus	25-d	Mortality	LOEC = 0.005	Laufer et al., 2012
		Metamorphosis	LOEC = 0.005	
<u>Mollusca</u>				
Mytilus galloprovincialis	48-h	Larval development	NOEC = 0,01	Fabbri et al., 2014
			LOEC = 0,1	
			$EC_{50} = 3,68$	
	12-h	Larval development	$EC_5 = 14$	Liu et al., 2011
			$EC_{50} = 31$	
Haliotis diversicolor	96-h	Larval development	$EC_5 = 0,18$	
			$EC_5 = 0,21$	
			$EC_{50} = 1,01$	
			$EC_{50} = 1,67$	
	1-h	Hatching	NOEC = 50	Zhou et al., 2011
			LOEC = 200	

	Time-scale	Endpoint	Toxicity (µg/L)	Source
	7.5-h	Larval development	NOEC = 50	
			LOEC = 200	
	5-d	Metamorphosis	NOEC = 50	
			LOEC = 200	
Echinoida				
Hemicentrotus pulcherrimus	80-d	Juvenile growth	NOEC = 114	Kiyomoto et al., 2006
Paracentrotus lividus	2-h	Development (larvae)	EC_{50} = 388	Bošnjak et al., 2014
Psammechinus miliaris	1-h	Fecundation	NOEC = 9.999	Schäfer et al., 2009
			LOEC = 99.999	
Strongylocentrotus purpuratus	96-h	Development	EC_{50} = 226,5	Roepke et al., 2005
Ascidiacea				
Ciona intestinalis	1-h	Development (larvae)	LOEC = 22,8	Cangialosi et al., 2013
	3-h			
	6-h			
	22-h			
	19-h	Mortality (embryos)	NOEC = 2.283	Matsushima et al., 2013
		Teratogenicity	NOEC = 228	
Fishes				
Rivulus marmoratus	24-h	Mortality (juveniles)	LC_{50} = 3.680	Rhee et al., 2011
	96-h	Mortality (embryos)	LC_{50} = 3.500	
	96-h	Mortality (adults)	LC_{50} = 8.200	
Menidia menidia	24-h	Mortality	LC_{50} = 12.000	Alexander et al., 1988
	48-h		LC_{50} = 11.000	
	72-h		LC_{50} = 9.400	

	Time-scale	Endpoint	Toxicity (µg/L)	Source
	96-h		$LC_{50} = 9.400$	

LC_{50}/EC_{50} = Lethal/Effective Concentration 50
LOEC/LOEL = Lowest Observed Effect Concentration/Level
NOEC/NOEL = Non Observed Effect Concentration/Level

5.4 Analytical methods employed

As reported in chapter 3 for Triallate, the results of the extensive bibliographical review indicate that the most widely used preanalytical procedures for the determination of BHT, EHMC, Triallate and the Fragrances in water samples use SPE extraction with Oasis HLB cartridges. These analytes are also effectively analysed by GC-MS, or GC-MS/MS, generally achieving lower detection limits. These techniques suggest a comprehensive multi-analyte method for their determination in water samples. Similarly the preparation of samples of solid matrices (sediments, biota) will be performed following a common procedure for BHT, EHMC, Triallate and Fragrances, using Accelerated Solvent Extraction (ASE).

Considering the literature, BSA determination is mainly performed using GC-MS or HPLC-MS in sediment, seawater, river water and biota samples. The instrumental detection limit (LOD) and method detection limit (MDL) are quite similar between GC-MS and HPLC-MS techniques, with values below of 10 ng/L for seawater, and of 10 ng/g for sediment and fish samples. BSA is usually extracted from water samples (volumes from 250 mL to 1L) using SPE cartridges. The treatment of sediment and biota samples consists in an extraction (i.e. using QUECHERS) followed by clean up using dispersive solid phase extraction. GC-MS analysis requires also a derivatization step. To minimize the pre-analytical steps, avoiding the derivatization procedure, HPLC-MS/MS will be used to analyse BSA in seawater, sediment and biota samples. Chromatographic separation is performed using C18 stationary phase, with methanol and water as mobile phase. The sample treatment will be similar to the methodology previously described.

5.5 References

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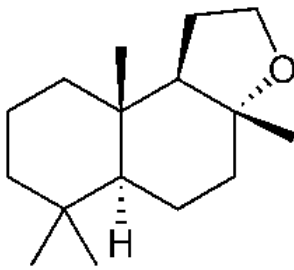Web site:

European Chemicals Agency (ECHA): echa.europa.eu

6 Fragrances

Fragrances are ubiquitous in daily life: the majority of cosmetics, toiletries, and a variety of household and Personal Care Products (PCPs) contain Fragrance Materials (FMs). 17 among the longest-lasting and most stable fragrance ingredients that are commercially available were originally selected to study their occurrence and distribution in the environment. The selected fragrances were recently found as contaminants at a global scale, being detected in the Venice Lagoon, Antarctica, Svalbard Islands and open Mediterranean Sea. Local emissions were revealed, together with evidences of long-range atmospheric transport (LRAT), supporting the hypothesis of the environmental persistence of the selected FMs. To fulfil the aims of the line 2.3, the research will focus on the 6 fragrances that in the preliminary studies were detected more frequently and at higher concentrations, namely Amyl Salicylate, Hexyl Salicylate, Benzyl Salicylate, Oranger Crystals, Ambrofix and Peonile. In particular, the allergenic and oestrogenic Salicylate compounds are High Production Volume (HPV) chemicals with a large global consumption (>5000 tons/year).

For the fragrances there are no ecotoxicological data in literature.

6.1 Ambrofix

Tab. 230. Substance identity.

Parameters	
Name	Ambrofix
Other names	Dodecahydro-3a,6,6,9a-tetramethylnaphtho[2,1-b]furan, Ambroxide, Ambrox, Cetalox
IUPAC name	3a,6,6,9a-tetramethyldodecahydronaphtho[2,1-b]furan
CAS number	6790-58-5
Molecular formula	C16H28O
Molecular weight	236
Structure	
SMILES	C[C@@]12CC[C@H]3C(C)(C)CCC[C@]3(C)[C@H]1CCO2

Tab. 231. Physico-chemical properties.

Endpoint	Value	Source
Vapour pressure (Pa)	0.066 Pa at 25 °C	ECHA
Water solubility (mg/L)	1.88 mg/L at 20 °C	ECHA
Log K_{ow}	5.09 at 25 °C	ECHA

Tab. 232. Environmental fate.

Endpoint	Value	Source
Sorption potential K_{OC}	5 250	ECHA
Biodegradability	Readily biodegradable	ECHA

Tab. 233. Analytical methods.

Method	LOD (µg/L)	Description	Reference
SPE + GC-MS	0.004	Prep. laboratory	(Vecchiato et al., 2016)
	0.0004	Prep. clean-room	(Vecchiato et al., 2018a)

6.1.1 Environmental exposure assessment
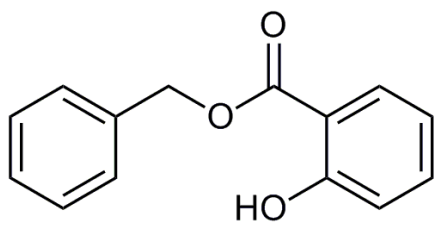
Tab. 234. Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source
Measured concentration in water MEC_w (µg/L)	0.0042 - 0.304	Transitional water bodies (open lagoon and urban canals)	Venice lagoon	(Vecchiato et al., 2016)
	0.0015 - 0.0072	Seawater	Sicily Channel (Mediterranean)	(Vecchiato et al., 2018b)
	0.0025 – 0.021	Seawater	Terranova Bay (Antarctica)	(Vecchiato et al., 2017)
	0.0008 – 0.0014	Seawater and Snow	Ny Alesund (Arctic)	(Vecchiato et al., 2018a)

6.2 Benzyl salicylate

Tab. 235. Substance identity.

Parameters	
Name	Benzyl salicylate

Other names	Salicylic acid, benzylester
IUPAC name	benzyl 2-hydroxybenzoate
CAS number	118-58-1
Molecular formula	C14H12O3
Molecular weight	228
Structure	
SMILES	OC1=C(C=CC=C1)C(=O)OCC1=CC=CC=C1

Tab. 236. Physico-chemical properties.

Endpoint	Value	Source
Vapour pressure (Pa)	0.01 Pa @ 25 °C	ECHA
Water solubility (mg/L)	8.8 mg/L @ 20 °C	ECHA
Log K_{ow}	4	ECHA

Tab. 237. Environmental fate.

Endpoint	Value	Source
Sorption potential K_{OC}	5 623	ECHA
Biodegradability	Readily biodegradable	ECHA
Bioconcentration (BCF)	311 L/kg ww	ECHA

Tab. 238. Analytical methods.

Method	LOD (µg/L)	Description	Reference
Water: SPE + GC-MS	0.011	Prep. laboratory	(Vecchiato et al., 2016)
Water: SPE + GC-MS	0.0008	Prep. clean-room	(Vecchiato et al., 2018a)
Water: USAEME + GC-MS/MS	0.0010	Ultrasound-assisted emulsification microextraction	(Vila et al., 2016)

Method	LOD (µg/L)	Description	Reference
Water: DLLME + GC-MS	0.003	Dispersive liquid–liquid microextraction	(Negreira et al., 2010)
Water: SPE + GC-MS	0.0001 – 0.003*	DSC-18LT, DSC-PH eluted with DCM	(Kameda et al., 2011)
Sediment: ultrasonic extraction + GC-MS	0.00005 –0.001 mg kg-1*	Extraction with DCM and multiple column purification	(Kameda et al., 2011)

* range of different analytes
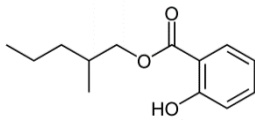
6.2.1 Environmental exposure assessment

Tab. 239. Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source
Measured concentration in water MEC_w (µg/L)	0.0011 – 2.4*	Transitional water bodies (open lagoon and urban canals)	Venice lagoon	(Vecchiato et al., 2016)
	0.0007 - 0.0056	Seawater	Sicily Channel (Mediterranean)	(Vecchiato et al., 2018b)
	0.0022 – 0.0045	Seawater	Terranova Bay (Antarctica)	(Vecchiato et al., 2017)
	0.0008 – 0.017	Seawater and Snow	Ny Alesund(Arctic)	(Vecchiato et al., 2018a)
	0.107 – 0.197	River	Japan	(Kameda et al., 2011)
	0.008 – 0.036	River	Spain	(Vila et al., 2016)
	0.006 – 0.189	River	Spain	(Negreira et al., 2010)
	0.0021 - 0.0060	River	Australia (Melbourne)	(Allinson et al., 2018)
	0.0011 – 2.4*	Transitional water bodies (open lagoon and urban canals)	Venice lagoon	(Vecchiato et al., 2016)

* PNEC marine water ECHA 0.103 µg/L

6.3 Amyl salicylate

Tab. 240. Substance identity.

Parameters	
Name	Amyl salicylate
Other names	Isopentyl 2-hydroxybenzoate 3-Methylbutyl 2-hydroxybenzoate
IUPAC name	3-methylbutyl 2-hydroxybenzoate
CAS number	87-20-7
Molecular formula	C12H16O3
Molecular weight	208
Structure	
SMILES	CC(C)CCOC(=O)C1=C(O)C=CC=C1

Tab. 241. Physico-chemical properties.

Endpoint	Value	Source
Vapour pressure (Pa)	8 Pa at 20 °C	ECHA
Water solubility (mg/L)	6.3 mg/L at 20 °C	ECHA
Log K_{ow}	4.78 at 23 °C	ECHA

Tab. 242. Environmental fate.

Endpoint	Value	Source
Biodegradability	Readily biodegradable	ECHA

Tab. 243 Analytical methods.

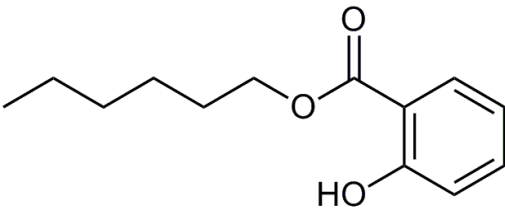| Method	LOD (µg/L)	Description	Reference
SPE + GC-MS	0.0095	Prep. laboratory	(Vecchiato et al., 2016)
	0.00024	Prep. clean-room	(Vecchiato et al., 2018a)

6.3.1 Environmental exposure assessment

Tab. 244. Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source
Measured concentration in water MEC_w (μg/L)	0.0017 – 6.75	Transitional water bodies (open lagoon and urban canals)	Venice lagoon	(Vecchiato et al., 2016)
	0.0070 - 0.059	Seawater	Sicily Channel (Mediterranean)	(Vecchiato et al., 2018b)
	0.0042 - 0.029	Seawater	Terranova Bay (Antarctica)	(Vecchiato et al., 2017)
	0.0030 – 0.032	Seawater and Snow	Ny Alesund	(Vecchiato et al., 2018a)

* PNEC marine water ECHA 0.103 μg/L

6.4 Hexyl salicylate

Tab. 245. Substance identity.

Parameters	
Name	Hexyl salicylate
Other names	Hexyl 2-hydroxybenzoate
IUPAC name	Hexyl 2-hydroxybenzoate
CAS number	6259-76-3
Molecular formula	C13H18O3
Molecular weight	222
Structure	
SMILES	CCCCCCOC(=O)C1=C(O)C=CC=C1

Tab. 246. Physico-chemical properties.

Endpoint	Value	Source
Vapour pressure (Pa)	0.077 Pa at 23 °C	ECHA

Endpoint	Value	Source
Water solubility (mg/L)	2 mg/L at 23 °C	ECHA
Log K_{ow}	5.5 at 30 °C	ECHA

Tab. 247. Environmental fate.

Endpoint	Value	Source
Biodegradability	Readily biodegradable	ECHA

Tab. 248. Analytical methods.

Method	LOD (µg/L)	Description	Reference
SPE + GC-MS	0.0049	Prep. laboratory	(Vecchiato et al., 2016)
	0.0034	Prep. clean-room	(Vecchiato et al., 2018a)

6.4.1 Environmental exposure assessment
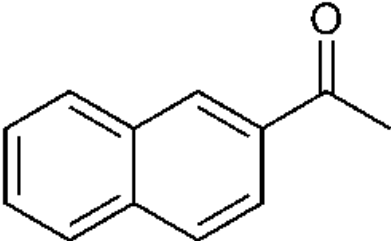
Tab. 249. Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source
Measured concentration in water MEC_w (µg/L)	0.0052 – 3.39*	Transitional water bodies (open lagoon and urban canals)	Venice lagoon	(Vecchiato et al., 2016)
	0.0032 - 0.037	Seawater	Sicily Channel (Mediterranean)	(Vecchiato et al., 2018b)
	0.0021 – 0.028	Seawater	Terranova Bay (Antarctica)	(Vecchiato et al., 2017)
	0.0019 – 0.016	Seawater and Snow	Ny Alesund (Arctic)	(Vecchiato et al., 2018a)

* PNEC marine water ECHA 0.0357 µg/L

6.5 Oranger Crystals

Tab. 250. Substance identity.

Parameters	
Name	2'-acetonaphthone
Other names	2-Acetonaphthone
IUPAC name	1-(naphthalen-2-yl)ethan-1-one
CAS number	93-08-3

Molecular formula	C12H10O
Molecular weight	170
Structure	
SMILES	CC(=O)C1=CC2=CC=CC=C2C=C1

Tab. 251. Physico-chemical properties.

Endpoint	Value	Source
Vapour pressure (Pa)	0.12 Pa at 25 °C	ECHA
Water solubility (mg/L)	133.3 mg/L at 25 °C	ECHA
Log K_{ow}	2.678 at 25 °C	ECHA

Tab. 252. Environmental fate.

Endpoint	Value	Source
Sorption potential K_{OC}	682	ECHA
Biodegradability	Inherently biodegradable; Half-life in freshwater: 15 days @ 25 °C; Half-life in freshwater sediment: 4.5 months at 25 °C	ECHA

Tab. 253. Analytical methods.

Method	LOD (µg/L)	Description	Reference
SPE + GC-MS	0.0012	Prep. laboratory	(Vecchiato et al., 2016)
	0.0003	Prep. clean-room	(Vecchiato et al., 2018a)

6.5.1 Environmental exposure assessment
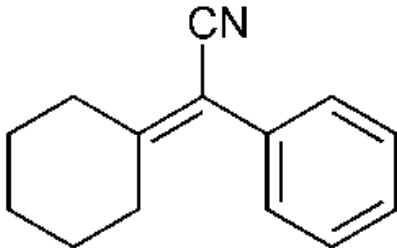
Tab. 254. Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source
Measured concentration in water MEC_w (µg/L)	0.0013 - 0.190	Transitional water bodies (open lagoon and urban canals)	Venice lagoon	(Vecchiato et al., 2016)

Value	Matrix	Region/area	Source
0.0020 - 0.0035	Seawater	Sicily Channel (Mediterranean)	(Vecchiato et al., 2018b)
0.0031 – 0.0035	Seawater and Snow	Ny Alesund (Arctic)	(Vecchiato et al., 2018a)

* PNEC marine water ECHA 3.6 µg/L

6.6 Peonile

Tab. 255. Substance identity.

Parameters	
Name	Peonile
Other names	2-cyclohexylidene-2-phenylacetonitrile; Rose Nitrile
IUPAC name	2-cyclohexylidene-2-phenylacetonitrile
CAS number	10461-98-0
Molecular formula	C14H15N
Molecular weight	197
Structure	
SMILES	N#CC(=C1CCCCC1)C1=CC=CC=C1

Tab. 256. Physico-chemical properties.

Endpoint	Value	Source
Vapour pressure (Pa)	0.043 Pa at 20 °C	ECHA
Water solubility (mg/L)	7.5 mg/L at 20 °C	ECHA
Log K_{ow}	2 at 30 °C	ECHA

Tab. 257. Environmental fate.

Endpoint	Value	Source

Endpoint	Value	Source
Sorption potential K_{OC}	2 630.26	ECHA
Biodegradability	Biodegradation in water: Under test conditions no biodegradation observed	ECHA

Tab. 258. Analytical methods.

Method	LOD (µg/L)	Description	Reference
SPE + GC-MS	0.001	Prep. clean-room	(Vecchiato et al., 2018a)

6.6.1 Environmental exposure assessment

Tab. 259. Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source
Measured concentration in water MEC_w (µg/L)	0.011 – 2.25*	Transitional water bodies (open lagoon and urban canals)	Venice lagoon	(Vecchiato et al., 2016)
	0.0013 - 0.0037	Seawater	Sicily Channel (Mediterranean)	(Vecchiato et al., 2018b)
	0.0007 – 0.014	Seawater and Snow	Ny Alesund	

* PNEC marine water ECHA 0.3 µg/L

6.7 Analytical methods employed

The most widely used preanalytical procedures for the determination of the Fragrances in water samples (as for BHT, EHMC, Triallate) use SPE extraction with Oasis HLB cartridges. These analytes are also effectively analyzed by GC-MS, or GC-MS/MS, generally achieving lower detection limits. These techniques suggest a comprehensive multi-analyte method for their determination in water samples. Similarly the preparation of samples of solid matrices (sediments, biota) will be performed following a common procedure for BHT, EHMC, Triallate and Fragrances, using Accelerated Solvent Extraction (ASE).

6.8 Ecotoxicological data

Tab. 260. Biochemical and genetic responses for fragrances.

Species	Concentrations	Days of exposure	Biochemical/molecular effects	Reference

Freshwater mussels *Dreissena polymorpha*	100 and 500 ng/L of galaxolide (HHCB) and 20 and 80 ng/L of tonalide (AHTN)	0, 1, 2, 3, 4, 11, 15, 18, and 21 days	HHCB induced significant increases in lipid peroxidation (LPO) and protein carbonyl content (PCC) levels, while AHTN enhanced only PCC. Moreover, significant increases in DNA strand breaks were caused by exposure to the highest concentrations of HHCB and AHTN, but no fixed genetic damage was observed.	Parolini et al., 2015.
Mussels *Mytilus californianus*	Nitromusks and polycyclic musks in the µM range (1-10).	90 min. (in vitro study)	Negative effects on the multixenobiotic defence systems (MXR transporters) in gills	Luckenbach et al., 2004.
Freshwater mussels *Lampsilis cardium*	Test with glochidia (400, 800, and 1600 µg HHCB/L or 300, 600, and 1200 µg AHTN/L)	24- and 48-h static tests	Regarding AHTN, 24-h LC50s were 454 to 850 µg/L and the range of 48-h LC50s was 281 to 1181 µg/L. As for HHCB, 24-h LC50s were 1000 µg/L to >1750 µg/L, and 48-h LC50s were 999 µg/L to >1750 µg/L	Gooding et al., 2006.
Freshwater mussels *Lampsilis cardium*	Test with juveniles (50, 100, 200, 400, 800, and 1600 µg HHCB/L or 38, 75, 150, 300, 600, and 1200 µg AHTN/L)	96-h static toxicity test	After 96 h, mean mortality of juveniles across all treatments ranged from 0 to 24%.	Gooding et al., 2006.

6.9   References

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Web site:

European Chemicals Agency (ECHA): echa.europa.eu

7   Perfluoroalkyl substances: PFASs

In recent years major efforts have been undertaken to study the so-called emerging pollutants, a heterogeneous group of chemical substances that have been recently discovered or which are spreading wider. In particular, perfluoroalkyl substances (PFASs) attracted increasing interest due to their widespread applications, environmental persistence and bioaccumulative properties, which make them a real threat for the human health.
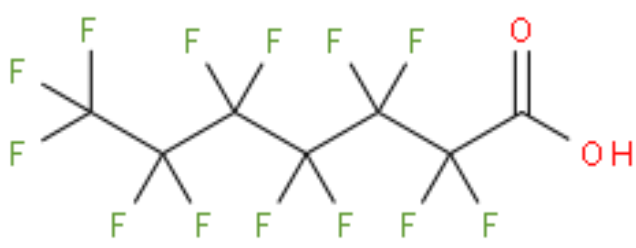
PFASs are a large group of anthropogenic organic chemicals widely used for a variety of industrial applications, which includes perfluorinated carboxylic acids (PFCAs) and perfluorinated sulfonic acids (PFSAs). Their unique physico-chemical and biological properties make them resistant to hydrolysis, photolysis and biodegradation, as well as to metabolic processes in living organisms. Unlike other persistent organic pollutants (POPs), PFASs are water-soluble, hence easily released into surface water and aquifers, which become the principal medium for their environmental transport (Prevedouros et al., 2006). For this reason, they can enter into the food chain through the reuse of this water to irrigate crops, intensifying the possible human exposure to PFASs.

In the last few years, a serious PFASs contamination affected a large area of the Veneto region among the provinces of Vicenza, Verona and Padua (about 1.800.000 inhabitants with 350.000 people involved) caused by industrial discharges that have contaminated rivers, aquifers and drinking water and led to concentrations in serum of the population about forty times higher than the tolerable values (World Health Organization, 2017). A characterization of the exposure to PFASs contamination of people in those areas has been developed by the Italian National Institute for Health (Istituto Superiore di Sanità, ISS) and showed a significant correlation between PFAS serum levels and drinking water consumption (Brambilla and De Filip, 2013; Ingelido et al., 2018), especially for some PFCAs (e.g., perfluorooctanoic acid, PFOA).

7.1   Perfluoroheptanoic acid: PFHpA

Tab. 261. Substance identity.

Parameters	
Name	Perfluoroheptanoic acid: PFHpA
Other names	Tridecafluoroheptanoic acid, Perfluoro-n-heptanoic acid, Perfluoroenanthic acid
IUPAC name	2,2,3,3,4,4,5,5,6,6,7,7,7-tridecafluoroheptanoic acid
CAS number	375-85-9
Molecular formula	C7HF13O2
Molecular weight	364.06

Structure	
SMILES	C(=O)(C(C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)O
Metabolites (or other related substances)	Not metabolized - Branched isomers

Tab. 262. Physico-chemical properties.

Endpoint	Value	Source
Vapour pressure (Pa)	17.73 at 25°C	Converted from PubChem, HSDB and EPA DSSTox
Water solubility (mg/L)	3.65 at 25°C	PubChem and HSDB
Log K_{ow}	4.15	PubChem and HSDB

Tab. 263. Environmental fate.

Endpoint	Value	Source
Sorption potential K_{OC}	Log K_{OC} (mL/g) 1.63 - 2.10	(Campos Pereira et al., 2018)
Biodegradability	NRB	ECHA

Tab. 24. Analytical methods.

Method	LOD	Description	Reference
Water SPE + LC/MS2	LOD: 1 - 8 pg/L	Extraction: SPE C18	(Moody et al., 2001)
Water SPE + LC-ESI-TOF/MS	LOD: 10 - 300 pg/L	Extraction: SPE C18	(Voogt et al., 2014)
Water SPE disk + GC-EI/MS	LOD: 18 µg/L	Extraction: SPE disk SAX Derivatization: Methyl ester	(Moody and Field, 1999)
Water SPME + GC-NCI/MS	LOD: 100 - 750 ng/L	Extraction: SPME PDMS fiber Derivatization: Buthyl ester	(Alzaga and Mar, 2004)
Water SPE + GC-EI/MS	LOD: 30 - 310 ng/L	Extraction: SPE HLB Derivatization: Isobuthyl ester	(Dufková et al., 2012, 2009)
Water SPE + GC-ECD	LOD: 0.2 - 0.7 µg/L	Extraction: SPE HLB Derivatization: Isobuthyl ester	(Dufková et al., 2012, 2009)

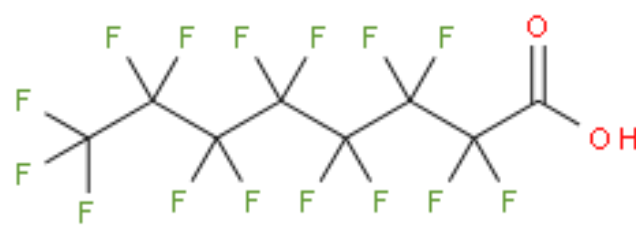| Method	LOD	Description	Reference
Sediment PLE + GC-NCI/MS	LOD: 0.5 - 0.8 ng/g	Extraction: PLE (ACE:MeOH + MeOH-H3PO4), Derivatization: Buthyl ester	(Alzaga et al., 2005)
Biota LLE + GC/MS2	LOD: 10 pg	Extraction: Ion-pairing agent MTBE Derivatization: Difluoro-anilides	(De Silva and Mabury, 2004)
Biota US + LC-TOF/MS	LOD: 1 - 8 pg	Extraction: Ultrasound assisted (MeOH/H_2O, NH_4Ac)	(Berger and Haukås, 2005)

7.1.1 Environmental exposure assessment

Tab. 265. Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source
Measured concentration in water MEC_w (µg/L)	0.011 - 0.208	Groundwater	Veneto Region, PFAS red zone	ARPAV monitoring (Zanon, 2017)
	0.010 - 0.260	Surface water	Veneto Region, PFAS red zone	ARPAV monitoring (Zanon, 2017)
	<10 - 16 ng/L	Groundwater	Venice	ARPAV monitoring (ARPAV, 2019)
	<5 ng/L	Surface water	Venice	ARPAV monitoring (ARPAV, 2019)
	0.328 ng/L	Marine water	Adriatic Sea (offshore from Venice)	(Loos et al., 2013)
	0.64 - 20.1 ng/L	Freshwater	Júcar river basin (East Spain)	(Campo et al., 2016)
Measured concentration in sediment MEC_{sed} (µg/kg dw)	0.39 - 1.06 ng/g	River sediment	Júcar river basin (East Spain)	(Campo et al., 2016)
	0.006 ng/g	Coastal sediment	South Bohai coastal watersheds (China)	(Zhu et al., 2014)
	0.008 ng/g	Riverine sediment	South Bohai coastal watersheds (China)	(Zhu et al., 2014)
Measured concentration in	1.18 - 111 µg kg-1	Fish	Júcar river basin (East Spain)	(Campo et al., 2016)

	Value	Matrix	Region/area	Source
biota MEC$_{biota}$ (µg/kg)	See also: Comments Concerning the National Swedish *Contaminant Monitoring Programme in Marine Biota*			(Bignert et al., 2016)

7.2 Perfluorooctanoic acid: PFOA

Tab. 266. Substance identity.

Parameters	
Name	Perfluorooctanoic acid: PFOA
Other names	Pentadecafluorooctanoic acid, Perfluoro-n-octanoic acid, Perfluorocaprylic acid
IUPAC name	2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-pentadecafluorooctanoic acid
CAS number	335-67-1
Molecular formula	C8HF15O2
Molecular weight	414.07
Structure	
SMILES	C(=O)(C(C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)O
Metabolites (or other related substances)	Not metabolized - Branched isomers

Tab. 267. Physico-chemical properties.

Endpoint	Value	Source
Vapour pressure (Pa)	70.66 at 25°C	Converted from PubChem and EPA DSSTox
Water solubility (mg/L)	2290 at 24°C 3300 at 25°C 4340 at 24°C	(Bhhatarai and Gramatica, 2011) (Inoue et al., 2012) (Rahman et al., 2013)
Log K$_{ow}$	4.81	PubChem and HSDB

Tab. 268. Environmental fate.

Endpoint	Value	Source

Endpoint	Value	Source
Sorption potential K_{OC}	Log K_{OC} (mL/g) 1.89 - 3.50	(Campos Pereira et al., 2018)
Biodegradability	NRB	ECHA
Bioaccumulation (BAF)	91 ± 20 L kg-1	(Dai et al., 2013)
Bioconcentration (BCF)	3.1 - 9.4	(Inoue et al., 2012)

Tab. 269. Analytical methods.

Method	LOD	Description	Reference
Water SPE + LC/MS[2]	LOD: 25 ng/L	Extraction: SPE C18	(Hansen et al., 2002, 2001; Risha et al., 2005)
Water SPE + LC/MS[2]	LOD: 1 - 8 pg/L	Extraction: SPE C18	(Moody et al., 2001)
Water SPE + LC-ESI-TOF/MS	LOD: 10 - 300 pg/L	Extraction: SPE C18	(Voogt et al., 2014)
Water SPE disk + GC-EI/MS	LOD: 18 µg/L	Extraction: SPE disk SAX Derivatization: Methyl ester	(Moody and Field, 1999)
Water SPME + GC-NCI/MS	LOD: 100 - 750 ng/L	Extraction: SPME PDMS fiber Derivatization: Buthyl ester	(Alzaga and Mar, 2004)
Water SPE + GC-EI/MS	LOD: 30 - 310 ng/L	Extraction: SPE HLB Derivatization: Isobuthyl ester	(Dufková et al., 2012, 2009)
Water SPE + GC-ECD	LOD: 0.2 - 0.7 µg/L	Extraction: SPE HLB Derivatization: Isobuthyl ester	(Dufková et al., 2012, 2009)
Water SPE + HPLC/MS[2]	LOQ: 2.5 ng/L	Pre-cleaning: SPE HLB and WAX Off-line Extraction: SPE HLB On-line pre-concentration: SPE WAX	(Dasu et al., 2017)
Sediment PLE + GC-NCI/MS	LOD: 0.5 - 0.8 ng/g	Extraction: PLE (ACE:MeOH + MeOH-H_3PO_4) Derivatization: Buthyl ester	(Alzaga et al., 2005)
Sediment US + SPE + LC/MS[2]	LOD: 0.01 - 0.25 ng/g	Extraction: Ultrasound assisted (9:1 MeOH, 1%Ac) Centrifugation Clean-up: SPE C18	(Higgins et al., 2005)
Biota LLE + GC/MS[2]	LOD: 10 pg	Extraction: Ion-pairing agent MTBE Derivatization: Difluoro-anilides	(De Silva and Mabury, 2004)

Method	LOD	Description	Reference
Biota US + LC-TOF/MS	LOD: 1 - 8 pg	Extraction: Ultrasound assisted (MeOH/H$_2$O, NH$_4$Ac)	(Berger and Haukås, 2005)

7.2.1 Environmental exposure assessment

Tab. 270. Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source
Measured concentration in water MEC$_w$ (µg/L)	0.010 - 1.377	Groundwater	Veneto Region, PFAS red zone	ARPAV monitoring (Zanon, 2017)
	0.010 - 3.417	Surface water	Veneto Region, PFAS red zone	ARPAV monitoring (Zanon, 2017)
	<10 - 40 ng/L	Groundwater	Venice	ARPAV monitoring (ARPAV, 2019)
	<5 ng/L	Surface water	Venice	ARPAV monitoring (ARPAV, 2019)
	1.475	Drinking water	Veneto Region Summer 2013	(World Health Organization, 2017)
	0.386	Drinking water	Veneto Region Spring 2014	(World Health Organization, 2017)
	2.505 ng/L	Marine water	Adriatic Sea (offshore from Venice)	(Loos et al., 2013)
	0.210	Freshwater	Lake Halmsjön nearby Stockholm Arlanda Airport	(Ahrens et al., 2015)
	0.07 - 52.2 ng/L	Freshwater	Júcar river basin (East Spain)	(Campo et al., 2016)
Measured concentration in sediment MEC$_{sed}$ (µg/kg dw)	0.15 - 6.69 ng/g	River sediment	Júcar river basin (East Spain)	(Campo et al., 2016)
	0.04 - 2.52 ng/g	Estuarine sediment	Charleston harbour (South Carolina, USA)	(White et al., 2015)

	Value	Matrix	Region/area	Source
	0.005 - 1.049 ng/g	Coastal sediment	South Bohai coastal watersheds (China)	(Zhu et al., 2014)
	0.005 - 0.221 ng/g	Riverine sediment	South Bohai coastal watersheds (China)	(Zhu et al., 2014)
Measured concentration in biota MEC_{biota} (µg/kg)	2.9 - 13 ng/g	Liver of Polar bear *Ursus maritimus*	Sanikiluaq, Nunavut (Canada)	(Martin et al., 2004)
	See also: Comments Concerning the National Swedish *Contaminant Monitoring Programme in Marine Biota*			(Bignert et al., 2016)

Tab. 271. Ecotoxicological data.

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
Algae				
Isochrysis galbana	72-h	Growth inhibition	NOEC = 25.000	Mhadhbi et al., 2012
			LOEC = 50.000	
			EC_{50} = 163.600	
Crustacea				
Siriella armata	96-h	Mortality	NOEC = 5.000	Mhadhbi et al., 2012
			LOEC = 10.000	
			EC_{50} = 15.500	
Mollusca				
Mytilus galloprovincialis	48-h	Larval development	NOEC = 0,01	Fabbri et al., 2014
			LOEC = 0,1	
Echinoida				
Paracentrotus lividus	48-h	Growth inhibition (larvae)	NOEC = 10.000	Mhadhbi et al., 2012
			LOEC = 20.000	

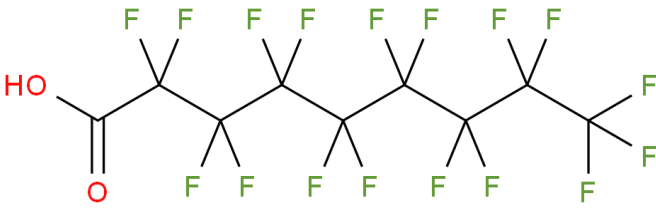| Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
			EC_{50} = 110.000	
Fishes				
Psetta maxima	144-h	Mortality	NOEC = 1.500	Mhadhbi et al., 2012
			LOEC = 3.000	
			EC_{50} = 11.900	

LC_{50}/EC_{50} = Lethal/Effective Concentration 50
LOEC/LOEL = Lowest Observed Effect Concentration/Level
NOEC/NOEL = Non Observed Effect Concentration/Level

7.3 Perfluorononanoic acid: PFNA

Tab. 272. Substance identity.

Parameters	
Name	Perfluorononanoic acid: PFNA
Other names	Heptadecafluorononanoic acid Perfluoro-n-nonanoic acid Perfluoropelargonic acid
IUPAC name	2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,9-heptadecafluorononanoic acid
CAS number	375-95-1
Molecular formula	C9HF17O2
Molecular weight	464.08
Structure	
SMILES	C(=O)(C(C(C(C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)O
Metabolites (or other related substances)	Not metabolized - Branched isomers

Tab. 273. Physico-chemical properties.

Endpoint	Value	Source

Endpoint	Value	Source
Vapour pressure (Pa)	11.07 at 25°C	Converted from PubChem and HSDB
Water solubility (mg/L)	6.25×10^{-2} at 25°C	PubChem and HSDB
Log K_{ow}	5.48	PubChem and HSDB

Tab. 274. Environmental fate.

Endpoint	Value	Source
Sorption potential K_{OC}	Log K_{OC} (mL/g) 2.36 - 4.00	(Campos Pereira et al., 2018)
Biodegradability	NRB	ECHA
Bioaccumulation (BAF)	152 ± 21 L kg^{-1}	(Dai et al., 2013)
Bioconcentration (BCF)	42 - 54 L kg^{-1}	(Ahrens et al., 2015)

Tab. 275. Analytical methods.

Method	LOD	Description	Reference
Water SPE + LC/MS[2]	LOD: 25 ng/L	Extraction: SPE C18	(Hansen et al., 2002, 2001; Risha et al., 2005)
Water SPE + LC-ESI-TOF/MS	LOD: 10 - 300 pg/L	Extraction: SPE C18	(Voogt et al., 2014)
Water SPME + GC-NCI/MS	LOD: 100 - 750 ng/L	Extraction: SPME PDMS fiber, Derivatization: Buthyl ester	(Alzaga and Mar, 2004)
Water SPE + GC-EI/MS	LOD: 30 - 310 ng/L	Extraction: SPE HLB, Derivatization: Isobuthyl ester	(Dufková et al., 2012, 2009)
Water SPE + GC-ECD	LOD: 0.2 - 0.7 µg/L	Extraction: SPE HLB, Derivatization: Isobuthyl ester	(Dufková et al., 2012, 2009)
Sediment PLE + GC-NCI/MS	LOD: 0.5 - 0.8 ng/g	Extraction: PLE (ACE: MeOH + MeOH-H_3PO_4), Derivatization: Buthyl ester	(Alzaga et al., 2005)
Sediment US + SPE + LC/MS[2]	LOD: 0.01 - 0.25 ng/g	Extraction: Ultrasound assisted (9:1 MeOH, 1%Ac), Centrifugation Clean-up: SPE C18	(Higgins et al., 2005)
Biota LLE + GC/MS[2]	LOD: 10 pg	Extraction: Ion-pairing agent MTBE, Derivatization: Difluoro-anilides	(De Silva and Mabury, 2004)
Biota US + LC-TOF/MS	LOD: 1 - 8 pg	Extraction: Ultrasound assisted (MeOH/H_2O, NH_4Ac)	(Berger and Haukås, 2005)

Method	LOD	Description	Reference
Water SPE + LC/MS[2]	LOD: 25 ng/L	Extraction: SPE C18	(Hansen et al., 2002, 2001; Risha et al., 2005)

7.3.1 Environmental exposure assessment

Tab. 276. Measured Environmental Concentrations.

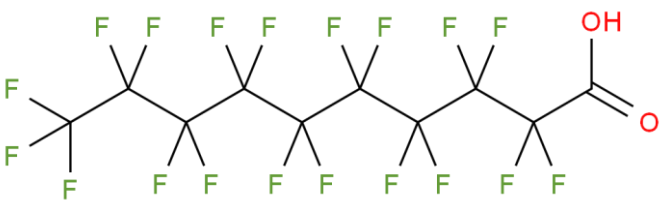|	Value	Matrix	Region/area	Source
Measured concentration in water MEC$_w$ (µg/L)	0.013 - 0.040	Groundwater	Veneto Region, PFAS red zone	ARPAV monitoring (Zanon, 2017)
	0.010 - 0.855	Surface water	Veneto Region, PFAS red zone	ARPAV monitoring (Zanon, 2017)
	<10 ng/L	Groundwater	Venice	ARPAV monitoring (ARPAV, 2019)
	<5 ng/L	Surface water	Venice	ARPAV monitoring (ARPAV, 2019)
	0.152 ng/L	Marine water	Adriatic Sea (offshore from Venice)	(Loos et al., 2013)
	0.85 - 19.8 ng/L	Freshwater	Júcar river basin (East Spain)	(Campo et al., 2016)
Measured concentration in sediment MEC$_{sed}$ (µg/kg dw)	3.63 ng/g	River sediment	Júcar river basin (East Spain)	(Campo et al., 2016)
	0.002 - 0.080 ng/g	Coastal sediment	South Bohai coastal watersheds (China)	(Zhu et al., 2014)
	0.002 - 0.087 ng/g	Riverine sediment	South Bohai coastal watersheds (China)	(Zhu et al., 2014)
Measured concentration in biota MEC$_{biota}$ (µg/kg)	71.5 µg kg^{-1}	Fish	Júcar river basin (East Spain)	(Campo et al., 2016)
	108 - 230 ng/g	Liver of Polar bear *Ursus maritimus*	Sanikiluaq, Nunavut (Canada)	(Martin et al., 2004)
	2.22 - 86 ng/g	Liver of Arctic fox *Alopex lagopus*	Arviat, Nunavut (Canada)	(Martin et al., 2004)

	Value	Matrix	Region/area	Source
	3.3 - 8.8 ng/g	Liver of Ringed seal *Phoca hispida*	Holman, Northwest Territories (Canada)	(Martin et al., 2004)
	2.4 - 8.1 ng/g	Liver of Ringed seal *Phoca hispida*	Grise Fjord, Nunavut (Canada)	(Martin et al., 2004)
	2.0 - 35 ng/g	Liver of Mink *Mustela vison*	Watson Lake Area, Yukon (Canada)	(Martin et al., 2004)
	0.50 ng/g	Liver of Northern fulmar *Fulmarus glacialis*	Prince Leopold Island, Nunavut (Canada)	(Martin et al., 2004)
	0.61 - 1.7 ng/g	Liver of White sucker *Catostomus commersoni*	Kuujjuarapik, Québec (Canada)	(Martin et al., 2004)
	5.9 - 6.5 ng/g	Liver of Brook trout *Salvelinus fontinalis*	Kuujjuarapik, Québec (Canada)	(Martin et al., 2004)
	2.4 - 4.0 ng/g	Liver of Lake whitefish *Coregonus clupeaformis*	Kuujjuarapik, Québec (Canada)	(Martin et al., 2004)
	3.4 ng/g	Liver of Lake trout *Salvelinus namaycush*	Lac Minto, Québec (Canada)	(Martin et al., 2004)
	2.2 ng/g	Liver of Arctic sculpin *Myoxocephalus scorpioides*	Kuujjuarapik, Québec (Canada)	(Martin et al., 2004)
	See also: *Comments Concerning the National Swedish Contaminant Monitoring Programme in Marine Biota*			(Bignert et al., 2016)

7.4 Perfluorodecanoic acid: PFDA

Tab. 277. Substance identity.

Parameters	
Name	Perfluorodecanoic acid: PFDA
Other names	Nonadecafluorodecanoic acid, Perfluoro-n-decanoic acid, Perfluorocapric acid

IUPAC name	2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-nonadecafluorodecanoic acid
CAS number	335-76-2
Molecular formula	C10HF19O2
Molecular weight	514.09
Structure	
SMILES	C(=O)(C(C(C(C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)O
Metabolites (or other related substances)	Not metabolized - Branched isomers

Tab. 278. Physico-chemical properties.

Endpoint	Value	Source
Vapour pressure (Pa)	0.23 at 25°C	(Bhhatarai and Gramatica, 2011; Rahman et al., 2013)
Water solubility (mg/L)	260 at 22.4°C	(Rahman et al., 2013)
Log K_{ow}	4.00	(Bhhatarai and Gramatica, 2011)

Tab. 279. Environmental fate.

Endpoint	Value	Source
Sorption potential K_{OC}	Log K_{OC} (mL/g) 2.96 - 4.60	(Campos Pereira et al., 2018)
Biodegradability	NRB	ECHA
Bioaccumulation (BAF)	175 ± 23 L kg^{-1}	(Dai et al., 2013)
Bioconcentration (BCF)	140 - 220 L kg^{-1}	(Ahrens et al., 2015)

Tab. 280. Analytical methods.

Method	LOD (µg/L)	Description	Reference
Water SPE + LC/MS[2]	LOD:25 ng/L	Extraction: SPE C18	(Hansen et al., 2002, 2001; Risha et al., 2005)
Water SPE + LC-ESI-TOF/MS	LOD:10 - 300 pg/L	Extraction: SPE C18	(Voogt et al., 2014)

Method	LOD (µg/L)	Description	Reference
Water SPME + GC-NCI/MS	LOD:100 - 750 ng/L	Extraction: SPME PDMS fiber, Derivatization: Buthyl ester	(Alzaga and Mar, 2004)
Water SPE + GC-EI/MS	LOD:30 - 310 ng/L	Extraction: SPE HLB, Derivatization: Isobuthyl ester	(Dufková et al., 2012, 2009)
Water SPE + GC-ECD	LOD:0.2 - 0.7 µg/L	Extraction: SPE HLB, Derivatization: Isobuthyl ester	(Dufková et al., 2012, 2009)
Sediment PLE + GC-NCI/MS	LOD:0.5 - 0.8 ng/g	Extraction: PLE (ACE: MeOH + MeOH-H_3PO_4), Derivatization: Buthyl ester	(Alzaga et al., 2005)
Sediment US + SPE + LC/MS[2]	LOD:0.01 - 0.25 ng/g	Extraction: Ultrasound assisted (9:1 MeOH, 1%Ac), Centrifugation, Clean-up: SPE C18	(Higgins et al., 2005)
Biota LLE + GC/MS[2]	LOD:10 pg	Extraction: Ion-pairing agent MTBE, Derivatization: Difluoro-anilides	(De Silva and Mabury, 2004)
Biota US + LC-TOF/MS	LOD: 1 - 8 pg	Extraction: Ultrasound assisted (MeOH/H_2O, NH_4Ac)	(Berger and Haukås, 2005)

7.4.1 Environmental exposure assessment

Tab. 281. Measured Environmental Concentrations.

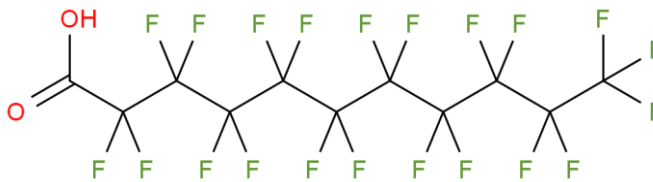|	Value	Matrix	Region/area	Source
Measured concentration in water MEC_w (µg/L)	0.010	Groundwater	Veneto Region, PFAS red zone	ARPAV monitoring (Zanon, 2017)
	0.010 - 0.037	Surface water	Veneto Region, PFAS red zone	ARPAV monitoring (Zanon, 2017)
	<10 ng/L	Groundwater	Venice	ARPAV monitoring (ARPAV, 2019)
	<5 ng/L	Surface water	Venice	ARPAV monitoring (ARPAV, 2019)
	0.019 ng/L	Marine water	Adriatic Sea (offshore from Venice)	(Loos et al., 2013)
	0.09 - 213 ng/L	Freshwater	Júcar river basin (East Spain)	(Campo et al., 2016)
Measured concentration in	0.37 - 1.65 ng/g	River sediment	Júcar river basin (East Spain)	(Campo et al., 2016)

	Value	Matrix	Region/area	Source
sediment MEC$_{sed}$ (µg/kg dw)	0.06 - 4.76 ng/g	Estuarine sediment	Charleston harbour (South Carolina, USA)	(White et al., 2015)
	0.025 ng/g	Coastal sediment	South Bohai coastal watersheds (China)	(Zhu et al., 2014)
	0.067 ng/g	Riverine sediment	South Bohai coastal watersheds (China)	(Zhu et al., 2014)
Measured concentration in biota MEC$_{biota}$ (µg/kg)	35 - 76 ng/g	Liver of Polar bear *Ursus maritimus*	Sanikiluaq, Nunavut (Canada)	(Martin et al., 2004)
	1.9 - 72 ng/g	Liver of Arctic fox *Alopex lagopus*	Arviat, Nunavut (Canada)	(Martin et al., 2004)
	0.98 - 3.1 ng/g	Liver of Ringed seal *Phoca hispida*	Holman, Northwest Territories (Canada)	(Martin et al., 2004)
	2.1 - 3.8 ng/g	Liver of Ringed seal *Phoca hispida*	Grise Fjord, Nunavut (Canada)	(Martin et al., 2004)
	0.69 - 9.0 ng/g	Liver of Mink *Mustela vison*	Watson Lake Area, Yukon (Canada)	(Martin et al., 2004)
	0.55 ng/g	Liver of Common loon *Gavia immer*	Kuujjuarapik, Québec (Canada)	(Martin et al., 2004)
	1.7 - 3.1 ng/g	Liver of White sucker *Catostomus commersoni*	Kuujjuarapik, Québec (Canada)	(Martin et al., 2004)
	2.3 - 2.8 ng/g	Liver of Brook trout *Salvelinus fontinalis*	Kuujjuarapik, Québec (Canada)	(Martin et al., 2004)
	1.2 - 1.8 ng/g	Liver of Lake whitefish *Coregonus clupeaformis*	Kuujjuarapik, Québec (Canada)	(Martin et al., 2004)

	Value	Matrix	Region/area	Source
	2.0 ng/g	Liver of Lake trout *Salvelinus namaycush*	Lac Minto, Québec (Canada)	(Martin et al., 2004)
	2.0 ng/g	Liver of Northern pike *Esox lucius*	Kuujjuarapik, Québec (Canada)	(Martin et al., 2004)
	0.52 ng/g	Liver of Arctic sculpin *Myoxocephalus scorpioides*	Kuujjuarapik, Québec (Canada)	(Martin et al., 2004)
	See also: *Comments Concerning the National Swedish Contaminant Monitoring Programme in Marine Biota*			(Bignert et al., 2016)

7.5 Perfluoroundecanoic acid: PFUnA

Tab. 282. Substance identity.

Parameters	
Name	Perfluoroundecanoic acid: PFUnA
Other names	Henicosafluoroundecanoic acid, Perfluoro-n-undecanoic acid, Perfluoroundecylic acid
IUPAC name	2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,11-henicosafluoroundecanoic acid
CAS number	2058-94-8
Molecular formula	C11HF21O2
Molecular weight	564.09
Structure	
SMILES	C(=O)(C(C(C(C(C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F) (F)F)O
Metabolites (or other related substances)	Not metabolized - Branched isomers

Tab. 283. Physico-chemical properties.

Endpoint	Value	Source

Endpoint	Value	Source
Vapour pressure (Pa)	0.10 at 25°C	(Bhhatarai and Gramatica, 2011; Rahman et al., 2013)
Water solubility (mg/L)	92.3 at 22.9°C	(Rahman et al., 2013)
Log K_{ow}	9.2	(Inoue et al., 2012)

Tab. 284. Environmental fate.

Endpoint	Value	Source
Sorption potential K_{OC}	Log K_{OC} (mL/g) 3.30 - 5.10	(Campos Pereira et al., 2018)
Biodegradability	NRB	ECHA
Bioaccumulation (BAF)	270 ± 18 L kg^{-1}	(Dai et al., 2013)
Bioconcentration (BCF)	2300 - 3700	(Inoue et al., 2012)

Tab. 285. Analytical methods.

Method	LOD	Description	Reference
Water SPE + LC/MS[2]	LOD: 25 ng/L	Extraction: SPE C18	(Hansen et al., 2002, 2001; Risha et al., 2005)
Water SPE + LC-ESI-TOF/MS	LOD: 10 - 300 pg/L	Extraction: SPE C18	(Voogt et al., 2014)
Water SPE + GC-EI/MS	LOD: 30 - 310 ng/L	Extraction: SPE HLB Derivatization: Isobuthyl ester	(Dufková et al., 2012, 2009)
Water SPE + GC-ECD	LOD: 0.2 - 0.7 µg/L	Extraction: SPE HLB Derivatization: Isobuthyl ester	(Dufková et al., 2012, 2009)
Sediment US + SPE + LC/MS[2]	LOD: 0.01 - 0.25 ng/g	Extraction: Ultrasound assisted (9:1 MeOH, 1%Ac) Centrifugation Clean-up: SPE C18	(Higgins et al., 2005)
Biota LLE + GC/MS[2]	LOD: 10 pg	Extraction: Ion-pairing agent MTBE Derivatization: Difluoro-anilides	(De Silva and Mabury, 2004)
Biota US + LC-TOF/MS	LOD: 1 - 8 pg	Extraction: Ultrasound assisted (MeOH/H_2O, NH_4Ac)	(Berger and Haukås, 2005)

7.5.1 Environmental exposure assessment

Tab. 286. Measured Environmental Concentrations.

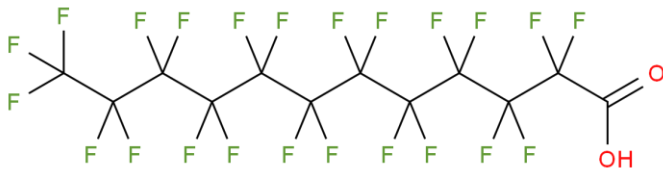|	Value	Matrix	Region/area	Source
Measured concentration in water MEC$_w$ (µg/L)	0.640	Groundwater	Veneto Region, PFAS red zone	ARPAV monitoring (Zanon, 2017)
	0.010 - 0.022	Surface water	Veneto Region, PFAS red zone	ARPAV monitoring (Zanon, 2017)
	<10 ng/L	Groundwater	Venice	ARPAV monitoring (ARPAV, 2019)
	<5 ng/L	Surface water	Venice	ARPAV monitoring (ARPAV, 2019)
	0.62 ng/L	Freshwater	Júcar river basin (East Spain)	(Campo et al., 2016)
Measured concentration in sediment MEC$_{sed}$ (µg/kg dw)	0.034 ng/g	Coastal sediment	South Bohai coastal watersheds (China)	(Zhu et al., 2014)
	0.084 ng/g	Riverine sediment	South Bohai coastal watersheds (China)	(Zhu et al., 2014)
Measured concentration in biota MEC$_{biota}$ (µg/kg)	56 - 78 ng/g	Liver of Polar bear *Ursus maritimus*	Sanikiluaq, Nunavut (Canada)	(Martin et al., 2004)
	0.78 - 55 ng/g	Liver of Arctic fox *Alopex lagopus*	Arviat, Nunavut (Canada)	(Martin et al., 2004)
	1.4 - 5.4 ng/g	Liver of Ringed seal *Phoca hispida*	Holman, Northwest Territories (Canada)	(Martin et al., 2004)
	2.0 - 5.9 ng/g	Liver of Ringed seal *Phoca hispida*	Grise Fjord, Nunavut (Canada)	(Martin et al., 2004)
	12 ng/g	Liver of Mink *Mustela vison*	Watson Lake Area, Yukon (Canada)	(Martin et al., 2004)
	2.2 ng/g	Liver of Common loon *Gavia immer*	Kuujjuarapik, Québec (Canada)	(Martin et al., 2004)

	Value	Matrix	Region/area	Source
	3.9 - 8.5 ng/g	Liver of White sucker *Catostomus commersoni*	Kuujjuarapik, Québec (Canada)	(Martin et al., 2004)
	4.9 - 6.5 ng/g	Liver of Brook trout *Salvelinus fontinalis*	Kuujjuarapik, Québec (Canada)	(Martin et al., 2004)
	2.7 - 4.7 ng/g	Liver of Lake whitefish *Coregonus clupeaformis*	Kuujjuarapik, Québec (Canada)	(Martin et al., 2004)
	6.1 ng/g	Liver of Lake trout *Salvelinus namaycush*	Lac Minto, Québec (Canada)	(Martin et al., 2004)
	2.9 ng/g	Liver of Northern pike *Esox lucius*	Kuujjuarapik, Québec (Canada)	(Martin et al., 2004)
	1.1 ng/g	Liver of Arctic sculpin *Myoxocephalus scorpioides*	Kuujjuarapik, Québec (Canada)	(Martin et al., 2004)
	See also: *Comments Concerning the National Swedish Contaminant Monitoring Programme in Marine Biota*			(Bignert et al., 2016)

7.6 Perfluorododecanoic acid: PFDoA

Tab. 287. Substance identity.

Parameters	
Name	Perfluorododecanoic acid: PFDoA
Other names	Tricosafluorododecanoic acid, Perfluoro-n-dodecanoic acid, Perfluorolauric acid
IUPAC name	2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,12,12,12-tricosafluorododecanoic acid
CAS number	307-55-1
Molecular formula	C12HF23O2
Molecular weight	614.10

Parameters	
Name	Perfluorododecanoic acid: PFDoA
Other names	Tricosafluorododecanoic acid, Perfluoro-n-dodecanoic acid, Perfluorolauric acid
IUPAC name	2,2,3,3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,11,11,12,12,12-tricosafluorododecanoic acid
Structure	
SMILES	C(=O)(C(C(C(C(C(C(C(C(C(C(C(C(F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)(F)F)O
Metabolites (or other related substances)	Not metabolized

Tab. 25. Physico-chemical properties.

Endpoint	Value	Source
Vapour pressure (Pa)	0.01 at 25°C	(Bhhatarai and Gramatica, 2011; Rahman et al., 2013)
Water solubility (mg/L)	0.52 at 25°C	(Inoue et al., 2012)
Log K_{ow}	10.2	(Inoue et al., 2012)

Tab. 26. Environmental fate.

Endpoint	Value	Source
Sorption potential K_{OC}	Log K_{OC} (mL/g) 5.6 ± 0.2	(Campos Pereira et al., 2018)
Biodegradability	NRB	ECHA
Bioaccumulation (BAF)	380 ± 22 L kg^{-1}	(Dai et al., 2013)
Bioconcentration (BCF)	16.000 - 10.000	(Inoue et al., 2012)

Tab. 27. Analytical methods.

Method	LOD	Description	Reference
Water SPE + LC/MS^2	LOD: 25 ng/L	Extraction: SPE C18	(Hansen et al., 2002, 2001; Risha et al., 2005)
Water SPE + LC/MS^2	LOD: 1 - 8 pg/L	Extraction: SPE C18	(Moody et al., 2001)

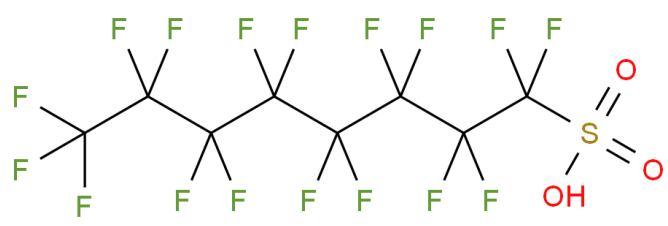| Method	LOD	Description	Reference
Water SPE + LC-ESI-TOF/MS	LOD: 10 - 300 pg/L	Extraction: SPE C18	(Voogt et al., 2014)
Water SPE disk + GC-EI/MS	LOD: 18 μg/L	Extraction: SPE disk SAX Derivatization: Methyl ester	(Moody and Field, 1999)
Water SPE + GC-EI/MS	LOD: 30 - 310 ng/L	Extraction: SPE HLB Derivatization: Isobuthyl ester	(Dufková et al., 2012, 2009)
Water SPE + GC-ECD	LOD: 0.2 - 0.7 μg/L	Extraction: SPE HLB Derivatization: Isobuthyl ester	(Dufková et al., 2012, 2009)
Sediment US + SPE + LC/MS^2	LOD: 0.01 - 0.25 ng/g	Extraction: Ultrasound assisted (9:1 MeOH, 1%Ac) Centrifugation Clean-up: SPE C18	(Higgins et al., 2005)
Biota LLE + GC/MS^2	LOD: 10 pg	Extraction: Ion-pairing agent MTBE Derivatization: Difluoro-anilides	(De Silva and Mabury, 2004)
Biota US + LC-TOF/MS	LOD: 1 - 8 pg	Extraction: Ultrasound assisted (MeOH/H$_2$O, NH$_4$Ac)	(Berger and Haukås, 2005)

7.6.1 Environmental exposure assessment

Tab. 28. Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source
Measured concentration in water MEC$_w$ (μg/L)	0.013	Groundwater	Veneto Region, PFAS red zone	ARPAV monitoring (Zanon, 2017)
	0.010 - 0.016	Surface water	Veneto Region, PFAS red zone	ARPAV monitoring (Zanon, 2017)
	<10 ng/L	Groundwater	Venice	ARPAV monitoring (ARPAV, 2019)
	<5 ng/L	Surface water	Venice	ARPAV monitoring (ARPAV, 2019)
Measured concentration in sediment MEC$_{sed}$ (μg/kg dw)	0.013 ng/g	Coastal sediment	South Bohai coastal watersheds (China)	(Zhu et al., 2014)
	0.027 ng/g	Riverine sediment	South Bohai coastal watersheds (China)	(Zhu et al., 2014)

	Value	Matrix	Region/area	Source
Measured concentration in biota MEC$_{biota}$ (µg/kg)	4.7 - 8.2 ng/g	Liver of Polar bear *Ursus maritimus*	Sanikiluaq, Nunavut (Canada)	(Martin et al., 2004)
	4.8 ng/g	Liver of Arctic fox *Alopex lagopus*	Arviat, Nunavut (Canada)	(Martin et al., 2004)
	0.74 ng/g	Liver of Ringed seal *Phoca hispida*	Holman, Northwest Territories (Canada)	(Martin et al., 2004)
	0.56 - 1.3 ng/g	Liver of Ringed seal *Phoca hispida*	Grise Fjord, Nunavut (Canada)	(Martin et al., 2004)
	0.76 ng/g	Liver of Mink *Mustela vison*	Watson Lake Area, Yukon (Canada)	(Martin et al., 2004)
	0.74 ng/g	Liver of Common loon *Gavia immer*	Kuujjuarapik, Québec (Canada)	(Martin et al., 2004)
	0.65 - 1.8 ng/g	Liver of White sucker *Catostomus commersoni*	Kuujjuarapik, Québec (Canada)	(Martin et al., 2004)
	0.83 - 2.2 ng/g	Liver of Brook trout *Salvelinus fontinalis*	Kuujjuarapik, Québec (Canada)	(Martin et al., 2004)
	0.69 - 1.8 ng/g	Liver of Lake whitefish *Coregonus clupeaformis*	Kuujjuarapik, Québec (Canada)	(Martin et al., 2004)
	2.30 ng/g	Liver of Lake trout *Salvelinus namaycush*	Lac Minto, Québec (Canada)	(Martin et al., 2004)
	0.83 ng/g	Liver of Northern pike *Esox lucius*	Kuujjuarapik, Québec (Canada)	(Martin et al., 2004)
	0.55 ng/g	Liver of Arctic sculpin *Myoxocephalus scorpioides*	Kuujjuarapik, Québec (Canada)	(Martin et al., 2004)
	See also: *Comments Concerning the National Swedish Contaminant Monitoring Programme in Marine Biota*			(Bignert et al., 2016)

7.7   Perfluorooctane sulfonic acid: PFOS

Tab. 29. Substance identity.

Parameters	
Name	Perfluorooctane sulfonic acid: PFOS
Other names	Heptadecafluorooctane sulfonic acid, Heptadecafluoro-1-octane sulfonic acid, Perfluorooctyl sulfonic acid, Perfluorooctane sulfonate
IUPAC name	1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-heptadecafluorooctane, -1-sulfonic acid
CAS number	1763-23-1
Molecular formula	C8HF17O3S
Molecular weight	500.13
Structure	
SMILES	C(C(C(C(C(C(F)(F)S(=O)(=O)O)(F)F)(F)F)(F)F)(C(C(C(F)(F)F)(F)F)(F)F)(F)F
Metabolites (or other related substances)	Not metabolized - Branched isomers

Tab. 30. Physico-chemical properties.

Endpoint	Value	Source
Vapour pressure (Pa)	0.27 at 25°C	Converted from PubChem and HSDB
Water solubility (mg/L)	3.2×10^{-3} at 25°C	PubChem and HSDB
Log K_{ow}	4.49	PubChem and HSDB

Tab. 31. Environmental fate.

Endpoint	Value	Source
Sorption potential K_{OC}	Log K_{OC} (mL/g) 2.6 - 3.8	(Campos Pereira et al., 2018)
Biodegradability	NRB	ECHA
Bioaccumulation (BAF)	179 ± 25 L kg-1	(Dai et al., 2013)
Bioconcentration (BCF)	720 - 1300	(Inoue et al., 2012)

Tab. 295. Analytical methods.

Method	LOD	Description	Reference
Water SPE + LC/MS[2]	LOD: 0.4 pg/L - 60 ng/L	Extraction: SPE C18	(Hansen et al., 2002, 2001; Taniyasu et al., 2003)
Water SPE + LC/MS[2]	LOD: 0.4 - 0.8 pg/L	Extraction: SPE HLB	(Yamashita et al., 2004)
Water SPE + LC/MS[2]	LOD: 3 - 5 pg/L	Extraction: SPE C18	(Moody et al., 2001)
Water SPE + HPLC/MS[2]	LOQ: 1.9 ng/L	Pre-cleaning: SPE HLB and WAX Off-line, Extraction: SPE HLB, On-line pre-concentration: SPE WAX	(Dasu et al., 2017)
Sediment US + SPE + LC/MS[2]	LOD: 0.04 - 0.11 ng/g	Extraction: Ultrasound assisted (9:1 MeOH, 1%Ac). Centrifugation, Clean-up: SPE C18	(Higgins et al., 2005)
Biota LLE + LC/MS[2]	LOD: 2 - 8 ng/g	Extraction: Ion-pairing agent MTBE	(Hansen et al., 2002, 2001)
Biota SPE + GC-ECNI/MS	LOD: 1.46 µg/L	Extraction: SPE WAX, In-Port-Derivatization: Buthyl ester	(Chu and Letcher, 2009)
Biota US + LC-TOF/MS	LOD: 0.2 - 0.5 pg	Extraction: Ultrasound assisted, (MeOH/H_2O, NH_4Ac)	(Berger and Haukås, 2005)

7.7.1   Environmental exposure assessment

Tab. 32. Measured Environmental Concentrations.

	Value	Matrix	Region/area	Source
Measured concentration in water MEC_w (µg/L)	0.010 - 0.026	Groundwater	Veneto Region, PFAS red zone	ARPAV monitoring (Zanon, 2017)
	0.010 - 0.424	Surface water	Veneto Region, PFAS red zone	ARPAV monitoring (Zanon, 2017)
	<10 ng/L	Groundwater	Venice	ARPAV monitoring (ARPAV, 2019)
	0.65 - 1.68 ng/L	Surface water	Venice	ARPAV monitoring (ARPAV, 2019)
	0.117	Drinking water	Veneto Region Summer 2013	(World Health Organization, 2017)

	Value	Matrix	Region/area	Source
	0.036	Drinking water	Veneto Region Spring 2014	(World Health Organization, 2017)
	1.343 ng/L	Marine water	Adriatic Sea (offshore from Venice)	(Loos et al., 2013)
	2.340	Freshwater	Lake Halmsjön nearby Stockholm Arlanda Airport	(Ahrens et al., 2015)
	0.01 - 128 ng/L	Freshwater	Júcar river basin (East Spain)	(Campo et al., 2016)
Measured concentration in sediment MEC_{sed} (µg/kg dw)	0.06 - 9.83 ng/g	River sediment	Júcar river basin (East Spain)	(Campo et al., 2016)
	0.09 - 7.37 ng/g	Estuarine sediment	Charleston harbour (South Carolina, USA)	(White et al., 2015)
	0.061 - 0.188 ng/g	Coastal sediment	South Bohai coastal watersheds (China)	(Zhu et al., 2014)
	0.027 - 0.435 ng/g	Riverine sediment	South Bohai coastal watersheds (China)	(Zhu et al., 2014)
	0.492 - 30.1 ng/g	Sediment core	Lake Ontario	(Yeung et al., 2015)
Measured concentration in biota MEC_{biota} (µg/kg)	0.56 - 8.13 µg kg^{-1}	Fish	Júcar river basin (East Spain)	(Campo et al., 2016)
	1245 - 1325 ng/g ww	Liver of Polar bear *Ursus maritimus*	Ittoqqortoormiit (Greenland)	(Bossi et al., 2005)
	52 - 67 ng/g ww	Liver of Ringed seal *Phoca hispida*	Ittoqqortoormiit (Greenland)	(Bossi et al., 2005)
	27 ng/g ww	Liver of Ringed seal *Phoca hispida*	Avanersuaq (Greenland)	(Bossi et al., 2005)
	10 - 13 ng/g ww	Liver of Ringed seal *Phoca hispida*	Qeqertarsuaq (Greenland)	(Bossi et al., 2005)

	Value	Matrix	Region/area	Source
	13 - 16 ng/g ww	Liver of Black guillemot *Cepphus grylle*	Ittoqqortoormiit (Greenland)	(Bossi et al., 2005)
	14 ng/g ww	Liver of Black guillemot *Cepphus grylle*	Qeqertarsuaq (Greenland)	(Bossi et al., 2005)
	13 - 18 ng/g ww	Liver of Shorthorn sculpin *Myoxocephalus scorpius*	Ittoqqortoormiit (Greenland)	(Bossi et al., 2005)
	28 - 39 ng/g ww	Liver of Long finned pilot whale *Globicephala melas*	Miðvágur (Greenland)	(Bossi et al., 2005)
	65 ng/g ww	Liver of Long finned pilot whale *Globicephala melas*	Bøur (Greenland)	(Bossi et al., 2005)
	24 - 29 ng/g ww	Liver of Fulmar *Fulmarus glacialis*	Nólsoy and Viðareiði (Greenland)	(Bossi et al., 2005)
	1700 - >4000 ng/g	Liver of Polar bear *Ursus maritimus*	Sanikiluaq, Nunavut (Canada)	(Martin et al., 2004)
	6.1 - 1400 ng/g	Liver of Arctic fox *Alopex lagopus*	Arviat, Nunavut (Canada)	(Martin et al., 2004)
	8.6 - 23 ng/g	Liver of Ringed seal *Phoca hispida*	Holman, Northwest Territories (Canada)	(Martin et al., 2004)
	10 - 37 ng/g	Liver of Ringed seal *Phoca hispida*	Grise Fjord, Nunavut (Canada)	(Martin et al., 2004)
	1.3 - 20 ng/g	Liver of Mink *Mustela vison*	Watson Lake Area, Yukon (Canada)	(Martin et al., 2004)
	11 - 26 ng/g	Liver of Common loon *Gavia immer*	Kuujjuarapik, Québec (Canada)	(Martin et al., 2004)

	Value	Matrix	Region/area	Source
	1.0 - 1.5 ng/g	Liver of Northern fulmar *Fulmarus glacialis*	Prince Leopold Island, Nunavut (Canada)	(Martin et al., 2004)
	6.5 - 8.6 ng/g	Liver of White sucker *Catostomus commersoni*	Kuujjuarapik, Québec (Canada)	(Martin et al., 2004)
	29 - 50 ng/g	Liver of Brook trout *Salvelinus fontinalis*	Kuujjuarapik, Québec (Canada)	(Martin et al., 2004)
	12 ng/g	Liver of Lake whitefish *Coregonus clupeaformis*	Kuujjuarapik, Québec (Canada)	(Martin et al., 2004)
	31 ng/g	Liver of Lake trout *Salvelinus namaycush*	Lac Minto, Québec (Canada)	(Martin et al., 2004)
	5.7 ng/g	Liver of Northern pike *Esox lucius*	Kuujjuarapik, Québec (Canada)	(Martin et al., 2004)
	12 ng/g	Liver of Arctic sculpin *Myoxocephalus scorpioides*	Kuujjuarapik, Québec (Canada)	(Martin et al., 2004)
	See also: *Comments Concerning the National Swedish Contaminant Monitoring Programme in Marine Biota*			(Bignert et al., 2016)

Tab. 33. Ecotoxicological data.

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
Algae				
Isochrysis galbana	72-h	Growth inhibition	NOEC = 7.500	Mhadhbi et al., 2012
			LOEC = 15.000	
			EC$_{50}$ = 37.500	
Crustacea				
Siriella armata	96-h	Mortality	NOEC = 1.250	Mhadhbi et al., 2012
			LOEC = 2.500	

Species	Time-scale	Endpoint	Toxicity (µg/L)	Source
			EC_{50} = 6.900	
Mollusca				
Mytilus galloprovincialis	48-h	Larval development	NOEC = 0,01	Fabbri et al., 2014
			LOEC = 0,1	
Echinoida				
Paracentrotus lividus	48-h	Growth inhibition (larvae)	NOEC = 1.000	Mhadhbi et al., 2012
			LOEC = 2.000	
			EC_{50} = 20.000	
Fishes				
Psetta maxima	144-h	Mortality	NOEC = 15	Mhadhbi et al., 2012
			LOEC = 30	
			EC_{50} = 110	
Gadus morhua	14-d	Mortality	NOEC = 200	Preus-Olsen et al., 2014
		Growth (length)	NOEC = 200	
		Growth (weight)	NOEC = 200	
		Condition index	NOEC = 200	

LC_{50}/EC_{50} = Lethal/Effective Concentration 50
LOEC/LOEL = Lowest Observed Effect Concentration/Level
NOEC/NOEL = Non Observed Effect Concentration/Level

7.8 Analytical methods employed

The liquid chromatography (LC) methods are the most commonly used analytical methods for the determination of PFASs. They can be employed with different detection methods, but determination with mass spectrometry (MS) detection, with different type and configuration of the analysers, are commonly considered as the reference methods.

Nevertheless, LC tubing and the internal LC parts could be responsible for high PFAS signals in blanks. Therefore, the LC tubing is usually replaced with PEEK (polyether ether ketone) and/or stainless steel tubing, while solvent inlet filters are replaced with stainless steel ones. Furthermore, all the Teflon® and other fluoropolymers parts, like vial caps and septa, are replaced with polyethylene ones.

Although analyses for PFASs are now mostly carried out by means of HPLC-MS(-MS) to meet the requirements of high sensitivity and selectivity, many laboratories are not equipped for this method and would prefer readily available, and less expensive, gas chromatography techniques.

GC is less common than LC methods but is also widely applied in determination of PFASs in different matrices, including environmental ones. If GC offers much larger efficiency of chromatographic separation, its practical limitation is given by the volatility of analytes to be determined that requires an additional derivatization step to convert the polar functional group to a non-polar derivative (usually ethers) prior to injection in GC columns.

Since in our laboratory routine practice we already successfully use a GC method which implies a simply micro-derivatization to convert PFAS in their equivalent isobutyl esters, as explained in (Pizzini et al., 2017), in this project we will use the GC technique for the PFCA quantification. This practice also helped to avoid background contamination from internal fluoropolymer parts of LC. Since GC determination of PFSAs is quite difficult because of the instability of its derivatives, which quickly undergo solvolysis and nucleophilic substitution reactions (Miller, 2010; Teasdale et al., 2010), where analytical difficulties arise (*i.e.* PFOS determination) the analysis will be carried out by means of HPLC-MS[2].

7.9   Ecotoxicological data

Tab. 34. Biochemical and genetic responses for PFASs.

Species	Concentrations	Days of exposure	Biochemical/molecular effects	Reference
Oysters *Crassostrea gigas*	20 mg/L of perfluorooctanoic acid (PFOA)	24h	Effects on development (alterations of haemocyte abnormal developed D-shelled larvae)	Vogeler et al., 2017
Mussels *Perna viridis*	0.1, 1, 10, 100, and 1000 µg/L of potassium perfluorooctanesulfonate (PFOS), PFOA, perfluorononanoic acid (PFNA) and perfluorodecanoic acid (PFDA)	24h	Immunotoxicity	Liu and Gin, 2018.
Freshwater mussels *Dreissena polymorpha*	1, 10 and 1000 µg/L of PFOS and PFOA	10 days	Alterations in multixenobiotic transporter activity (MXR) and filtration and oxygen consumption rates	Fernández-Sanjuan et al., 2013.
Mussels *Mytilus galloprovincialis*	0.01–0.1–1–10–100–1000 µg/L of PFOS and PFOA	48 h	PFOS and PFOA interfered with normal larval development (presence of not fully developed D-larvae)	Fabbri et al., 2014.

7.10   References

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HSDB, Hazardous Substances Data Bank: https://toxnet.nlm.nih.gov/newtoxnet/hsdb.htm.

PubChem: https://pubchem.ncbi.nlm.nih.gov/.

8   Microplastics

Environmental contamination by plastic debris is documented in marine environment from the 1970's and now dispersion in aquatic environments shows a worldwide diffusion, including pristine areas such as deep sea, Arctic Ocean and Antarctica.

Microplastics are the most abundant and pervasive components, because these small particles can be ingested and accumulated within organisms, causing physical and mechanical damages, obstructions of gastrointestinal tract and a consequent pseudo-satiation resulting in reduced food intake that may lead to mortality. Toxic effects due to organic compounds and trace elements adsorbed on the microplastics may be a potential hazard, as well.

Microplastic particles are generally classified according their sizes, but the classification is still a work in progress. The European Chemical Agency (ECHA, 2019) propose the definition of microplastic as "a material composed of solid polymer-containing particles, to which additives or other substances may have been added, with particle dimensions ranging from 1 nm to 5 mm and with fiber lengths ranging from 3 nm to 15 mm and length to diameter ratio of >3".

Primary sources of microplastics are cosmetics, personal care products and fibers from household washing (washing machines and hand-washing); it is assessed that 35% of primary microplastics released in the environments derives from the shedding of synthetic fibers being washed, which are eventually discharged in rivers and oceans. Once in the ocean, fibers may be ingested by the biota, entering then the trophic net and becoming a relevant environmental problem.

Since microplastics are emerging pollutants, an accurate estimate of the amount of microplastics in the environment it is fundamental, as well as a precise polymer identification so that the problem could be assessed correctly and adequate measures taken.
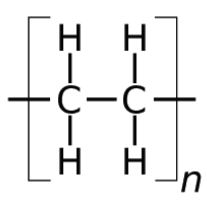
In literature several methods have been employed, especially microscopic methods which do not allow to identify polymers. In fact, in several studies a subset of samples was analysed via FTIR or via FTIR-ATR, after the microscopic observations. The analysis via μ-FTIR is a non-destructive technique and it allows a quantification of microplastic and a simultaneous polymer identification, since μ-FTIR instruments couple microscopy with FTIR Spectroscopy.

To sample microplastics in sediments. box corer, Van Benn grab or iron scoop can be employed, in relation to the sampling depth to be investigated. Sediments will be then stored in glass containers or alumin foils. To sample microplastics in water, trawls with different mesh will be employed. The finest mesh of the trawl net is 100 μm and microplastic particles <100 μm, which can be ingested by biota, cannot be sampled and analysed; hence, for the quantification and the identification of microplastics <100 μm water can be sampled with plastic free pumps. Water samples will be stored in glass containers at 4°C until the filtration and the analysis.

In the subsequent tables microplastics found in water-bodies, seawater, sediments and biota are reported, together with their sources and the methods employed; their abundance are reported as percentage (%). In another set of tables polymer characteristics are reported as well; for some polymers it was not possible to retrieve complete information, since they are not widespread and they may be degradation products of primary polymers. When the CAS number cannot be retrieved, the EC number of ECHA (European Chemical Agency) is shown.

8.1 Polyethylene

Tab. 35. Substance identity.

Parameters	
Name	Polyethylene
Other names	PE
IUPAC name	Polymethylene
CAS number	9002-88-4
Molecular formula	$(C_2H_4)_n$
Structure	

Tab. 300. Physico-chemical properties.

Endpoint	Value	Source
Melting point	115–135 °C	Batra, Kamal (2014).
Boiling point	120-180 °C	MSDS Total PE0016, Validation date 2013
Relative density	0.88–0.96 g/cm^3	Batra, Kamal (2014
Vapour pressure (Pa)	Negligible	MSDS Total PE0016, Validation date 2013
Water solubility (mg/L)	Insoluble	MSDS Total PE0016, Validation date 2013
Flash point	341 °C	MSDS Total PE0016, Validation date 2013
Autoflammability	349 °C	MSDS Total PE0016, Validation date 2013

Tab. 301. Measured Environmental Concentrations.

	Abundance	Matrix	Region/area	Source of emission	Method	Source
Water	66 %	water-column and surface	coastal waters of Tuscany (Italy)	the riverine inputs, the terrestrial pollution	Microscopy FTIR	Baini et al., 2018

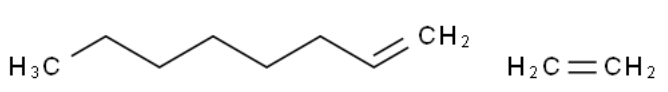|	Abundance	Matrix	Region/area	Source of emission	Method	Source
	>80% (* other 14% PP, PO,PS, PVC, ABS.	Sea surface water	Slovenian part of the Trieste Bay in the Northern Adriatic Sea	sea-current	Microscopy	Gajšta et al., 2016
	41.3%	Surface water	Lake Iseo	municipal discharges, sewage, urban runoff and storm water	Microscopy FTIR	Sighicelli et al., 2018
	48%	Surface water	Lake Maggiore	municipal discharges, sewage, urban runoff and storm water	Microscopy FTIR	Sighicelli et al., 2018
	45.4%	Surface water	Lake Garda	municipal discharges, sewage, urban runoff and storm water	Microscopy FTIR	Sighicelli et al., 2018
	34 to 74% off Pellestrina and from 41 to 79% off the Po Delta	Sea surface water	Lagoon of Venice and off the Po Delta	maritime traffic; tourism-related impacts, intense fishing and mussel farming.	µFT-IR	Vianello et al., 2018
	52%	Sea surface water	Mediterranean Sea	packaging industry and ship pollution	FTIR-ATR	Suaria et al., 2018

	Abundance	Matrix	Region/area	Source of emission	Method	Source
	66.5%	Sea surface water	Adriatic Sea: Gulf of Venice (Italy); Gulf of Trieste; (Slovenian waters); Gulf of Split (Croatia); Gulf of Kotor (Montenegro)	food products, coatings, plastics colorants and additives		Zeri et al., 2018
	26%	Sea surface water	Italian minor islands, Mediterranean Sea	Washing-machine discharge and ship	µFT-IR	De Lucia et al., 2018.
	67.2%	Sea surface water	Mediterranean Sea	Agriculture, fisheries, aquaculture, maritime transport, and tourism	Microscopy FTIR	Digka et al.,
Sediment	48.4% - 42-445 µm	Superficial sediment	Lagoon of Venice	Urban discharges, port, industry, mussel farming, land anthropogenic materials packaging and breakdown of rigid plastics	µFT-IR	Vianello et al., 2013

	Abundance	Matrix	Region/area	Source of emission	Method	Source
	18% (abundance) 61.4% (weight)	Marine sediments	Pianosa Island (Central Adriatic Sea)	marine-based sources including fishing vessels, merchant vessels and recreational boats, shipping traffic	Microscopy FTIR	Mistri et al., 2018
	43.5%	Beach sediment	Mediterranean Sea	Agriculture, fisheries, aquaculture, maritime transport, and tourism	Microscopy FTIR	Digka et al.,
	85.71%	Sediment	littoral zone of the north Tunisian coast (Mediterranean Sea)	textile, plastic and electronic industries, fishing activities and shellfish production.	Microscopy FTIR-ATR	Abidli et al., 2018
	16.25%	Beach sediment	central Italy coast	packaging, plastic bottles, cups, cotton buds or containers, fhishin net	Microscopy FTIR	Pietrelli et al., 2018
Biota	1.85±0.04 items per fish (2014); 1.71±0.08 items per fish (2015)	Gastrointestinal tract of Solea solea	central and northern Adriatic Sea	Sea hydrodynamic circulation, especially the near-shore currents and gyres mussel farms	µFT-IR	Pellinia et al., 2017

	Abundance	Matrix	Region/area	Source of emission	Method	Source
	61.5%	Mussels and fish	Mediterranean Sea	Agriculture, fisheries, aquaculture, maritime transport, and tourism	Microscopy FTIR	Digka et al.,
	29.86%	Posidonia oceanica spheroids (egagropiles, EG)	Central Italy coast	packaging, plastic bottles, cups, cotton buds or containers, fhishin net	Microscopy FTIR	Pietrelli et al., 2018.

8.2 Linear low-density polyethylene-octene copolymer (LLDP/Oct)

Tab. 302. Substance identity.
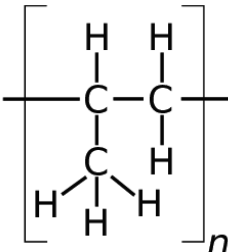
Parameters	
Name	Linear low-density polyethylene-octene copolymer
Other names	LLDP/Oct, Dow 13;Dow 2045;Dow 2032;Dow 2001;Dowlex 2027;Dowlex 2032;Dowlex 2045;Dowlex 2035;Dowlex 2037;Dowlex 2038
IUPAC name	POLY(ETHYLENE-CO-1-OCTENE)
CAS number	26221-73-8
Molecular formula	$(C_{10}H_{20})_n$
Structure	

Tab. 303. Measured Environmental Concentrations.

	Abundance	Matrix	Region/area	Source of emission	Method	Source
Sediment	2.2% (abundance) 9,0 % (weight)	Marine sediments	Pianosa Island (Central Adriatic Sea)	marine-based sources including fishing vessels, merchant vessels and recreational boats, shipping traffic	Microscopy FTIR	Mistri et al., 2018

8.3 Polypropylene (PP)

Tab. 304. Substance identity.

Parameters	
Name	Polypropylene
Other names	PP, Polypropene; Polipropene 25 [USAN]; Propene polymers; Propylene polymers; 1-Propene; [-Ch2-Ch(Ch3)-]n
IUPAC name	Poly(propene)
CAS number	9003-07-0
Molecular formula	$[CH_2CH(CH_3)]_n$
Structure	

Tab. 305. Physico-chemical properties.

Endpoint	Value	Source
Melting point	130 to 165°C	MSDS Sasol, Revision 2011
Boiling point	Not available	MSDS Sasol, Revision 2011
Relative density	0.88-0.92 g/m^3	MSDS Sasol, Revision 2011
Vapour pressure (Pa)	Not applicable	MSDS Sasol, Revision 2011
Water solubility (mg/L)	Insoluble in water	MSDS Sasol, Revision 2011
Flash point	>350 °C	MSDS Sasol, Revision 2011
Autoflammability	>390 °C	MSDS Sasol, Revision 2011

Tab. 306. Measured Environmental Concentrations.

	Abundance	Matrix	Region/area	Source of emission	Method	Source
Water	28%	water-column and surface	coastal waters of Tuscany (Italy)	the riverine inputs, the terrestrial pollution	Microscopy FTIR	Baini et al., 2018

	Abundance	Matrix	Region/area	Source of emission	Method	Source
	5.4%	Surface water	Lake Iseo	municipal discharges, sewage, urban runoff and storm water	Microscopy FTIR	Sighicelli et al., 2018
	17.2%	Surface water	Lake Maggiore	municipal discharges, sewage, urban runoff and storm water	Microscopy FTIR	Sighicelli et al., 2018
	21.8%	Surface water	Lake Garda	municipal discharges, sewage, urban runoff and storm water	Microscopy FTIR	Sighicelli et al., 2018
	5 - 30%	Sea surface water	Lagoon of Venice and off the Po Delta	maritime traffic; tourism-related impacts, intense fishing and mussel farming.	µFT-IR	Vianello et al., 2018
	16%	Sea surface water	Mediterranean Sea	packaging industry and ship pollution	FTIR-ATR	Suaria et al., 2018
	17.9%	Sea surface water	Adriatic Sea: Gulf of Venice (Italy); Gulf of Trieste; (Slovenian waters); Gulf of Split (Croatia); Gulf of Kotor (Montenegro)	food products, coatings, plastics' colorants and additives		Zeri et al., 2018
	11%	Sea surface water	Italian minor islands, Mediterranean Sea	Washing-machine discharge and ship	µFT-IR	De Lucia et al., 2018.
	17.3%	Sea surface water	Mediterranean Sea		Microscopy FTIR	Digka et al.,

	Abundance	Matrix	Region/area	Source of emission	Method	Source
Sediment	34.1 % 15-1660 µm	Superficial sediment	Lagoon of Venice	Urban discharges, port, industry, mussel farming, land anthropogenic, textile floor covering, carpets, rugs, sportswear, fishing nets	µFT-IR	Vianello et al., 2013
	3% (abundance) 19.6% (weight)	Marine sediments	Pianosa Island (Central Adriatic Sea)	Packaging and marine-based sources including fishing vessels, merchant vessels and recreational boats, shipping traffic	Microscopy FTIR	Mistri et al., 2018
	38%	Beach sediment	Mediterranean Sea	Agriculture, fisheries, aquaculture, maritime transport, and tourism	Microscopy FTIR	Digka et al.,
	14.29%	Sediment	littoral zone of the north Tunisian coast (Mediterranean Sea)	textile, plastic and electronic industries, fishing activities and shellfish production.	Microscopy FTIR-ATR	Abidli et al., 2018
	14.47%	Beach sediment	central Italy coast	packaging, plastic bottles, cups, cotton buds or containers, fishing net	Microscopy FTIR	Pietrelli et al., 2018

	Abundance	Matrix	Region/area	Source of emission	Method	Source
Biota	1.85±0.05 items per fish (2014); 1.72±0.08 items per fish (2015)	gastrointestinal tract of Solea solea	central and northern Adriatic Sea	Sea hydrodynamic circulation, especially the near-shore currents and gyres mussel farms	µFT-IR	Pellini et al., 2017
	50%	stomach content of sardines (Sardina pilchardus)	central Adriatic Sea	Environmental conditions, human impacts, flooding events and current pattern in marine and coastal areas	Microscopy, µFT-IR	Renzi et al., 2018
	23,07%	Mussels and fish	Mediterranean Sea	Agriculture, fisheries, aquaculture, maritime transport, and tourism	Microscopy FTIR	Digka et al.,
	6.33%	Posidonia oceanica spheroids (egagropiles, EG)	Central Italy coast	packaging, plastic bottles, cups, cotton buds or containers, fishing net	Microscopy FTIR	Pietrelli et al., 2018.

8.4 Poly(ethylene-propylene)

Tab. 307. Substance identity.

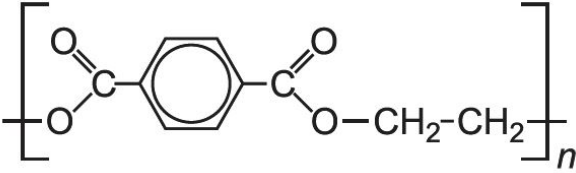| Parameters	
Name	Poly(ethylene-propylene)
Other names	Propylene Ethylene Polymer (PP Block Copolymer, PP Random Copolymer), Ethylene-propylene rubber
CAS number	9010-79-1

Tab. 308. Physico-chemical properties.

Endpoint	Value	Source
Melting point	130~170 °C	MSDS LG Chem, 2010
Boiling point	Not available	MSDS LG Chem, 2010
Vapour pressure (Pa)	Not applicable	MSDS LG Chem, 2010
Water solubility (mg/L)	Insoluble in water	MSDS LG Chem, 2010
Log K_{ow}	Not applicable	MSDS LG Chem, 2010
Flash point	> 340 °C	MSDS LG Chem, 2010
Autoflammability	Not available	MSDS LG Chem, 2010

Tab. 309. Measured Environmental Concentrations.

	Abundance	Matrix	Region/area	Source of emission	Method	Source
Sediment	5.2% 5-244 µm	Superficial sediment	Lagoon of Venice	Urban discharges, port, industry, mussel farming, land anthropogenic	µFT-IR	Vianello et al., 2013

8.5 Polyester (PL)

Tab. 310. Substance identity.

Parameters	
Name	Polyester
Other names	PL
CAS number	25038-59-9
Structure	

Tab. 311. Physico-chemical properties.

Endpoint	Value	Source
Melting point	250 °C	MSDS Akra Polyester, 2010

Endpoint	Value	Source
Boiling point	Not applicable	MSDS Akra Polyester, 2010
Relative density	1.38-1.42	MSDS Akra Polyester, 2010
Vapour pressure (Pa)	Not applicable	MSDS Akra Polyester, 2010
Water solubility (mg/L)	Insoluble in water	MSDS Akra Polyester, 2010
Log K_{ow}	Not applicable	MSDS Akra Polyester, 2010
Flash point	350 °C	MSDS Akra Polyester, 2010
Autoflammability	420 °C	MSDS Akra Polyester, 2010

Tab. 312. Measured Environmental Concentrations.
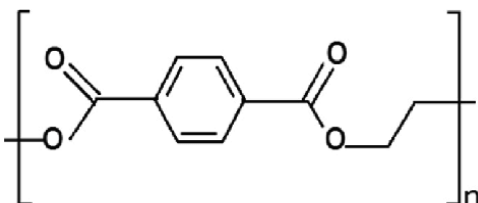
	Abundance	Matrix	Region/area	Source of emission	Mehod	Source
Water	9,0 %	Surface water	Lake Iseo	municipal discharges, sewage, urban runoff and storm water	Microscopy FTIR	Sighicelli et al., 2018
	0.6%	Surface water	Lake Garda	municipal discharges, sewage, urban runoff and storm water	Microscopy FTIR	Sighicelli et al., 2018
	1.6%	Sea surface water	Adriatic Sea: Gulf of Venice (Italy); Gulf of Trieste; (Slovenian waters); Gulf of Split (Croatia); Gulf of Kotor (Montenegro)	food products, coatings, plastics' colorants and additives		Zeri et al., 2018
	8%	Sea surface water	Italian minor islands, Mediterranean Sea	Washing-machine discharge and ship	µFT-IR	De Lucia et al., 2018.

	Abundance	Matrix	Region/area	Source of emission	Mehod	Source
Sediment	3.6% 15-2413 µm	Superficial sediment	Lagoon of Venice	Urban discharges, port, industry, mussel farming, land anthropogenic	µFT-IR	Vianello et al., 2013
	0.14%	Beach sediment	central Italy coast	packaging, plastic bottles, cups, cotton buds or containers, fhishin net	Microscopy FTIR	Pietrelli et al., 2018
Biota	1.74 ± 0.05 items per fish (2014); 1.61 ± 0.09 items per fish (2015)	gastrointestinal tract of Solea solea	central and northern Adriatic Sea	Sea hydrodynamic circulation, especially the near-shore currents and gyres mussel farms	µFT-IR	Pellinia et al., 2017
	6.34%	Posidonia oceanica spheroids (egagropiles, EG)	Central Italy coast	packaging, plastic bottles, cups, cotton buds or containers, fhishin net	Microscopy FTIR	Pietrelli et al., 2018.

8.6   Polyethylene terephthalate (PET)

Tab. 313. Substance identity.

Parameters	
Name	Polyethylene terephthalate
Other names	PET, PETE, PETP or PET-P
IUPAC name	Poly(ethyl benzene-1,4-dicarboxylate)
CAS number	25038-59-9
Molecular formula	$(C_{10}H_8O_4)_n$

Parameters	
Name	Polyethylene terephthalate
Other names	PET, PETE, PETP or PET-P
IUPAC name	Poly(ethyl benzene-1,4-dicarboxylate)
Structure	

Tab. 314. Physico-chemical properties.

Endpoint	Value	Source
Melting point	> 250 °C (482 °F; 523 K)	GESTIS Substance Database
Boiling point	> 350 °C (662 °F; 623 K)	GESTIS Substance Database
Relative density	1.38 g/cm^3 (20 °C)	GESTIS Substance Database
Water solubility (mg/L)	insoluble	GESTIS Substance Database

Tab. 315. Measured Environmental Concentrations.
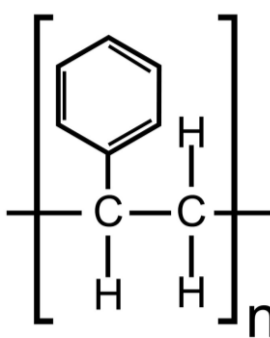
	Abundance	Abundance	Region/area	Source of emission	Method	Source
Water	0.6%	Surface water	Lake Garda	municipal discharges, sewage, urban runoff and storm water	Microscopy FTIR	Sighicelli et al., 2018
	<1%	Sea surface water	Mediterranean Sea	packaging industry and ship pollution	FTIR-ATR	Suaria et al., 2018
	1%	Sea surface water	Adriatic Sea: Gulf of Venice (Italy); Gulf of Trieste; (Slovenian waters); Gulf of Split (Croatia); Gulf of Kotor (Montenegro)	food products, coatings, plastics' colorants and additives		Zeri et al., 2018

	Abundance	Abundance	Region/area	Source of emission	Method	Source
	0.6%	Sea surface water	Mediterranean Sea	Agriculture, fisheries, aquaculture, maritime transport, and tourism	Microscopy FTIR	Digka et al.,
Sediment	6%	Beach sediment	Mediterranean Sea	Agriculture, fisheries, aquaculture, maritime transport, and tourism	Microscopy FTIR	Digka et al.,
	0.66%	Beach sediment	central Italy coast	packaging, plastic bottles, cups, cotton buds or containers, fhishin net	Microscopy FTIR	Pietrelli et al., 2018
Biota	7%	stomach content of anchovies (Engraulis encrasicolus)	central Adriatic Sea	Environmental conditions, human impacts, flooding events and current pattern in marine and coastal areas	Microscopy, µFT-IR	Renzi et al., 2018
	3.8%	Mussels and fish	Mediterranean Sea	Agriculture, fisheries, aquaculture, maritime transport, and tourism	Microscopy FTIR	Digka et al.,
	5.90%	Posidonia oceanica spheroids (egagropiles, EG)	Central Italy coast	packaging, plastic bottles, cups, cotton	Microscopy FTIR	Pietrelli et al., 2018.

8.7 Polystyrene (PS)

Tab. 316. Substance identity.

Parameters	
Name	Polystyrene
IUPAC name	Poly(1-phenylethene)
CAS number	9003-53-6
Molecular formula	$(C_8H_8)_n$
Structure	

Tab. 317. Physico-chemical properties.

Endpoint	Value	Source
Melting point	~ 240 °C (464 °F; 513 K)	ISBN 978-1-85957-191-0
Relative density	0.96–1.04 g/cm^3	ISBN 978-1-85957-191-0
Water solubility (mg/L)	insoluble	ISBN 978-1-85957-191-0

Tab. 318. Measured Environmental Concentrations.

	Abundance	Matrix	Region/area	Source of emission	Method	Source
Water	5%	water-column and surface	coastal waters of Tuscany (Italy)	the riverine inputs, the terrestrial pollution	Microscopy FTIR	Baini et al., 2018
	1.8%	Surface water	Lake Iseo	municipal discharges, sewage, urban runoff and storm water	Microscopy FTIR	Sighicelli et al., 2018

	Abundance	Matrix	Region/area	Source of emission	Method	Source
	4.9%	Surface water	Lake Maggiore	municipal discharges, sewage, urban runoff and storm water	Microscopy FTIR	Sighicelli et al., 2018
	1.9%	Surface water	Lake Garda	municipal discharges, sewage, urban runoff and storm water	Microscopy FTIR	Sighicelli et al., 2018
	0-9%	Sea surface water	Lagoon of Venice and off the Po Delta	maritime traffic; tourism-related impacts, intense fishing and mussel farming.	µFT-IR	Vianello et al., 2018
	2.8%	Sea surface water	Mediterranean Sea	packaging industry and ship pollution	FTIR-ATR	Suaria et al., 2018
	0.2%	Sea surface water	Mediterranean Sea	Agriculture, fisheries, aquaculture, maritime transport, and tourism	Microscopy FTIR	Digka et al.,
Sediment	3.5% 42-259 µm	Superficial sediment	Lagoon of Venice	Urban discharges, port, industry, mussel farming, land anthropogenic, packaging, disposable items,	µFT-IR	Vianello et al., 2013
	5.7%	Beach sediment	Mediterranean Sea	Agriculture, fisheries, aquaculture, maritime transport, and tourism	Microscopy FTIR	Digka et al.,

	Abundance	Matrix	Region/area	Source of emission	Method	Source
	1.41%	Beach sediment	central Italy coast	packaging, plastic bottles, cups, cotton buds or containers, fishing net	Microscopy FTIR	Pietrelli et al., 2018
Biota	4.2%	Mussels and fish	Mediterranean Sea	Agriculture, fisheries, aquaculture, maritime transport, and tourism	Microscopy FTIR	Digka et al.,

8.8 Expanded polystyrene (EPS)

Tab. 319. Measured Environmental Concentrations.

	Abundance	Matrix	Region/area	Source of emission	Method	Source
Water	24.6%	Surface water	Lake Iseo	municipal discharges, sewage, urban runoff and storm water	Microscopy FTIR	Sighicelli et al., 2018
	4.2%	Sea surface water	Adriatic Sea: Gulf of Venice (Italy); Gulf of Trieste; (Slovenian waters); Gulf of Split (Croatia); Gulf of Kotor (Montenegro)	food products, coatings, plastics' colorants and additives	Microscopy FTIR-ATR	Zeri et al., 2018
Sediment	9%	Surface water	Lake Maggiore	municipal discharges, sewage, urban runoff and storm water	Microscopy FTIR	Sighicelli et al., 2018
Biota	21.7%	Surface water	Lake Garda	municipal discharges, sewage, urban runoff and storm water	Microscopy FTIR	Sighicelli et al., 2018

8.9 Polyacrylonitrile (PAN)

Tab. 320. Substance identity.

Parameters	
Name	Polyacrylonitrile
IUPAC name	poly(1-acrylonitrile)
Molecular formula	C_3H_3N
Structure	

Tab. 321. Physico-chemical properties.

Endpoint	Value
Melting point	300 °C (572 °F; 573 K)
Boiling point	Degrades
Relative density	1.184 g/cm³
Water solubility (mg/L)	Insoluble

Tab. 322. Measured Environmental Concentrations.

	Abundance	Matrix	Region/area	Source of emission	Method	Source
Water	3,1%	Sea surface water	Adriatic Sea: Gulf of Venice (Italy); Gulf of Trieste; (Slovenian waters); Gulf of Split (Croatia); Gulf of Kotor (Montenegro)	food products, coatings, plastics' colorants and additives	Microscopy FTIR-ATR	Zeri et al., 2018
Sediment	2.6 % 18-950 µm	Superficial sediment	Lagoon of Venice	Urban discharges, port, industry, mussel farming, land anthropogenic	µFT-IR	Vianello et al., 2013
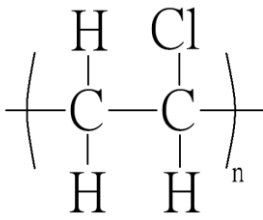
8.10 Alkyd resin

Tab. 323. Measured Environmental Concentrations.

	Abundance	Matrix	Region/area	Source of emission	Method	Source
Sediment	1.4% 55-203 µm	Superficial sediment	Lagoon of Venice	Urban discharges, port, industry, mussel farming, land anthropogenic	µFT-IR	Vianello et al., 2013

8.11 Polyvinylchloride (PVC)

Tab. 324. Substance identity.

Parameters	
Name	Polyvinyl chloride
IUPAC name	poly(1-chloroethylene)
CAS number	9002-86-2
Molecular formula	$(C_2H_3Cl)_n$
Structure	

Tab. 325. Measured Environmental Concentrations.

	Abundance	Matrix	Region/area	Source of emission	Method	Source
Water	5.4%	Surface water	Lake Iseo	municipal discharges, sewage, urban runoff and storm water	Microscopy FTIR	
	3.7%	Surface water	Lake Maggiore	municipal discharges, sewage, urban runoff and storm water	Microscopy FTIR	
	0.6%	Surface water	Lake Garda	municipal discharges, sewage, urban runoff and storm water	Microscopy FTIR	
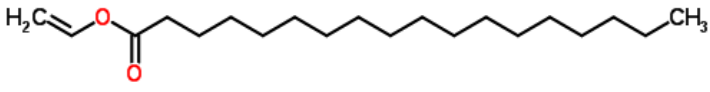
	Abundance	Matrix	Region/area	Source of emission	Method	Source
	2.6%	Sea surface water	Mediterranean Sea	packaging industry and ship pollution	FTIR-ATR	Suaria et al., 2018
	0.2%	Sea surface water	Adriatic Sea: Gulf of Venice (Italy); Gulf of Trieste; (Slovenian waters); Gulf of Split (Croatia); Gulf of Kotor (Montenegro)	food products, coatings, plastics' colorants and additives	Microscopy FTIR-ATR	Zeri et al., 2018
	0.8%	Sea surface water	Mediterranean Sea	Agriculture, fisheries, aquaculture, maritime transport, and tourism	Microscopy FTIR	Digka et al.,
Sediment	0.5 % 60-163 µm	Superficial sediment	Lagoon of Venice	Urban discharges, port, industry, mussel farming, land anthropogenic	µFT-IR	Vianello et al., 2013
	0.98%	Beach sediment	central Italy coast	packaging, plastic bottles, cups, cotton buds or containers, fishing net	Microscopy FTIR	Pietrelli et al., 2018
Biota	1.45±0.04 items per fish (2014) 1.5±0.08 items per fish (2015)	gastrointestinal tract of Solea solea	central and northern Adriatic Sea	Sea hydrodynamic circulation, especially the near-shore currents and gyres mussel farms	µFT-IR	Pellinia et al., 2017

	Abundance	Matrix	Region/area	Source of emission	Method	Source
	50%	stomach content of sardines (Sardina pilchardus)	central Adriatic Sea	Environmental conditions, human impacts, flooding events and current pattern in marine and coastal areas	Microscopy, µFT-IR	Renzi et al., 2018
	93%	stomach content of anchovies (Engraulis encrasicolus)	central Adriatic Sea	Environmental conditions, human impacts, flooding events and current pattern in marine and coastal areas	Microscopy, µFT-IR	Renzi et al., 2018

8.12 Polyvynil Stearate (PVS)

Tab. 326. Substance identity.

Parameters	
Name	Polyvynil Stearate
Other names	Poly(octadecanoic acid ethenyl ester)
CAS number	9003-95-6
Molecular formula	$C_{20}H_{38}$
Structure	
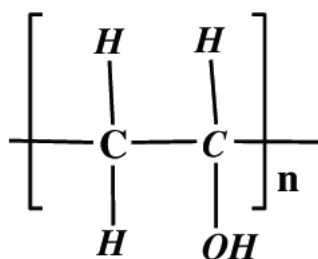
Tab. 327. Measured Environmental Concentrations.

	Abundance	Matrix	Region/area	Source of emission	Method	Source
Water	52%	Sea surface water	Mediterranean Sea	packaging industry and ship pollution	FTIR-ATR	Suaria et al., 2018

	Abundance	Matrix	Region/area	Source of emission	Method	Source
	0.4%	Sea surface water	Adriatic Sea: Gulf of Venice (Italy); Gulf of Trieste; (Slovenian waters); Gulf of Split (Croatia); Gulf of Kotor (Montenegro)	dentistry as a moulding material	Microscopy FTIR-ATR	Zeri et al., 2018

8.13 Polyvinyl alcohol (PVA)

Tab. 328. Substance identity.

Parameters	
Name	Polyvinyl alcohol, PVOH, PVA, PVAl
Other names	PVOH; Poly(Ethenol), Ethenol, homopolymer; PVA; Polyviol; Vinol; Alvyl; Alcotex; Covol; Gelvatol; Lemol; Mowiol; Mowiflex, Alcotex, Elvanol, Gelvatol, Lemol, Mowiol, Nelfilcon A, Polyviol und Rhodoviol
CAS number	9002-89-5
Molecular formula	$(C_2H_4O)_x$
Structure	

Tab. 329. Physico-chemical properties.

Endpoint	Value
Melting point	200 °C (392 °F; 473 K)
Relative density	1.19-1.31 g/cm^3
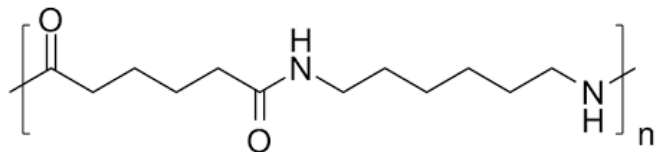
Tab. 330. Measured Environmental Concentrations.

	Abundance	Matrix	Region/area	Source of emission	Method	Source
Water	1.2%	Sea surface water	Mediterranean Sea	packaging industry and ship pollution	FTIR-ATR	Suaria et al., 2018

	Abundance	Matrix	Region/area	Source of emission	Method	Source
	0.4%	Sea surface water	Adriatic Sea: Gulf of Venice (Italy); Gulf of Trieste; (Slovenian waters); Gulf of Split (Croatia); Gulf of Kotor (Montenegro).	coating	Microscopy FTIR-ATR	Zeri et al., 2018
Sediment	0.4% 93 μm	Superficial sediment	Lagoon of Venice	Urban discharges, port, industry, mussel farming, land anthropogenic	μFT-IR	Vianello et al., 2013

8.14 Polyamide (PA)

Tab. 331. Substance identity.

Parameters	
Name	Polyamide
Other names	Hexanedioic acid, polymer with hexahydro-2H-azepin-2-one and 1,6-hexanediamine
IUPAC name	Nylon 6,6 (Polyamide)
CAS number	24993-04-2
Molecular formula	$(C_{12}H_{22}N_2O_2)_n$
Structure	

Tab. 332. Measured Environmental Concentrations.
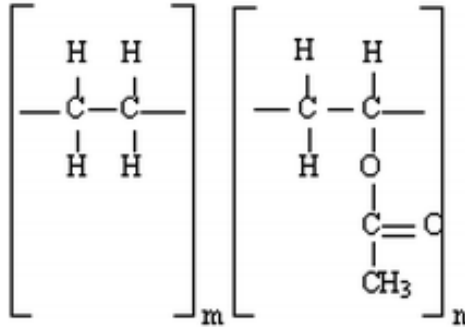
	Abundance	Matrix	Region/area	Source of emission	Method	Source
Water	4.7% (1.9% nylon)	Sea surface water	Mediterranean Sea	packaging industry and ship pollution	FTIR-ATR	Suaria et al., 2018

	Abundance	Matrix	Region/area	Source of emission	Method	Source
	Nylon: 3.1%	Sea surface water	Adriatic Sea: Gulf of Venice (Italy); Gulf of Trieste; (Slovenian waters); Gulf of Split (Croatia); Gulf of Kotor (Montenegro).	food products, coatings, plastics' colorants and additives	Microscopy FTIR-ATR	Zeri et al., 2018
Sediment	0.3% 715 µm	Superficial sediment	Lagoon of Venice	Urban discharges, port, industry, mussel farming, land anthropogenic	µFT-IR	Vianello et al., 2013
	Nylon: 53.2% (abundance) 5.9% (weight)	Marine sediments	Pianosa Island (Central Adriatic Sea)	Making ropes and fishing lines	Microscopy FTIR	Mistri et al., 2018
	Nylon 0.37%	Beach sediment	central Italy coast	packaging, plastic bottles, cups, cotton buds or containers, fishing net	Microscopy FTIR	Pietrelli et al., 2018
Biota	1.76±0.04 items per fish (2014) 1.65±0.07 items per fish (2015)	gastrointestinal tract of Solea solea	central and northern Adriatic Sea	Sea hydrodynamic circulation, especially the near-shore currents and gyres mussel farms	µFT-IR	Pellinia et al., 2017

	Abundance	Matrix	Region/area	Source of emission	Method	Source
	10%	stomach content of sardines (Sardina pilchardus)	central Adriatic Sea	Environmental conditions, human impacts, flooding events and current pattern in marine and coastal areas	Microscopy, µFT-IR	Renzi et al., 2018
	Nylon 14.4%	Posidonia oceanica spheroids (egagropiles, EG)	Central italy coast	packaging, plastic bottles, cups, cotton buds or containers, fishing net	Microscopy FTIR	Pietrelli et al., 2018.

8.15 Ethylene-vinyl acetate (EVA)

Tab. 333. Substance identity.

Parameters	
Name	Ethylene-vinyl acetate
Other names	Poly(ethylene-vinyl acetate); Poly(ethylene-co-vinyl acetate); Polyethylene-vinyl acetate copolymer
IUPAC name	but-3-enoic acid; ethane, but-3-enoic acid; ethene polymer.
CAS number	24937-78-8
Molecular formula	$(C_2H_4)_n(C_4H_6O_2)_m$
Structure	
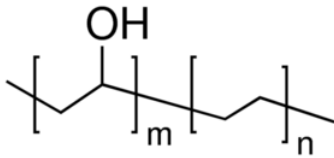
Tab. 36. Measured Environmental Concentrations.

	Abundance	Matrix	Region/area	Source of emission	Method	Source
Water	1%	water-column and surface	coastal waters of Tuscany (Italy)	the riverine inputs, the terrestrial pollution	Microscopy FTIR	Baini et al., 2018
	5-30%	Sea surface water	Lagoon of Venice and off the Po Delta	maritime traffic; tourism-related impacts, intense fishing and mussel farming.	μFT-IR	Vianello et al., 2018
	<1%	Sea surface water	Mediterranean Sea	packaging industry and ship pollution	FTIR-ATR	Suaria et al., 2018
	0.4%	Sea surface water	Adriatic Sea: Gulf of Venice (Italy); Gulf of Trieste; (Slovenian waters); Gulf of Split (Croatia); Gulf of Kotor (Montenegro).	packaging	Microscopy FTIR-ATR	Zeri et al., 2018
	5%	Sea surface water	Italian minor islands, Mediterranean Sea	Washing-machine discharge and ship	μFT-IR	De Lucia et al., 2018.

8.16 Ethylene vinyl alcohol (EVOH)

Tab. 335. Substance identity.

Parameters	
Name	Ethylene vinyl alcohol
Other names	Ethenol, polymer with ethene
CAS number	25067-34-9
Molecular formula	$(C_2H_4O\text{-}C_2H_4)_x$
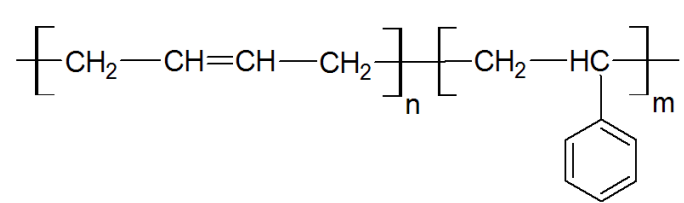
Parameters	
Name	Ethylene vinyl alcohol
Other names	Ethenol, polymer with ethene
Structure	

Tab. 336. Measured Environmental Concentrations.

	Abundance	Matrix	Region/area	Source of emission	Method	Source
Sediment	12.9% (abundance) 3.8% (weight)	Marine sediments	Pianosa Island (Central Adriatic Sea)	marine-based sources including fishing vessels, merchant vessels and recreational boats, shipping traffic	Microscopy FTIR	Mistri et al., 2018

8.17 Styrene-butadiene (SBR)

Tab. 337. Substance identity.

Parameters	
Name	Styrene-butadiene
Other names	Styrene-butadiene rubber (SBR)
CAS number	9003-55-8
Molecular formula	$C_{12}H_{14}$ (probable formula)
Structure	

Tab. 338. Measured Environmental Concentrations.
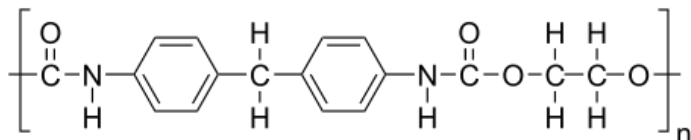
	Abundance	Matrix	Region/area	Source of emission	Method	Source

	Abundance	Matrix	Region/area	Source of emission	Method	Source
Water	1%	water-column and surface	coastal waters of Tuscany (Italy)	Source of emission	Microscopy FTIR	Baini et al., 2018

8.18 Polyurethane (PU)

Tab. 339. Substance identity.

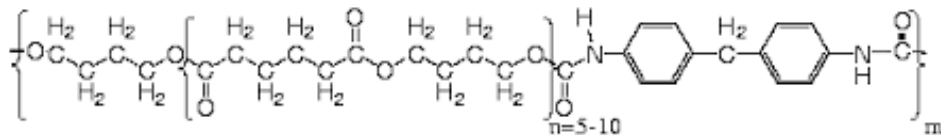| Parameters	
Name	Polyurethane
Other names	-Etheron sponge; Etheron; Polyurethane foam [USAN]; Polyurethane A; Polyfoam plastic sponge; Spenlite; Spenkel; Isourethane; Polyurethane sponge; Andur; Polylurethane; Polyurethane ester foam; Ostamer; NCI-C56451; Polyurethane ether foam; Polyfoam sponge; Urethane polymers; Curene; Pliogrip; Polyether-based
Molecular formula	$C_3H_8N_{2O}$
Structure	

Tab. 340. Measured Environmental Concentrations.

	Abundance	Matrix	Region/area	Source of emission	Method	Source
Water	1.2%	Surface water	Lake Maggiore	municipal discharges, sewage, urban runoff and storm water	Microscopy FTIR	Sighicelli et al., 2018
	1.2%	Surface water	Lake Garda	municipal discharges, sewage, urban runoff and storm water	Microscopy FTIR	Sighicelli et al., 2018
Sediment	0.7%	Beach sediment	Mediterranean Sea	Agriculture, fisheries, aquaculture, maritime transport, and tourism	Microscopy FTIR	Digka et al.,

	Abundance	Matrix	Region/area	Source of emission	Method	Source
	1.36%	Beach sediment	central Italy coast	packaging, plastic bottles, cups, cotton	Microscopy FTIR	Pietrelli et al., 2018
Biota	1.13%	Posidonia oceanica spheroids (egagropiles, EG)	Central italy coast	packaging, plastic bottles, cups, cotton buds or containers, fishing net	Microscopy FTIR	Pietrelli et al., 2018.

8.19 Thermoplastic Polyurethane (TPU)

Tab. 341. Substance identity.

Parameters	
Name	Thermoplastic Polyurethane
Structure	
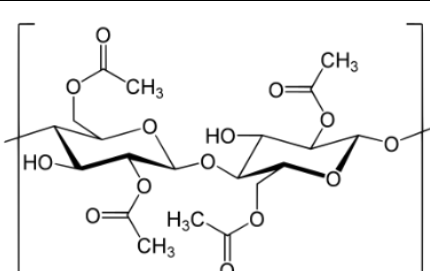
Tab. 342. Measured Environmental Concentrations.

	Abundance	Matrix	Region/area	Source of emission	Method	Source
Sediment	10.6% (abundance) 0.2% (weight)	Marine sediments	Pianosa Island (Central Adriatic Sea)	marine-based sources including fishing vessels, merchant vessels and recreational boats, shipping traffic	Microscopy FTIR	Mistri et al., 2018

8.20 Cellulose Acetate (CA)

Tab. 343. Substance identity.

Parameters	
Name	Cellulose Acetate

IUPAC name	1,2,4-benzenetricarboxylate
Molecular formula	$[C_6H_7O_2(OH)_3\text{-}m(OOCCH_3)_m]$, m = 0~3
Structure	

Tab. 344. Measured Environmental Concentrations.

	Abundance	Matrix	Region/area	Source of emission	Method	Source
Water	0.6%	Surface Water	Lake Garda	municipal discharges, sewage, urban runoff and storm water	Microscopy FTIR	Sighicelli et al., 2018
	<1%	Sea surface water	Mediterranean Sea	packaging industry and ship pollution	FTIR-ATR	Suaria et al., 2018
	0.1%	Sea surface water	Adriatic Sea: Gulf of Venice (Italy); Gulf of Trieste; (Slovenian waters); Gulf of Split (Croatia); Gulf of Kotor (Montenegro).	food products, coatings, plastics' colorants and additives	Microscopy FTIR-ATR	Zeri et al., 2018

8.21 Acrylonitrile-butadiene styrene (ABS)

Tab. 345. Substance identity.

Parameters	
Name	Acrylonitrile butadiene styrene
IUPAC name	buta-1,3-diene;prop-2-enenitrile;styrene
CAS number	9003-56-9
Molecular formula	$(C_8H_8\cdot C_4H_6\cdot C_3H_3N)_n$

Structure	
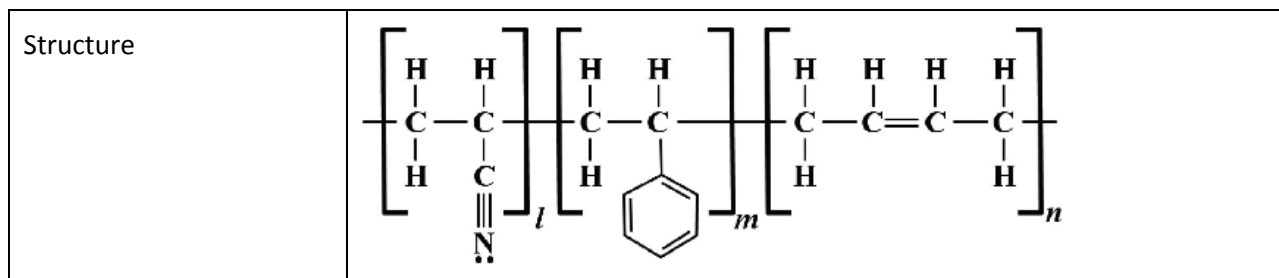
Tab. 346. Physico-chemical properties.

Endpoint	Value
Relative density	1.060–1.080 g·cm^{-3}
Water solubility (mg/L)	Insoluble
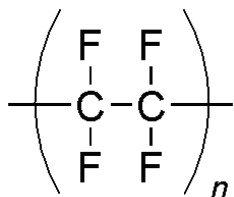
Tab. 347. Measured Environmental Concentrations.

	Abundance	Matrix	Region/area	Source of emission	Method	Source
Water	1.2%	Surface water	Lake Maggiore	municipal discharges, sewage, urban runoff and storm water	Microscopy FTIR	Sighicelli et al., 2018
Sediment	0.05%	Beach sediment	central Italy coast	packaging, plastic bottles, cups, cotton buds or containers, fishing net	Microscopy FTIR	Pietrelli et al., 2018

8.22 Polytetrafluoroethylene (PTFE)

Tab. 348. Substance identity.

Parameters	
Name	Polytetrafluoroethylene
Other names	Syncolon, Fluon, Poly(tetrafluroethene), Poly(difluoromethylene), Poly(tetrafluoroethylene), teflon
IUPAC name	Poly(tetrafluoroethylene)
CAS number	9002-84-0
Molecular formula	$(C_2F_4)_n$

Structure	

Tab. 349. Physico-chemical properties.
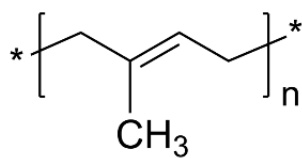
Endpoint	Value
Melting point	600 K, 327 °C
Relative density	2200 kg/m^3

Tab. 350. Measured Environmental Concentrations.

	Abundance	Matrix	Region/area	Source of emission	Method	Source
Biota	10%	stomach content of sardines (Sardina pilchardus)	central Adriatic Sea	Environmental conditions, human impacts, flooding events and current pattern in marine and coastal areas	Microscopy, µFT-IR	Renzi et al., 2018

8.23 Polyisoprene

Tab. 351. Substance identity.

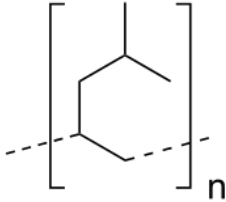| Parameters	
Name	Polyisoprene
Other names	isoprene rubber, 1,3-butadiene, 2-methyl-, homopolymer
IUPAC name	Polyisoprene
CAS number	9003-31-0; EC/List no.: 618-362-9
Molecular formula	(C_5H_8)
Structure	

Tab. 352. Measured Environmental Concentrations.

	Abundance	Matrix	Region/area	Source of emission	Method	Source

	Abundance	Matrix	Region/area	Source of emission	Method	Source
Water	<1%	Sea surface water	Mediterranean Sea	packaging industry and ship pollution	FTIR-ATR	Suaria et al., 2018

8.24 Polymethylpenthene (PMP)

Tab. 353. Substance identity.

Parameters	
Name	Polymethylpentene
Other names	Poly(4-methyl-1-pentene); PMP
CAS number	25068-26-2
Molecular formula	$(C_6H_{12})_n$
Structure	

Tab. 354. Physico-chemical properties.

Endpoint	Value
Melting point	240 °C (464 °F; 513 K)
Relative density	0.833 g/mL

Tab. 355. Measured Environmental Concentrations.

	Abundance	Matrix	Region/area	Source of emission	Method	Source
Water	0.1%	Sea water surface	Adriatic Sea: Gulf of Venice (Italy); Gulf of Trieste, (Slovenian waters); Gulf of Split (Croatia); Gulf of Kotor (Montenegro).	food products, coatings, plastics' colorants and additives	Microscopy FTIR-ATR	Zeri et al., 2018

8.25 Ecotoxicological data

Tab. 356. Biochemical and genetic responses for microplastics.

Species	Concentrations	Days of exposure	Biochemical/molecular effects	Reference
Mytilus galloprovincialis	4.6 E + 5 polyethylene microbeads/L (1–50 µm in size)	1) 18 days exposure; 2) 28 days recovery; 3) additional 18 days exposure	Trascriptomic profiling showed: after 18 d, disruption of global homeostasis with production of stress and immune-related proteins; after recovery, activation of apoptotic processes and up-regulation of immune-receptors and stress-related proteins (glutathione peroxidase, hsp70); ability to establish a stress-memory upon microplastics exposure.	Detree and Gallardo-Escarate 2018.
Corbicula fluminea (freshwater bivalve)	Microplastics (0.13 mg/L; 1-5 µm diameter) alone and in combination with mercury (30 µg/L)	8 days exposure; 6 days recovery	Microplastics reduced the bioconcentration of mercury; they decreased filtration rate, increased oxidative stress and lipid peroxidation, reduced adductor muscle ChE activity. Recovery was not enough to totally reverse the toxic effects.	Oliveira et al. 2018.
Ennucula tenuis Abra nitida	1, 10 and 25 mg polyethylene microplastics/kg of sediment. Three size classes (4-6; 20-25 and 125-500 µm) were used.	4 weeks	Survival, condition index or burrowing behaviour not affected; significant changes in energy reserves; more severe effects due to largest particles and higher concentrations	Bour et al. 2018.

Corbicula fluminea (freshwater bivalve)	Microplastics (0.2 and 0.7mg/l) alone and in mixture with the antimicrobial florfenicol (1.8 and 7.1 mg/l) Microplastics were red fluorescent polymer microspheres with 1–5 µm diameter	96 h	Microplastics (0.2 mg/l) inhibited ChE activity by 31%. Mixtures caused feeding inhibition (57–83%), significant inhibition of ChE (44–57%) and of isocitrate dehydrogenase activity, and increased anti-oxidant enzymes activity and lipid peroxidation levels	Guilhermino et al, 2018.
Corbicula fluminea (freshwater bivalve)	4 types of microplastics: polyethylene terephthalate, PET (mean size 198 µm), polyethylene (mean size 209 µm), polyvinylchloride, PVC (mean size 169 µm) and polystyrene (mean size 179 µm) with and without polychlorinated biphenyls (PCBs). Exposure concentrations of 4.1 mg/L for PET, 2.8 mg/L for polyethylene, 4.2 mg/L for PVC and 3.2 mg/L for polystyrene.	28 days	The feeding behaviour was not significantly different amongst treatments; no significant differences across treatments for CYP450 and vitellogenin were observed; histological changes were seen in the digestive glands, but no significant differences in the number of anomalies were found among treatments; clams exposed to plastic had 3 times more histological abnormalities than controls	Rochman et al. 2017.
Scrobicularia plana	polystyrene 1 mg/L(20 µm in size)	2 weeks of exposure 1 week depuration	Effects on antioxidant capacity, DNA damage, neurotoxicity and oxidative damage revealed by a battery of biomarkers; inefficient detoxification process during depuration	Ribeiro et al. 2017.

Mytilus galloprovincialis	1.5E+7 microbeads of polyethylene/L (1 to 50 µm in size)	24h	Changes at the transcriptome level in four tissues: up-regulation of genes relative to carbon metabolism, oxidative stress, immune response and apoptosis in the mantle and digestive gland; a global down-regulation of genes involved in carbon metabolism in haemolymph and gills	Detree and Gallardo-Escarate 2017.
Perna viridis	polyvinylchloride (PVC) particles 0 mg/l, 21.6 mg/l, 216 mg/l, 2160 mg/l (1-50 µm in size)	two 2-hour-time-periods per day for 91days	Filtration and respiration rates and byssus production were decreased with increasing particle concentration (after 44 days) Survival decreased with increasing particle concentration (alter 91 days)	Rist et al 2016.
Mytilus spp.	polystyrene microbeads (mix of 2 and 6 µm in size); final concentration: 32 µg/L) alone or in combination with fluoranthene (30 µg/L)	7 days exposure, 7 days depuration	Exposure to microbeads alone led to increased hemocyte mortality and triggered substantial modulation of cellular oxidative balance: increase in reactive oxygen species production in hemocytes and enhancement of anti-oxidant and glutathione-related enzymes in mussel tissues. Highest histopathological damages and levels of anti-oxidant markers were observed in mussels exposed to micro-beads together with fluoranthene.	Paul-Pont et al. 2016.

Crassostrea gigas	polystyrene microspheres (2 and 6 μm in size; 0.023 mg/L)	2 months during a reproductive cycle	Cellular, transcriptomic, and proteomic responses; fecundity; and offspring development were assessed. Smaller particle (2 μm) were mostly ingested. Consumption of microalgae and absorption efficiency were higher in exposed oysters. Oocyte number and diameter, and sperm velocity decreased. D-larval yield and larval development decreased in offspring from exposed parents compared with control offspring. Shift in energy allocation from reproduction to growth and molecular signatures of endocrine disruption were revealed.	Sussarellu et a. 2016.
Atactodea striata	Polystyrene with size 63 - 250 μm (10 items/L and 1000 items/L)	2 weeks	Reduction in clearance rate and thus energy intake; no effects on respiration rate and absorption efficiency; low retention in the body	Xu et al. 2016.

Mytilus	Polystyrene amino-modified nanoparticles (50 nm in size; 1, 5, 50 µg/ml)	Haemocyte in vitro exposure	Clear signs of cytoxicity evident only at the highest concentration; dose dependent decrease in phagocytic activity and increase in lysozyme activity; increase in extracellular ROS and NO production, with maximal effects at lower concentrations; apoptotic process at the highest concentration	Canesi et al. 2015.
Mytilus galloprovincialis	Polyethylene (PE) and polystyrene (PS) microplastics (< 100 µm in size), both virgin and pyrene-contaminated (microplastic concentration: 1.5 g/L)	7 days	Capability of contaminated microplastics to transfer PAH to exposed mussels, mostly in digestive tissue. Cellular effects included alterations of immunological responses, lysosomal compartment, peroxisomal proliferation, antioxidant system, neurotoxic effects, onset of genotoxicity; changes in gene expression profile demonstrated through a DNA microarray platform.	Avio et al. 2015.

Mytilus edulis	High-density poly-ethylene (HDPE) particles (>0-80 μm in size) at a nominal concentration of 2.5 g/L	3, 6, 12, 24, 48, 96h	Notable histological changes upon uptake in gills and digestive gland; strong inflammatory response demonstrated by the formation of granulocytomas after 6 h exposure and lysosomal membrane destabilization, which significantly increased with longer exposure times.	Von Moos et al. 2012.
Mytilus edulis	0, 0.1, 0.2, and 0.3 g/L of polystyrene nanoparticles (30 nm)	8 hours	Effects on feeding behaviour were assessed. Total weight of the feces and pseudofeces increased with increasing nano PS concentration in the medium. Filtering activity decreased at all nano PS concentrations tested respect to controls	Wegner et at., 2012.

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