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Selection of substances for the 3rd Watch List under the Water Framework Directive

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Executive summary

The 1st Watch List (WL) was established by the Commission Implementing Decision (EU) 2015/495[1] in March 2015. The list was updated in June 2018 by the Commission Implementing Decision (EU) 2018/840[2]. During the WL update, the Commission concluded that the substances diclofenac, oxadiazon, 2,6-di-tert-butyl-4-methylphenol, tri-allate and 2-ethylhexyl-4-methoxycinnamate should be removed from the WL, while the insecticide metaflumizone and the antibiotics amoxicillin and ciprofloxacin were included in the WL (EU 2018/840[2]).

The period of a continuous monitoring for any WL substance should not exceed four years (Article 8b in Directive 2008/105/EC[3] as amended by Directive 2013/39/EU[4]). Thus, by the end of the 4th reporting year for the WL (2019) the substances in the 1st WL should have been removed and a maximum of 12 substances or groups of substances may be listed in the 3rd WL. However, the three substances included during the first WL update (EU 2018/840[2]) should be carried over to the 3rd WL to ensure that enough high-quality monitoring data are collected for their risk assessment.

The purpose of this report is to propose candidate substances for the 3rd WL.

Three pillars of information were used to select the candidate substances (Chapter 2 of the report). The first pillar is the outcome of the last prioritisation exercise[5,6], the second includes the outcome of the review of the 1st WL and recommendations for the 3rd WL[7], and the third is based on a literature search and/or other sources (for instance information from MS) for emerging substances.

Five criteria for the identification of candidate WL substances, as discussed and adopted in the first revision of the WL[7] were used by the JRC:

1. Substances that met the criteria for prioritisation previously but were not shortlisted because there were few or low-quality monitoring data.

2. Substances shortlisted but with uncertainties for the monitoring data.

3. Substances considered in the modelling-based exercise[6] for which:

   a. the monitoring data met the criteria for the representativeness (number of MS, sites and samples) in Scenario 2 (Sc2) but not in Scenario 3 (Sc3), and

   b. in Sc2 the Spatial, Temporal and Extent of PNEC exceedance (STE) score[5,7] was high and the modelled Risk Quotient (RQ) was high;

and substances which went directly to the modelling stream (measured below 4 MS in Sc2 during the ongoing prioritisation) with modelled RQ above 5 but not further selected because of lack of monitoring data.

4. Substances shortlisted but not included in the 1st and 2nd WL because of limitations of monitoring methods available at the time:

4.1) availability of analytical methods,

4.2) reliability of the PNEC.

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5. Substances of emerging concern identified based on research projects and articles, in line with the article 8b of Directive 2008/105/EC[3] as amended by Directive 2013/39/EU[4] (e.g. industrial products, pharmaceuticals, plant protection products and biocides).

Please note that banned substances fulfilling the aforementioned criteria will not be taken into consideration as potential candidates for the WL following the final recommendation cited in the document on the development of the 1st Watch List[8]. To prioritise substances for the inclusion in the WL, the relevant matrix and stability of the substance were taken into account in addition to the hazard properties and the availability of a reliable PNEC and an appropriate analytical method. The data scenario Sc2 includes all quantified and non-quantified monitoring samples (the non-quantified measurements are set to half of the LOQ as stipulated in Directive 2009/90/EC[9]). The Sc3 involves the quantified measurements plus only the non-quantified samples where ½LOQ≤PNEC and it is considered as a more relevant data scenario for making a risk assessment[5,7]

The preferred monitoring matrix for candidate substances was decided according to their log K_{OW}. Accordingly, substances with log K_{OW} > 5 should preferably be measured in sediments, or in Suspended particulate matter (SPM), those with a log K_{OW} < 3 should be monitored preferably in water, while for substances with a log K_{OW} between 3 and 5, the choice of sediment or SPM is optional and will depend on the degree of contamination.

The selection of candidate substances took into consideration their hazard properties (PBT, CMR, ED) as well as the availability of reliable PNECs (including AMR for antibiotics) and the availability of relevant analytical methods for monitoring in the appropriate environmental matrix.

All details of the selection process, including a rationale for each individual substance selected, are described in Chapters 3 and 4 of the report.

The **candidate substances, fulfilling the selection criteria and identified by the JRC as most likely to be proposed for the next WL**, are listed in Table S1 showing their group/class, name, use and matrix (environmental compartment) in which the given compound should be monitored.

Table S1: A list of candidate substances, fulfilling the selection criteria and identified by the JRC as most likely to be proposed for the next WL. The table shows for candidate substances the group/class, name, use and matrix (environmental compartment) where to be monitored. (PPP = Plant Protection Product.)

Group	Name	Use	Matrix
	EHMC (2-Ethylexyl 4-methoxycinnamate)	UV filter	Sediment
Pyrethroids	Bifenthrin, Deltamethrin, Esfenvalerate, Permethrin	PPP	Sediment
Industrial products	Cr(VI) and Cr(III)	Industrial chemical	Coastal/transitional water (as Cr total dissolved

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			fraction)
Anti-Microbial pharmaceuticals	Sulfamethoxazole, Trimethoprim	Antibiotic	Water (inland whole water)
	Clotrimazole, Fluconazole, Miconazole	Antifungal	
Other pharmaceuticals	Proton pump inhibitors (PPI): Omeprazole and its metabolite 4-hydroxy omeprazole sulphide (OM14)	Human medicine	Water (inland whole water)
	Norethisterone	Synthetic hormone	
	Venlafaxine	Antidepressant	
PPP and biocides (azole compounds)	Epoxiconazole, Imazalil, Ipconazole, Metconazole, Penconazole, Prochloraz, Tetraconazole	PPP Biocides	Water (inland whole water)
Other PPP and biocides	Free cyanide	Inorganic biocide	Water (inland dissolved fraction/ coastal waters)
	Dimoxystrobin	PPP	Water (inland whole water)
	Famoxadone	PPP	Water (inland whole water)

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1 Introduction

The surface water Watch List (WL) under the Water Framework Directive (WFD) is a mechanism for obtaining high-quality Union-wide monitoring data on emerging pollutants and substances that may pose a significant risk at Union level to or via the aquatic environment, but for which available monitoring data are insufficient to draw conclusions on the actual risk posed. According to the amended Environmental Quality Standards (EQS) Directive (Article 8b[3]), the WL should be updated every 2 years. When updating the WL, the Commission should remove any substance for which a risk-based assessment can be concluded without additional monitoring data. New substances or groups of substances can be added to the WL during each update. The maximum number of substances or groups of substances that the Commission is allowed to include in the list increases by one at each update to a maximum of 14 substances or groups of substances. The duration of a continuous WL monitoring period for any individual substance may not exceed four years.

The first WL was established by Commission Implementing Decision (EU) 2015/495 in March 2015[1] and replaced in June 2018 by the list in Commission Implementing Decision (EU) 2018/840[2]. During the WL update, the Commission concluded that the substances diclofenac, oxadiazon, 2,6-di-tert-butyl-4-methylphenol, tri-allate and 2-ethylhexyl-4-methoxycinnamate should be removed from the WL, while the insecticide metaflumizone and the antibiotics amoxicillin and ciprofloxacin were identified as suitable candidates and then included (EU 2018/840[2]). As the continuous WL monitoring period for any individual substance may not exceed four years, after the current WL update the substances from the 1st WL should be removed and a maximum of 12 substances or groups of substances can be listed in the 3rd WL. However, the three substances included during the first WL update (EU 2018/840[2]) should be carried over to the 3rd WL to ensure that enough high-quality monitoring data are collected for their risk assessment.

The purpose of the present report is to propose candidate substances to be included in the new WL.

The report is structured as follows:

Chapter 2 Process for selecting candidate substances for the WL. This chapter describes the overall process for selecting candidate substances for the WL. Section 2.1 provides a description of the sources of information and databases for ecotoxicology data and hazard properties. Section 2.2 provides a description of the sources of information and databases for analytical methods.

Chapter 3 Substances selected during the previous review of the WL to be monitored in sediment. Section 3.1 describes the criteria for selecting substances for sediment monitoring. Section 3.2 presents the list of substances proposed for sediment monitoring. It also provides available PNEC values and analytical methods. Section 3.3 describes the rationale for the selection.

Chapter 4 Selection of new candidate substances for the third WL. Section 4.1 describes the criteria followed for the selection of candidates for the 3rd WL. Section 4.2 presents the list of substances fulfilling the criteria and provides available PNEC values and analytical methods. Section 4.3 explains the rationale for the selection.

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Chapter 5 Conclusions. This chapter describes the conclusions and the recommendations for the next WL.

The report also includes annexes and factsheets that show all supportive information:

Annex I: Outcome of the workshop "Analytical methods for substances in the Watch List under the Water Framework Directive" (JRC-Ispra, Italy, October 2018).

Annex II: Tables summarising the hazard properties, and showing the available monitoring data, risk quotients and STE scores of the candidate substances.

Annex III: Factsheets for the candidate substances.

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2 Process for selecting candidate substances for the WL

To select the substances, three pillars as source of information were considered (Figure 1). One pillar is the priority substances prioritisation exercise[5,6], the second is the outcome of the review of the 1st WL and recommendations for the 3rd WL[7], and the third is literature search and other information[10]. The criteria shown in each box are going to be described in Chapter 4. In the dashed box above the first pillar, there are grouped substances, i.e. the pyrethroid and sunscreen ingredient (2-ethylhexyl 4-methoxycinnamate (EHMC)), that are described separately (see Chapter 3) because they were already identified as potential candidates to be measured in the sediment[7].

Figure 1. Overall process for the selection of candidate substances for the WL.

2.1 Sources of information and databases for hazard properties and analytical methods

A search for information on exposure to each substance in the aquatic environment was carried out. For the freshwater compartment, environmental quality standards (EQS) or predicted no-effect concentration (PNEC) values have been collected or derived considering toxicity effects to aquatic freshwater organisms ($PNEC_{fw,eco}$). For highly hydrophobic substances, the EQS or PNEC values were also considered for sediment organisms ($PNEC_{eco,sed}$). EQS or PNEC values should protect freshwater and marine ecosystems from possible adverse effects of chemicals.

Hazard properties such as Persistence (P), Bioaccumulation (B), Toxicity (T), Carcinogenicity (C), Mutagenicity (M), Reproductive Toxicity (R) and Endocrine Disruption (ED), substances' type of usage and status were also investigated.

2.1.1 Hazard information

Hazard information was collected from different sources (Table 1) for all the potential candidates.

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First, EQS were collected from reports or online databases (see Table 1). Second, PNEC values were collected, with a particular focus on the substances where no EQS value was available. Furthermore, PNEC values were searched for in the literature, with preference given to those used already in European monitoring campaigns or prioritisation exercises.

Third, PNECs were collected from European Chemicals Agency (ECHA) dossiers (http://echa.europa.eu/) and European Food Safety Authority (EFSA) risk assessment reports (http://www.efsa.europa.eu/), when available.

Fourth, for pharmaceuticals, the Swedish FASS database was considered. In the case of antimicrobials, PNEC values were retrieved from the antimicrobial resistance (AMR) industry alliance list.

Fifth, literature was screened, particularly studies following the technical guidance document (TGD)-EQS (2018) for their PNEC derivation.

Finally, for those substances where information was not available from any of the sources listed above, PNECs were derived by the JRC using studies that were considered reliable or reliable with restrictions according to the TGD-EQS (2018.

Then, information about the PBT properties was retrieved from ECHA (industrial chemicals) or EFSA (plant protection products, PPP), while the "2012-2015 Environmentally classified pharmaceuticals document" from the Stockholm County Council was the source for human pharmaceuticals. Carcinogenicity (C), Mutagenicity (M) and Reproductive Toxicity (R) are in accordance with Globally Harmonised System (GHS) categories from ECHA dossiers. For EDs the Endocrine Disruptor Strategy (EDS) database and categorisation of the European Commission was used (EDS database, EC). Concerning PPP if EFSA dossiers were available, CMR scores were set accordingly.

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Table 1: Sources for EQS/PNEC values and hazard information

Source	Description
AgriTox ANSES FR 2019	Plant protection products http://www.agritox.anses.fr/php/data-criteria.php
AMR Industry alliance	Anti-Microbial pharmaceuticals https://www.amrindustryalliance.org/wp-content/uploads/2018/09/AMR_Industry_Alliance_List-of-Predicted-No-Effect-Concentrations-PNECs.pdf
ECHA	All substances https://echa.europa.eu/home
ECOSAR	Pharmaceuticals
EDS database, EC	All substances https://ec.europa.eu/environment/chemicals/endocrine/strategy/substances_en.htm
Swiss ECOTOX centre	All substances https://www.ecotoxcentre.ch/expert-service/quality-standards/proposals-for-acute-and-chronic-quality-standards/
ECOTOX Database US EPA	All substances
EFSA	All substances http://dar.efsa.europa.eu/dar-web/provision
EU Pesticides database	Plant protection products https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.selection&language=EN
FASS	Pharmaceuticals https://www.fass.se/LIF/startpage
INERIS	All substances https://substances.ineris.fr/fr/
Janusinfo, Stockholm County Council	Pharmaceuticals https://www.janusinfo.se/environment
JRC	All substances
OSPAR	All substances
Research articles and reports	All substances
RIVM	Pharmaceuticals https://www.rivm.nl/

2.1.2 Analytical methods

A literature review of available analytical methods was carried out for all the candidate substances (Table 2)

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Table 2: Sources for analytical methods.

Source	Description
Companies	Plant protection products and industrial products
EFSA	Plant protection products
Research articles and reports	All substances
USGS	Plant protection products and industrial products
US EPA	Plant protection products

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3 Candidate substances identified which should be monitored in sediment

The first potential candidates for the 3rd WL were identified during the review of the 1st WL[7].

3.1 Criteria for selecting substances for sediment monitoring

In the previous WL report[7], the JRC recommended sediment or biota as the preferred monitoring matrix for hydrophobic substances with high log K_{OW} values (i.e. pyrethroid insecticides and 2-ethylhexyl 4-methoxycinnamate (EHMC)). Pyrethroids were shortlisted in the prioritisation exercise for priority substances due to the high risk quotient (PEC/PNEC) calculated in the modelling-based exercise for three of them (bifenthrin, esfenvalerate and deltamethrin) and the high STE score for permethrin[5,6]. Due to the lack of good monitoring data, the experts involved in the exercise proposed their inclusion in the next WL. The sunscreen ingredient EHMC was already in the WL, but most of the monitoring was being done in water despite a recommendation to monitor it in sediment. For the above reasons, the pyrethroids and the sunscreen ingredient EHMC were recommended in 2018 as potential candidates for the 3rd WL to be measured in sediment[7], but not included because of a need to ensure the availability of appropriate monitoring methods.

Sediment monitoring was discussed during the workshop "Analytical methods for substances in the Watch List under the Water Framework Directive" held at the JRC (Ispra, Italy) in October 2018. During the workshop, analytical methods to measure pyrethroids and EHMC in sediment were discussed. The outcome of the workshop is reported in Annex I. Briefly, the experts reached a general consensus on the definition of hydrophobicity of the analyte, as also recommended in the WFD CIS Guidance document No. 25 on sediment and biota monitoring (2010)[11] and on sediment sampling, storage and extraction. For the hydrophobicity, the proposed rule of thumb also described in the JRC workshop report[12] is that compounds with log $K_{OW} > 5$ should preferably be measured in sediments, or in SPM, while compounds with a log $K_{OW} < 3$ should preferably be measured in water. Then, for compounds with a log K_{OW} between 3 and 5, either the sediment matrix or SPM may be used depending on the degree of contamination.

3.2 List of substances to be monitored in sediment

Table 3 shows the potential candidates for the next WL which should be monitored in sediment. These substances were listed by the JRC in 2018[7]. For each substance, the table includes the group, name, uses, CAS number, PNEC value, analytical methods and status. The column on the right is dedicated to comments or other relevant information.

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Table 3: Potential candidates for the 3rd WL which should be monitored in sediment

Group	Name	Use	CAS	PNEC water (µg/L) PNEC sediments (µg/kg)	Available Analytical Method (LOQ µg/L or µg/kg)	Status
	EHMC (2-Ethylexyl 4-methoxycinnamate) (2-Ethylexyl trans-4-methoxycinnamate)	Sunscreen ingredient Substance is known to be on the EEA market in nanomaterial form (ECHA).	5466-77-3 83834-59-7	**water** 6 (Carvalho et al., 2015)[8] **sediments** 200 (specific organism, *Melanoides tuberculata*, 28d, AF 10; JRC factsheet)[8]	**sediments** HPLC-MS2 (0.0001) (Mandaric et al., 2017)[13]	Authorised
Pyrethroid insecticides	**Bifenthrin**	PPP Biocide	82657-04-3	**water** 0.00002 (JRC draft dossier, 2016)[14] **sediments** 0.4 dw (*Chironomus riparus*, AF 100; JRC draft dossier, 2016)[14]	**surface water** GC-APCI-MS/MS (0.000025) (Rösch et al., 2019)[15] **sediments** GC-MS/MS (MDL 0.2) (USGS, 2007, 2009)[16-18]	**NOT APPROVED as PPP** app 01/08/2012 exp 31/07/2019 (2009/887/EC,Reg. (EU) 2017/195,Reg. (EU) 2018/291,Reg. (EU) 2019/324,Reg. (EU) No 582/2012). In progress for: AT, IT, SK **APPROVED as BIOCIDE**. This substance is approved for use as a biocide in the EEA and/or Switzerland for a wood preservation.

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	Deltamethrin	PPP Biocide	52918-63-5	**water** 0.00007 (JRC draft dossier, 2016)[14] **sediments** 6.2 ww (Equilibrium partitioning, SE, assessment report, 2011) 0.54 dw (*Chironomus riparus*, AF 100; JRC draft dossier, 2016)[14]	**surface water** GC-APCI-MS/MS (0.000025) (Rösch et al., 2019)[15] **sediments** GC-MS/MS (MDL 0.2) (USGS, 2007, 2009)[16-18]	**APPROVED as PPP** app 01/11/2003 exp 31/10/2020 03/5/ECReg. (EU) No 2018/1262Reg. (EU) No 540/2011Reg. (EU) No 823/2012 (Reg. (EU) 2016/950,Reg. (EU) 2017/1511). Authorised in: AT, BE, BG, CY, CZ, DE, DK, EE, EL, ES, FI, FR, HR, HU, IE, IT, LT, LU, LV, MT, NL, PL, PT, RO, SE, SI, SK, UK (28 MS) **APPROVED as BIOCIDE** in the EEA and/or Switzerland for controlling insects, ants, etc.
	Esfenvalerate	PPP Biocide	66230-04-4	**water** 0.0001 (JRC draft dossier, 2016)[14] **sediments** 1.25866 dw (Equilibrium partitioning; JRC draft dossier, 2016)[14]	**surface water** GC-APCI-MS/MS (0.000025) (Rösch et al., 2019) [15] **sediments** GC-MS/MS (MDL 0.2) (USGS, 2007, 2009)[16-18]	**APPROVED as PPP** app 01/01/2016 exp 31/12/2022 00/67/ECReg. (EU) 2015/2047Reg. (EU) No 540/2011 (2010/77/EU,Reg. (EU) 2015/1885). Authorised in: AT, BE, BG, CY, CZ, DE, EL, ES, FI, FR, HR, HU, IE, IT, LU, NL, PL, PT, RO, SE, SK, UK (22 MS) **BEING REVIEWED as BIOCIDE** (ECHA)

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	Permethrin	PPP Biocide	52645-53-1	**water** 0.00047 (JRC draft dossier, 2016)[14] **sediments** 0.2 ww (specific organism, INERIS, 2011) 1 dw (*Chironomus riparus*, AF 100; JRC draft dossier, 2016)[14]	**surface water** GC-APCI-MS/MS (0.000125) (Rösch et al., 2019) [15] **sediments** GC-MS/MS (MDL 0.2) (USGS, 2007, 2009)[16-18]	**NOT APPROVED as PPP** 00/817/EC In progress for: IT (1 MS). **APPROVED as BIOCIDE** This substance is approved for use as a biocide in the EEA and/or Switzerland, for: wood preservation, controlling insects, ants, etc.

dw: dry weight; ww: wet weight; AF: assessment factor; PNEC: predicted no effect concentration; LOQ: limit of quantification; MDL: method detection limit: PPP: plant protection product.

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3.3 Rationale for the selection

2-Ethylhexyl 4-methoxycinnamate (EHMC, sunscreen agent)

2-ethylhexyl-4-methoxycinnamate (EHMC) is a sunscreen ingredient. According to ECHA, this substance is known to be on the European Economic Area (EEA) market in nanomaterial form. This substance has ED properties and was ranked with high RQ in sediment matrix[8]. For the above reason, EHMC was included in the 1st WL but it was delisted in 2018, because, although monitoring in sediment or SPM had been recommended, the data were mainly from inland water. Indeed, the few sediment data reported to the JRC were not enough to carry out a risk evaluation for that matrix (see Annex II, Table 2.1). It was therefore decided to remove EHMC from the WL and to consider its re-inclusion in 2019/20 for sediment monitoring[6]. This would ensure the timely and cost-efficient development/validation of analytical methods (in particular by optimising sediment sampling) and sediment PNECs.

Conclusion: 2-ethylhexyl-4-methoxycinnamate (EHMC) is most likely to be proposed for reinclusion in the WL for monitoring in sediment or SPM.

Group of pyrethroids (bifenthrin, permethrin, deltamethrin and esfenvalerate)

The pyrethroids were identified as group of substances of high concern for aquatic organisms and indirectly for human health. These compounds are highly hydrophobic and more frequently detected in sediments[19] than in water. The pyrethroids were shortlisted in the prioritisation exercise[5,6]. However, they were not included in the priority substances list due to the lack of good monitoring data for inland water or sediments (see Annex II, Table 2.1). The experts involved concluded that the pyrethroids should first be included in the WL.

Following that recommendation, the JRC proposed during the first revision of the WL to include them in the WL when an adequate analytical method became available[7]. A new analytical method (LLE-GC-APCI-MS/MS) has been recently developed by the Swiss Federal Institute of Aquatic Science and Technology (Eawag[15]) for the detection of pyrethroids at low concentration (pg/L) in the water phase. On the other hand, there is also an available analytical method for monitoring pyrethroids in sediments using GC-MS/MS (MDL=0.2 µg/kg) (USGS, 2009[16-18]) with a sufficient sensitivity. Therefore, the JRC considers that the pyrethroids could now be included in the new WL.

Conclusion: The pyrethroids (bifenthrin, deltamethrin, esfenvalerate and permethrin) are most likely to be proposed for the next WL as a group of substances to be monitored in sediment, the more appropriate matrix for hydrophobic substances with high log K_{OW} values.

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4 Selection of new substances for the WL

This chapter describes a set of criteria for identification of candidate substances to update the WL and presents a list of substances that fulfil the selection criteria.

4.1 Criteria for identification of candidate substances for WL update

The JRC proposes five criteria for the identification of new WL substances. The criteria proposed in the present report generally follow the approach described in the 1st and 2nd JRC WL reports[7,8]. These criteria build on the monitoring and modelling-based exercises carried out by the JRC with the support of the SG-R[5,6] for the review of the priority substances list. For more details on the methodologies, please see the summary available at the following link: https://circabc.europa.eu/w/browse/0f6b893e-b0ab-46cb-a631-c3e1e55c7514.

Respecting the requirements of the EQS Directive[3,4], the JRC is proposing the following **criteria** for identifying potential candidates for inclusion in the WL:

1. Substances that met the criteria for prioritisation previously but were not shortlisted because of few or low-quality monitoring data.

2. Substances shortlisted but with uncertainties for the monitoring data.

3. Substances considered in the modelling-based exercise[6] for which:

a. the monitoring data met the criteria for the representativeness (number of MS, sites and samples) in Sc2 but not in Sc3, and

b. in Sc2 the STE (Spatial, Temporal and Extent of PNEC exceedance[5,7]) score was high and the modelled RQ was high;

and substances which went directly to the modelling stream (measured below 4 MS in Sc2 during the ongoing prioritisation) with modelled RQ above 5 but not further selected because of lack of monitoring data.

4. Substances shortlisted, but not included in the 1st and 2nd WL because of limitations of monitoring methods available at the time:

4.1) availability of analytical methods,

4.2) reliability of the PNEC.

5. Substances of emerging concern identified based on research projects and articles, in line with the article 8b of Directive 2008/105/EC[3] as amended by Directive 2013/39/EU[4] (e.g. industrial products, pharmaceuticals, plant protection products and biocides).

Please note that banned substances fulfilling the criteria above will not be taken into consideration as potential candidates for the WL following the final recommendation cited in the document on the development of the 1st Watch List[8]. To establish a priority for the

inclusion in the WL, the relevant matrix and stability of the substance should be taken into account, considering in addition the availability of a reliable PNEC and an appropriate analytical method. The data scenario Sc2 includes all quantified and non-quantified monitoring samples (the non-quantified measurements are set to half of the LOQ as stipulated in Directive 2009/90/EC[9]). The Sc3 involves the quantified measurements and only the non-quantified samples where ½LOQ≤PNEC, and it is considered as a more relevant data scenario for making a risk assessment[5,7]

4.2 List of substances fulfilling the criteria

Table 4 summarises potential candidates identified by the JRC for the next WL (in addition to the pyrethroids mentioned in section 3). The substances have been selected according to the above criteria. To facilitate discussion, the substances have been grouped according to their use/type of substance (class). The table includes the name of the substance, use, CAS number, PNEC value, available analytical method, status and selection criteria.

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Table 4: Potential candidates for the WL identified following the new criteria defined by the JRC. The **names of substances most likely to be proposed are written in bold** characters; the other good candidates are in non-bold characters.

Group	**Name**	**Use**	**CAS**	**PNEC water** (µg/L)	**Available Analytical Method** (LOQ µg/L)	**Status**	**Selection criteria**
Industrial products	4-chloroaniline	Industrial (ECHA)	106-47-8	0.05 (prioritisation exercise RBSP-ECOSTAT, UBA, 2014)[5,6] 1 (INERIS)	Isocratic reversed-phase HPLC (RPHPLC) (LOD 0.036) (Börnick et al., 2001)[20] LC-MS/MS (0.00013) (Rimayi et al., 2019)[21]	This substance is manufactured and/or imported in the European Economic Area for industrial use resulting in the manufacture of another substance (use of intermediates).	criterion 5
	3,4-dichloroaniline	Industrial (ECHA)	95-76-1	0.2 (water) and 0.039 mg/kg ww (sediment) (Risk Assessment Report, JRC, 2006) 0.02 (water, monitoring exercise INERIS, 2012)[5,6]	Isocratic reversed-phase HPLC (RPHPLC) (LOD 0.033) (Börnick et al., 2001)[20] LC-MS/MS (LOD 0.0052) (USGS, 2012)[22]	This substance is manufactured and/or imported in the European Economic Area for industrial use resulting in the manufacture of another substance (use of intermediates). This substance is used at industrial sites and in manufacturing.	criterion 5

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	Cr (III) and Cr (VI)	Industrial (ECHA)	Cr III (CAS 16065-83-1) Cr VI (CAS 18540-29-9) CrO_3 (CAS 1333-82-0)	Inland water: Cr (III): 1.8 (JRC derived, 2018)[7]; Cr (VI): 2.06 (JRC derived, 2018)[7]; Coastal water: Cr (VI): 0.6 (JRC Dossier; Env. Agen. UK)[7] Cr (III): The QS derived for Cr (III) in freshwater may be used as an indicative value for marine water bodies until sufficient long-term studies with marine organisms are available (UK EA 2007).	EPA method 218.7 (LOD 0.0044 to 0.015) LC-ICP-MS (LOD 0.001 to 0.01) (Perkin Elmer Application note)[23]	Cr (III) **Authorised.** This substance is known to be on the EEA market in nanomaterial form. Cr (VI) and its compounds are included in the REACH restricted substance list (entry 47, Annex XVII of REACH regulation)	criterion 1
Anti-Microbial (AM) pharmaceuticals: antibiotics	**Sulfamethoxazole**	Antibiotic Antibacterials for systemic use	723-46-6	0.6 (EQS chronic, Swiss ECOTOX centre 2016) 0.4 (EQS 0.4 Substance factsheet 2015 from modelling-based exercise 2016)[5,6] 0.59 (FASS and RIVM, 2011) 16 (PNEC-MIC, AMR industry alliance)[24] 0.1 (JRC derivation,	LC–MS/MS (0.0030) (Chitescu et al., 2015)[26] LC-MS/MS (0.0022) (Papageorgiou et al., 2019)[27] SPE followed by UHPLC-QqLIT-MS (river water 0.0008) (Mandaric et al., 2017)[13]	**Authorised**	criteria 4, 5

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				2019) 2.4 (Zhou et al. 2019)[25]			
	Trimethoprim	Antibiotic Antibacterials for systemic use	738-70-5	120 (EQS chronic, Swiss ECOTOX centre 2015) 60 (Swiss ECOTOX centre modelling-based exercise 2016)[5,6] 0.5 (PNEC-MIC, AMR industry alliance)[24] 43.3 (JRC derivation 2019) 16 (RIVM, 2011) 15.7 (Zhou et al., 2019)[25]	LC–MS/MS (0.01721) (Chitescu et al., 2015)[26] LC-MS/MS (0.0005) (Papageorgiou et al., 2019)[27] SPE followed by UHPLC-QqLIT-MS (river water 0.0002) (Mandaric et al., 2017)[13]	**Authorised**	criterion 5
Anti-Microbial pharmaceuticals: azole pharmaceuticals (antifungal agents)	**Clotrimazole**	Human medicine Dermatologicals-antifungals for dermatological use	23593-75-1	1 (OSPAR, 2015) 0.02 (JRC derivation, 2019) 0.036 (Zhou et al., 2019)[25]	LC–MS/MS (0.02261) (Chitescu et al., 2015)[26]	**Authorised**	criterion 5

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	Fluconazole	Human medicine Antimycotics for systemic use	86386-73-4	0.25 (PNEC-MIC, AMR industry alliance)[24] 9.46 (JRC derivation, 2019) 0.613 (Zhou et al., 2019)[25]	LC–MS/MS 0.00501 (Chitescu et al., 2015)[26] LC-MS/MS (0.0014) (Papageorgiou et al., 2019)[27]	**Authorised**	criterion 5
	Miconazole **Miconazole nitrate**	Human medicine Dermatologicals-antifungals for dermatological use	22916-47-8 22832-87-7	0.4 (Minguez et al., 2014 acute) 0.2 (FASS SE database) 0.044 (Zhou et al. 2019)[25]	LC–MS/MS 0.00171 (Chitescu et al., 2015)[26]	**Authorised**	criterion 5
Other pharmaceuticals	Benzimidazoles: Anthelmintics: Mebendazole	Human medicine Antiparasitic Products, Insecticides and Repellents - Anthelmintics	31431-39-7	0.088 (FASS SE database)	LC-IonTrap-MS 0.00037 (Zrnčić et al., 2014)[28]	**Authorised**	criterion 5
	Benzimidazoles: Proton pump inhibitors (PPIs): Lansoprazole	Human medicine Alimentary Tract and Metabolism - Drugs for acid-related disorders	103577-45-3	18 (acute, Pharmaceuticals in the environment. Chapter 16. Webb, 2004) 0.192 (Zhou et al., 2019)[25]	LC-MS/MS (0.0012) (Papageorgiou et al., 2019)[27]	**Authorised**	criterion 5

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	Benzimidazoles: Proton pump inhibitors (PPIs): Omeprazole and its metabolite 4-hydroxy omeprazole sulphide (OM14)	Human medicine Alimentary Tract and Metabolism - Drugs for acid-related disorders	73590-58-6 (Omeprazole) 103876-98-8 (4-hydroxy omeprazole sulphide)	Omeprazole: 41.9 (FASS) 2.1 (Zhou et al., 2019)[25] 4-hydroxy omeprazole sulphide: 0.28 (Wielens Becker et al., 2020)[29]	UHPLC-QTOF MS (surface and wastewater) (Boix et al., 2014)[30] LC-MS/MS (0.00157) (Kosma et al., 2016)[31]	**Authorised**	criterion 5
	Fentanyl	Human medicine Nervous System - Anaesthetics	437-38-7	11.1 (FASS SE database) 0.295 (Zhou et al., 2019)[25]	LC–MS/MS (0.0001) (Krizman-Matasic et al., 2017)[32]	**Authorised**	criterion 5
	Gemfibrozil	Human medicine Cardiovascular System – Lipid-modifying agents	25812-30-0	0.8519 (JRC derivation, prioritisation exercise, 2016)[5,6] 1.56 (Zhou et al., 2019)[25]	SPE followed by UHPLC-QqLIT-MS (river water 0.0034) (Mandaric et al., 2017)[13]	**Authorised**	criterion 5
	Norethisterone	Industrial (ECHA) Human medicine Genito-Urinary System and Sex Hormones - Sex hormones and modulators of the genital system	68-22-4	0.0354 (Prioritisation exercise, 2016)[5,6] 0.51 (freshwater, ECHA) 0.0148 (Zhou et al., 2019)[25]	LC-MS/MS (0.00001) (Vulliet et al., 2011)[33]	**Authorised** This is substance is manufactured and/or imported in the European Economic Area in 1-10 tonnes per year. This substance is used at industrial sites and in manufacturing.	criterion 5

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	Venlafaxine	Human medicine Nervous System-Psychoanaleptics	93413-69-5	0.03835 (prioritisation exercise)[5,6] 0.0061 (Zhou et al., 2019)[25] 0.650 µg/L (Wielens Becker et al., 2020)[29]	SPE-LC-MS-MS (0.0005) (Loos et al., 2013)[34] LC-MS/MS (0.0004) (Papageorgiou et al., 2019)[27] SPE followed by UHPLC-QqLIT-MS (river water 0.0015) (Mandaric et al., 2017)[13]	**Authorised**	criteria 3, 4 and 5
Plant protection products and biocides: azole compounds	**Epoxiconazole**	Plant protection product	106325-08-0 133855-98-8 135319-73-2	0.2 (EQS chronic, Swiss ECOTOX centre, 2016) 0.18 (INERIS, 2017)	LC–MS/MS (0.0083) (Chitescu et al., 2015)[26] LC-ESI-Q-Orbitrap-MS (0.0025) (Casado et al., 2019)[35]	**APPROVED** app 01/05/2009 exp **30/04/2020** 2008/107Reg. (EU) 2019/168Reg. (EU) No 540/2011 . **Authorised in**: AT, BE, BG, CZ, DE, DK, EE, EL, ES, FR, HR, HU, IE, IT, LT, LU, LV, NL, PL, PT, RO, SI, SK, UK (24 MS)	criterion 5
	Imazalil (enilconazole)	Plant protection product	35554-44-0	2.5 (INERIS, 2015) 0.8 (monitoring exercise, JRC derivation from EFSA report)[5,6]	LC-ESI-Q-Orbitrap-MS (0.001) (Casado et al., 2019)[35]	**APPROVED as PPP** app 01/01/2012 exp **31/12/2024** Reg. (EU) No 2019/291Reg. (EU) No 540/2011Reg. (EU) No 705/2011 (1997/73/EC,2007/21/EC,2010/57/EU) **Authorised in**: AT, BE, BG, CY, CZ, DE, DK, EE, EL, ES, FI, FR, HR, HU, IE, IT, LT, LU, NL, PL, PT, RO, SE, SK, UK (25	criterion 5

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						MS) In progress: LV **APPROVED as BIOCIDE** reviewed for use as a biocide in the EEA and/or Switzerland, for: veterinary hygiene	
	Ipconazole	Plant protection product	125225-28-7	0.044 (AgriTox ANSES FR, 2019)	LC-MS/MS (0.05) (DAR, 2011)	**APPROVED** app 01/09/2014 exp **24/08/2024** Reg. (EU) No 571/2014 (Dossier complete 08/20/EC) **Authorised in**: AT, BE, BG, CY, CZ, DE, EL, ES, FR, HR, HU, IE, IT, PL, PT, RO, SE, SK, UK (19 MS) In progress for: FI	criterion 5
	Metconazole	Plant protection product	125116-23-6	0.0582 (Prioritisation exercise, 2016)[5,6] 0.582 (AgriTox ANSES FR 2019) 0.0291 (JRC derivation, 2019)	LC–MS/MS 0.0108 (Chitescu et al., 2015)[26] LC-ESI-Q-Orbitrap-MS (0.0025) (Casado et al., 2019)[35]	**APPROVED** app 01/06/2007 exp **30/04/2020**2006/74/ECReg. (EU) No 540/2011Reg. (EU) no 2019/168 (Reg. (EU) No 2018/524,Reg. (EU) No 878/2014) **Authorised in**: AT, BE, BG, CZ, DE, DK, EE, ES, FI, FR, HR, HU, IE, IT, LT, LU, LV, NL, PL, PT, RO, SE, SI, SK, UK (25 MS)	criteria 3, 4, 5

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	Penconazole	Plant protection product	66246-88-6	6 (AgriTox ANSES FR and INERIS)	LC–MS/MS (0.0095) (Chitescu et al., 2015)[26]	**APPROVED** app 01/01/2010 exp **31/12/2021** 2009/77/EC2010/34/ EUReg. (EU) No 540/2011 **Authorised in**: AT, BE, BG, CY, CZ, DE, EE, EL, ES, FI, FR, HR, HU, IT, LT, LU, LV, MT, NL, PL, PT, RO, SE, SI, SK, UK (26 MS)	criterion 5
	Prochloraz	Plant protection product	67747-09-5	10 (AgriTox ANSES FR) 0.161 (Zhou et al., 2019)[25]	LC–MS/MS (0.00851) (Chitescu et al., 2015)[26]	**APPROVED** app 01/01/2012 exp **31/12/2023** Reg. (EU) No 1143/2011Reg. (EU) No 2019/291Reg. (EU) No 540/2011 (2008/934) **Authorised in**: AT, BE, BG, CZ, DE, EE, EL, ES, FI, FR, HR, HU, IE, IT, LT, LU, LV, MT, NL, PL, RO, SI, SK, UK (24 MS)	criterion 5
	Tetraconazole	Plant protection product	112281-77-3	1.9 (Prioritisation exercise, 2016)[5,6] 4.2 (AgriTox ANSES FR) 3.2 (INERIS)	LC-ESI-Q-Orbitrap-MS (0.0025) (Casado et al., 2019)[35]	**APPROVED** app 01/01/2010 exp **31/12/2021** 2009/82/EUReg. (EU) No 540/2011 **Authorised in**: AT, BE, BG, CZ, DE, EL, ES, FR, HR, HU, IT, MT, PL, PT, RO, SI,	criterion 5

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						SK, UK (18 MS)	
Plant protection products and biocides: other substances	Copper (I) oxide (Cu_2O) Copper (II) oxide (CuO)	Industrial (ECHA) Biocide (ECHA) Plant protection product	1317-39-1 1317-38-0	7.8 (Cu2O and CuO freshwater ECHA) 1.6 (Cu2O and CuO statistic approach, INERIS)	ICP-MS (0.02) (US EPA)	**APPROVED as BIOCIDE** This substance is manufactured and/or imported in the European Economic Area in 1 000 - 10 000 tonnes per year. This substance is used by consumers, in articles, by professional workers (widespread uses), in formulation or re-packing, at industrial sites and in manufacturing. Cu2O substance is approved for use as a biocide in the EEA and/or Switzerland, for preventing fouling. **APPROVED as PPP** app 01/01/2019 exp **31/12/2025** 2009/37/ECReg. (EU) No 2018/1981Reg. (EU) No 232/2015Reg. (EU) No 540/2011	criterion 5

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						(Reg.(EU) No 84/2018) **Authorised in**: AT, BE, BG, CY, CZ, DE, EL, ES, FR, HR, HU, IE, IT, LT, LU, LV, MT, PL, PT, RO, SI, SK, UK (23 MS) CuO is known to be on the EEA market in nanomaterial form (ECHA)	
	Free cyanide	Inorganic biocide	CN- 57-12-5 CNH 74-90-8	0.26 (JRC Factsheet 2015-2018/WFD-UK TAG report 2012)[7,8] 5 (fresh water ECHA dossier) **0.5** (JRC Dossier https://circabc.europa.eu/faces/jsp/extension/wai/navigation/container.jsp 2015)	Continuous Flow Analysis (CFA) method according to ISO 14403-2:2012) modified (0.14-0.30) (Fraunhofer Institute, 2018)[36]	**NOT APPROVED as PPP** (2004/129/EC) No authorisation in place **APPROVED AS BIOCIDE.** This substance is approved for use as a biocide in the EEA and/or Switzerland, for: wood preservation, controlling rodents, controlling insects, ants, etc. (ECHA)	criterion 4

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	Dimoxystrobin	Plant protection product	149961-52-4	0.0316 (ETOX: Information System Ecotoxicology and Environmental Quality Targets, UBA) 1.67 (AgriTox ANSES FR)	LC-MS/MS 0.01 (Loos et al., 2018)[7] LC-ESI-Q-Orbitrap-MS (0.0010) (Casado et al., 2019)[35]	**APPROVED** app 01/10/2006 exp **31/01/2020** 06/75/ECReg. (EU) No 2018/1796Reg. (EU) No 540/2011 (Reg. (EU) No 1136/2013, Reg.(EU) No 84/2018) **Authorised in**: AT, BE, BG, CZ, DE, EE, FR, HR, HU, LT, LU, LV, PL, RO, SK, UK (16 MS)	criteria 3, 4
	Famoxadone	Plant protection product	131807-57-3	0.14 (JRC derivation, prioritisation exercise)[5,6] 0.11 (AgriTox ANSES FR)	LC/MS/MS (0.1) (EPA, 2015)	**APPROVED** app 01/10/2002 exp **30/06/2020** 02/64/ECReg. (EU) No 2018/917Reg. (EU) No 2019/707Reg. (EU) No 540/2011 (2010/77/EU, Reg. (EU) No 2015/1885, Reg. (EU) No 2016/549, Reg. (EU) No 2017/841) **Authorised in:** AT, BE, BG, CY, CZ, DE, EL, ES, FR, HR, HU, IT, MT, NL, PL, PT, RO, SI, SK, UK (20 MS)	criterion 4

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	Proquinazid	Plant protection product	189278-12-4	0.18 (Oecotoxzentrum, Eagaw/EPFL, CH) 0.18 (AgriTox ANSES FR)	GC-MS (0.1) (EFSA, 2009)	**APPROVED** app 01/08/2010 exp **31/07/2022** 2010/25/EUReg. (EU) 2017/2069Reg. (EU) No 540/2011 A**uthorised in**: AT, BG, CY, CZ, DE, EE, EL, ES, FI, FR, HR, HU, IE, IT, LT, LU, LV, MT, PL, PT, RO, SE, SI, SK, UK (25 MS)	criteria 3, 4

dw: dry weight; ww: wet weight; PNEC: predicted no effect concentration; LOQ: limit of quantification; MDL: method detection limit; MIC: minimum inhibitory concentration.

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4.3 Rationale for the selection

Industrial Products

4-Chloroaniline and 3,4-dichloroaniline

4-Chloroaniline (CAS 106-47-8) and 3,4-dichloroaniline (CAS 95-76-1) are industrial chemicals (aromatic amines) primarily used as chemical intermediates in the synthesis of pigments, dyes, pesticides, drugs and rubber products, as well as in laboratory chemicals. These substances are manufactured in and/or imported into the European Economic Area (EEA) for industrial use, in particular the manufacture of other substances (ECHA[a]). Due to their high solubility in water, they can be easily released into surface waters through runoff either as the parent substance or as transformation products and metabolites (e.g. aromatic amines can be found as degradation products and intermediates of various pesticides).

Both substances (4-chloroaniline and 3,4-dichloroaniline) are persistent. 4-Chloroaniline is classified as carcinogenic (ECHA) and 3,4-dichloroaniline is a suspected endocrine disruptor. These substances were selected and fulfil criterion 5.

The quality of available data is low/poor (3,4-dichloroaniline) and acceptable (4-chloroaniline) but for both the data are not Union-representative for making a risk assessment (see Annex II, Table 2.2).

Conclusion: At present, 4-chloroaniline and 3,4-dichloroaniline are considered as other good candidates for the WL.

Chromium (VI) and chromium (III)

Chromium (VI) (CAS 18540-29-9) and chromium (III) (CAS 16065-83-1) are two oxidation states of the element chromium. Chromium (III) is the state in which chromium is found in nature. Chromium (VI), also known as hexavalent chromium, is the second most stable oxidation state of chromium. Rarely occurring naturally, most chromium (VI) compounds are manufactured (products or by-products).

Chromium (VI) was shortlisted during the review of the PS list[5] but not considered for EQS derivation (criterion 1). It was recommended to deselect this substance because restrictions on its use had already been imposed in EU. Its possible selection for the WL is discussed in the JRC reports[7,8]. Chromium (VI) and its compounds are considered substances of very high concern (SVHC[b]) because they are carcinogenic and mutagenic. These substances are included in the REACH restricted substance list (entry 47, Annex XVII of REACH regulation).

According to the WHO, chromium (VI) causes more ecotoxicological concern than chromium (III). However, other studies[37] observed higher toxicity of chromium (III) to aquatic organisms. The JRC reviewed the ecotoxicological data available for chromium (VI) and chromium (III). This led to an update for the PNEC in freshwaters of 2.06 µg/L and 1.8 µg/L for chromium (VI) and chromium (III), respectively (the PNECs derived by the JRC will need to be confirmed via consultation with the WG Chemicals). The PNEC for

[a]European Chemicals Agency (ECHA). https://echa.europa.eu/es/substance-information/ /substanceinfo/100.003.093
[b] Article 57, REACH Regulation, at pp. 141–42.

chromium (III) oxide is authorised and known to be on the European Economic Area (EEA) market in nanomaterial form (ECHA).

For chromium (VI) and its compounds, 735 samples are available from 4 MS and 148 sites in the prioritisation exercise (Inland whole water; Sc3 with PNEC = 2.06 µg/L) (see Annex II, Table *2.2*). About 51% of samples are quantified. The data quality seems to be good since all non-quantified samples are measured with LOQ < PNEC, however the data are not representative for the EU since about 61% of all samples originate from 1 MS; another MS has a share of 29%; the remaining 2 MS hold only 10% of all samples (one of them contributed with only 2 samples).

For chromium (III) oxide, 798 samples are available from 1 MS and 56 sites in the prioritisation exercise (Inland whole water; Sc2) (see Annex II, Table 2.2). About 19% of samples are quantified. The data quality seems to be good since all non-quantified samples are measured with LOQ < PNEC (1.8 µg/L), however the data are not Union-representative since all samples originate from 1 MS.

For Cr total inland dissolved (Sc3, PNEC = 1.8 µg/L), monitoring data from 24 MS (11058 sites) with 174070 samples (22.8% quantified) are available in the prioritisation exercise. The data quality seems acceptable but 51% of all samples originate from 1 MS, other 2 MS hold about 31% of data (see Annex II, Table 2.2).

For Cr total coastal dissolved (Sc3, PNEC = 0.6 µg/L), monitoring data from 6 MS (52 sites) with 370 samples (23% quantified) are available in the prioritisation exercise (see Annex II, Table 2.2). The data quality seems acceptable but 75% of all samples originate from 1 MS, therefore the data can not be considered as Union-representative.

Thus, accepting the difficulties for a separate monitoring of chromium (VI) and chromium (III) in the inland surface water and acknowledging the sufficient amount of data for Cr total inland dissolved, the JRC proposes the final evaluation of chromium (VI) and chromium (III) to be developed, considering the Cr total dissolved in coastal/transitional waters.

Conclusion: Chromium (VI) and chromium (III) are most likely to be proposed for the next WL to be monitored together as Cr total dissolved fraction in coastal/transitional waters.

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Pharmaceuticals

Different types of pharmaceuticals (e.g. antimicrobials, antidepressants) commonly found in surface waters, groundwaters and soils across the EU are considered for inclusion in the WL. The selection of pharmaceuticals is in line with the Commission Communication on the Strategic Approach to Pharmaceuticals in the Environment (COM/2019/128 final[10])[a].

In this document, the pharmaceuticals are grouped according to their therapeutic use. The antibiotics and antifungal agents are grouped as Anti-Microbial pharmaceuticals while the remaining pharmaceuticals are listed as other pharmaceuticals (Figure 2). The pharmaceuticals are selected under criterion 5.

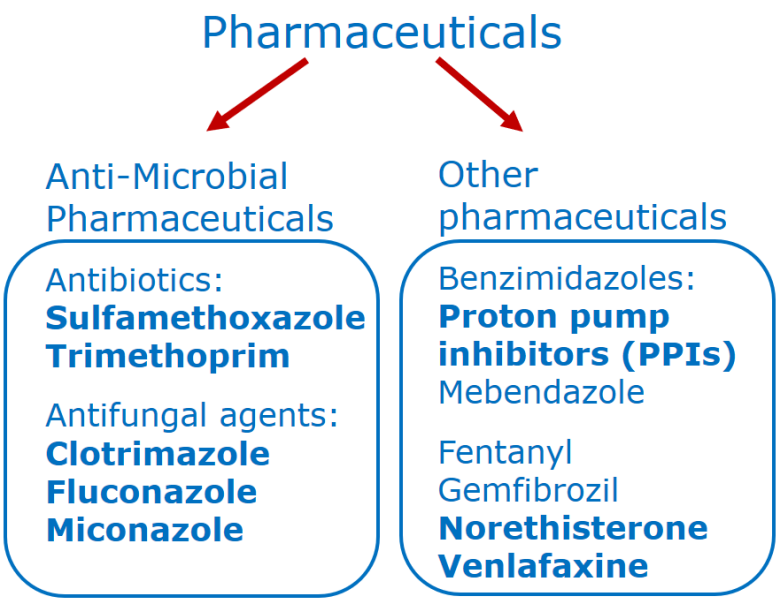

Figure 2: Classification of pharmaceuticals. In bold the most likely to be proposed; not in bold - other good candidates.

Anti-Microbial pharmaceuticals (antibiotics and antifungal)

Antibiotics sulfamethoxazole (CAS 723-46-6) and trimethoprim (CAS 738-70-5), and the antifungal agents (azole pharmaceuticals): clotrimazole (CAS 23593-75-1), fluconazole (CAS 86386-73-4) and miconazole (CAS 22916-47-8) are frequently detected in the water and apart from being toxic they may contribute to the spread and persistence of AMR[38]. The selection of Anti-Microbial pharmaceuticals (antibiotics and antifungal agents) is also in line with the European One Health Action Plan against antimicrobial resistance[b] (COM/2017/0339 final[39]).

[a] The European Union Strategic Approach to Pharmaceuticals in the Environment states: "The Commission will: Consider additional potentially relevant pharmaceuticals, such as cytotoxic pharmaceuticals and X-ray contrast media, in the work supporting the review of the surface water Watch List under the Water Framework Directive, as well as the feasibility of monitoring antimicrobial resistant microorganisms and antimicrobial resistance genes;"(https://eur-lex.europa.eu/legal-content/EN/ALL/?uri=COM:2019:128:FIN)

[b] The Action Plan states: "maximise the use of data from existing monitoring, e.g. Watch List monitoring under the Water Framework Directive, to improve knowledge of the occurrence and spread of antimicrobials in the environment". COM/2017/0339 final: Communication from the Commission to the Council and the European

The available monitoring data in the prioritisation dataset (Sc2; inland surface water) for the foregoing Anti-Microbial pharmaceuticals are not representative and/or are insufficient for making a Union-wide risk assessment (moreover, miconazole is missing any monitoring data) (see Annex II, Table 2.2).

These substances can be monitored using the same analytical method (LC-MS/MS[26]).

Risk assessment for antibiotics

Antimicrobials are natural, semi-synthetic or synthetic compounds that can kill or inhibit the growth of microorganisms including bacteria and fungi. As other pharmaceuticals, antibiotics enter the environment via wastewater effluents, runoff, through manufacturing plants and/or improper disposal. Antibiotics have been detected in aquatic systems around the world, with concentrations ranging between 0.01 to 1 µg/L[38,40-42], and in some cases, like effluents from antibiotic manufacturing sites, could reach higher concentrations, in the milligram per litre range[41,43].

Antibiotics present a potential risk to the ecosystem's health because their mode of toxic action is conserved for the environmental microorganisms[44] and some of them are persistent in the environment[45]. Furthermore, several studies have shown that antimicrobials could increase, maintain and spread antibiotic-resistant bacteria (ARB) in the environment even at low, sub-lethal or sub-inhibitory exposure concentrations and thereby pose a risk to human health[46].

The current Environmental Risk Assessment (ERA) for antibiotics has been developed based on the existing guidelines for other chemicals (e.g. pesticides or industrial chemicals) which typically involve ecotoxicological tests using different organisms like fish, *Daphnia* and algae, including cyanobacteria. The effects on microorganisms are assessed by functional endpoints such as nitrogen transformation in soil, and respiration in activated sludge[46]. Antibiotic's modes of action are generally highly specific, especially for bacteria, but test on bacterial toxicity plays a minor role during the current ecotoxicological assessment, leaving the possibility to overlook an adverse effect of antibiotics on environmental bacteria.

Minimum Inhibitory Concentration (MIC)

To ensure protection to the environment, a PNEC for antimicrobial resistance (AMR) derived using the minimum inhibitory concentration (MIC) has been proposed to predict upper boundaries for resistance[47]. The group of Bengtsson-Palme and Larsson[47] collected MIC data from the public EUCAST database, identified the lowest MIC, compensated for the limited species coverage and predicted the lowest MIC adjusted for the number of tested species. The PNECs for resistance selection (PNEC-MIC) were assessed using an assessment factor of 10 to account for the differences between inhibitory concentration and selective concentration of antibiotics. In some cases, the PNEC-MIC were below the available PNEC for ecotoxicological effects.

In order to be more protective with environmental ecosystems, it is suggested to derive PNECs, determine ecotoxicological and resistant selection, and use the lower value for the ERA (AMR industry alliance[24]).

Parliament: A European One Health Action Plan against Antimicrobial Resistance (AMR) https://eur-lex.europa.eu/legal-content/GA/TXT/?uri=CELEX:52017DC0339

Conclusion: The antibiotics (sulfamethoxazole and trimethoprim) and the antifungal agents (azole pharmaceuticals): clotrimazole, fluconazole and miconazole, are most likely to be proposed for the next WL to be monitored in inland surface waters.

Other pharmaceuticals

Other pharmaceuticals have also been selected according to their occurrence and hazard properties.

Benzimidazoles

Anthelmintics: Mebendazole

Mebendazole (CAS 31431-39-7) is persistent, bioaccumulative and toxic (Stockholm County Council[a]). It is suspected of being carcinogenic, mutagenic and toxic to reproduction (CMR, in Annex III inventory, ECHA[b]).

No data are available for this substance in the dataset of the prioritization exercise (see Annex II; Table 2.2).

Conclusion: At present, mebendazole is considered amongst the other good candidates for the WL.

Proton pump inhibitors (PPI): lansoprazole and omeprazole

Proton pump inhibitors, e.g. lansoprazole (CAS 103577-45-3) and omeprazole (CAS 73590-58-6), are commonly prescribed, and thus, widely used for the treatment of acid-related disorders. According to several studies[29-31,48,49], PPIs are easily metabolised in the human body and easily transformed in the environment. For this reason, even though they are widely used, PPIs occur at low concentrations in wastewater and surface water. It has been suggested that their most abundant and frequent metabolites and transformation products should be monitored in water together with the parent compounds to better assess the risk that these substances pose to aquatic organisms. In the case of omeprazole, the most abundant and frequently detected metabolites in wastewater and surface water are the transformation product omeprazole sulphide OTP5[49] along with the metabolites OM10 and 4-hydroxy omeprazole sulphide OM14[30]. According to a recently published study[29], the metabolite 4-hydroxy omeprazole sulphide (OM14, CAS number 103876-98-8) identified as potentially mutagenic poses a higher risk to aquatic organisms than its parent compound.

No available data exist for omeprazole and lansoprazole nor for their metabolites in the dataset of the prioritisation exercise (see Annex II; Table 2.2).

Conclusion: Omeprazole and its metabolite 4-hydroxy omeprazole sulphide (OM14) are most likely to be proposed for the next WL to be monitored in inland surface waters.

[a] https://politiquedesante.fr/wp-content/uploads/2014/05/PBT-2014-2015-copie.pdf
[b] https://echa.europa.eu/information-on-chemicals/annex-iii-inventory

Fentanyl

Fentanyl (CAS 437-38-7) is an opioid used in anaesthetics. It is also employed as a recreational drug and shows persistent and toxic (PT) properties according to the Stockholm County Council[a], and elicits possibly toxic effects to reproduction (R) (Annex III inventory, ECHA[b]).

Two MS expressed a concern that fentanyl is subject to the controlled substance law (the narcotics act), therefore difficulties could be encountered to purchase standard solutions for chemical analysis.

No monitoring data are available for this substance in the dataset of the prioritisation exercise (see Annex II; Table 2.2).

Conclusion: At present, fentanyl is considered amongst the other good candidates for the WL.

Gemfibrozil

Gemfibrozil (CAS 25812-30-0) is a human medicine used for the treatment of abnormal blood lipid levels. It is persistent and toxic (PT, Stockholm County Council[c]) and possibly carcinogenic (C) and toxic to reproduction (R).

According to the prioritisation dataset Sc2 (inland whole water), it is monitored in 3 MS at 251 sites (see Annex II; Table 2.2) with 2476 samples (only 2% quantified). About 97% of all samples come from one MS, meaning that the data are not Union-representative.

Conclusion: Gemfibrozil is considered at present amongst the other good candidates for the WL.

Norethisterone

Norethisterone (CAS 68-22-4) is a human pharmaceutical belonging to the group of sex hormones and modulators of the reproductive system used for the treatment of different hormonal disorders. As a synthetic progesterone (progestin), it is used alone or in combination with some oral contraceptive pills. The presence of this substance in the aquatic environment raises concern due to its ability to act as endocrine disrupter by mimicking and/or disrupting the activity of endogenous progestogens, which play critical roles in modulating sexual development and maturation in fish[50,51].

In Sc2 (inland whole water) of the prioritisation dataset, there are available 20 samples from 1 MS (19 sites) (see Annex II; Table 2.2). The data quality is good (100% quantified samples), however, the quantity of data is insufficient and they are not representative for the EU to perform risk assessment.

Conclusion: Norethisterone is most likely to be proposed for the next WL for monitoring in inland surface waters.

[a] https://politiquedesante.fr/wp-content/uploads/2014/05/PBT-2014-2015-copie.pdf
[b] https://echa.europa.eu/information-on-chemicals/annex-iii-inventory
[c] https://politiquedesante.fr/wp-content/uploads/2014/05/PBT-2014-2015-copie.pdf

Venlafaxine

Venlafaxine (CAS 93413-69-5) is an antidepressant that was identified as a potential candidate in the previous review of the WL[7]. This substance is considered persistent and toxic (PT, Stockholm County Council[a]) and toxic to reproduction (R, ECHA[b]). It fulfils criterion 3 (substances from the modelling exercise measured below 4 MS with modelled RQ above 5), however it was not selected for the WL in 2018 because the PNEC value was considered not reliable. The JRC has reviewed the available ecotoxicological information and found a reliable PNEC of 0.0061 (Zhou et al., 2019), which, if confirmed upon consultation with the MS and stakeholder, should suggest the substance to be considered for the next WL.

The available monitoring data came from 1 MS (93 sites) with 1395 samples (about 77% quantified) (see Annex II; Table 2.2) and are not representative for making a Union-wide risk assessment.

Conclusion: Venlafaxine is most likely to be proposed for the next WL for monitoring in inland surface waters.

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[a] https://politiquedesante.fr/wp-content/uploads/2014/05/PBT-2014-2015-copie.pdf
[b] https://echa.europa.eu/es/brief-profile/-/briefprofile/100.122.418

Plant protection products and biocides

Azole compounds: epoxiconazole, imazalil, ipconazole, metconazole, penconazole, prochloraz and tetraconazole

Due to their antifungal properties, azole fungicides are extensively used in plant protection products and biocides. Europe is considered the dominant market for fungicides with major applications on grains and cereals, fruits (with particularly intensive use in viticulture), and vegetables. In urban areas, fungicides are used in paints and coatings on walls, flat roofs, and basement seals. Consequently, fungicides can enter aquatic ecosystems via discharge from wastewater treatment plants following domestic and agricultural use and directly from surface runoff, primarily from agricultural use sources. Azole fungicides can be harmful to a broad range of non-target organisms and have also been studied for their possible endocrine-disrupting properties. Moreover, their use is predicted to increase due to climate change and to contribute to the development of fungicide resistance and to the propagation of invasive fungal species[52]. Azole compounds are selected under criterion 5.

The available monitoring data in the prioritisation dataset (Sc2; inland surface water) for the azole compounds (epoxiconazole, imazalil, ipconazole, metconazole, penconazole, prochloraz and tetraconazole) are either insufficient or not overall representative for making a Union-wide risk assessment (ipconazole is missing any monitoring data). In addition, the data quality seems poor because there are many repeated non-quantified samples for these compounds in the dataset (see Annex II; Table 2.3).

These substances can be measured using the same analytical method (LC–MS/MS) with limits of quantification ranging from 0.001 to 0.05 µg/L depending on the substance[26,35]. See Annex I for more detailed information.

Conclusion: The azole compounds (epoxiconazole, imazalil, ipconazole, metconazole, penconazole, prochloraz and tetraconazole) are most likely to be proposed for the next WL to be monitored in inland surface waters.

Copper oxides

Copper occurs in nature in four oxidation states: elemental copper Cu (0) (solid metal), Cu (I) cuprous ion (Cu_2O; CAS 1317-39-1), Cu (II) cupric ion (CuO; CAS 1317-38-0), and rarely Cu (III). In water, Cu (II) is the most prevalent form of copper[53]. Two forms of copper oxide (i.e. copper (I) oxide and copper (II) oxide) are approved in the European Economic Area (EEA) and/or Switzerland for use as active ingredients in plant protection products and biocides. Copper (I) oxide is approved as a biocide for preventing fouling, while copper (II) oxide is approved as a biocide for wood preservation. Dicopper oxide is manufactured and/or imported in the European Economic Area in 1000-10000 tonnes per year, while copper oxide is manufactured and/or imported in the European Economic Area in 1000+ tonnes per year (ECHA). These substances may be washed into the aquatic environment from agricultural and urban application sites and may also enter into the water when used as a biocide in antifouling paint formulations.

Besides, copper (II) oxide is known to be on the EEA market in nanomaterial form (ECHA). Metal nanoparticles can induce toxicity by mechanisms that are different from those of soluble ions. A Danish investigation into the environmental risk posed by engineered nanomaterials found that release patterns and hazard properties of copper nanomaterials may cause a future concern[54].

Moreover, the environmental pollution caused by heavy metals such as copper can co-select for antimicrobial resistance (AMR)[38].

No available data for copper oxides are present in the dataset of the prioritization exercise (see Annex II; Table 2.3).

For Cu total inland dissolved fraction (Sc3; PNEC = 7.8 µg/L), overall 97036 samples from 24 MS (7009 sites) are available in the dataset (inland surface water) of the prioritisation exercise. About 50% of all samples are quantified. The data quality seems good, however the risk evaluation outcome depends on the choice of PNEC (see Annex II; Table 2.3).

Conclusion: At present, copper oxides are considered amongst the other good candidates for the WL.

Free cyanide

Free cyanide (CAS CN- 57-12-5; CNH CAS 74-90-8) is approved for use as a biocide in the European Economic Area (EEA) for wood preservation, controlling rodents, controlling insects and ants (ECHA). Furthermore, the cyanide is used as a raw material in many products leading to the release in aquatic environments through effluents[55] as cyanide ions[56]. Free cyanide has been identified as the most toxic form derived from HCN, NaCN and KCN. This substance was identified as a good candidate for the 1st WL[8] however it was not recommended due to the lack of an appropriate analytical method. In 2015, a project was launched by the stakeholder in collaboration with the Fraunhofer Institute entitled "Monitoring program for the determination of the natural background concentrations of free cyanide in surface waters". The overall goal of this study was to validate a method to determine the natural background (Fraunhofer Institute, 2018[36]). The project successfully could develop a sensitive method for the free cyanide measurements with LOQ below 0.3 µg/L.

For cyanide anion, in the prioritisation dataset Sc2 (inland dissolved fraction; see Annex II; Table 2.3) data from 2 MS with 340 samples are available (18.5% quantified samples). The data quality is low since about 64% of non-quantified samples have LOQ/LOD ≥ PNEC (PNEC = 0.5 µg/L) and not Union representative (monitored only in 2 countries). Therefore, there is insufficient amount of good quality and representative data for free cyanide to develop a Union-wide risk assessment.

Besides, there are no available data for cyanide anion in coastal/transitional water (dissolved fraction). All these motivate the need of a Union-wide data collection for cyanide anion (inland and/or coastal water; dissolved fraction) for the purpose of risk evaluation.

Conclusion: The analytical method is available, with a Limit of Quantification (LOQ) mostly < 0.3 µg/L (PNEC value for freshwater is 0.5 µg/L), thus confirming a sufficient sensitivity of the analytical method to reach a value below the PNEC in freshwater. Free cyanide is most likely to be proposed for the next WL to be monitored in coastal and inland surface waters (dissolved fraction).

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Dimoxystrobin

Dimoxystrobin (CAS 149961-52-4) is approved as a plant protection product in the UE. It is authorised in 16 Member States. Dimoxystrobin fulfils two of the PBT (persistent, bioaccumulative and toxic) criteria according to the EU pesticides database[a] and it is a candidate for substitution. Furthermore, it is an endocrine disruptor, and is possibly carcinogenic and toxic to reproduction (ECHA[b]). It fulfils criteria 3 and 4. Dimoxystrobin was not recommended for the WL during the last update[7] because of the expiry date of the approval as a plant protection product. The approval for this substance was renewed in January 2019 and it will be reviewed again in January 2020. If it is again renewed, dimoxystrobin should be considered for inclusion in the next WL.

The available monitoring data in the prioritisation dataset (Sc2; inland surface water) are not representative (6078 samples from only 1 MS) for making a Union-wide risk assessment. In addition, the data quality seems poor because there are 3890 repeated non-quantified samples (64% from total) (see Annex II; Table 2.3).

Conclusion: Dimoxystrobin is most likely to be proposed for the next WL to be monitored in inland surface waters.

Famoxadone

Famoxadone (CAS 131807-57-3) is authorised as plant protection product in 20 Member States. Moreover, this substance fulfils two of the PBT criteria according to the EU pesticides database[c] and it is a candidate for substitution. This substance has also been listed in the Annex III inventory (ECHA[d]) as a suspected carcinogen, mutagen and hazardous to the aquatic environment. Famoxadone is selected under criterion 4.

According to the last review of the WL (Loos et al., 2018), famoxadone could be considered for inclusion in the 3rd WL, if its approval is renewed and if a reliable PNEC and an appropriate analytical method are available. This substance is approved until June 2020 when the approval will be reviewed. If it is renewed, it should be considered for inclusion in the next WL, although it might have to wait until the 4th WL.

The available monitoring data in the prioritisation dataset (Sc2; inland surface water) are not representative (overall 5528 samples from 3 MS; 98% of samples originate from one MS) for making a Union-wide risk assessment. In addition, the data quality is poor because there are numerous repeated non-quantified samples (5422; about 98% from total) (see Annex II; Table 2.3).

Conclusion: Famoxadone is most likely to be proposed for the next WL to be monitored in inland surface waters.

Proquinazid

Proquinazid (CAS 189278-12-4) is authorised as plant protection product in 25 Member States. This substance is persistent, toxic and possibly carcinogenic (ECHA[e]) and should

[a] https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=homepage&language=EN
[b] https://echa.europa.eu/es/substance-information/-/substanceinfo/100.128.660
[c] https://ec.europa.eu/food/plant/pesticides/eu-pesticides
[d] https://echa.europa.eu/es/information-on-chemicals/annex-iii-inventory/-/dislist/details/AIII-100.114.714
[e] https://echa.europa.eu/es/substance-information/-/substanceinfo/100.113.680

be considered for the WL if reliable information for the PNEC is available[7]. Proquinazid fulfils criteria 3 and 4.

The available monitoring data in the prioritisation dataset (Sc2; inland surface water) are not representative for making a Union-wide risk assessment (see Annex II; Table 2.3).

Conclusion: Proquinazid is considered at present amongst the other good candidates for the WL.

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5 Conclusions

In 2020, the WL, according to Directive 2008/105/EC (Article 8b[8]) has to be revised and, except for three substances included in 2018 (amoxicillin, ciprofloxacin and metaflumizone), all existing substances must be removed.

JRC recommends 12 substances/groups of substances selected based on the criteria described in sections 3.1 and 4.1 for inclusion in the next WL.

- Group of pyrethroids and the sunscreen ingredient. These substances are hydrophobic and, to gather good data quality in order to evaluate whether they pose an ecotoxicological or human health risk, they should be measured in sediment or biota. JRC would recommend measurement in sediment. Recently, Rösch et al. developed a very sensitive method to measure the pyrethroids in water, reaching a LOQ of pg/L (below the PNEC values) (Rösch et al., 2019[15]). However, this method requires very sophisticated and expensive instruments which are not available in all laboratories. Participants in the workshop "Analytical methods for substances in the Watch List under the Water Framework Directive" held at the JRC (Ispra, Italy) in October 2018, agreed that compounds with log K_{OW} > 5 should preferably be measured in sediments or in SPM, and that a method for sediments exists.
- Antibiotics (sulfamethoxazole, trimethoprim) and antifungal pharmaceuticals (clotrimazole, fluconazole, miconazole). These substances have been selected because of their wide use and release into water, their toxicity to aquatic life and their possible contribution to the spread of antimicrobial and antifungal resistance. In the context of action to address in a more holistic way the rising threat from AMR, the environment, and particularly water, has been identified as a potential reservoir of resistance whose role needs to be better understood (A EU One Health Action Plan)[39]. Their inclusion in the WL will provide a picture of their concentration at EU level.
- Other pharmaceuticals. Venlafaxine was identified as a good candidate since this substance is PT and fulfils criterion 3 (measured in fewer than 4 MS during the ongoing priority substances prioritisation exercise and with a modelled RQ higher than 5). However, it was excluded because the PNEC was not reliable. The JRC, based on available ecotoxicological data, derived a PNEC. Omeoprazole and its metabolite 4-hydroxy omeprazole sulphide have been identified for their hazard properties and for their wide uses. Norethisterone is a synthetic hormone and its ED properties could pose a risk to aquatic organisms.
- PPP (azole compounds). Epoxiconazole, imazalil, ipconazole, metconazole, penconazole, prochloraz and petraconazole are widely used as PPP and biocides. They have been selected due to their hazard properties. Many of them are PT and some of them have ED properties. Moreover, they may contribute to antifungal resistance.
- Dimoxystrobin and famoxadone. These two substances are PPP and they were identified and selected for their hazard properties and potential risk inthe modelling-based exercise. In the first review of the WL, they were not further proposed due to expired data. Recently, their use in Europe has been renewed and JRC would recommend their inclusion due to common use in 16 Member States (MS) (dimoxystrobin) and 20 MS (famoxadone).
- Chromium (III) and chromium (VI). In 2018[7], JRC revised the PNEC value for Cr (III) which currently corresponds to 1.8 µg/L and is lower than the PNEC value for Cr (VI) (2.06 µg/L) considered so far the most toxic form. Indeed, the use of hexavalent chromium has been restricted due to its toxicity effects, however, according to the more recent ecotoxicological data, trivalent chromium poses a

major risk. For this reason, JRC recommends to gather more data on these two forms of chromium, particularly for coastal and transitional waters, since no good data are available to evaluate the risk.

- Free cyanide is one of the most toxic cyanide forms in aquatic environment. This substance was identified as a potentially risk during the prioritisation exercise (2011), but questions were raised about the form of cyanide covered by the available monitoring data. The substance was not further considered in the 1st WL because of the lack of a good analytical method. Thanks to the efforts of stakeholders, a method is now available and the selection of this substance would result in monitoring data collected across Europe. However, the surrounding environment and potential natural background should be considered.

In conclusion, Table 5 shows the suggested candidate substances and group/class of substances with respective names, uses and matrices (environmental compartment) where the JRC would recommend that monitoring be performed.

Table 5: A list of candidate substances fulfilling the selection criteria and identified by the JRC as most likely to be proposed for the next WL. The table shows for each candidate substance the group/class, name, use and matrix (environmental compartment) where it should be monitored.

Group	Name	Use	Matrix
	EHMC (2-Ethylexyl 4-methoxycinnamate)	UV filter	Sediment
Pyrethroids	Bifenthrin, Deltamethrin, Esfenvalerate, Permethrin	PPP	Sediment
Industrial products	Cr (VI) and Cr (III)	Industrial chemical	Coastal/transitional water (as Cr total dissolved fraction)
Anti-Microbial Pharmaceuticals	Sulfamethoxazole, Trimethoprim	Antibiotic	Water (inland whole water)
	Clotrimazole, Fluconazole, Miconazole	Antifungal	
Other Pharmaceuticals	Proton pump inhibitors (PPI): Omeprazole and its metabolite 4-hydroxy omeprazole sulphide (OM14)	Human medicine	Water (inland whole water)
	Norethisterone	Synthetic Hormone	
	Venlafaxine	Antidepressant	
PPP and Biocides (Azole compounds)	Epoxiconazole, Imazalil, Ipconazole, Metconazole, Penconazole, Prochloraz, Tetraconazole	PPP Biocides	Water (inland whole water)
Other PPP and	Free Cyanide	Inorganic biocide	Water (inland dissolved

Biocides			fraction/coastal waters)
	Dimoxystrobin	PPP	Water (inland whole water)
	Famoxadone	PPP	Water (inland whole water)

Table 6 lists other substances classified as good candidates that are not further considered in this exercise following some comments of MS and stakeholders as explained in section 4.3.

Table 6: List of substances assessed by the JRC as other good candidates for the next WL (not proposed for now to be included in the WL). For each substance, the table shows the group/class, name, use and matrix (environmental compartment) where it should be monitored.

Group	Name	Use	Matrix
Industrial products	4-chloroaniline 3,4-dichloroaniline	Industrial	Water (inland whole water)
Pharmaceuticals	Mebendazole	Human medicine	Water (inland whole water)
	Fentanyl	Human medicine	
	Gemfibrozil	Human medicine	
PPP and Biocides	Copper (I) oxide (Cu_2O) Copper (II) oxide (CuO)	PPP Biocide	Water (inland dissolved fraction)
	Proquinazid	PPP	Water (inland whole water)

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List of abbreviations and definitions

AMR Antimicrobial resistance

APCI Atmospheric pressure chemical ionisation

ARB Antibiotic resistant bacteria

B Bioaccumulation

C Carcinogenicity

CMR Carcinogenic, mutagenic and toxic to reproduction

CAS Chemical Abstract Service

Eawag Swiss Federal Institute of Aquatic Science and Technology

EE2 17-alpha-Ethinylestradiol

E1 Estrone

E2 17-beta-Estradiol

ECHA European Chemicals Agency

ECOSAR

ED Endocrine disruptor

EDS Endocrine Disruptors Strategy

EEA European Environment Agency

EEA European Economic Area

EFSA European Food Safety Authority

EFTA European Free Trade Association

EHMC 2-ethylhexyl-4-methoxycinnamate

EQS Environmental quality standard

EQSD Environmental quality standard Directive

ERA Environmental Risk Assesment

FASS Swedish Medicines Information Engine

GC-MS Gas chromatography mass spectrometry

INERIS Institut national de l'environnement industriel et des risques

JRC Joint Research Centre

K_{OW} N-octanol/water partition coefficient

LC-MS-MS Liquid chromatography (tandem) triple quadrupole mass spectrometry

LLE Liquid-liquid extraction

LOD Limit of detection

LOQ Limit of quantification

M Mutagenicity

MDL Method detection limit

MEC Measured environmental concentration

MIC Minimum inhibitory concentration

MS Member State

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OM Omeprazole metabolite

OT Omeprazole transformation product

OSPAR Convention for the Protection of the Marine Environment of the North-East Atlantic

PBT Persistent, bioaccumulative and toxic

PEC Predicted environmental concentration

PNEC Predicted no-effect concentration

P Persistence

PPI Proton pump inhibitor

PPP Plant protection product

PS Priority Substance

R Reproduction Toxicity

RIVM National Institute for Public Health and the Environment (NL)

RQ Risk Quotient

Sc2 and Sc3 Scenario 2 and Scenario 3

SG-R Sub-group on revision (of the priority substance list)

SoE State of the Environment

SPE Solid-phase extraction

SPM Suspended particulate matter

STE Spatial, Temporal and Extent of PNEC exceedance

SVHC Substance of very high concern

T Toxicity

TGD Technical guidance document

UBA German Environment Agency

USGS United States Geological Survey

US EPA United States Environmental Protection Agency

WFD Water Framework Directive

WL Watch List

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Supplementary information

The annexes below present additional information for the WL candidate substances.

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Annex I: Outcome of the workshop "Analytical methods for substances in the Watch List under the Water Framework Directive" held at the JRC (Ispra, Italy) in October 2018

The workshop was held at the JRC (Ispra, Italy), on the 9-10 October 2018. It was attended by 22 experts from 14 countries. Teresa Lettieri chaired the meeting.

The objectives of the Workshop were: i) to discuss the feedback received from MS in order to get better measurements for the five substances for which it is difficult to reach the LOQ ≤ PNEC (in particular methiocarb, imidacloprid, EE2); ii) to discuss the analytical methods for the pyrethroid insecticides and the sunscreen (UV-filter) agent 2-ethylhexyl 4-methoxycinnamate (EHMC) in the appropriate matrix (sediment or biota).

During the meeting, the experts gave several presentations which are summarised as follows.

Robert Loos (JRC) presented the substances proposed for the next round of the WL to be measured in sediment: pyrethroids (etofenprox, permethrin, esfenvalerate, deltamethrin, bifenthrin) and EHMC, a UV-filter sunscreen ingredient. In particular, he discussed the analytical methods (including extraction, clean-up and determination) and the sampling strategies reported in scientific articles and indicated the MS that currently analyse pyrethroids (FR and CH (method in development)) or EHMC (CZ; DE, SE (method in development)).

Isabella Sanseverino discussed the PNEC values derived by the JRC for pyrethroids in marine water, freshwater and sediments. All the studies (acute and chronic) were retrieved from institutional dossiers.

Francois Lestremeau (INERIS-FR) presented the institutional method (GC-MS/MS) used to analyse pyrethroids in sediment, which is part of the regular monitoring in France since 2015. With this method, the MS is able to reach an LOQ of 1-5 µg/kg. To avoid sticking of the substances to the analytical part of the instrument (GC liner), sorbitol alcohol is used as analytical protectant.

Silwan Daouk (CH) presented the method (GC-APCI or NCI MS/MS) developed in CH for analysing pyrethroids in water. With this method, it was possible to reach LOQ ≤ PNEC (around 25 pg/l) for many compounds except for permethrin, bifenthrin and deltamethrin. He suggested to use tap water instead of MilliQ water as a matrix for making the calibration process and to analyse the samples within 24 hours. If measurement is not performed, it is recommended to store samples at -20°C for a maximum of 1 week and to avoid sample storage at +4°C. He also remarked that pyrethroids stick to the glass and that it is possible to recover the substances by shaking. The method for detecting pyrethroids in sediment is under development. Some detections and PNEC exceedances in water were reported.

Martin Fereneik (CZ) presented the method developed for detecting EHMC in sediment, based on lyophilisation, LLE with hexane/acetone and GC-MS. He pointed out that it is critical to evaluate laboratory blanks (therefore no clean-up is used) because they can be easily contaminated with cosmetic products used by operators. The method LOQ was set at 50 µg/kg to avoid false positive samples. The concentration levels at the majority of the sampling sites were below the LOQ.

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Ola Swahn (SE) presented an analytical method (in-house built method is in development) for detecting EHMC in sediment, based on superheated water extraction (SHWE), followed by SPE clean-up and UHPLC-MS/MS analysis (use of HPLC degasser, GC oven, extraction cell and a cooling coil). The samples can be extracted in wet conditions and it takes 20 minutes to extract 1 sample without the use of organic solvents. As the results have not been published yet, slides cannot be circulated.

After the presentations, several aspects of the sediment analysis (e.g. fraction to be analysed, number of sampling points, normalisation, storage) were discussed with specific focus on EHMC in sediments.

For pyrethroids, the measurement in biota was also mentioned considering their bioaccumulation potential in fish. However, sediment was indicated as matrix of choice because there is already analytical methodology available, while measurement in biota would be more difficult. When analysed in water, it is recommended to perform the analysis of pyrethroids within 24h or store them at -20°C (for a maximum of one week). It was also remarked that pyrethroids stick to the glass, but it is possible to recover the substance by shaking.

For the analysis in sediments, the importance of defining the fraction to be analysed was mentioned and how to normalise the data to the organic carbon. Different methodologies used to measure pyrethroids and EHMC in sediments were also presented with following discussion on drafting recommendations for sediment analysis. It was suggested to consult the CIS sediment and biota guidance document Nº 25.

Finally, the participants split in two different groups to draft guidelines for sediment analysis. All participants agreed on the following points:

1. Use of sediment fraction below 2 mm;

2. Normalisation of the concentration results respect to the dry matter and Total Organic Carbon (TOC);

3. Selection of a proper sampling site ensuring at least 20% of fine particles;

4. Creation of a composite sample with a minimum of three sampling points located close by;

5. Sample storage at -20°C in amber glass (if not possible to analyse them within 24 hours);

6. Sampling period dependent on the use of pesticides, and for EHMC after the summer;

7. Importance of internal standards: recovery standards should be spiked the day before and left over night, normal internal standard can be spiked just before extraction; use of reference materials;

8. Extraction method is up to the laboratories (different methods possible).

The **main conclusions** of the Workshop were the following:

1. Proposal for introducing the LOQ value in the WL Decision;

2. Ask MS to provide information about LOD, LOQ and concentrations between LOD and LOQ to understand if non-quantified samples are detected or non-detected samples;

3. Recommendation for sediment analysis to be drafted;

4. Look for PNEC to propose new substances for the next round of the WL;

5. Promote the exchange of information and improve communication and collaboration (service, training, protocols) between MS for substances for which it is difficult to reach the LOQ≤PNEC.

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Annex II: Hazard properties, available monitoring data, RQ, and STE scores

The tables below give information relative to the hazard properties (PBT/CMR/ED), available monitoring data, RQs, and STE scores for the candidate substances.

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Table 2.1: Candidate substances to be monitored in the sediments.

Group	Name	CAS	PNEC water(µg/L) PNEC sediments (µg/kg)	Hazard (PBT/CMR/ED)	Data (prioritisation exercise)	RQ (MEC(P95)/PNEC)	STE score
	EHMC (2-Ethylexyl 4-methoxycinnamate) **(2-Ethylexyl trans-4-methoxycinnamate)**	5466-77-3 83834-59-7	**water** 6 (EU 2015/495) **sediments** 200 (specific organism, *Melanoides tuberculata*, 28d, AF 10; JRC factsheet Carvalho et al., 2015)	Not in Annex III inventory (ECHA) ED properties (Several studies, the endocrine disruption exchange, TEDX endocrine) ED according to the JRC factsheet (Carvalho et al., 2015) ED (ECHA)	Inland whole water: WL combined dataset (after 3rd reporting year): for Sc3 1583 samples (13.4% quantified) from 23 MS; Median = 0.3 µg/L; MEC(p95) = 1.8 µg/L. Sediments: No available data in the dataset of the prioritization exercise. WL dataset: reported 31 samples from 3 MS; max concentration = 35 µg/kg	0.3 (PNEC = 6 µg/L) <1	0 (PNEC = 6 µg/L) 0
Pyrethroid insecticides	**Bifenthrin**	82657-04-3	**water** 0.00002 (JRC FactSheet; prioritisation 2016) **sediments** 0.4 dw (specific organism, INERIS, 2011) 0.4 dw (*Chironomus riparus*, AF 100; JRC dossier, 2016)	2 PBT criteria (PT EU Pesticides database); PT CMR in Annex III inventory (ECHA) Possibly C (ECHA); Possible ED properties	Inland whole water: In Sc2 dataset 7572 samples from 3 MS (1132 sites) are available. Only 2 quantified samples. The data quality of Sc2 is not good (for majority of non-quantified samples LOQs > PNEC). The data are not Union-representative. Sc3 was not developed since low data quality. Median conc = 0.01 µg/L; MEC(p95) = 0.025 µg/L Sediments: No available data in the dataset of the prioritisation exercise.	1250 (PNEC = 0.00002 µg/L)	3 (PNEC = 0.00002 µg/L)

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	Deltamethrin	52918-63-5	**water** 0.00007 (JRC FactSheet; prioritisation 2016) **sediments** 6.2 ww (Equilibrium partitioning, SE, assessment report 2011) 0.54 dw (Chironomus riparus, AF 100; JRC dossier 2016)	P (suspected) BT C (suspected) in Annex III inventory (ECHA); Possible ED properties (one study)	Inland whole water: In Sc2 dataset 28842 samples from 7 MS (2766 sites) are available. Only 0.7% quantified samples. Data quality in Sc2 is not good since 96.6% of non-quantified samples have LOQs>PNEC. The data are not Union-representative because 1 MS holds 89.2% from all samples. Median conc = 0.01 µg/L; MEC(p95) = 0.05 µg/L. Sc3 was worked out but it is not representative for EU-wide assessment (3 MS with 3520 samples; 6% quantified). Sediments: No available data in the dataset of the prioritisation exercise.	714 (Sc2; PNEC = 0.00007 µg/L) 1.4 (Sc3; PNEC = 0.00007 µg/L)	2.69 (Sc2; PNEC= 0.00007 µg/L) 1.2 (Sc3; PNEC= 0.00007 µg/L)
	Esfenvalerate	66230-04-4	**water** 0.0001 (JRC FactSheet prioritisation 2016) **sediments** 1.25866 (dw) (Equilibrium partitioning; JRC dossier, 2016)	2 PBT criteria (EU Pesticides database) PB (suspected) T C (suspected) in Annex III inventory (ECHA) Possible ED properties (one study)	Inland whole water: In Sc2 data from 4 MS (1152 sites) with 8661 samples are available. Only 0.5% quantified samples. Data quality in is not good since 98.9% from all non-quantified samples have LOQs > PNEC. The data are not union representative (one MS holds 76% from all measurements). In Sc3 (PNEC = 0.0001 µg/L) data from only 2 MS (26 sites) with 87 samples are available (53% quantified samples). These data are insufficient and Sc3 is not representative for EU-wide assessment. Sediments: No available data in the dataset of the prioritisation exercise.	500 (Sc2) 170 (Sc3)	2.6 (Sc2; PNEC = 0.0001 µg/L) 2.5 (Sc3; PNEC = 0.0001 µg/L)

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	Permethrin	52645-53-1	**water** 0.00047 (derived by the JRC) 0.0015 (UK) **sediments** 0.2 ww (specific organism, INERIS, 2011) 1 dw (*Chironomus riparus,* AF 100; JRC substance dossier, 2016)	PB (suspected) T M(suspected) in Annex III inventory (ECHA) Possible ED properties (two studies)	Inland whole water: In Sc2 dataset 29730 samples from 7 MS are available. Only 0.4% quantified samples. Data quality is not good since only 2 non-quantified samples have LOQ < PNEC. The data are not Union-representative because one MS holds 90.7% from all samples. Median = 0.0125 µg/L; MEC(p95) = 0.025 µg/L; Sc3 contains 117 samples from 4MS. The available data are insufficient for a reliable risks assessment. Median = 0.01 µg/L; MEC(p95) = 0.09 µg/L; Sediments: No available data in the dataset of the prioritisation exercise.	53 (Sc2) 191 (Sc3)	2.41 (Sc2; PNEC = 0.00047 µg/L) 2.29 (Sc3; PNEC = 0.00047 µg/L)

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Table 2.2: Industrial products and pharmaceuticals.

Group	Name	CAS	PNEC (µg/L)	Hazard (PBT/CMR/ED)	Data (prioritisation exercise)	RQ (MEC(P95)/PNEC)	STE score
Industrial products	4-Chloroaniline	106-47-8	0.05 (prioritisation exercise RBSP-ECOSTAT, UBA, 2014) 1 (INERIS)	PT, C, possible M C (ECHA). Not in Annex III inventory (ECHA)	In Sc2 (inland whole water) monitored in 5 MS (2323 sites); available 26925 samples; only 0.8% quantified samples; the data quality is acceptable but the data are not Union-representative since one MS holds about 90% from all samples; Median = 0.05 µg/L; MEC(p95) = 0.15 µg/L; Sc3 is expected to be similar to Sc2 for PNEC = 0.05 µg/L.	3 (PNEC = 0.05 µg/L)	0.97 (PNEC = 0.05 µg/L)
	3,4-dihloroaniline	95-76-1	0.2 (water) and 0.039 mg/kg ww (sediment) (Risk Assessment Report, JRC 2006) 0.02 (water, monitoring exercise INERIS, 2012)	P, vP Endocrine disruptor (INERIS). Not in Annex III inventory (ECHA)	In Sc2 (inland whole water) monitored in 9 MS; available 13348 samples; only 0.7% are quantified samples; the data quality is poor since 71.5% from non-quantified samples were measured with LOQ > PNEC (PNEC = 0.02 µg/L); the data are not Union-representative (79% from all samples originate from 2 MS); Median = 0.025 µg/L; MEC(p95) = 0.15 µg/L. Sc3 is not developed since the low data quality.	7.5 (PNEC = 0.02 µg/L)	1.6 (PNEC = 0.02 µg/L)
	Cr (III) and Cr (VI)	Cr (III) (CAS 16065-83-1) Cr (VI) (CAS 18540-29-9) CrO_3 (CAS 1333-82-0)	Inland surface water: Cr (III): 1.8 (JRC derived, 2018); 4.7 (INERIS) Cr (VI): 2.06 (JRC derived, 2018); 3.4 (INERIS, ECHA) Coastal/Transitional water: Cr (VI): 0.6 (JRC Dossier; Env. Agen. UK)	P and T (FactSheet) Cr (III) suspected R (ECHA) Cr (VI) suspected C Annex III inventory (ECHA) Cr (VI) trioxide is CM and possible R (ECHA) Cr (VI) and its compounds were included in the SVHC (substance of very high concern) list (Annex XV REACH in 2010) because they are carcinogenic and mutagenic	Cr (VI) and CrO_3 (inland whole water, Sc3, PNEC = 2.06 µg/L): 735 samples are available from 4 MS and 148 sites; about 51 % of samples are quantified; the data quality seems to be good since all non-quantified samples are measured with LOQ < PNEC, however the data are not Union-representative since about 61% of all samples originate from 1 MS; another MS has a share of 29%; the remaining 2 MS hold only 10% of all samples (one of them contributed with only 2 samples); Median = 1 µg/L; MEC(p95) = 5 µg/L. Cr (III) (inland whole water, Sc2): 798 samples are available from 1 MS and 56 sites; about 19 % of samples are quantified; the data quality seems to be good since all non-quantified samples are measured with LOQ < PNEC, however the data	Cr (VI) (inland whole water; Sc3; PNEC = 2.06 µg/L): 2.4 Cr (III) (inland whole water; Sc2; PNEC = 1.8 µg/L): 0.44 Cr total (inland dissolved; Sc3; PNEC = 1.8 µg/L): 0.83	Cr (VI) (inland whole water; Sc3; PNEC = 2.06 µg/L): 1.1 Cr (III) (inland whole water; Sc2; PNEC = 1.8 µg/L): STE is not calculated but is expected to be low since MEC(p95) < PNEC Cr total (inland dissolved; Sc3; PNEC = 1.8 µg/L): 0.2 Cr total (coastal

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					are not Union-representative since all samples originate from 1 MS; Median = 0.05 µg/L; MEC(p95) = 0.783 µg/L. Cr total (inland dissolved; Sc3; PNEC = 1.8 µg/L): 24 MS, 11058 sites, 174070 samples (22.8% quantified); the data quality seems acceptable; 51% of all samples originate from 1 MS, other 2 MS hold about 31% of data; Median = 0.25 µg/L; MEC(p95) = 1.5 µg/L. Cr total (coastal dissolved; Sc3; PNEC = 0.6 µg/L): 6 MS, 52 sites, 370 samples (23% quantified); the data quality seems acceptable; 75% of all samples originate from 1 MS; Median = 0.5 µg/L; MEC(p95) = 0.7 µg/L.	Cr total (coastal dissolved; Sc3; PNEC = 0.6 µg/L): 1.2	dissolved; Sc3; PNEC = 0.6 µg/L): 0.57
Anti-Microbial (AM) pharmaceuticals: antibiotics	**Sulfamethoxazole**	723-46-6	2.7 (EQS acute, Swiss ECOTOX centre 2016) 0.6 (EQS chronic, Swiss ECOTOX centre 2016) 0.4 (EQS 0.4 Substance factsheet 2015 from modelling-based exercise 2016) and 0.2 (prioritisation) 0.59 (FASS) 16 (PNEC-MIC, AMR industry alliance) 0.1 (JRC derivation 2019) 2.4 (Zhou et al. 2019)	P(3/3)T(3/3) Stockholm County Council. Suspected P(suspected hazardous for aquatic environment) suspected CMR in Annex III inventory (ECHA). No information about ED properties	In Sc2 (inland whole water) data from 14 MS (1023 sites) with 11684 samples are available. About 65% of samples are quantified. The non-quantified samples were measured with LOQ < PNEC (0.1 µg/L or lower). The quality of monitoring is acceptable (LOQ < PNEC) but the data are not Union-representative (65% of all samples originate from one MS; 18.6% from another MS; the remaining 13 MS have a share less than 16.4%). Sc3 is equal to Sc2 (for PNEC considered). Median = 0.025 µg/L; MEC(p95) = 1.17 µg/L	2.9 (PNEC = 0.4 µg/L) 11.7 (PNEC = 0.1 µg/L)	0.42 (PNEC = 0.4 µg/L) (not calculated for PNEC = 0.1 µg/L)

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	Trimethoprim	738-70-5	210 (EQS acute, Swiss ECOTOX centre 2015) 120 (EQS acute, Swiss ECOTOX centre 2015) 60 (Swiss ECOTOX centre modelling-based exercise 2016) 0.5 (PNEC-MIC, AMR industry alliance) 43.3 (JRC derivation 2019) 15.7 (Zhou et al. 2019)	P(3/3)(T(1/3) Stockholm County Council. Suspected P; suspected CMR in Annex III inventory (ECHA). No information about ED properties	In Sc2 (inland whole water) data from 4 MS (352 sites) with 4613 samples are available. About 26% of samples are quantified. All non-quantified samples were measured with LOQ < PNEC (0.03 µg/L or lower). Data quality in Sc2 seems to be acceptable (LOQ < PNEC) but the data are not Union-representative (76% of all samples originate from one MS; 21% from another MS; the remaining 2 MS have a share less than 3%). Median = 0.0125 µg/L; MEC(p95) = 0.0674 µg/L Sc3 is not developed but is expected to be equal to Sc2 (since for non-quantified samples LOQ < PNEC).	0.001 (PNEC = 60 µg/L) 0.13 (PNEC = 0.5 µg/L)	0 (PNEC = 60 µg/L) (not calculated for PNEC = 0.5 µg/L)
Anti-Microbial pharmaceuticals: azole pharmaceuticals (antifungal agents)	**Clotrimazole**	23593-75-1	1 (OSPAR 2015) 0.02 (JRC derivation 2019) 0.036 (Zhou et al. 2019)	P(3/3)B(3/3)T(3/3) Stockholm County Council Suspected PT; suspected CM in Annex III inventory (ECHA) database of modelling exercise: PBT. Possible ED only one study	In Sc2 (inland dissolved) data from 2 MS (19 sites) with 45 samples are available. About 47% of samples are quantified. Data quality in Sc2 seems to be acceptable but the amount of data is very low. Median = 0.0008 µg/L; MEC(p95) = 0.016 µg/L. Sc3 was not developed since the data are not representative.	0.016 (PNEC = 1 µg/L) 0.8 (PNEC = 0.02 µg/L)	STE (Sc2) is not calculated (should be low since MEC(p95) < PNECs)
	Fluconazole	86386-73-4	0.25 (PNEC-MIC, AMR industry alliance) 9.46 (JRC derivation 2019) 0.613 (Zhou et al. 2019)	P(3/1 uncertain)T(1/3) Stockholm County Council R - a majority of data submitters agree this substance is Toxic to Reproduction (ECHA) Not in Annex III inventory (ECHA). Not in database of the modelling exercise. No information about ED	In Sc2 (inland whole water) data from 1 MS (26 sites) with 436 samples are available. 40% of samples are quantified. The data quality is acceptable but the data are not union representative. Median = 0.01 µg/L; MEC(p95) = 0.06 µg/L. Sc3 was not developed since the data are not representative.	0.24 (PNEC = 0.25 µg/L)	STE (Sc2) is not calculated (expected be low since MEC(p95) < PNECs)

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	Miconazole **Miconazole nitrate**	22916-47-8 22832-87-7	0.4 (Minguez et al. 2014 acute) 0.2 (FASS SE database) 0.044 (Zhou et al. 2019)	PBT, possible MR P(3/3uncertain) B(3/3) T(3/3) Stockholm County Council. Suspected PBT; suspected R in Annex III inventory (ECHA)	No available data in the dataset of the prioritisation exercise		
Other pharmaceuticals	Benzimidazoles: Anthelmintics: Mebendazole	31431-39-7	0.088 (FASS SE database)	PBT, possible R (modelling exercise) P(3/3uncertain) B(3/1) T(1/3) Stockholm County Council. Suspected P suspected CMR in Annex III inventory (ECHA)	No available data in the dataset of the prioritisation exercise		
	Benzimidazoles: Proton pump inhibitors (PPIs): Lansoprazole and its metabolites	103577-45-3	18 (acute, Pharmaceuticals in the environment. Chapter 16. Webb, 2004) 0.192 (Zhou et al. 2019)	PT P(3/3)T(1/3) Stockholm County Council No information about ED properties	No available data in the dataset of the prioritisation exercise		
	Benzimidazoles: Proton pump inhibitors (PPIs): Omeprazole and its metabolites	73590-58-6	41.9 (FASS) 2.1 (Zhou et al. 2019)	T (modelling exercise) possible M and R. No information about ED properties	No available data in the dataset of the prioritisation exercise		
	Fentanyl	437-38-7	11.1 (FASS SE database) 0.295 (Zhou et al. 2019)	PT, possible R Not PBT (FASS) P(3/3) T(1/3) uncertain) Stockholm County Council P R Annex III inventory (ECHA) No information about ED properties	No available data in the dataset of the prioritisation exercise		

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	Gemfibrozil	25812-30-0	0.8519 (JRC derivation, Prioritisation) 1.56 (Zhou et al. 2019)	PBT, possible C and R (modelling exercise) P(3/3) T(2/3) Stockholm County Council. No information about ED properties	In Sc2 (inland whole water) monitored in 3 MS (251 sites); available 2476 samples; only 2% quantified samples; 97% of all samples coming from one MS; the data are not union representative; Median = MEC(p95) = 0.0125 µg/L; Sc3 is equal to Sc2 (PNEC = 0.8519 µg/L)	0.015 (PNEC = 0.8519 µg/L)	0.16 (PNEC = 0.8519 µg/L)
	Norethisterone	68-22-4	0.0354 (Prioritisation) 0.51 (freshwater ECHA) 0.00148 (Zhou et al. 2019)	PBT, possible C, R, ED (modelling exercise) P(3/3) B(3/3) T(3/3) Stockholm County Council	In Sc2 (inland whole water) monitored in 1 MS (19 sites); available 20 samples; the data quality is good; 100% quantified samples. However, the data are insufficient and are not Union-representative. Median = 0.003 µg/L; MEC(p95) = 0.0034 µg/L;	0.1 (PNEC = 0.0354 µg/L) 0.23 (PNEC=0.0148 µg/L)	0 (PNEC = 0.0354 µg/L)
	Venlafaxine	93413-69-5	0.03835 (prioritisation exercise, not reliable) 0.1 (JRC derivation 2019) 0.0061 (Zhou et al. 2019)	PT Stockholm County Council R (ECHA dossier) P(3/3) T(2/3) Stockholm County Council. No information about ED properties	In Sc2 (inland whole water) data from only 1 MS (93 sites) with 1395 samples are available. 76.8% quantified samples. The quality of monitoring in this country is acceptable but data are not representative for an EU-wide assessment. Sc3 was not developed since data are not representative. Median = 0.03 µg/L; MEC(p95) = 0.19 µg/L	5 (PNEC = 0.03835 µg/L) 31 (PNEC = 0.0061 µg/L)	1.36 (PNEC = 0.03835 µg/L)

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Table 2.3: PPP and biocides.

Group	Name	CAS	PNEC (µg/L)	Hazard (PBT/CMR/ED)	Data (prioritisation exercise)	RQ (MEC(P95)/PNEC)	STE score
Plant protection products and biocides: azole compounds	**Epoxiconazole**	106325-08-0 133855-98-8 205862-63-1	0.24 (EQS acute, Swiss ECOTOX centre 2016) 0.2 (EQS chronic, Swiss ECOTOX centre 2016) 0.18 (INERIS 2017)	PT, possible CR (modelling exercise) possibly P, R Annex III inventory (ECHA) two PBT criteria, toxic for reproduction 1A/1B ED properties (EU Pesticides database)	In Sc2 (inland whole water) monitored in 7 MS (2385 sites); available 26476 samples; only 1.3% quantified samples; the data quality seems poor although that 95% of non-quantified samples were measured with LOQ < PNEC (LOQ ≤ 0.1); there is a lot repeated non-quantified samples (17682; about 67% from all samples) coming from 2 MS; the data are not Union-representative (1 MS holds 53% of all samples, other 40% originate from 2 MS); Median = 0.01 µg/L; MEC(p95) = 0.05 µg/L. Sc3 is not developed since the low data quality but is expected to be similar to Sc2 for considered PNECs. FOCUS Step 3 PEC: 0.001 - 0.9 µg/L (EFSA, 2008)	0.28 (PNEC = 0.18 µg/L) RQ(PEC) 0.005 - 5 (PNEC = 0.18 µg/L)	0.46 (PNEC = 0.18 µg/L)
	Imazalil (enilconazole)	35554-44-0	2.5 (INERIS, 2015) 0.8 (monitoring exercise, JRC derivation from EFSA report)	possibly C (modelling exercise) possibly ED (ECHA) suspected P T suspected R in Annex III inventory (ECHA)	In Sc2 (inland whole water) are available 7197 samples from 6 MS. Only 0.1% quantified samples. The data have a poor quality and are not Union-representative (91.6% of samples originate from 1 MS). About 75% (5421) from all samples are repeated non-quantified samples having LOQ of 0.02 or 0.05 µg/L. Median = 0.01 µg/L; MEC(p95) = 0.075 µg/L. Sc3 was not developed since the low data quality. FOCUS PEC (EFSA; 2011) Step 2: 0.43 µg/L Step 3: 0.001 - 0.13 µg/L	0.09 (PNEC = 0.8 µg/L) RQ(PEC) (PNEC = 0.8 µg/L) Step 2: 0.54 Step 3: 0.00125 - 0.1625	0 (PNEC = 0.8 µg/L)

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	Ipconazole	125225-28-7	0.044 (AgriTox ANSES FR 2019)	PT, vP, possible R (modelling exercise). Suspected P suspected CR in Annex III inventory (ECHA)	No available data in the dataset of the prioritisation exercise FOCUS PEC, Step 2 (EFSA; 2013) N Europe, October-February, PECmax = 0.2719 µg/L N Europe, March - May, PEC max = 0.1088 µg/L N Europe, June - September, PEC max = 0.1088 µg/L S Europe, October-February, PEC max = 0.2175 µg/L S Europe, March - May, PEC max = 0.2175 µg/L S Europe, June - September, PEC max = 0.1631 µg/L	RQ(PEC) 2.5 (PEC = 0.11 µg/L) 6.1 (PEC = 0.27 µg/l)	
	Metconazole	125116-23-6	0.0582 (prioritisation) 0.582 (AgriTox ANSES FR 2019) 0.0291 (JRC derivation 2019)	Suspected PT suspected CR in Annex III inventory (ECHA) two PBT criteria (EU Pesticides database); R possibly toxic for reproduction (ECHA); database of modelling exercise: PT, vP, possible R. No information about ED properties	In Sc2 (inland whole water) data from 3 MS (702 sites) with 5742 samples are available. Only 3 samples are quantified. The data quality in Sc2 is not good. There are 4108 (70% from total) repeated non-quantified samples with LOQ = 0.05 µg/L coming from 1 MS. The data are not Union-representative. Median = MEC(p95) = 0.025 µg/L. Sc3 is not developed since the low data quality. FOCUS PEC (EFSA, 2006) 0.1 - 1.2 µg/L	0.43 (PNEC = 0.0582 µg/L) 0.86 (PNEC = 0.0291 µg/L) RQ(PEC) 1.7 - 20.6 (PNEC = 0.0582 µg/L) 3.4 - 41 (PNEC = 0.0291 µg/L)	0 (PNEC = 0.0582 µg/L)

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	Penconazole	66246-88-6	6 (AgriTox ANSES FR and INERIS)	PT, possible R (modelling exercise)	In Sc2 (inland whole water) monitored in 5 MS (1547 sites); available 14037 samples; only 2.8% quantified samples; the data quality seems poor, although all non-quantified samples were measured with LOQ ≤ 0.23 µg/L; there is a lot repeated non-quantified samples (7184; about 70.5% from all samples) with LOQ = 0.05 µg/L or LOQ = 0.02 µg/L;); the data are not Union-representative (1 MS holds 52% of all samples, other 45% originate from 2 MS); Median = 0.025 µg/L; MEC(p95) = 0.05 µg/L. Sc3 is not developed since the low data quality but is expected to be equal to Sc2 for considered PNECs. FOCUS PEC (EFSA; 2008) Step 2: 2 - 3.3 µg/L Step 3: 0.184 - 0.556 µg/L	0.008 (PNEC = 6 µg/L) RQ(PEC) (PNEC=6 µg/L) Step 2: 0.33 - 0.55 Step 3: 0.03 - 0.09	STE (Sc2) is not calculated (expected to be low since MEC(p95) < PNEC)
	Prochloraz	67747-09-5	10 (AgriTox ANSES FR) 0.161 (Zhou et al., 2019)	PT, vP, possible CR, possible ED (modelling exercise) two PBT criteria (EU Pesticides database)	In Sc2 (inland whole water) monitored in 7 MS (2557 sites); available 32674 samples; only 1.6% quantified samples; the data quality is not good, although all non-quantified samples have LOQ ≤ 0.4 µg/L; there are many repeated non-quantified samples (23462; about 72% from total) with LOQs from 0.01 µg/L to 0.1 µg/L; the data are not Union-representative since one MS holds 84% of samples; Median = 0.02 µg/L; MEC(p95) = 0.05 µg/L. Sc3 is not developed since the low data quality. FOCUS Step 3 calculations of PEC applied in Winter cereals: 0.1 - 3 µg/L (EFSA, 2011)	0.005 (PNEC = 10 µg/L) 0.3 (PNEC = 0.161 µg/L) RQ(PEC) 0.01 - 0.3 (PNEC = 10 µg/L) 0.6 - 18.6 (PNEC = 0.161 µg/L)	STE (Sc2) is not calculated (expected to be low since MEC(p95) < PNEC)

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	Tetraconazole	112281-77-3	1.9 (Prioritisation) 4.2 (AgriTox ANSES FR) 3.2 (INERIS)	PT, vP, possible R (modelling exercise)	In Sc2 (inland whole water) monitored in 2 MS (1132 sites); available 11075 samples; only 0.1% quantified samples; the data quality seems poor since there is a lot repeated non-quantified samples (9778; about 88% from total) with LOQs of 0.02; 0.05 and 0.1 µg/L coming from 1 MS; the data are not Union-representative; Median = 0.02 µg/L; MEC(p95) = 0.05 µg/L. Sc3 is not developed since the low data quality but is expected to be equal to Sc2. FOCUS Step 2 PEC: 2 - 3 µg/L (EFSA, 2008)	0.03 (PNEC = 1.9 µg/L) RQ(PEC) 1.1 - 1.6 (PNEC = 1.9 µg/L)	0 (PNEC = 1.9 µg/L)
Plant protection products and biocides: other substances	Copper (I) oxide (Cu_2O) Copper (II) oxide (CuO)	1317-39-1 1317-38-0	7.8 (Cu_2O and CuO freshwater ECHA) 1.6 (Cu_2O and CuO statistic approach, INERIS)	P two PBT criteria (EU Pesticides database)	No available data for Cu_2O and CuO in the dataset of the prioritisation exercise (probably these substances were reported together with Cu (CAS 7440-50-8)). Copper Cu (CAS 7440-50-8). Inland whole water (Sc3; PNEC = 7.8 µg/L): 151392 samples from 27 MS (9079 sites); 79% of all samples are quantified; the data quality seems good; Median = 1.7 µg/L, MEC(p95) = 6 µg/L. Inland dissolved (Sc3; PNEC = 7.8 µ g/L): 97036 samples from 24 MS (7009 sites); 50% of all samples are quantified; the data quality seems good; Median = 1.7 µg/L, MEC(p95) = 6 µg/L.	0.94 (Sc3; PNEC = 7.8 µg/L) 16 (Sc3; PNEC = 1.6 µg/L) 0.77 (Sc3; PNEC = 7.8 µg/L) 16 (Sc3; PNEC = 1.6 µg/L)	0.36 (Sc3; PNEC = 7.8 µg/L) 0.4 (Sc3; PNEC = 7.8 µg/L)

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	Free cyanide	CN- 57-12-5 CNH 74-90-8	0.26 (JRC Factsheet 2015 2018/WFD-UK TAG report 2012) 5 (fresh water ECHA dossier) 0.6 (INERIS 2018) **0.5** (JRC Dossier https://circabc.europa.eu/faces/jsp/extension/wai/navigation/container.jsp 2015)	T (ECHA) HCN does not display properties of environmental persistence or bioaccumulation, although it is highly toxic to aquatic organisms. It does not meet the criteria for classification as PBT.	Cyanide (as total CN): In Sc2 (inland whole water) data from 14 MS with 17568 samples are available; 23.4% quantified samples. The data quality is low since about 77% of non-quantified samples have LOQ/LOD ≥ PNEC (PNEC = 0.5 µg/L). The data seems not Union-representative since 3 MS hold about 70% from all samples; Median = 2.15 µg/L; MEC(p95) = 7.5 µg/L. Sc3 was not worked out since low data quality. Cyanide anion (CN-): In Sc2 (inland dissolved fraction) data from 2 MS with 340 samples are available (18.5% quantified samples). The data quality is low since about 64% of non-quantified samples have LOQ or LOD ≥ PNEC (PNEC = 0.5 µg/L). The data are not representative. Median = 1 µg/L; MEC(p95) = 11.7 µg/L. Sc3 was not worked out since low data quality.	Cyanide (inland dissolved; NORMAN; WATERBASE): 10-40 (MEC = 5-20 µg/L and PNEC = 0.5 µg/L) 19.2-76.8 (MEC = 5 - 20 µg/L and PNEC = 0.26 µg/L). Cyanide anion: 23.4 (PNEC = 0.5 µg/L) 45 (PNEC = 0.26 µg/l)	STE(Sc2) is not calculated for CN- but it is expected to be high since the median-conc. > PNEC
	Dimoxystrobin	149961-52-4	0.0316 (ETOX: Information System Ecotoxicology and Environmental Quality Targets, UBA) 1.67 (AgriTox ANSES FR)	2 PBT criteria (PT), endocrine disrupting properties (EU Pesticides database); T CR M(suspected) in Annex III inventory (ECHA) ; C Possibly Carcinogenic ; R Possibly Toxic to Reproduction ; database of modelling exercise: PT. No information about ED properties	In Sc2 (inland whole water) data from 1 MS (6078 samples); 2.8% quantified samples. The data quality seems acceptable (LOQs < PNEC) but there are 3890 (64% from total) repeated non-quantified samples (LOQ = 0.01 µg/L or 0.02 µg/L) the data are not union representative; Median = 0.01 µg/L; MEC(p95) = 0.025 µg/L; Sc3 is not developed since the scarcity of data.	0.79 (PNEC = 0.0316 µg/L)	0 (PNEC = 0.0316 µg/L) (since MEC(p95) < PNEC)

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	Famoxadone	131807-57-3	0.14 (JRC derivation) 0.11 (AgriTox ANSES FR)	PBT CM in Annex III inventory (ECHA) 2 PBT criteria (EU Pesticides database). No information about ED properties	In Sc2 (inland whole water) data from 3 MS (5528 samples) are available; no any quantified samples; the data quality seems acceptable since LOQs < PNEC (0.14 µg/L) but there are a lot repeated non-quantified samples (5422; about 98% from total) The data are not union representative (98% of samples originate from one MS). Median = 0.01 µg/L; MEC(p95) = 0.025 µg/L; Sc3 is not developed since insufficient data quality.	0.18 (PNEC = 0.14 µg/L)	0 (PNEC = 0.14 µg/L)
	Proquinazid	189278-12-4	0.18 (not reliable, Oecotoxzentrum, Eagaw/EPFL, CH) 0.18 (AgriTox ANSES FR)	PT C in Annex III inventory (ECHA); C Possibly Carcinogenic (ECHA); database of modelling exercise: PBT. No information about ED properties	In Sc2 data from 1 MS (1285 samples); very low data quality; no any quantified samples; the data are not union representative Median = MEC(p95) = 0.01 µg/L; Sc3 is not developed since low data quality	0.056 (PNEC = 0.18 µg/L)	0 (PNEC = 0.18 µg/L)

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Annex III: Factsheets

This Annex shows factsheets only for candidate substances fulfilling the selection criteria and identified by the JRC as most likely to be proposed for the next WL.

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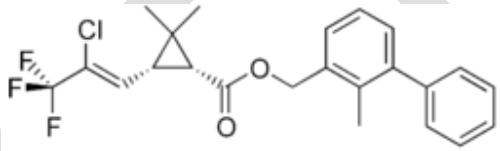
Bifenthrin (CAS N. 82657-04-3)

1. Substance identity

EC name	(2-methylbiphenyl-3-yl)methylrel-(1R,3R)-3-[(1Z)-2-chloro-3,3,3-trifluoroprop-1-en-1-yl]-2,2-dimethylcyclopropanecarboxylate; bifenthrin (ISO)
EC number	617-373-6
CAS number	82657-04-3
Molecular formula	$C_{23}H_{22}ClF_3O_2$
Molecular weight	422.87 g/mol
Structure	 Bifenthrin is a mixture of 2 optical isomers, (Z)-(1R)-cis-acid and (Z)-(1S)-cis-acid (enantiomers)
SMILES	CC1=C(C=CC=C1COC(=O)C2C(C2(C)C)C=C(C(F)(F)F)Cl)C3=CC=CC=C3

2. Physico-chemical properties

Endpoint	**Value**	**Source**
Vapour Pressure (Pa)	1780 at 20°C 1.78 x 10^{-5} at 20°C (purity 98.8%)	HSDB EFSA Conclusion, 2011
Water solubility (mg/L)	< 0.001	http://npic.orst.edu/factsheets/archive/biftech.html EFSA, 2011
logK_{ow}	6.0 6.6 6.6 (comparative HPLC method)	https://pubchem.ncbi.nlm.nih.gov/compound/bifenthrin EFSA, 2011 EFSA Conclusion, 2011

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3. Environmental fate

Endpoint	Value	Source
Sorption potential K_{oc}	236610 8387-14332 236610 (arithmetic mean) ($logK_{oc}$ = 5.37)	EFSA, 2011 HSDB EFSA Conclusion, 2011
Partition coefficient solid-water in sediment Kp_{sed} (L/kg)	2.24e5 ($logK_{oc}$)	https://comptox.epa.gov/dashboard/dsstoxdb/results?search=DTXSID9020160#env-fate-transport
Biodegradability	Not readily biodegradable	EFSA Conclusion, 2011
Bioaccumulation (BCF)	1703 4.68e4 (predicted) 1709 (mesured)	EFSA, 2011 https://comptox.epa.gov/dashboard/dsstoxdb/results?search=DTXSID9020160#env-fate-transport EFSA Conclusion, 2011 According to the BCF value exceeding the trigger of 100 and to the value of the log K_{ow} which is higher than 3, the potential risk to biota and humans from secondary poisoning should be assessed (EFSA Conclusion, 2011 and PubChem).

4. Environmental exposure assessment

4.1 Predicted Environmental Concentration

	Description	Source
Tonnes/year	1 - 10 tonne registered substances	ECHA https://echa.europa.eu/it/substance-information/-/substanceinfo/100.120.070
Uses	NOT APPROVED as PPP (2009/887/EC,Reg. (EU) 2017/195,Reg. (EU) 2018/291,Reg. (EU) 2019/324,Reg. (EU) No 582/2012) Authorisation in progress for: AT, IT, SK (3 MS)	http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.detail&language=EN&selectedID=1026
	APPROVED as BIOCIDE.	https://echa.europa.eu/it/su

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	Biocidal active substance and product. This substance is approved for use as a biocide in the EEA and/or Switzerland, for: wood preservation. Only uses as insecticide may be authorised.	bstance-information/ /substanceinfo/100.120.070
Spatial usage (by MS)		
Banned uses		
ERC code		
PEC_{fw} (µmg/L)	0.0005 - 0.0049 (values predicted for risk assessment using FOCUS Step 4)	EFSA Conclusion, 2011
PEC_{sed} (mg/kg dw)	0.0030 – 0.495 (values predicted for risk assessment using FOCUS Step 4)	EFSA Conclusion, 2011
PEC_{biota} (mg/kg)		

4.2 Measured Environmental Concentration

n. of MS	Source of monitoring data	MEC values
In Sc2 dataset (inland whole water) 7572 samples from 3 MS (1132 sites) are available. Only 2 quantified samples. Data quality of Sc2 is not good. Sc3 was not developed since data scarcity.	Dataset of monitoring prioritisation 2014	MEC(P95) = 0.025 µg/L (Sc2)

Note: Sc2 includes all reported quantified and non-quantified samples. The data quality for Sc2 is verified by controlling the data accuracy, checking quantification frequency of sampling and applying the LOQ-PNEC criterion to non-quantified samples (½ LOQ ≤ PNEC).

Sc3 is the main decisive dataset which includes the quantified measurements and these non-quantified samples when ½ LOQ ≤ PNEC (i.e. avoiding the non-confirmed exceedances when the non-quantified concentrations are set up equal to half of LOQ).

4.3 Analytical Methods

Method	LOQ (µg/L)	Description/Reference

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GC-MS	0.001	In surface water (EFSA, 2008 and EFSA, 2011).
GC-NCI-MS	0.00004	Extraction by ultrasound-assisted emulsification-extraction of a water-immiscible solvent (chloroform) in 20 mL water (Feo et al., 2010).
GC-ECD/MS	0.00006 – 0.00098 (LOD)	SPE (Zheng et al., 2016).
n.a.	0.005	Finland
GC-APCI-MS/MS	0.0000025	Surface water (Rösch et al., 2019)
GC-MS/MS (0.2)	0.2 (MDL)	Sediment (USGS, 2007, 2009)

5. P, B, T, C, M, R, ED properties

Substance	Persistent (P) Bioaccumulative (B) Toxic (T)	Carcinogenic (C) Mutagenic (M) Reproduction toxicity (R)	Endocrine Disruptive (ED)	Comment
Bifenthrin	B and T Suspected P	C Suspected M and R	ED**	

Note: Not listed in the PBT list from ECHA https://echa.europa.eu/it/information-on-chemicals/pbt-vpvb-assessments-under-the-previous-eu-chemicals-legislation. Harmonised classification for acute toxicity# Harmonised classification for aquatic toxicity# Harmonised classification for carcinogenicity# Harmonised classification for skin sensitisation# Harmonised classification for specific target organ toxicity# Suspected carcinogen# Suspected hazardous to the aquatic environment# Suspected mutagen# Suspected persistent in the environment# Suspected skin sensitiser# Suspected toxic for reproduction (ECHA. Annex III inventory)

**https://endocrinedisruption.org/interactive-tools/tedx-list-of-potential-endocrine-disruptors/search-the-tedx-list#sname=BIFENTHRIN&searchfor=any&sortby=chemname&action=search&searchcats=all&sortby=chemname

6. Hazard assessment

6.1 Ecotoxicology data

Freshwater

Species	Time-scale	Endpoint	Toxicity (µg/L)
Invertebrates			
Daphnia magna	21 d	NOEC	0.00095
Daphnia magna	21 d	NOEC	0.0013
Corbicula	21 d	NOEC	2.58
Mysidopsis bahia	28 d	NOEC	0.0012
Chironomus riparius	28 d	NOEC	0.32

Fish			
Pimephales promelas	21 d	NOEC	1.86
Pimephales promelas	368 d	NOEC	0.04

Sediment

Species	**Time-scale**	**Endpoint**	**Toxicity (µg/L)**
Chironomus riparius	28 d	NOEC	0.04

6.2 Mammalian toxicology data

		Master reference
Mammalian toxicity	Rat, acute toxicity, oral, LD_{50} 54.5 mg/kg (diluted in corn oil); 186.1 mg/kg (undiluted)	EFSA Conclusion, 2011
	Rat, acute toxicity, dermal, LD_{50} >2000 mg/kg	
	Rat, acute toxicity, inhalation, LC_{50} 1.01 mg/l/4h	
	Dog, short-term toxicity, oral, tremors; reduction in tail latency; staggered gait and exaggerated hindlimb flexion, NOAEL 2.5 mg/kg/day (90-day dog) NOAEL 1.5 mg/kg/day (1-year dog)	
	Rat, short-term toxicity, dermal, tremors; reduction in tail latency; staggered gait and exaggerated hindlimb flexion, NOAEL 50 mg/kg/day	
	Rabbits, short-term toxicity, dermal, tremors; reduction in tail latency; staggered gait and exaggerated hindlimb flexion, NOAEL 100 mg/kg/day	
	Rat, long-term toxicity, tremors, NOAEL 4.7 mg/kg bw/d for males and 3 mg/kg bw/d for females (2-yr rat)	
	Mouse, long-term toxicity, tremors, NOAEL 7.6 mg/kg bw/d for males and 37 mg/kg bw/d for females (18-m mice)	
	Mouse, carcinogenicity, bladder tumors in male mice (statistically significant at 92 mg/kg bw/d)	
	Mouse, acute, LD_{50} 42.5 mg/kg bw (Bifenthrin, a.s.)	
	Rat, reproductive, NOAEL 3 mg/kg bw/day (Bifenthrin, a.s.)	

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	Rat, acute neurotoxicity, NOAEL 35 mg/kg bw/d	EFSA Conclusion, 2011 and DAR, 2006
	Mouse, long-term toxicity, oral; tremors, reduction in weight, NOAEL 7.6 mg/kg bw/day for males and 37 mg/kg bw/day for females (Bifenthrin, 88.35% purity)	Geiger L.E. (1986), cited in DAR, 2006 and in INERIS, 2011
	Rat, oral, 2-year, tremors, NOAEL 3 mg/kg bw/day for males and 4.7 mg/kg bw/day for females	INERIS, 2011
	Oryctolagus cuniculus, oral, 29-day, convulsive movements, no teratogenic effects, NOAEL 2.67 mg/kg bw/day	INERIS, 2011
	Rat, oral, 29-day; tremors, reduction in weight, no teratogenic effects, NOAEL 1 mg/kg bw/day (Bifenthrin, 88.35% purity)	DeProspo J.R. (1984) cited in DAR, 2006 and in INERIS, 2011
	Rat, oral, tremors, reduction in weight, no teratogenic effects, NOAEL 7.4 mg/kg bw/day (Bifenthrin, 95.3% purity)	Watt B. and Freeman C. (2001) cited in DAR, 2006 and in INERIS, 2011
	Rat, oral, long-term toxicity, tremors and reduction in body weight in parental line and in F1 generation of females during gestation and lactation, reproductive NOAEL 5 mg/kg bw/day and systemic NOAEL 3 mg/kg bw/day (Bifenthrin, 88.35% purity)	DeProspo J.R. (1986) cited in DAR, 2006 and in INERIS, 2011

6.3 PNEC derivation

PNEC	**Endpoint**	**Endpoint value**	**AF**	**PNEC value**
$PNEC_{fw}$	NOEC, 21 d (*Daphnia magna*)	0.00095 µg/L	50	0.00002 (µg/L) (JRC draft dossier, 2016)
$PNEC_{sed}$	*NOEC, 28 d (Chironomus riparius)*	0.04 mg/kg	100	0.4 µg/kg dw (JRC draft dossier, 2016)
$PNEC_{biota,sec\ pois}$				
$PNEC_{biota,\ hh}$				
$PNEC_{dw,\ hh}$				

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7. Risk Quotient (MEC or PEC/PNEC)

RQ	**Value**
RQ_{fw} (for MEC(P95) and PNEC = 0.00002 µg/L)	1250 (Sc2)
RQ_{fw} (for PEC = 0.054 µg/L and PNEC = 0.00002 µg/L)	2700
RQ_{fw} (for PEC = 0.0049 µg/L and PNEC = 0.00002 µg/L)	245

Note: PEC values are taken from Lettieri, T., Chirico, N., Carvalho, R.N., Napierska, D., Loos, R., Sanseverino, I., Marinov, D., Ceriani, L., Umlauf, G. 2016. *Modelling-based strategy for the prioritisation exercise under the Water Framework Directive,* https://circabc.europa.eu/w/browse/85b46283-9353-4e67-bf56-e4d18b32cbaf.

8. STE score

3 (Sc2; PNEC = 0.00002 µg/L)

Note: STE is a risk-evaluation method/tool developed by the JRC (Loos et al., 2018, EUR 29173 EN). Minimal score = 0 (no risk); Maximal score = 3 (very high risk).

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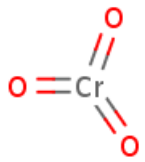
Chromium trioxide and other Cr (VI) compounds (CAS N. 1333-82-0; 18540-29-9)

1. Substance identity

EC name	
EC number	
CAS number	1333-82-0; 18540-29-9 (Chromium(VI))
Molecular formula	CrO_3; Cr(VI)
Molecular weight	99.99; Cr(VI): 51.9
Structure	
SMILES	[Cr](=O)(=O)=O

2. Physico-chemical properties

Endpoint	**Value**	**Source**
Vapour Pressure (Pa)	Not available (inorganic ionic compound)	EU-RAR, 2005
Water solubility (mg/L)	1667 mg/L	EU-RAR, 2005
logK_{ow}	Not available (inorganic ionic compound)	EU-RAR, 2005

3. Environmental fate

Endpoint	**Value**	**Source**
Sorption potential K_{oc}	Not available	EU-RAR, 2005
Partition coefficient solid-water in sediment Kp_{sed} (L/kg)	1000	EU-RAR, 2005
Biodegradability	N.a.	EU-RAR, 2005
Bioaccumulation (BCF)	2.8	EU-RAR, 2005

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Chromium is a relatively common element and occurs in the earth's crust at an average concentration of 200 mg/kg. In soils one finds in general contents of 10 to 90 mg/kg.

Trivalent chromium is an essential trace element for humans and animals. Hexavalent chromium compounds cause allergic and asthmatic reactions and are considered carcinogenic.

Chromium occurs in waters in trivalent and hexavalent form. Under aerobic conditions chromium (VI) is stable. Under anaerobic conditions, it is reduced to chromium (III). Under oxidising conditions, a transformation from chromium (III) to chromium (VI) is also possible. The distribution between chromium (III) and chromium (VI) of the total chromium concentration in flowing waters is not constant, chromium (VI) has a share of 30-70%.

Due to the formation of poorly soluble chromium (III) compounds and adsorption of chromium in suspended solids, a large part of the chromium is particulate bound.

There is a wide range of background values ("ambient background concentrations") within Europe. For the dissolved concentration of chromium in uncontaminated waters, values of < 0.1 µg/L to 0.5 µg/L are given. The FOREGS study gives for European waters for > 0.45 µm filtered concentration a median value (n = 806) of 0.38 µg/L (Internationale Kommission zum Schutz des Rheins, 2009).

4. Environmental exposure assessment

4.1Predicted Environmental Concentration

	Description	**Source**
Tonnes/year	114 (2010) in CZ	CZ
Uses	Manufacture of substances and of preparations, formulation of preparations and materials, industrial use resulting in inclusion into or onto a matrix, use as laboratory reagent. Chromium trioxide meets the criteria for inclusion in Annex XIV to Regulation (EC) N. 1906/2006. In 2015 the latest application date were expected for chromium trioxide is 21 March 2016, and the sunset date is 21 September 2017, but exemptions have been granted for certain uses.	ECHA, 2013 Regulation (EC) N. 1906/2006 COMMISSION REGULATION (EU) No 348/2013
	Electroplating	CZ
	Main source is leather tanning industry and other industries using chromium.	DK
Spatial usage (by MS)	Not known	-
Banned uses	Cement and cement-containing mixtures shall not be placed on the market, or used, if they contain, when hydrated, more than 2 mg/kg (0.0002%) soluble chromium VI of the total dry weight of	ECHA, List of substances restricted under REACH

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	the cement. Leather articles coming into contact with the skin shall not be placed on the market where they contain chromium VI in concentrations equal to or greater than 3 mg/kg (0.0003% by weight) of the total dry weight of the leather. Articles containing leather parts coming into contact with the skin shall not be placed on the market where any of those leather parts contains chromium VI in concentrations equal to or greater than 3 mg/kg (0.0003% by weight) of the total dry weight of that leather part.	
ERC code	-	-
PEC_{fw} (mg/L)		
PEC_{sed} (mg/kg dw)		
PEC_{biota} (mg/kg)	0.98 (N.R.)	Calculation based on Equation L (Section 3.4.3)

N.R. Not required based on BCF value not reaching the trigger value required for biota assessment

4.2 Measured Environmental Concentrations

Chromium is analysed in most countries as total chromium (VI+III). In the prioritisation exercise 2014, Cr (VI) data were only available for non-filtered water samples (whole water fraction) from 4 countries.

In 2018, one MS (England) submitted Cr (VI) data for dissolved water samples, and 9 MS total chromium (VI+III) data.

The use of monitored concentrations for chromium total in dissolved fraction, and the use of monitored concentration for Cr (VI) in whole water, below, gives an overestimation of the risk posed by Chromium VI in dissolved fraction.

n. of MS	Source of monitoring data	MEC values
Cr (VI) and CrO_3 in Sc3 (inland whole water; PNEC = 2.06 µg/L) from 4 MS (148 sites)	735 samples (51% quantified). The data quality seems to be good (non-quantified samples are measured with LOQ < PNEC) but about 61% of all samples originate from 1 MS; another MS has a share of 29%. (Dataset of monitoring prioritisation 2014 plus additionally submitted data 2017-2018)	5 µg/L (P95)

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Cr(total) in Sc3 (inland dissolved fraction; PNEC = 1.8 µg/L) from 24 MS (11058 sites)	174070 samples (22.8% quantified). The data quality seems acceptable but 51% of all samples originate from 1 MS, other 2 MS hold about 31% of data (Dataset of monitoring prioritisation 2014 plus data submitted in 2018; years 2010-2018)	1.5 µg/L (P95) 0.25 µg/L (median)
Cr (total) in Sc3 (coastal and transitional water; dissolved fraction; PNEC = 0.6 µg/L) in 6 MS (52 sites)	370 samples (23% quantified). The data quality seems acceptable but 75% of all samples originate from 1 MS. (Dataset of monitoring prioritisation 2014)	0.7 µg/L (P95) 0.5 µg/L (median)
Cr (total) in CZ	Waste water; measured in industrial waste water not in surface water. Year 2015.	0.02-497 µg/L
Cr (VI) in England (probably inland dissolved phase)	Approx. 170 sites monitored quarterly in water body's deemed at risk from Cr (VI) via permitted discharges.	Results mostly show below LOD, however 1 site exceeds AA EQS, and 2 others record values above this limit.

4.3 Analytical Methods

Method	**LOQ (µg/L)**	**Description/Reference**
EPA method 218.7 (2011)	0.0044 to 0.015 (LOD)	Samples are preserved with a combined buffer/dechlorinating reagent which complexes free chlorine and increases the pH to a value greater than eight. A measured volume (usually 1 mL) of the sample is introduced into an ion chromatograph. CrO_4^{2-} is separated from other matrix components on an anion exchange column. CrO_4^{2-} is derivatised with 1,5-diphenylcarbazide in a post-column reactor and is detected spectrophotometrically at a wavelength of 530 nm. Cr (VI) is qualitatively identified via retention time, and the concentration of CrO_4^{2-} in the sample is calculated using the integrated peak area and the external standard technique. Results are reported in units of µg/L of Cr (VI) (EPA method 218.7; 2011).
Ion chromatography	LOD: 0.050 LOQ: 0.16	Cr (VI) determination in water samples with ion chromatography followed by post-column derivatisation of the Cr (VI) with diphenylcarbazide and detection of the coloured

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		complex at 530 nm (Mamais et al., 2016).
LC-ICP-MS	0.001 to 0.01 (LOD)	Perkin Elmer Application note; Vonderheide et al., 2004.
ISO method 23913:2006 Flow analysis (FIA and CFA) and spectrometric detection	2-200 (LOD)	ISO 23913:2006 specifies flow injection analysis (FIA) and continuous flow analysis (CFA) methods for the determination of Cr (VI) in various types of water. The method applies to the following mass concentration ranges: for FIA (20 to 200 micrograms per litre and 200 to 2 000 micrograms per litre for surface water, leachates and waste water) and for CFA (2 to 20 micrograms per litre and 20 to 200 micrograms per litre for drinking water, ground water, surface water, leachates and waste water). The range of application may be changed by varying the operating conditions. Seawater may be analysed by these methods with changes in sensitivity and after adaptation of the reagent and calibration solutions to the salinity of the samples.
Ion chromatography	1	Ionic chromatography to separate Cr6+ and interfering compounds. Measure by spectrometry (540nm) after derivation post column by 1.5-diphenylcarbazide solution (Belgium-Wallonia).

5. P, B, T, C, M, R, ED properties

Substance	**Persistent(P) Bioaccumulative (B) Toxic (T)**	**Carcinogenic (C) Mutagenic (M) Reproduction toxicity (R)**	**Endocrine Disruptive (ED)**
Chromium (VI)	P and T	M and R	Not investigated

The evidence clearly indicates that highly water-soluble Cr (VI) compounds can produce significant mutagenic activity in vitro and in vivo (EU-RAR, 2005). The Cr (VI) compounds under consideration are therefore regarded as in vivo somatic cell mutagens (EU-RAR, 2005). In addition, toxicokinetic and dominant lethal data suggest that water-soluble Cr (VI) has the potential to be an in vivo germ cell mutagen (EU-RAR, 2005). Chrome plating workers exposed to chromium (VI) trioxide in aqueous solution have shown a clear excess in mortality from lung cancer (EU-RAR, 2005). Therefore chromium (VI) trioxide should be regarded as a human carcinogen (EU-RAR, 2005). Adverse effects on fertility have been found in studies in mice following repeated oral exposure (EU-RAR, 2005). In addition, adverse effects on the testes have been seen following repeated oral exposure in the rat (EU-RAR, 2005). The substance is not readily biodegradable (P). It shows a low potential to bioaccumulate in aquatic organism (EU-RAR, 2005).

6. Hazard assessment

6.1 Ecotoxicology data

Chromium (VI)

The PNEC previously used for chromium (VI) in the 2014 prioritisation report has been updated by JRC after a literature search and the evaluation of new chronic toxicity data. The assessment performed in the European Risk Assessment Report (EU 2005), by the Environment Agency in 2007 (UK EA 2007) and in the UBA Dossier 2015 have been taken into consideration, with the inclusion of additional chronic data assessed to be adequate and relevant. On this basis, the JRC has derived a new PNEC of 2.06 µg/L for chromium (VI).

In addition to the previous chronic quality standard derivation (EU 2005), 31 freshwater and 2 marine water chronic toxicity values have been found from 17 studies published after 2005. A literature evaluation of these studies has been performed by using the LET tool in-house developed by the JRC, and based on the work of Kase et al. (2015), and three of them were deemed to be not reliable. Freshwater and marine water datasets have been treated separately, in accordance with the EQS Technical Guidance Document (EC 2011).

An overall dataset of 73 freshwater chronic toxicity values are available for 35 species of 8 different taxonomic groups, i.e. 7 algae species, 2 cnidarian species, 5 crustaceans, 11 fish species, 4 higher aquatic plants, 2 insects, 2 molluscs, and 2 amphibians.

After selecting the most sensitive geometric mean endpoints per species, a probabilistic approach has been undertaken with 35 freshwater chronic data points, giving an HC5 value of 0.006 mg/L. An AF of 3 has been applied to the HC5 value giving a chronic freshwater QS of 2.06 µg/L.

Regarding the marine water chronic toxicity dataset, only a deterministic approach could be applied, since data are available for 15 species of 5 taxonomic groups. The lowest value has been observed for the polychaete worm *Nereis arenaceodentata* with a 2-week NOEC of 0.006 mg/L. In accordance with the EQS Technical Guidance Document (EC 2011), an AF of 10 has been applied, giving a chronic marine water QS of 0.6 µg/L.

Chromium (III)

In addition a new PNEC of 1.8 µg/L has been derived by JRC for chromium (III) after a literature search and the evaluation of new chronic ecotoxicological data.

In addition to the chronic toxicity values reported in the European Assessment report of 2005 (EU 2005), four toxicological data have been retrieved (2 from the ECHA's dissemination website, and 2 from recent publications), giving a final dataset of 9 freshwater and 2 marine water chronic toxicity values.

The available dataset could not enable the derivation of an SSD curve, since only data from 7 species of three taxonomic groups have been found. Therefore, the deterministic approach has been carried out in the present assessment.

The 30-day time-to-hatch NOEC 0.018 mg/L for the fish *Danio rerio* (Study report 1990, ECHA DB 2018b) has been determined to be the lowest chronic freshwater value in the new dataset. Because data are available from each trophic level of the base set, an AF of 10 has been applied (EC 2011), giving a QS of 1.8 µg/L.

The only value available for the marine water is the 7-day mortality NOEC 40 mg/L of the crustacean *Petrolisthes laevigatus* (Urrutia et al., 2008). Based on these data, it has been yet deemed to be insufficient to derive QS for marine water bodies.

6.2 PNEC derivation (Cr (VI))

PNEC	Endpoint	Endpoint value (µg/L)	AF	PNEC value (µg/L)
$PNEC_{fw}$	$HC_{5\text{-}50\%}$	6.0	3 (SSD)	2.06 (Loos et al., 2018)
$PNEC_{t+cw}$	NOEC (*Nereis arenaceodentata* /2-week)	6.0	10	0.6 (Loos et al., 2018)

PNEC derivation (Cr (III))

PNEC	Endpoint	Endpoint value (µg/L)	AF	PNEC value (µg/L)
$PNEC_{fw}$	NOEC (*Danio rerio* /30 d)	18	10	1.8 (Loos et al., 2018)

7. Risk Quotient (MEC or PEC/PNEC)

RQ	Value
RQ_{fw} (CrVI, inland whole water) (for MEC(P(95) data from 4MS and PNEC = 2.06 µg/L)	2.4 (Sc3)
RQ_{fw} (Cr total, inland dissolved) (for MEC(P(95) data from 24 MS for time period 2010-2018, and PNEC = 1.8 µg/L)	0.83 (Sc3)
RQ_{c+tw} (Cr total, coastal dissolved) (for MEC(P(95) data from 6 MS and PNEC = 0.6 µg/L)	1.17 (Sc3)
RQ_{fw} (PEC/PNEC)	102.94[a]

[a] PEC has been derived for the 1st WL and it doesn't consider the restricted use. (Carvalho, et al., WL report 2015)

8. STE score (Sc3)

1.099 (PNEC = 2.06 µg/L) (Cr (VI) inland whole water; data from 4 countries).

0.203 (PNEC = 1.8 µg/L) (Cr (total) inland dissolved phase; data from 24 countries).

0.564 (PNEC = 0.6 µg/L) (Cr (total) coastal and transitional dissolved phase; data from 6 countries).

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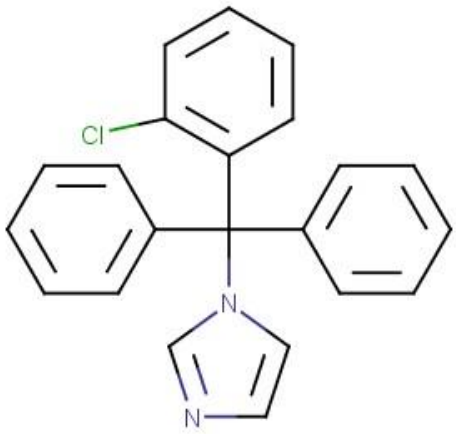
Clotrimazole (CAS N. 23593-75-1)

1. Substance identity

EC name	Clotrimazole
EC number	245-764-8
CAS number	23593-75-1
Molecular formula	$C_{22}H_{17}ClN_2$
Molecular weight	344.8 g/mol
Structure	
SMILES	C1=CC=C(C=C1)C(C2=CC=CC=C2)(C3=CC=CC=C3Cl)N4C=CN=C4

2. Physico-chemical properties

Endpoint	**Value**	**Source**
Vapour Pressure (Pa)	3,31E-07	(OSPAR, 2015)
Water solubility (mg/L)	0,49	(OSPAR, 2015)
logK_{ow}	4,1	(OSPAR, 2015)

3. Environmental fate

Endpoint	**Value**	**Source**
Sorption potential K_{oc}		
Partition coefficient solid-water in sediment Kp_{sed} (L/kg)		

Biodegradability	not biodegradable	(OSPAR, 2015)
Bioaccumulation (BCF)	610 L/kg	(OSPAR, 2015)

4. Environmental exposure assessment

4.1 Predicted Environmental Concentration

	Description	**Source**
Tonnes/year	10 tonnes are produced in the EU each year, and almost the same quantity is imported.	(OSPAR, 2015)
Uses	Its main use is for treatment of dermatological and gynaecological fungal infections.	(OSPAR, 2015)
Spatial usage (by MS)		
Banned uses		
ERC code		
PEC_{fw} (mg/L)	8,6E-5	(OSPAR, 2015)
PEC_{sed} (mg/kg dw)		
PEC_{biota} (mg/kg)		

4.2 Measured Environmental Concentration

n. of MS	**Source of monitoring data**	**MEC values**
In Sc2 (inland dissolved) data from 2 MS (19 sites) with 45 samples are available. About 47% of samples are quantified. Data quality in Sc2 seems to be acceptable but the amount of data is very low. The data are not union representative. Sc3 was not developed since the data scarcity.	Dataset of monitoring prioritisation 2014	MEC(P95) = 0.016 µg/L (Sc2)

4.3 Analytical Methods

Method	**LOQ (µg/L)**	**Description/Reference**
LC–MS/MS	0.02261	Chitescu et al. 2015

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5. P, B, T, C, M, R, ED properties

Substance	Persistent (P)Bioaccumulative (B) Toxic (T)	Carcinogenic (C) Mutagenic (M) Reproduction toxicity (R)	Endocrine Disruptive (ED)	Comment
Clotrimazole	P and B	C and M	ED	

NOTE: Suspected bioaccumulative #Suspected carcinogen #Suspected mutagen #Suspected persistent in the environment #Suspected skin sensitiser (ECHA Annex II inventory). https://endocrinedisruption.org/interactive-tools/tedx-list-of-potential-endocrine-disruptors/search-the-tedx-list#sname=CLOTRIMAZOLE&searchfor=any&sortby=chemname&action=search&searchcats=all&sortby=chemname. POSSIBLE ED (ONLY 1 STUDY)

6. Hazard assessment

6.1 PNEC derivation

PNEC	Endpoint	Endpoint value (µg/L)	AF	PNEC value (µg/L)
$PNEC_{fw}$	NOEC 66 Nieuwkoop-faber-stage (*Xenopus tropicalis*)	1.96	100	0.02 (JRC derivation, 2019)
$PNEC_{fw}$	EC_{50} (Fish)	36	1000	0.036 (Zhou et al., 2019)
$PNEC_{fw}$	NOEC 21d (*Daphnia magna*)	10	10	1 (OSPAR, 2015)
$PNEC_{sed}$				31.6 µg/kg wwt (EqP, OSPAR, 2015)
$PNEC_{biota,sec\ pois}$				
$PNEC_{biota,\ hh}$				
$PNEC_{dw,\ hh}$				

7. Risk Quotient (MEC or PEC/PNEC)

RQ	Value
RQ_{fw} (MEC(P95)/PNEC)	0.016 (PNEC = 1 µg/L) 0.8 (PNEC = 0.02 µg/L, JRC derivation 2019)
RQ_{fw} (PEC/PNEC; PEC = 0.086 µg/L)	0.086 (PNEC = 1 µg/L)

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	4.3 (PNEC = 0.02 µg/L, JRC derivation 2019)
RQ_{sed}	
$RQ_{biota,sec\ pois}$	
$RQ_{biota,\ hh}$	
$RQ_{dw,\ hh}$	

8. STE score

STE (Sc2) is not calculated (according to available data it is expected to be low since MEC(P95) < PNEC (1 µg/L and 0.02 µg/L))

9. References

Chitescu, C. L., Kaklamanos, G., Nicolau, A. I. & Stolker, A. A. M. High sensitive multiresidue analysis of pharmaceuticals and antifungals in surface water using U-HPLC-Q-Exactive Orbitrap HRMS. Application to the Danube river basin on the Romanian territory. Science of The Total Environment 532, pp. 501-511, doi: https://doi.org/10.1016/j.scitotenv.2015.06.010 (2015).

OSPAR Commission. OSPAR background document on clotrimazole. 2005

Zhou, S. et al. Optimization of screening-level risk assessment and priority selection of emerging pollutants – The case of pharmaceuticals in European surface waters. Environment International 128, pp. 1-10, doi: https://doi.org/10.1016/j.envint.2019.04.034 (2019).

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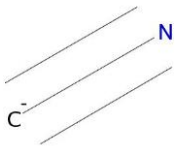
Cyanide-Free (CAS N. 57-12-5)/ Hydrogen Cyanide (CAS N. 74-90-8)

1. Substance identity

EC name	Cyanide
EC number	200-821-6 (Hydrogen cyanide)
CAS number	57-12-5 (free cyanide) 74-90-8 (hydrogen Cyanide)
Molecular formula	HCN, CN^-
Molecular weight	26.02 g/mol (free cyanide) 27.03 g/mol (hydrogen cyanide)
Structure	
SMILES	C#N

2. Physico-chemical Properties for hydrogen cyanide (HCN)

Endpoint	Value	Source
Vapour Pressure	620 mmHg at 20°C (as HCN) 830 hPa at 20°C	WFD – UK TAG Report, 2012 https://echa.europa.eu/it/registration-dossier/-/registered-dossier/14996/2/3
Water solubility (mg/L)	1,000,000 at 25°C (as HCN)	WFD – UK TAG Report, 2012
logK_{ow}	0.35 – 1.07 (as HCN) -0.25 to 0.66	WFD – UK TAG Report, 2012 https://www.canada.ca/en/environment-climate-change/services/evaluating-existing-substances/screening-assessment-cyanides.html

3. Environmental fate

Endpoint	Value	Source

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Sorption potential Log K_{oc}	0.45 to 1.17	https://www.canada.ca/en/environment-climate-change/services/evaluating-existing-substances/screening-assessment-cyanides.html
Partition coefficient solid-water in sediment Kp_{sed} (L/kg)		
Biodegradability	Biodegradation is an important transformation process for cyanide in natural surface waters and is dependent on such factors as cyanide concentrations, pH, temperature, availability of nutrients and acclimation of microbes.	WFD – UK TAG Report, 2012
Bioaccumulation (BCF)	Experimental BCF values for rainbow trout range from 1.69–4.12.	WFD – UK TAG Report, 2012

4. Environmental exposure assessment

4.1 Predicted Environmental Concentration

	Description	**Source**
Tonnes/year	11894 (2010) in CZ	CZ
Uses	Cyanides are used extensively in industry and are also emitted from car exhaust fumes. They also occur ubiquitously in the environment and are found in a range of aquatic organisms such as arthropods, macrophytes, fungi and bacteria. Cyanide is used in the following MS: CZ, IRL	WFD – UK TAG Report, 2012
	Electroplating	CZ
Spatial usage (by MS):	Widespread use	
Banned uses	**-**	
ERC code	-	
Fraction of tonnage to region	-	
PEC_{fw} (mg/L)	-	

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PEC_{sed} (mg/kg dw)	-	
PEC_{biota} (mg/kg)	-	

4.2 Measured Environmental Concentration

n. of MS	Source of monitoring data	MEC values	RBSP
CZ	Waste water	2.5 - 11 µg/L (2015)	
14 (CZ, SI, EL, FR, DE, AT, ES, UK, IE, NL, PL, RO, SK, IT) Reported as cyanide in the databases	NORMAN DB, 2014	$MEC_{95, whole}$: 1.07 µg/L $MEC_{95, dissolved}$: 5 µg/L	10 MS (RBSP EQS ECOSTAT – UBA report) EQS set for cyanide ion and total (WRc, 2012)
	WATERBASE, 2014	$MEC_{95, whole}$: 20 µg/L $MEC_{95, dissolved}$: 20 µg/L	
	IPCheM	MEC_{95}: 14 µg/L	

n. of MS	Source of monitoring data	MEC values
<u>Cyanide (as total CN)</u> In Sc2 (inland whole water) data from 14 MS with 17568 samples are available (23.4% quantified samples). The data quality is low (about 77% of non-quantified samples have LOQ/LOD ≥ PNEC (0.5 µg/L)). 3 MS hold about 70% from all samples. Sc3 was not worked out since low data quality.	Dataset of monitoring prioritisation 2014	MEC(P95) = 7 µg/L
<u>Cyanide anion (CN-)</u> In Sc2 (inland dissolved fraction) data from 2 MS with 340 samples are available (18.5% quantified samples). The data quality is low (about 64% of non-quantified samples have LOQ/LOD ≥ PNEC (0.5 µg/L)). The data are not union representative. Sc3 was not worked out since low data quality.	Dataset of monitoring prioritisation 2014	MEC(P95) = 11.7 µg/L (Median = 1 µg/L)

4.3 Analytical Methods

Method	LOQ (µg/L)	Description/Reference
Free cyanide: CSN ISO 6703 Total cyanides: CSN 757415, CSN EN ISO 14403-2	Free cyanide: 5 Total cyanides: 1 – 5	CZ
Spectrophotometric measure of total and free cyanide by molecular absorption	LOD: 0.1 LOQ: 0.5	BE-Wallonia
SPEK (CFA), SIST EN ISO 14403-2:2013	LOD: 0.1 LOQ: 0.5	Slovenia
Continuous flow analysis (CFA) with photometric detection	LOQ: 0.14 - 0.30	Fraunhofer Institute, 2017

5. P, B, T, C, M, R, ED properties

Substance	Persistent (P) Bioaccumulative (B) Toxic (T)	Carcinogenic (C) Mutagenic (M) Reproduction toxicity (R)	Endocrine Disruptive (ED)	Comment
Free cyanide	T	-	-	-

NOTE: Not listed in the PBT list from ECHA https://echa.europa.eu/it/information-on-chemicals/pbt-vpvb-assessments-under-the-previous-eu-chemicals-legislation.

Volatilisation and biodegradation are important transformation processes for cyanide in ambient waters. Hydrogen cyanide can be biodegraded by acclimated microbial cultures, but is usually toxic to unacclimated microbial systems at high concentrations (WFD-UK TAG Report, 2012).

6. Hazard assessment

6.1 Ecotoxicology data

Trophic level	Endpoint	Value	Reference
Fish	Rainbow trout, 20 d, LOEC	5 µg/L	WFD- UK TAG Report, 2012
Fish	***Lepomis macrochirus*, 289 d, total inhibiotin of spawning, LOEC**	**5.2 µg/L**	WFD- UK TAG Report, 2012
Fish	*Salvelinus fontinalis*, egg production, NOEC	5.7 µg/L	WFD- UK TAG Report, 2012

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Aquatic Invertebrates	*Moinodaphnia macleayi*, 5 d, reproduction, NOEC	9.6 µg/L	WFD- UK TAG Report, 2012
Aquatic Invertebrates	*Gammarus pseudolimnaeus,* 98 d, growth, NOEC	4 µg/L	WFD- UK TAG Report, 2012
Aquatic Invertebrates	*Hydra viridissima*, 6 d, population growth, NOEC	110 µg/L	WFD- UK TAG Report, 2012
Algae	*Pseudokirchneriella subcapitata*, 72 h,growth rate and biomass, NOEC	10 µg/L	WFD- UK TAG Report, 2012

6.2 PNEC derivation

PNEC	**Endpoint**	**Endpoint value**	**AF**	**PNEC value**
$PNEC_{fw}$	*Lepomis macrochirus*, 289 d, LOEC	5.2 µg/L	20	0.26 (µg/L)[a]
$PNEC_{sed}$	-	-	-	-
$PNEC_{biota,sec\ pois}$	-	-	-	-
$PNEC_{biota,\ hh}$	-	-	-	-
$PNEC_{dw,\ hh}$	-	-	-	50 (µg/L)[b]

N.R. Not required based on Koc and BCF values not reaching the trigger values required for sediment and biota assessment

[a] Value retrieved from WFD- UK TAG Report (2012)[1]. A more recent freshwater AA-EQS derivation of 5E-04 mg/L needs also to be considered (JRC substance dossier, 2012).

[b] EU Drinking Water QS, referred to cyanide.

6.3 PNEC derivation SSD method (JRC dossier, 2012)

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Trophic level	Endpoint	**Klimish code**	Reference
Algae & aquatic plants (mg/L)	*Chlamydomonas*/10d $NOEC_{pop}$ = 0.010	1 ([57])	[58]
	Chlorococcales/24h $NOEC_{physiology}$ = 0.024	2 ([57])	Krebbs, 1991
	Lemna gibba/7d $E_rC_{10\ (biomass)}$ = 0.00899 [CN^-] E_yC_{10} (biomass) = 0.00358[3] [CN^-]	1 (INERIS, 2011)	[59]
	Champia parvula/14d $NOEC_{growth}$ = 0.0039	2 ([57])	[60]
	Nitzschia closterium/72h $LOEC_{growth}$ = 0.010	2 (Sorokin, 2007)	Pablo et al., 1997a
Invertebrates (mg/L)	*Gammarus pseudolimnaeus*/98d $NOEC_{reproduction}$ = 0.0039 [HCN]	2 ([57])	[61]
	Moinodaphnia macleayi/5d $NOEC_{reproduction}$ = 0.0058	2 ([57])	Rippon et al., 1992
	Asellus communis/112d $NOEC_{reproduction}$ = 0.0279	2 (Sorokin, 2007)	Oseid and Smith, 1979
	Chironomous riparius/ 8d $NOEC_{reproduction} \geq$ 0.005	1 (INERIS, 2011)	[62]
	No information available		
	No information available		
Fish (mg/L)	*Oncorhynchus mykiss*/20d $NOEC_{growth}$ = 0.0048	2 (Sorokin, 2007)	Kovacs, 1979
	Salvelinus fontinalis/144d $NOEC_{reproduction}$ = 0.0054 [CN^-]	2 ([57])	[63]
	Lepomis macrochirus/289d $LOEC_{reproduction}$ = 0.005 **Extrapolation to $NOEC_{repro}$ = 0.001[2)]**	2 ([57], [57])	[64]
	No information available		
	No information available		

(1) www.epa.gov/ecotox

(2) [57], proposed to add an extrapolation factor of 2 from the LOEC to the NOEC, whereas [57] used an extrapolation factor of 5. The worst-case of 5 was retained.

(3) Estimated from the lowest test concentration (3.7 µg/L).

- **Chronic toxicity:**

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According to the TGD-EQS, when sufficient data are available, two calculation methods can be used to calculate AA-$QS_{freshwater}$ and AA-$QS_{saltwater}$ values:

- Assessment Factor Method

Chronic toxicity values are available on 3 freshwater trophic levels and 1 marine trophic level. The lowest value was obtained on the crustacean *Lepomis macrochirus* / 289d: $NOEC_{repro}$ = **1 µg/L**.

According to the TGD-EQS ([65]1), a default assessment factor of 10 and 100 applies for freshwater and marine water, respectively. The information on the chronic toxicity of cyanides to marine species is insufficient to reduce the assessment factor.

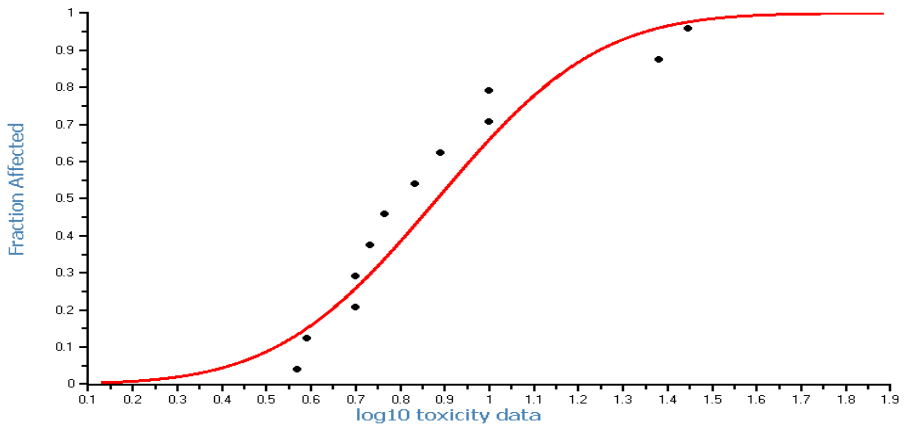
$QS_{freshwater}$ (assessment factor method) = 1 / 10 = 0.1 µg/L

$QS_{saltwater}$ (assessment factor method) = 1 / 100 = 0.01 µg/L

- Species Sensitivity Distribution (SSD) Method

Toxicity data are log-transformed and fitted to a distribution function from which the 5th percentile (referred to as the HC_5) of that distribution is used as the basis for an EQS.

Species sensitivity distribution of NOECs for freshwater and saltwater species



Champia parvula
Chlamydomonas
Chlorococcales
Asellus communis
Gammarus
pseudolimnaeus
Moinodaphnia macleayi
Nitzchia closterium
Lepomis macrochirus
Oncorhynchus mykiss
Salvelinus fontinalis
Chironomus riparius
Lemna gibba

As no significant difference can be demonstrated between freshwater and saltwater sensitivities, it is deemed more relevant to base the QS derivation on the freshwater and saltwater SSD including a higher number of species. This SSD, consisting of the most reliable data (Klimisch code 1 – 2), results in an HC_5 of 2.5 µg.l^{-1}.

It is noted however that mollusk species are missing to complete the TGD-EQS ([65]1) requirements for SSD derivation. For this reason, the maximum assessment factor of 5 is used to determine the AA-QS from the SSD.

$QS_{freshwater}$ (SSD method) = 2.5/5 = 0.5 µg/L

$QS_{saltwater}$ (SSD method) = 2.5/50 = 0.05 µg/L

The QS determined using the SSD are more than 3 times higher than the QS derived with the method of the assessment factors. However, it is noted that these QS would be

sufficiently protective to protect the most sensitive data (*Lepomis macrochirus*/289d: $NOEC_{repro}$ = 1 µg/L) among the species tested.

Although the dataset lacks mollusc ecotoxicity data, the *Chironomus riparius* and *Lemna gibba* data recently provided a comprehensive dataset and the use of the maximum assessment factor applied on the HC_5 should be considered as protective enough. It is thus proposed to use the QS derived using the SSD method. Consequently, the following QS are proposed for the protection of aquatic organisms:

PNEC	Relevant study for derivation of QS	AF	Tentative QS
AA-QS$_{freshwater, eco}$	SSD – HC_5 = 0.0025 mg/L	5	0.5 µg/L

(JRC Dossier https://circabc.europa.eu/faces/jsp/extension/wai/navigation/container.jsp 2015)

6.3 PNEC derivation

PNEC	Endpoint	Endpoint value (µg/L)	AF	PNEC value (µg/L)
PNEC$_{fw}$	LOEC, 289 d *(Lepomis macrochirus*)	5.2	20	0.26 (JRC Factsheet 2015)
PNEC$_{fw}$				0.5 (SSD Approach, JRC Dossier, 2015)
PNEC$_{fw}$	-	50	10	5 (freshwater ECHA dossier)
PNEC$_{sed}$				
PNEC$_{biota,sec\ pois}$				
PNEC$_{biota,\ hh}$				
PNEC$_{dw,\ hh}$				

7. Risk Quotient (PEC/PNEC)

RQ	Value
RQ$_{fw}$ (NORMAN MEC 5-20 µg/L)[c] and PNEC 0.5 µg/L	10-40
RQ$_{fw}$ (NORMAN MEC 5-20 µg/L)[c] and PNEC 0.26 µg/L	19.2-76.8
RQ$_{fw}$ (MEC(P95) CN-)[c] and PNEC 0.5 µg/L	23.4
RQ$_{fw}$ (MEC(P95) CN-)[c] and PNEC 0.26 µg/L	45

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RQ_{sed}	-
$RQ_{biota,sec\ pois}$	-
$RQ_{biota,\ hh}$	-
$RQ_{dw,\ hh}$	-

[c] Dissolved fraction

8. STE score

STE score for Cyanide anion (Sc2) is not calculated since the data scarcity (however, considering the data from these 2 MS, STE is expected to be high since the Median > PNEC (0.5 µg/L)).

9. References

EQS set for cyanide ion and total, WRc, 2012. Contract No. 070311/2011/603663/ETU/D1 "Comparative Study of Pressures and Measures in the Major River Basin Management Plans' - Task 2c (Comparison of Specific Pollutants and EQS): Final Report". WRc Ref: UC8981/1 October 2012. Available at http://ec.europa.eu/environment/archives/water/implrep2007/pdf/P_M%20Task%202c.pdf

EU Drinking Water QS. COUNCIL DIRECTIVE 98/83/EC of 3 November 1998 on the quality of water intended for human consumption, Official Journal of the European Communities. Available at http://europa.eu/legislation_summaries/environment/water_protection_management/l28079_en.htm

Fraunhofer Institute, 2017. Rüdel, H., Knopf, B. Monitoring program for the determination of the natural background concentrations of free cyanide in surface waters. Report on work package 3: Characterization of parameters influencing cyanide levels in natural waters.

IPCheM database at http://ipchem.jrc.ec.europa.eu/JRC Dossier, 2015 at https://circabc.europa.eu/faces/jsp/extension/wai/navigation/container.jsp 2015

NORMAN Database http://www.norman-network.net/?q=node/24

RBSP EQS ECOSTAT – UBA report - Ecological Environmental Quality Standards of "River Basin Specific Pollutants" in Surface Waters - Update and Development analysis of a European Comparison between Member States, by U. Irmer, F. Rau, J. Arle, U. Claussen, V. Mohaupt – Annex WATERBASE Database http://www.eea.europa.eu/data-and-maps/data/waterbase-rivers-6.

WFD – UK TAG Report, Proposed EQS for Water Framework Directive Annex VIII substances: cyanide (free) (For consultation), Water Framework Directive - United Kingdom Technical Advisory Group, 2012. Available at http://www.wfduk.org/sites/default/files/Media/Cyanide_Final_.pdf.

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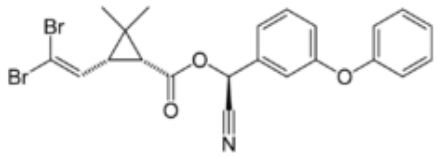
Deltamethrin (CAS N. 52918-63-5)

1. Substance identity

EC name	α-cyano-3-phenoxybenzyl [1R-[1α(S*),3α]]-3-(2,2-dibromovinyl)-2,2-dimethylcyclopropanecarboxylate
EC number	258-256-6
CAS number	52918-63-5
Molecular formula	$C_{22}H_{19}Br_2NO_3$
Molecular weight	505.21 g/mol
Structure	
SMILES	CC1(C(C1C(=O)OC(C#N)C2=CC(=CC=C2)OC3=CC=CC=C3)C=C(Br)Br)C

2. Physico-chemical Properties

Endpoint	**Value**	**Source**
Vapour Pressure (Pa)	1.24 x 10^{-8} at 25°C	Biocide Assessment Report, 2011
Water solubility (mg/L)	0.0002 0.0002 at 25°C; solubility not pH dependent (determined at pH 7.49 - 7.85) < 0.005 at 20ºC by column elution method, pH 6.2	http://npic.orst.edu/factsheets/archive/Deltatech.html EC Review Report, 2002
logK_{ow}	4.6 6.1	http://ceqg-rcqe.ccme.ca/download/en/170 http://npic.orst.edu/factsheets/archive/Deltatech.html

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3. Environmental fate

Endpoint	Value	Source
Sorption potential K_{oc} (L/kg)	408250 L/kg EU dossier K_{oc} range 460000-16300000 mL/g 10240000	Biocide Assessment Report, 2011 PPDB: Pesticide Properties DataBase. University of Hertfordshire http://sitem.herts.ac.uk/aeru/ppdb/en/Reports/205.htm
Partition coefficient solid-water in sediment Kp_{sed} (L/kg)		
Biodegradability	Not readily biodegradable	EC Review Report, 2002
Bioaccumulation (BCF)	1400 *Lepomis macrochirus,* 28 days: 310, 2800 and 1400 for edible, non-edible and whole body tissue, respectively. Clearance time: 4.3 days; by day 14 of the depuration period 7 6% of the ^{14}Cresidues present on the last day of exposure had been eliminated from the whole body tissue.	http://sitem.herts.ac.uk/aeru/ppdb/en/Reports/205.htm EC Review Report, 2002 Biocide Assessment Report, 2011

4. Environmental exposure assessment

4.1 Predicted Environmental Concentration

	Description	Source
Tonnes/year	1 - 10 tonne registered substances	ECHA https://echa.europa.eu/it/substance-information/-/substanceinfo/100.052.943
Uses	Deltamethrin is approved as PPP in the EU (in agriculture to protect crops or kill livestock parasites). Deltamethrin is authorised in 28 MS (AT, BE, BG, CY, CZ, DE, DK, EE, EL, ES, FI, FR, HR, HU, IE, IT, LT, LU, LV, MT, NL, PL, PT, RO, SE, SI, SK, UK). This substance is approved for use as a biocide in the EEA and/or	http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.detail&language=EN&selectedID=1197 https://echa.europa.eu/it/substance-information/-/substanceinfo/100.052.9

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	Switzerland, for: controlling insects, ants, etc..	43
	Expiration of approval: 31/10/2020	
Spatial usage (by MS)		
Banned uses		
ERC code		
PEC_{fw} (mg/L)		
PEC_{sed} (mg/kg dw)		
PEC_{biota} (mg/kg)		

4.2 Measured Environmental Concentration

n. of MS	Source of monitoring data	MEC values
In Sc2 dataset (inland whole water) 28842 samples from 7 MS (2766 sites) are available. Only 0.7% quantified samples. Data quality in Sc2 is not good. Sc3 was worked out but it is not representative for EU-wide assessment (3 MS with 3520 samples; 6% quantified).	Dataset of monitoring prioritisation 2014	MEC(P95) = 0.05 µg/L (Sc2) MEC(P95) = 0.0001 µg/L (Sc3)

Note: Sc2 includes all reported quantified and non-quantified samples. The data quality for Sc2 is verified by controlling the data accuracy, checking quantification frequency of sampling and applying the LOQ-PNEC criterion to non-quantified samples (½ LOQ ≤ PNEC).

Sc3 is the main decisive dataset which includes the quantified measurements and these non-quantified samples when ½ LOQ ≤ PNEC (i.e. avoiding the non-confirmed exceedances when the non-quantified concentrations are set up equal to half of LOQ).

4.3 Analytical Methods

Method	LOQ	Description/Reference
GC-NCI-MS	0.00038 **µg/L**	Extraction by ultrasound-assisted emulsification-extraction of a water-immiscible solvent (chloroform) in 20 mL water (Feo et al., 2010).
GC-NCI-MS	0.001 **µg/L**	SPE of 1 L water (Elfman et al., 2011).
GC-ECD/MS	0.00006 – 0.00098	SPE (Zheng et al., 2016).

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	µg/L (LOD)	
n.a.	0.005 **µg/L**	Finland
n.a.	0.001 – 0.02 **µg/L**	CZ
GC-APCI-MS/MS	0.000025 **µg/L**	Surface water (Rösch et al. 2019)
GC-MS/MS	0.2 **µg/kg**	Sediment (USGS, 2009)

5. P, B, T, C, M, R, ED properties

Substance	**Persistent (P)Bioaccumulative (B) Toxic (T)**	**Carcinogenic (C) Mutagenic (M) Reproduction toxicity (R)**	**Endocrine Disruptive (ED)**	**Comment**
Deltamethrin	P, B and T	C and M	ED	

NOTE: Not listed in the PBT list from ECHA https://echa.europa.eu/it/information-on-chemicals/pbt-vpvb-assessments-under-the-previous-eu-chemicals-legislation. #Harmonised classification for aquatic toxicity #Suspected bioaccumulative #Suspected carcinogen #Suspected hazardous to the aquatic environment #Suspected mutagen #Suspected persistent in the environment #Suspected skin sensitiser (ECHA Annex II inventory).

**https://endocrinedisruption.org/interactive-tools/tedx-list-of-potential-endocrine-disruptors/search-the-tedx-list#sname=Deltamethrin&searchfor=any&sortby=chemname&action=search&searchcats=all&sortby=chemname possible ED

6. Hazard assessment

6.1 Ecotoxicology data

Freshwater

Species	**Time-scale**	**Endpoint**	**Toxicity (µg/L)**
Algae			
Chlorella vulgaris	96 h	NOEC	470
Invertebrates			
Daphnia magna	21 d	NOEC	0.0041
Chironomus riparius	28 d	NOEC	0.010
Chironomus riparius	28 d	NOEC	0.0035
Gammarus pulex	21 d	NOEC	0.009
Tisbe battagliai	6 d	EC10	0.0161
Tisbe battagliai	6 d	EC10	0.0087

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Tisbe battagliai	6 d	EC10	0.0281
Tisbe battagliai	6 d	LC10	0.0641
Fish			
Pimephales promelas	260 d	NOEC	0.017

Sediment

Species	**Time-scale**	**Endpoint**	**Toxicity (µg/kg dw)**
Chironomus riparius	28 d	EC10	54.2

6.2 Mammalian toxicology data

Mammalian oral toxicity	Rat, acute, LD_{50}: 87 mg/kg bw	EC Review Report, 2002
	Dog, 13-week, oral, NOEL: 2.5 mg/kg bw/day (supported by observations of maternal toxicity in teratogenicity studies)	
	Dog, 1-year, oral, NOAEL: 1 mg/kg bw/day (neurological effects)[a]	
	Rat, 90-day, oral, NOAEL: 1 mg/kg bw/day (neurological effects)	
	Rat, 2-year, oral, NOAEL: 1 mg/kg bw/day (neurological effects) [b]	
	Rat, reproductive toxicity, diet, NOEL: 4.2 mg/kg bw/day (adults and offspring)[c]	
	Rat, maternal toxicity, NOAEL: 2.5 mg/kg bw/day	
	Rat, developmental toxicity, NOEL: > 5 mg/kg bw/day	
	Rat, 13-week, oral, NOEL: 4 mg/kg bw/day (neurotoxicity)	
	Mice, 2-year, dietary study, NOAEL: 12 mg/kg	EFSA Opinion,

[a] Lowest NOAEL value which had also been identified in the EFSA Opinion (2009) and used for risk assessment. This NOAEL value of 1 mg/kg bw/day was reported to be related to altered behaviour and liquid faeces (EFSA Opinion, 2009).

[b] Lowest NOAEL value which had also been identified in the EFSA Opinion (2009), and used for risk assessment. This NOAEL value of 1 mg/kg bw/day was reported to be related to reduced body weight and food consumption, and changes in heamatological parameters (EFSA Opinion, 2009).

[c] This two*generation study was also commented in the EFSA Opinion, 2009. The NOAEL 4.2 mg/kg bw/day for parental and offspring toxicity was based on clinical signs, reduced body weight and increased mortality. The NOAEL for reproductive toxicity was found to be 18 mg/kg bw/day, the highest dose tested (EFSA Opinion, 2009).

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	bw/day (males, highest dose tested)	2009
	Mice, 97-week, dietary study, NOAEL: 16 mg/kg bw/day (males, skin ulceration)	
	Rat, 2-year, dietary study, NOAEL: 1 mg/kg bw/day (males, reduced body weight and food consumption, changes in haematological parameters)	
	Rat, acute neurotoxicity test, gavage, NOAEL: 5 mg/kg bw/day (effects in the functional observation battery and on locomotor activity)	
	Rat, short-term dietary neurotoxicity, diet, 13-week, NOAEL: 4 mg/kg bw/day (systemic toxicity and neurotoxicity)	
	Rat, two-generation reproductive study, diet, NOAEL: 18 mg/kg bw/day (highest dose tested, reproductive toxicity)	
	Mice, developmental toxicity, gavage, NOAEL: 3 mg/kg bw/day (maternal toxicity, based on absence of malformations and developmental variations in the foetuses at the highest dose tested)	
	Rats / developmental toxicity / gavage / NOAEL: 2.5 mgkg bw/day (neonatal toxicity, based on reduced body weight gain and mild salivation)	
	Rats, developmental toxicity, gavage, NOAEL: 5 mgkg bw/day (maternal toxicity, based on reduced body weight gain and mild salivation)	
	Rat, developmental toxicity, gavage, NOAEL: 3.3 mgkg bw/day (maternal toxicity, based on clinical signs (e.g. moribundity, convulsions, increased salivation, hypersensitivity, staining), reduced body weight gain, deaths	
	Rats, developmental toxicity, gavage, NOAEL: 11 mgkg bw/day (developmental toxicity, no malformation and developmental variations in foetuses at the highest dose tested)	
	Rabbit, developmental toxicity, NOAEL: 25 mg/kg bw/day (maternal toxicity, based on death of one female; developmental toxicity, based on retardation of ossification)	
	Rabbit, developmental toxicity, NOAEL: 10 mg/kg bw/day (maternal toxicity, based on decreased food consumption and body weight gain)	
	Rabbit, developmental toxicity, NOAEL: 32 mg/kg	

	bw/day (developmental toxicity, highest dose tested)	
	Rat, developmental neurotoxicity study, diet, NOAEL: 6.78 mg/kg bw/day (maternal toxicity, based on reduced body weight gain in dams)	
	Rat, developmental neurotoxicity study, diet, NOAEL: 6.78 mg/kg bw/day (offspring toxicity, based on reduced body weight gain and delayed balanopreputial separation)	

6.3 PNEC derivation

PNEC	**Endpoint**	**Endpoint value**	**AF**	**PNEC value**
$PNEC_{fw}$	28 d, NOEC *(Chironomus riparius)*	0.0035 µg/L	50	0.00007 µg/L (JRC draft dossier, 2016)
$PNEC_{sed}$	*28 d, EC10* *(Chironomus riparius)* (mortality)	54.2 µg/kg dw	100	0.54 µg/kg dw (JRC draft dossier, 2016)
$PNEC_{biota,sec\ pois}$				
$PNEC_{biota,\ hh}$				
$PNEC_{dw,\ hh}$				

7. Risk Quotient (MEC or PEC/PNEC)

RQ	**Value**
RQ_{fw} (MEC(P95)/PNEC)	714 (Sc2); 1.4 (Sc3)
RQ_{fw} (PEC/PNEC; PEC = 0.03 µg/L)	429
RQ_{fw} PEC/PNEC; PEC = 0.36 µg/L)	5143

Note: PEC values are taken from Lettieri, T., Chirico, N., Carvalho, R.N., Napierska, D., Loos, R., Sanseverino, I., Marinov, D., Ceriani, L., Umlauf, G. 2016. *Modelling-based strategy for the prioritisation exercise under the Water Framework Directive,* https://circabc.europa.eu/w/browse/85b46283-9353-4e67-bf56-e4d18b32cbaf.

8. STE score

2.69 (Sc2; PNEC = 0.00007 µg/L)

1.2 (Sc3; PNEC = 0.00007 µg/L)

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Note: STE is a risk-evaluation method/tool developed by the JRC (Loos et al., 2018, EUR 29173 EN). Minimal score = 0 (no risk); Maximal score = 3 (very high risk).

9. References

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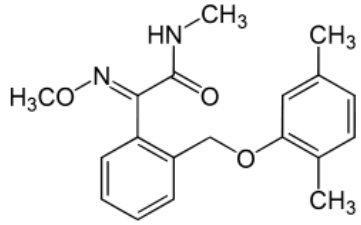
DRAFT

Dimoxystrobin (CAS N. 149961-52-4)

1. Substance identity

EC name	Dimoxystrobin
EC number	604-712-8
CAS number	149961-52-4
Molecular formula	$C_{19}H_{22}N_2O_3$
Molecular weight	326,39 g·mol^{-1}
Structure	
SMILES	CC1=CC(=C(C=C1)C)OCC2=CC=CC=C2C(=NOC)C(=O)NC

2. Physico-chemical Properties

Endpoint	**Value**	**Source**
Vapour Pressure (Pa)		
Water solubility (mg/L)	4.3	http://sitem.herts.ac.uk/aeru/iupac/Reports/246.htm
logK_{ow}	3.6	http://sitem.herts.ac.uk/aeru/iupac/Reports/246.htm

3. Environmental fate

Endpoint	**Value**	**Source**
Sorption potential K_{oc}	486.2 mL/g	EFSA, 2005
Partition coefficient solid-water in sediment Kp_{sed} (L/kg)	Photolysis and partition to sediment was considered the main routes of dissipation of dimoxystrobin from the water phase in the outdoor water sediment study. A first order water phase $DT_{50water}$ = 15.3 d was calculated using only 0-58 d data.	EFSA, 2005
Biodegradability	Not readily biodegradable	EFSA, 2005

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Bioaccumulation (BCF)	48	EFSA, 2005

4. Environmental exposure assessment

4.1 Predicted Environmental Concentration

	Description	**Source**
Tonnes/year	Use: 8.485 in 2016. 18.572 in 2015.	CZ RO
Uses	Dimoxistrobin is approved as PPP in EU (16 MS: AT, BE, BG, CZ, DE, EE, FR, HR, HU, LT, LU, LV, PL, RO, SK, UK) Strobilurin funcicide with the main uses in oilseed rape. Approval expiration date: 31/01/2019.	http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.detail&language=EN&selectedID=1251 EU pesticides database BASF, 2013 DG Sante
Spatial usage (by MS)	Not in PPP register, not sold as PPP in the 2000's. In Finland, the compound is not use.	FI
	Uses registered for oil-seed rape, sunflower.	SK
	Admission for rapeseed.	BE-Fl
	Not approved in DK and SE.	SE; DK
Banned uses		
ERC code		
PEC_{fw} (mg/L)		
PEC_{sed} (mg/kg dw)		
PEC_{biota} (mg/kg)		

4.2 Measured Environmental Concentration

n. of MS	**Source of monitoring data**	**MEC values**
In Sc2 (inland whole water) data from only 1 MS (720 sites) with 6078 samples are available. 2.8% quantified samples.	Dataset of monitoring prioritisation 2014	MEC(P95) = 0.025 µg/L (Sc2)

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The data quality seems acceptable (LOQs<PNEC) but there are 3890 (64% from total) repeated non-quantified samples (LOQ = 0.01 µg/L or 0.02 µg/L) Sc3 was not developed since the data are not union representative.

4.3 Analytical Methods

Method	**LOQ (µg/L)**	**Description/Reference**
SPE-LC-MS-MS	0.025	Extraction of 10 mL water; elution with methanol (BASF, 2013)
LC-MS-MS	0.01	CZ
SPE-LC-MS-MS	0.01	BE-Wallonia
LC-ESI-Q-Orbitrap-MS	0.0010	Casado et al., 2019

Dimoxystrobin has mainly been analysed in food products (Lozowicka et al., 2014; Schurek et al., 2008; Wang et al., 2012; 2017).

Lozowicka et al. (2014) analysed pesticide residues (including dimoxystrobin) in grain (barley, oat, rye, and wheat) from Kazakhstan.

5. P, B, T, C, M, R, ED properties

Substance	**Persistent (P) Bioaccumulative (B) Toxic (T)**	**Carcinogenic (C) Mutagenic (M) Reproduction toxicity (R)**	**Endocrine Disruptive (ED)**	**Comment**
Dimoxystrobin	P and T			

Dimoxystrobin is stable to hydrolysis at all environmental relevant pHs. Photolysis may moderately contribute to the degradation of dimoxystrobin in water. Degradation of dimoxystrobin in water/sediment systems was very limited. Only 10-15% of the applied dimoxystrobin degrades after 100 d. Disappearance from the water phase is mainly attributed to partition with sediment. Additionally an outdoor water sediment study and an outdoor mesocosm study in Germany were used to investigate the aquatic dissipation of dimoxystrobin. Photolysis and partition to sediment were considered the main routes of dissipation of dimoxystrobin from the water phase in the outdoor water sediment study. In the mesocosm study dimoxystrobin was applied in early May and a dissipation DT_{50} = 60 – 69 d was calculated for the water phase (EFSA, 2005).

The hydrolytic stability of dimoxystrobin was studied in sterile aqueous buffer solutions (pH 4, 5, 7, and 9) at 25ºC and 50ºC. Dimoxystrobin is stable at all environmental relevant pHs. Photolysis in water was investigated in two different studies. Photolysis may moderately contribute to the degradation of dimoxystrobin in water. Measured half-life under continuous irradiation under laboratory conditions was 14.1 d (pond water) and 64.8 d (sterile buffer pH 7, extrapolated) (EFSA, 2005).

6. Hazard assessment

6.1 Ecotoxicology data

Species	Time-scale	Endpoint	Toxicity (µg/L)
Algae & aquatic plants			
Pseudokirchneriella subcapitata	96 h	EC10	13.3
Invertebrates			
Daphnia magna	21 d, reproduction	NOEC	12.5
Daphnia magna	10 d, growth	NOEC	0.5
Chironomus riparius	28 d, emergence rate	NOEC	10
Fish			
Oncorhynchus mykiss	97 d, growth	NOEC	0.316
Oncorhynchus mykiss	97 d	NOEC	1
Acipenser ruthenus L.	7 d	NOEC (weight) NOEC (growth)	0.1 1
Oncorhynchus mykiss	28 d	NOEC	10
Pimephales promelas	36 d	NOEC	16

Data used for PNEC derivation

Source: UBA 2014 and EFSA 2005

6.2 PNEC derivation

PNEC	Endpoint	Endpoint value (µg/L)	AF	PNEC value (µg/L)
$PNEC_{fw}$	97-d NOEC (body length, ELS*, *Oncorhynchus mykiss*)	0.316	10	0.0316 (ETOX: Information System Ecotoxicology and Environmental Quality Targets, UBA)
$PNEC_{fw}$				1.67 (AgriTox ANSES FR)

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$PNEC_{sed}$				
$PNEC_{biota,sec\ pois}$				
$PNEC_{biota,\ hh}$				
$PNEC_{dw,\ hh}$				

7. Risk Quotient (MEC or PEC/PNEC)

RQ	**Value**
RQ_{fw} (MEC(P(95))/PNEC)	0.79 (Sc2; PNEC = 0.0316 µg/L)
RQ_{fw} (PEC/PNEC; PEC = 16.42 µg/L)	519.6 (PNEC = 0.0316 µg/L)

Note: PEC value is taken from Lettieri et al., 2016.

8. STE score

0 (Sc2; PNEC = 0.0316 µg/L)

9. References

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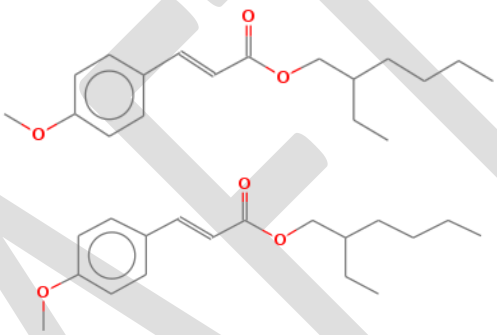
DRAFT

2-Ethylhexyl-4-methoxycinnamate, EHMC (CAS N. 5466-77-3)/2-Ethylhexyl trans 4-methoxycinnamate (CAS N. 83834-59-7)

1. Substance identity

Chemical name (IUPAC)	2-Ethylhexyl 4-methoxycinnamate
EC number	226-775-7
CAS number	5466-77-3
Molecular formula	$C_{18}H_{26}O_3$
Molecular weight	290.4 g/mol
Structure	
SMILES	CCCCC(CC)COC(=O)/C=C/C1=CC=C(C=C1)OC

2. Physico-chemical Properties

Endpoint	**Value**	**Source**
Vapour Pressure (Pa)	30	ECHA, 2014
Water solubility (mg/L)	0.75	ECHA, 2014
logK_{ow}	>6	ECHA, 2014

3. Environmental fate

Endpoint	**Value**	**Source**
Sorption potential (K_{oc})	13290	ECHA, 2014
Partition coefficient solid-water in sediment Kp_{sed} (L/kg)		
Biodegradability	Readily biodegradable	ECHA, 2014

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Bioaccumulation (BCF)	433	ECHA, 2014
BMF	1	GD No. 27 (2011)

4. Environmental exposure assessment

4.1 Predicted Environmental Concentration

	Description	**Source**
Tonnes/year	7500 (year 2000)	Prioritisation exercise (Carvalho et al., 2016 and Lettieri et al. 2016)
Uses	Sunscreen ingredient in personal care products	
Spatial usage (by MS):	Widespread use (worldwide)	Sevin, I. (2006)
Banned uses	-	
ERC code	ERC8a	
Fraction of tonnage to region	0.1	
PEC_{fw} (mg/L)	0.0063	ECETOC (Carvalho et al., 2015)
PEC_{sed} (mg/kg dw)	8.39	ECETOC (Carvalho et al., 2015)
PEC_{biota} (mg/kg)	2.73 (N.R.)	Calculation based on Equation L (Carvalho et al., 2015)

N.R. Not Required because readily biodegradable.

4.2 Measured Environmental Concentration

n. of MS	**Source of monitoring data**	**MEC values**	**RBSP**
	NORMAN DB, 2014	$MEC_{95,\ whole}$: 3.98E-04 mg/L (DE)	
2 (DE, SE)	SE National Screening Programme 2009: UV-filters	MEC_{95}: 3.03E-05 mg/L (surface water) MEC_{95}: 0.043 mg/kg dw (sediment)	-

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	MEC_{95}: 7.8E-04 mg/kg ww (biota)	
MS	**Source of monitoring data**	**MEC values**
Water: In Sc3 (inland whole water) 1583 samples (13.4% quantified) from 23 MS (335 sites) are available; the data quality is good (LOQ < PNEC) and data are union representative; Median conc. = 0.3 µg/L.	Combined WL dataset (after 3rd reporting year of the WL)	MEC(P95) = 1.8 µg/L (Sc3)
Sediments: In Sc2 reported 31 samples from 3 MS; Max conc. = 35 µg/kg	Combined WL dataset (after 3rd reporting year of the WL)	MEC(P95) < 35 µg/kg (Sc2)

4.3 Analytical Methods

Method	**LOQ**	**Description/Reference**
HPLC-MS2 (sediment)	0.0001 ng/g	(Mandaric et al., 2017)

5. P, B, T, C, M, R, ED properties

Substance	**Persistent (P) Bioaccumulative (B) Toxic (T)**	**Carcinogenic (C) Mutagenic (M) Reproduction toxicity (R)**	**Endocrine Disruptive (ED)**	**Comment**
EHMC	Suspected PBT		Suspected ED	

NOTE: Endocrine disruptor-Category 1 both for human health and aquatic organisms (Endocrine Disruptor database of the EU Commission, 2011). In the latter case, an increase in plasma VTG + and increased mRNA expression levels of estrogen receptor (ER) alpha, among sex hormone receptors in the liver (Endocrine Disruptor database of the EU Commission, 2011).

EHMC has been reported to display low but multiple hormonal activities in fish including vitellogenin induction, histological changes in gonads and effects on the expression of genes involved in different hormonal pathways in fathead minnows (Christen V. et al., 2011). EHMC has also caused toxic effects on reproduction in snails (Kaiser D. et al., 2012).

Negative results for genotoxicity. (ECHA, 2014). Suspected PBT, potential endocrine disruptor, possible risk, wide dispersive use, consumer use, environmental exposure, high (aggregated) tonnage (Draft Community Rolling Action Plan (CoRAP) update for years 2016-2018).

6. Hazard assessment

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6.1 Ecotoxicology data

Trophic level	Endpoint	Value	Reference
Algae	*Selenastrum capricornutum*, 72 h, growth rate, EC_{50}	32 mg/L	ECHA, 2014
Algae	*Selenastrum capricornutum*, 72 h, growth rate, NOEC	> 100000 µg/L	ECHA, 2014
Aquatic invertebrates	***Melanoides tuberculata*, 28 d, number of embryos per snail, sediment toxicity test, NOEC**	**2 mg/kg**	**Kaiser et al., (2012)** **(R2)**
Aquatic invertebrates	*Potamopyrgus antipodarum*, 56 d, number of embryos per snail, sediment toxicity test, NOEC	0.08 mg/kg[a]	Kaiser et al., (2012) (R2)
Aquatic invertebrates	*Daphnia magna*, 48 h, EC_{50}	> 0.0271 mg/L	ECHA, 2014
Fish	*Danio rerio*, 48 h, sediment contact test, sublethal effects, NOEC	100 mg/kg	Kaiser et al., (2012) (R2)
Fish	*Cyprinus carpio*, 96 h, LC_{50}	> 100000 µg/L	ECHA, 2014

[a] Even though this value was lower, it was not selected for the risk assessment, because no dose-effect curve was seen, in contrast with the one chosen (in bold).

(R2) Relevance and reliability were assessed using a literature evaluation tool (LET) based on the CRED system (Kase et al., unpublished). Assessed to be reliable with restrictions (Klimisch score 2).

6.2 Mammalian toxicology data

Type of test	Endpoint	Value	Reference
Repeated dose toxicity	Rat, oral, min 90 d, NOAEL	450 mg/kg bw/day	ECHA, 2014
Reproductive toxicity	Rat, oral, 2 generation study, NOAEL	450 mg/kg bw/day	ECHA, 2014

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Developmental toxicity	Rabbit, oral, NOAEL	500 mg/kg bw/day	ECHA, 2014

6.3 PNEC derivation

PNEC	Endpoint	Endpoint value	AF	PNEC value	Comment
$PNEC_{fw}$	-	-	-	6 µg/L	Carvalho et al., 2015
$PNEC_{sed}$	*Melanoides tuberculata*, 28 d, sediment toxicity test, NOEC	2000 µg/kg	10[a]	200 µg/kg	Kaiser et al., (2012)
$PNEC_{biota,sec\ pois}$	N.R.	-	-	-	RB
$PNEC_{biota,\ hh}$	N.R.	-	-	-	RB
$PNEC_{dw,\ hh}$	DNEL, repeated dose toxicity, oral	2.25 mg/kg bw/day	-	7.875 mg/kg bw/day	ECHA, 2014 (for DNEL & AF)[b]

N.R. Not required because the substance is readily biodegradable.

[a] Two long-term endpoints were available for two snail species *Potamopyrgus antipodarum* and *Melanoides tuberculata* at concentrations below water solubility. For *P. antipodarum*, although the NOEC was lower (0.08mg/kg), there was no clear dose response, and for this reason it was not selected. Additionally, for *Chironomus riparius* and *Lumbriculus variegatus* no effects were observed over 28 days for concentrations up to 50 mg/kg dw. Thus, there is data for three long-term tests with species representing different living and feeding conditions and an AF of 10 was selected.

[b] DNEL, retrieved from ECHA, 2014 used in equation F as TL_{hh} (Carvalho et al., 2015)

7. Risk Quotient (MEC or PEC/PNEC)

RQ	Value
RQ_{fw}	0.3
RQ_{sed}	7.1 (SE Screening Programme) < 1 (WL sediments data)
$RQ_{biota,sec\ pois}$	N.R.
$RQ_{biota,\ hh}$	N.R.
$RQ_{dw,\ hh}$	8E-04

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8. STE score

Water: 0 (PNEC = 6 µg/L)

Sediments: Not calculated since insufficient data are available

9. References

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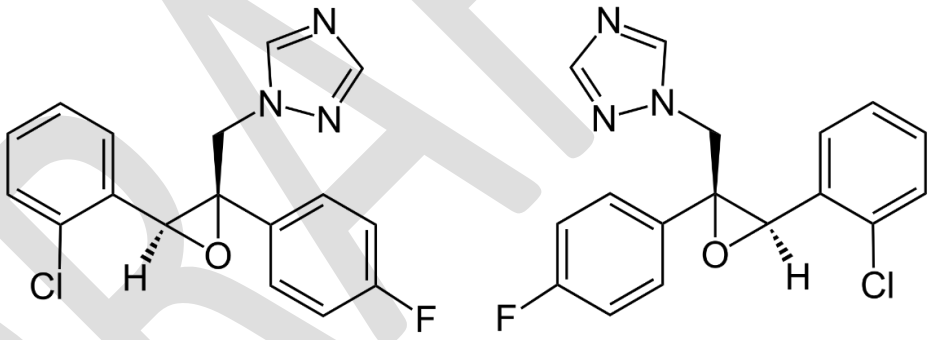
Epoxiconazole (CAS N. 133855-98-8)

1. Substance identity

EC name	(2RS,3SR)-1-[3-(2-chlorophenyl)-2,3-epoxy-2-(4-fluorophenyl)propyl]-1H-1,2,4-triazole
EC number	600-739-4 603-768-0 603-915-9
CAS number	133855-98-8 106325-08-0 135319-73-2
Molecular formula	$C_{17}H_{13}ClFN_3O$
Molecular weight	329.76 g/mol
Structure	
SMILES	C1=CC=C(C(=C1)C2C(O2)(CN3C=NC=N3)C4=CC=C(C=C4)F)Cl

2. Physico-chemical properties

Endpoint	**Value**	**Source**
Vapour Pressure (Pa)	< 1.10^{-5} at 20°C	INERIS, 2011 EFSA, 2008
Water solubility (mg/L)	7.1 (demineralised water) at 20°C, 8.4 at pH 3 and 20°C	INERIS, 2011 EFSA, 2008
logK_{ow}	3.3	INERIS, 2011 JRC, 2009

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3. Environmental fate

Endpoint	Value	Source
Sorption potential K_{oc} (L/kg)	280 – 2647 1802	EFSA, 2008 INERIS, 2011
Partition coefficient solid-water in sediment Kp_{sed} (L/kg)	3.3 at 25°C (demineralised water)	EFSA, 2008 INERIS, 2011
Biodegradability	Not easily biodegradable	INERIS, 2011 EFSA, 2006 and 2008
Bioaccumulation (BCF)	70	INERIS, 2011 EFSA, 2006 and 2008

4. Environmental exposure assessment

4.1 Predicted Environmental Concentration

	Description	Source
Tonnes/year		
Uses		
Spatial usage (by MS)	APPROVED as PPP app 01/05/2009 exp 30/04/2020 2008/107Reg. (EU) 2019/168Reg. (EU) No 540/2011. Authorised in: AT, BE, BG, CZ, DE, DK, EE, EL, ES, FR, HR, HU, IE, IT, LT, LU, LV, NL, PL, PT, RO, SI, SK, UK (24 MS)	EU pesticides database
Banned uses		
ERC code		
PEC_{fw} (µg/L)	0.001 - 0.9	FOCUS Step 3 (EFSA, 2008)
PEC_{sed} (mg/kg dw)		
PEC_{biota} (mg/kg)		

4.2 Measured Environmental Concentration

n. of MS	Source of monitoring data	MEC values
In Sc2 (inland whole water) monitored in 7 MS (2385 sites); available 26476	Prioritisation	Median = 0.01 µg/L;

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samples; only 1.3% quantified samples; the data quality seems poor although that 95% of non-quantified samples were measured with LOQ < PNEC (LOQ ≤ 0.1 µg/L); There is a lot repeated non-quantified samples (17682; about 67% from all samples) coming from 2 MS; the data are not union representative (1 MS holds 53% of all samples, other 40% originate from 2 MS); Sc3 is not developed since the low data quality but is expected to be similar to Sc2 for considered PNECs.	exercise	MEC(p95) = 0.05 µg/L;

4.3 Analytical Methods

Method	**LOQ (µg/L)**	**Description/Reference**
LC–MS/MS	0.0083	Chitescu et al., 2015
LC-ESI-Q-Orbitrap-MS	0.0025	Casado et al., 2019

5. P, B, T, C, M, R, ED properties

Substance	**Persistent (P) Bioaccumulative (B) Toxic (T)**	**Carcinogenic (C) Mutagenic (M) Reproduction toxicity (R)**	**Endocrine Disruptive (ED)**	**Comment**
	PT	CM (suspected) R (suspected)	ED	

Note: Harmonised classification for aquatic toxicity #Harmonised classification for carcinogenicity #Harmonised classification for reprotoxicity #Suspected carcinogen #Suspected hazardous to the aquatic environment #Suspected mutagen #Suspected persistent in the environment #Suspected respiratory sensitiser #Suspected skin sensitiser #Suspected toxic for reproduction (ECHA Annex III inventory). ED (EU Pesticides Database)

Hazard assessment

6.1 Ecotoxicology data

Trophic level	**Endpoint**	**Value (µg/L)**	**Reference**
Algae	LC/EC_{50} *Ankistodesmus bibraianus*	1900	INERIS, 2011
Algae	$NOEC/EC_{10}$ *Pseudokirchneriella subcapitata*	1.8	INERIS, 2011
Invertebrate	LC/EC_{50} *Daphnia magna*	8690	INERIS, 2011
Invertebrate	$NOEC/EC_{10}$ *Chironomus riparus*	62.5	INERIS, 2011

Fish	LC/EC_{50} *Oncorhynchus mykiss*	3140	INERIS, 2011
Fish	NOEC/EC_{10} *Oncorhynchus mykiss*	10	INERIS, 2011

6.2 Mammalian toxicology data

6.3 PNEC derivation

PNEC	**Endpoint**	**Endpoint value (µg/L)**	**AF**	**PNEC value**
$PNEC_{fw}$	chronic			0.2 µg/L (Swiss ECOTOX centre, 2016)
$PNEC_{fw}$	Chronic NOEC/CE10 algae *Pseudokirchneriella subcapitata*	1.8	10	0.18 µg/L (INERIS, 2011)
$PNEC_{sed}$				3 µg/kg (EqP dw, INERIS, 2011)
$PNEC_{biota,sec\ pois}$				
$PNEC_{biota,\ hh}$				
$PNEC_{dw,\ hh}$				

7. Risk Quotient (MEC or PEC/PNEC)

RQ	**Value**
RQ_{fw} (MEC(P95)/PNEC)	0.28 (PNEC = 0.18 µg/L)
RQ_{fw} (PEC/PNEC)	0.005 – 5 (PNEC = 0.18 µg/L)
RQ_{sed}	
$RQ_{biota,sec\ pois}$	
$RQ_{biota,\ hh}$	
$RQ_{dw,\ hh}$	

8. STE score

0.46 (PNEC = 0.18 µg/L)

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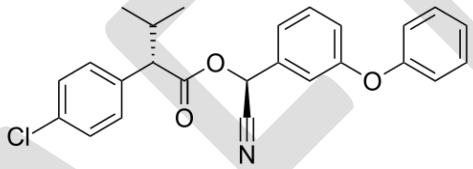
Esfenvalerate (CAS N. 66230-04-4)

1. Substance identity

EC name	(S)-a-cyano-3-phenoxybenzyl-(S)-2-(4-chlorophenyl)-3-methylbutyrate
EC number	613-911-9
CAS number	66230-04-4
Molecular formula	$C_{25}H_{22}ClNO_3$
Molecular weight	419.91 g/mol
Structure	
SMILES	CC(C)C(C1=CC=C(C=C1)Cl)C(=O)OC(C#N)C2=CC(=CC=C2)OC3=CC=CC=C3

2. Physico-chemical Properties

Endpoint	Value	Source
Vapour Pressure (Pa)	1.17×10^{-9} at 20°C purity 99.9% 2.84×10^{-9} at 25°C purity 99.9%	EFSA Conclusion, 2014
Water solubility (mg/L)	< 0.001 at pH 5, 20°C; nearly insoluble in water	EFSA Conclusion, 2014
logK_{ow}	6.24	EFSA Conclusion, 2014

3. Environmental fate

Endpoint	Value	Source
Sorption potential K_{oc}	251700 mL/g	EFSA Conclusion, 2014
Partition coefficient solid-water in sediment Kp_{sed} (L/kg)		

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Biodegradability	Not readily biodegradable	EFSA Conclusion, 2014
Bioaccumulation (BCF)	3369	http://www.rivm.nl/bibliotheek/rapporten/601716017.pdf EFSA, 2014

4. Environmental exposure assessment

4.1 Predicted Environmental Concentration

	Description	**Source**
Tonnes/year	1 - 10 tonne registered substances	ECHA https://echa.europa.eu/it/substance-information/-/substanceinfo/100.118.804
Uses	Esfenvalerate is approved as PPP in the EU (in agriculture to protect crops or kill livestock parasites). Esfenvalerate is authorised in 25 MS AT, BE, BG, CY, CZ, DE, EL, ES, FI, FR, HR, HU, IE, IT, LU, NL, PL, PT, RO, SE, SK, UK	http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.detail&language=EN&selectedID=1286
	Only uses as insecticide may be authorised.	http://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:32011R0540&from=EN
	Expiration of approval: 31/12/2022 (00/67/ECReg. (EU) 2015/2047Reg. (EU) No 540/2011 (2010/77/EU, Reg. (EU) 2015/1885))	http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.detail&language=EN&selectedID=1286
	BEING REVIEWED AS BIOCIDE	ECHA https://echa.europa.eu/it/substance-information/-/substanceinfo/100.118.804
Spatial usage (by MS)		
Banned uses		
ERC code		

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PEC_{fw} (mg/L)	0.000774 - 0.00539 (values predicted for risk assessment using FOCUS Step 4)	EFSA Conclusion, 2014
PEC_{sed} (mg/kg dw)	0.00244 - 1.090 (values predicted for risk assessment using FOCUS Step 4)	EFSA Conclusion, 2014
PEC_{biota} (mg/kg)		

4.2 Measured Environmental Concentration

n. of MS	Source of monitoring data	MEC values
In Sc2 (inland whole water) data from 4 MS (1152 sites) with 8661 samples are available. Only 0.5% quantified samples. The data quality in Sc2 is not good. In Sc3 (inland whole water; PNEC = 0.0001 µg/L) data from only 2 MS (26 sites) with 87 samples are available; 53% quantified samples. Sc3 is not representative for EU-wide assessment.	Dataset of monitoring prioritisation 2014	MEC(P95) = 0.05 µg/L (Sc2) MEC(P95) = 0.017 µg/L (Sc3)

Note: Sc2 includes all reported quantified and non-quantified samples. The data quality for Sc2 is verified by controlling the data accuracy, checking quantification frequency of sampling and applying the LOQ-PNEC criterion to non-quantified samples (½ LOQ ≤ PNEC).

Sc3 is the main decisive dataset which includes the quantified measurements and these non-quantified samples when ½ LOQ ≤ PNEC (i.e. avoiding the non-confirmed exceedances when the non-quantified concentrations are set up equal to half of LOQ).

4.3 Analytical Methods

Method	LOQ	Description/Reference
GC-NCI-MS	0.0001 **µg/L**	Extraction by ultrasound-assisted emulsification-extraction of a water-immiscible solvent (chloroform) in 20 mL water (Feo et al., 2010).
GC-MS	0.06 **µg/L**	SPE of water (Bereswill et al., 2013).
GC-ECD	0.001 **µg/L**	Surface water and drinking water analysis (EFSA, 2014).
GC-APCI-MS/MS	0.000025 **µg/L**	Surface water (Rösch et al., 2019)
GC-MS/MS	0.2 µg/kg	Sediment (USGS, 2009)

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5. P, B, T, C, M, R, ED properties

Substance	Persistent (P)Bioaccumulative (B) Toxic (T)	Carcinogenic (C) Mutagenic (M) Reproduction toxicity (R)	Endocrine Disruptive (ED)	Comment
Esfenvalerate	P (suspected), B (suspected) and T*	C (suspected)	ED**	

*Not listed in the PBT list from ECHA https://echa.europa.eu/it/information-on-chemicals/pbt-vpvb-assessments-under-the-previous-eu-chemicals-legislation. Harmonised classification for acute toxicity# Harmonised classification for aquatic toxicity# Harmonised classification for skin sensitisation# Suspected bioaccumulative# Suspected carcinogen# Suspected hazardous to the aquatic environment# Suspected persistent in the environment# Suspected skin sensitiser (ECHA. Annex III inventory).

**https://endocrinedisruption.org/interactive-tools/tedx-list-of-potential-endocrine-disruptors/search-the-tedx-list#sname=ESFENVALERATE&searchfor=any&sortby=chemname&action=search&searchcats =all&sortby=chemname

6. Hazard assessment

6.1 Ecotoxicology data

Freshwater

Species	Time-scale	Endpoint	Toxicity (µg/L)
Algae			
Pseudokirchneriella subcapitata	48 hr, growth rate	NOEC	1.0
Invertebrates			
Daphnia magna	21 d, reproduction	NOEC	0.052
Daphnia magna	21 d, reproduction	NOEC	0.056
Chironomus riparius	28 d	NOEC	0.16
Fish			
Lepomis macrochirus	30 d, mortality	NOEC	0.092
Lepomis macrochirus	60 d, mortality	NOEC	0.052
Lepomis macrochirus	90 d, mortality	NOEC	0.010
Oncorhynchus mykiss	21 d, mortality	NOEC	0.001
Pimephales promelas	260 d, survival	NOEC	0.090
Salmo gairdneri	21 d	NOEC	0.001

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Mesocosm study			
Aquatic insects	-	NOEC	0.01

6.2 Mammalian toxicology data

Mammalian toxicity	Rat, long-term toxicity, systemic toxicity and carcinogenic effects, 104-week NOAEL 2.3 mg/kg bw/day	EFSA Conclusion, 2014
	Mouse, long-term toxicity, systemic toxicity and carcinogenic effects, 18-month, NOAEL 4.3 mg/kg bw/day	
	Mouse, reproductive toxicity, parental NOAEL 2.45 mg/kg bw/day, reduction in body weight; relevant reproductive NOAEL 6 mg/kg bw/day, no adverse effect; relevant offspring NOAEL 2.45 mg/kg bw/day, decreased body weight	
	Rat, developmental toxicity, maternal NOAEL 3 mg/kg bw/day; relevant developmental NOAEL 20 mg/kg bw/day. Clinical signs of neurotoxicity have been described for the maternal toxicity while no adverse effects have been reported for the developmental toxicity	
	Rabbit, developmental toxicity, maternal NOAEL 2 mg/kg bw/day; relevant developmental NOAEL 20 mg/kg bw/day. Clinical signs of neurotoxicity have been described for the maternal toxicity while no adverse effects have been reported for the developmental toxicity	
	Rat, acute neurotoxicity, NOAEL 1.75 mg/kg bw/day on the basis of clinical signs of neurotoxicity (***)	
	Rat, repeated neurotoxicity, 13-week, NOAEL 3.2 mg/kg bw/day on the basis of clinical signs of neurotoxicity (reduced forelimb grip strength, reduced motor activity)	
	Rat, acute toxicity, LD_{50} 88.5 mg/kg bw	EFSA Conclusion, 2014
	Mouse, acute toxicity, LD_{50} 250 mg/kg bw	EFSA Conclusion, 2014
	Rat, short term toxicity, 90-day, NOAEL 2.5 mg/kg bw/day	EFSA Conclusion, 2014
	Mouse, short term toxicity, 90-day, NOAEL 30.5 mg/kg bw/day	EFSA Conclusion, 2014
	Dog, short term toxicity, 1 year (highest dose), NOAEL 5 mg/kg bw/day	EFSA Conclusion,

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		2014

6.3 PNEC derivation

PNEC	Endpoint	Endpoint value	AF	PNEC value
$PNEC_{fw}$	21-day, mortality (*Oncorhynchus mykiss*)	0.001 µg/L	10	0.0001 µg/L (JRC draft dossier, 2016)
$PNEC_{sed}$		EqP		0.4841 µg/kg_{ww} 1.25866 µg/kg_{dw} (JRC draft dossier, 2016)
$PNEC_{biota,sec\ pois}$				
$PNEC_{biota,\ hh}$				
$PNEC_{dw,\ hh}$				

7. Risk Quotient (MEC or PEC/PNEC)

RQ	Value
RQ_{fw} (for MEC(P95) and PNEC = 0.0001 µg/L)	500 (Sc2) 170 (Sc3)
RQ_{fw} (for PEC = 0.0634 µg/L and PNEC = 0.0001 µg/L)	634
RQ_{fw} (for PEC = 0.0054 µg/L and PNEC = 0.0001 µg/L)	54

Note: PEC values are taken from Lettieri, T., Chirico, N., Carvalho, R.N., Napierska, D., Loos, R., Sanseverino, I., Marinov, D., Ceriani, L., Umlauf, G. 2016. *Modelling-based strategy for the prioritisation exercise under the Water Framework Directive,* https://circabc.europa.eu/w/browse/85b46283-9353-4e67-bf56-e4d18b32cbaf.

8. STE scores

2.6 (Sc2; PNEC = 0.0001 µg/L)

2.5 (Sc3; PNEC = 0.0001 µg/L)

Note: STE is a risk-evaluation method/tool developed by the JRC (Loos et al., 2018, EUR 29173 EN). Minimal score = 0 (no risk); Maximal score = 3 (very high risk).

9. References

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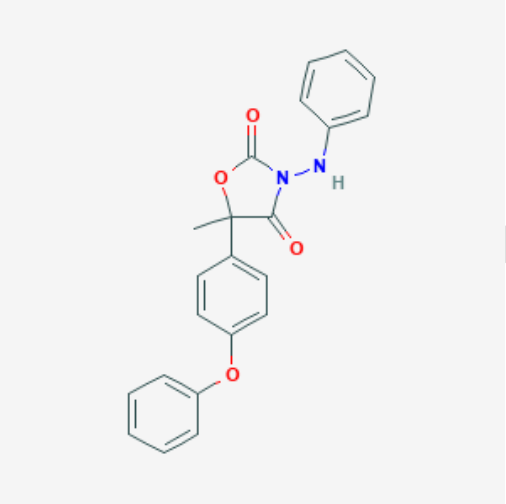
Famoxadone (CAS N.131807-57-3)

1. Substance identity

EC name	3-anilino-5-methyl-5-(4-phenoxyphenyl)-1,3-oxazolidine-2,4-dione
EC number	603-520-1
CAS number	131807-57-3
Molecular formula	$C_{22}H_{18}N_2O_4$
Molecular weight	374.4 g/mol
Structure	
SMILES	CC1(C(=O)N(C(=O)O1)NC2=CC=CC=C2)C3=CC=C(C=C3)OC4=CC=CC=C4

2. Physico-chemical properties

Endpoint	Value	Source
Vapour Pressure (Pa)	$6.4x10^{-7}$ (at 20°C)	PubChem
Water solubility (mg/L)	0.0520	PubChem
logK_{ow}	4.65 (at pH7) 4.65 (at pH7)	PubChem

3. Environmental fate

Endpoint	Value	Source
Sorption potential K_{oc}	3300-4030	PubChem

Partition coefficient solid-water in sediment Kp_{sed} (L/kg)		
Biodegradability	Substance considered not readily biodegradable in the absence of a specific experiment.	EFSA, 2015
Bioaccumulation (BCF)	971 to 1,286 measured in edible bluegill sunfish tissue 3,327 to 3,608 for the nonedible tissue and 2,434 to 3,425 for the whole fish tissues	PubChem

4. Environmental exposure assessment

4.1 Predicted Environmental Concentration

	Description	**Source**
Tonnes/year	Criteria for 1-10 tonne registered substance	ECHA
Uses	Substance approved on 01/10/2002 with expiration date on 30/06/202002/64/EC Reg. (EU) No 2018/917Reg. (EU) No 2019/707 Reg. (EU) No 540/2011 (2010/77/EU, Reg. (EU) No 2015/1885, Reg. (EU) No 2016/549, Reg. (EU) No 2017/841). Substance authorised in 20 MS (AT, BE, BG, CY, CZ, DE, EL, ES, FR, HR, HU, IT, MT, NL, PL, PT, RO, SI, SK, UK)	EU Pesticides Database
Spatial usage (by MS)		
Banned uses		
ERC code		
PEC_{fw} (mg/L)		
PEC_{sed} (mg/kg dw)		
PEC_{biota} (mg/kg)		

4.2 Measured Environmental Concentration

n. of MS	**Source of monitoring data**	**MEC values**
In Sc2 (inland whole water) data from 3 MS (5528 samples) are available; no any quantified samples; the data quality	Dataset of monitoring prioritization 2014	MEC(P95) = 0.025 µg/L (Sc2)

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seems acceptable since LOQs < PNEC (0.14 µg/L) but there are a lot repeated non-quantified samples (5422; about 98% from total) The data are not union representative (98% of samples originate from one MS). Sc3 was not developed since lower data quality.	

4.3 Analytical Methods

Method	**LOQ (µg/L)**	**Description / Reference**
LC/MS/MS	0.10	Samples were adjusted to approximately 5% acetonitrile and 0.01 % formic acid. The analytes were extracted from the solution onto a C18-SPE cartridge and recovered in acidified acetonitrile and acidified methanol (EPA, 2015).

5. P, B, T, C, M, R, ED properties

Substance	**Persistent (P)Bioaccumulative (B) Toxic (T)**	**Carcinogenic (C) Mutagenic (M) Reproduction toxicity (R)**	**Endocrine Disruptive (ED)**	**Comment**
Famoxadone	P, B,T	C*, M*		2 PBT criteria (EU Pesticides Database)

NOTA: *Suspected. Harmonised classification for aquatic toxicity #Harmonised classification for specific target organ toxicity #Suspected bioaccumulative #Suspected carcinogen #Suspected hazardous to the aquatic environment #Suspected mutagen #Suspected persistent in the environment #Suspected skin sensitiser (ECHA Annex III inventory)

6.Hazard assessment

6.1PNEC derivation

PNEC	**Endpoint**	**Endpoint value (µg/L)**	**AF**	**PNEC value (µg/L)**
$PNEC_{fw}$				0.14 (JRC Derivation, prioritization exercise Lettieri et al., 2016)
				0.11 (AgriTox ANSES FR)

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$PNEC_{sed}$				
$PNEC_{biota,sec\ pois}$				
$PNEC_{biota,\ hh}$				
$PNEC_{dw,\ hh}$				

7. Risk Quotient (MEC or PEC/PNEC)

RQ	**Value**
RQ_{fw} (MEC(P95)/PNEC)	0.18 (PNEC = 0.14 µg/L)
RQ_{fw} (PEC/PNEC)	
RQ_{sed}	
$RQ_{biota,sec\ pois}$	
$RQ_{biota,\ hh}$	
$RQ_{dw,\ hh}$	

8. STE score

0 (Sc2; PNEC = 0.14 µg/L)

9. References

ECHA. Annex III inventory. https://echa.europa.eu/information-on-chemicals/annex-iii-inventory/-/dislist/details/AIII-100.047.817

EPA, 2015. https://www.epa.gov/pesticide-analytical-methods/ecm-famoxadone-degradates-soilwater-mrid-49970601

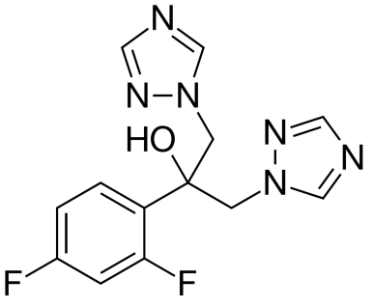
EU Pesticides database. https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.selection&language=EN

Lettieri, T. et al. Modelling-based strategy for the prioritisation exercise under the Water Framework Directive, https://circabc.europa.eu/w/browse/85b46283-9353-4e67-bf56-e4d18b32cbaf) (2016).

DRAFT

Fluconazole (CAS N. 86386-73-4)

1. Substance identity

EC name	1H-1,2,4-Triazole-1-ethanol, alpha-(2,4-difluorophenyl)-alpha-(1H-1,2,4-triazol-1-ylmethyl)-
EC number	627-806-0
CAS number	86386-73-4
Molecular formula	$C_{13}H_{12}F_2N_6O$
Molecular weight	306.2708
Structure	
SMILES	OC(CN1C=NC=N1)(CN1C=NC=N1)C1=C(F)C=C(F)C=C1

2. Physico-chemical properties

Endpoint	**Value**	**Source**
Vapour Pressure (Pa)	$3.0x10^{-9}$ mm Hg at 25°C (est)	US EPA, 2004
Water solubility (mg/L)	4.363 mg/L at 25°C (est) Slightly soluble in water	US EPA, 2004
logK_{ow}	0.25 at 25°C (est)	US EPA, 2004

3. Environmental fate

Endpoint	**Value**	**Source**
Sorption potential K_{oc}	estimated Koc of $5.3x10^4$	ToxNet https://toxnet.nlm.nih.gov/cgi-bin/sis/search2/r?dbs+hsdb:@term+@rn+@rel+86386-73-4
Partition coefficient solid-water in sediment Kp_{sed} (L/kg)		

DRAFT

Biodegradability		
Bioaccumulation (BCF)	estimated BCF of 3.2	ToxNet https://toxnet.nlm.nih.gov/cgi-bin/sis/search2/r?dbs+hsdb:@term+@rn+@rel+86386-73-4

4. Environmental exposure assessment

4.1 Predicted Environmental Concentration

	Description	**Source**
Tonnes/year		
Uses		
Spatial usage (by MS)		
Banned uses		
ERC code		
PEC_{fw} (mg/L)		
PEC_{sed} (mg/kg dw)		
PEC_{biota} (mg/kg)		

4.2 Measured Environmental Concentration

n. of MS	**Source of monitoring data**	**MEC values**
In Sc2 (inland whole water) data from 1 MS (26 sites) with 436 samples are available. 40%of samples are quantified. The data quality seems acceptable but the data are not union representative. Sc3 was not developed since data scarcity.	Dataset of monitoring prioritisation 2014	MEC(P95) = 0.06 µg/L (Sc2)

4.3 Analytical Methods

Method	**LOQ (µg/L)**	**Description/Reference**
LC–MS/MS	0.00501	Chitescu et al., 2015
LC-MS/MS	0.0014	Papageorgiou et al., 2019

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5. P, B, T, C, M, R, ED properties

Substance	Persistent (P) Bioaccumulative (B) Toxic (T)	Carcinogenic (C) Mutagenic (M) Reproduction toxicity (R)	Endocrine Disruptive (ED)	Comment
Fuconazole	PT	R		

NOTE: PT according to https://noharm-global.org/sites/default/files/documents-files/2633/Environmental%20classified%20pharmaceuticals%202014-2015%20booklet.pdf A majority of data submitters agree this substance is Toxic to Reproduction. (ECHA)

6.Hazard assessment

6.1PNEC derivation

PNEC	Endpoint	Endpoint value (µg/L)	AF	PNEC value (µg/L)
$PNEC_{fw}$				0.25 (PNEC-MIC) (AMR industry alliance)
$PNEC_{fw}$	NOEC (Fish)	30.63	50	0.613 (Zhou et al., 2019)
$PNEC_{fw}$	EC10 7d (*Lemna minor*)	473	50	9.46 (JRC derivation, 2019)
$PNEC_{sed}$				
$PNEC_{biota,sec\ pois}$				
$PNEC_{biota,\ hh}$				
$PNEC_{dw,\ hh}$				

7. Risk Quotient (MEC or PEC/PNEC)

RQ	Value
RQ_{fw} (MEC(P95)/PNEC)	0.24 (PNEC MIC = 0.25 µg/L)
RQ_{fw} (PEC/PNEC)	
RQ_{sed}	
$RQ_{biota,sec\ pois}$	
$RQ_{biota,\ hh}$	
$RQ_{dw,\ hh}$	

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8. STE score

STE (Sc2) is not calculated since data scarcity (only 1 MS) considering only data from this MS, STE is expected be low since MEC(p95) < PNEC (0.25 µg/L).

9. References

AMR Industry Alliance Antibiotic Discharge Targets. List of Predicted No-Effect Concentrations (PNECs) (2018).

Chitescu, C. L., Kaklamanos, G., Nicolau, A. I. & Stolker, A. A. M. High sensitive multiresidue analysis of pharmaceuticals and antifungals in surface water using U-HPLC-Q-Exactive Orbitrap HRMS. Application to the Danube river basin on the Romanian territory. Science of The Total Environment 532, pp. 501-511, doi: https://doi.org/10.1016/j.scitotenv.2015.06.010 (2015).

Papageorgiou, M., Zioris, I., Danis, T., Bikiaris, D. & Lambropoulou, D. Comprehensive investigation of a wide range of pharmaceuticals and personal care products in urban and hospital wastewaters in Greece. Science of The Total Environment 694, 133565. doi: https://doi.org/10.1016/j.scitotenv.2019.07.371 (2019).

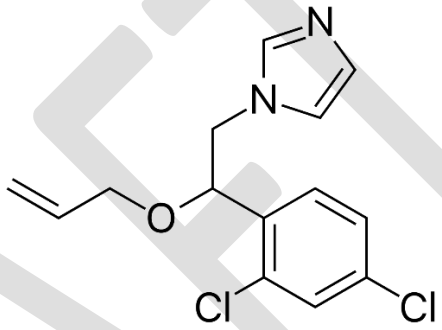
US EPA, 2004; Estimation Program Interface (EPI) Suite. Ver.3.12. Nov 30, 2004. Available from, as of Dec 19, 2005: http://www.epa.gov/oppt/exposure/pubs/episuitedl.htm

Zhou, S. et al. Optimization of screening-level risk assessment and priority selection of emerging pollutants – The case of pharmaceuticals in European surface waters. Environment International 128, pp. 1-10. doi: https://doi.org/10.1016/j.envint.2019.04.034 (2019).

DRAFT

Imazalil (enilconazole) (CAS N. 125116-23-6)

1. Substance identity

EC name	1-[2-(allyloxy)-2-(2,4-dichlorophenyl)ethyl]-1H-imidazole
EC number	252-615-0
CAS number	35554-44-0
Molecular formula	$C_{14}H_{14}Cl_2N_2O$
Molecular weight	297.18 g/mol
Structure	
SMILES	C=CCOC(CN1C=CN=C1)C2=C(C=C(C=C2)Cl)Cl

2. Physico-chemical properties

Endpoint	**Value**	**Source**
Vapour Pressure (Pa)	1.58 10^{-4} at 25°C	EFSA, 2010 INERIS, 2015
Water solubility (mg/L)	184 at pH 7.6 and 20°C	EFSA, 2010 INERIS, 2015
logK_{ow}	3.82	FOOTPRINT, INERIS

3. Environmental fate

Endpoint	**Value**	**Source**
Sorption potential K_{oc}	5115 4753 (mean, soils)	FOOTPRINT, INERIS EFSA, 2010
Partition coefficient solid-water in sediment Kp_{sed} (L/kg)		

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Biodegradability	Not rapidly biodegradable	EFSA, 2010 and INERIS, 2015
Bioaccumulation (BCF)	154 48,7-63,8 (*Oncorhynchus mykiss*), low risk of bioconcntration	US EPA, 2011 cited by INERIS EFSA, 2010 and INERIS, 2015

4. Environmental exposure assessment

4.1 Predicted Environmental Concentration

	Description	**Source**
Tonnes/year	1-10 tonne registered substance	ECHA
Uses	**APPROVED as PPP** approval 01/01/2012 expiration 31/12/2024 Reg. (EU) No 2019/291Reg. (EU) No 540/2011Reg. (EU) No 705/2011 (1997/73/EC,2007/21/EC,2010/57/EU)	EU pesticides database
	This substance is being reviewed for use as a biocide in the EEA and/or Switzerland, for: veterinary hygiene.	ECHA
Spatial usage (by MS)	Authorised as PPP in: AT, BE, BG, CY, CZ, DE, DK, EE, EL, ES, FI, FR, HR, HU, IE, IT, LT, LU, NL, PL, PT, RO, SE, SK, UK (25 MS) In progress: LV	EU pesticides database
Banned uses		
ERC code		
PEC_{fw} (µg/L)	Step 2: 0.43 Step 3: 0.001 - 0.13	FOCUS PEC (EFSA; 2011)
PEC_{sed} (mg/kg dw)		
PEC_{biota} (mg/kg)		

4.2 Measured Environmental Concentration

n. of MS	**Source of monitoring data**	**MEC values**
In Sc2 (inland whole water) are available 7197 samples from 6 MS. Only 0.1% quantified samples. The data have a poor quality and are not union	Dataset of monitoring prioritisation 2014	Median = 0.01 µg/L MEC(p95) = 0.075 µg/L

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representative (91.6% of samples originate from 1 MS). About 75% (5421) from all samples are repeated non-quantified samples having LOQ of 0.02 or 0.05 µg/L. Sc3 was not developed since the low data quality but is expected to be similar to Sc2 for considered PNEC.	

4.3 Analytical Methods

Method	**LOQ (µg/L)**	**Description/Reference**
LC-ESI-Q-Orbitrap-MS	0.001	Casado et al., 2019

5. P, B, T, C, M, R, ED properties

Substance	**Persistent (P) Bioaccumulative (B) Toxic (T)**	**Carcinogenic (C) Mutagenic (M) Reproduction toxicity (R)**	**Endocrine Disruptive (ED)**	**Comment**
	P (suspected) T	CR (suspected)	ED	

NOTE: Suspected to be Carcinogenic and under assessment as Endocrine Disrupting (ECHA). Harmonised classification for acute toxicity #Harmonised classification for aquatic toxicity #Harmonised classification for eye damage #Suspected hazardous to the aquatic environment #Suspected persistent in the environment #Suspected toxic for reproduction (ECHA Annex III Inventory)

6. Hazard assessment

6.1 Ecotoxicology data

Freshwater

Trophic level	**Endpoint**	**Value (µg/L)**	**Reference**
Algae	LC/EC_{50} *Pseudokirchneriella subcapitata*	870	INERIS, 2015
Algae	$NOEC/EC_{10}$ *Pseudokirchneriella subcapitata*	457	INERIS, 2015
Invertebrate	$NOEC/EC_{10}$ *Daphnia magna*	3500	INERIS, 2015
Invertebrate	$NOEC/EC_{10}$ *Daphnia magna*	25	INERIS, 2015
Fish	LC/EC_{50} *Oncorhynchus mykiss*	1480	INERIS, 2015

Fish	*NOEC/EC_{10} Oncorhynchus mykiss*	225	INERIS, 2015

Sediment

Trophic level	**Endpoint**	**Value (mg/kg)**	**Reference**
Invertebrate	NOEC/EC_{10} *Chironomus riparus*	27.5 (dw)	INERIS, 2015

6.2 Mammalian toxicology data
6.3 PNEC derivation

PNEC	**Endpoint**	**Endpoint value (µg/L)**	**AF**	**PNEC value**
$PNEC_{fw}$	NOEC/LOEC *Daphnia magna*	25	10	2.5 µg/L (INERIS, 2015)
$PNEC_{fw}$				0.8 µg/L monitoring exercise (Carvalho et al., 2016) JRC derivation from EFSA report
$PNEC_{sed}$				275 µg/kg (EqP dw, INERIS, 2015)
$PNEC_{biota,sec\ pois}$				
$PNEC_{biota,\ hh}$				
$PNEC_{dw,\ hh}$				

7. Risk Quotient (MEC or PEC/PNEC)

RQ	**Value**
RQ_{fw} (MEC(P95)/PNEC)	0.09 (PNEC = 0.8 µg/L)
RQ_{fw} (PEC/PNEC; PNEC = 0.8 µg/L)	Step 2: 0.54 Step 3: 0.00125 - 0.1625
RQ_{sed}	
$RQ_{biota,sec\ pois}$	

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$RQ_{biota, hh}$	
$RQ_{dw, hh}$	

8. STE score

0 (PNEC = 0.8 µg/L)

9. References

Carvalho, R. N. et al. Monitoring-based exercise: second review of the priority substances list under the Water Framework Directive (https://circabc.europa.eu/w/browse/52c8d8d3-906c-48b5-a75e-53013702b20a) (2016).

Casado, J., Brigden, K., Santillo, D. & Johnston, P. Screening of pesticides and veterinary drugs in small streams in the European Union by liquid chromatography high resolution mass spectrometry. Science of The Total Environment 670, pp. 1204-1225. doi: https://doi.org/10.1016/j.scitotenv.2019.03.207 (2019).

ECHA. Annex III inventory. https://echa.europa.eu/information-on-chemicals/annex-iii-inventory/-/dislist/details/AIII-100.047.817

EFSA, 2010. Conclusion on the peer review of the pesticide risk assessment of the active substance imazalil. European Food Safety Authority, EFSA Journal 8(3), 1526 http://www.efsa.europa.eu/en/efsajournal/doc/1526.pdf.

EU Pesticides database. https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.selection&language=EN

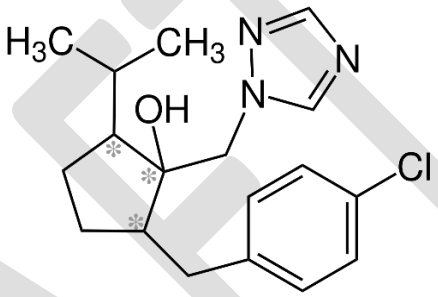
INERIS, 2015. Validation groupe d'experts: Juillet 2014. Version 1: 21/12/2015. DRC-15-136849-12775A. https://substances.ineris.fr/fr/substance/nom/imazalil

EPA (2011). EPI Suite, v.4.10, EPA's office of pollution prevention toxics and Syracuse Research Corporation (SRC).

DRAFT

Ipconazole (CAS N. 125116-23-6)

1. Substance identity

EC name	ipconazole (ISO); (1RS,2SR,5RS;1RS,2SR,5SR)-2-(4-chlorobenzyl)-5-isopropyl-1-(1H-1,2,4-triazol-1-ylmethyl)cyclopentanol
EC number	603-038-1
CAS number	125225-28-7
Molecular formula	$C_{18}H_{24}ClN_3O$
Molecular weight	333.9 g/mol
Structure	
SMILES	CC(C)C1CCC(C1(CN2C=NC=N2)O)CC3=CC=C(C=C3)Cl

2. Physico-chemical properties

Endpoint	**Value**	**Source**
Vapour Pressure (Pa)	3 x 10^{-6} Pa at 25°C (99.7% pure)	EFSA, 2013
Water solubility (mg/L)	11 mg/L (20°C)	EFSA, 2013
logK_{ow}	Log Pow = 4.49 at 20°C	EFSA, 2013

3. Environmental fate

Endpoint	**Value**	**Source**
Sorption potential K_{oc} (L/kg)	2431	EFSA, 2013
Partition coefficient solid-water in sediment Kp_{sed} (L/kg)		
Biodegradability	Not readily biodegradable	EFSA, 2013
Bioaccumulation (BCF)	283 (whole fish)	EFSA, 2013

DRAFT

4.Environmental exposure assessment

4.1 Predicted Environmental Concentration

	Description	**Source**
Tonnes/year	1-10 tonne registered substance	ECHA
Uses	Approved as PPP **APPROVED** approved 01/09/2014 expiration **24/08/2024** Reg. (EU) No 571/2014 (Dossier complete 08/20/EC)	EU Pesticides database
Spatial usage (by MS)	Authorised as PPP in: AT, BE, BG, CY, CZ, DE, EL, ES, FR, HR, HU, IE, IT, PL, PT, RO, SE, SK, UK (19 MS) In progress for: FI	EU Pesticides database
Banned uses		
ERC code		
PEC_{fw} (µg/L)	N Europe, October-February, PECmax = 0.2719 µg/L N Europe, March - May, PEC max = 0.1088 µg/L N Europe, June - September, PEC max = 0.1088 µg/L S Europe, October-February, PEC max = 0.2175 µg/L S Europe, March - May, PEC max = 0.2175 µg/L S Europe, June - September, PEC max = 0.1631 µg/L	FOCUS PEC, Step 2 (EFSA, 2013)
PEC_{sed} (mg/kg dw)		
PEC_{biota} (mg/kg)		

4.2 Measured Environmental Concentration

n. of MS	**Source of monitoring data**	**MEC values**
No available monitoring data	Prioritisation dataset	

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4.3 Analytical Methods

Method	LOQ (µg/L)	Description/Reference
LC-MS/MS	0.05	DAR, 2011

5. P, B, T, C, M, R, ED properties

Substance	Persistent (P) Bioaccumulative (B) Toxic (T)	Carcinogenic (C) Mutagenic (M) Reproduction toxicity (R)	Endocrine Disruptive (ED)	Comment
	P (suspected)	CR (suspected)		

NOTE: Suspected carcinogen #Suspected hazardous to the aquatic environment #Suspected persistent in the environment #Suspected toxic for reproduction (ECHA Annex III Inventory)

6. Hazard assessment

6.1 Ecotoxicology data

Freshwater

Trophic level	Endpoint	Value (µg/L)	Reference
Algae	EC_{50} *Pseudokirchneriella subcapitata*	620	EFSA, 2013
Invertebrates	Chronic 21 d reproduction NOEC *Daphnia magna*	10.9	EFSA, 2013
Fish	Chronic NOEC *Pimephales promelas*	0.44	EFSA, 2013

Sediment

Trophic level	Endpoint	Value (µg/L)	Reference
Invertebrate	Chronic 28d (spiked water) emergence and development rate NOEC *Chironomus ruparus*	3520	EFSA, 2013

DRAFT

6.2 Mammalian toxicology data

6.3 PNEC derivation

PNEC	Endpoint	Endpoint value (µg/L)	AF	PNEC value (µg/L)
$PNEC_{fw}$	NOEC *Pimephales promelas*	0.44	10	0.044 (AgriTox ANSES FR, 2019)
$PNEC_{sed}$				
$PNEC_{biota,sec\ pois}$				
$PNEC_{biota,\ hh}$				
$PNEC_{dw,\ hh}$				

7. Risk Quotient (MEC or PEC/PNEC)

RQ	Value
RQ_{fw} (MEC(P95)/PNEC)	
RQ_{fw} (PEC/PNEC; PNEC = 0.044 µg/L)	2.5 (PECmax = 0.11 µg/L) 6.1 (PECmax = 0.27 µg/L)
RQ_{sed}	
$RQ_{biota,sec\ pois}$	
$RQ_{biota,\ hh}$	
$RQ_{dw,\ hh}$	

8. STE score

Not calculated since missing monitoring data.

9. References

AGRITOX-Database on active plant protection substances. ANSES. http://www.agritox.anses.fr/php/data-criteria.php

DAR, 2011. Report and Proposed Decision of the United Kingdom made to the European Commission under Regulation 1107/2009.

ECHA. Annex III inventory. https://echa.europa.eu/information-on-chemicals/annex-iii-inventory/-/dislist/details/AIII-100.047.817

DRAFT

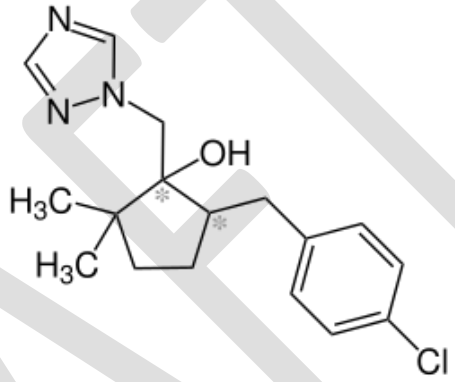
EFSA, 2013. European Food Safety Authority; Conclusion on the peer review of the pesticide risk assessment of the active substance [ipconazole]. EFSA Journal 11(4), 3181, 76 pp. doi: 10.2903/j.efsa.2013.3181. Available online: www.efsa.europa.eu/efsajournal.

EU Pesticides database. https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.selection&language=EN

DRAFT

Metconazole (CAS N. 125116-23-6)

1. Substance identity

EC name	(1RS,5RS;1RS,5SR)-5-(4-chlorobenzyl)-2,2-dimethyl-1-(1H-1,2,4-triazol-1-ylmethyl)cyclopentanol
EC number	603-031-3
CAS number	125116-23-6
Molecular formula	$C_{17}H_{22}ClN_3O$
Molecular weight	319.8 g/mol
Structure	
SMILES	CC1(CCC(C1(CN2C=NC=N2)O)CC3=CC=C(C=C3)Cl)C

2. Physico-chemical properties

Endpoint	**Value**	**Source**
Vapour Pressure (Pa)	2.1 x 10-8 Pa at 20°C	EFSA, 2006
Water solubility (mg/L)	30.4 mg/L at 20°C in distilled Milli-Q water (pH ca. 7.5)	EFSA, 2006
logK_{ow}	3.85 at 20°C (pH 7.2 - 8)	EFSA, 2006

3. Environmental fate

Endpoint	**Value**	**Source**
Sorption potential K_{oc} (L/kg)	726-1718	EFSA, 2006
Partition coefficient solid-water in sediment Kp_{sed} (L/kg)		
Biodegradability		
Bioaccumulation (BCF)	129	EFSA, 2006

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4. Environmental exposure assessment

4.1 Predicted Environmental Concentration

	Description	**Source**
Tonnes/year	1-10 tonne registered substances	ECHA
Uses	APPROVED as PPP approval 01/06/2007 expiration 30/04/2020 2006/74/ECReg. (EU) No 540/2011Reg. (EU) no 2019/168(Reg. (EU) No 2018/524,Reg. (EU) No 878/2014)	EU Pesticides database
Spatial usage (by MS)	Authorised AS PPP in: AT, BE, BG, CZ, DE, DK, EE, ES, FI, FR, HR, HU, IE, IT, LT, LU, LV, NL, PL, PT, RO, SE, SI, SK, UK (25 MS)	EU Pesticides database
Banned uses		
ERC code		
PEC_{fw} (µg/L)	0.1–1.2	FOCUS (EFSA, 2006)
PEC_{sed} (mg/kg dw)		
PEC_{biota} (mg/kg)		

4.2 Measured Environmental Concentration

n. of MS	**Source of monitoring data**	**MEC values**
In Sc2 (inland whole water) data from 3 MS (702 sites) with 5742 samples are available. Only 3 samples are quantified. The data quality in Sc2 is not good. There are 4108 (70% from total) repeated non-quantified samples with LOQ = 0.05 µg/L coming from 1 MS. The data are not union representative. Sc3 is not developed since the low data quality.	Dataset of monitoring prioritisation 2014	MEC(P95) = 0.025 µg/L (Sc2)

4.3 Analytical Methods

Method	**LOQ (µg/L)**	**Description/Reference**

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Q Exactive high-performance benchtop quadrupole-Orbitrap LC–MS/MS	0.0108	Chitescu et al., 2015
LC-ESI-Q-Orbitrap-MS	0.0025	Casado et al., 2019

5. P, B, T, C, M, R, ED properties

Substance	**Persistent (P) Bioaccumulative (B) Toxic (T)**	**Carcinogenic (C) Mutagenic (M) Reproduction toxicity (R)**	**Endocrine Disruptive (ED)**	**Comment**
	PT	CR		

Note: Harmonised classification for acute toxicity #Harmonised classification for aquatic toxicity #Harmonised classification for reprotoxicity #Suspected carcinogen #Suspected hazardous to the aquatic environment #Suspected persistent in the environment #Suspected toxic for reproduction

6. Hazard assessment

6.1 Ecotoxicology data

Freshwater

Trophic level	**Endpoint**	**Value (µg/L)**	**Reference**
Algae	EC_{50} *Pseudokirchneriella subcapitata*		EFSA, 2006
Invertebrates	Chronic 21d reproduction NOEC *Daphnia magna*	160	EFSA, 2006
Fish	Chronic 95d survival NOEC *Onchorhynchus mykiss*	2.91	EFSA, 2006
Fish	Chronic 28d mortality NOEC *Onchorhynchus mykiss*	1140	EFSA, 2006

Sediment

Trophic level	**Endpoint**	**Value (µg/L)**	**Reference**
Invertebrates	Chronic 28d emergence NOEC *Chironomus riparus*	2120	EFSA, 2006

DRAFT

6.2 Mammalian toxicology data

6.3 PNEC derivation

PNEC	Endpoint	Endpoint value (µg/L)	AF	PNEC value (µg/L)
$PNEC_{fw}$	Chronic 95d survival NOEC *Onchorhynchus mykiss*	2.91	50	0.0582 (JRC derivation prioritization, Lettieri et al., 2016)
$PNEC_{fw}$	Chronic 95d survival NOEC *Onchorhynchus mykiss*	2.91	5	0.582 (AgriTox ANSES FR 2019)
$PNEC_{fw}$	Chronic 95d survival NOEC *Onchorhynchus mykiss*	2.91	100	0.0291 (JRC derivation, 2019)
$PNEC_{sed}$				
$PNEC_{biota,sec\ pois}$				
$PNEC_{biota,\ hh}$				
$PNEC_{dw,\ hh}$				

7. Risk Quotient (MEC or PEC/PNEC)

RQ	Value
RQ_{fw} (MEC(P95)/PNEC)	0.43 (PNEC = 0.0582 µg/L) 0.86 (PNEC = 0.0291 µg/L)
RQ_{fw} (PEC/PNEC)	1.7-20.6 (PNEC = 0.0582 µg/L) 3.4-41 (PNEC = 0.0291 µg/L)
RQ_{sed}	
$RQ_{biota,sec\ pois}$	
$RQ_{biota,\ hh}$	
$RQ_{dw,\ hh}$	

DRAFT

8. STE score

0 (PNEC = 0.0582 µg/L)

Not calculated for PNEC = 0.0291 µg/L (according to available data it is expected to be low since MEC(p95) < PNEC)

9. References

AGRITOX-Database on active plant protection substances. ANSES. http://www.agritox.anses.fr/php/data-criteria.php

Casado, J., Brigden, K., Santillo, D. & Johnston, P. Screening of pesticides and veterinary drugs in small streams in the European Union by liquid chromatography high resolution mass spectrometry. Science of The Total Environment 670, pp. 1204-1225. doi: https://doi.org/10.1016/j.scitotenv.2019.03.207 (2019).

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ECHA. Annex III inventory. https://echa.europa.eu/information-on-chemicals/annex-iii-inventory/-/dislist/details/AIII-100.047.817

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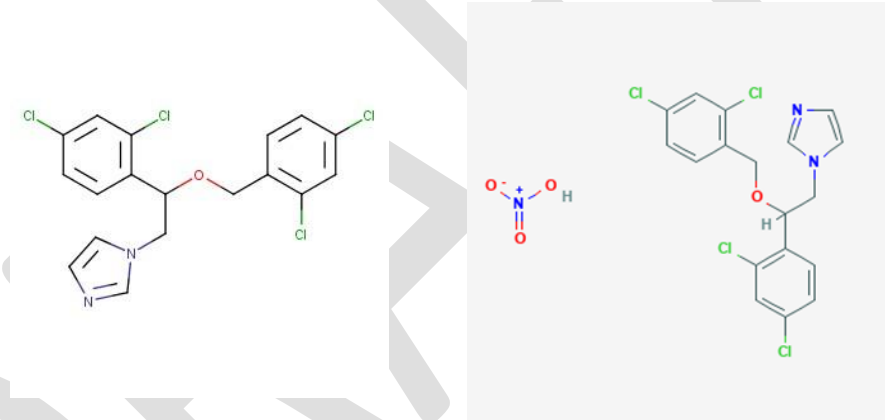
DRAFT

Miconazole (CAS N. 22916-47-8) and Miconazole Nitrate (CAS N.22832-87-7)

1. Substance identity

EC name	Miconazole
EC number	245-324-5 (Miconazole) 245-256-6 (Miconazole nitrate)
CAS number	22916-47-8 (Miconazole) 22832-87-7 (Miconazole nitrate)
Molecular formula	$C_{18}H_{14}Cl_4N_2O$ (Miconazole) $C_{18}H_{15}Cl_4N_3O_4$ (Miconazole nitrate)
Molecular weight	416.1 g/mol (Miconazole) 479.1 g/mol (Miconazole nitrate)
Structure	
SMILES	C1=CC(=C(C=C1Cl)Cl)COC(CN2C=CN=C2)C3=C(C=C(C=C3)Cl)Cl (Miconazole) C1=CC(=C(C=C1Cl)Cl)COC(CN2C=CN=C2)C3=C(C=C(C=C3)Cl)Cl.[N+](=O)(O)[O-] (Miconazole nitrate)

2. Physico-chemical properties

Endpoint	Value	Source
Vapour Pressure (Pa)	$2.36x10^{-8}$	Chen and Ying, 2015
Water solubility (mg/L)	0.01 1g/100mL (20ºC; Experimental properties) 0.763 (Predicted properties)	Chen and Ying, 2015 DrugBank (https://www.drugbank.ca/drugs/DB01110)
logK_{ow}	6.25	Chen and Ying, 2015

3. Environmental fate

Endpoint	Value	Source
Sorption potential K_{oc} (L/kg)	554800	INERIS https://substances.ineris.fr/fr/substance/nom/nitrate-de-miconazole
Partition coefficient solid-water in sediment Kp_{sed} (L/kg)		
Biodegradability	0.77 (Estimated rate in WWTP) Not ready biodegradable	Chen and Ying, 2015 Drugbank (https://www.drugbank.ca/drugs/DB01110)
Bioaccumulation (BCF)	6192	INERIS https://substances.ineris.fr/fr/substance/nom/nitrate-de-miconazole

4. Environmental exposure assessment

4.1 Predicted Environmental Concentration

	Description	Source
Tonnes/year		
Uses	Synthetic antifungal agent with broad spectrum of activity against pathogenic fungi and gram-positive bacteria. Used to treat mycotic vulvovaginitis. Miconazole is classified as POM (List I or List II) in most of the member states.	EDQM, 2017
Spatial usage (by MS)		
Banned uses		
ERC code		
PEC_{fw} (µg/L)	0.032	Minguez et al., 2016
PEC_{sed} (mg/kg dw)		
PEC_{biota} (mg/kg)		

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4.2 Measured Environmental Concentration

n. of MS	Source of monitoring data	MEC values
No available data in the dataset of the prioritisation exercise		

4.3 Analytical Methods

Method	LOQ (µg/L)	Description/Reference
LC–MS/MS	0.00171	Q-Exactive high-performance benchtop quadrupole-Orbitrap (Chitascu et al., 2015)

5. P, B, T, C, M, R, ED properties

Substance	Persistent (P)Bioaccumulative (B) Toxic (T)	Carcinogenic (C) Mutagenic (M) Reproduction toxicity (R)	Endocrine Disruptive (ED)	Comment
Miconazole	P*, B*, T*	R*		ECHA

NOTE: *Suspected. Miconazole: Suspected bioaccumulative #Suspected hazardous to the aquatic environment #Suspected persistent in the environment #Suspected toxic for reproductionMiconazole Nitrate: Suspected bioaccumulative #Suspected hazardous to the aquatic environment t#Suspected persistent in the environment #Suspected toxic for reproduction (ECHA. Annex III inventory)

6. Hazard assessment

6.1 Ecotoxicology data

Trophic level	Endpoint	Value (mg/L)	Reference
Aquatic Invertebrates	*Daphnia magna,* immobilisation, 48h, EC_{50}	0.40	Minguez et al., 2014
Algae	*Pseudokirchneriella subcapitata,* growth inhibition 72h, EC_{50}	1.35	Minguez et al., 2014
Fish	Acute E(L)C50 (Miconazole nitrate)	0.144	Vestel et al., 2016
Fish	Chronic NOEC (Miconazole nitrate)	0.012	Vestel et al., 2016
Green algae	Acute E(L)C50	0.03	Vestel et

	(Miconazole nitrate)		al., 2016
Green algae	Chronic NOEC (Miconazole nitrate)	0.01	Vestel et al., 2016
Algae	Acute EC_{50} ECOSAR	0.049	Zhou et al., 2019
Crustacean	Acute EC_{50} ECOSAR	0.128	Zhou et al., 2019
Fish	Acute EC_{50} ECOSAR	0.044	Zhou et al., 2019

6.2 PNEC derivation

PNEC	**Endpoint**	**Endpoint value (µg/L)**	**AF**	**PNEC value (µg/L)**
$PNEC_{fw}$	Chronic NOEC green algae (Miconazole nitrate)	10	50	0.2 (FASS SE database)
$PNEC_{fw}$	48h EC_{50} (*Daphnia magna*)	400	1000	0.4 (Minguez et al., 2014)
$PNEC_{fw}$	Acute EC_{50}, Fish ECOSAR	44	1000	0.044 (Zhou et al., 2019)
$PNEC_{sed}$				
$PNEC_{biota,sec\ pois}$				
$PNEC_{biota,\ hh}$				
$PNEC_{dw,\ hh}$				

7. Risk Quotient (MEC or PEC/PNEC)

RQ	**Value**
RQ_{fw} (MEC(P95)/PNEC)	
RQ_{fw} (PEC/PNEC; PEC^{a} = 0.032 µg/L; $PNEC^{a}$ = 0.4 µg/L)	0.079^{a}
RQ_{fw}(PEC/PNEC; PEC^{a} = 0.032 µg/L; $PNEC^{b}$ = 0.044 µg/L)	0.73^{b}

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RQ_{sed}	
$RQ_{biota,sec\ pois}$	
$RQ_{biota,\ hh}$	
$RQ_{dw,\ hh}$	

[a] Minguez et al., 2014

[b] Zhou et al., 2019

8. STE score

Not calculated since missing monitoring data.

9. References

Chen, Z.-F. and G.-G. Ying. Occurrence, fate and ecological risk of five typical azole fungicides as therapeutic and personal care products in the environment: A review. Environment International, 84, pp. 142-153 (2015).

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ECHA. Annex III inventory. https://echa.europa.eu/information-on-chemicals/annex-iii-inventory/-/dislist/details/AIII-100.047.817

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Minguez, L., et al. Toxicities of 48 pharmaceuticals and their freshwater and marine environmental assessment in northwestern France. Environmental Science and Pollution Research 23(6), pp. 4992-5001 (2016).

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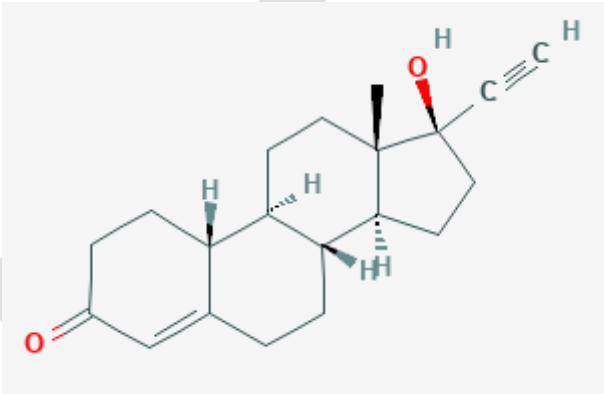
Zhou, S. et al. Optimization of screening-level risk assessment and priority selection of emerging pollutants – The case of pharmaceuticals in European surface waters. Environment International 128, pp. 1-10. doi: https://doi.org/10.1016/j.envint.2019.04.034 (2019).

DRAFT

Norethisterone (CAS N. 68-22-4)

1. Substance identity

EC name	Norethisterone
EC number	200-681-6
CAS number	68-22-4
Molecular formula	$C_{20}H_{26}O_2$
Molecular weight	298.4 g/mol
Structure	
SMILES	CC12CCC3C(C1CCC2(C#C)O)CCC4=CC(=O)CCC34

2. Physico-chemical properties

Endpoint	**Value**	**Source**
Vapour Pressure (Pa)	$4.18x10^{-5}$	PubChem (https://pubchem.ncbi.nlm.nih.gov/compound/6230#section=Vapor-Pressure)
Water solubility (mg/L)	7.04 mg/L (at 25°C)	PubChem (https://pubchem.ncbi.nlm.nih.gov/compound/6230#section=Solubility)
logK_{ow}	2.97	PubChem (https://pubchem.ncbi.nlm.nih.gov/compound/6230#section=Octanol-Water-Partition-Coefficient)

3. Environmental fate

Endpoint	**Value**	**Source**
Sorption potential K_{oc}	220	PubChem (https://pubchem.ncbi.nlm.nih.gov/co

		mpound/6230#section=Environmental-Fate)
Partition coefficient solid-water in sediment Kp_{sed} (L/kg)		
Biodegradability	Data not available	PubChem (https://pubchem.ncbi.nlm.nih.gov/compound/6230#section=Ecological-Information)
Bioaccumulation (BCF)	37.5 (at 25°C; experimental) 42 (predicted)	US EPA (https://comptox.epa.gov/dashboard/dsstoxdb/results?search=DTXSID9023380#env-fate-transport)

4. Environmental exposure assessment

4.1 Predicted Environmental Concentration

	Description	**Source**
Tonnes/year	Manufactured and/or imported in the European Economic Area in 1-10 tonnes per year.	ECHA (https://echa.europa.eu/substance-information/-/substanceinfo/100.000.619)
Uses		
Spatial usage (by MS)		
Banned uses		
ERC code		
PEC_{fw} (mg/L)		
PEC_{sed} (mg/kg dw)		
PEC_{biota} (mg/kg)		

4.2 Measured Environmental Concentration

n. of MS	**Source of monitoring data**	**MEC values**
In Sc2 (inland whole water) monitored in 1 MS (19 sites); available 20 samples. The data quality is good (100% quantified samples), however, the data are insufficient and not union representative for making a risk	Prioritisation exercise 2014	0.0034 µg/L

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assessment.

4.3 Analytical Methods

Method	**MDL (µg/L)**	**Description/Reference**
LC-MS/MS	0.00001	Vulliet et al., 2011

5. P, B, T, C, M, R, ED properties

Substance	**Persistent (P)Bioaccumulative (B) Toxic (T)**	**Carcinogenic (C) Mutagenic (M) Reproduction toxicity (R)**	**Endocrine Disruptive (ED)**	**Comment**
Norethisterone	PBT	C*, R*	ED*	Stockholm Country Council

NOTE: *Possible

6. Hazard assessment

6.1 Ecotoxicology data

Trophic level	**Endpoint**	**Value (mg/L)**	**Reference**
Algae	Acute EC_{50} (Ecosar)	18.768	Zhou et al., 2019
Crustacean	Chronic NOEC	500	Zhou et al., 2019
Fish	**Chronic NOEC**	**0.00074**	**Zhou et al., 2019**

6.2 Mammalian toxicology data

6.3 PNEC derivation

PNEC	**Endpoint**	**Endpoint value (µg/L)**	**AF**	**PNEC value (µg/L)**
$PNEC_{fw}$	Fish chronic NOEC	0.74	50	0.0148 (Zhou et al., 2019)
$PNEC_{fw}$				0.0354 (Prioritisation exercise, Lettieri et al., 2016 and Carvalho et al., 2016)
$PNEC_{fw}$	EC_{50} (72 h)	510	1000	0.51(freshwater, ECHA)

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$PNEC_{sed}$				
$PNEC_{biota,sec\ pois}$				
$PNEC_{biota,\ hh}$				
$PNEC_{dw,\ hh}$				

7. Risk Quotient (MEC or PEC/PNEC)

RQ	**Value**
RQ_{fw} (MEC(P95)/PNEC)	0.1 (PNEC = 0.0354 µg/L) 0.23 (PNEC = 0.0148 µg/L)
RQ_{fw} (PEC/PNEC)	
RQ_{sed}	
$RQ_{biota,sec\ pois}$	
$RQ_{biota,\ hh}$	
$RQ_{dw,\ hh}$	

8. STE score

STE is not calculated since the insufficient amount of data.

9. References

Carvalho, R. N. et al. Monitoring-based exercise: second review of the priority substances list under the Water Framework Directive (https://circabc.europa.eu/w/browse/52c8d8d3-906c-48b5-a75e-53013702b20a) (2016).

Lettieri, T. et al. Modelling-based strategy for the prioritisation exercise under the Water Framework Directive, https://circabc.europa.eu/w/browse/85b46283-9353-4e67-bf56-e4d18b32cbaf). (2016).

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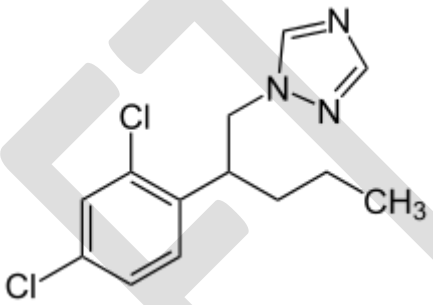
Zhou, S. et al. Optimization of screening-level risk assessment and priority selection of emerging pollutants – The case of pharmaceuticals in European surface waters. Environment International 128, pp. 1-10. doi: https://doi.org/10.1016/j.envint.2019.04.034 (2019).

DRAFT

Penconazole (CAS N. 66246-88-6)

1. Substance identity

EC name	1-[2-(2,4-dichlorophenyl)pentyl]-1H-1,2,4-triazole
EC number	266-275-6
CAS number	66246-88-6
Molecular formula	$C_{13}H_{15}Cl_2N_3$
Molecular weight	284.2
Structure	
SMILES	CCCC(CN1C=NC=N1)C2=C(C=C(C=C2)Cl)Cl

2. Physico-chemical properties

Endpoint	**Value**	**Source**
Vapour Pressure (Pa)	$3.7x10^{-5}$ at 25°C	INERIS, 2012
Water solubility (mg/L)	73 at pH 6-7 and 20°C	INERIS, 2012
logK_{ow}	3.72 at 25°C	INERIS, 2012

3. Environmental fate

Endpoint	**Value**	**Source**
Sorption potential K_{oc} (L/kg)	786 - 4120	INERIS, 2012
Partition coefficient solid-water in sediment Kp_{sed} (L/kg)		
Biodegradability	Not readily biodegradable	INERIS, 2012
Bioaccumulation (BCF)	320	INERIS, 2012

4. Environmental exposure assessment

4.1 Predicted Environmental Concentration

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	Description	Source
Tonnes/year	1 - 10 tonne registered substances	ECHA
Uses	APPROVED as PPP approved 01/01/2010 expexpiration 31/12/2021 2009/77/EC2010/34/EU Reg. (EU) No 540/2011	EU Pesticides database
Spatial usage (by MS)	Authorised as PPP in: AT, BE, BG, CY, CZ, DE, EE, EL, ES, FI, FR, HR, HU, IT, LT, LU, LV, MT, NL, PL, PT, RO, SE, SI, SK, UK (26 MS)	EU Pesticides database
Banned uses		
ERC code		
PEC_{fw} (µg/L)	Step 2: 2 - 3.3 Step 3: 0.184 - 0.556	FOCUS PEC (EFSA, 2008)
PEC_{sed} (mg/kg dw)		
PEC_{biota} (mg/kg)		

4.2 Measured Environmental Concentration

n. of MS	Source of monitoring data	MEC values
In Sc2 (inland whole water) monitored in 5 MS (1547 sites); available 14037 samples; only 2.8% quantified samples; the data quality seems poor, although all non-quantified samples were measured with LOQ ≤ 0.23 µg/L; there is a lot repeated non-quantified samples (7184; about 70.5% from all samples) with LOQ = 0.05 µg/L or LOQ = 0.02 µg/L; the data are not union representative (1 MS holds 52% of all samples, other 45% originate from 2 MS); Sc3 is not developed but is expected to be equal to Sc2 for considered PNEC.	Prioritisation dataset	Median = 0.025 µg/L MEC(p95) = 0.05 µg/L

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4.3 Analytical Methods

Method	LOQ (µg/L)	Description/Reference
Q Exactive high-performance benchtop quadrupole-Orbitrap LC–MS/MS	0.0095	Chitescu et al., 2015

5. P, B, T, C, M, R, ED properties

Substance	Persistent (P) Bioaccumulative (B) Toxic (T)	Carcinogenic (C) Mutagenic (M) Reproduction toxicity (R)	Endocrine Disruptive (ED)	Comment
	PT	R (suspected)		

Note: Suspected acutely toxic via the oral route #Harmonised classification for acute toxicity #Harmonised classification for aquatic toxicity #Harmonised classification for reprotoxicity #Suspected bioaccumulative #Suspected carcinogen #Suspected hazardous to the aquatic environment #Suspected persistent in the environment #Suspected toxic for reproduction (ECHA Annex III inventory)

6. Hazard assessment

6.1 PNEC derivation

PNEC	Endpoint	Endpoint value (µg/L)	AF	PNEC value
$PNEC_{fw}$	*NOEC Daphnia magna*	60	10	6 µg/L (AgriTox ANSES FR and INERIS, 2012)
$PNEC_{sed}$				0.252 mg/kg dw (EqP, INERIS, 2012)
$PNEC_{biota,sec\ pois}$				
$PNEC_{biota,\ hh}$				
$PNEC_{dw,\ hh}$				

7. Risk Quotient (MEC or PEC/PNEC)

RQ	Value
RQ_{fw} (MEC(P95)/PNEC)	0.008 (PNEC = 6 µg/L)
RQ_{fw} (PEC/PNEC; PNEC = 6 µg/L)	Step 2: 0.33 - 0.55 Step 3: 0.03 - 0.09

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RQ_{sed}	
$RQ_{biota,sec\ pois}$	
$RQ_{biota,\ hh}$	
$RQ_{dw,\ hh}$	

8. STE score

STE (Sc2) is not calculated (according to available data it is expected to be low since MEC(P95) < PNEC).

9. References

Chitescu, C. L., Kaklamanos, G., Nicolau, A. I. & Stolker, A. A. M. High sensitive multiresidue analysis of pharmaceuticals and antifungals in surface water using U-HPLC-Q-Exactive Orbitrap HRMS. Application to the Danube river basin on the Romanian territory. Science of The Total Environment 532, pp. 501-511. doi: https://doi.org/10.1016/j.scitotenv.2015.06.010 (2015).

ECHA. Annex III inventory. https://echa.europa.eu/information-on-chemicals/annex-iii-inventory/-/dislist/details/AIII-100.047.817

EFSA, 2008. Conclusion regarding the peer review of the pesticide risk assessment of the active substance penconazole. doi: 10.2903/j.efsa.2008.175r.

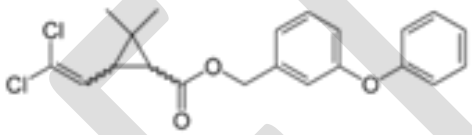
EU Pesticides database. https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.selection&language=EN

INERIS, 2012. Penconazole. Validation groupe d'experts: Novembre 2012. Version 2: 24/03/2013. DRC-13-126836-03549A

DRAFT

Permethrin (CAS N. 52645-53-1)

1. Substance identity

EC name	m-phenoxybenzyl 3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropane carboxylate
EC number	258-067-9
CAS number	52645-53-1
Molecular formula	$C_{21}H_{20}Cl_2O_3$
Molecular weight	391.28 g/mol
Structure	
SMILES	CC1(C(C1C(=O)OCC2=CC(=CC=C2)OC3=CC=CC=C3)C=C(Cl)Cl)C

2. Physico-chemical Properties

Endpoint	**Value**	**Source**
Vapour Pressure (Pa)	2.155 x 10^{-6} at 20°C, purity 99.30%	EU Assessment report, 2014
Water solubility (mg/L)	0.006 - 0.2; nearly insoluble in water 0.006 mg/L at 20°C	CCME, 2006
Log K_{ow}	6.1	

3. Environmental fate

Endpoint	**Value**	**Source**
Sorption potential K_{oc}	26.930 (log K_{oc} = 4.43)	EU Assessment report, 2014
Partition coefficient solid-water in sediment Kp_{sed} (L/kg)		
Biodegradability	Not readily biodegradable (Log P_{ow} > 3, BCF > 100)	
Bioaccumulation (BCF)	500 – 570[m] L/kg (fish)	EU Assessment report

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	(Bayer/Sumitomo) 166[m] L/kg (chironomid in water) (published study) 415[m] L/kg (chironomid in sediment) (published study) 166[m] L/kg (chironomid in porewater) (published study) 15108[e] L/kg (earthworm) (Bayer/Sumitomo)	2014

4. Environmental exposure assessment

4.1 Predicted Environmental Concentration

	Description	**Source**
Tonnes/year	1 - 10 tonne registered substances	ECHA https://echa.europa.eu/it/substance-information/-/substanceinfo/100.052.771
Uses	Permethrin is not approved anymore as PPP in the EU (in agriculture to protect crops or kill livestock parasites).	http://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.detail&language=EN&selectedID=1687
	The authorisations for permethrin as a PPP were withdrawn by a Commission decision in 2000	http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32000D0817
	Permethrin is approved in IE for use in biocidal products, wood preservatives (Product Typ 8), insecticides, acaricides and products to control other arthropods (Product Typ 18). Substance explicitly approved as biocide only.	http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32014R1090&from=EN https://echa.europa.eu/it/information-on-chemicals/biocidal-active-substances?p_p_id=echarevbiocides_WAR_echarevbiocidesportlet&p_p_lifecycle=0&p_p_col_id=column-1&p_p_col_pos=1&p_p_col_count=2&_echarevbiocides_WAR_echarevbiocidesportlet_rml_id=100.052.771
Spatial usage (by MS)		

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Banned uses		
ERC code		
PEC_{fw} (mg/L)	250 (secondary poisoning) 0.225 (ECETOC calculations, tier 2)	EU Assessment report, 2014 (page 50) Calculations of JRC
PEC_{sed} (mg/kg dw)		
PEC_{biota} (mg/kg)		

4.2 Measured Environmental Concentration

n. of MS	Source of monitoring data	MEC values
In Sc2 (inland whole water) data from 7 MS (2431 sites) with 29730 samples are available. Only 0.4% quantified samples. Data quality in Sc2 is not good. In Sc3 (inland whole water; PNEC = 0.00047 µg/L) data from 4 MS (74 sites) with 117 samples (98% quantified samples). Sc3 is not representative for EU-wide assessment.	Dataset of monitoring prioritisation 2014	MEC(P95) = 0.025 µg/L (Sc2) MEC(P95) = 0.09 µg/L (Sc3)

Note: Sc2 includes all reported quantified and non-quantified samples. The data quality for Sc2 is verified by controlling the data accuracy, checking quantification frequency of sampling and applying the LOQ-PNEC criterion to non-quantified samples (½ LOQ ≤ PNEC).

Sc3 is the main decisive dataset which includes the quantified measurements and these non-quantified samples when ½ LOQ ≤ PNEC (i.e. avoiding the non-confirmed exceedances when the non-quantified concentrations are set up equal to half of LOQ).

4.3 Analytical Methods

Method	LOQ	Description/Reference
LLE followed by HRGC/HRMS	0.000044 **µg/L** (LOD)	US EPA method 1699 (2007)
LLE-GC-MS	0.0015 **µg/L**	LLE of 1 L water; silica gel clean-up (Kupper et al., 2006)
n.a.	0.005 **µg/L**	Finland

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GC-APCI-MS/MS	0.000125 **µg/L**	Surface water (Rösch et al., 2019)
GC-MS/MS	0.2 µg/kg	Sediment (USGS, 2009)

5. P, B, T, C, M, R, ED properties

Substance	Persistent (P) Bioaccumulative (B) Toxic (T)	Carcinogenic (C) Mutagenic (M) Reproduction toxicity (R)	Endocrine Disruptive (ED)	Comment
Permethrin	P, B and T*	M	ED	

* Not listed in the PBT list from ECHA https://echa.europa.eu/it/information-on-chemicals/pbt-vpvb-assessments-under-the-previous-eu-chemicals-legislation. Harmonised classification for acute toxicity#Harmonised classification for aquatic toxicity#Harmonised classification for skin sensitisation#Suspected bioaccumulative#Suspected hazardous to the aquatic environment#Suspected mutagen#Suspected persistent in the environment#Suspected skin sensitiser (ECHA Annex III inventory)

6. Hazard assessment

6.1 Ecotoxicology data

Freshwater

Species	Time-scale	Endpoint	Toxicity (µg/L)
Algae			
Pseudokirchneriella subcapitata	72 h, cell density	NOEC	< 3.1
Invertebrates			
Daphnia magna	21 d, reproduction	NOEC	0.0047
Fish			
Zebrafish	35 d, survival	NOEC	0.41
Pimephales promelas	32 d, survival	NOEC	0.66
Cyprinodon variegatus	28 d, survival	NOEC	10

Sediment

Species	Time-scale	Endpoint	Toxicity (µg/L)
Chironomus riparius	5-day after last emergence	NOEC	< 3.1

6.2 Mammalian toxicology data

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Mammalian toxicity	Rat, acute toxicity, oral, LD_{50} 480 mg/kg bw/day	EU Assessment report 2014 (Bayer/Sumitomo)
	Rat, chronic toxicity, NOAEL 5 mg/kg bw/day	EU Assessment report 2014
	Rat, acute toxicity, oral, LD_{50} 554 mg/kg bw/day	EU Assessment report 2014 (Tagros)
	Rat, acute toxicity, dermal, LD_{50} > 2000 mg/kg bw/day	EU Assessment report 2014 (Bayer/Sumitomo and Tagros)
	Rat, acute toxicity, inhalation, LC_{50} 23.5 mg/L	EU Assessment report 2014 (Bayer/Sumitomo)
	Rat, acute toxicity, inhalation, LC_{50} > 4.638 (MAC) mg/L	EU Assessment report 2014 (Tagros)
	Dog, oral, adaptive hepatic changes, 1-year, NOAEL 5 mg/kg bw/day	EU Assessment report 2014 (Bayer/Sumitomo)
	Dog, increased liver weight, 6-month, NOAEL 10 mg/kg bw/day	EU Assessment report 2014
	Rat, dermal study, 90-day, NOAEL 1000 mg/kg bw/day, LOAEL 2000 mg/kg bw/day	EU Assessment report 2014 (Tagros)
	Rat, inhalation, 90-day, NOAEL 0.2201 mg/L (equivalent to 59.43 mg/kg bw/day); LOAEL 0.4363 mg/L (equivalent to 117.8 mg/kg bw/day)	EU Assessment report 2014 (Tagros)
	Rat, reproductive toxicity, NOAEL 180 mg/kg bw/day (high dose); LOAEL > 180 mg/kg bw/day (high dose)	EU Assessment report 2014 (Bayer/Sumitomo)
	Rat, reproductive toxicity, NOAEL 500 mg/kg bw/day (high dose); LOAEL > 500 mg/kg bw/day (high dose)	EU Assessment report 2014 (Tagros)
	Rabbit, developmental NOAEL 400 mg/kg bw/day	EU Assessment report 2014
	Rat, carcinogenicity, 104-week, NOAEL 50 mg/kg bw/day	EU Assessment report 2014 and WHO, 2014
	Mouse, carcinogenicity, 98-week, NOAEL 150	EU Assessment report 2014 and

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	mg/kg bw/day	WHO, 2014

6.3 PNEC derivation

PNEC	Endpoint	Endpoint value	AF	PNEC value
$PNEC_{fw}$	21 d, reproduction (*Daphnia magna*)	0.0047 µg/L	10	0.00047 µg/L (JRC draft dossier, 2016)
$PNEC_{sed}$	5-day (*Chironomus riparus*)	0.1 mg/kg	100	0.001 $mg.kg^{-1}$ (JRC draft dossier, 2016)
$PNEC_{biota,sec\ pois}$				
$PNEC_{biota,\ hh}$				
$PNEC_{dw,\ hh}$				

7. Risk Quotient (MEC or PEC/PNEC)

RQ	Value
RQ_{fw} (for MEC(P95) and PNEC = 0.00047 µg/L)	53 (Sc2) 191 (Sc3)
RQ_{fw} (PEC/PNEC)	

8. STE scores

2.41 (Sc2; PNEC=0.00047 µg/L)

2.29 (Sc3; PNEC=0.00047 µg/L)

Note: STE is a risk-evaluation method/tool developed by the JRC (Loos et al., 2018, EUR 29173 EN). Minimal score = 0 (no risk); Maximal score = 3 (very high risk).

9. References

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EU Assessment report, 2014. Regulation (EU) No 528/2012 concerning the making available on the market and use of biocidal products. Evaluation of active substances. Assessment Report. Permethrin. Product-Type 8 (Wood Preservative); Rapporteur: Ireland.

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USGS. 2007. Hladik, M. & USGS. Methods Development for the Analysis of Pyrethroid Pesticides in Environmental Samples. FINAL REPORT FOR CALFED Recipient Agreement No. ERP-02-P42.

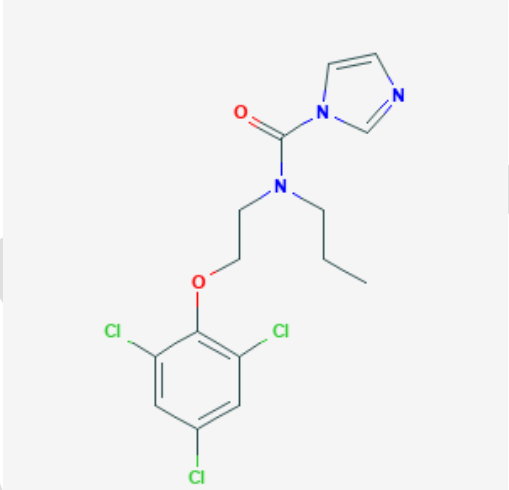
USGS. Hladik, M. L. & Kuivila, K. M. Assessing the Occurrence and Distribution of Pyrethroids in Water and Suspended Sediments. Journal of Agricultural and Food Chemistry 57, pp. 9079-9085. doi: 10.1021/jf9020448 (2009).

USGS. Hladik, M. L., Smalling, K. L. & Kuivila, K. M. Methods of Analysis—Determination of Pyrethroid Insecticides in Water and Sediment Using Gas Chromatography/Mass Spectrometry. Techniques and Methods 5–C2. U.S. Department of the Interior. U.S., Geological Survey, Reston, Virginia (2009).

DRAFT

Prochloraz (CAS N. 67747-09-5)

1. Substance identity

EC name	N-propyl-N-[2-(2,4,6-trichlorophenoxy)ethyl]imidazole-1-carboxamide
EC number	266-994-5
CAS number	67747-09-5
Molecular formula	$C_{15}H_{16}Cl_3N_3O_2$
Molecular weight	376.7 g/mol
Structure	
SMILES	CCCN(CCOC1=C(C=C(C=C1Cl)Cl)Cl)C(=O)N2C=CN=C2

2. Physico-chemical properties

Endpoint	**Value**	**Source**
Vapour Pressure (Pa)	1.5	PubChem (https://pubchem.ncbi.nlm.nih.gov/compound/Prochloraz#section=Vapor-Pressure)
Water solubility (mg/L)	9.03	PubChem (https://pubchem.ncbi.nlm.nih.gov/compound/Prochloraz#section=Solubility)
logK_{ow}	4.12	Cravedi et al., 2001

3. Environmental fate

Endpoint	**Value**	**Source**
Sorption potential K_{oc}	1440.5 -5650.5 mL/g	EFSA, 2011

Partition coefficient solid-water in sediment Kp_{sed} (L/kg)		
Biodegradability	No biodegradable	EFSA, 2011
Bioaccumulation (BCF)	196.5	EFSA, 2011

4. Environmental exposure assessment

4.1 Predicted Environmental Concentration

	Description	**Source**
Tonnes/year	Criteria for 1-10 tonne registered substance	ECHA (https://echa.europa.eu/substance-information/-/substanceinfo/100.060.885)
Uses	Approved on 01/01/2012 with expiration date on 31/12/2023 Reg. (EU) No 1143/2011Reg. (EU) No 2019/291Reg. (EU) No 540/2011 (2008/934) Use authorised in: AT, BE, BG, CZ, DE, EE, EL, ES, FI, FR, HR, HU, IE, IT, LT, LU, LV, MT, NL, PL, RO, SI, SK, UK"	EU Pesticides Database (https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.detail&language=EN&selectedID=1753)
Spatial usage (by MS)		
Banned uses		
ERC code		
PEC_{fw} (µg/L)	0.1 - 3	FOCUS Step 3 of PEC for winter cereals (EFSA, 2011)
PEC_{sed} (mg/kg dw)		
PEC_{biota} (mg/kg)		

4.2 Measured Environmental Concentration

n. of MS	**Source of monitoring data**	**MEC values**
In Sc2 (inland whole water) monitored in 7 MS (2557 sites); available 32674	Prioritisation dataset	Median = 0.02 µg/L; MEC(P95) = 0.05 µg/L

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samples; only 1.6% are quantified samples; the data quality is not good, although all non-quantified samples have LOQ ≤ 0.4 µg/L; there are many repeated non-quantified samples (23462; about 72% from total) with LOQs from 0.01 µg/L to 0.1 µg/L; the data are not union representative since one MS holds 84% of samples; Sc3 is not developed since the low data quality.	

4.3 Analytical Methods

Method	**LOQ (µg/L)**	**Description/Reference**
Q Exactive high-performance benchtop quadrupole-Orbitrap LC–MS/MS	0.00851	Chitescu et al., 2015

5. P, B, T, C, M, R, ED properties

Substance	**Persistent (P) Bioaccumulative (B) Toxic (T)**	**Carcinogenic (C) Mutagenic (M) Reproduction toxicity (R)**	**Endocrine Disruptive (ED)**	**Comment**
Prochloraz	P, vP, T	C*, R*	ED*	Two PBT criteria (EU Pesticides database)

*possible

6. Hazard assessment

6.1 Ecotoxicology data

Trophic level	**Endpoint**	**Value (µg/L)**	**Reference**
Algae	Short term L(E)C_{50}	192	Zhou et al., 2019
Crustacean	Short term L(E)C_{50}	1290	Zhou et al., 2019
Fish	**Short term L(E)C_{50}**	**161**	**Zhou et al., 2019**

6.2 PNEC derivation

PNEC	**Endpoint**	**Endpoint value (µg/L)**	**AF**	**PNEC value (µg/L)**

$PNEC_{fw}$	Fish, Short term $L(E)C_{50}$	161	1000	0.161 (Zhou et al., 2019)
				10 (AgriTox ANSES FR)
$PNEC_{sed}$				
$PNEC_{biota,sec\ pois}$				
$PNEC_{biota,\ hh}$				
$PNEC_{dw,\ hh}$				

7. Risk Quotient (MEC or PEC/PNEC)

RQ	**Value**
RQ_{fw} (MEC(P95)/PNEC)	0.005 (PNEC = 10 µg/L) 0.3 (PNEC = 0.161 µg/L)
RQ_{fw} (PEC/PNEC)	0.01 - 0.3 (PNEC = 10 µg/L) 0.6 - 18.6 (PNEC = 0.161 µg/L)
RQ_{sed}	
$RQ_{biota,sec\ pois}$	
$RQ_{biota,\ hh}$	
$RQ_{dw,\ hh}$	

8. STE score

STE (Sc2) is not calculated (according to available data it is expected to be low since MEC(P95) < PNECs).

9. References

AgriTox ANSES FR. http://www.agritox.anses.fr/php/donnees-essentielles.php.

Chitescu, C.L., et al., High sensitive multiresidue analysis of pharmaceuticals and antifungals in surface water using U-HPLC-Q-Exactive Orbitrap HRMS. Application to the Danube river basin on the Romanian territory. Science of The Total Environment 532, pp. 501-511 (2015).

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Cravedi, J.P., et al., Metabolic fate of 2,4-dichloroaniline, prochloraz and nonylphenol diethoxylate in rainbow trout: a comparative in vivo/in vitro approach. Aquatic Toxicology 53(3), pp. 159-172 (2001).

EFSA European Food Safety Authority. Conclusion on Pesticide peer review: Conclusion on the peer review of the pesticide risk assessment of the active substance prochloraz. EFSA Journal 9(7), 2323. https://efsa.onlinelibrary.wiley.com/doi/pdf/10.2903/j.efsa.2011.2323 (2011).

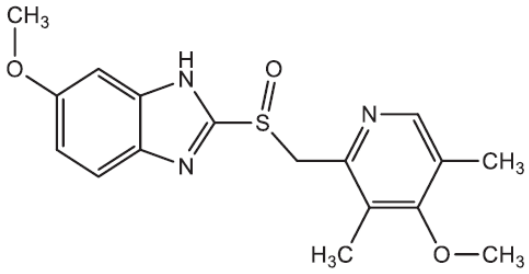
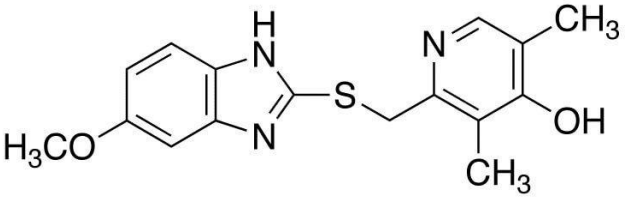
EU Pesticides database. https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.detail&language=EN&selectedID=1753

Zhou, S., et al., Optimization of screening-level risk assessment and priority selection of emerging pollutants – The case of pharmaceuticals in European surface waters. Environment International 128, pp. 1-10 (2019).

DRAFT

Omeprazole (CAS N. 73590-58-6) and 4-hydroxy omeprazole sulphide (CAS N. 103876-98-8)

Substance identity

EC name	
EC number	615-996-8
CAS number	73590-58-6 (Omeprazole) 103876-98-8 (4-hydroxy omeprazole sulphide)
Molecular formula	$C_{17}H_{19}N_3O_3S$ (Omeprazole) $C_{16}H_{17}N_3O_2S$ (4-hydroxy omeprazole sulphide)
Molecular weight	345.4 g/mol (Omeprazole) 315.39 g/mol (4-hydroxy omeprazole sulphide)
Structure	 Omeprazole  4-hydroxy omeprazole sulphide
SMILES	CC1=CN=C(C(=C1OC)C)CS(=O)C2=NC3=C(N2)C=C(C=C3)OC (Omeprazole) CC1=CNC(=C(C1=O)C)CSC2=NC3=C(N2)C=C(C=C3)OC (4-hydroxy omeprazole sulphide)

Physico-chemical properties

Endpoint	**Value**	**Source**
Vapour Pressure (Pa)		
Water solubility (mg/L)		
logK_{ow}	3.4 (Omeprazole, Theoretical)	Becker et al., 2020

	2.23 (Omeprazole, Experimental) 3.59 (4-hydroxy omeprazole sulphide, Theoretical)	

Environmental fate

Endpoint	**Value**	**Source**
Sorption potential K_{oc}	871.3 kg/L	Domènech et al., 2011
Partition coefficient solid-water in sediment Kp_{sed} (L/kg)		
Biodegradability		
Bioaccumulation (BCF)		

Environmental exposure assessment

4.1 Predicted Environmental Concentration

	Description	**Source**
Tonnes/year		
Uses		
Spatial usage (by MS)		
Banned uses		
ERC code		
PEC_{fw} (mg/L)		
PEC_{sed} (mg/kg dw)		
PEC_{biota} (mg/kg)		

4.2 Measured Environmental Concentration

n. of MS	**Source of monitoring data**	**MEC values**
No available data in the dataset of the prioritization exercise.		

4.3 Analytical Methods

Method	**LOQ (µg/L)**	**Description/Reference**

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UHPLC-QTOF MS (surface and wastewater)		Boix et al., 2014
LC-MS/MS	0.00157	Kosma et al., 2016

P, B, T, C, M, R, ED properties

Substance	**Persistent (P) Bioaccumulative (B) Toxic (T)**	**Carcinogenic (C) Mutagenic (M) Reproduction toxicity (R)**	**Endocrine Disruptive (ED)**	**Comment**
Omeprazole	T	M*, R*		
4-hydroxy omeprazole sulphide		M*		

*Suspected

Hazard assessment

6.1 Ecotoxicology data

Trophic level	**Endpoint**	**Value (mg/L)**	**Reference**
Green algae	Green algae, EC_{50} Omeprazole (Ecosar)	0.38	Wielens Becker et al., 2020
Aquatic Invertebrate	*Daphnid, L*C_{50} Omeprazole (Ecosar)	3.26	Wielens Becker et al., 2020
Fish	Fish*, L*C_{50} Omeprazole (Ecosar)	0.78	Wielens Becker et al., 2020
Algae	**Acute EC_{50} Omeprazole (Ecosar)**	**0.21**	**Zhou et al., 2019**
Crustacean	Acute EC_{50} Omeprazole (Ecosar)	1.27	Zhou et al., 2019
Fish	NOEC Omeprazole (Ecosar)	4.99	Zhou et al., 2019
Green algae	**Green algae, EC_{50} 4-hydroxy omeprazole sulphide (Ecosar)**	**0.28**	**Wielens Becker et al., 2020**
Aquatic Invertebrate	*Daphnid, L*C_{50} 4-hydroxy omeprazole	2.27	Wielens Becker et al., 2020

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	sulphide (Ecosar)		
Fish	Fish, *LC*$_{50}$ 4-hydroxy omeprazole sulphide (Ecosar)	0.46	Wielens Becker et al., 2020

6.2 Mammalian toxicology data

6.3 PNEC derivation

PNEC	**Endpoint**	**Endpoint value (µg/L)**	**AF**	**PNEC value (µg/L)**
PNEC$_{fw}$	Algae Acute EC$_{50}$ Omeprazole (Ecosar)	210	100	2.1
	Green algae, EC$_{50}$ 4-hydroxy omeprazole sulphide (Ecosar)	280	1000	0.28
PNEC$_{sed}$				
PNEC$_{biota,sec\ pois}$				
PNEC$_{biota,\ hh}$				
PNEC$_{dw,\ hh}$				

7. Risk Quotient (MEC or PEC/PNEC)

RQ	**Value**
RQ$_{fw}$ (MEC(P95)/PNEC)	
RQ$_{fw}$ (PEC/PNEC)	
RQ$_{sed}$	
RQ$_{biota,sec\ pois}$	
RQ$_{biota,\ hh}$	
RQ$_{dw,\ hh}$	

8. STE score

Not calculated since missing monitoring data.

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9. References

Boix, C. et al. Identification of new omeprazole metabolites in wastewaters and surface waters. Science of The Total Environment 468-469, pp. 706-714. doi: https://doi.org/10.1016/j.scitotenv.2013.08.095 (2014).

Domènech, X., M. Ribera, and J. Peral, Assessment of Pharmaceuticals Fate in a Model Environment. Water, Air, & Soil Pollution 218(1), pp. 413-422 (2011).

Kosma, C. I., Lambropoulou, D. A. & Albanis, T. A. Analysis, occurrence, fate and risks of proton pump inhibitors, their metabolites and transformation products in aquatic environment: A review. Science of The Total Environment 569-570, pp. 732-750. doi: https://doi.org/10.1016/j.scitotenv.2016.06.160 (2016).

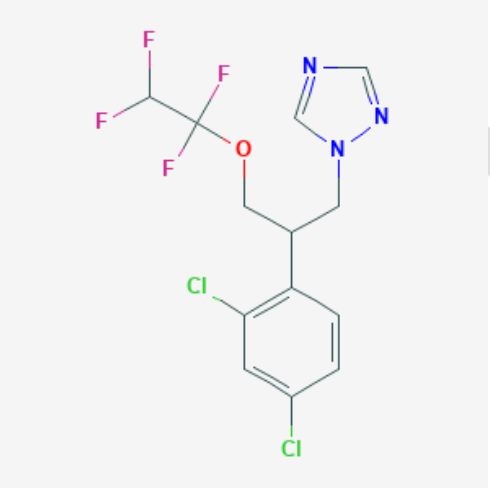
Wielens Becker, R., et al., Investigation of pharmaceuticals and their metabolites in Brazilian hospital wastewater by LC-QTOF MS screening combined with a preliminary exposure and in silico risk assessment. Science of The Total Environment 699, 134218 (2020).

Zhou, S., et al., Optimization of screening-level risk assessment and priority selection of emerging pollutants – The case of pharmaceuticals in European surface waters. Environment International 128, pp. 1-10 (2019).

DRAFT

Tetraconazole (CAS N. 112281-77-3)

1. Substance identity

EC name	
EC number	407-760-6 691-058-1
CAS number	112281-77-3
Molecular formula	$C_{13}H_{11}Cl_2F_4N_3O$
Molecular weight	372.14 g/mol
Structure	
SMILES	C1=CC(=C(C=C1Cl)Cl)C(CN2C=NC=N2)COC(C(F)F)(F)F

2. Physico-chemical properties

Endpoint	Value	Source
Vapour Pressure (Pa)	$1.8x10^{-4}$	INERIS, 2011 PubChem (https://pubchem.ncbi.nlm.nih.gov/compound/Tetraconazole#section=Vapor-Pressure)
Water solubility (mg/L)	150 (at 20°C) 156.6 (at 20°C, pH 7)	PubChem (https://pubchem.ncbi.nlm.nih.gov/compound/Tetraconazole#section=Density) INERIS, 2011

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Log K_{ow}	3.56	PubChem (https://pubchem.ncbi.nlm.nih.gov/compound/Tetraconazole#section=Octanol-Water-Partition-Coefficient)

3. Environmental fate

Endpoint	**Value**	**Source**
Sorption potential K_{oc}	531-1922	PubChem (https://pubchem.ncbi.nlm.nih.gov/compound/Tetraconazole#section=Environmental-Fate-Exposure-Summary)
Partition coefficient solid-water in sediment Kp_{sed} (L/kg)		
Biodegradability	Non biodegradable	INERIS, 2011
Bioaccumulation (BCF)	110 42	PubChem (https://pubchem.ncbi.nlm.nih.gov/compound/Tetraconazole#section=Environmental-Fate-Exposure-Summary) INERIS, 2011

4. Environmental exposure assessment

4.1 Predicted Environmental Concentration

	Description	**Source**
Tonnes/year	Registred substance 1-10 Tonne	ECHA (https://echa.europa.eu/substance-information/-/substanceinfo/100.218.522)
Uses	Approved as PPP on 01/01/2010, expiration of approval 31/12/2021 Legislation: 2009/82/EUReg. (EU) No 540/2011 Authorised in: AT, BE, BG, CZ, DE, EL, ES, FR, HR, HU, IT, MT, PL, PT, RO, SI, SK, UK	EU Pesticides Database (https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.detail&language=EN&selectedID=1928)
Spatial usage (by MS)		
Banned uses		

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ERC code		
PEC_{fw} (µg/L)	2 - 3	FOCUS Step 2 PEC (EFSA, 2008)
PEC_{sed} (mg/kg dw)		
PEC_{biota} (mg/kg)		

4.2 Measured Environmental Concentration

n. of MS	Source of monitoring data	MEC values
In Sc2 (inland whole water) monitored in 2 MS (1132 sites); available 11075 samples; only 0.1% quantified samples; the data quality seems poor since there is a lot repeated non-quantified samples (9778; about 88% from total) with LOQs of 0.02; 0.05 and 0.1 µg/L coming from 1 MS; the data are not union representative; Sc3 is not developed since the low data quality but is expected to be equal to Sc2 for considered PNECs.	Prioritisation datasset	MEC(P95) = 0.05 µg/L

4.3 Analytical Methods

Method	LOQ (µg/L)	Description/Reference
LC-ESI-Q-Orbitrap-MS	0.0025	Casado et al., 2019

5. P, B, T, C, M, R, ED properties

Substance	Persistent (P) Bioaccumulative (B) Toxic (T)	Carcinogenic (C) Mutagenic (M) Reproduction toxicity (R)	Endocrine Disruptive (ED)	Comment
Tetraconazole	P,T, vP	R*		Substances predicted as likely to meet criteria for category 1A or 1B (ECHA: https://echa.europa.eu/substance-information/-/substanceinfo/

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Substance	Persistent (P) Bioaccumulative (B) Toxic (T)	Carcinogenic (C) Mutagenic (M) Reproduction toxicity (R)	Endocrine Disruptive (ED)	Comment
				100.218.522)

*suspected

6. Hazard assessment

6.1 Ecotoxicology data

Trophic level	Endpoint	Value (µg/L)	Reference
Algae	*Scenedesmus subspicatus* EC_{50}	410	INERIS, 2011
Algae	*Lemna gibba* EC_{10}	32	INERIS, 2011
Aquatic invertebrate	*Daphnia magna* EC_{50}	3000	INERIS, 2011
Aquatic invertebrate	*Daphnia magna* EC_{10}	190	INERIS, 2011
Fish	*Lepomis macrochirus* EC_{50}	4300	INERIS, 2011
Fish	*Pimephales promelas* *EC_{10}*	300	INERIS, 2011

6.2 Mammalian toxicology data

6.3 PNEC derivation

PNEC	Endpoint (µg/L)	Endpoint value (µg/L)	AF	PNEC value (µg/L)
$PNEC_{fw}$				1.9 (JRC Prioritisation, Carvalho et al., 2016 and Lettieri et al., 2016)

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	Lemna gibba EC_{10}	32	10	3.2 (INERIS, 2011)
				4.2 (AgriTox ANSES FR)
$PNEC_{sed}$				
$PNEC_{biota,sec\ pois}$				
$PNEC_{biota,\ hh}$				
$PNEC_{dw,\ hh}$				

7. Risk Quotient (MEC or PEC/PNEC)

RQ	**Value**
RQ_{fw} (MEC(P95)/PNEC)	0.03 (PNEC= 1.9 µg/L)
RQ_{fw} (PEC/PNEC)	1.1 - 1.6 (PNEC= 1.9 µg/L)
RQ_{fw}	

8. STE score

0 (PNEC = 1.9 µg/L)

9. References

Casado, J., Brigden, K., Santillo, D. & Johnston, P. Screening of pesticides and veterinary drugs in small streams in the European Union by liquid chromatography high resolution mass spectrometry. Science of The Total Environment 670, pp. 1204-1225. doi: https://doi.org/10.1016/j.scitotenv.2019.03.207 (2019).

Carvalho, R. N. et al. Monitoring-based exercise: second review of the priority substances list under the Water Framework Directive (https://circabc.europa.eu/w/browse/52c8d8d3-906c-48b5-a75e-53013702b20a) (2016).

EFSA, 2008. Conclusion regarding the peer review of the pesticide risk assessment of the active substance Tetraconazole. EFSA Scientific Report (2008) 152, 1-86

EU Pesticides Database https://ec.europa.eu/food/plant/pesticides/eu-pesticides-database/public/?event=activesubstance.detail&language=EN&selectedID=1928

INERIS, 2011. Tetraconazole. Validation groupe d'experts: Octobre 2011. Version 1: 06/01/2012. DRC-12-118981-00250.

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Lettieri, T. et al. Modelling-based strategy for the prioritisation exercise under the Water Framework Directive, https://circabc.europa.eu/w/browse/85b46283-9353-4e67-bf56-e4d18b32cbaf) (2016).

DRAFT

Trimethoprim (CAS N. 738-70-5)

1.Substance identity

EC name	Trimethoprim
EC number	212-006-2
CAS number	738-70-5
Molecular formula	$C_{14}H_{18}N_4O_3$
Molecular weight	290.323 g/mol
Structure	
SMILES	COC1=CC(=CC(=C1OC)OC)CC2=CN=C(N=C2N)N

2. Physico-chemical properties

Endpoint	**Value**	**Source**
Vapour Pressure (Pa)	1.00E-06 (at 25°C) 4.97E-07(at 15°C)	https://www.rivm.nl/bibliotheek/rapporten/601711003.pdf
Water solubility (mg/L)	400 (at 25°C)	HSDB (https://toxnet.nlm.nih.gov/cgi-bin/sis/search2/r?dbs+hsdb:@term+@rn+@rel+738-70-5)
logK_{ow}	0.91 0.64 to 1.15	RIVM, 2011 Straub, 2013

3. Environmental fate

Endpoint	Value	Source
Sorption potential K_{oc} (L/kg)	760	RIVM, 2011
Partition coefficient solid-water in sediment Kp_{sed} (L/kg)	22.8 Raw sewage 28.12 Act. Sludge	RIVM, 2011
Biodegradability	TMP is recalcitrant to biodegradation in standard ready and inherent tests and also in a standard sewage treatment plants model test at low concentration. However, good removal (> 50%) was seen in tests performed with aerobic activated sludge with a long sludge retention time.	Straub, 2013
Bioaccumulation (BCF)	3	HSDB (https://toxnet.nlm.nih.gov/cgi-bin/sis/search2/r?dbs+hsdb:@term+@rn+@rel+738-70-5)

4. Environmental exposure assessment

4.1 Predicted Environmental Concentration

	Description	Source
Tonnes/year		
Uses		
Spatial usage (by MS)		
Banned uses		
ERC code		
PEC_{fw} (µg/L)	0.0734	RIVM, 2011
PEC_{sed} (mg/kg dw)		
PEC_{biota} (mg/kg)		

4.2 Measured Environmental Concentration

n. of MS	Source of monitoring	MEC values

DRAFT

	data	
In Sc2 (inland whole water) data from 4 MS (352 sites) with 4613 samples are available. About 26% of samples are quantified. Data quality in Sc2 seems to be acceptable (LOQs ≤ 0.03 µg/L for non-quantified samples) but the data are not union representative (76% of all samples originate from one MS; 21% from another MS). Sc3 is expected to be equal to Sc2 for considered PNECs.	Dataset of monitoring prioritisation 2014	MEC(P95) = 0.07 µg/L (Sc2)

4.3 Analytical Methods

Method	**LOQ (µg/L)**	**Description/Reference**
LC–MS/MS	0.01721	Chitescu et al., 2015
LC-MS/MS	0.0005	Papageorgiou et al., 2019
SPE followed by UHPLC-QqLIT-MS	river water 0.0002	Mandaric et al., 2017

5. P, B, T, C, M, R, ED properties

Substance	**Persistent (P) Bioaccumulative (B) Toxic (T)**	**Carcinogenic (C) Mutagenic (M) Reproduction toxicity (R)**	**Endocrine Disruptive (ED)**	**Comment**
Trimethoprim	P (suspected)TP	C (suspected) M and R		

NOTE: Suspected carcinogen #Suspected hazardous to the aquatic environment #Suspected mutagen #Suspected persistent in the environment #Suspected toxic for reproduction.

6. Hazard assessment

Trophic level	**Endpoint**	**Value (mg/L)**	**Reference**
Algae	Chronic NOEC *Pseudokirchneriella subcapitata* growth inhibition	16	Young et al., 2008
Invertebrate	Chronic NOEC Crustacea	3.12	De Liguoro et al., 2012
Fish	Chronic NOEC	0.157	Zhou et al., 2019

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6.1 PNEC derivation

PNEC	Endpoint	Endpoint value	AF	PNEC value (µg/L)
$PNEC_{fw}$	Acute algae	16	1000	16 (RIVM, 2011)
$PNEC_{fw}$				0.5 (PNEC-MIC, AMR industry alliance)
$PNEC_{fw}$	NOEC (Fish)	157 µg/L	10	15.7 (Zhou et al., 2019)
$PNEC_{fw}$	NOEC 21 d (*Daphnia magna*)	4326.66 µg/L	100	43.3 (JRC derivation 2019)
$PNEC_{fw}$				60 (Swiss ECOTOX centre modelling-based exercise 2016)
$PNEC_{fw}$				120 (EQS chronic, Swiss ECOTOX centre 2015)
$PNEC_{sed}$				
$PNEC_{biota,sec\ pois}$				
$PNEC_{biota,\ hh}$				
$PNEC_{dw,\ hh}$				

7. Risk Quotient (MEC or PEC/PNEC)

RQ	Value
RQ_{fw} (MEC(P95)/PNEC)	0.001 (Sc2; PNEC = 60 µg/L) 0.13 (PNEC = 0.5 µg/L)
RQ_{fw}(PEC/PNEC)	0.0046 (PNEC = 16 µg/L (RIVM, 2011)
RQ_{sed}	
$RQ_{biota,sec\ pois}$	
$RQ_{biota,\ hh}$	
$RQ_{dw,\ hh}$	

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8. STE score

0 (Sc2; PNEC = 60 µg/L)

9. References

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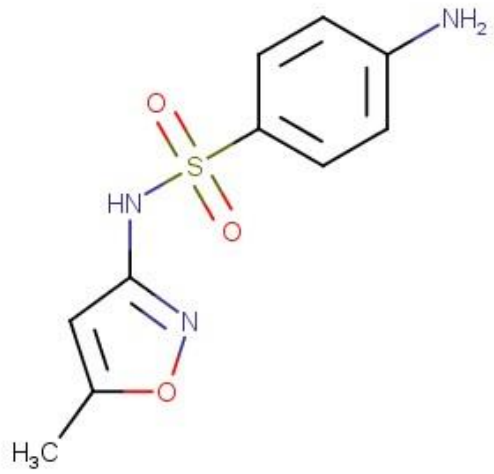
DRAFT

Sulfamethoxazole (CAS N. 723-46-6)

1. Substance identity

EC name	Sulfamethoxazole
EC number	211-963-3
CAS number	723-46-6
Molecular formula	$C_{10}H_{11}N_3O_3S$
Molecular weight	253.276 g/mol
Structure	
SMILES	CC1=CC(=NO1)NS(=O)(=O)C2=CC=C(C=C2)N

2. Physico-chemical properties

Endpoint	**Value**	**Source**
Vapour Pressure (Pa)	1.74E-05 (at 25°C) 3.96E-06 (at 15°C)	https://www.rivm.nl/bibliotheek/rapporten/601711003.pdf
Water solubility (mg/L)	610 (at 37°C) 454 (at 15°C)	https://www.drugbank.ca/drugs/DB01015 https://www.rivm.nl/bibliotheek/rapporten/601711003.pdf
logK_{ow}	0.89	HSDB (https://toxnet.nlm.nih.gov/cgi-bin/sis/search2/r?dbs+hsdb:@term+@rn+@rel+723-46-6) https://www.rivm.nl/bibliotheek/rapporten/601711003.pdf

3. Environmental fate

Endpoint	Value	Source
Sorption potential K_{oc}	258	https://www.rivm.nl/bibliotheek/rapporten/601711003.pdf
Partition coefficient solid-water in sediment Kp_{sed} (L/kg)	77.49 raw sewage 95.571 act. sludge	https://www.rivm.nl/bibliotheek/rapporten/601711003.pdf
Biodegradability	Sulfonamide antimicrobials are not readily biodegraded and persist in soils	https://pubchem.ncbi.nlm.nih.gov/compound/Sulfamethoxazole#section=Artificial-Pollution-Sources
Bioaccumulation (BCF)	3	HSDB (https://toxnet.nlm.nih.gov/cgi-bin/sis/search2/r?dbs+hsdb:@term+@rn+@rel+723-46-6)

4. Environmental exposure assessment

4.1 Predicted Environmental Concentration

	Description	Source
Tonnes/year	1 - 10 tonne registered substances	ECHA https://echa.europa.eu/it/substance-information/-/substanceinfo/100.010.877
Uses	Antibacterial drug used since the 1960s to treat Acute urinary tract infections, gonorrhoea, meningitis and serious respiratory tract infections (Pneumocystis carinii) and prophylactically against susceptible meningococci. The combination with trimethoprim is used mainly for the treatment of urinary tract infections, with pyrimethamine, it is used in the treatment of chloroquine-resistant *Plasmodium falciparum* malaria.	https://monographs.iarc.fr/wp-content/uploads/2018/06/mono79-15.pdf
Spatial usage (by MS)	Listed in the pharmacopoeias of France, Germany, Italy, Poland, and Czech Republic. Registered for human use in	https://monographs.iarc.fr/wp-content/uploads/2018/06/mono79-15.pdf

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	Finland, Ireland, Netherlands, Portugal, Spain and Sweden.	
Banned uses		
ERC code		
PEC_{fw} (µg/L)	0.0513	RIVM, 2011 It should be noted that hospital use is not included in this study, nor are over-the-counter use or veterinarian use. Including these in the calculations would lead to higher PEC.
PEC_{sed} (mg/kg dw)		
PEC_{biota} (mg/kg)		

4.2 Measured Environmental Concentration

n. of MS	Source of monitoring data	MEC values
In Sc2 (inland whole water) data from 14 MS (1023 sites) with 11684 samples are available. About 65% of samples are quantified. The data quality in Sc2 seems to be acceptable (LOQs ≤ 0.1 µg/L for non-quantified samples; lowest PNEC = 0.1 µg/L) but the data are not union representative (65% of all samples originate from one MS; 18.6% from another MS). Sc3 is expected to be equal to Sc2 for considered PNECs.	Dataset of monitoring prioritisation 2014	MEC(P95) = 1.17 µg/L (Sc2)

4.3 Analytical Methods

Method	LOQ (µg/L)	Description/Reference
Q Exactive high-performance benchtop quadrupole-Orbitrap LC–MS/MS	0.0030	Chitescu et al., 2015
LC-MS/MS	0.0022	Papageorgiou et al., 2019
SPE followed by UHPLC-QqLIT-MS	0.0008 (river water)	Mandaric et al., 2017

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5. P, B, T, C, M, R, ED properties

Substance	Persistent (P) Bioaccumulative (B) Toxic (T)	Carcinogenic (C) Mutagenic (M) Reproduction toxicity (R)	Endocrine Disruptive (ED)	Comment
Sulfamethoxazole	P, T	C*, M*, R*		

NOTE: *Suspected in ECHA. Suspected carcinogen #Suspected hazardous to the aquatic environment #Suspected mutagen #Suspected persistent in the environment #Suspected toxic for reproduction (ECHA. Annex III inventory)

6. Hazard assessment

Trophic level	Endpoint	Value (mg/L)	Reference
Algae	Chronic	0.5	Zhou et al., 2019
Algae	Chronic NOEC	0.22	RIVM, 2011
Invertebrate	Chronic NOEC Crustacea	0.0059	RIVM, 2011
Invertebrate	Chronic Crustacea	0.120	Zhou et al., 2019
Fish	Chronic NOEC	0.01	RIVM, 2011
Fish	Chronic NOEC	0.533	Zhou et al., 2019

6.1 PNEC derivation

PNEC	Endpoint	Endpoint value (µg/L)	AF	PNEC value (µg/L)
$PNEC_{fw}$	NOEC 21 d (*Limnodynastes peronei*)	10	100	0.1 (JRC derivation, 2019)
$PNEC_{fw}$				0.48 (SSD approach, EQS JRC dossier, 2015)
$PNEC_{fw}$	Chronic NOEC Crustacea	5.9	10	0.59 (RIVM, 2011)
$PNEC_{fw}$	Chronic NOEC Crustacea	5.9	10	0.6 (EQS chronic, Swiss ECOTOX centre, 2016/JRC dossier, 2015)

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$PNEC_{fw}$	NOEC (Crustaceans)	120	50	2.4 (Zhou et al., 2019)
$PNEC_{fw}$				16 (PNEC-MIC, AMR industry alliance)
$PNEC_{sed}$				
$PNEC_{biota,sec\ pois}$				
$PNEC_{biota,\ hh}$				
$PNEC_{dw,\ hh}$				

7. Risk Quotient (MEC or PEC/PNEC)

RQ	**Value**
RQ_{fw} (MEC(P95)/PNEC)	2.9 (Sc2; PNEC = 0.4 µg/L) 11.7 (PNEC = 0.1 µg/L)
RQ_{fw}(PEC/PNEC)	0.13 (PNEC = 0.4 µg/L) (RIVM, 2011)
RQ_{sed}	
$RQ_{biota,sec\ pois}$	
$RQ_{biota,\ hh}$	
$RQ_{dw,\ hh}$	

8. STE score

0.42 (Sc2; PNEC = 0.4 µg/L)

9. References

AMR Industry Alliance Antibiotic Discharge Targets. List of Predicted No-Effect Concentrations (PNECs) (2018).

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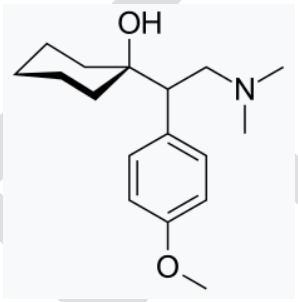
DRAFT

Venlafaxine (CAS N. 93413-69-5)

1. Substance identity

EC name	1-[2-(dimethylamino)-1-(4-methoxyphenyl)ethyl]cyclohexanol
EC number	618-944-2
CAS number	93413-69-5
Molecular formula	$C_{17}H_{27}NO_2$
Molecular weight	277.4 g/mol
Structure	
SMILES	CN(C)CC(C1=CC=C(C=C1)OC)C2(CCCCC2)O

2. Physico-chemical properties

Endpoint	**Value**	**Source**
Vapour Pressure (Pa)	2.46X10-7 mm Hg at 25°C (est) 32.9 mPa	US EPA, 2011
Water solubility (mg/L)	230 mg/L predicted) 267 mg/L at 25°C (est)	https://www.drugbank.ca/salts/DBSALT000186 https://www.drugbank.ca/drugs/DB00285 US EPA, 2011
logK_{ow}	0.43 3.2	http://datasheets.scbt.com/sc-201102.pdf Sangster J; LOGKOW Database. A databank of evaluated octanol-water partition coefficients (Log P). Available from, as of Oct 26, 2011: http://logkow.cisti.nrc.ca/logkow/search.html

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3. Environmental fate

Endpoint	Value	Source
Sorption potential K_{oc}	190	Estimated Koc value of 190(SRC), determined from a log K_{ow} of 3.20 and a regression-derived equation ToxNet https://toxnet.nlm.nih.gov/cgi-bin/sis/search2/r?dbs+hsdb:@term+@DOCNO+6699
Partition coefficient solid-water in sediment Kp_{sed} (L/kg)		
Biodegradability		
Bioaccumulation (BCF)	28.93 60	US EPA, 2011 through INERIS https://substances.ineris.fr/fr/substance/3171 https://toxnet.nlm.nih.gov/cgi-bin/sis/search2/r?dbs+hsdb:@term+@DOCNO+6699

4. Environmental exposure assessment

4.1 Predicted Environmental Concentration

	Description	Source
Tonnes/year		
Uses	Antidepressant drug Venlafaxine is used in the following MS: CZ, FI, IRL, RO, SK	
Spatial usage (by MS)	Not known	-
Banned uses		
ERC code		
PEC_{fw} (mg/L)		
PEC_{sed} (mg/kg dw)		
PEC_{biota} (mg/kg)		

4.2 Measured Environmental Concentration

n. of MS	Source of monitoring data	MEC values
Europe (90 samples from 18 countries)	WWTP effluents Loos et al., 2013	0.119 µg/L (mean) 0.548 µg/L (max.)
DE	WWTP effluents (Germany; DE)	0.225 µg/L (mean)

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	Schlüsener et al., 2015	
DE	Rhine River Schlüsener et al., 2015	0.014 µg/L (annual mean)
DE	Emscher River (small river) Schlüsener et al., 2015	0.180 µg/L (mean)
SE	Surface waters downstream WWTPs; also found in blood samples from otters (in 10/10 pooled samples).	< LOQ (0.1 ng/L) up to 0.440 µg/L

n. of MS	Source of monitoring data	MEC values
In Sc2 (inland whole water) data from only 1 MS (93 sites) with 1395 samples are available. 76.8% quantified samples. The quality of monitoring in this country is acceptable but data are not representative for an EU-wide assessment. Sc3 was not developed since data scarcity but it is expected to be similar to Sc2 since the majority of samples are quantified.	Dataset of monitoring prioritisation 2014	Median=0.03 µg/L (Sc2) MEC(P95)= 0.19 µg/L (Sc2)

4.3 Analytical Methods

Method	LOQ (µg/L)	Description/Reference
SPE-LC-MS-MS	0.0007	Extraction of 100 mL water (Gros et al., 2012)
SPE-LC-MS-MS	0.0005	Extraction of 100 mL water (Loos et al., 2013)
SPE-LC-MS-MS	0.0003	Extraction of 1 L water (Schlüsener et al., 2015)
LC-MS/MS	0.0004	Papageorgiou et al., 2019
SPE followed by UHPLC-QqLIT-MS	0.0015 (river water)	Mandaric et al., 2017
LC-MS-MS	0.01	CZ
n.a.	0.0001	SE
n.a.	0.0005	BE-Wallonia

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5. P, B, T, C, M, R, ED properties

Substance	Persistent (P) Bioaccumulative (B) Toxic (T)	Carcinogenic (C) Mutagenic (M) Reproduction toxicity (R)	Endocrine Disruptive (ED)	Comment
Venlafaxine	P and T*	R		

NOTE: REACH registration dossiers notifications

6. Hazard assessment

6.1 Ecotoxicology data

Trophic level	Endpoint	Value (mg/L)	Reference
Green algae	**EC_{50} (Ecosar)**	**0.65**	**Wielens Becker et al., 2020**
Aquatic invertebrate	*Daphnid,* EC_{50} (Ecosar)	1.06	Wielens Becker et al., 2020
Fish	EC_{50} (Ecosar)	7.68	Wielens Becker et al., 2020
Green algae	LC_{50} (Ecosar)	265.34	Zhou et al., 2019
Aquatic invertebrate	NOEC	141.28	Zhou et al., 2019
Fish	**NOEC**	**0.000305**	**Zhou et al., 2019**

6.2 Mammalian toxicology data

6.3 PNEC derivation

PNEC	Endpoint	Endpoint value	AF	PNEC value
$PNEC_{fw}$	Long Term NOEC (Fish)	0.305 µg/L	50	0.0061 µg/L (Zhou et al., 2019)
$PNEC_{fw}$				0.03835 (prioritisation exercise, Carvalho et al., 2016 and Lettieri et al., 2016)
$PNEC_{fw}$	EC_{50} (green algae, ECOSAR)	650 µg/L	1000	0.650 µg/L (Wielens Becker et al., 2020)
$PNEC_{sed}$				

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$PNEC_{biota,sec\ pois}$				
$PNEC_{biota,\ hh}$				
$PNEC_{dw,\ hh}$				

7. Risk Quotient (MEC or PEC/PNEC)

RQ	**Value**
RQ_{fw} (MEC(P95)/PNEC)	5 (Sc2; PNEC = 0.03835 µg/L) 31 (Sc2; PNEC = 0.0061 µg/L)
RQ_{fw}(PEC/PNEC)	
RQ_{sed}	
$RQ_{biota,sec\ pois}$	
$RQ_{biota,\ hh}$	
$RQ_{dw,\ hh}$	

8. STE score

1.36 (Sc2; PNEC = 0.03835 µg/L)

STE score is not calculated for PNEC = 0.0061 µg/L but it is expected to be high because Median (0.03 µg/L) > PNEC.

9. References

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