European Commission

JRC TECHNICAL REPORT

Development of the first Watch List under the Environmental Quality Standards Directive

Directive 2008/105/EC, as amended by Directive 2013/39/EU, in the field of water policy

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Abstract

According to Directive 2008/105/EC (the Environmental Quality Standards Directive, EQSD), a new mechanism is needed to provide high-quality monitoring information on the concentrations of polluting substances in the aquatic environment across the EU. The aim of this mechanism is to support the identification of priority substances for regulation under the Water Framework Directive. A restricted number of substances (up to 10) are to be included in a dynamic Watch List, remaining there for limited time. Three compounds, i.e. diclofenac, 17-beta-estradiol (E2), and 17-alpha-ethinylestradiol (EE2) have already been identified for inclusion in the first Watch List, for the specific purpose of better informing the determination of suitable risk reduction measures. Therefore, up to seven additional substances should be identified for inclusion.

This report describes the procedure to identify a short-list of substances, based on the suspected risk to or via the aquatic environment, as well as on the unavailability of sufficient monitoring data or data of sufficient quality to identify the risk posed by those substances, and to prioritise them at EU level. From the short-list, seven additional substances are proposed for inclusion in the first Watch List.

Development of the first Watch List under the Environmental Quality Standards Directive

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Abbreviations

ADI	Acceptable Daily Intake
BCF	Bioaccumulation Factor
BMF	Biomagnification Factor
CIS	Common Implementation Strategy
dw	Drinking Water
EMA	European Medicines Agency
EqP	Equilibrium Partitioning method
fw `	Freshwater
hh	Human Health
Koc	Organic carbon adsorption coefficient
LOD	Limit Of Detection
LOQ	Limit Of Quantification
MS	Member States
NOAEL	No-Observed Adverse Effect Level
NOEC	No-Observed Effect Concentration
PEC	Predicted Environmental Concentration
PNEC	Predicted No Effect Concentration
PPP	Plant Protection Products
PS	Priority Substance
RBSP	River Basin Specific Pollutants
RQ	Risk Quotient (PEC/PNEC)
sec pois	Secondary poisoning
sed	Sediment
TDI	Tolerable Daily Intake
TG n. 27	Reference no. 18
WFD	Water Framework Directive

1. Introduction

According to the Environmental Quality Standards Directive 2008/105/EC as amended by Directive 2013/39/EU (EQSD) [1], a new mechanism is needed to provide high-quality monitoring information on the concentrations of potentially polluting substances in the aquatic environment to support future prioritisation exercises in line with Article 16(2) of Directive 2000/60/EC (Water Framework Directive, WFD) [2], and thereby to improve the protection of the aquatic environment and of human health via the environment. The mechanism is aimed at emerging pollutants and other substances for which the available monitoring data are either insufficient or of insufficient quality for the purpose of identifying the risk posed across the EU. It involves creating a Watch List with a limited number of such substances and monitoring them EU-wide for up to 4 years. A maximum number of 10 substances or groups of substances shall be included in the first Watch list, increasing by one at each update, up to a maximum of 14 substances or groups of substances [1]. Frequent reviews of the list will ensure that substances are not monitored longer than necessary, and that substances for which a significant risk at EU level is confirmed are identified as candidate priority substances with as little delay as possible.

However, three compounds, i.e. diclofenac (CAS n. 15307-79-6), 17-beta-estradiol (E2) (CAS n. 50-28-2), and 17-alpha-ethinylestradiol (EE2) (CAS n. 57-63-3), have already been selected for inclusion in the first list in order to collect sufficient monitoring data for the determination of risk reduction measures. The Joint Research Centre (JRC) has been tasked with proposing 7 substances as candidates for the completion of the first Watch List and identifying analytical methods for their monitoring.

This report describes the procedure and criteria used to identify a short-list of substances, proposed for inclusion in the Watch list.

2. Initial List of Substances

The main criteria for inclusion in the initial list of candidate substances were that i) the substance is suspected of posing a significant risk to, or via, the aquatic environment, meaning there is reliable evidence of hazard and of a possible exposure to aquatic organisms and mammals, but ii) there is not enough information to assess the EU-wide exposure for the substance, i.e. insufficient monitoring data or data of insufficient quality, nor sufficient modelled exposure data to decide whether to prioritise the substance.

Article 8b of the EQSD [1] sets out a comprehensive list of information sources to be considered when establishing the Watch List. These were further elaborated in the Document on the Development of the 1st Watch List under the EQS Directive, produced by DG ENV and presented at the 2nd Meeting of the WFD CIS Working Group Chemicals in March 2014 [3], and include:

(a) the results of the most recent regular review of Annex X to Directive 2000/60/EC provided for in Article 16(4) of that Directive (in particular substances ranked highly but not prioritised because of a paucity of monitoring data);

(b) research projects (even though these are likely to be the same research projects assessed in the priority substances review, the results would be considered more frequently for the watch list updates; their reliability should be considered);

(c) recommendations from the stakeholders referred to in Article 16(5) of Directive 2000/60/EC (these may include recommendations from the SCHER, MS, the EP, EEA, research programmes, international organisations, European business organisations inc SMEs, and environmental organisations);

(d) Member States' characterisation of river basin districts and the results of monitoring programmes, under Articles 5 and 8 of Directive 2000/60/EC respectively (consideration of river basin specific pollutants (RBSPs) if there is not already enough evidence from enough MS);

(e) Information on production volumes, use patterns, intrinsic properties (including, where relevant, particle size), concentrations in the environment and effects, including information gathered in accordance with Directives 98/8/EC, 2001/82/EC and 2001/83/EC, and with Regulations (EC) No 1907/2006 and (EC) No 1107/2009.

The above information sources have been considered for the compilation of the initial list of candidate substances (Table 1). Firstly, substances short-listed during the last review of priority substances, but not finally proposed for prioritisation [5] have been considered for the Watch List. Secondly, substances highlighted in some pieces of literature regarding research projects were considered, in particular those identifying emerging substances of concern. Thirdly, a few MS and Stakeholders have suggested substances for inclusion in the Watch List.

The document on the Development of the 1st Watch List included, in addition to the main (primary) criteria for identifying substances, the following secondary criteria: i) the need for a sufficiently sensitive analytical method to be available by the time monitoring has to begin (e.g. LoD less than or equal to PNEC or 2xPNEC, depending upon likely concentrations and nature of substance); and ii) no immediate ban on the production or use of the substance in the EU to be foreseen (unless, in the event of a ban, emissions from secondary sources such as imported products might be expected, and/or the substance is PBT or vPvB). As regards the first point, the JRC has done a preliminary assessment, and the second point has been taken into account in the final recommendation, having in mind that changes in the authorisation conditions for some substances could lead to future changes in concentrations of substances beyond the Watch List monitoring period.

The above document also identified some further criteria for prioritising substances, suggesting that account be taken of the particular hazardous properties of each substance, the relevance of the substance to drinking water quality, the irreversibility or severity of potential effects on ecosystems, the extent and nature of use; the possibility that monitoring data might very soon become available from other sources, and the ease of monitoring substances together, e.g. in same sample matrix (therefore for similar periods), at similar locations, as groups of substances. Some of the comments received from WG Chemicals members queried the value or precise meaning of some of these points, other comments were largely supportive. In line with the overall message, the approach presented in this document has focussed mainly on the risk quotient, on resolving information gaps identified during the last priority substances review, and on trying to give some attention to "emerging" pollutants.

Table 1. Initial list of substances

CAS n.	Substance name	Source [a]
294-62-2	Cyclododecane	[5]
60207-90-1	Propiconazole	[5]
731-27-1	Tolylfluanid	[5]
1066-51-9	Amino-methyl phosphonic acid (AMPA)	[5]
25057-89-0	Bentazone	[5]
80-05-7	Bisphenol A	[5]
298-46-4	Carbamazepine	[5]
1897-45-6	Chlorothalonil	[5]
1333-82-0	Chromium trioxide	[5]
81103-11-9	Clarithromycin	[5]
1085-98-9	Dichlofluanid	[5]
60-00-4	Edetic Acid (EDTA)	[5]
1071-83-6	Glyphosate	[5]
15687-27-1	Ibuprofen	[5]
93-65-2; 7085-19-0	Mecoprop (MCPP)	[5]
1113-02-6	Omethoate	[5]
2303-17-5	Tri-allate	[5]
52-68-6	Trichlorfon	[5]
7440-66-6	Zinc and its compounds	[5]
57-12-5	Cyanide – free (HCN and CN-)	[5]
723-46-6	sulfamethoxazole	[5]
53-16-7	Estrone	[6-8]
128-37-0	2,6-di-tert-butyl-4-methylphenol	MS
50-00-0	Formaldehyde	MS
85-01-8; 90640-80-5	Phenanthrene	MS
52645-53-1	Permethrin	EEB
121-75-5	Malathion	EEB
61-82-5	Aminotriazole	NORMAN
83905-01-5	Azithromycin	NORMAN
5466-77-3	2-ethylhexyl 4-methoxycinnamate	NORMAN
83164-33-4	Diflufenican	NORMAN
82419-36-1	Ofloxacin	NORMAN
114-07-8	Erythromycin	NORMAN
115-86-6	Triphenyl phosphate	NORMAN
85721-33-1	Ciprofloxacin	NORMAN
87674-68-8/163515-14-8	Dimethenamid/ dimethenamid-P	NORMAN
2032-65-7	Methiocarb	NORMAN
19666-30-9	Oxadiazon	NORMAN
105827-78-9; 138261-41-3	Imidacloprid	[9-11]

153719-23-4	Thiametoxam	[9-11]
210880-92-5	Clothianidin	[9-11]
111988-49-9	Thiacloprid	[11]
135410-20-7/160430-64-8	Acetamiprid	[11]

[a] Sources indicated as reference [5] are those listed in Table 4.1 of that document.

2.1 Substances from the last review of the PS list

During the last review of the priority substances list in accordance with Article 16(2) of the WFD [2], 12 priority substances (PS) were added to the initial list of 33 PS in Annex X to that Directive. Both modelling- and monitoring-based exercises, starting from initial lists of 2014 and 316 substances, respectively, were performed during the prioritisation process [4], resulting in a short-list of substances. However, not all of those substances were ultimately prioritised, in several cases because hazard information was lacking or monitoring data were available for too few Member States.

Therefore, the substances short-listed during the last review of the PS but not finally proposed for prioritisation, for which a detailed dossier had been produced and sometimes EQS had been derived, were included in the Initial List of substances as candidates for the Watch List. These substances have been identified in Table 4.1 of the Prioritisation scoping report [5], and are also listed above in Table 1. An exception is the substance musk xylene (CAS n. 81-15-2), which despite having been short-listed in the last prioritisation exercise, was not included in the current list of candidate substances because a ban has been imposed on its use in Europe. Firstly, the International Fragrance Association decided in their 44th amendment a voluntary ban on the use of musk xylene in fragrance products. Secondly, the European Commission has issued a ban on musk xylene with a sunset date of 21/07/2014.

2.2 Substances proposed by MS and other stakeholders and/or flagged in the literature

Member States representatives and other stakeholders which are part of the WFD Common Implementation Strategy (CIS) Working Group Chemicals were invited to propose substances for the Watch List based on the experience gained in the implementation of monitoring programs under the WFD, and previous prioritisation schemes followed in Europe. The proposed substances are listed in Table 1, as well as some substances flagged in the literature as being of possible concern.

The estrogenic hormone estrone (E1) is a product of E2 oxidation and although it has lower estrogen receptor binding/transactivation potency than E2 *in vitro* [6,7], it is usually found at higher concentrations (by a factor of about 10) in WWTP effluents and surface waters [6-8]. Because of its chemical similarity, E1 is usually analysed together with E2 and EE2.

Other substances proposed for inclusion in the initial candidate list were 2,6-di-tert-butyl-4-methylphenol (UV stabilizer and fuel antioxidant), formaldehyde, phenanthrene, the insecticides permethrin and malathion, and five neonicotinoid pesticides. The use of three of these neonicotinoids (imidacloprid, thiamethoxam, clothianidin) was recently restricted for two years (Regulation (EU) No 485/2013, Art. 2) by prohibition of seed treatment, soil treatment and foliar application before flowering for specific crops, to address concern that they pose a risk to bees [9]. Risks to other organisms have also been identified, and laboratory studies suggest that some of these substances have a half-life in soil that

can reach three years [10], while the field DT_{50soil} values in the EU Review Report 2005 were up to 305 d for clothianidin [11]. Use of the two other neonicotinoids, thiacloprid and acetamiprid, has not been restricted because they show lower toxicity to bees [12].

The initial list also includes top-ranked substances in "Category 2" [1] of the NORMAN Prioritisation scheme, including the plant protection products aminotriazole, diflufenican, dimethenamid, methiocarb and oxadiazon, the flame retardant triphenyl phosphate, the sun screen ingredient 2-ethylhexyl 4-methoxycinnamate and the antibiotics azithromycin, ofloxacin, erythromycin and ciprofloxacin. Moreover, antibiotics as a group and mixtures of unknown composition were also suggested by a stakeholder for inclusion in the initial list. Information on exposure to antibiotics in the environment is needed not only because of their potential direct toxic effects, but also because of the increasing concern regarding antimicrobial resistance (AMR), although the latter is not the issue in the present risk assessment [13-15].

2.3 Criteria for De-selection of Substances

From the initial list of 43 candidate substances for the Watch List, a criterion was defined to de-select substances with sufficient monitoring data available to conclude on a European-wide risk, i.e. with monitoring data from at least four MS. This is because a threshold for availability of monitoring data relating to at least four MS has been proposed as a criterion for including substances in the monitoring-based ranking of the next prioritisation exercise [16]. Therefore, such substances are considered to have sufficient monitoring data for a possible prioritisation and were therefore excluded from the Watch List. To identify the number of MS for which monitoring data are available, the period 2006-2014 was considered, and three databases were searched, i) WATERBASE, hosted by the European Environment Agency (EEA) and containing official monitoring data, aggregated by year, gathered under the State of the Environment (SoE) reports by MS, ii) IPCheM, with regard to the monitoring data compiled during the previous prioritisation exercise and iii) NORMAN database containing monitoring data from official sources, projects and literature.

Even though several substances on the initial list have been identified as River Basin Specific Pollutants (RBSP) in some MS [17], few additional data on those substances, apart from those available in the above databases, were forthcoming.

The selection criteria for consideration of monitoring data were the following:

1. Clear indication of the sampling site (site name, code, etc)
2. Clear identification of the analysed substance (determinand)
3. Clear identification of the measurement unit
4. Samples collected from 2006 on

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[1] The substances have been selected on the basis of the occurrence data available in the NORMAN EMPODAT database and they fulfil the following criteria: a) hazard assessment is based on experimental data (AF maximum 50 for the derivation of the Lowest PNEC, mostly based on existing Assessment Reports) AND b) there is at least 1 site with exceedance of the Lowest PNEC (evidence of a potential risk) AND c) further monitoring data are needed for better assessment of exposure and risk at the European scale.

5. Either LOD or LOQ (at least one) clearly reported

6. Identification of the analysed fraction (only for NORMAN, such information was not available for WATERBASE)

7. LOD or LOQ ≤ substance-specific limits[2] when the value is reported to be below LOD or LOQ[3]

8. LOD or LOQ < PNEC when the value is reported to be below LOD or LOQ[3]

2.4 Dataset Filtered

After the application of the above criteria, 16 substances were de-selected based on availability of sufficient monitoring data. These substances are estrone, propiconazole, AMPA, bentazone, bisphenol A, carbamazepine, chlorothalonil, glyphosate, ibuprofen, mecoprop, omethoate, zinc, sulfamethoxazole, phenanthrene, permethrin and malathion. Monitoring data were available for dimethenamid from four MS, and only dimethenamid-P was considered for further assessment in this exercise. Therefore, a final number of 27 substances were taken forward for the purpose of ranking according to the risk they pose to the environment.

3. Methodology for Ranking of Substances

3.1 Overall Methodology

A risk assessment of all the substances in the filtered dataset was done by combining the substance-specific hazard data and information on exposure to the substance in or via the aquatic environment. According to the substance's physico-chemical properties, the receptors and compartments at risk were identified and an assessment done for each route of exposure, including the estimation of specific PEC and PNEC values, as summarized in Figure 1. In general, the criteria to identify the required assessments followed those specified in the Technical Guidance No. 27 of the Common Implementation Strategy (CIS) of the WFD [19].

The risk for direct toxicity to pelagic organisms from the presence of substances in the water column was always assessed, considering both a PEC_{fw} and a $PNEC_{fw}$ for surface water.

Depending on the sorption potential of a substance, a risk assessment for the sediment compartment was performed, i.e. whenever the organic carbon adsorption coefficient trigger value (Log K_{oc} or Log K_{ow}) ≥ 3, by estimating a PEC_{sed} and the $PNEC_{sed}$.

For the protection of organisms from secondary poisoning, an assessment was made for those substances with a potential to bioaccumulate, using as trigger value a bioconcentration factors (BCF) $\geq$

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[2] Two substance-specific limits were calculated as the 99th percentile of all LOD and LOQ values for a certain substance (for NORMAN database separate limits were calculated for the dissolved fraction and for the "whole water" fraction).

[3] In WATERBASE data are aggregated by year, but information is available on the number of samples collected and the number of samples resulting below the LOQ. Hence these criteria were only applied if all samples were reported to be below LOQ.

100 or if no valid measured BCF was available a Log $K_{ow} \geq 3$ and the substance being not readily biodegradable [20]. In this case, a PEC_{biota} was considered and a $PNEC_{biota, sec\,pois}$ was estimated for top predators, as well as a $PNEC_{biota, hh}$ to assess the risk for human health arising from the consumption of fishery products.

Finally, an effect assessment was conducted for all substances regarding the protection of human health from consumption of drinking water, by estimating a $PNEC_{dw, hh}$ to be compared to the PEC_{fw}.

After estimating all the above PEC and PNEC values, risk quotients (PEC/PNEC) were calculated for the different compartment and receptor scenarios. The highest risk quotient calculated for a substance was used in the final ranking of substances (from highest to lowest risk).
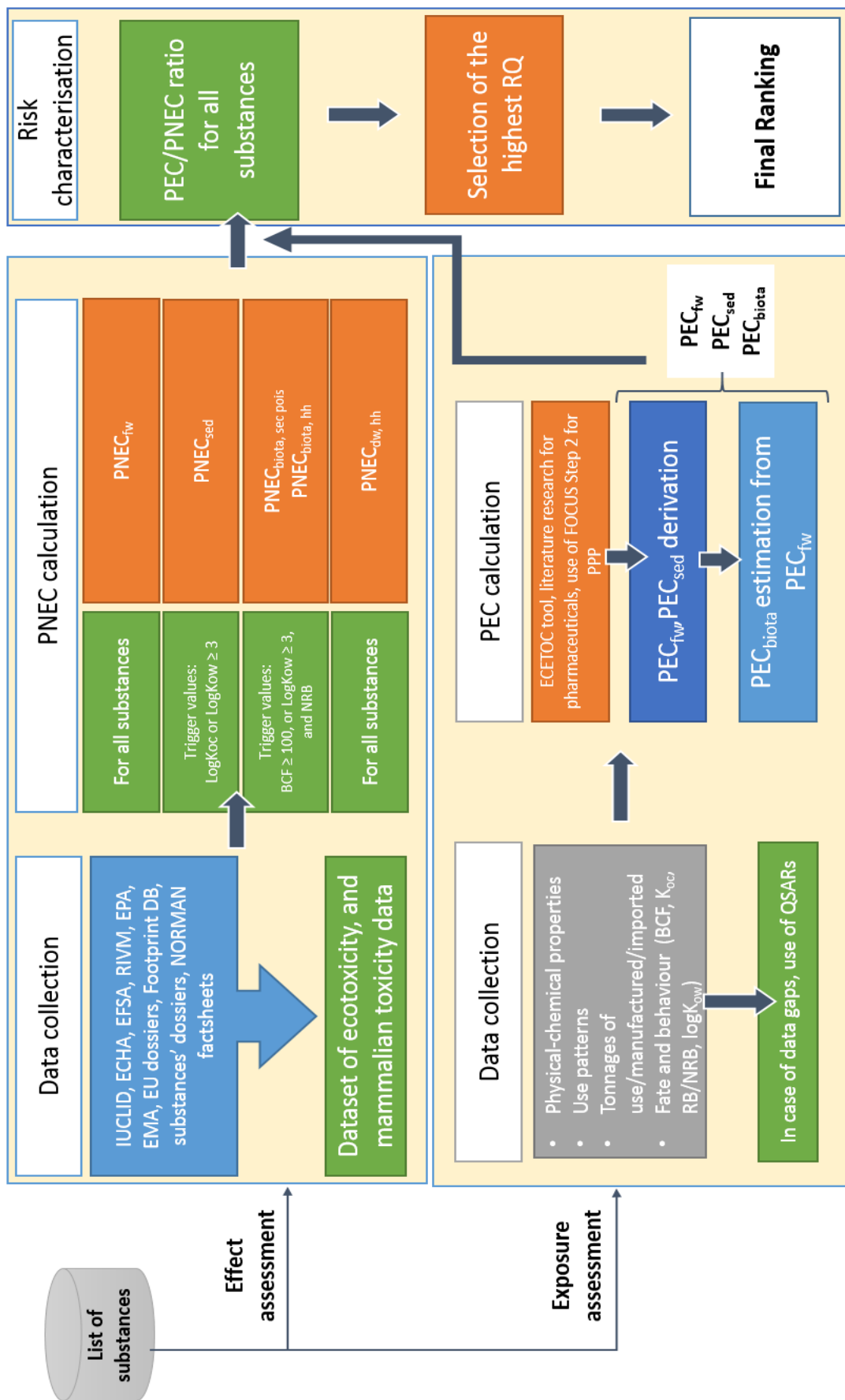
Figure 1. Summary of the overall methodology for the risk assessment of candidate substances for the Watch List.

3.2 Data Collection

For the collection of data, information was retrieved from several databases and reports, including IUCLID, ECHA, EFSA, RIVM, EMA, EU-Review reports, EU-RAR, EU Pesticides DB, Footprint Pesticides Properties DB, EPA, substances dossiers prepared during the last prioritisation exercise and substances factsheets provided by NORMAN. The relevance and reliability of the data retrieved from the above sources was deemed acceptable for the purpose of this exercise, since it was considered that the data had been reviewed by a competent authority, and no further review of the original study reports was conducted.

Data collected for the exposure assessment and PEC calculation comprised physical and chemical properties (molecular weight, water solubility, vapour pressure, biodegradability, sorption potential and bioaccumulation potential), tonnage (of use, manufacture and import) and Environmental Release Category (ERC) codes.

The collection of hazard data for the aquatic and sediment compartments included acute and chronic ecotoxicity (typically the most sensitive LC/EC50 or NOEC/EC10 endpoints). Regarding mammalian or human toxicity effects from oral exposure, data were collected for repeated dose toxicity, carcinogenicity, mutagenicity and effects on reproduction, focusing on typical endpoints such as NOAL, DNEL, ADI and TDI values. When new literature was considered that had not been retrieved from the sources listed above, reliability assessment of the ecotoxicological data was done by using a literature evaluation tool (LET), based on the Criteria for Reporting and Evaluating ecotoxicity Data (CRED) check list (Kase et al., personal communication).

3.3 Hazard assessment – estimation of PNEC values

3.3.1 PNEC for direct toxicity to freshwater organisms

Chemical risk assessment in the water compartment is relevant for the protection of organisms inhabiting the water column. Therefore, the protection threshold concentrations $PNEC_{fw}$ have been estimated for all substances.

For the estimation of the $PNEC_{fw}$, a deterministic approach has been used by selecting the most stringent valuable endpoint from the available aquatic toxicity data, and applying an assessment factor (AF), which was chosen based on the guidelines for the derivation of the $QS_{fw, eco}$ retrieved from the TG n. 27 - CIS WFD [18]. However, for some substances for which the PNEC was retrieved directly from other sources, a probabilistic method was used.

3.3.2 PNEC for the toxicity to benthic species

The threshold safety value for the protection of benthic organisms $PNEC_{sed}$ has been derived for those substances with a potential for sorption into the sediment compartment using as trigger values: logKoc or LogKow $\geq$ 3. The $PNEC_{sed}$ has been calculated following the TG n. 27- CIS WFD [18] and the ECHA Guidance (2012) [21], using equation A.

$$PNEC_{sed} = \frac{K_{\text{sed-water}}}{RHO_{sed}} \times PNEC_{fw} \times 1000 \qquad (A)$$

RHO_{sed} is the bulk density of wet sediment, $K_{\text{sed-water}}$ is the partition coefficient between sediment and water and 1000 is the conversion factor from m^3 to litre.

Since the final $PNEC_{sed}$ was calculated in terms of dry weight, a conversion step was required, by using the following equations B and C.

$$CONVsed = \frac{RHO_{sed}}{Fsolid_{sed} \times RHOsolid} \qquad (B)$$

$$PNEC_{Sed} = CONVsed \times PNEC_{sed-ww} \qquad (C)$$

For the calculation of $K_{\text{Sed-water}}$, the following equation D was used.

$$K_{sed-water} = Fair_{sed} \times K_{air-water} + Fwater_{sed} + Fsolid_{sed} \times \frac{Kp_{Sed}}{1000} \times RHO_{solid} \qquad (D)$$

Default values for $Fair_{sed}$, RHO_{solid}, $Fwater_{sed}$, $Fsolid_{sed}$ and Foc_{sed} were taken from TG n. 27 - CIS WFD [18]. Since the given default value for $Fair_{sed}$ was *zero* [18], the first part of the equation ($Fair_{sed} \times K_{air-water}$) is not reported in the description of the calculations in the substances' factsheets.

3.3.3 PNEC for the toxicity to top predators from secondary poisoning

The WFD provides for the protection of top predators such as birds and mammals from risks of secondary poisoning arising from the consumption of aquatic organisms from lower trophic levels contaminated with toxic substances.

A $PNEC_{biota, sec pois}$ has been derived for all substances with a potential to bioaccumulate, as indicated under section 3.1.

The derivation of a $PNEC_{biota, sec pois}$ started from toxicological endpoints reporting on dietary and oral exposure such as the no-observed adverse effect level (NOAEL) or no observed effect concentration for ingestion ($NOEC_{oral}$). Since the $PNEC_{biota, sec pois}$ is expressed as concentration in food, conversion factors from NOAEL to NOEC have been used, for bird and mammalian toxicity studies, following the TG n. 27 - CIS WFD [18].

3.3.4 PNEC for hazard to human health via consumption of fishery products

Regarding the protection of human health from the consumption of contaminated fishery products, a $PNEC_{biota, hh}$ has been derived in a similar manner as the $QS_{biota, hh food}$ in the TG n. 27 - CIS WFD [18], by using endpoints such as the acceptable daily intake (ADI), tolerable daily intake (TDI) or $NOAEL_{oral}$ (divided by an AF).

$$PNEC_{biota,\,hh} = \frac{0.1 \times TL \times 70}{0.115} \qquad\qquad (E)$$

The PNEC$_{biota,\,hh}$ is expressed in µg·kg^{-1}, and uses a default value of human body weight of 70 kg, and a daily consumption of fishery products of 0.115 kg. In addition, it is assumed that fishery products make up no more than 10% of the threshold level value (0.1 × TL) [18].

3.3.5 PNEC for hazard to human health via drinking water consumption

Drinking water is a possible route of human exposure to substances in water, and protection threshold concentrations PNEC$_{dw,\,hh}$ have been derived for all substances, based on human toxicity data. If available, WHO [21] or EU [22] drinking water standards have been used as the PNEC$_{dw,\,hh}$ values for that substance.

When a WHO drinking water standard was not available, the PNEC$_{dw,\,hh}$ was calculated according to the following equation F, retrieved from the TG n. 27 - CIS WFD [19].

$$PNEC_{dw,\,hh} = \frac{0.1 \times TL_{hh} \times bw}{uptake_{dw}} \qquad\qquad (F)$$

A human body weight (bw) of 70 kg and a daily uptake of drinking water (uptake$_{dw}$) of 2 litres were used. A fraction of 0.1 of the human toxicological standard (TL$_{hh}$, usually the acceptable daily intake (ADI) or the tolerable daily intake (TDI)) is allocated to intake of the substance via drinking water.

3.4 Exposure assessment – estimation of PEC values

Regarding the exposure assessment, information on tonnage and use pattern for all substances was searched for. To facilitate the ranking of substances based on risk, it was attempted to use a similar method for the PEC calculation for all substances, the ECETOC PEC calculation tool based on EUSES [23] This tool requires tonnage information, as well as usage information as input values. Unfortunately, the required input information was not available for all substances, and additional models were required, as detailed below. When more than one PEC value was calculated by different methods, the worst case value was generally used for the ranking of substances.

3.4.1 PEC for freshwater

Tonnages and usage information were retrieved from IUCLID for six substances, also for an additional seven substances from the last prioritisation exercise. Thus, for these substances, with the exception of PPPs, the ECETOC tool was used for the PEC calculation with the respective ERC codes (when more than one use was reported, the ERC corresponding to the worst-case scenario was selected for the calculation).

Unfortunately, the required input information for the remaining substances was not sufficient to run the model, and additional methods were sought for the PEC calculation depending on the availability of input data.

For one substance the PEC was retrieved from European Union Risk Assessment Reports (EU-RAR), while for eleven pesticides, the PEC was calculated with the model FOCUS Step 2 [24]. Finally, for four

antibiotics, given the unavailability of information on production or sales at European level, PEC values were calculated by using the following equation G, retrieved from the publication of Besse et al, 2008 [25]

$$PEC_{fw}= (consumption \times F_{excreta}) / (WWinhab \times hab \times dilution \times 365) \qquad (G)$$

where *WWinhab* is the volume of wastewater per person per day (default value of 200 [L/(hab*day)]), *hab* are the number of inhabitants, $F_{excreta}$ is the excretion factor of the active substance (retrieved from the same publication), *dilution* is the dilution factor (default value of 10), consumption is the quantity (mg/year) of active ingredient consumed by the population during 1 year.

Data on human consumption of antibiotics in the list were available for six MS (France, Greece, Portugal, Latvia, Germany and Denmark), retrieved respectively from Besse et al, 2008 [25], Iatrou et al, 2014 [26], UBA report [27], and directly provided to the JRC for PT, LV and DK.

The worst case PEC value among those estimated for each antibiotic was selected for the risk quotient (RQ) calculation. However, human consumption is not the only use for the considered pharmaceuticals, and veterinary uses and intermediate uses (for erythromycin and azithromycin), are not accounted for in the above mentioned calculated PEC. Moreover, data on human consumption at European scale are still lacking. For this reason, the upper end values from the available monitoring data were used to calculate the risk, which is shown for comparison in the final ranking.

A summary of the sources of information and the models used for the PEC calculation are given in Table 2.

Table 2. Data sources and methods used for PEC calculation.

CAS n.	Substance name	Tonnage source	ERC code used	PEC calculation method
128-37-0	2,6-di-tert-butyl-4-methylphenol	IUCLID	ERC8d [a]	ECETOC [b]
135410-20-7/ 160430-64-8	Acetamiprid	-	-	FOCUS Step 2
61-82-5	Aminotriazole	(Last prioritisation exercise)[c]	(ERC8d)[c]	FOCUS Step 2
83905-01-5	Azithromycin	-	-	Eq. G
1333-82-0	Chromium trioxide	-	-	EU-RAR
85721-33-1	Ciprofloxacin	-	-	Eq. G
81103-11-9	Clarithromycin	-	-	Eq. G
210880-92-5	Clothianidin	-	-	FOCUS Step 2
57-12-5	Cyanide- free (HCN and CN-	-	-	-
294-62-2	Cyclododecane	IUCLID	ERC6a	ECETOC [b]
1085-98-9	Dichlofluanid	Last prioritisation exercise	ERC8b	ECETOC [b]
83164-33-4	Diflufenican	-	-	FOCUS Step 2 [d]

163515-14-8	Dimethenamid-P	-	-	FOCUS Step 2
60-00-4	Edetic Acid (EDTA)	IUCLID	ERC10b [a]	ECETOC [b]
114-07-8	Erythromycin	IUCLID	ERC8a	ECETOC [b] and Eq. G
5466-77-3	2-ethylhexyl 4-methoxycinnamate	Last prioritisation exercise	ERC8a	ECETOC [b]
50-00-0	Formaldehyde	IUCLID	ERC8d [a]	ECETOC [b]
105827-78-9/ 138261-41-3	Imidacloprid	-	-	FOCUS Step 2
2032-65-7	Methiocarb	(Last prioritisation exercise)[c]	(ERC8d[c]	FOCUS Step 2
82419-36-1	Ofloxacin	-	-	Eq. G
19666-30-9	Oxadiazon	-	-	FOCUS Step 2 [d]
111988-49-9	Thiacloprid	-	-	FOCUS Step 2
153719-23-4	Thiamethoxam	-	-	FOCUS Step 2
731-27-1	Tolylfluanid	Last prioritisation exercise	ERC8b	ECETOC [b]
2303-17-5	Tri-allate	(Last prioritisation exercise)[c]	(ERC8d[c]	FOCUS Step 2
52-68-6	Trichlorfon	Last prioritisation exercise	ERC8a	ECETOC [b]
115-86-6	Triphenyl phosphate	IUCLID	ERC8a [a]	ECETOC [b]

[a] Worst-case use scenario was selected among many others

[b] Koc value were used, in addition to default input values

[c] Calculations with ECETOC were made for comparison with FOCUS Step 2 results. However, the latter was used for the risk assessment.

[d] Output from FOCUS Step 2 retrieved from EFSA conclusion report

3.4.2 PEC for sediment

For the calculation of the PEC$_{sed}$ ECETOC results were used whenever available, and for pesticides the results were retrieved from Focus Step 2. Similar to the PEC$_{fw}$, PEC$_{sed}$ values for chromium trioxide were retrieved from the EU-RAR. For those pharmaceutical substances passing the trigger value Log Koc and Log Kow ≥3, the sediment equilibrium partition method (EqP) was used considering the PEC$_{fw}$. Similar to what was done for the PNEC sediment in Section 3.3.2 (equations B-D), the PEC$_{sed-ww}$ in terms of wet weight (ww) was calculated using equation G:

$$PEC_{sed-ww} = \frac{K_{sed\text{-}water}}{RHO_{sed}} \times PEC_{fw} \times 1000 \qquad (H)$$

Since the final PEC$_{sed}$ was calculated in terms of dry weight, a conversion step was required, by using the following equations I and J.

$$CONVsed = \frac{RHO_{sed}}{Fsolid_{Sed} \times RHOsolid} \qquad (I)$$

$$PEC_{Sed} = CONVsed \times PEC_{sed-ww} \qquad (J)$$

For the calculation of K$_{Sed-water}$, the following equation K was used.

$$K_{sed-water} = Fair_{sed} \times K_{air-water} + Fwater_{sed} + Fsolid_{sed} \times \frac{Kp_{Sed}}{1000} \times RHO_{solid} \qquad (K)$$

Default values for Fair$_{sed}$, RHO$_{solid}$, Fwater$_{sed}$, Fsolid$_{sed}$ and Foc$_{sed}$ were taken from TG n. 27 - CIS WFD [18]. Since the given default value for Fair$_{sed}$ was *zero* [18], the first part of the equation (Fair$_{sed}$ × K$_{air-water}$) is not reported in the description of the calculations in the substances' factsheets.

3.4.3 PEC for biota

For the calculation of the PEC$_{biota}$ the following equation L was used [28].

$$PEC_{biota} = PEC_{fw} \times BCF \times BMF \qquad (L)$$

BCF values were retrieved when available or, for 5 substances, calculated from QSARS.
Default BMF values were retrieved from TG n. 27 - CIS WFD [18].

3.5 Final Ranking

Risk quotients (RQ) were estimated for all the relevant receptors at risk, i.e. RQ$_{fw}$, RQ$_{sed}$, RQ$_{biota, sec pois}$, RQ$_{biota, hh}$, RQ$_{dw, hh}$, and are available in the substances fact sheets, in Annex I. The highest RQ for the different compartments and/or receptors was selected for the final ranking of substances (Table 3).

4. Results

4.1 Overview of the exposure, hazard and risk assessment

The current exercise has attempted to quantify the risk associated with the substances in the candidate list, for which a lack of EU-wide monitoring data has been identified that makes it difficult to decide whether to propose them as priority substances in the EU.

Details of the considered sources of information on hazard and exposure, as well as the calculations of PEC and PNEC done for each individual substance for the different receptors and compartments, can be found in the factsheets in the Annex.

First results for the estimated PEC and PNEC values, as well as the different RQ, were presented and discussed at the Working Group Chemicals meeting (16-17 October 2014), following which Member States and Stakeholders provided additional comments and information in writing. New information on exposure or hazard has been considered and used to update the substance assessments. The final results are summarised in Table 3. Substances are ranked from the highest to the lowest RQ. The provision of additional monitoring data for several substances means that there are now sufficient data to evaluate some of them in the monitoring-based exercise of the ongoing review of PS. These substances have been deselected from the candidate list (Table 4). However, a detailed factsheet is still presented in the Annex for these substances, including information on the measured environmental concentrations. For the two substances with the lowest ranking, ofloxacin and EDTA, the risk quotient was below 1 in the present assessment and they have also been excluded from the candidate list.

In addition to the ranking based on the risk quotient, the uncertainty of the PEC and PNEC calculations was also taken into account for the final recommendation. Additionally, existing or imminent non-authorisation of use was taken into account to avoid proposing substances for inclusion in the Watch List for which measures are already in place that are expected to reduce the risk to the environment. Finally, it was considered whether methods are available to allow the monitoring of each proposed substance at concentrations close to its PNEC.

A number of specific issues were identified during the risk assessment of the candidate substances, or brought to our attention by Member States and Stakeholders during or following the WG Chemicals Meeting (16-17 October 2014). In several cases, these issues relate to uncertainties in the PEC and PNEC calculation due to unavailability of data that could result in over or underestimation of the risk. These issues are discussed in more detail below by substance.

Table 3. Results from the risk-based ranking of substances using the highest risk quotient calculated for each substance

ID Rank	Substance	$PNEC_{fw}$ [a] (mg/L)	$PNEC_{sed}$ (mg/kg dw)	$PNEC_{biota, sec\ pois}$ (mg/kg food)	$PNEC_{biota, hh}$ (mg/kg food)	$PNEC_{dw, hh}$ (mg/L)	PEC_{fw} [b] (mg/L)	SOURCE of PEC_{fw}	PEC_{Sed} [b] (mg/kg)	SOURCE of PEC_{sed}	PEC_{biota} (mg/kg$_{wet\ fish}$)	Highest RQ for ranking		Comment
1	Trichlorfon	9.6E-07	NR	N.R.	N.R.	0.158	0.034	ECETOC	0.120	ECETOC	0.09	35312	RQ_{fw}	High uncertainty regarding its spatial use, and AF 1000 for $PNEC_{fw}$
2	Cyclododecane	NA	NA	5	38.043	2.188	0.468	ECETOC	306.45	ECETOC	64074.9	12815	$RQ_{biota, sec\ pois}$	No effects on aquatic organisms found at concentrations below water solubility. Doubts regarding analytical methods
3	Imidacloprid	9E-06	N.R.	N.R.	N.R.	0.21	0.008	FOCUS Step 2	0.018	FOCUS Step 2	0.005	889	RQ_{fw}	Sufficient monitoring data only pre-restriction
4	Diflufenican	1E-05	0.02	16.7	12.174	0.7	0.006	FOCUS Step 2	0.112	FOCUS Step 2	9.18	575	RQ_{fw}	Sufficient monitoring data
5	Oxadiazon	8.8E-05	0.05	0.24	0.219	0.0126	0.039	FOCUS Step 2	0.496	FOCUS Step 2	9.48	443	RQ_{fw}	Evaluation process of Confirmatory data is on-going.
6	Methiocarb	1E-05	0.0005	0.591	0.791	0.0455	0.004	FOCUS Step 2	0.026	FOCUS Step 2	0.30	395	RQ_{fw}	Sufficient monitoring data

#	Name													Comment
														only pre banning as molluscicide
7	2,6-ditert-butyl-4-methylphenol	3.16E-03	1.290	16.7	15.217	0.875	0.423	ECETOC	367.640	ECETOC	2115	283	RQ_{sed}	
8	Thiacloprid	5E-05	N.R.	N.R.	N.R.	0.035	0.011	FOCUS Step 2	0.042	FOCUS Step 2	0.03	218	RQ_{fw}	
9	Tri-allate	6.7E-04	0.145	1.67	1.522	0.0875	0.118	FOCUS Step 2	2.560	FOCUS Step 2	165.20	176.12	RQ_{fw}	
10	Aminotriazole	3.20E-02	N.R.	N.R.	N.R.	0.004	0.501	FOCUS Step 2	0.459	FOCUS Step 2	1.19	143	$RQ_{dw,hh}$	Commission vote is expected in Dec 2014, regarding the renewal of the authorisation.
11	Chromium trioxide	3.4E-03	3.4	17	0.055	0.003	0.350	EU-RAR	0.152	EU-RAR	0.98	111	$RQ_{dw,hh}$	Last application date in 2016, sunset date 2017.
12	Thiamethoxam	1.4E-04	N.R.	N.R.	N.R.	0.091	0.011	FOCUS Step 2	0.007	FOCUS Step 2	0.03	78.6	RQ_{fw}	
13	Clothianidin	1.3E-04	N.R.	N.R.	N.R.	0.340	0.008	FOCUS Step 2	0.014	FOCUS Step 2	0.03	61.54	RQ_{fw}	
14	Erythromycin	0.0002	0.006	No info	0.043	0.002	0.005 [c]	ECETOC	0.3185	ECETOC	0.255	52.9	RQ_{sed}	
							0.0002 [d]	Eq. G	0.006	EqP	0.01	1.00	$RQ_{fw/sed}$	Human consumption
							0.0006	MEC	0.0185	EqP	0.03	3.07	$RQ_{fw/sed}$	Monitoring
15	2-ethylhexyl 4-methoxycinnamate	NA	0.2	N.R.	N.R.	7.875	0.006	ECETOC	8.390	ECETOC	2.73	41.9	RQ_{sed}	
16	Dichlofluanid	2.65E-04	0.018	3.33	21.30	1.225	0.005	ECETOC	0.732	ECETOC	0.38	40.2	RQ_{sed}	
17	Formaldehyde	4.7E-01	2.44	N.R.	N.R.	0.525	13.53	ECETOC	70.200	ECETOC	13.53	28.8	RQ_{fw}	
18	Dimethenamid-p	2.70E-03	0.005	N.R.	N.R.	0.070	0.066	FOCUS Step 2	0.109	FOCUS Step 2	3.81	24.3	RQ_{fw}	Sufficient monitoring data

#	Substance													
19	Triphenyl phosphate	3.70E-03	0.240	N.R.	N.R.	0.140	0.015	ECETOC	5.490	ECETOC	2.16	22.9	RQ$_{sed}$	
20	Acetamiprid	5E-04	N.R.	N.R.	N.R.	0.245	0.005	FOCUS Step 2	0.005	FOCUS Step 2	0.02	10.0	RQ$_{fw}$	
21	Ciprofloxacin	8.9E-05	0.272	N.R.	N.R.	0.006	5.4E-04 [d]	Eq. G	1.642	EqP	0.0017	6.04	RQ$_{fw/sed}$	Human consumption
		8.9E-05	0.272	N.R.	N.R.	0.006	0.0012	MEC	3.78	EqP	0.004	13.93	RQ$_{fw/sed}$	Monitoring
22	Tolylfluanid	2.65E-04	0.058	8	6.087	0.350	9.7E-04	ECETOC	0.217	ECETOC	0.07	3.66	RQ$_{fw}$	Sufficient monitoring data
23	Clarithromycin	1.3E-04	0.0012	No info	0.012	0.001	4.38E-04 [d]	Eq. G	0.004	EqP	0.025	3.37	RQ$_{fw/sed}$	Human consumption
							6E-04	MEC	0.006	EqP	0.036	4.96	RQ$_{fw/sed}$	Monitoring
24	Azithromycin [c]	9E-05	0.014	No info	0.103	0.006	1.3E-04 [d]	Eq. G	0.020	EqP	0.03	1.42	RQ $_{fw/sed}$	Human consumption
		9E-05	0.014	No info	0.103	0.006	5.83E-04	MEC	0.09	EqP	0.117	6.48	RQ $_{fw/sed}$	Monitoring
25	Ofloxacin	1.3E-04	N.R.	N.R.	N.R.	No info	9.4E-05 [d]	Eq. G	0.0002	EqP	0.0003	0.72	RQ$_{fw}$	RQ < 1
26	Edetic Acid (EDTA)	2.2	118.58	N.R.	N.R.	0.6	0.2486	ECETOC	26.93	ECETOC	0.447	0.41	RQ$_{dw,hh}$	RQ < 1
27	Cyanide-free	0.00026	-	-	-	-	-	-	-	-	-	-	-	Many MS are monitoring CN, a few are already monitoring free CN. Improvements in analytical capabilities are likely to soon generate sufficient data.

[a] PNEC values were updated according to the comments received. New monitoring data from Sweden and Italy were considered as well, and therefore 5 substances may be moved to the priority substances review because there are monitoring data from at least 4 MS.

[b] PEC$_{fw,sed}$ values for plant protection products were calculated using FOCUS Step2.

[c] Erythromycin and azithromycin are registered in ECHA as having an intermediate use.

[d] PEC$_{fw}$ values for antibiotics were re-calculated by using the following formula: PEC$_{fw}$= *(consumption X F$_{excreta}$) / (WWinhab X hab X dilution X 365)* from Besse et al. (2008)[25]

where *WWinhab* is the volume of wastewater per person per day (default value of 200 [L/(hab*day]), *hab* are the number of inhabitants, *F$_{excreta}$* is the excretion factor of the active substance, *consumption* is the quantity (mg/year) of active ingredient consumed by the population during 1 year.

Besse et al (2008)[25] made calculations based on data of consumption from France. Consumption data were taken from Iatrou et al, 2014[26] for EL, from UBA report for DE[27], and directly provided to JRC for PT, DK and LV by the respective MS. A similar calculation was done for these MS. The worst case PEC$_{fw}$ value, calculated with the consumption data from single MS, was selected for the risk assessment.

The above calculations of PEC values for antibiotics do not consider any veterinary use. In fact, the MEC, based on monitoring data from just a few MS, show that the calculated PEC are likely an underestimation of the real environmental concentrations.

5. Discussion and Recommendations

- **Trichlorfon**: this substance has been banned as a PPP since 2007 but is currently still used as a veterinary pharmaceutical. For the PEC calculation, only a pre-banning tonnage was available (year 2000), and no PEC value was available from the literature related to its current use. For this reason, the available tonnage value was used for the PEC calculation, even though it is likely an overestimation, and an ERC code applicable to veterinary pharmaceuticals was selected (ERC8a). Additionally, as suggested at the WG Chemicals meeting 16-17 Oct 2014, a simulation was done to calculate the risk considering a reduction in the tonnage. From this simulation, it could be seen that even reducing the tonnage by 80%, the substance would still rank in the 2nd position in this exercise. It should be noted that six Member States (MS) have derived an EQS for trichlorfon, but it is unclear whether monitoring data have been collected by at least four MS for the time period 2006-2014, in which case the substance could automatically be considered under the monitoring-based exercise of the ongoing PS review. There is also significant uncertainty in the derivation of the PNEC, with the use of an AF of 1000. Regarding the available analytical methods, there are some difficulties reported with the extraction and analysis and in reaching the low PNEC of the substance [29]. It is considered that additional data are required on tonnage and hazard to better identify the risk from trichlorfon, before recommending its inclusion into the Watch List, and for this reason, the substance has been deselected from the candidate list.

- **Cyclododecane**: No effects on aquatic organisms found at concentrations below water solubility and no reliable QSARs predictions were found for the substance. Therefore, it was not possible to calculate $PNEC_{fw}$. The highest risk was calculated for biota. Even though cyclododecane has a high BCF and is expected to accumulate in biota, the derived PEC_{biota}, seems like an overestimation. The PEC_{biota} was calculated from the PEC_{fw} using ECETOC. However, the PEC_{fw} (also calculated using ECETOC) is about 30 times higher than the water solubility. In addition, there is no information on how widespread the use of cyclododecane is in Europe and no analytical methods could be retrieved from the literature [29]. For the reasons stated above, it is recommended to deselect cyclododecane from the candidate list for the WL.

- **Diflufenican**: The exposure of diflufenican was assessed using different FOCUS Step models and a risk was identified even using the high-tier FOCUS Step 3, considering the derived PNEC. The number of MS with monitoring data for the water compartment in the period 2006-2014 has been reassessed, and now reaches four MS, which is considered sufficient to assess the risk posed by the substance based on measured environmental concentrations in this compartment in the monitoring-based exercise of the ongoing review of the PS list. Even though the substance is likely to partition into the sediment (high Koc and DT50 sed values, see factsheet), a higher risk has been derived for the water compartment. However, PNEC exceedances were found in the two compartments (water and sediment).

- **Oxadiazon**: The substance is a RBSP in one MS, and monitoring data are available for only two MS, while there is information that the substance is used in nine MS. The exposure of oxadiazon was assessed using FOCUS models and a risk was identified even using the high-tier FOCUS Step 3, considering the derived PNEC. The available monitoring data, particularly those retrieved from IPChem,

also indicate a risk from this substance. Furthermore, a risk was determined for drinking water (RQ_{dw} 3.1). There are analytical methods capable of analysing the substance at low concentrations [29]. Although, an evaluation process of Confirmatory data on the substance is currently on-going, oxadiazon is still recommended for inclusion in the Watch List because of the apparently very high RQ, which could remain high even if the conditions of approval are changed.

- **Tri-allate**: The substance was evaluated during the last review of the PS list. The highest RQ calculated in the present report is for surface water (RQ_{fw}). The substance seems to be in use in eight MS, while monitoring data are available from only two MS (for water), with no PNEC exceedance. By contrast, the PEC calculation with FOCUS Step models indicates an exceedance of the PNEC even using FOCUS Step 3. There are analytical methods capable of analysing the substance at low concentrations in both water and soil [29].

- **Methiocarb**: Following the WG Chemicals meeting (16-17 October 2014), new monitoring data have become available and the total number of MS with monitoring data for methiocarb is now five. A PEC_{fw} has been calculated using both ECETOC and FOCUS Step 1 and Step 2 models. The results from the first two models were quite in agreement with the measured concentrations (MEC_{95}), except for SE, where all the measurements were below LOQ. Thus, both predicted and most measured concentrations are consistent with a risk for the water compartment in several MS. However, recently, the Commission Implementing Regulation (EU) No 187/2014 has restricted the uses of this active substance by withdrawing the authorisation for its use as a molluscicide. It is likely that this restriction will reduce the use of this substance in Europe and given the fast degradation of Methiocarb in the environment, no further aquatic exposure is expected from former use as a molluscicide. It is recommended that methiocarb is still considered for the Watch List to gather information on the post-banning environmental concentration (which at the moment is not available for any MS), in order to assess whether the banning as a molluscicide has been effective in eliminating the risk from this substance. In this respect, there are analytical methods capable of analysing the substance at low concentrations [29].

- **Imidacloprid**: This neonicotinoid has a widespread use in Europe as PPP and biocide, and some of its uses are currently restricted [30]. The PEC was derived using FOCUS Step models, where the PEC calculation was based on crop applications that accounted for the restriction in the uses of the substance. The calculated PEC shows an exceedance of the PNEC, even using FOCUS Step 3. Monitoring data are available for 5 MS (pre-restriction), and even though the MEC is lower than the predicted concentration, it still shows an exceedance of the PNEC. The PNEC has been derived using a probabilistic method and an AF of 3. Although there are monitoring data from more than 4 MS, the risk assessment of this substance in the prioritisation process may need to take account of the effects of the restriction, if it is extended, therefore monitoring data under those conditions should be obtained. There are analytical methods capable of analysing the substance at low concentrations [29].

- **2,6-ditert-butyl-4-methylphenol**: The substance is classified as having industrial uses with applications in a broad range of products. However, no monitoring data are available for the surveyed period (2006-2014), except from SE, for sludge and treatment plant effluents.

A recent tonnage value is available in IUCLID and this was used to calculate the PEC using an ECETOC model. Both $PNEC_{fw}$ and $PNEC_{sed}$ were retrieved from the ECHA file, with an AF of 100. The risk was higher for the sediment fraction. Given the high risk calculated for this substance, its widespread use and the fact that it is not readily biodegradable, and has a high BCF value, its inclusion into the Watch List is recommended. The literature indicates that methods are available for analysing the substance at the low ng/L level [29].

- **Thiacloprid**: The substance has a widespread use in Europe as PPP and biocide. Since no tonnage was available for its use as biocide, the PEC calculation was done with the application rate considering its use as PPP only using FOCUS Step models. Even using the higher-tier Step 3, the calculated PEC exceeded the PNEC. Monitoring data are available from four MS, in two of which there was exceedance of the PNEC. Hazard data for PNEC calculation were retrieved from the Biocide Assessment report for the substance and the lowest endpoint from the aquatic species tested corresponded to the midge *Chironomus riparius* to which an AF of 10 was applied to derive the PNEC. Although having sufficient monitoring data to be included in the monitoring-based exercise, it is recommended to keep thiacloprid on the candidate list, since the predicted risk is already reinforced by exceedances of the PNEC in 50% of the four MS with monitoring data. There are analytical methods capable of analysing the substance at low concentrations [29].

- **Aminotriazole**: A significant risk was calculated for this substance, even considering a high-tier FOCUS step 3 for the calculation of the PEC. However, monitoring data are only available from one MS, where the MEC_{95} is slightly below the PNEC. A high risk was determined for drinking water (RQ_{dw} 143). It was brought to our attention that a Commission vote is expected in December 2014, regarding the renewal of the authorisation of aminotriazole. For this reason, it is recommended to postpone the decision on an eventual proposal of aminotriazole for the WL until it is known whether a restriction on its use will be issued. The aminotriazole factsheet could then be reassessed on the occasion of the first revision of the WL. Furthermore, there seem to be some issues with the extraction and analysis of aminotriazole [29].

- **Clothianidin**: The substance has a widespread use in Europe (20 MS, according to the EU pesticides database) as PPP and biocide. A restriction on the use of clothianidin was imposed in 2013 [30]. The PEC has been calculated considering the application rate as PPP using the FOCUS Step models; the crop used for the PEC calculation was not listed in the restricted uses. Even using the higher-tier Step 3, the calculated PEC exceeded the PNEC. Monitoring data are available from only one MS, where all values were below the LOQ (which was below the PNEC). As for other neonicotinoid substances, the midge *Chironomus riparius* was the most sensitive species from all the hazard data in the Bioacide assessment report of the substance, and the PNEC was calculated using the deterministic approach with an AF of 10. Due to the high risk calculated for the aquatic environment, and insufficient information on environmental concentrations, it is considered that clothianidin is a good candidate for the WL, despite some of its uses currently being restricted. There are analytical methods capable of analysing the substance at low concentrations [29].

- **Chromium trioxide**: Chromium trioxide was short-listed during the last review of the PS list. A ban on the use of chromium trioxide and other hexavalent ions has been recently introduced, with the last application date in 2016, and a sunset date of 2017. Since there are already measures in place that are expected to decrease the environmental concentrations for this substance, it is recommended to deselect chromium trioxide as candidate for the Watch List and from the review of the PS list.

- **Thiamethoxam**: This neonicotinoid has a widespread use in Europe as PPP and biocide, and some of its uses are currently restricted [30]. The PEC was derived using FOCUS Step models, where the PEC calculation was based on crop applications that accounted for the restriction in the uses of the substance. The calculated PEC shows an exceedance of the PNEC, even using a PEC calculated from Step 3. Monitoring data are available for four MS, in one of which the PNEC has been exceeded. The highest MEC_{95} is lower than the predicted concentration, and also lower than the PNEC. The PNEC was derived using the deterministic approach with an AF of 100, following the Biocide Assessment report. Given its widespread use, and significant calculated RQ, the risk assessment of this substance could benefit from more extensive monitoring across Europe, to resolve the discrepancy between the PEC and the MEC, therefore it is recommended to consider thiamethoxam as a candidate for the Watch list. There are analytical methods capable of analysing the substance at low concentrations [29].

- **2-Ethylhexyl 4-methoxycinnamate**: This substance and UV filters in general have a widespread use worldwide. The tonnage value used for the PEC calculation was relative to year 2000, and considering the increase in the use of UV-filters in recent years, the tonnage could be even higher currently. The highest risk has been calculated for the sediment fraction from the PEC estimated with ECETOC and estimated $PNEC_{sed}$ and no toxicity was found for pelagic organisms below the water solubility of the substance. There are monitoring data for only two MS, where the MEC_{95} was lower than the PNEC for the substance. Even though other UV filters (eg. octocrylene) are found in the environment at higher concentrations than 2-ethylhexyl 4-methoxycinnamate, the latter is one that shows toxicity at lower concentrations (see factsheet for references). Furthermore EHMC is a suspected PBT and an endocrine disruptor, and more information on the exposure of aquatic ecosystems is required, and for this reason it is suggested as a good candidate for the Watch list. The available literature indicates that the substance can be measured at sufficiently low concentrations, including in sediment [29].

- **Dichlofluanid**: this substance was short-listed under the last review of PS. Dichlofluanid is currently used as a biocide and has been banned as a PPP since 2003. However, for the PEC calculation, only a pre-banning tonnage was available (from year 1997), and no PEC value was available from the literature related to its current use. For this reason, the available tonnage value was used for the PEC calculation, even though it is likely an overestimation. As suggested at the WG Chemicals meeting 16-17 Oct 2014, a simulation was done to calculate the risk considering a reduction in the tonnage. From this simulation, it could be seen that a 50% reduction in the tonnage would shift the ranking in this exercise from 16th to the 19th position. There is monitoring data from three MS for the time period 2006-2014, and the highest concentration measured is below the derived PNEC, while most measurements were below LOQ, even for sediment. Considering a broader time scale, also the PEC1 and PEC2 calculated from the monitoring data of the substance during the last review of the PS list were similar to more recent values

and still below the PNEC. It was also reported in the Biocide Assessment report that dichlofluanid rapidly degrades in aerobic aquatic systems, and that dichlofluanid does not have the potential to cause long-lasting contamination of surface water or sediment [31]. It is considered that the risk assessment of this substance requires an update in tonnage values relative to its current use. The available literature indicates that the substance can be measured in the low ng/l and μg/kg ranges for water and sediment, respectively [29].

- **Formaldehyde**: The substance was suggested for the WL by a MS. It is used in many different products, EU-wide. A confidential updated tonnage value was used for calculation of the PEC with the ECETOC model. However, in recent years different uses of formaldehyde have been banned (see factsheet). Formaldehyde is reported as a RBSP in three MS, and monitoring data in the period 2006-2014 is available for three MS. The MEC_{95} from all the databases screened in this report is below the PNEC. Furthermore, a decreasing trend in measured concentrations (MEC_{95}) in surface water was apparent (FR: from 17.6 μg/L (2008) to 7.6 μg/L(2012); UK: from 26.2 μg/L(2010) to 21.2 μg/L(2011); SK: from 6.5 μg/L(2007) to 0.2 μg/L(2010)). The PNEC was retrieved from ECHA and was estimated using the probabilistic approach with an AF of 10. A considerable risk was determined for drinking water, with a RQ_{dw} similar to the one for freshwater (25.8 and 28.8, respectively). It is likely that environmental exposure to formaldehyde will occur in many MS but it is less likely that exceedances of the PNEC are detected considering the restricted uses. There seem to be no issues in measuring this substance with the analytical methods available [29].

- **Dimethenamid-P**: dimethenamid was banned in 2006 [32] and since replaced by its active isomer dimethenamid-P. The PNEC values were estimated based on combined data from dimethenamid and dimethenamid-P, since the toxicological reference values established for dimethenamid have been considered applicable to dimethenamid-P by EFSA [33]. The initial assessment of the number of MS for which monitoring data are available was done by considering the monitoring data for dimethenamid and dimethenamid-P separately. In doing so, it was realised that there were monitoring data from four MS for dimethenamid, and only from two MS for dimethenamid-P (NL and IT). However, it was brought to our attention that monitoring data after the latest sales date established for dimethenamid (22 June 2008) can only relate to uses of dimethenamid-P PPPs, even if it has been attributed to "dimethenamid" (stakeholder comment (BASF)). Therefore, monitoring data after 2008 are available from five MS, and is considered sufficient for the evaluation of the substance in the ongoing review of PS. For this reason it is recommended to deselect dimethenamid-P as candidate substance for the Watch list.

- **Triphenyl phosphate**: The use pattern is not clearly stated in the ECHA dossier, but an ERC code related to wide dispersive use is given. An updated tonnage value retrieved from IUCLID was used for the PEC calculation with ECETOC. Triphenyl phosphate is readily biodegradable and the DT50 water < 28 days. The Koc value is very high and its accumulation in sediment is expected. Indeed, the highest risk was calculated for sediment, but no monitoring data were available for this compartment. For the water compartment, monitoring data are available for two MS, in both cases with concentrations lower than the PNEC, and the substance is reported as RBSP in 1 MS. Additional monitoring data could help in the risk

assessment of the substance. There seem to be no issues in measuring this substance with the analytical methods available, even in sediment [29].

- **Acetamiprid**: This neonicotinoid has a widespread use in Europe as PPP and it has not been subject to any restriction. The PEC calculation was done with the application rate considering its use as PPP using FOCUS Step models. Even using the higher-tier Step 3, the calculated PEC exceeded the PNEC. Monitoring data are available from only two MS, in one of which the PNEC has been exceeded. The lowest endpoint retrieved from the EU Review report related to *Chironomus riparius* and an AF of 10 was used to derive the PNEC. It is considered that acetamiprid is a good candidate for the Watch list and there are analytical methods capable of analysing the substance at low concentrations [29].

- **Erythromycin**: This pharmaceutical substance is registered in IUCLID with tonnage value given for an intermediate use (associated code ERC6a). By using ECETOC and ERC6a code to estimate the PEC value, an extremely high PEC_{sed} (50.89 mg/kg), and therefore a considerable risk, would be calculated for this substance, which would become the highest ranked in this exercise. However, the high PEC_{sed} value seemed an overestimated value and therefore, it was decided to use a different ERC code, applicable to pharmaceuticals, i.e. ERC8a. In addition to its intermediate use, erythromycin is a human and veterinary antimicrobial. Sales data were provided by PT, DK and LV and retrieved from the literature for EL [26] and from a report for DE [27]. The PEC calculated considering human use and excretion rates, by using a simplified EMA calculation retrieved from literature (see factsheet) were at least 1-order of magnitude lower than those using ECETOC ERC8a. The substance showed exceedance of the PNEC in measured concentrations in the NORMAN database (since 2002) and in monitoring data from SE, although the concentrations in the NORMAN database in the period 2006-2014 were all <LOQ. No consumption data were available for the use of erythromycin as a veterinary medicine. The risk assessment of this substance would greatly benefit from more information regarding both its use and environmental prevalence, and the inclusion into the Watch List could inform the risk assessors on the latter. There seems to be analytical methods available to analyse the substance at low concentrations, even regarding the LOQ for sediment [29].

- **Clarithromycin**: this pharmaceutical is used both as human and veterinary antimicrobial. Six PEC_{fw} values were calculated by using a simplified EMA calculation retrieved from the literature (see factsheet). According to the information available, only sales data related to human consumption from four MS were used for the PEC calculations, since no consumption values were available for the use of clarithromycin as veterinary medicine. The highest PEC value selected among those calculated was found to be lower than the highest MEC_{95} measured in SE, underlying that there may likely be an underestimation in the PEC calculation, due also to the missing information. The substance showed exceedance of the PNEC both in predicted and in measured concentrations in one MS out of three countries for which monitoring data are available. The risk assessment process of this substance would greatly benefit from more information regarding both its use and environmental prevalence, and the inclusion into the Watch List could inform the risk assessors on the latter. There are analytical methods capable of analysing the substance at low concentrations [29].

- **Ciprofloxacin**: this pharmaceutical is used both as human and veterinary antimicrobial. Five PEC_{fw} values were calculated by using a simplified EMA calculation retrieved from literature (see factsheet). Only sales data relating to human consumption in those MS were available for the PEC calculations. The highest PEC value selected among those calculated was found to be lower than the highest MEC_{95} measured in SE (NORMAN database), underlining that there may likely be an underestimation in the PEC calculation, due at least in part to the missing information. The predicted concentrations and the measured concentrations in the NORMAN database and in SE exceeded the PNEC. Additional monitoring data gained through the inclusion of ciprofloxacin into the Watch List would greatly benefit the risk assessment. There are analytical methods capable of analysing the substance at low concentrations [29].

- **Azithromycin**: this pharmaceutical is used both as human and veterinary antimicrobial. Five PEC_{fw} values were calculated by using a simplified EMA calculation retrieved from literature (see factsheet). Only sales data relating to human consumption in those MS were available for the PEC calculations. The highest PEC value selected among those calculated was found to be lower than the highest dissolved MEC_{95} measured in PT (NORMAN database), underlying that there may likely be an underestimation in the PEC calculation, due at least in part to the missing information. The substance showed exceedance of the PNEC both in predicted and in dissolved measured concentrations in the NORMAN database. Also in the case of azithromycin, it would be advantageous to have additional monitoring data, and the substance is considered a good candidate for the Watch List. There are analytical methods capable of analysing the substance at low concentrations [29].

- **Free cyanides**: Even though there are monitoring available data for total cyanides from > four MS, there appears to be insufficient information with regard to the most bioavailable cyanide species. Furthermore, no tonnage in Europe was available in IUCLID for free cyanides and therefore ECETOC could not be used for PEC calculation. Moreover, no PEC value could be found in the literature. Improved monitoring strategies focused on free cyanide would facilitate the estimation of environmental concentrations, particularly considering the concern for drinking water exposure and the available drinking water standard in Europe for cyanides [22]. Continuous improvements in sampling and analytical methodologies and capabilities in the different MS promise to allow widespread adequate measurement of free cyanides in the near future.

- For **ofloxacin** and **EDTA**, no risk was found in the present assessment (RQ < 1), and consequently they have been excluded from the candidate list.

Table 4. Final ranking after removal of substances with high uncertainty (trichlorfon, cyclododecane), facing a total ban (chromium trioxide), having a RQ < 1 (EDTA and ofloxacin), or with sufficient monitoring data (diflufenican, dimethenamid-P, tolylfluanid). For Cyanide-free, it is expected that appropriate data will soon become available. To be noted that the five substances imidacloprid, thiacloprid, clothianidin, thiamethoxam, and acetamiprid have been grouped together under the "*neonicotinoid class*".

Substance	Cas n.	Critical PNEC value	AF	Critical PEC value	Highest RQ for ranking		Recommended fraction	Analytical method [29]	LOQ (ng/L)	Comment
Oxadiazon	19666-30-9	8.8E-05 mg/L	10	0.039 mg/L	443.18	RQ_{fw}	water	yes	low	
Methiocarb	2032-65-7	1E-05 mg/L	10	0.004 mg/L	395.0	RQ_{fw}	water	yes	low	To determine environmental concentrations post banning as molluscicide.
2,6-ditert-butyl-4-methylphenol	128-37-0	1.290 mg/kg dw	100*	367.640 mg/kg dw	283.24	RQ_{sed}	water/sediment	yes	low	
Tri-allate	2303-17-5	6.7E-04 mg/L	10	0.118	176.12	RQ_{fw}	water	yes	10	
Imidacloprid	105827-78-9/ 138261-41-3	9E-06 mg/L	3	0.008 mg/L	889	RQ_{fw}	water	yes	low	RQs pre-partial restriction. Possible grouping as neonicotinoids. A common analytical method for monitoring is available.
Thiacloprid	111988-49-9	5.0E-05 mg/L	10	0.0109 mg/L	218.0	RQ_{fw}	water	yes	low	
Thiamethoxam	153719-23-4	1.4E-04 mg/L	100	0.0110 mg/L	78.57	RQ_{fw}	water	yes	low	
Clothianidin	210880-92-5	1.3E-04 mg/L	5	0.0080 mg/L	61.54	RQ_{fw}	water	yes	low	
Acetamiprid	135410-20-7/ 160430-64-8	5.0E-04 mg/L	10	0.0050 mg/L	10.0	RQ_{fw}	water	yes	low	
Erythromycin	114-07-8	0.0060 mg/kg dw	10*	0.318 mg/kg dw	52.9	RQ_{sed}	water/sediment	yes	10	ECETOC
		2 E-04 mg/L	10	0.0006 mg/L	3.07	$RQ_{fw/sed}$				Monitoring
2-ethylhexyl 4-methoxycinnamate	5466-77-3	0.2 mg/kg dw	10	8.390 mg/kg dw	41.95	RQ_{sed}	sediment	yes	low	
Dichlofluanid	1085-98-9	0.018 mg/kg dw	10*	0.732 mg/kg dw	40.2	RQ_{sed}	sediment	yes	low	
Formaldehyde	50-00-0	0.47 mg/L	10	13.5 mg/L	28.8	RQ_{fw}	water	yes	low	
Triphenyl phosphate	115-86-6	0.24 mg/kg dw	10*	0.015 mg/kg dw	22.9	RQ_{sed}	sediment	yes	low	

Ciprofloxacin	85721-33-1	8.9E-05 mg/L	50	5.4E-04 mg/L	6.04	$RQ_{fw/sed}$	water/sediment	yes	low	Human consumption
				0.0012 mg/L	13.93					Monitoring
Clarithromycin	81103-11-9	1.3E-04 mg/L	20	4.4E-04 mg/L	3.37	$RQ_{fw/sed}$	water/sediment	yes	low	Human consumption
				6E-04 mg/L	4.96					Monitoring
Azithromycin	83905-01-5	9E-05 mg/L	50	1.3E-04 mg/L	1.42	$RQ_{fw/sed}$	water/sediment	yes	low	Human consumption
				5.83E-04 mg/L	6.48					Monitoring

* The $PNEC_{sed}$ was calculated with the Equilibrium Partitioning method from the $PNEC_{fw}$

It is recommended that in addition to diclofenac, E2 and EE2, already proposed for the Watch List, the list also includes the substances with the highest risk, and not excessive uncertainty in the PEC or PNEC calculation in this exercise.

Even though E1 has been excluded from the list of candidate substances due to availability of monitoring data, it is a transformation product of E2 and is a considerable contributor to estrogenic activity in the aquatic environment. Therefore, it is recommended that E1 be analysed together with E2 to gather data for risk management following the reasons for inclusion of E2 into the Watch List. Both substances may be analysed with the same method in the same run, by GC-MS or LC-MS, without considerable additional burden.

Regarding neonicotinoids, a risk has been predicted for all five substances in the initial list, and their use in Europe is widespread. Even though for imidacloprid and thiamethoxam apparently the monitoring data would be sufficient to consider the substances under the monitoring exercise of the ongoing review of PS, these are related to a period prior to the implementation of the restriction on their use. If the restriction were to be extended, consideration of the substances in the priority substances review would have to be based on updated monitoring data. For thiacloprid, sufficient data also exist, but the exposure situation could also change in the light of the above restrictions. Since the neonicotinoids have similar properties and a similar mode of action and can be measured together with the same method, and without excessive costs, they could be included as a group of substances in the Watch List (Table 4). It is of note that just three of them were restricted due to the risk they pose for bees. However, a risk is identified for all five substances when other insects, relevant to the aquatic environment, are considered.

For substances with more individual uses, the estimation of a more realistic risk is complicated by the lack of sufficient monitoring data. However, the risk estimated for the four antimicrobials was in the same range considering the upper-end measured concentrations in Europe. Erythromycin, clarithromycin, and azithromycin are members of the same class, i.e. macrolide antibiotics, and share the same mode of action. Since it has been suggested by some MS and stakeholders, both in the initial proposal of substances and during the commenting phase of the report, to consider antibiotics as a group for the Watch List, those three substances are now proposed as a group of substances. This proposal is also supported by the availability of a single analytical method [29]. The significant risk estimated for ciprofloxacin would also support its inclusion in the Watch List. However, since it is in a different class of antimicrobials from the above group, it would need to be included as a separate substance.

In conclusion, the ten substances/groups of substances most recommended for the first Watch List are listed below, subject to the availability of the analytical methodology to monitor them:

Diclofenac
17-Beta-estradiol (E2), Estrone (E1)
17-Alpha-ethinylestradiol (EE2)

Oxadiazon

Methiocarb

2,6-ditert-butyl-4-methylphenol

Tri-allate

Imidacloprid, Thiacloprid, Thiamethoxam, Clothianidin, Acetamiprid

Erythromycin Clarithromycin, Azithromycin

2-Ethylhexyl 4-methoxycinnamate

6. Acknowledgements

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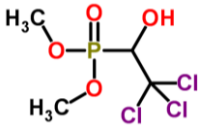
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Annex – Substances factsheets

Information on exposure, hazard and risk for the Watch List candidate substances (except for substances with RQ <1)

Trichlorfon (CAS N. 52-68-6)

1. Substance identity

Chemical name (IUPAC)	Dimethyl 2,2,2-trichloro-1-hydroxyethylphosphonate
EC number	200-149-3
CAS number	52-68-6
Molecular formula	C4H8Cl3O4P
Molecular weight	257.437
Structure	
SMILES	COP(=O)(C(C(Cl)(Cl)Cl)O)OC

2. Physico-chemical Properties

Endpoint	Value	Source
Vapour Pressure (Pa)	2.1E-04	EFSA conclusion, 2006[1]
Water solubility (mg/L)	120000	EFSA conclusion, 2006[1]
logK$_{ow}$	0.43	EFSA conclusion, 2006[1]

3. Environmental fate

Endpoint	Value	Source
Sorption potential (K$_{oc}$)	0	EFSA conclusion, 2006[1]
Biodegradability	NRB	EFSA conclusion, 2006[1]
Bioaccumulation (BCF)	2.74	Consensus between ADMET Predictor v. 7, VEGA Nic software, EPI Suite BCFBAF v. 3.01
BMF	1	Default value, TG n. 27 - CIS WFD[2]

4. Environmental exposure assessment

	Description	Source
Tonnes/year	1050 (year 2000)	From previous exercise
Uses	Insecticide used as veterinary pharmaceutical	
Spatial usage (by MS):	Not known	
Banned uses	PPP	(Commission Decision, C (2007)2096)[3]
ERC code	ERC8a	

Fraction of tonnage to region	0.1	

4.1 Predicted Environmental Concentration

	Description	Source
PEC_{fw} (mg/L)	0.034	ECETOC
PEC_{sed} (mg/kg dw)	0.12 (N.R.)	ECETOC
PEC_{biota} (mg/kg)	0.093 (N.R.)	Calculation based on Equation L (Section 3.4.3)

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

4.1.1 ECETOC simulation with lower tonnages

From 25 May 2007 no authorisation for plant protection products containing trichlorfon are granted or renewed. Any period of grace granted by Member States shall be as short as possible and shall expire not later than 21 November 2008 (Commission Decision, C (2007)2096)[3].

However, the available tonnage of 1050 relates to the year 2000, which is prior to the banning of the substance as PPP. At the WG Chem meeting 16-17/10/2014, it was suggested to perform a simulation on the PEC calculated with ECETOC using reduced tonnage values of trichlorfon that could be closer to the actual tonnage after the banning, i.e. related to the use as veterinary pharmaceutical only. Since no tonnage value specific for this particular use was available, it was decided to perform the simulation considering a 30%, 50% or 80% decrease in tonnage values. The results of the simulations are compared with the pre-banning tonnage scenario in the following Table.

Tonnes/year	1050	735	525	210
Decrease respective to pre-banning tonnage	-	30%	50%	80%
PEC_{fw} (mg/L)	0.034	0.024	0.017	0.007
RQ_{fw}	35312	24781.25	17697.92	7083.33
Position in the ranking (higher RQ)	1 (RQ_{fw})	1 (RQ_{fw})	1 (RQ_{fw})	2 (RQ_{fw})

4.2 Measured Environmental Concentration

Trichlorfon has been reported as a RBSP, with 6 MS having set EQSs ranging from 0.001 µg/L and 0.01 µg/L[4]. However, monitoring data was available only for 3 MS during the period surveyed (2006-2014).

n. of MS	Source of monitoring data	MEC values	RBSP
3 (FR, NL, IT)	NORMAN DB, 2014[5]	$MEC_{95, whole}$: 0.428 µg/L	6 MS[4]
	IT monitoring programme[6]	All values < LOQ	

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

Trichlorfon is listed as Endocrine disruptor category 2 in the Endocrine Disruptor's Access Database of the European Commission[7].

In the EFSA Conclusion 2006[1], it was reported that, with respect to gene mutation in vitro, equivocal results were obtained in the cultured mammalian cells (Chinese hamster lung cells). Positive results were obtained for in vitro chromosome aberrations in human lymphocytes, with and without metabolic activation. However the clastogenicity could not have been confirmed *in vivo* for somatic cells (micronucleus test) or germ cells (dominant lethal assay) since the studies were considered as non acceptable due to major deviations from the guidelines. Therefore, the genotoxic potential of trichlorfon *in vivo* could not be concluded in the EFSA Conclusion, 2006[1]. In the same document, it was concluded that trichlorfon is not a carcinogenic compound and has no developmental toxicity.

Trichlorfon is not readily biodegradable (P), and a BCF value of 2.74 L/kg (the mean value of the three results was used) was estimated by using VEGA Nic, ADMET and EPI Suite models.

6. Hazard assessment

6.1 Ecotoxicology data

Trophic level	Endpoint	Value	Reference
Fish	*Oncorynchus mykiss*, 96 h, LC_{50}	0.7 mg/L	EFSA conclusion, 2006[1]
Aquatic invertebrates	***Daphnia magna*, 48 h, EC_{50}**	**0.00096 mg/L**	**Footprint Pesticides Database[8]**
Algae	*Scenedesmus subspicatus*, 120 h, EC_{50}	10 mg/L	EFSA conclusion, 2006[1]

6.2 Mammalian toxicology data

Type of test	Endpoint	Value	Reference
Acute toxicity	Rat, LD50, oral	212 mg/kg bw	EFSA conclusion, 2006[1]
Long term toxicity	**Rat, NOAEL, 2 years, oral [a]**	**4.5 mg/kg bw/day**	**EFSA conclusion, 2006[1]**
Developmental toxicity	Rabbit, NOAEL, maternal toxicity	15 mg/kg bw/day	EFSA conclusion, 2006[1]
Developmental toxicity	Rabbit, NOAEL, offspring toxicity	45 mg/kg bw/day	EFSA conclusion, 2006[1]
Sub-chronic neurotoxicity	Rat, NOAEL, oral, 90 d	6.08 mg/kg bw/day	EFSA conclusion, 2006[1]
Long-term toxicity	Rat, NOAEL	13.2 mg/kg bw/day	EFSA conclusion, 2006[1]
Reproduction toxicity	Rat, NOEL	300 ppm	EFSA conclusion, 2006[1]

[a] Value used for ADI calculation in EFSA conclusion (2006) [1]

6.3 PNEC derivation

The most sensitive endpoint is for acute toxicity in *Daphnia magna.*

To be noted that in the EFSA conclusion (2006)[1], the study on *Daphnia magna* was considered of poor quality. In the U.S. EPA ECOTOX DB[9] the LC50/EC50 values with the same organism ranged from 0.01

µg/L to 750 µg/L. Evidence that *D. magna* showed highest sensitivity among organisms tested with trichlorfon are reported in Coelho et al. (2011)[10].

PNEC	Endpoint	Endpoint value	AF	PNEC value
PNEC$_{fw}$	*Daphnia magna*, 48 h, EC$_{50}$	0.00096 mg/L	1000 [a]	9.6E-07 mg/L
PNEC$_{sed}$	-	-	-	N.R.
PNEC$_{biota,sec\ pois}$	-	-	-	N.R.
PNEC$_{biota,\ hh}$	-	-	-	N.R.
PNEC$_{dw,\ hh}$	ADI	0.045 mg/kg bw/day	-	0.158 mg/L [b]

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

[a] Assessment factor 1000 was chosen because there was just acute toxicity data available for the main trophic levels.

[b] ADI value, retrieved from EFSA Conclusion, 2006[1], used in equation F as TL$_{hh}$. See section 3.3.5 for calculation.

7.   Risk Quotient (PEC/PNEC)

RQ	Value
RQ$_{fw}$	**35312**
RQ$_{sed}$	N.R.
RQ$_{biota,sec\ pois}$	N.R.
RQ$_{biota,\ hh}$	N.R.
RQ$_{dw,\ hh}$	0.22

8.   References

[1] EFSA Scientific Report (2006) 76, 1-62, Conclusion on the peer review of trichlorfon. Available at http://www.efsa.europa.eu/it/efsajournal/pub/76r.htm

[2] Technical Guidance for Deriving Environmental Quality Standards – Guidance Document No. 27 (2011) Common Implementation Strategy of the Water Framework Directive (2000/60/EC). Available at http://ec.europa.eu/environment/water/water-dangersub/lib_pri_substances.htm

[3] COMMISSION DECISION of 21 May 2007 concerning the non-inclusion of trichlorfon in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance (notified under document number C(2007) 2096). Available at http://eur-lex.europa.eu/legal-content/EN/ALL/?uri=CELEX:32007D0356

[4] NORMAN database at http://www.norman-network.net/?q=node/24

[5] Irmer U, Rau F, Arle J, Claussen U, Mohaupt V. (2013) Ecological Environmental Quality Standards of "River Basin Specific Pollutants" in Surface Waters - Update and Development Analysis of a European Comparison between Member States. ECOSTAT- UBA report.

[6] Italian Monitoring Programme (data provided directly to the JRC)

[7] Endocrine Disruptor database of the EU Commission), available at: http://ec.europa.eu/environment/chemicals/endocrine/documents/index_en.htm

[8] http://www.eu-footprint.org/it/index.html

[9] http://cfpub.epa.gov/ecotox/
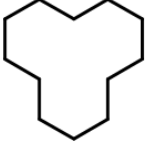
[10] Coelho S, Oliveira R, Pereira S, Musso C, Domingues I, Bhujel RC, Soares AM, Nogueira AJ. Assessing lethal and sub-lethal effects of trichlorfon on different trophic levels. Aquatic Toxicology 103 (2011) 191–198.

Cyclododecane (CAS N. 294-62-2)

1. **Substance identity**

Chemical name (IUPAC)	Cyclododecane
EC number	206-033-9
CAS number	294-62-2
Molecular formula	C12H24
Molecular weight	168.32
Structure	
SMILES	C1CCCCCCCCCCC1

2. **Physico-chemical Properties**

Endpoint	Value	Source
Vapour Pressure (Pa)	9.83	ECHA, 2013[1]
Water solubility (mg/L)	0.016	ECHA, 2013[1]
logK$_{ow}$	7.6	ECHA, 2013[1]

3. **Environmental fate**

Endpoint	Value	Source
Sorption potential (K$_{oc}$)	6513	ECHA, 2013[1]
Biodegradability	NRB	ECHA, 2013[1]
Bioaccumulation (BCF)	13700	ECHA, 2013[1]
BMF	10	Default value, TG n. 27 - CIS WFD[2]

4. **Environmental exposure assessment**

	Description	Source
Tonnes/year	Confidential tonnage used for calculation	IUCLID, 2013
Uses	Industrial use resulting in manufacture of another substance (use of intermediates)	IUCLID, 2013
Spatial usage (by MS)	Not known	
Banned uses	-	
ERC code	ERC6a	
Fraction of tonnage to region	0.1	

4.1   Predicted Environmental Concentration

	Description	Source
PEC_{fw} (mg/L)	0.4677	ECETOC
PEC_{sed} (mg/kg dw)	306.44	ECETOC
PEC_{biota} (mg/kg)	**64074.90**	Calculation based on Equation L (Section 3.4.3)

4.2 Measured Environmental Concentration

n. of MS	Source of monitoring data	MEC values	RBSP
None	-	-	-

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

Both in the ECHA dossier[1] and in the SVHC report[3], cyclododecane is considered to be not readily biodegradable, according to the biodegradability screening tests available.It was also concluded that cyclododecane has a very high bioaccumulation potential and fulfils the B and vB criteria[3]. The properties of persistency, liability to bioaccumulate and toxicity justified placing cyclododecane in the OSPAR list of Chemical for Priority Action, although no background document was prepared on the grounds that the substance is used as an intermediates in closed systems[4].

The ECHA Member State Committee (MSC) unanimously agreed that there was no sufficient scientific data to justify identification of cyclododecane as a substance of very high concern (SVHC)[5].

6.   Hazard assessment

6.1 Ecotoxicology data

No effects found in aquatic organisms at concentrations below water solubility[1].

6.2 QSARS for predicting ecotoxicity values

Software	Endpoint	Endpoint value	Reliability	Conclusions
ADMET predictor v. 7	LC_{50}, fish, 96 h	0.51 mg/L	The substance is within the scope (applicability domain) of the model	The endpoint value is above the water solubility of the substance. Therefore, it cannot be used
ADMET predictor v. 7	$pIGC_{50}$, *Tetrahymena pyriformis*, growth inhibition toxicity	0.247 mg/L	The substance is outside the scope (applicability domain) of the model	The prediction is not reliable.
ADMET predictor v. 7	pLC_{50}, *Daphnia magna*, 48 h	1565.30 g/L	The substance is within the scope (applicability domain) of the model	The endpoint value is above the water solubility of the substance. Therefore, it

				cannot be used
VEGA Nic	*Fathead minnow*, LC50, 96 h (from T.E.S.T tool)	0.78 mg/L	The substance is outside the applicability domain of the model.	The prediction is not reliable
VEGA Nic	*Daphnia magna*, LC50, 48 h (from T.E.S.T tool)	81.25 mg/L	The substance is outside the applicability domain of the model.	The prediction is not reliable
VEGA Nic	*Daphnia magna*, LC50, 48 h (from DEMETRA tool)	1.11 mg/L	The substance is outside the applicability domain of the model.	The prediction is not reliable
VEGA Nic	Fish, classification of toxicity (from SarPy tool)	Tox-2 (toxicity between 1-10 mg/L)	The substance is within the applicability domain of the model.	The prediction should be reliable
ECOSAR v. 1.11	Fish, *Daphnia*, Algae Acute toxicity estimation	< 0.01 mg/L	According to the $\log K_{ow}$ value of the substance (log K_{ow} 7.6), no effects at saturation are expected.	The predictions are not reliable.
ECOSAR v. 1.11	Fish, *Daphnia*, Algae chronic toxicity estimation	0.232 µg/L (fish) 0.506 µg/L (*Daphnia*) 6 µg/L (Green algae)	None of the chemical classes used for the models development seems to be representative of the molecular structure of the substance, leading to the consideration that cyclododecane could be outside of the structural domain of the models. Although both molecular weight and $\log K_{ow}$ of the substance are below the cut-off values related to the chronic endpoints, the predictions are considered not reliable.	

6.3 Mammalian toxicology data

Type of test	Endpoint	Value	Reference
Acute toxicity	Rat, oral, LD50	>1000 mg/kg bw	ECHA, 2013[1]
Repeated dose toxicity	Rat, oral, 29 d, NOAEL	150 mg/kg bw/day	ECHA, 2013[1]

6.4 PNEC derivation

PNEC	Endpoint	Endpoint value	AF	PNEC value
PNEC_fw	-	-	-	N.A.
Due to the fact that no effects have been seen at concentrations below solubility, it is not possible to calculate PNEC_fw (ECHA, 2013)[1]. No reliable QSARs predictions were found for the substance.				
PNEC_sed	-	-	-	N.A.
See comment above for PNEC_fw				
PNEC_biota,sec pois	Rats, repeated dose toxicity, conversion	150 mg/kg bw/day	300	5 mg/kg food [a]

	factor 10, 29 d, NOAEL			
PNEC_{biota, hh}	DNEL, from repeated dose toxicity, oral, NOAEL 150 mg/kg bw/day, AF 240 [b]	0.625 mg/kg bw/day	-	38.04 mg/kg bw/day [c]
PNEC_{dw, hh}	DNEL, same as above	0.625 mg/kg bw/day	-	2.19 mg/kg bw/day [d]

[a] The following steps were followed for PNEC$_{biota,sec pois}$ calculation: a) conversion of NOAEL (150 mg/kg bw/day) retrieved from ECHA, 2013 into NOEC (1500 mg/kg) by using the conversion factor of 10 (taken from TG n. 27- CIS WFD); b) To the NOEC value (1500 mg/kg), an appropriate AF$_{oral}$ (300) (selected according to the duration test (29 days) (TG n. 27 - CIS WFD) was applied.

[b] At the beginning the DNEL value was estimated from NOAEL value of 150 mg/kg bw/day (repeated dose toxicity study, oral gavage, rat, 29 d), by using an AF of 600. The latter value was calculated by using the default values reported in Table R.8-6 of the ECHA document "Guidance on information requirements and chemical safety assessment Chapter R.8: characterisation of dose [concentration]-response for human health", available at http://echa.europa.eu/documents/10162/13632/information_requirements_r8_en.pdf. Specifically, an AF of 4 was used for the correction of differences in metabolic body weight from rat to human, an AF of 2.5 for remaining interspecies differences, an AF of 10 was chosen for intraspecies differences related to general population, an AF of 6 was used for accounting differences from sub-acute to chronic study, and AF of 1 was selected both for dose-response differences and for issues related to the quality of the whole database. The total multiplication led to a value of 600. However, it was finally decided to remove the AF of 2.5(remaining interspecies differences) leading to a total AF value of 240, with a DNEL value of 0.624 mg/kg bw/day instead of 0.25 mg/kg bw/day. The final ranking would not change. However, the last considerations were included in the final risk assessment of the substance. Therefore, the factsheet has been amended accordingly.

[c] DNEL value used for PNEC calculation according to Equation E (see section 3.3.4)

[d] The DNEL value was calculated from the NOAEL value (ECHA, 2013[1]), and thenused in equation F as TL$_{hh}$ for PNEC calculation. See section 3.3.5 for calculation.

7. Risk Quotient (PEC/PNEC)

RQ	Value
RQ_{fw}	N.A.
RQ_{sed}	N.A.
RQ_{biota,sec pois}	**12814.98**
RQ_{biota, hh}	1684.25
RQ_{dw, hh}	0.21

8. References

[1] ECHA dissemination website: http://apps.echa.europa.eu/registered/data/dossiers/DISS-9d827c78-e4a2-5770-e044-00144f67d249/DISS-9d827c78-e4a2-5770-e044-00144f67d249_DISS-9d827c78-e4a2-5770-e044-00144f67d249.html

[2] Technical Guidance for Deriving Environmental Quality Standards – Guidance Document No. 27 (2011) Common Implementation Strategy of the Water Framework Directive (2000/60/EC). Available at http://ec.europa.eu/environment/water/water-dangersub/lib_pri_substances.htm

[3] SVHC_SUPPORT DOCUMENT, Member State Committee Support document for Agreement on cyclododecane. Adopted on 8 October 2008. Available at http://echa.europa.eu/documents/10162/13638/svhc_supdoc_cyclododecane_en.pdf[4] OSPAR list of Chemicals for Priority Action (Revised 2011). Available at: http://www.google.it/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&ved=0CCMQFjAA&url=http%3A%2F%2Fww w.ospar.org%2Fdocuments%2Fdbase%2Fdecrecs%2Fagreements%2F04-
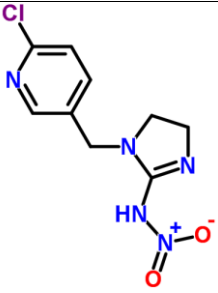
12e_list%2520of%2520chemicals%2520for%2520priority%2520action.doc&ei=mw5aVPHZL8TKaOXPgugD&usg=A
FQjCNE2l36bdrzuRahZmGXf-2BL5Gt-zA&sig2=4FsSESi1UTzEdCoXlAt0cg&bvm=bv.78677474,d.d2s

5 ECHA Press Release (ECHA/PR/08/34). ECHA Member State Committee Agrees On The Identification Of 14
Substances Of Very High Concern. Available at:
http://www.bssa.org.uk/cms/File/msc_indentification_svhc_20081009%20%282%29.pdf

Imidacloprid (CAS N. 105827-78-9/138261-41-3)

1. Substance identity

EC name	1-(6-chloropyridin-3-ylmethyl)-N-nitroimidazolidin-2-ylidenamine
EC number	428-040-8
CAS number	105827-78-9/138261-41-3
Molecular formula	C9H10ClN5O2
Molecular weight	255.7
Structure	
SMILES	C1CN(C(=N1)N[N+](=O)[O-])CC2=CN=C(C=C2)Cl

2. Physico-chemical Properties

Endpoint	Value	Source
Vapour Pressure (Pa)	4E-10	EFSA conclusion, 2008 [1]
Water solubility (mg/L)	610	EFSA conclusion, 2008 [1]
logK$_{ow}$	0.57	EFSA conclusion, 2008 [1]

3. Environmental fate

Endpoint	Value	Source
Sorption potential (K$_{oc}$)	225 (mean)	EFSA conclusion, 2008 [1]
Biodegradability	NRB	EFSA conclusion, 2008 [1]
Bioaccumulation (BCF)	0.61	FOOTPRINT PPDB[2]

4. Environmental exposure assessment

	Description	Source
Tonnes/year	-	
Uses	Insecticide (PPP and biocide)	
Spatial usage (by MS)	AT, BE, BG, CY, CZ, DE, DK, EE, EL, ES, FI, FR, HU, IE, IT, LT, LU, LV, MT, NL, PL, PT, RO, SE, SI, SK, UK	EU Pesticides DB [3]
Banned uses	Restriction of uses[a]	EU n. 485/2013 [4]
ERC code	ERC8d (N.R.)	

[a] the use as a seed treatment or soil treatment of plant protection products containing imidacloprid is prohibited for crops attractive to bees and for cereals except for uses in greenhouses and for winter cereals. Foliar treatments with plant protection products containing imidacloprid are prohibited for crops attractive to bees and for cereals with the exception of uses in greenhouses and uses after flowering[4].

4.1 Predicted Environmental Concentration

PEC_{fw} (mg/L)	0.008	FOCUS Step 2
PEC_{sed} (mg/kg dw)	0.0.018 (N.R.)	FOCUS Step 2
PEC_{biota} (mg/kg)	0.005 (N.R.)	Calculation based on Equation L (Section 3.4.3)

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

4.1.1 Comparison of FOCUS Pesticides models

FOCUS Step 1

Crop	Application Rate (g/ha)[1]	Water solubility (mg/L)[1]	K_{oc} (L/kg) [1]	DT_{50} whole system (d) [1]
Pome and Stone Fruits (late)	1st appln 70 2nd appln 105 (40 d application interval)	610	225 (mean)	90

FOCUS Step 2

Same parameters and conditions as above, in addition to DT_{50soil} 82 d (although being normalized with the older Q_{10} value of 2.2, this field DT_{50} value was kept for Step1&2 calculations, since the PEC_{fw} value of Step3 retrieved from the EFSA conclusion, 2014[5] was based on the same value), $DT_{50water}$: 90 d [1], $DT_{50sediment}$ 1000 d (conservative value)[1]. In the EFSA Conclusion, 2008[1], an earlier growth stage was reported for apples. However, we have considered a full canopy for FOCUS Step 1-2 calculations, in order to account for the restriction in the uses of the substance (post-flowering application).

FOCUS Step 3 – SWASH Package

No new calculations were made, PEC_{fw} value was retrieved from EFSA Conclusion, 2014[5].

Results

Tier	PEC_{fw} (mg/L)	PEC_{sed} (mg/kg)
FOCUS Step 1	0.054	0.116
FOCUS Step 2	**0.008**	0.018
FOCUS Step 3	0.006187 (single application - R3 stream	NA

4.2 Measured Environmental Concentration

n. of MS	Source of monitoring data	MEC values	RBSP
5 (FR, PT, NL, SE, IT)	NORMAN DB, 2014 [6]	$MEC_{95, dissolved}$: 0.114 µg/L	1 MS[10] EQS set (WRc, 2012) [11]
	WATERBASE, 2014 [7]	$MEC_{95, whole}$: 0.08 µg/L	
	SE pesticide monitoring programme [8]	MEC_{95}: 0.21 µg/L	
	IT Monitoring Programme [9]	MEC_{95}: 0.099 µg/L	

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

No evidence of genotoxic or carcinogenic effects was observed with imidacloprid[1]. Likewise it did not affect the reproductive parameters in rats, or the embryofoetal development in rats and rabbits[1]. In neurotoxicity studies, effects occurred in the functional observational battery, without histopathological findings in the nervous tissues[1]. Imidacloprid is not readily biodegradable (P). It shows a low potential to bioaccumulate in aquatic organism[1].

6. Hazard assessment

6.1 Ecotoxicology data

Trophic level	Endpoint	Value	Reference
Aquatic invertebrates	*Daphnia magna*, NOEC, reproduction	6 mg/L	EFSA Conclusion, 2014[5]
Aquatic invertebrates	*Daphnia magna*, NOEC, reproduction	1.8 mg/L	EFSA Conclusion, 2014[5]
Aquatic invertebrates	*Daphnia magna*	2 mg/L	EFSA Conclusion, 2014[5]
Aquatic invertebrates	*Daphnia magna*	6 mg/L	EFSA Conclusion, 2014[5]
Aquatic invertebrates	*Gammarus pulex*, NOEC, swimming/behaviour	0.064 mg/L	EFSA Conclusion, 2014[5]
Aquatic invertebrates	***Gammarus pulex*, EC_{10}, immobilisation**	**0.00295 mg/L**	**EFSA Conclusion, 2014[5], RIVM Report[12]**
Aquatic invertebrates	***Hyalella azteca*, NOEC, survival**	**0.00047 mg/L**	**EFSA Conclusion, 2014[5], RIVM Report[12]**
Aquatic invertebrates	***Asellus aquaticus*, EC_{10}, immobilisation**	**0.00171 mg/L**	**EFSA Conclusion, 2014[5], RIVM Report[12]**
Aquatic invertebrates	*Chironomus riparius*, EC_{10}, emergence	0.00209 mg/L	EFSA Conclusion, 2014[5]
Aquatic invertebrates	*Chironomus riparius*, 10 d, NOEC, recovery after 4 d exposure	< 0.00215 mg/L	EFSA Conclusion, 2014[5]
Aquatic invertebrates	***Chironomus riparius*, NOEC, emergence, growth**	**0.0004 mg/L**	**EFSA Conclusion, 2014[5], RIVM Report[12]**
Aquatic invertebrates	***Chironomus tentans*, EC_{10}, survival**	**0.00042 mg/L**	**EFSA Conclusion, 2014[5], RIVM Report[12]**
Aquatic invertebrates	***Caenis horaria*, EC_{10}, immobilisation**	**0.000024 mg/L**	**EFSA Conclusion, 2014[5], RIVM Report[12]**

Aquatic invertebrates	*Chaoborus obscuripes*, EC$_{10}$, immobilisation	0.00457 mg/L	EFSA Conclusion, 2014[5], RIVM Report[12]
Aquatic invertebrates	*Cloeon dipterum*, EC$_{10}$, immobilisation	0.000033 mg/L	EFSA Conclusion, 2014[5], RIVM Report[12]
Aquatic invertebrates	*Sialis lutaria*, EC$_{10}$, immobilisation	0.00128 mg/L	EFSA Conclusion, 2014[5], RIVM Report[12]
Aquatic invertebrates	*Plea minutissima*, EC$_{10}$, immobilisation	0.00203 mg/L	EFSA Conclusion, 2014[5], RIVM Report[12]

Values in bold were used in the SSD (EFSA Conclusion, 2014[5])

6.2 Mammalian toxicology data

Type of test	Endpoint	Value	Reference
Acute oral toxicity	Rat, LD$_{50}$	500 mg/kg bw	EFSA Conclusion, 2008[1]
Short-term toxicity (neurotoxicity)	Rat, oral, 90 d, NOAEL	9.3 mg/kg bw/day	EFSA Conclusion, 2008[1]
Short-term toxicity	Dog, oral, 28 d and 90 d, NOAEL	8 mg/kg bw/day	EFSA Conclusion, 2008[1]
Long-term toxicity	**Rat, 2 years, NOAEL. Value used for ADI calculation in the EFSA Conclusion, 2008[1]**	**5.7 mg/kg bw/day**	**EFSA Conclusion, 2008[1]**
Long-term toxicity	Mouse, 2 years, NOAEL	208 mg/kg bw/day	EFSA Conclusion, 2008[1]
Reproductive toxicity	Rat, 2 generation study, a)parent NOAEL b)reproductive NOAEL c)offspring NOAEL	a)20 mg/kg bw/day b)50 mg/kg bw/day c)20 mg/kg bw/day	EFSA Conclusion, 2008[1]
Developmental toxicity	Rat, maternal and developmental NOAEL	30 mg/kg bw/day	EFSA Conclusion, 2008[1]
Developmental toxicity	Rabbit, a)maternal NAOEL b)developmental NOAEL	a)8 mg/kg bw/day b)24 mg/kg bw/day	EFSA Conclusion, 2008[1]

6.3 PNEC derivation

PNEC	Endpoint	Endpoint value	AF	PNEC value
PNEC$_{fw}$	HC$_5$[a]	0.027 µg/L	3	0.009 µg/L [b]
PNEC$_{sed}$	-	-	-	N.R.
PNEC$_{biota,sec pois}$	-	-	-	N.R.
PNEC$_{biota, hh}$	-	-	-	N.R.
PNEC$_{dw, hh}$	ADI [1]	0.06 mg/kg bw/day	-	0.210 mg/L [c]

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

[a] HC5 from chronic SSD suggested by NL. Value retrieved from the new EFSA conclusion, 2014[5]

[b] Value retrieved from the new EFSA conclusion, 2014[5], as Tier-2B RAC$_{sw;ch}$

[c] ADI value, retrieved from EFSa conclusion, 2008[1], used in equation F as TL$_{hh}$. See section 3.3.5 for calculation.

7. Risk Quotient (PEC/PNEC)
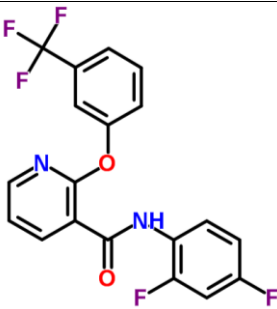
RQ	Value
RQ_{fw}	**888.9**
RQ_{sed}	N.R.
$RQ_{biota,sec\ pois}$	N.R.
$RQ_{biota,\ hh}$	N.R.
$RQ_{dw,\ hh}$	0.04

8. References

[1] EFSA Scientific Report (2008) 148, 1-120, Conclusion on the peer review of imidacloprid. Available at http://www.efsa.europa.eu/it/efsajournal/doc/148r.pdf

[2] FOOPRINT Pesticides DataBase, available at http://www.eu-footprint.org/it/ppdb.html

[3] European Pesticides Database: http://ec.europa.eu/sanco_pesticides/public/?event=homepage

[4] COMMISSION IMPLEMENTING REGULATION (EU) No 485/2013 of 24 May 2013 amending Implementing Regulation (EU) No 540/2011, as regards the conditions of approval of the active substances clothianidin, thiamethoxam and imidacloprid, and prohibiting the use and sale of seeds treated with plant protection products containing those active substances. Available at http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32013R0485

[5] EFSA (European Food Safety Authority), 2014. Conclusion on the peer review of the pesticide risk assessment for aquatic organisms for the active substance imidacloprid. EFSA Journal 2014;12(10):3835, 49 pp. doi:10.2903/j.efsa.2014.3835.

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

[7] WATERBASE Database http://www.eea.europa.eu/data-and-maps/data/waterbase-rivers-6

[8] Swedish National Screening Programme Pesticides (data provided directly to the JRC)

[9] Italian Monitoring Programme (data provided directly to the JRC)

[10] Irmer U, Rau F, Arle J, Claussen U, Mohaupt V. (2013) Ecological Environmental Quality Standards of "River Basin Specific Pollutants" in Surface Waters - Update and Development Analysis of a European Comparison between Member States. ECOSTAT- UBA report

[11] 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

[12] Water quality standards for imidacloprid, Proposal for an update according to the Water Framework Directive, RIVM Letter report 270006001/2014, C.E. Smit. Available at http://www.rivm.nl/en/Documents_and_publications/Scientific/Reports/2014/april/Water_quality_standards_for_imidacloprid_Proposal_for_an_update_according_to_the_Water_Framework_Directive

Diflufenican (CAS N. 83164-33-4)

1. **Substance identity**

EC name	
EC number	
CAS number	83164-33-4
Molecular formula	C19H11F5N2O2
Molecular weight	394.3
Structure	
SMILES	C1=CC(=CC(=C1)OC2=C(C=CC=N2)C(=O)NC3=C(C=C(C=C3)F)F)C(F)(F)F

2. **Physico-chemical Properties**

Endpoint	Value	Source
Vapour Pressure (Pa)	4.25E-06	EFSA conclusion, 2007 [1]
Water solubility (mg/L)	0.05	EFSA conclusion, 2007 [1]
logK$_{ow}$	4.2	EFSA conclusion, 2007 [1]

3. **Environmental fate**

Endpoint	Value	Source
Sorption potential (K$_{oc}$)	1989	EFSA conclusion, 2007 [1]
Biodegradability	NRB	EFSA conclusion, 2007 [1]
Bioaccumulation (BCF)	1596	EFSA conclusion, 2007 [1]
BMF	1	Default value, TG n. 27 - CIS WFD[2]

4. **Environmental exposure assessment**

	Description	Source
Tonnes/year	-	
Uses	Herbicide (PPP)	
Spatial usage (by MS)	AT, BE, BG, CZ, DE, DK, EE, EL, ES, FI, FR, HU, IE, IT, LT, LU, LV, NL, PL, PT, RO, SE, SI, SK, UK	EU Pesticides DB [2]

Banned uses	-	
ERC code	ERC8d	
Fraction of tonnage to region		

4.1 Predicted Environmental Concentration

PEC_{fw} (mg/L)	0.00575	FOCUS Step 2
PEC_{sed} (mg/kg dw)	0.112	FOCUS Step 2
PEC_{biota} (mg/kg)	9.18	Calculation based on Equation L (Section 3.4.3)

4.1.1 Comparison of FOCUS Pesticides models

FOCUS Step 1 [a]

Crop[1]	Application Rate (g/ha)[1]	Water solubility (mg/L)[1]	K_{oc} (L/kg) [1]	DT_{50} whole system (d) [1]
Wheat	1×120	0.05	1989	214

FOCUS Step 2 [a]

Same parameters and conditions as above, in addition to DT_{50soil} 141.8 d [1], $DT_{50water}$: 31.7 d [1], $DT_{50sediment}$ 338.7 d [1], no crop interception[1].

FOCUS Step 3 – SWASH Package[a]

[a] No new calculations were performed, since PEC value were retrieved from EFSA conclusion, 2007 [1]

Results

Tier	PEC_{fw} (mg/L)	PEC_{sed} (mg/kg)
FOCUS Step 1	0.012	0.218
FOCUS Step 2	0.00575	0.112
FOCUS Step 3	0.000835 D2 ditch	0.0304 R3 stream

4.2 Measured Environmental Concentration

n. of MS	Source of monitoring data	MEC values	RBSP
4 (FR, DE, FI, SE)*	NORMAN DB, 2014 [3]	$MEC_{95, whole}$: 0.09 µg/L $MEC_{95, dissolved}$: 0.152 µg/L	1 MS [6]
	WATERBASE, 2014 [4]	$MEC_{95, whole}$: 0.029 µg/L	
	SE pesticide monitoring programme [5]	MEC_{95}: 0.0314 µg/L	

* Monitoring data for the sediment compartment are available from only 1 MS (FR) from NORMAN and from IPChem, where PNEC exceedances were found.

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

There was no concern about the genotoxic properties of diflufenican[1]. Diflufenican did not show any carcinogenic potential in the studies reported in the EFSA Conclusion, 2007[1]. There might be some indications of endocrine disruption at high doses but in view of the potential link with systemic toxicity, no classification for fertility was proposed. In developmental studies with rats and rabbits, there was no evidence of teratogenic activity in the absence of maternal toxicity (EFSA Conclusion, 2007[1]). Diflufenican is not readily biodegradable. Since the BCF in fish was > 1000 and the DT_{90} in sediment was >100 days the risk of bioaccumulation in terrestrial food chains was assessed[1]. The BAF (bioaccumulation factor) was calculated as 0.77. Since the BAF is <1 the risk of bioaccumulation is considered to be low (EFSA Conclusion, 2007[1]).

5.1 Ecotoxicology data

Trophic level	Endpoint	Value	Reference
Fish	*Cyprinus carpio*, 96 h, LC_{50}	0.098 mg/L	INERIS, 2012[7]
Fish	*Pimephales promelas*, ELS	0.015 mg/L	INERIS, 2012[7]
Aquatic invertebrates	*Daphnia magna*, 48 h, EC_{50}	>0.24 mg/L	INERIS, 2012[7]
Aquatic invertebrates	*Daphnia magna*, 21 d, NOEC	0.052 mg/L	INERIS, 2012[7]
Algae	*Scenedesmus subspicatus*, 72 h, growth rate, EC_{50}	0.00045 mg/L	INERIS, 2012[7]
Algae	***Scenedesmus subspicatus*, 72 h, NOEC**	**0.0001 mg/L**	**INERIS, 2012[7]**
Aquatic plants	*Lemna gibba*, 14 d, EC_{50}	0.039 mg/L	INERIS, 2012[7]
Sediment dwelling organisms	***Chironomus riparius*, 28 d, NOEC**	**2 mg/kg**	**INERIS, 2012[7]**

5.2 Mammalian toxicology data

Type of test	Endpoint	Value	Reference
Acute oral toxicity	Rat, LD_{50}	>5000 mg/kg bw	EFSA Conclusion, 2007[1]
Short-term toxicity	**Rat, oral, 13 weeks, NOAEL**	**19.47 mg/kg bw/day**	**EFSA Conclusion, 2007[1]**
Short-term toxicity	Dog, oral, 1 year, NOAEL	100 mg/kg bw/day	EFSA Conclusion, 2007[1]
Long-term toxicity	**Rat, 2 years, NOAEL**	**23.27 mg/kg bw/day (rounded to 25 mg/kg bw/day)**	**EFSA Conclusion, 2007[1] INERIS, 2012[7]**
Long-term toxicity	Mouse, 2 years, NOAEL	62.2 mg/kg bw/day	EFSA Conclusion, 2007[1]
Reproductive toxicity	a)Parental NOAEL b)Reproductive NOAEL c)Offspring NOAEL	a)35.5 mg/kg bw/day b)206.1 mg/kg bw/day c)41.9 mg/kg bw/day	EFSA Conclusion, 2007[1] INERIS, 2012[7]
Developmental toxicity	Rat, a)maternal NOAEL b)developmental NOAEL	a)50 mg/kg bw/day b)500 mg/kg bw/day	EFSA Conclusion, 2007[1]
Developmental toxicity	Rabbit, maternal and developmental NOAEL	350 mg/kg bw/day	EFSA Conclusion, 2007[1]
Reproductive toxicity	*Colinus virginianus*, 20 weeks, NOAEL	91.84 mg/kg bw	EFSA Conclusion, 2007[1] INERIS, 2012[7]

Both studies in bold were used for calculation of the ADI (EFSA Conclusion, 2007[1]).

5.3 PNEC derivation

PNEC	Endpoint	Endpoint value	AF	PNEC value
PNEC$_{fw}$	*Scenedesmus subspicatus*, 72 h, NOEC	0.0001 mg/L	10 [a]	1.00E-05 mg/L[7]
PNEC$_{sed}$	*Chironomus riparius*, 28 d, NOEC	2 mg/kg	100 [b]	0.020 mg/kg dw [7]
PNEC$_{biota,sec pois}$	Rats, chronic toxicity, conversion factor 20, 2 years, NOAEL	25 mg/kg day	30	16.7 mg/kg food [7]
PNEC$_{biota, hh}$	ADI[1]	0.2 mg/kg bw/day	- [c]	12.174 mg/kg food
PNEC$_{dw, hh}$	ADI [1]	0.2 mg/kg bw/day	- [d]	0.7 mg/L

[a] Three long term values were available from the main trophic levels

[b] One long term test available

[c] ADI value used in equation B as TL. See section 3.3.4 for calculation

[d] ADI value used in equation C as TL$_{hh}$. See section 3.3.5 for calculation

6. Risk Quotient (PEC/PNEC)

RQ	Value
RQ$_{fw}$	**575**
RQ$_{sed}$	5.6
RQ$_{biota,sec pois}$	0.55
RQ$_{biota, hh}$	0.75
RQ$_{dw, hh}$	0.01

7. References

[1] EFSA Scientific Report (2007) 122, 1-84, Conclusion on the peer review of diflufenican. Available at http://www.efsa.europa.eu/de/scdocs/doc/122r.pdf

[2] European Pesticides Database http://ec.europa.eu/sanco_pesticides/public/?event=homepage

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

[4] WATERBASE Database http://www.eea.europa.eu/data-and-maps/data/waterbase-rivers-6
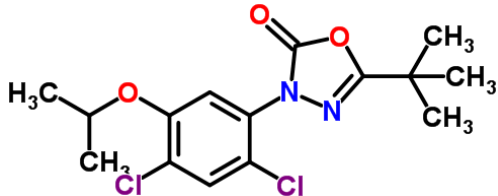
[5] Swedish National Screening Programme Pesticides (data provided directly to the JRC)

[6] Irmer U, Rau F, Arle J, Claussen U, Mohaupt V. (2013) Ecological Environmental Quality Standards of "River Basin Specific Pollutants" in Surface Waters - Update and Development Analysis of a European Comparison between Member States. ECOSTAT- UBA report.

[7] INERIS DIFLUFENICANIL – N° CAS : 83164-33-4 (April, 2012). Available at : http://www.ineris.fr/substances/fr/substance/getDocument/2990

Oxadiazon (CAS N. 19666-30-9)

1. Substance identity

EC name	3-[2,4-dichloro-5-(1-methylethoxy)phenyl]-5-(1,1-dimethylethyl)-1,3,4-oxadiazol-2(3H)-one
EC number	243-215-7
CAS number	19666-30-9
Molecular formula	C15H18Cl2N2O3
Molecular weight	345.22
Structure	
SMILES	CC(C)Oc1cc(c(cc1Cl)Cl)n2c(=O)oc(n2)C(C)(C)C

2. Physico-chemical Properties

Endpoint	Value	Source
Vapour Pressure (Pa)	1.035E-04	EFSA Conclusion, 2010 [1]
Water solubility (mg/L)	0.57	EFSA Conclusion, 2010 [1]
logK$_{ow}$	5.33	EFSA Conclusion, 2010 [1]

3. Environmental fate

Endpoint	Value	Source
Sorption potential (K$_{oc}$)	1294	EFSA Conclusion, 2010 [1]
Biodegradability	NRB	EFSA Conclusion, 2010 [1]
Bioaccumulation (BCF)	243	EFSA Conclusion, 2010 [1]
BMF	1	Default value, TG n. 27 - CIS WFD [2]

4. Environmental exposure assessment

	Description	Source
Tonnes/year	-	
Uses	Herbicide (PPP)	
Spatial usage (by MS)	BE, CY, ES, FR, IT, LU, PT, SK, UK	EU Pesticides DB[3]
Banned uses	-	
ERC code	ERC8d	

4.1   Predicted Environmental Concentration

PEC_{fw} (mg/L)	0.039	FOCUS Step 2
PEC_{sed} (mg/kg dw)	0.496	FOCUS Step 2
PEC_{biota} (mg/kg)	9.477	Calculation based on Equation L (Section 3.4.3)

4.11 Comparison of FOCUS Pesticides models

FOCUS Step 1 [a]

Crop [1]	Application Rate (g/ha)[1]	Water solubility (mg/L)[1]	K_{oc} (L/kg) [1]	DT_{50} whole system (d) [1]
Sunflower	1×750 g/ha (pre-emergence)	0.57	1294	127

FOCUS Step 2 [a]

Same parameters and conditions as above, in addition to DT_{50soil} 120 d [1], $DT_{50water}$: 127 d [1], $DT_{50sediment}$ 999 d [1], no crop interception [1].

FOCUS Step 3 – SWASH Package [a]

[a] No new calculations were made, since PEC_{fw} and PEC_{sed} values were retrieved from EFSA Conclusion, 2010 [1].

Results

Tier	PEC_{fw} (mg/L)	PEC_{sed} (mg/kg)
FOCUS Step 1	0.0986	1.19
FOCUS Step 2	**0.039**	0.496
FOCUS Step 3	0.0084 (R4 stream)	0.025

4.2 Measured Environmental Concentration

n. of MS	Source of monitoring data	MEC values	RBSP
2 (FR, IT)	NORMAN DB, 2014[4]	$MEC_{95, whole}$: 0.07 µg/L $MEC_{95, dissolved}$: 0.168 µg/L	1 MS [7] EQS set (WRc, 2012)[8]
	IPCheM[5]	MEC_{95}: 12.8 µg/L	
	IT Monitoring Programme[6]	MEC_{95}: 0.376 µg/L	

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

Oxadiazon itself did not present genotoxic potential[1]. Liver tumours were observed in both the rat and mouse species; mechanistic studies confirmed that oxadiazon is a peroxisome proliferator[1]. Although peroxisome proliferators are hepatocarcinogens in rodents, the current scientific opinion is that humans are not responsive to this class of non-genotoxic carcinogens and therefore, oxadiazon is unlikely to present a carcinogenic risk to humans[1]. Effects on the reproduction (increase in gestation length and

irregular oestrus cycle) were more prominent in a preliminary dose-range finding study to the multigeneration study where total litter losses were observed at ca. 30 mg/kg bw/day, as the main study was conducted with much lower dose levels. On this basis a classification with the risk phrase R62 "possible risk of impaired fertility" was proposed[1]. Oxadiazon was considered to be very toxic to aquatic organisms, with algae and fish reproduction as the most sensitive endpoints. It is not reaily biodegradable (P).A bioaccumulation study with bluegill sunfish (*Lepomis macrochirus*) gave BCF values of 243 (not B) based on measured oxadiazon residues in fish (EFSA Conclusion, 2010[1]).

6   Hazard assessment

6.1 Ecotoxicology data

Trophic level	Endpoint	Value	Reference
Fish	*Lepomis macrochirus*, 96 h, LC_{50}	1.2 mg/L	EFSA Conclusion, 2010[1]
Fish	*Oncorhynchus mykiss*, 96 h, LC_{50}	1.2 mg/L	EFSA Conclusion, 2010[1]
Fish	***Oncorhynchus mykiss*, 60 d, ELS NOEC**	**0.00088 mg/L**	**EFSA Conclusion, 2010[1]**
Aquatic invertebrates	*Daphnia magna*, 48 h, EC_{50}, mortality	> 2.4 mg/L	EFSA Conclusion, 2010[1]
Aquatic invertebrates	*Daphnia magna*, 21 d, NOEC, reproduction	0.03 mg/L	EFSA Conclusion, 2010[1]
Algae	*Anabaena flos-aquae,* 120 h, EC_{50}, growth rate	>3.7 mg/L	EFSA Conclusion, 2010[1] DAR, 2006[9]
Algae	*Selenastrum capricornutum,* 120 h, a) EC_{50} biomass, b) EC_{50} growth rate	a)0.0082 mg/L b)0.021 mg/L	EFSA Conclusion, 2010[1]
Algae	*Navicula pelliculosa*, 120 h, a) EC50, b) NOEC	a)0.128 mg/L b) 0.027 mg/L	DAR, 2006[9]
Algae	*Scenedesmus subspicatus*, 72 h, a) EC_{50} biomass, b) EC_{50} growth rate, c) NOEC	a)0.00318 mg/L b) 0.00423 c) 0.002 mg/L	EFSA Conclusion, 2010[1] DAR, 2006[9]
Algae with sediment	*Scenedesmus subspicatus*, 72 h, a) EC_{50} biomass, b) EC_{50} growth rate, c) NOEC	a)0.0096 mg/L b)0.0108 mg/L c) 0.005 mg/L	EFSA Conclusion, 2010[1] DAR, 2006[9]
Aquatic plants	*Lemna gibba*, 14 d, frond count, a) EC_{50}, b) NOEC	a)0.057 mg/L b) 0.0082 mg/L	EFSA Conclusion, 2010[1] DAR, 2006[9]
Sediment dwelling organisms	*Chironomus riparius*, 28 d, NOEC	5 mg/L	EFSA Conclusion, 2010[1]

6.2 Mammalian toxicology data

Type of test	Endpoint	Value	Reference
Acute oral toxicity	Rat, LD_{50}	>5000 mg/kg bw/day	EFSA Conclusion, 2010[1]
Chronic	**Rat, 2 years, NOAEL**	**0.36 mg/kg bw/day**	**EFSA Conclusion, 2010[1]**
Chronic	Mouse, 2 years, NOAEL	0.92 mg/kg bw/day	EFSA Conclusion, 2010[1]
Chronic	Dog, 2 years, NOAEL	1.2 mg/kg bw/day	EFSA Conclusion, 2010[1]
Combined repeated dose and reproduction / developmental screening	Rat, NOAEL	12 mg/kg bw/day	EFSA Conclusion, 2010[1]
Long-term toxicity (reproductive toxicity)	Rat, NOAEL, parental and offspring toxicity	15 mg/kg bw/day	EFSA Conclusion, 2010[1]
Long-term toxicity (reproductive toxicity)	Rat, NOAEL, reproductive toxicity	5 mg/kg bw/day	EFSA Conclusion, 2010[1]

6.3 PNEC derivation

PNEC	Endpoint	Endpoint value	AF	PNEC value
$PNEC_{fw}$	***Oncorhynchus mykiss*, 60 d, ELS NOEC**	0.00088 mg/L	10 [a]	0.000088 mg/L
$PNEC_{sed}$	*Chironomus riparius*, 28 d, NOEC	5 mg/L	100 [b]	0.05 mg/L
$PNEC_{biota,sec pois}$	Rat, 2 years, NOAEL	0.36 mg/kg bw/day	30 [c]	0.24 mg/kg [d]
$PNEC_{biota, hh}$	ADI	0.0036 mg/kg bw/day	-	0.22 mg/kg food [e]
$PNEC_{dw, hh}$	ADI	0.0036 mg/kg bw/day	-	0.0126 [f]

[a] Three NOEC values (including algae). AF selected according to ECHA guidance and to TG n.27- CIS WFD, pg 38

[b] Since just 1 NOEC value was available, used an AF of 100. Followed TG n.27- CIS WFD, pg. 96

[c] AF selected based on the duration of the test of 2 y

[d] The following steps were followed for $PNEC_{biota,sec pois}$ calculation: a) conversion of NOAEL (0.36 mg/kg bw/day) value into NOEC (7.2 mg/kg) by using the conversion factor of 20 (taken from TG n. 27- CIS WFD); b) Application of appropriate AF_{oral} (30) to the NOEC value (see Note c).

[e] ADI value retrieved from EFSA Conclusion, 2010 used for PNEC calculation according to Equation E (see section 3.3.4)

[f] ADI value used in equation F as TL_{hh}. See section 3.3.5 for calculation.

7 Risk Quotient (PEC/PNEC)
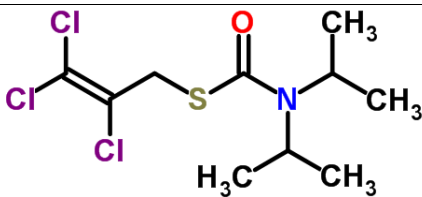
RQ	Value
RQ_{fw}	**443.18**
RQ_{sed}	9.92
$RQ_{biota,sec pois}$	39.49
$RQ_{biota, hh}$	43.25
$RQ_{dw, hh}$	3.10

8   References

[1] EFSA Journal 2010; 8(2):1389, available at http://www.efsa.europa.eu/it/efsajournal/pub/1389.htm

[2] Technical Guidance for Deriving Environmental Quality Standards – Guidance Document No. 27 (2011) Common Implementation Strategy of the Water Framework Directive (2000/60/EC). Available at http://ec.europa.eu/environment/water/water-dangersub/lib_pri_substances.htm

[3] EU Pesticides Database http://ec.europa.eu/sanco_pesticides/public/?event=homepage

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

[5] IPCheM database at http://ipchem.jrc.ec.europa.eu/

[6] Italian Monitoring Programme (data provided directly to the JRC)

[7] Irmer U, Rau F, Arle J, Claussen U, Mohaupt V. (2013) Ecological Environmental Quality Standards of "River Basin Specific Pollutants" in Surface Waters - Update and Development Analysis of a European Comparison between Member States. ECOSTAT- UBA report

[8] 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

[9] DAR Oxadiazon, Volume 3 – Annex B.9 (2006).

Tri-allate (CAS N. 2303-17-5)

1. Substance identity

EC name	S-2,3,3-trichloroallyl diisopropylthiocarbamate
EC number	218-962-7
CAS number	2303-17-5
Molecular formula	C10H16Cl3NOS
Molecular weight	304.7
Structure	
SMILES	CC(C)N(C(C)C)C(=O)SCC(=C(Cl)Cl)Cl

2. Physico-chemical Properties

Endpoint	Value	Source
Vapour Pressure (Pa)	0.012	EFSA conclusion, 2008 [1]
Water solubility (mg/L)	4.1	EFSA conclusion, 2008 [1]
logK$_{ow}$	4.06	EFSA conclusion, 2008 [1]

3. Environmental fate

Endpoint	Value	Source
Sorption potential (K$_{oc}$)	4301.4	EFSA conclusion, 2008 [1]
DT50 water	103.8 d	EFSA conclusion, 2008 [1]
Biodegradability	NRB	EFSA conclusion, 2008 [1]
Bioaccumulation (BCF)	1400	EFSA conclusion, 2008 [1]
BMF	1	Default value, TG n. 27 - CIS WFD [2]

4. Environmental exposure assessment

	Description	Source
Tonnes/year	10150 (year 2003)	From previous prioritisation exercise
Uses	Herbicide (PPP)	
Spatial usage (by MS)	AT, BE, CZ, FR, IE, IT, NL, UK	EU Pesticides DB [3]
Banned uses	-	
ERC code	ERC8d	

4.1 Predicted Environmental Concentration

PEC_{fw} (mg/L)	0.118	FOCUS Step 2
PEC_{sed} (mg/kg dw)	2.56	FOCUS Step 2
PEC_{biota} (mg/kg)	165.2	Calculation based on Equation L (Section 3.4.3)

4.1.1 Comparison of FOCUS Pesticides models with ECETOC model

FOCUS Step 1

Crop [1]	Application Rate (g/ha)[1]	Water solubility (mg/L)[1]	K_{oc} (L/kg) [1]	DT_{50} whole system (d) [1]
Winter cereals (for Step 1 calculations, used Pome & Stone Fruits late, as reported in the EFSA Conclusion, 2008[1])	1×2250 g/ha	4.1	4301.4	68.2

FOCUS Step 2

Same parameters and conditions as above, in addition to DT_{50soil} 58.2 d [1], $DT_{50water}$: 103.8 d [1], $DT_{50sediment}$ 210.9 d [1], no crop interception [1].

FOCUS Step 3 – SWASH Package

No new calculations were made, since PEC_{fw} and PEC_{sed} values were retrieved from EFSA Conclusion, 2008[1].

Results

Tier	PEC_{fw} (mg/L)	PEC_{sed} (mg/kg)
ECETOC	0.19	86
FOCUS Step 1	0.229	5.49
FOCUS Step 2	**0.118**	2.56
FOCUS Step 3 (D2, ditch-Brimstone)	0.042	0.089

4.2 Measured Environmental Concentration

n. of MS	Source of monitoring data	MEC values	RBSP
2 (FR, NL)	NORMAN DB, 2014 [4]	$MEC_{95, whole}$: 0.1875 µg/L	-

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

Tri-allate is unlikely to be genotoxic[1]. Tri-allate is unlikely to pose carcinogenic risk to humans[1]. No evidence of treatment-related oncogenicity was found in either rats, mice or hamsters[1]. No classification proposed for reproductive toxicity[1]. The substance is not readily biodegradable (P). It has a BCF value of 1400[1].

6. Hazard assessment

6.1 Ecotoxicology data

Trophic level	Endpoint	Value	Reference
Fish	*Oncorhynchus mykiss*, 96 h, LC_{50}	0.95 mg/L	EFSA conclusion, 2008[1]
Fish	*Oncorhynchus mykiss*, 88 d , NOEC, growth	0.038 mg/L	EFSA conclusion, 2008[1]
Aquatic invertebrates	*Daphnia magna*, 48 h, EC_{50}	0.091 mg/L	EFSA conclusion, 2008[1]
Aquatic invertebrates	*Daphnia magna*, 21 d, NOEC, reproduction	0.013 mg/L	EFSA conclusion, 2008[1]
Algae	***Pseudokirchneriella subcapitata*, 96 h,** measured concentrations, a) EC_{50} biomass, b) NOEC biomass, c) EC_{50} growth rate, d) **NOEC growth rate**	a) 0.013 mg/L b) 0.0034 mg/L c) 0.036 mg/L **d) 0.0067 mg/L**	EFSA conclusion, 2008[1] **DAR, 2007 [5]**
Algae	*Anabaena flos-aquae*, 96 h, measured concentrations, a) NOEC growth rate, b) EC_{50} growth rate;, c) NOEC biomass, d) EC_{50} biomass	a) 1.6 mg/L b) >3.7 mg/L c) 1.6 mg/L d) 2.6 mg/L	DAR, 2007 [5]
Aquatic plants	*Lemna gibba*, EC_{50}	2.3 mg/L	EFSA conclusion, 2008[1]
Sediment dwelling organisms	*Chironomus riparius*, 28 d, NOEC, EMERGENCE	0.583 mg/L	EFSA conclusion, 2008[1]

6.2 Mammalian toxicology data

Type of test	Endpoint	Value	Reference
Acute oral toxicity	Rat, LD_{50}	1100 mg/kg bw	EFSA conclusion, 2008[1]
Short term oral toxicity	Rat, 90 d, NOAEL	6.4 mg/kg bw/day	EFSA conclusion, 2008[1]

(neurotoxicity)			
Short term oral toxicity	Dog, 8-weeks capsule study, NOAEL	12 mg/kg bw/day	EFSA conclusion, 2008[1]
Short term oral toxicity	**Dog, 1-year capsule study, NOAEL**	**2.5 mg/kg bw/day**	**EFSA conclusion, 2008[1]**
Short term oral toxicity	Mice, 8-weeks, NOAEL	11.5 mg/kg bw/day	EFSA conclusion, 2008[1]
Short term oral toxicity	Hamster, 90 d, NOAEL	43.2 mg/kg bw/day	EFSA conclusion, 2008[1]
Chronic	Rat, NOAEL, 2 years	2.5 mg/kg bw/day	EFSA conclusion, 2008[1]
Chronic	Mice, 2-year, NOAEL	12.4 mg/kg bw/day	EFSA conclusion, 2008[1]
Chronic	Hamster, 79-95 weeks, NOAEL	16.2 mg/kg bw/day	EFSA conclusion, 2008[1]
Reproductive toxicity	NOAEL	7.7 mg/kg bw/day	EFSA conclusion, 2008[1]
Developmental toxicity	Rat, NOAEL	30 mg/kg bw/day	EFSA conclusion, 2008[1]
Developmental toxicity	Rabbit, NOAEL a)maternal toxicity b)developmental toxicity	a)15 mg/kg bw/day b)5 mg/kg bw/day	EFSA conclusion, 2008[1]
Long-term toxicity	Rat, NOEL	9 mg/kg bw/day	EFSA conclusion, 2008[1]

6.3 PNEC derivation

PNEC	Endpoint	Endpoint value	AF	PNEC value
PNEC$_{fw}$	*Pseudokirchneriella subcapitata, 96 h, NOEC*[5]	0.0067 mg/L	10	0.00067 mg/L [a]
PNEC$_{sed}$	-	-	-	0.145 mg/kg [b]
PNEC$_{biota,sec\ pois}$	Rats, chronic toxicity, conversion factor 20, 2 years, NOAEL [1]	2.5 mg/kg bw/day	30	1.67 mg/kg food [c]
PNEC$_{biota,\ hh}$	ADI	0.025 mg/kg bw/day	-	1.522 mg/kg food [d]
PNEC$_{dw,\ hh}$	ADI	0.025 mg/kg bw/day	-	0.088 mg/L [e]

[a] Three NOEC values available from the three main trophic levels (fish, aquatic invertebrates, algae)

[b] PNEC$_{sed}$ calculated with the Equilibrium Partitioning Method, where $K_{sed-water}$= 108.34 m^{3}m^{-3} (Eq. D), RHO$_{sed}$= 1300 kg m^{-3} (default value), Fsolid$_{sed}$= 0.2 (default value), RHO$_{solid}$= 2500 kg m^{-3} (default value), Kp$_{sed}$= 215.07 L/kg (calculated, K_{oc} x Foc$_{sed}$), K_{oc}= 4301.4 L/kg [1], Foc$_{sed}$= 0.05 kg kg^{-1} (default value). Conversion from wet weight to dry weight was done with eq. B (Section 3.3.2).

[c] The AF of 30 was selected according to the duration test (2 years) (TG n. 27 - CIS WFD)[2] The following steps were followed for PNEC$_{biota,sec\ pois}$ calculation: a) conversion of NOAEL (2.5 mg/kg bw/day) value into NOEC (50 mg/kg) by using the conversion factor of 20 (taken from TG n. 27- CIS WFD); b) Application of appropriate AF$_{oral}$ (30) to the NOEC value (The AF of 30 was selected according to the duration test (2 years) (TG n. 27 - CIS WFD)[4]

[d] ADI value retrieved from EFSA Conclusion, 2008 used for PNEC calculation according to Equation E (see section 3.3.4)

[e] ADI value used in equation F as TL$_{hh}$. See section 3.3.5 for calculation.

7. Risk Quotient (PEC/PNEC)

RQ	Value
RQ_{fw}	**176.12**
RQ_{sed}	17.63
$RQ_{biota,sec\ pois}$	99.12
$RQ_{biota,\ hh}$	108.56
$RQ_{dw,\ hh}$	1.35

8. References

[1] EFSA Scientific Report (2008) 181, 1-100 Conclusion on the peer review of tri-allate. Available at http://www.efsa.europa.eu/it/efsajournal/pub/181r.htm

[2] Technical Guidance for Deriving Environmental Quality Standards – Guidance Document No. 27 (2011) Common Implementation Strategy of the Water Framework Directive (2000/60/EC). Available at http://ec.europa.eu/environment/water/water-dangersub/lib_pri_substances.htm

[3] EU Pesticides Database http://ec.europa.eu/sanco_pesticides/public/?event=homepage

[4] NORMAN Database http://www.norman-network.net/?q=node/24
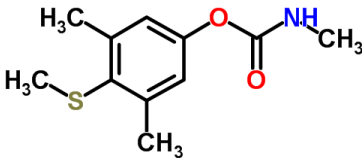
[5] DAR Tri-allate, Volume 3, Annex B.9 : Ecotoxicology (2007)

Methiocarb (CAS N. 2032-65-7)

1. **Substance identity**

Chemical name (IUPAC)	Mercaptodimethur/ 3,5-Dimethyl-4-methylthiophenyl N-methylcarbamate
EC number	217-991-2
CAS number	2032-65-7
Molecular formula	C11H15NO2S
Molecular weight	225.3
Structure	
SMILES	CNC(=O)Oc1cc(C)c(SC)c(C)c1

2. **Physico-chemical Properties**

Endpoint	Value	Source
Vapour Pressure (Pa)	1.5E-05	EFSA Conclusion, 2010[1]
Water solubility (mg/L)	27	EFSA Conclusion, 2010[1]
$logK_{ow}$	3.18	EFSA Conclusion, 2010[1]

3. **Environmental fate**

Endpoint	Value	Source
Hydrolysis (DT50)	9.1 d	EFSA Conclusion, 2010[1]
Sorption potential (K_{oc})	Highest value: 1000 Mean value: 660 (used for PEC calculation Step 2)	EFSA Conclusion, 2010[1]
Biodegradability	NRB	EFSA Conclusion, 2010[1]
Bioaccumulation (BCF)	75.86	Source: Experimental value retrieved from VegaNIC vers. 1.0.8
BMF	1	Default value, TG n. 27 - CIS WFD [2]

4. **Environmental exposure assessment**

	Description	Source
Tonnes/year	1500 (year 2000)	From previous prioritisation exercise
Uses	Insecticide, Repellant (PPP)	
Spatial usage (by MS):	Authorised in: AT, BE, BG, CY, CZ, DE, DK, EE, EL, ES, FI, FR, HU, IE, IT, LV, NL, PL, PT, RO, SI, SK, UK	EU Pesticides DB [3]

Banned uses	Moluscicide	Commission Implementing Regulation (EU) No 187/2014 [4]
ERC code	ERC8d	
Fraction of tonnage to region	0.1	

4.1 Predicted Environmental Concentration

PEC_{fw} (mg/L)	0.00395	FOCUS Step 2
PEC_{sed} (mg/kg dw)	0.026	FOCUS Step 2
PEC_{biota} (mg/kg)	0.30	Calculation based on Equation L (Section 3.4.3)

4.1.1 Comparison of FOCUS Pesticides models with ECETOC model

FOCUS Step 1

Crop[1]	Application Rate (g/ha)[1]	Water solubility (mg/L)[1]	K_{oc} (L/kg) [1]	DT_{50} (d) [1]
Maize	2×150 (seed treatment)	27	660 (mean)	15.3 d (whole system)

FOCUS Step 2

Same parameters and conditions as above, in addition to DT_{50soil} 2.8 d [1], $DT_{50water}$: 8.5 d [1], $DT_{50sediment}$ 20.1 d [1], no crop interception (seed treatment) [1].

Results

Tier	PEC_{fw} (mg/L)	PEC_{sed} (mg/kg)
ECETOC	0.044	4.54
FOCUS Step 1	0.0266	0.176
FOCUS Step 2	0.00395	0.026

4.2 Measured Environmental Concentration

n. of MS	Source of monitoring data	MEC values	RBSP
5 (FR, NL, UK, SE, IT)	NORMAN DB, 2014 [5]	$MEC_{95, whole}$: 0.0585 µg/L	1 MS [9]
	IPCheM [6]	MEC_{95}: 0.095 µg/L	
	SE pesticide monitoring programme [7]	All values < LOQ	
	IT Monitoring Programme [8]	MEC_{site}: 0.02 µg/L	

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

Methiocarb is acutely very toxic by oral route and toxic after inhalation in rats[1]. Methiocarb was clastogenic in the chromosomal aberration assay in CHO cells but this was not confirmed in cytological

analysis in a micronucleus test[1]. There was no evidence of genotoxicity in other in vitro and in vivo studies[1]. There was no evidence of carcinogenicity in mice and rats[1]. Methiocarb did not affect reproductive and developmental parameters and did not show any potential to cause delayed neurotoxicity[1]. The substance is not readily biodegradable.It has a BCF that ranges from 60 to 90 in fish[1]. However, also a BCF experimental value of 75.86 L/kg was reported in the VEGA Nic software, and used for calculations.

6. Hazard assessment

6.1 Ecotoxicology data

Trophic level	Endpoint	Value	Reference
Fish	*Lepomis macrochirus*, 96 h, LC_{50}	0.65 mg/L	EFSA Conclusion, 2006[1] DAR, 2004[10]
Fish	*Oncorhyncus mykiss*, 56 d, NOEC	0.05 mg/L	EFSA Conclusion, 2006[1] DAR, 2004[10]
Aquatic invertebrates	*Daphnia magna*, 48 h, EC_{50}	0.0077 mg/L	EFSA Conclusion, 2006[1] DAR, 2004[10]
Aquatic invertebrates	***Daphnia magna*, 21 d NOEC, reproduction**	**0.0001 mg/L**	**EFSA Conclusion, 2006[1] DAR, 2004[10]**
Algae	*Scenedesmus subspicatus*, 72 h, a) EC_{50} growth rate, b) EC_{50} biomass, c) NOEC based on biomass	a)2.2 mg/L b)0.82 mg/L c) 0.052 mg/L	EFSA Conclusion, 2006[1] DAR, 2004[10]

6.2 Mammalian toxicology data

Type of test	Endpoint	Value	Reference
Acute oral toxicity	Rat, LD50	19 mg/kg bw (based on weight of evidence of published data with range of 13–135 mg/kg bw).	EFSA Conclusion, 2006[1]
Sub-chronic toxicity (with investigation of neurofunction)	**Dog, 90 d, dietary study, NOAEL. Value also used for ADI calculation in the EFSA Conclusion.**	**1.33 mg/kg bw/day**	**EFSA Conclusion, 2006[1]**
Long term toxicity	Dog, 2-year, dietary study, NOAEL	2.2 mg/kg bw/day	EFSA Conclusion, 2006[1]
Reproductive toxicity	NOAEL	4.3 mg/kg bw/day	EFSA Conclusion, 2006[1]
Developmental toxicity	NOAEL, a) parental toxicity, b) developmental toxicity	a)0.5 mg/kg bw/day b)10 mg/kg bw/day	EFSA Conclusion, 2006[1]

6.3 PNEC derivation

PNEC	Endpoint	Endpoint value	AF	PNEC value
PNEC_fw	*Daphnia magna*, 21 d, NOEC	0.0001 mg/L	10 [a]	1.00E-05 mg/L [a]
PNEC_sed	-	-	-	0.001 mg/kg dw [b]
PNEC_biota,sec pois	Dog, 90 d, conversion factor 40, NOAEL	1.33 mg/kg bw/day	90	0.591 mg/kg food [c]
PNEC_biota, hh	ADI	0.013 mg/kg bw/day	-	0.791 mg/kg food [d]
PNEC_dw, hh	ADI	0.013 mg/kg bw/day	-	0.046 mg/L [e]

[a] An AF of 10 was chosen based on the availability of three NOEC values from the three main trophic levels (fish, aquatic invertebrates, algae), according to TG n. 27- CIS WFD

[b] $K_{sed-water}$= 25.8 m³m⁻³ (calculated with eq. D), RHO_{sed}= 1300 kg m⁻³ (default value), $Fsolid_{sed}$= 0.2 (default value), RHO_{solid}= 2500 kg m⁻³ (default value), Kp_{sed}= 50 L/kg (calculated, K_{oc} x Foc_{sed}), K_{oc}= 1000 L/kg, Foc_{sed}= 0.05 kg kg⁻¹ (default value). Conversion from wet weight to dry weight was done with eq. B (Section 3.3.2).

[c] The following steps were followed for PNEC_biota,sec pois calculation: a) conversion of NOAEL (1.33 mg/kg bw/day) value into NOEC (53.2 mg/kg) by using the conversion factor of 40 (taken from TG n. 27- CIS WFD); b) Application of appropriate AF_{oral} (90) to the NOEC value. The AF was selected according to the duration of the test (90 d)

[d] ADI value retrieved from EFSA Conclusion, 2006 used for PNEC calculation according to Equation E (see section 3.3.4)

[e] ADI value used in equation F as TL_{hh}. See section 3.3.5 for calculation.

7. Risk Quotient (PEC/PNEC)

RQ	Value
RQ_fw	**395**
RQ_sed	50.39
RQ_biota,sec pois	0.51
RQ_biota, hh	0.38
RQ_dw, hh	0.09

8. References

[1] EFSA Scientific Report (2006) 79, 1-82, Conclusion on the peer review of methiocarb. Available at http://www.efsa.europa.eu/it/efsajournal/doc/79r.pdf

[2] Technical Guidance for Deriving Environmental Quality Standards – Guidance Document No. 27 (2011) Common Implementation Strategy of the Water Framework Directive (2000/60/EC). Available at http://ec.europa.eu/environment/water/water-dangersub/lib_pri_substances.htm

[3] European Pesticides Database: http://ec.europa.eu/sanco_pesticides/public/?event=homepage

[4] Commission Implementing Regulation (EU) No 187/2014 of 26 February 2014 amending Implementing Regulation (EU) No 540/2011 as regards the conditions of approval of the active substance methiocarb. Available at: http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32014R0187&from=EN

[5] NORMAN database at http://www.norman-network.net/?q=node/24

[6] IPCheM database at http://ipchem.jrc.ec.europa.eu/

[7] Swedish National Screening Programme Pesticides (data provided directly to the JRC)
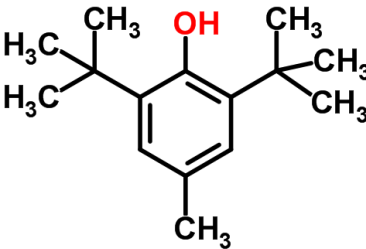
[8] Italian Monitoring Programme (data provided directly to the JRC)

[9] Irmer U, Rau F, Arle J, Claussen U, Mohaupt V. (2013) Ecological Environmental Quality Standards of "River Basin Specific Pollutants" in Surface Waters - Update and Development Analysis of a European Comparison between Member States. ECOSTAT- UBA report

[10] DAR Methiocarb – Volume 3, Annex B, Ecotoxicology (June 2004)

2,6-di-tert-butyl-4-methylphenol (CAS N. 128-37-0)

1. Substance identity

EC name	2,6-di-tert-butyl-p-cresol
EC number	204-881-4
CAS number	128-37-0
Molecular formula	C15H24O
Molecular weight	220.350
Structure	
SMILES	c1(c(O)c(C(C)(C)C)cc(c1)C)C(C)(C)C

2. Physico-chemical Properties

Endpoint	Value	Source
Vapour Pressure (Pa)	1.1	ECHA, 2013[1]
Water solubility (mg/L)	0.76	ECHA, 2013[1]
logK$_{ow}$	5.1	ECHA, 2013[1]

3. Environmental fate

Endpoint	Value	Source
Sorption potential (K$_{oc}$)	8183	ECHA, 2013[1]
Biodegradability	NRB	ECHA, 2013[1]
Bioaccumulation (BCF)	2500	ECHA, 2013[1]
BMF	2	Default value, TG n. 27 - CIS WFD[2]

4. Environmental exposure assessment

	Description	Source
Tonnes/year	A confidential and recent tonnage value was used for calculation	IUCLID, 2013[3]
Uses	Industrial uses, use in plastics, rubber products, adhesives, coatings, dyes, fuel (biodiesel), use for the formulation of PPP	ECHA, 2013[1]

	and biocides, use as laboratory reagent. Used as antioxidant in food. Uses in Europe (UK communication): Stabiliser for rubber (largely during polymerisation) (50%) Stabiliser for oils, lubricants and fuels (25%) Stabiliser for plastics (10%) Food additive/others (15%)	
Spatial usage (by MS)	Not known	
Banned uses	-	
ERC code	ERC8d	
Fraction of tonnage to region	0.1	

4.1   Predicted Environmental Concentration

PEC_{fw} **(mg/L)**	0.423	ECETOC
PEC_{sed} **(mg/kg dw)**	367.64	ECETOC
PEC_{biota} **(mg/kg)**	2115	Calculation based on Equation L (Section 3.4.3)

4.2 Measured Environmental Concentration

n. of MS	Source of monitoring data	MEC values	RBSP
None[a]	-	-	-

[a] Monitoring data was provided by SE but only regarding sewage treatment effluent and sludge

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

IARC classification: group 3, as not classifiable as to its carcinogenicity to humans. There is limited evidence for the carcinogenicity of butylated hydroxytoluene in experimental animaIs.[3]

Not genotoxic[1]. The substance is not readily biodegradable. The highest BCF value was of 2500 L/kg (ECHA, 2013[1]).

6.   Hazard assessment

6.1 Ecotoxicology data

Trophic level	Endpoint	Value	Reference
Fish	*Danio rerio*, 96 h, LC_0	≥0.57 mg/L	ECHA, 2013[1]
Aquatic invertebrates	*Daphnia magna*, 48 h, EC_{50}, mobility	0.48 mg/L	ECHA, 2013[1]
Aquatic invertebrates	***Daphnia magna*, 21 d, NOEC, reproduction**	**0.316 mg/L**	**ECHA, 2013[1]**
Algae	*Scenedesmus subspicatus*, 72 h, EC_{50}, biomass and growth rate	>0.4 mg/L	ECHA, 2013[1]

6.2 Mammalian toxicology data

Type of test	Endpoint	Value	Reference
Acute toxicity	Rat, oral, LD_{50}	>2930 mg/L	ECHA, 2013[1]
Repeated dose toxicity, carcinogenicity	**Rat, oral, two-generation carcinogenicity study, 22 months, NOAEL. The effect value was used for DMEL calculation in the ECHA report.**	**25 mg/kg bw/day**	**ECHA, 2013[1]**
Repeated dose toxicity, carcinogenicity	Rat, oral, two-generation carcinogenicity study, 22 months, NOAEL	100 mg/kg bw/day	ECHA, 2013[1]
Reproductive toxicity	Rat, oral, 22 months, NOAEL	500 mg/kg bw/day	ECHA, 2013[1]
Developmental toxicity	Rat, oral, 22 months, NOAEL	100 mg/kg bw/day	ECHA, 2013[1]

6.3 PNEC derivation

PNEC	Endpoint	Endpoint value	AF	PNEC value
$PNEC_{fw}$	*Daphnia magna*, 21 d, NOEC	0.316 mg/L	100 [a]	3.16E-03 mg/L [b]
$PNEC_{sed}$	-	-	-	1.290 mg/kg dw [c]
$PNEC_{biota,sec\ pois}$	-	-	30	16.7 mg/kg food [d]
$PNEC_{biota,\ hh}$	DMEL	0.25 mg/kg bw/day	-	15.217 mg/kg food [e]
$PNEC_{dw,\ hh}$	DMEL	0.25 mg/kg bw/day	-	0.875 mg/L [f]

[a] One long term value from *Daphnia magna* was available.

[b] In IUCLID, three different $PNEC_{fw}$ were reported. Two were calculated from QSAR estimations, and the third one was calculated from the same study on *Daphnia magna*, as reported in the table above, with the same AF.

[c] Equilibrium partitioning method used in the ECHA dossier[1]. No new calculations were performed.

[d] All values used were retrieved from ECHA dossier[1]

[e] DMEL value, retrieved from ECHA, 2013[1], used for PNEC calculation according to Equation E (see section 3.3.4)

[f] DMEL value used in equation F as TL_{hh}. See section 3.3.5 for calculation.

7. Risk Quotient (PEC/PNEC)

RQ	Value
RQ_{fw}	133.86
RQ_{sed}	**283.24**
$RQ_{biota,sec\ pois}$	126.65
$RQ_{biota,\ hh}$	138.99
$RQ_{dw,\ hh}$	0.48

8. References

[1] ECHA Dissemination website: http://apps.echa.europa.eu/registered/data/dossiers/DISS-9d82f461-e7b6-3a89-e044-00144f67d249/AGGR-7097be3d-db74-4fb0-9968-20bfdf833cb2_DISS-9d82f461-e7b6-3a89-e044-00144f67d249.html#AGGR-7097be3d-db74-4fb0-9968-20bfdf833cb2

[2] Technical Guidance for Deriving Environmental Quality Standards – Guidance Document No. 27 (2011) Common Implementation Strategy of the Water Framework Directive (2000/60/EC). Available at http://ec.europa.eu/environment/water/water-dangersub/lib_pri_substances.htm
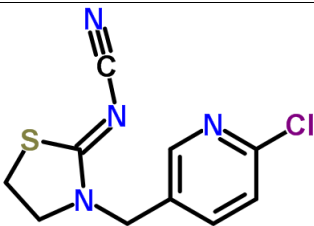
[3] Complete IUCLID dossier of 2,6-di-tert-butyl-4-methylphenol

[4] Swedish National Screening Programme Pesticides (data provided directly to the JRC)

[5] IARC monograph Vol. 40 available at http://monographs.iarc.fr/ENG/Monographs/vol1-42/mono40.pdf, and http://monographs.iarc.fr/ENG/Classification/ClassificationsCASOrder.pdf).

Thiacloprid (CAS N. 111988-49-9)

1. **Substance identity**

EC name	(Z)-3-(6-chloro-3-pyridylmethyl)-1,3-thiazolidin-2-ylidenecyanamide
EC number	
CAS number	111988-49-9
Molecular formula	C10H9ClN4S
Molecular weight	252.7
Structure	
SMILES	S1C(\N(CC1)Cc1ccc(nc1)Cl)=N\C#N

2. **Physico-chemical Properties**

Endpoint	Value	Source
Vapour Pressure (Pa)	3×10^{-10}	EU List of Endpoints (LoE), 2002[1]
Water solubility (mg/L)	184	EU List of Endpoints (LoE), 2002[1]
logK$_{ow}$	1.26	EU List of Endpoints (LoE), 2002[1]

3. **Environmental fate**

Endpoint	Value	Source
DT50 (whole system) (d)	27	EU List of Endpoints (LoE), 2002[1]
Sorption potential (K$_{oc}$)	615	EU List of Endpoints (LoE), 2002[1]
Biodegradability	NRB	
Bioaccumulation (BCF)	3.15	EPI Suite, BCFBAF vers. 3.01
BMF	1	Default value, TG n. 27 - CIS WFD[2]

4. **Environmental exposure assessment**

	Description	Source
Tonnes/year	-	
Uses	Insecticide (Biocide and PPP)	
Spatial usage (by MS)	AT, BE, BG, CY, CZ, DE, DK, EE, EL, ES, FI, FR, HU, IE, IT, LT, LU, LV, MT, NL, PL, PT, RO, SE, SI, SK, UK	EU Pesticides DB [3]

Banned uses	-	
ERC code	ERC8d (N.R.)	

4.1 Predicted Environmental Concentration

PEC_{fw} (mg/L)	0.0109	FOCUS Step 2
PEC_{sed} (mg/kg dw)	0.042 (N.R.)	FOCUS Step 2
PEC_{biota} (mg/kg)	0.034 (N.R.)	Calculation based on Equation L (Section 3.4.3)

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

4.11 Comparison of FOCUS Pesticides models

FOCUS Step 1

Crop [1]	Application Rate (g/ha)[1]	Water solubility (mg/L)[1]	K_{oc} (L/kg) [1]	DT_{50} whole system (d) [1]
Pome & Stone Fruits late	2×180 (14 d application interval full canopy)	184	615	27

FOCUS Step 2

Same parameters and conditions as above, in addition to DT_{50soil} 1.30 d [1], $DT_{50water}$: 31 d [1], $DT_{50sediment}$ 62 d[1]

FOCUS Step 3 – SWASH Package

In addition to the input values listed above, it was considered an application window of 44 d (30+(n. of applications-1) x application interval)[4], with a foliar application and a pre-harvest interval (PHI) of 14 d. In accordance both with the FOCUS SW Appendix C and D[5] and with the BBCH of 54-75 related to pome and stone fruits (as reported in the GAP table of the LoE, 2002[3]). The following application windows were selected for the relevant crop scenarios for the PAT calculator: D3, D4, D5, R1, R2 from 18/06 to 31/07; R3 and R4 from 24/06 to 07/08. Just for the runs of D4 and D5 scenarios, no results were achieved due to some software errors.

Results

Tier	PEC_{fw} (mg/L)	PEC_{sed} (mg/kg)
FOCUS Step 1	0.085	0.457
FOCUS Step 2	**0.0109**	0.042
FOCUS Step 3	0.0057 (R3 stream)	0.004 (D3 pond)

It is acknowledged that even though thiacloprid is used as PPP and biocide, the application rate approach is not suitable for the calculation of PEC values for biocides, but just for PPP, so the results could be an underestimation. However, the tonnage values related to the biocide use were not available and therefore, no further calculation could be done.

4.2 Measured Environmental Concentration

n. of MS	Source of monitoring data	MEC values	RBSP
4(FI, SE, IT, NL)	WATERBASE, 2014 [6]	All values < LOQ	-
	SE pesticide monitoring programme [7]	MEC_{95}: 0.116 µg/L	
	IT Monitoring Programme [8]	MEC_{95}: 0.03 µg/L	
	NORMAN DB, 2014[9]	MEC_{95}: 0.14 µg/L (NL)	

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

Increase in malignant uterine adenocarcinomas and thyroid adenomas in rats and ovarian luteomas in mice was observed for thiacloprid[9]. Tumours occur by a non-genotoxic mechanism and a threshold can be identified for the onset of tumours. Based on the T25 estimate of carcinogenic potency, thiacloprid is considered to be of medium potency within the EU. Classified as Carc Cat 3. (R40)[9]. Data indicate that thiacloprid is not mutagenic in vitro. In addition, a negative result was obtained in a standard in vivo micronucleus test. No classification was proposed for reproductive toxicity[9]. The substance is not readily biodegradable, however data presented in the Biocide Assessment Report show that thiacloprid did degrade reasonably rapidly in the aquatic environment with DT_{50} values of 31 and 62 d derived from an outdoor microcosm for the water and sediment compartments respectively. Thiacloprid has a low potential for bioconcentration with a mean measured log P_{ow} = 1.26 (Biocide Assessment Report[9]). An estimated BCF value of 3.16 was provided by Episuite. Finally, according to the available data, the most sensitive chronic endpoint for thiacloprid is that derived for a 28 d Chironomus study (NOEC of 0.0005 mg L^{-1}). This means that the trigger of < 0.01 mg l-1 given in the TGD is exceeded and thiacloprid fulfils the toxic criterion[9].

6   Hazard assessment

6.11 Ecotoxicology data

Trophic level	Endpoint	Value	Reference
Fish	*Lepomis macrochirus*, 96 h, LC_{50}	25.2 mg/L	Biocide Assessment Report, 2008[9]
Fish	*Oncorhyncus mykiss*, 97 d, a)LC_{50}, b) NOEC	a)>3.91 mg/L b)0.24 mg/L	Biocide Assessment Report, 2008[9]
Aquatic invertebrates	*Daphnia magna*, 48 h, immobility, EC_{50}	≥85.1 mg/L	Biocide Assessment Report, 2008[9]
Aquatic invertebrates	*Daphnia magna*, 48 h, immobility, EC_{50}	≥100 mg/L	Biocide Assessment Report, 2008[9]
Aquatic invertebrates	*Hyalella azteca*, 96 h, immobility, EC_{50}	0.0407 mg/L	Biocide Assessment Report, 2008[9]
Aquatic invertebrates	*Hyalella azteca*, 96 h, immobility, EC_{50}	≥47 mg/L	Biocide Assessment Report, 2008[9]
Aquatic invertebrates	*Asellus aquaticus*, 48h, mortality & immobility,	0.0758 mg/L	Biocide Assessment Report, 2008[9]

	EC$_{50}$		
Aquatic invertebrates	*Gammarus pulex*, 48 h, mortality & immobility, EC$_{50}$	0.027 mg/L	Biocide Assessment Report, 2008[9]
Aquatic invertebrates	*Ecydonurus pulex*, 48 h, immobility, EC$_{50}$	0.0077 mg/L	Biocide Assessment Report, 2008[9]
Aquatic invertebrates	*Daphnia magna*, 21 d, survival, reproduction and growth, NOEC	0.58 mg/L	Biocide Assessment Report, 2008[9]
Algae	*Scenedesmus subspicatus*, 72 h, growth inhibition, a) NOEC, b) EC$_{50}$ biomass, c) EC$_{50}$ growth rate	a)32 mg/L b)44.7 mg/L c)96.7 mg/L	Biocide Assessment Report, 2008[9]
Aquatic plants	*Lemna gibba,* 15 d, reduced frond number, EC$_{50}$	>95.4 mg/L	Biocide Assessment Report, 2008[9]
Sediment dwelling organisms	***Chironomus riparius, 28 d, a) NOEC number and time of emergence***, b)EC$_{50}$ emergence rate c) EC$_{50}$ development	**a)0.0005 mg/L** b)0.00218 mg/L c)≥0.0018 mg/L	**Biocide Assessment Report, 2008[9]**
Insects, sediment dwellers, zooplankton, phytoplankton	Outdoor microcosm study. Most sensitive group: Ceratopogonidae (insects), e.g. increase of number of species, 98 d, EAC	0.0016 mg/L	Biocide Assessment Report, 2008[9]

6.12 Mammalian toxicology data

Type of test	Endpoint	Value	Reference
Acute oral toxicity	Rat, LD$_{50}$	444 mg/kg	Biocide Assessment Report, 2008[9]
Repeated oral dose toxicity	**Rat, 2 year, NOAEL. Values used for ADI calculation in the EU Review Report, 2003[8]**	**1.2 mg/kg/day**	**Biocide Assessment Report, 2008[9]**
Carcinogenicity	Rat, lowest dose with tumours	25 mg/kg bw/day	Biocide Assessment Report, 2008[9]
Reproductive toxicity	NOAEL	2 mg/kg/day 3.7 mg/kg/day (dystocia)	Biocide Assessment Report, 2008[9]
Developmental toxicity	NOAEL	2 mg/kg/day	Biocide Assessment Report, 2008[9]

6.13 PNEC derivation

PNEC	Endpoint	Endpoint value	AF	PNEC value
PNEC$_{fw}$	*Chironomus riparius*, 28 d, NOEC [a], number and	0.0005 mg/L	10 [b]	5E-05 mg/L [9]

	time of emergence			
PNEC_sed	-	-	-	N.R.
PNEC_biota,sec pois	-	-	-	N.R.
PNEC_biota, hh	-	-	-	N.R.
PNEC_dw, hh	ADI [c]	0.01 mg/kg bw/day	-	0.035 mg/L

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

[a] Due to the mode of action of neonicotinoids, the lowest endpoint from the aquatic species tested corresponds to the midge *Chironomus riparius*. Therefore, it was selected for PNEC_fw calculation.

[b] Three long term values were available.

[c] ADI value, retrieved from EU Review Report 2003[10], used in equation F as TL_hh. See section 3.3.5 for calculation.

7   Risk Quotient (PEC/PNEC)

RQ	Value
RQ_fw	**218.00**
RQ_sed	N.R.
RQ_biota,sec pois	N.R.
RQ_biota, hh	N.R.
RQ_dw, hh	0.31

8   References

[1] List of end points, 2002 (based on doc 1654/VI/94, Rev. 7, 22 Apr 1998)

[2] Technical Guidance for Deriving Environmental Quality Standards – Guidance Document No. 27 (2011) Common Implementation Strategy of the Water Framework Directive (2000/60/EC). Available at http://ec.europa.eu/environment/water/water-dangersub/lib_pri_substances.htm

[3] European Pesticides Database: http://ec.europa.eu/sanco_pesticides/public/?event=homepage

[4] Generic guidance for FOCUS surface water scenarios 2011. Available at: http://focus.jrc.ec.europa.eu/sw/index.html

[5] Appendix C and D for parameterisation of drainage and run-off inputs, respectively. Available at: http://focus.jrc.ec.europa.eu/sw/index.html

[6] WATERBASE Database http://www.eea.europa.eu/data-and-maps/data/waterbase-rivers-6

[7] Swedish National Screening Programme Pesticides (data provided directly to the JRC)
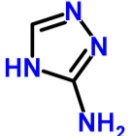
[8] Italian Monitoring Programme (data provided directly to the JRC)

[9] Directive 98/8/EC concerning the placing of biocidal products on the market. Inclusion of active substances in Annex I or IA to Directive 98/8/EC. Assessment report, THIACLOPRID Product-type 8 (Wood Preservative) 2008. Available at: http://dissemination.echa.europa.eu/Biocides/factsheet?id=0053-08

[10] EUROPEAN COMMISSION Review report for the active substance thiacloprid SANCO/4347/2000 – Final. Available at http://ec.europa.eu/food/plant/protection/evaluation/newactive/thiacloprid.pdf

Aminotriazole (CAS N. 61-82-5)

1. **Substance identity**

Chemical name (IUPAC)	1H-1,2,4-Triazol-3-amine
EC number	200-521-5
CAS number	61-82-5
Molecular formula	C2H4N4
Molecular weight	84.08
Structure	
SMILES	n1nc(N)nc1

2. **Physico-chemical Properties**

Endpoint	Value	Source
Vapour Pressure (Pa)	3.3E-05	INERIS, 2011 [1]
Water solubility (mg/L)	2.6E+05	EC Review report, 2001 [2]
logK$_{ow}$	-0.97	INERIS, 2011 [1]

3. **Environmental fate**

Endpoint	Value	Source
Hydrolysis (DT50)	86.1	EC Review report, 2001 [2]
Sorption potential (K$_{oc}$)	94	EFSA conclusion, 2014 [3]
Biodegradability	NRB	INERIS, 2011 [1]
Bioaccumulation (BCF)	2.38 (whole fish) in 7 days	EC Review report, 2001 [2]

4. **Environmental exposure assessment**

	Description	Source
Tonnes/year	22550 (year 1994)	From previous prioritisation exercise
Uses	Herbicide (PPP)	
Spatial usage (by MS):	BE, EL, ES, FR, HU, IT, LU, NL, PT, UK	EU Pesticides DB [4]
Banned uses	-	
ERC code	ERC8d	
Fraction of tonnage to region	0.1	

4.1 Predicted Environmental Concentration

PEC$_{fw}$ (mg/L)	0.501	FOCUS Step 2 (see Table below for details)
PEC$_{sed}$ (mg/kg dw)	0.459 (N.R.)	FOCUS Step 2
PEC$_{biota}$ (mg/kg)	1.192 (N.R.)	Calculation based on Equation L (Section 3.4.3)

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

4.1.1 Comparison of FOCUS Pesticides models with ECETOC model

FOCUS Step 1

Crop [3]	Application Rate (g/ha)[3]	Water solubility (mg/L)[3]	K$_{oc}$ (L/kg) [3]	DT$_{50}$ whole system (d) [3]
Orchards (citrus fruits, pome and stone fruits, assorted fruits-edible or inedible peel, tree nuts). For calculations, use of pome and stone fruits (early)	1 x 2977 g/ha	264000	94	86.1

FOCUS Step 2

Same parameters and conditions as above, in addition to DT$_{50soil}$ 7.4 d [3], DT$_{50water}$: 86.1 d [3], DT$_{50sediment}$ 86.1 d [3], no crop interception [3].

FOCUS Step 3 – SWASH Package

No new calculations were made, since PEC$_{fw}$ and PEC$_{sed}$ values were retrieved from EFSA Conclusion, 2014 [3]. The worst case values were from orchards, Autumn application.

Results

Tier	PEC$_{fw}$ (mg/L)	PEC$_{sed}$ (mg/kg)
ECETOC	0.73	9.27
FOCUS Step 1	1.17	1.06
FOCUS Step 2	**0.501**	0.459
FOCUS Step 3 (D3 stream)	0.0176	0.0028

4.2 Measured Environmental Concentration

n. of MS	Source of monitoring data	MEC values	RBSP
1 (FR)	NORMAN DB, 2014 [5]	MEC$_{95, whole}$: 0.873 µg/L	-

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

Aminotriazole is classified, in accordance with the provisions of Regulation (EC) No 1272/2008, as toxic for reproduction category 2 and toxic effects were observed in endocrine organs[3]. It is also listed in the Endocrine Disruptor's Database of the European Commission[6] as an ED Category 1 (Cat. 1 Human Health, Cat. 3 Wildlife, Cat. 1 overall). No evidence of a genotoxic potential relevant to humans[3]. The substance is not readily biodegradable (P). It has a low BCF of 2.38 (not B) (EFSA conclusion, 2014)[3].

6. Hazard assessment

6.1 Ecotoxicology data

Trophic level	Endpoint	Value	Reference
Fish	*Oncorhyncus mykiss*, 96 h, LC_{50}	>1000 mg/L	EFSA Conclusion, 2014[3]
Fish	*Oncorhyncus mykiss*, 21 d, NOEC	100 mg/L	EFSA Conclusion, 2014[3]
Fish	*Oncorhyncus mykiss*, 96 h, LC_{50}	>22.15 mg/L	EFSA Conclusion, 2014[3]
Aquatic invertebrate	*Daphnia magna*, 48 h, EC_{50}	6.1 mg/l	EFSA Conclusion, 2014[3]
Aquatic invertebrate	*Mysidopsis bahia,* 96 h, EC_{50}	2.8 mg/l	EFSA Conclusion, 2014[3]
Aquatic invertebrate	***Daphnia magna*, 21 d, NOEC**	**0.32 mg/L**	**EFSA Conclusion, 2014[3]**
Aquatic invertebrate	*Daphnia magna*, 48 h, EC_{50}	2.66 mg/L	EFSA Conclusion, 2014[3]
Algae	*Scenedesmus subspicatus*, 72 h, growth, EC_{50}	2.3 mg/L	EFSA Conclusion, 2014[3]
Algae	*Anabaena flos-aquae*. 120 h, a) EC_{50} biomass, b) EC_{50} growth rate	a)3.9 mg/L b)>4.8 mg/L	EFSA Conclusion, 2014[3]
Algae	*Selenastrum capricornutum*, 72 h growth, a) EC_{50} biomass, b) EC_{50} growth rate	a)1.6 mg/L b)>5.1 mg/L	EFSA Conclusion, 2014[3]
Algae	*Selenastrum capricornutum*, 8 d, a) EC_{50} growth rate and biomass, b)NOEC	a)>6 mg/L b)6 mg/L	EFSA Conclusion, 2014[3]
Algae	*Navicula pelliculosa*, 72 h, a) EC_{50} biomass, b) EC_{50} growth rate	a)1.3 mg/L b)>5.1 mg/L	EFSA Conclusion, 2014[3]
Algae	*Selenastrum capricornutum*, 72 h, a) EC_{50} biomass, b) EC_{50} growth rate	a)1.5 mg/L b)>3.1 mg/L	EFSA Conclusion, 2014[3]
Algae	*Selenastrum capricornutum*, 72 h, a) EC_{50} biomass, b) EC_{50} growth rate	a)27.9 mg/L b)>44.3 mg/L	EFSA Conclusion, 2014[3]

6.2 Mammalian toxicology data

Type of test	Endpoint	Value	Reference
Acute oral toxicity	Rat, LD_{50}	>5000 mg/kg bw	EFSA Conclusion, 2014[3]
Short term oral toxicity	**Rat, 90 d, NOAEL. Use for ADI calculation in the EFSA conclusion.**	**0.1 mg/kg bw/day**	**EFSA Conclusion, 2014[3]**
Short term oral toxicity	Dog, 1 year, NOAEL	0.3 mg/kg bw/day	EFSA Conclusion, 2014[3]
Long term toxicity	Rat, 2 year, NOAEL	0.5 mg/kg bw/day	EFSA Conclusion, 2014[3]
Long term toxicity	Mice, 18 months, NOAEL	1.5 mg/kg bw/day	EFSA Conclusion, 2014[3]
Long term toxicity	Hamster, 18 months, NOAEL	1 mg/kg bw/day	EFSA Conclusion, 2014[3]
Reproductive toxicity	Rat, 2 generation, NOAEL, a)parental toxicity, b) Reproductive toxicity, c) Offspring toxicity	a)0.12 mg/kg bw/day b)0.9 mg/kg bw/day c)0.9 mg/kg bw/day	EFSA Conclusion, 2014[3]
Developmental toxicity	Rabbit, NOAEL	3 mg/kg bw/day	EFSA Conclusion, 2014[3]

6.3 PNEC derivation

PNEC	Endpoint	Endpoint value	AF	PNEC value
$PNEC_{fw}$	*Daphnia magna,* chronic study, 21 d, NOEC	0.32 mg/L	10	0.032 mg/L [a]
$PNEC_{sed}$	-	-	-	N.R.
$PNEC_{biota,sec pois}$	-	-	-	N.R.
$PNEC_{biota, hh}$	-	-	-	N.R.
$PNEC_{dw, hh}$	ADI [b]	0.001 mg/kg bw/day	-	0.004 mg/L [c]

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

[a] An AF of 10 was chosen based on the availability of three NOEC values from the three main trophic levels (fish, aquatic invertebrates, algae).

[b] ADI retrieved from the European review report (2001)

[c] ADI value used in equation F as TLhh. See section 3.3.5 for calculation.

7. Risk Quotient (PEC/PNEC)

RQ	Value
RQ_{fw}	15.66
RQ_{sed}	N.R.
$RQ_{biota,sec pois}$	N.R.
$RQ_{biota, hh}$	N.R.
$RQ_{dw, hh}$	**143.14**

8. References

[1] INERIS Aminotriazole n. CAS: 61-82-5 (June, 2011). Available at:

http://www.ineris.fr/substances/fr/substance/getDocument/3068

[2] EUROPEAN COMMISSION Review report for the active substance amitrole 6839/VI/97-final (2001). Available at http://ec.europa.eu/sanco_pesticides/public/?event=activesubstance.detail

[3] EFSA (European Food Safety Authority), 2014. Conclusion on the peer review of the pesticide risk assessment of the active substance amitrole. EFSA Journal 2014;12(7):3742, 84 pp. doi:10.2903/j.efsa.2014.3742

[4] EU Pesticides Database http://ec.europa.eu/sanco_pesticides/public/?event=homepage
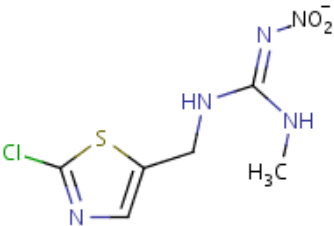
[5] NORMAN database at http://www.norman-network.net/?q=node/24

[6] Endocrine Disruptor database of the EU Commission), available at:

http://ec.europa.eu/environment/chemicals/endocrine/documents/index_en.htm

Clothianidin (CAS N. 210880-92-5)

1. **Substance identity**

EC number	433-460-1
CAS number	210880-92-5
Molecular formula	C6H8Cl N5O2S
Molecular weight	249.7
Structure	
SMILES	CN/C(=N\N(=O)[O-])/NCc1cnc(s1)Cl

2. **Physico-chemical Properties**

Endpoint	Value	Source
Vapour Pressure (Pa)	1.3E-10	Biocide Assessment Report, 2007[1]
Water solubility (mg/L)	327	Biocide Assessment Report, 2007[1]
$logK_{ow}$	0.7	Biocide Assessment Report, 2007[1]

3. **Environmental fate**

Endpoint	Value	Source
Sorption potential (K_{oc})	160	EU Review Report, 2005[2]
Biodegradability	NRB	Biocide Assessment Report, 2007[1]
Bioaccumulation (BCF)	a) BCF_{fish} 0.78 b) BCF 3.16 (estimated)	a) Biocide Assessment Report, 2007[1] b) EPI Suite, BCFBAF V3.01[3]

4. **Environmental exposure assessment**

4.1 **Predicted Environmental Concentration**

	Description	Source
Tonnes/year	-	
Uses	Insecticide (PPP and biocide)	
Spatial usage (by MS)	AT, BE, BG, CZ, DE, DK, EL, ES, FI, FR, HU, IE, IT, LT, NL, PL, PT, RO, SK, UK	EU Pesticides DB[4]

Banned uses	Restriction of uses	EU n. 485/2013[5]
ERC code	ERC8d (N.R.)	
PEC$_{fw}$ (mg/L)	0.008	FOCUS Step 2
PEC$_{sed}$ (mg/kg dw)	0.014 (N.R.)	FOCUS Step 2
PEC$_{biota}$ (mg/kg)	0.025 (N.R.)	Calculation based on Equation L (Section 3.4.3)

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

4.1.1 Comparison of FOCUS Pesticides models

FOCUS Step 1

Crop [2]	Application Rate (g/ha)[2]	Water solubility (mg/L)[2]	K$_{oc}$ (L/kg) [2]	DT$_{50}$ whole system (d) [2]
Sugar beet (seed treatment)	1×78	327	160	64.8

FOCUS Step 2

Same parameters and conditions as above, in addition to DT$_{50soil}$ 274 d (geometric mean from field studies)[1], DT$_{50water}$: 64.8 d[2], DT$_{50sediment}$ 1000 d (conservative value), no crop interception (seed treatment). The crop used is not listed in the restricted uses.

FOCUS Step 3 – SWASH package

Due the type of treatment, soil incorporation method was selected for all scenarios in SWASH and the chemical application method (CAM) was set to 8, "soil incorporation at one depth" with a depth of 3 cm for the PRZM scenarios, as specified in comments from a stakeholder. The definition of the application window was made by using the default application dates given by FOCUS SWASH, since the first useful date corresponded to a growth stage of zero, prior to the emergence date for each specific crop scenario (D3, D4, R1, R3). Since drift is assumed to be zero and surface runoff is assumed to be negligible due to the soil depth at which the seeds are drilled, only drainage scenarios were taken into account. Just for D4 run, no results were achieved due to some software error.

Results

Tier	PEC$_{fw}$ (mg/L)	PEC$_{sed}$ (mg/kg)
FOCUS Step 1	0.021	0.034
FOCUS Step 2	**0.008**	0.014
FOCUS Step 3	0.000248 D3 pond	0.0018 D3 pond

It is acknowledged that even though clothianidin is used as PPP and biocide, the application rate approach is not suitable for the calculation of PEC values for biocides, but just for PPP, so the results could be an underestimation. However, the tonnage values related to the biocide use were not available and therefore, no further calculation could be done.

4.2 Measured Environmental Concentration

n. of MS	Source of monitoring data	MEC values	RBSP
1 (SE)	SE monitoring programme[6]	All value < LOQ	

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

Based on the results of in vitro and in vivo genotoxicity tests, clothianidin is unlikely to pose a genotoxic risk to humans[7]. Clothianidin is unlikely to pose a carcinogenic risk to humans, and is unlikely to pose a teratogenic risk to humans at doses below those inducing toxic effects in the mother[7]. Clothianidin is also unlikely to affect fertility and developmental parameters in humans at doses below a range that elicits other toxic effects in adults[7]. The substance is not readily biodegradable (P) [7]. The low P_{ow} indicates that clothianidin has low potential to bioaccumulate in organisms[7]. Both estimated bioconcentration factors for the aquatic (BCF_{fish} = 0.78) and the terrestrial compartment ($BCF_{earthworm}$ = 0.9) can be classified as low. (Biocide Assessment Report, 2007[1]). An estimated BCF value of 3.16 L/kg was retrieved from EPI Suite[3].

6. Hazard assessment

6.1 Ecotoxicology data

Trophic level	Endpoint	Value	Reference
Fish	*Oncorhyncus mykiss*, 96 h, mortality, LC_{50}	>100 mg/L	Biocide Assessment Report, 2007[1]
Fish	*Pimephales promelas*, 33 d, hatching, mortality and growth, NOEC	≥20 mg/L	Biocide Assessment Report, 2007[1]
Aquatic invertebrates	*Daphnia magna*, 48 h, immobility, EC_{50}	26 mg/L	Biocide Assessment Report, 2007[1]
Aquatic invertebrates	*Daphnia magna*, 21 d, mortality and reproduction, NOEC	0.12 mg/L	Biocide Assessment Report, 2007[1]
Algae	*Selenastrum capricornutum*, 96 h, growth inhibition a) NOEC b)EC_{50}	a)15 mg/L b)56 mg/L	Biocide Assessment Report, 2007[1]
Sediment dwelling organisms	***Chironomus riparius*, 28 d, emergence and development, EC_{10}**	**0.00065 mg/L**	**Biocide Assessment Report, 2007[1]**
Sediment dwelling organisms, phytoplankton and zooplankton	Mesocosm study, 14 weeks, NOEC	0.001 mg/L	Biocide Assessment Report, 2007[1]

6.2 Mammalian toxicology data

Type of test	Endpoint	Value	Reference
Acute oral toxicity	Rat, LD_{50}	523 mg/kg bw	Biocide Assessment

			Report, 2007[1]
Short-term oral repeated dose toxicity	Dog, 90 d, NOAEL	20 mg/kg bw/day	Biocide Assessment Report, 2007[1]
Short-term oral repeated dose toxicity	Mouse, 90 d, mortality, NOEL	16 mg/kg bw/day	Biocide Assessment Report, 2007[1]
Long-term toxicity	**Rat, 2 year, dermal, NOAEL. Value used for ADI calculation in the EU Review Report, 2005[2].**	**9.7 mg/kg bw/day**	**EU Review Report, 2005[2] Biocide Assessment Report, 2007[1]**
Reproductive toxicity	Rat, NOAEL, a) parental, b) reproduction, c) offspring	a)31 mg/kg bw/day b) 31 mg/kg bw/day c) 10 mg/kg bw/day	Biocide Assessment Report, 2007[1]
Developmental toxicity	Rabbit, NOAEL, a) maternal, b) foetal	a)25 mg/kg bw/day b)25 mg/kg bw/day	Biocide Assessment Report, 2007[1]

6.3 PNEC derivation

PNEC	Endpoint	Endpoint value	AF	PNEC value
PNEC$_{fw}$	*Chironomus riparius*, 28 d, EC$_{10}$	0.00065 mg/L	5[a]	1.3E-04 mg/L[b]
PNEC$_{sed}$	-	-	-	N.R.
PNEC$_{biota,sec pois}$	-	-	-	N.R.
PNEC$_{biota, hh}$	-	-	-	N.R.
PNEC$_{dw, hh}$	ADI	0.097 mg/kg bw/day	-	0.340 mg/L[c]

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

[a] Due to the mode of action of neonicotinoids, the lowest endpoint from the aquatic species tested corresponds to the midge *Chironomus riparius*. Therefore, it was selected for PNEC$_{fw}$ calculation. A lower AF of 5 was selected, due to the availability of the mesocosm study. The same PNEC value was used in the Biocide Assessment Report[1].

[b] Three long term values were available.

[c] ADI value, retrieved from EU Review Report 2005[2], used in equation F as TL$_{hh}$. See section 3.3.5 for calculation.

7. Risk Quotient (PEC/PNEC)

RQ	Value
RQ$_{fw}$	**61.54**
RQ$_{sed}$	N.R.
RQ$_{biota,sec pois}$	N.R.
RQ$_{biota, hh}$	N.R.
RQ$_{dw, hh}$	0.02

8. References

[1] Directive 98/8/EC concerning the placing of biocidal products on the market Inclusion of active substances in Annex I to Directive 98/8/EC Assessment Report CLOTHIANIDIN Product-Type 8 (Wood Preservative) 13 September 2007 Annex I. Available at http://dissemination.echa.europa.eu/Biocides/factsheet?id=0015-08

[2] EUROPEAN COMMISSION Review report for the active substance clothianidin. SANCO/10533/05 – Final Available at http://ec.europa.eu/food/plant/protection/evaluation/newactive/list_clothianidin.pdf

[3] EPI Suite, BCFBAF v3.01
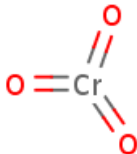
[4] European Pesticides Database: http://ec.europa.eu/sanco_pesticides/public/?event=homepage

[5] the use as a seed treatment or soil treatment of plant protection products containing clothianidin is prohibited for crops attractive to bees and for cereals except for uses in greenhouses and for winter cereals. Foliar treatments with plant protection products containing clothianidin are prohibited for crops attractive to bees and for cereals with the exception of uses in greenhouses and uses after flowering, from COMMISSION IMPLEMENTING REGULATION (EU) No 485/2013 of 24 May 2013 amending Implementing Regulation (EU) No 540/2011, as regards the conditions of approval of the active substances clothianidin, thiamethoxam and imidacloprid, and prohibiting the use and sale of seeds treated with plant protection products containing those active substances. Available at http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32013R0485.

[6] Swedish National Screening Programme Pesticides (data provided directly to the JRC)

Chromium trioxide (CAS N. 1333-82-0)

1. **Substance identity**

EC name	
EC number	
CAS number	1333-82-0
Molecular formula	CrO3
Molecular weight	99.99
Structure	
SMILES	[Cr](=O)(=O)=O

2. **Physico-chemical Properties**

Endpoint	Value	Source
Vapour Pressure (Pa)	Not available (inorganic ionic compound)	EU-RAR, 2005[1]
Water solubility (mg/L)	1667 mg/L	EU-RAR, 2005[1]
logK$_{ow}$	Not available (inorganic ionic compound)	EU-RAR, 2005[1]

3. **Environmental fate**

Endpoint	Value	Source
Sorption potential K$_{oc}$	Not available	EU-RAR, 2005[1]
Partition coefficient solid-water in sediment Kp$_{sed}$ (L/kg)	1000	EU-RAR, 2005[1]
Biodegradability	NRB	EU-RAR, 2005[1]
Bioaccumulation (BCF)	2.8	EU-RAR, 2005[1]

4. **Environmental exposure assessment**

4.1 **Predicted Environmental Concentration**

	Description	Source
Tonnes/year	-	-
Uses	Manufacture of substances and of	ECHA, 2013[2]

	preparations, formulation of preparations and materials, industrial use resulting in inclusion into or onto a matrix, use as laboratory reagent.	
Spatial usage (by MS)	Not known	-
Banned uses	All consumer uses, and all professional uses except as laboratory substance[2]. Chromium trioxide meets the criteria for inclusion in Annex XIV to Regulation (EC) N. 1906/2006[3]. Furthermore, the latest application date expected for chromium trioxide is 21 March 2016, and the sunset date is 21 September 2017[4].	ECHA, 2013[2] Regulation (EC) N. 1906/2006[3] COMMISSION REGULATION (EU) No 348/2013[4]
ERC code	-	-
PEC$_{fw}$ (mg/L)	0.35	EU-RAR, 2005[1]
PEC$_{sed}$ (mg/kg dw)	0.152	EU-RAR, 2005[1]
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 Concentration

n. of MS	Source of monitoring data	MEC values	RBSP
None	-	-	-

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

The evidence clearly indicates that highly water-soluble Cr(VI) compounds can produce significant mutagenic activity in vitro and in vivo[1]. The Cr (VI) compounds under consideration are therefore regarded as in vivo somatic cell mutagens[1]. In addition, toxicokinetic and dominant lethal data suggest that water-soluble Cr (VI) has the potential to be an in vivo germ cell mutagen[1]. Chrome plating workers exposed to chromium (VI) trioxide in aqueous solution have shown a clear excess in mortality from lung cancer[1]. Therefore chromium (VI) trioxide should be regarded as a human carcinogen[1]. Adverse effects on fertility have been found in studies in mice following repeated oral exposure[1]. In addition, adverse effects on the testes have been seen following repeated oral exposure in the rat (EU-RAR, 2005[1]). The substance is not readily biodegradable (P). It shows a low potential to bioaccumulate in aquatic organism[1].

6. Hazard assessment

6.1 Ecotoxicology data

Since chromium trioxide is recommended for deselection as candidate substance for the Watch List, because of the imminent ban (Last application date in 2016, sunset date 2017), no ecotoxicity data are reported at this stage.

6.2 Mammalian toxicology data

No mammalian toxicity data are reported at this stage due to imminent ban and deselection as Watch List candidate.

6.3 PNEC derivation

PNEC	Endpoint	Endpoint value	AF	PNEC value
$PNEC_{fw}$	$HC_{5-50\%}$	0.0102 mg/L	3	3.40E-03 mg/L[a]
$PNEC_{sed}$	-	-	-	6.80 mg/kg dw[b]
$PNEC_{biota,sec\ pois}$	Mouse, oral, conversion factor 8.3, NOAEL	20 mg/kg bw/day	10	17 mg/kg food[c] (N.R.)
$PNEC_{biota,\ hh}$	TDI	0.0009 mg/kg bw/day	-	0.055 mg/kg food[d] (N.R.)
$PNEC_{dw,\ hh}$	TDI	0.0009 mg/kg bw/day	-	0.003 mg/L[e]

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

[a]No new calculations were made. PNEC value retrieved from EU-RAR, 2005[1] with a probabilistic approach.

[b] Equilibrium partitioning method used, with the following values: $K_{sed-water}$= 500 m³m⁻³ (from EU-RAR, 2005), RHO_{sed}= 1300 kg m⁻³ (default value), $Fsolid_{sed}$= 0.2 (default value), RHO_{solid}= 2500 kg m⁻³ (default value). Conversion from wet weight to dry weight was done with eq. B of section 3.3.2

[c]No new calculations were performed. Value retrieved from EU-RAR, 2005[1]

[d] TDI value, retrieved from WHO Report 2013[6], used for PNEC calculation according to Equation E (see section 3.3.4)

[e] TDI value used in equation F as TL_{hh}. See section 3.3.5 for calculation.

7. Risk Quotient (PEC/PNEC)

RQ	Value
RQ_{fw}	102.94
RQ_{sed}	0.045
$RQ_{biota,sec\ pois}$	0.058
$RQ_{biota,\ hh}$	17.89
$RQ_{dw,\ hh}$	**111.11**

8. References

[1]European Risk Assessment Report on Chromium Trioxide, Sodium chromate, Sodium dichromate, Ammonium dichromate and Potassium dichromate (2005) EUR 21508 EN, and Brussels, C7/VR/csteeop/Cr/100903 D(03) Available at http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32013R0348&from=EN

2   ECHA   dissemination   website: http://apps.echa.europa.eu/registered/data/dossiers/DISS-9c7ac228-b090-229d-e044-00144f67d249/DISS-9c7ac228-b090-229d-e044-00144f67d249_DISS-9c7ac228-b090-229d-e044-00144f67d249.html

3 REGULATION (EC) No 1907/2006 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 18 December 2006, Official Journal of the European Union. Available at http://faolex.fao.org/docs/pdf/eur68317.pdf

4 COMMISSION REGULATION (EU) No 348/2013 of 17 April 2013 amending Annex XIV to Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), 2013

5 Technical Guidance for Deriving Environmental Quality Standards – Guidance Document No. 27 (2011) Common Implementation Strategy of the Water Framework Directive (2000/60/EC). Available at http://ec.europa.eu/environment/water/water-dangersub/lib_pri_substances.htm

6Inorganic chromium(VI) compounds; Concise International Chemical Assessment Document 78. IPCS, WHO (2013)

2   ECHA   dissemination   website: http://apps.echa.europa.eu/registered/data/dossiers/DISS-9c7ac228-b090-229d-e044-00144f67d249/DISS-9c7ac228-b090-229d-e044-00144f67d249_DISS-9c7ac228-b090-229d-e044-00144f67d249.html

3 REGULATION (EC) No 1907/2006 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 18 December 2006, Official Journal of the European Union. Available at http://faolex.fao.org/docs/pdf/eur68317.pdf

4 COMMISSION REGULATION (EU) No 348/2013 of 17 April 2013 amending Annex XIV to Regulation (EC) No 1907/2006 of the European Parliament and of the Council on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH), 2013

5 Technical Guidance for Deriving Environmental Quality Standards – Guidance Document No. 27 (2011) Common Implementation Strategy of the Water Framework Directive (2000/60/EC). Available at http://ec.europa.eu/environment/water/water-dangersub/lib_pri_substances.htm

Thiamethoxam (CAS N. 153719-23-4)

1. **Substance identity**

EC name	Thiamethoxam
EC number	428-650-4
CAS number	153719-23-4
Molecular formula	C8H10ClN5O3S
Molecular weight	291.71
Structure	
SMILES	CN1COCN(C1=N[N+](=O)[O-])Cc2cnc(s2)Cl

2. **Physico-chemical Properties**

Endpoint	Value	Source
Vapour Pressure (Pa)	6.6 E-09	Biocide Assessment Report[1]
Water solubility (mg/L)	4100	Biocide Assessment Report[1]
logK$_{ow}$	-0.13	Biocide Assessment Report[1]

3. **Environmental fate**

Endpoint	Value	Source
Sorption potential (K$_{oc}$)	56.2	Biocide Assessment Report[1]
Biodegradability	NRB	Biocide Assessment Report[1]
Bioaccumulation (BCF)	3.16 (estimated)	EPI Suite BCFBAF, v.3.01
BMF	1	Default value, TG n. 27 - CIS WFD[2]

4. **Environmental exposure assessment**

	Description	Source
Tonnes/year		
Uses	Insecticide (PPP and biocide)	
Spatial usage (by MS):	AT, BE, BG, CY, CZ, DE, DK, EE, EL, ES, FI, FR, HU, IT, LT, LV, MT, NL, PL, PT, RO, SE, SI, SK, UK	EU Pesticides DB[3]
Banned uses	Restriction of uses[a]	EU n. 485/2013[4]
ERC code	ERC8d	

Fraction of tonnage to region	-	

[a]The use as a seed treatment or soil treatment of plant protection products containing thiamethoxam is prohibited for crops attractive to bees and for cereals except for uses in greenhouses and for winter cereals. Foliar treatments with plant protection products containing thiamethoxam are prohibited for crops attractive to bees and for cereals with the exception of uses in greenhouses and uses after flowering[4].

4.1 Predicted Environmental cCncentration

	Value	Source
PEC_{fw} (mg/L)	0.011	FOCUS Step 2
PEC_{sed} (mg/kg dw)	0.0074 (N.R.)	FOCUS Step 2
PEC_{biota} (mg/kg)	0.035 (N.R.)	Calculation based on Equation L (Section 3.4.3)

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

4.1.1 Comparison between FOCUS Pesticides models

FOCUS Step 1

Crop	Application Rate (g/ha)[5]	Water solubility (mg/L)[5]	K_{oc} (L/kg) [5]	DT_{50} whole system (d)[5]
Pome & Stone Fruits (late)	2×100 (14 d application interval)	4100	56.2	46.4

FOCUS Step 2

Same parameters and conditions as above, in addition to DT_{50soil} 156 d (mean)[5], $DT_{50water}$ 38.2 d[5], $DT_{50sediment}$ 1000 d (conservative value), full crop interception.

FOCUS Step 3 – SWASH package

In addition to the input values listed above, foliar application, and a pre-harvest interval (PHI) of 14 days. In accordance both with the FOCUS SW Appendix C and D[6], and with a growth stage corresponding to post blosson (approximately BBCH 70) related to pome and stone fruits (as reported in the GAP table of the EU LoE[5]), the following application windows were selected for the relevant scenarios for the PAT calculator: D3 and D4 from 15.06 to 16.10, D5 from 15.06 to 26.09, R1 from 15.06 to 16.10, R2 from 15.07 to 16.09, R3 and R4 from 15.07 to 01.10. Just for runs of D4 and D5 no results were achieved due to some software error.

Results

Tier	PEC_{fw} (mg/L)	PEC_{sed} (mg/kg)
FOCUS Step 1	0.071	0.048
FOCUS Step 2	0.011	0.007
FOCUS Step 3	0.005 D3 pond	0.008 D3 pond

4.2 Measured Environmental Concentration

n. of MS	Source of monitoring data	MEC values	RBSP
4 (FI, SE, IT, NL)	WATERBASE, 2014[7]	$MEC_{95, whole}$: 0.03 µg/L	-
	SE pesticide monitoring programme [8]	MEC_{95}: 0.014 µg/L	
	IT monitoring programme[9]	MEC_{95}: 0.0365 µg/L	
	NORMAN DB, 2014[10]	MEC_{95}: 0.35 µg/L (NL)	

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

Thiamethoxam is not clastogenic or aneugenic[1]. On the basis of the absence of genotoxicity in vivo, the absence of carcinogenicity in rats and the mode of action by which liver tumours arise in mice, it was concluded that thiamethoxam is unlikely to pose a carcinogenic risk at human dietary exposure levels[11]. The Joint FAO/WHO Meeting concluded that thiamethoxam can cause fetotoxicity and skeletal anomalies (malformations and variants), but only at maternally toxic doses[11]. Thiamethoxam is not a neurotoxin in mammals at the tested dose levels, although it is a member of the neonicotinoid chemical class[11]. The substance is not readily biodegradable (P). It shows a low potential for bioaccumulation (not B) (Biocide Assessment Report, 2008[1]). A BCF value of 3.16 L/kg was also estimated with EPI Suite.

6.   Hazard assessment

6.1   Ecotoxicology data

Trophic level	Endpoint	Value	Reference
Fish	96 h, LC_{50}	>125 mg/L	Biocide Assessment Report, 2008[1]
Fish	88 d, NOEC	20 mg/L	Biocide Assessment Report, 2008[1]
Aquatic invertebrates	Ostracoda, 48 h, EC_{50}	0.18 mg/L	Biocide Assessment Report, 2008[1]
Aquatic invetebrates	*Gammarus* sp., 48 h, EC_{50}	2.8 mg/L	Biocide Assessment Report, 2008[1]
Aquatic invertebrates	*Daphnia magna,* 21 d, NOEC	100 mg/L	Biocide Assessment Report, 2008[1]
Aquatic invertebrates	*Lymnea stagnalis*, 48 h, EC50	100 mg/L	Biocide Assessment Report, 2008[1]
Aquatic invetebrates	***Cloeon* Sp., 48 h, EC_{50}**	**0.014 mg/L**	**Biocide Assessment Report, 2008[1]**
Sediment dwelling organisms	*Chironomus riparius*, 30 d, NOEC	0.01 mg/L	Biocide Assessment Report, 2008[1]
Algae	*Selenastrum capricornutum*, 72 h, NOEC	81.8 mg/L	Biocide Assessment Report, 2008[1]
Aquatic plants	*Lemna gibba*, 7 d, EC_{50}	>90.2 mg/L	Biocide Assessment Report, 2008[1]

6.2 Mammalian toxicology data

Type of test	Endpoint	Value	Reference
Acute oral toxicity	Rat, LD50	1563 mg/kg bw	Biocide Assessment Report, 2008[1]
Repeated oral dose toxicity	Mouse, 90 d, NOAEL	1.41 mg/kg bw/day	Biocide Assessment Report, 2008[1]
Repeated oral dose toxicity	Dog, 1 year, NOAEL	4.05 mg/kg bw/day	Biocide Assessment Report, 2008[1]
Carcinogenicity	**Mouse, 18 months, NOAEL. Value used for ADI calculation in the EU Review Report[4]**	**2.63 mg/kg bw/day**	Biocide Assessment Report, 2008[1]
Reproductive toxicity	Rat, 2 generation study, NOAEL	62 mg/kg bw/day	Biocide Assessment Report, 2008[1]
Developmental toxicity	Rabbit, NOAEL	50 mg/kg bw/day	Biocide Assessment Report, 2008[1]

6.3 PNEC derivation

PNEC	Endpoint	Endpoint value	AF	PNEC value
PNEC$_{fw}$	*Cleon* sp. (Ephemeroptera), 48 h, EC$_{50}$	0.014 mg/L	100	0.00014 mg/L[a]
PNEC$_{sed}$	-	-	-	N.R.
PNEC$_{biota,sec pois}$	-	-	-	N.R.
PNEC$_{biota, hh}$	-	-	-	N.R.
PNEC$_{dw, hh}$	ADI[b]	0.026 mg/kg bw/day	-	0.091 mg/L[c]

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

[a] Due to the mode of action of neonicotinoids, the lowest endpoint from the aquatic species tested corresponds to *Cleon* species. Therefore, it was selected for PNEC$_{fw}$ calculation. An assessment factor of 100 was used instead of the TGD (Technical Guidance Document) recommended 1000 because this taxa was regarded with high probability as being the most sensitive and a further long-term NOEC from different taxonomic group would not be lower than the data already available (Biocide Assessment Report, 2008)[1].

[b] ADI from EU LoE, 2006[5].

[c] ADI value used in equation F as TL$_{hh}$. See section 3.3.5 for calculation.
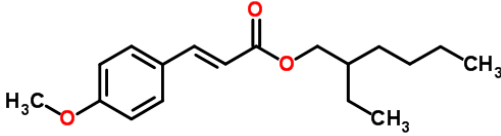
7. Risk Quotient (PEC/PNEC)

RQ	Value
RQ$_{fw}$	**78.57**
RQ$_{sed}$	N.R.
RQ$_{biota,sec pois}$	N.R.
RQ$_{biota, hh}$	N.R.

RQ$_{dw, hh}$	0.12

8. References

[1] Assessment Report Thiamethoxam Product-type 8 (Wood preservative) (2008) - Directive 98/8/EC concerning the placing of biocidal products on the market Inclusion of active substances in Annex I or IA to Directive 98/8/EC

[2] Technical Guidance for Deriving Environmental Quality Standards – Guidance Document No. 27 (2011) Common Implementation Strategy of the Water Framework Directive (2000/60/EC). Available at http://ec.europa.eu/environment/water/water-dangersub/lib_pri_substances.htm

[3] EU Pesticides Database http://ec.europa.eu/sanco_pesticides/public/?event=homepage

[4] COMMISSION IMPLEMENTING REGULATION (EU) No 485/2013 of 24 May 2013 amending Implementing Regulation (EU) No 540/2011, as regards the conditions of approval of the active substances clothianidin, thiamethoxam and imidacloprid, and prohibiting the use and sale of seeds treated with plant protection products containing those active substances. Official Journal of the European Union. Available at http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32013R0485

[5] EUROPEAN COMMISSION Review report for the active substance thiamethoxam, SANCO/10390/2002 - rev. final. Available at http://ec.europa.eu/food/plant/protection/evaluation/newactive/thiamethoxam_en.pdf

[6] Appendix C and D for parameterisation of drainage and run-off inputs, respectively. Available at: http://focus.jrc.ec.europa.eu/sw/index.html

[7] WATERBASE Database http://www.eea.europa.eu/data-and-maps/data/waterbase-rivers-6

[8] Swedish National Screening Programme Pesticides (data provided directly to the JRC)

[9] Italian Monitoring Programme (data provided directly to the JRC)

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

[11] Joint FAO/WHO Meeting report. Available at http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/JMPR/Report10/Thiamethoxam.pdf.

2-Ethylhexyl 4-methoxycinnamate (CAS N. 5466-77-3)

1. Substance identity

Chemical name (IUPAC)	2-Ethylhexyl 4-methoxycinnamate
EC number	226-775-7
CAS number	5466-77-3
Molecular formula	C18H26O3
Molecular weight	290.4
Structure	
SMILES	CCCCC(CC)COC(=O)/C=C/C1=CC=C(C=C1)OC

2. Reasons for proposal as candidate for the Watch list and suspected environmental risk

2-Ethylhexyl 4-methoxycinnamate (EHMC) is an organic sun-blocking agent derived from cinnamic acid that absorbs ultraviolet radiation in the UV-B range. It is used in sunscreen lotions to protect human skin from solar radiation, and to protect cosmetics and personal care products from photodegradation.

It is part of the Draft Community Rolling Action Plan (CoRAP)[1], where the initial grounds of concerned are listed as environment/suspected PBT, potential endocrine disruptor, possible risk; exposure/wide dispersive use, consumer use environmental exposure and high (aggregated) tonnage.

UV filters may enter the aquatic environment directly, as a result of bathing and washing activities in seas, rivers, lakes and swimming pools, as well as industrial discharges. Alternatively, they can enter the aquatic environment indirectly via domestic wastewater discharges and via wastewater treatment plants (Giokas, 2007)[2]. The Cosmetics Directive 92/8/EEC restricts the use of EHMC at a maximum concentration of 10%[3].

EHMC is a ubiquitous sunscreen filter in European environment, having been detected in surface waters, sediment and biota[4-10]. Due to its physic-chemical properties, EHMC is expected to accumulate in sediments. This substance has been measured up to 4 μg/kg in river sediments[5] and 34 μg/kg in lake sediments in Germany[10] and 79 μg/kg in Tokyo bay sediments[11]. A seasonal variation in the concentrations of UV filters (including EHMC) in the aquatic environment has been observed in many cases with a peak during the summer period.

3. Physico-chemical Properties

Endpoint	Value	Source
Vapour Pressure (Pa)	30	ECHA, 2014[12]
Water solubility (mg/L)	0.75	ECHA, 2014[12]
logK$_{ow}$	>6	ECHA, 2014[12]

4. Environmental fate

Endpoint	Value	Source
Sorption potential (K_{oc})	13290	ECHA, 2014[12]
Biodegradability	RB	ECHA, 2014[12]
Bioaccumulation (BCF)	433	ECHA, 2014[12]
BMF	1	Default value, TG n. 27 - CIS WFD[13]

5. Environmental exposure assessment

	Description	Source
Tonnes/year	7500 (year 2000)	Previous prioritisation exercise
Uses	Sunscreen ingredient in personal care products	
Spatial usage (by MS):	Widespread use (worldwide)	Sunscreen Ingredients, 2006[14]
Banned uses	-	
ERC code	ERC8a	
Fraction of tonnage to region	0.1	

5.1 Predicted Environmental Concentration

PEC_{fw} **(mg/L)**	0.0063	ECETOC
PEC_{sed} **(mg/kg dw)**	8.39	ECETOC
PEC_{biota} **(mg/kg)**	2.73 (N.R.)	Calculation based on Equation L (Section 3.4.3)

N.R. Not required because readily biodegradable.

4.2 Measured Environmental Concentration

n. of MS	Source of monitoring data	MEC values	RBSP
2(DE, SE)	NORMAN DB, 2014 [15]	$MEC_{95, whole}$: 3.98E-04 mg/L (DE)	-
	SE National Screening Programme 2009: UV-filters[4]	MEC_{95}: 3.03E-05 mg/L (surface water) MEC_{95}: 0.043 mg/kg dw (sediment) MEC_{95}: 7.8E-04 mg/kg ww (biota)	

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

Endocrine disruptor-Category 1 both for human health and aquatic organisms[16]. 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)[16].

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[17]. EHMC has also caused toxic effects on reproduction in snails[18].

Negative results for genotoxicity[12]. The substance is readily biodegradable (not P),. It has a BCF value of 433 L/kg (ECHA, 2014[12]).

7. Hazard assessment

7.1 Ecotoxicology data

Trophic level	Endpoint	Value	Reference
Algae	*Selenastrum capricornutum*, 72 h, growth rate, EC_{50}	32 mg/L	ECHA, 2014[12]
Algae	*Selenastrum capricornutum*, 72 h, growth rate, NOEC	>100000 µg/L	ECHA, 2014[12]
Aquatic invertebrates	***Melanoides tuberculata*, 28 d, number of embryos per snail, sediment toxicity test, NOEC**	**2 mg/kg**	**Kaiser et al. (2012)[18] (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)[18] (R2)
Aquatic invertebrates	*Daphnia magna*, 48 h, EC_{50}	>0.0271 mg/L	ECHA, 2014[12]
Fish	*Danio rerio*, 48 h, sediment contact test, sublethal effects, NOEC	100 mg/kg	Kaiser et al. (2012)[18] (R2)
Fish	*Cyprinus carpio*, 96 h, LC_{50}	>100000 µg/L	ECHA, 2014[12]

[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).

7.2 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[12]
Reproductive toxicity	Rat, oral, 2 generation study, NOAEL	450 mg/kg bw/day	ECHA, 2014[12]
Developmental toxicity	Rabbit, oral, NOAEL	500 mg/kg bw/day	ECHA, 2014[12]

7.3 PNEC derivation

PNEC	Endpoint	Endpoint value	AF	PNEC value	Comment
$PNEC_{fw}$	-	-	-	-	[a]
$PNEC_{sed}$	*Melanoides tuberculata*, 28 d, sediment toxicity	2 mg/kg	10 [b]	0.2 mg/kg	Kaiser et al. (2012)[18]

	test, NOEC				
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[12] (for DNEL & AF)[c]

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

[a] The substance showed no inhibitory effect in the range of the water solubility (ECHA, 2014)[12]

[b] 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.

[c] DNEL, retrieved from ECHA, 2014[12], used in equation F as TL_{hh} (see section 3.3.5)

8. Risk Quotient (PEC/PNEC)

RQ	Value
RQ_fw	-
RQ_sed	**41.95**
RQ_biota,sec pois	N.R.
RQ_biota, hh	N.R.
RQ_dw, hh	8E-04

9. References

[1] ECHA Draft Community Rolling Action Plan (CoRAP) update for years 2015-2017. Available at: http://echa.europa.eu/documents/10162/13628/corap_2015_2017_en.pdf

[2] Giokas DL, Salvador A, Chisvert, A. (2007) UV filters: From sunscreens to human body and the environment. Trends in Analytical Chemistry, 26(5): 360-374.

[3] http://ec.europa.eu/consumers/cosmetics/cosing/index.cfm?fuseaction=search.details&id=31273

[4] Remberger M, Lilja K, Kaj L, Viktor T, Brorström-Lundén E. (2011) Results from the Swedish National Screening Programme 2009. Subreport 3: UV-filters. IVL Swedish Environmental Research Institute. http://www.ivl.se/download/18.7df4c4e812d2da6a416800088960/B1971.pdf

[5] Ricking M, Schwarzbauer J, Franke S. (2003) Molecular markers of anthropogenic activity in sediments of the Havel and Spree Rivers (Germany). Water Res. 2003 Jun;37(11):2607-17.

[6] Langford KH, Thomas KV. (2008) Inputs of chemicals from recreational activities into the Norwegian coastal zone. J Environ Monit. 10(7):894-8.
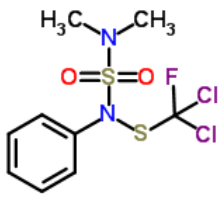
[7] Zenker A, Schmutz H, Fent K. (2008) Simultaneous trace determination of nine organic UV-absorbing compounds (UV filters) in environmental samples. J Chromatogr A. 1202(1):64-74.

[8] Fent K, Zenker A, Rapp M. (2010) Widespread occurrence of estrogenic UV-filters in aquatic ecosystems in Switzerland. Environ Pollut. 158(5):1817-24.

[9] Thomas K, Schlabach M, Langford K, Fjeld E, Øxnevad S, Rundberget T, Bæk K, Rostkowski P, Harju M. (2014) Screening program 2013 New bisphenols, organic peroxides, fluorinated siloxanes, organic UV filters and selected PBT substances. Report M-176/2014. http://www.miljodirektoratet.no/Documents/publikasjoner/M176/M176.pdf

[10] Rodil R, Moeder M. (2008) Development of a simultaneous pressurised-liquid extraction and clean-up procedure for the determination of UV filters in sediments. Anal. Chim. Acta 612, 152e159.

[11] Kameda Y, Tamada M, Kanai Y, Masunaga S. (2007) Occurence of organic UV filters in surface waters, sediments and core sediments in Tokyo bay, -organic UV filters are new POPs? Organhalogen Compd. 69, 263e266.

[12] ECHA dissemination website: http://apps.echa.europa.eu/registered/data/dossiers/DISS-9ea053bf-39e2-163b-e044-00144f67d031/DISS-9ea053bf-39e2-63b-e044-00144f67d031_DISS-9ea053bf-39e2-163b-e044-00144f67d031.html

[13] Technical Guidance for Deriving Environmental Quality Standards – Guidance Document No. 27 (2011) Common Implementation Strategy of the Water Framework Directive (2000/60/EC). Available at http://ec.europa.eu/environment/water/water-dangersub/lib_pri_substances.htm

[14] Update of Sunscreen Ingredients Nomination to NTP. Imogene Sevin, Ph.D. Technical Resources International, Inc., 2006

[15] NORMAN database at http://www.norman-network.net/?q=node/24

[16] Endocrine Disruptor database of the EU Commission), available at http://ec.europa.eu/environment/chemicals/endocrine/documents/index_en.htm

[17] Christen V, Zucchi S, Fent K. (2011) Effects of the UV-filter 2-2thyl-4-trimethoxycinnamate (EHMC) on expression of genes involved in hormonal pathways in fathead minnows (Pimephales promelas) and link to vitellogenic induction and histology. Aq. Tox. 102:167-176.

[18] Kaiser D, Sieratowicz A, Zielke H, Oetken M, Hollert H, Oehlmann J. (2012) Ecotoxicological effect characterisation of widely used organic UV filters. Environmental Pollution 163:84-90.

Dichlofluanid (CAS N. 1085-98-9)

1. Substance identity

EC name	
EC number	214-118-7
CAS number	1085-98-9
Molecular formula	C9H11Cl2FN2O2S2
Molecular weight	333.2
Structure	
SMILES	CN(C)S(=O)(=O)N(c1ccccc1)SC(F)(Cl)Cl

2. Physico-chemical Properties

Endpoint	Value	Source
Vapour Pressure (Pa)	2.15E-05 Pa at 20 °C	Biocide Assessment Report, 2006[1]
Water solubility (mg/L)	1.58 mg/l at 20 °C	Biocide Assessment Report, 2006[1]
logK$_{ow}$	3.5	Biocide Assessment Report, 2006[1]

3. Environmental fate

Endpoint	Value	Source
Sorption potential (K$_{oc}$)	1344	Biocide Assessment Report, 2006[1]
Biodegradability	NRB	Biocide Assessment Report, 2006[1]
Bioaccumulation (BCF)	72	Biocide Assessment Report, 2006[1]
DT$_{50}$ water/sediment systems	< 1 d Dichlofluanid was very rapidly degraded in aerobic aquatic systems to DMSA. DMSA stayed mainly in the water phase.	Biocide Assessment Report, 2006[1]
BMF	1	Default value, TG n. 27 - CIS WFD[2]

4. Environmental exposure assessment

4.1 Predicted Environmental Concentration

	Description	Source
Tonnes/year	10000 (year 1997)	From previous prioritization exercise
Uses	Wood preservative (Biocide)	

Spatial usage (by MS):	Not known	
Banned uses	Fungicide- PPP	(Commission Regulation (EC) No 2076/2002)[3]
ERC code	ERC8b	
Fraction of tonnage to region	0.1	
PEC_{fw} (mg/L)	0.0053	ECETOC
PEC_{sed} (mg/kg dw)	0.732	ECETOC
PEC_{biota} (mg/kg)	0.38	Calculation based on Equation L (Section 3.4.3)

4.1.1 ECETOC simulation with lower tonnages

Authorisations for plant protection products containing the active substance dichlofluanid were withdrawn by 25 July 2003[3]. However, the available tonnage of 10000 relates to the year 1997, which is prior to the banning of the substance as PPP.

At the WG Chem meeting 16-17/10/2014 it was suggested to perform a simulation on the PEC calculated with ECETOC using reduced tonnage values of dichlofluanid that could be closer to the actual tonnage after the banning, i.e. related to the use as biocide only. Since no tonnage value specific for this particular use was available, it was decided to perform the simulation considering a 20%, and 30% or 50% decrease in tonnage values. The results of the simulations are compared with the pre-banning tonnage scenario in the following Table.

Tonnes/year	10000	8000	7000	5000
Decrease respective to pre-banning tonnage	-	20%	30%	50%
PEC_{sed} (mg/kg dw)	0.732	0.586	0.513	0.366
RQ_{sed}	40.17	32.14	28.14	20.07
Position in the ranking (higher RQ)	16 (RQ_{sed})	16 (RQ_{sed})	17 (RQ_{sed})	19 (RQ_{sed})

4.2 Measured Environmental Concentration

n. of MS	Source of monitoring data	MEC values	RBSP
3 (FR, FI, IT)	NORMAN DB, 2014[4]	MEC_{site}: 0.03 µg/L MEC_{sed}: < LOD	-
	WATERBASE, 2014[5]	Values below LOQ	
	Italian Monitoring Programme[6]	Values below LOQ	

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

Following repeated oral administration of dichlofluanid, the most prominent finding was fluorosis caused by the release of fluoride from the dichlofluanid molecule during its metabolism[1]. This resulted in skeletal osteosclerosis, observed in lifetime dietary studies in both rats and mice[1]. Chronic nephropathy was also observed following repeated oral administration, but in dogs only[1]. The mode of action for the nephropathy is uncertain and possible explanations include direct nephrotoxicity of the active substance or a secondary consequence of elevated systemic fluoride levels[1]. Dichlofluanid is not genotoxic in vivo[1]. In terms of carcinogenicity, dichlofluanid induced thyroid tumours in rats at high doses, but by a mechanism not considered to be relevant for human health[1]. No increase in tumour incidence was observed in mice. Overall, dichlofluanid does not show any carcinogenic potential of relevance to human health[1]. In experimental animal studies dichlofluanid did not affect fertility and did not cause developmental toxicity[1]. The evidence suggests that this substance does not possess significant potential with respect to toxicity for reproduction[1].

The substance is not readily biodegradable (P). It has a low BCF of 72 L/kg (not B) [1].

6. Hazard assessment

6.1 Ecotoxicology data

Trophic level	Endpoint	Value	Reference
Fish	*Salmo gairdneri*, 96 h, LC_{50}	0.01 mg/L	Biocide Assessment Report, 2006[1]
Fish	*Salmo gairdneri*, 21 d, NOEC	0.00455 mg/L	Biocide Assessment Report, 2006[1]
Fish	*Pimephales promelas*, 33 d, body length and weight, NOEC	0.00407 mg/L	Biocide Assessment Report, 2006[1]
Aquatic invertebrates	*Daphnia magna*, 48 h, EC_{50}	0.42 mg/L	Biocide Assessment Report, 2006[1]
Aquatic invertebrates	***Daphnia magna*, 21 d, NOEC**	**0.00265 mg/L**	Biocide Assessment Report, 2006[1]
Algae	*Scenedesmus subspicatus*, 96 h, growth rate, a)NOEC, b)72 h EC_{50}	a)1 mg/L b)15 mg/L	Biocide Assessment Report, 2006[1]

6.2 Mammalian toxicology data

Type of test	Endpoint	Value	Reference
Acute oral toxicity	Rat, LD_{50}	>5000 mg/kg	Biocide Assessment Report, 2006[1]
Repeated dose toxicity	Dog, 90 d NOAEL, subchronic	20 mg/kg/day	Biocide Assessment Report, 2006[1]

Repeated dose toxicity	**Dog, 365 d, NOAEL, chronic. Value used for DNEL calculation**	**2.5 mg/kg/day**	Biocide Assessment Report, 2006[1]
Reproductive toxicity	Rat, NOAEL	16 mg/kg/day	Biocide Assessment Report, 2006[1]
Developmental toxicity	Rat, NOAEL	30 mg/kg/day	Biocide Assessment Report, 2006[1]

6.3 PNEC derivation

PNEC	Endpoint	Endpoint value	AF	PNEC value
PNEC$_{fw}$	*Daphnia magna*, 21 d, reproduction, NOEC	0.00265 mg/L	10[a]	2.65E-04 mg/L
PNEC$_{sed}$	-	-	-	0.018 mg/kg dw[b]
PNEC$_{biota,sec\,pois}$	Dog, repeated dose toxicity, 365 d, oral, conversion factor 40, NOAEL	2.5 mg/kg bw/day	30[c]	3.3 mg/kg food[d]
PNEC$_{biota,\,hh}$	ADI	0.35mg/kg bw/day	-	21.304 mg/kg food[e]
PNEC$_{dw,\,hh}$	ADI	0.35mg/kg bw/day	-	1.225 mg/L[f]

[a]Three long term values available from the three main trophic levels.

[b]Equilibrium partitioning method used for PNEC$_{sed}$ calculation, with the following values: $K_{sed\text{-}water}$= 34.4 m^{3}m^{-3} (calculated with eq. D of section 3.3.2), RHO_{sed}= 1300 kg m^{-3} (default value), $Fsolid_{sed}$= 0.2 (default value), RHO_{solid}= 2500 kg m^{-3} (default value), Kp_{sed}= 67.2 L/kg (calculated, K$_{oc}$ x Foc$_{sed}$), K_{oc}= 1344 L/kg[4], Foc_{sed}= 0.05 kg kg^{-1} (default value). Conversion from wet weight to dry weight was done with eq. B of section 3.3.2.

[c]The AF of 30 was selected according to the duration of the test (365 days). See TG n. 27- CIS WFD[2]

[d] The following steps were followed for PNEC$_{biota,sec\,pois}$ calculation: a) conversion of the NOAEL (2.5 mg/kg bw/day) value retrieved from the Biocide Assessment Report (2006)[1], into NOEC (100 mg/kg) by using the conversion factor of 40 (taken from TG n. 27- CIS WFD, and it depends both on species tested and age/study); b) Application of appropriate AF$_{oral}$ (30) to the NOEC value.

[e] ADI value retrieved from Biocide Assessment Report (2006) [1], used for PNEC calculation according to Equation E (see section 3.3.4)

[f] ADI value used in equation F as TL$_{hh}$. See section 3.3.5 for calculation.

7. Risk Quotient (PEC/PNEC)

RQ	Value
RQ$_{fw}$	20.04
RQ$_{sed}$	**40.17**
RQ$_{biota,sec\,pois}$	0.11
RQ$_{biota,\,hh}$	0.02
RQ$_{dw,\,hh}$	0.004

8. References

[1] Directive 98/8/EC concerning the placing of biocidal products on the market - Inclusion of active substances in Annex I to Directive 98/8/EC. Assessment Report, DICHLOFLUANID PT8 (2006). Available at http://dissemination.echa.europa.eu/Biocides/factsheet?id=0025-08

[2] Technical Guidance for Deriving Environmental Quality Standards – Guidance Document No. 27 (2011) Common Implementation Strategy of the Water Framework Directive (2000/60/EC). Available at http://ec.europa.eu/environment/water/water-dangersub/lib_pri_substances.htm

[3] COMMISSION REGULATION (EC) No 2076/2002 of 20 November 2002 extending the time period referred to in Article 8(2) of Council Directive 91/414/EEC and concerning the non-inclusion of certain active substances in Annex I to that Directive and the withdrawal of authorisations for plant protection products containing these substances. Available at http://ec.europa.eu/sanco_pesticides/public/?event=activesubstance.detail
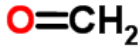
[4] NORMAN database at http://www.norman-network.net/?q=node/24

[5] WATERBASE Database http://www.eea.europa.eu/data-and-maps/data/waterbase-rivers-6

[6] Italian Monitoring Programme (data provided directly to the JRC)

Formaldehyde (CAS N. 50-00-0)

1. Substance identity

EC name	Formaldehyde
EC number	200-001-8
CAS number	50-00-0
Molecular formula	CH2O
Molecular weight	30.03
Structure	O=CH$_2$
SMILES	C=O

2. Physico-chemical Properties

Endpoint	Value	Source
Vapour Pressure (Pa)	131.87 Pa	ECHA, 2014[1]
Water solubility (mg/L)	550000	ECHA, 2014[1]
logK$_{ow}$	0.35	ECHA, 2014[1]

3. Environmental fate

Endpoint	Value	Source
Sorption potential (K$_{oc}$)	15.9	ECHA, 2014[1]
Biodegradability	RB	ECHA, 2014[1]
Bioaccumulation (BCF)	<1	ECHA, 2014[1]

4. Environmental exposure assessment

4.1   Predicted Environmental Concentration

	Description	Source
Tonnes/year	A confidential tonnage value was used for calculation	IUCLID, 2014[2]
Uses	Manufacture of substances, formulation in preparations and in materials, such as wood-based materials, paper, impregnated paper, bonded fibers or fiber mats, bonded	ECHA, 2014[1]

	particulates, rubber, leather foam, firelighters, fertilized granules, cleaning agents (ECHA, 2014)[1].	
Spatial usage (by MS)	Not known	
Banned uses	As biocide (PT1 Human hygiene, PT4 Food and feed area, PT5 Disinfection of Drinking water, PT6 Preservatives for products during storage, PT9 Fibre, leather, rubber and polymerised materials preservatives, PT11 Preservatives for liquid-cooling and processing systems, PT12 Slimicides, PT13 Working or cutting fluid preservatives, PT18 Insecticides, acaricides and products to control other arthropods, PT21 Antifouling products, PT23 Control of other vertebrates)	Consolidated list of non-inclusion decisions, 2013[3]
ERC code	ERC8d	
Fraction of tonnage to region	0.1	
PEC$_{fw}$ (mg/L)	13.53	ECETOC
PEC$_{sed}$ (mg/kg dw)	70.2 (N.R.)	ECETOC
PEC$_{biota}$ (mg/kg)	13.53 (N.R.)	Calculation based on Equation L (Section 3.4.3)

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

4.2 Measured Environmental Concentration

n. of MS	Source of monitoring data	MEC values	RBSP
3 (FR, UK, SK)	NORMAN DB, 2014[4]	MEC$_{95, whole}$: 7.165 µg/L	3 MS[7] EQS set (WRc, 2012)[8]
	WATERBASE, 2014[5]	MEC$_{95, whole}$: 22.75 µg/L	
	IPCheM[6]	MEC$_{95}$: 119.75 µg/L	

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

In the ECHA dissemination website, formaldehyde is classified as: Carc. 2 H351: Suspected of causing cancer <state route of exposure if it is conclusively proven that no other routs of exposure cause the hazard> Route of exposure: inhalation (ECHA, 2014[1]).

Potential mechanisms underlying formaldehyde-induced reproductive and developmental toxicities, including chromosome and DNA damage (genotoxicity), oxidative stress, altered level and/or function of

enzymes, hormones and proteins, apoptosis, toxicogenomic and epigenomic effects (such as DNA methylation), were identified (Duong A. et al.[9]).

Formaldehyde is not persistent, and not bioaccumulative (BCF < 1) (ECHA, 2014[1]).

6. Hazard assessment

6.1 Ecotoxicology data

Trophic level	Endpoint	Value	Reference
Fish	*Morone saxatilis*, 96 h, LC_{50}	6.7 mg/L	ECHA, 2014[1]
Fish	*Rasbora heteromorpha*, LC_{50}, 48 h	50 mg/L	ECHA, 2014[1]
Fish	*Ictalurus punctatus*, LC_{50}, 96 h	25.5 mg/L	ECHA, 2014[1]
Fish	*Ictalurus melas*, LC_{50}, 96 h	25 mg/L	ECHA, 2014[1]
Fish	*Leuciscus idus melanotus*, LC_{50}, 48h	15 mg/L	ECHA, 2014[1]
Fish	*Pimephales promelas*, LC_{50}, 96 h	24.1 mg/L	ECHA, 2014[1]
Fish	*Danio rerio*, LC_{50}, 96 h	41 mg/L	ECHA, 2014[1]
Fish	*Oryzias latipes*, NOEC, 28 d, mortality, target organ pathologies	≥48 mg/L	ECHA, 2014[1]
Fish	*Danio rerio*, 144 h, LC_{50}, Mortality of embryos/larvae	6.9 mg/L	ECHA, 2014[1]
Aquatic invertebrates	*Daphnia pulex*, 48 h, mobility, a) EC_{10} b) EC_{50}	a)1.9 mg/L b)5.8 mg/L	ECHA, 2014[1]
Aquatic invertebrates	*Pinctada fucata martensii* 96 h, LC_{50}	5.3 mg/L	ECHA, 2014[1]
Aquatic invertebrates	*Ceriodaphnia cf. dubia*, 48 h, mobility, EC_{50}	12.98 mg/L	ECHA, 2014[1]
Aquatic invertebrates	*Daphnia magna*, 24 h, LC_{50}	52 mg/L	ECHA, 2014[1]
Aquatic invertebrates	*Streptocephalus seali*, EC_{10}	25 mg/L	ECHA, 2014[1]
Aquatic invertebrates	*Daphnia magna*,48 h, EC_{50}	29 mg/L	ECHA, 2014[1]
Aquatic invertebrates	*Daphnia magna*, 24h, EC_{50}	14.7 mg/L	ECHA, 2014[1]
Algae	*Scenedesmus subspicatus*, 72 h, a) EC_{50} biomass, b) EC_{50} growth rate	a)3.48 mg/L b)4.89 mg/L	ECHA, 2014[1]
Algae	*Pseudokirchnerella subcapitata*, 48 h, a) EC_{50} growth rate, b) EC_{50} dissolved oxygen production	a)2.49 mg/L b)2.627 mg/L	ECHA, 2014[1]

Studies assigned as not reliable, or not assignable in the ECHA, 2013[1] were not reported.

6.2 Mammalian toxicology data

Type of test	Endpoint	Value	Reference
Acute oral toxicity (weight of evidence)	Rat, LD_{50}	460 mg/kg bw	ECHA, 2014[1]
Acute oral toxicity (weight of evidence)	Rat, LD_{50}	800 mg/kg bw	ECHA, 2014[1]
Repeated oral toxicity	Rat, oral drinking water, 105 weeks, NOAEL	15 mg/kg bw/day	ECHA, 2014[1]
Carcinogenicity	Rat, oral, 13 weeks, 1) LOAEC toxicity, 2)LOAEC carcinogenicity	a)17 ppm b)20ppm	ECHA, 2014[1]

Carcinogenicity	Rat, inhalation, 13 weeks, 1)NOAEC toxicity, 2)LOAEC toxicity, 2)LOAEC carcinogenicity	a)1 ppm b)10ppm c)10ppm	ECHA, 2014[1]
Carcinogenicity	Rat, oral drinking water, 32 weeks non-effective dose level for promoting activity	5000 mg/L drinking water	ECHA, 2014[1]
Reproductive toxicity	Mouse, oral, a) NOAEL, b) LOAEL maternal toxicity	a)185 mg/kg bw/day b)74 mg/kg bw/day	ECHA, 2014[1]

6.3 PNEC derivation

PNEC	Endpoint	Endpoint value	AF	PNEC value
$PNEC_{fw}$	-	-	10[a]	0.47mg/L[b]
$PNEC_{sed}$	-	-	-	2.440 mg/kg dw[c] (N.R.)
$PNEC_{biota,sec pois}$	-	-	-	N.R.
$PNEC_{biota, hh}$	-	-	-	N.R.
$PNEC_{dw, hh}$	TDI	0.15 mg/kg bw	-	0.525 mg/L[d]

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

[a] The AF was reported in the ECHA dossier, 2014[1]

[b] In the ECHA report, the PNEC value was estimated with a probabilistic approach. No new calculations were performed.

[c] No new calculations were done, because value was retrieved from ECHA, 2014[1]. The equilibrium partitioning method was used in the dossier.

[d] TDI value, retrieved from EFSA opinion, 2006[11], was used in equation F as TL_{hh}. See section 3.3.5 for calculation.

7. Risk Quotient (PEC/PNEC)

RQ	Value
RQ_{fw}	**28.79**
RQ_{sed}	N.R.
$RQ_{biota,sec pois}$	N.R.
$RQ_{biota, hh}$	N.R.
$RQ_{dw, hh}$	25.77

8. References

[1] ECHA dissemination website: http://apps.echa.europa.eu/registered/data/dossiers/DISS-9daa7594-c409-0ed0-e044-00144f67d249/DISS-9daa7594-c409-0ed0-e044-00144f67d249_DISS-9daa7594-c409-0ed0-e044-00144f67d249.html

[2] Complete IUCLID dossier of formaldehyde.

[3] Existing active substances for which a decision of non-inclusion into Annex I or Ia of Directive 98/8/EC has been adopted - In accordance with Article 4(2) of Regulation (EC) No 2032/2003, biocidal products containing active substances for which a non-inclusion decision was taken shall be removed from the market within 12 months of the entering into force of such decision; unless otherwise stipulated in that non-inclusion decision-Dates by which

products containing these active substances shall no longer be placed on the market for the relevant product-types (February 2013). Available at: http://ec.europa.eu/environment/chemicals/biocides/pdf/list_dates_product_2.pdf

[4] NORMAN database at http://www.norman-network.net/?q=node/24

[5] WATERBASE Database http://www.eea.europa.eu/data-and-maps/data/waterbase-rivers-6

[6] IPCheM database at http://ipchem.jrc.ec.europa.eu/

[7] Irmer U, Rau F, Arle J, Claussen U, Mohaupt V. (2013) Ecological Environmental Quality Standards of "River Basin Specific Pollutants" in Surface Waters - Update and Development Analysis of a European Comparison between Member States. ECOSTAT- UBA report.

[8] 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
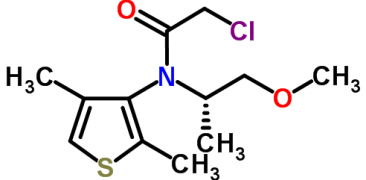
[9] Reproductive and Developmental Toxicity of Formaldehyde: A Systematic Review by Anh Duong, Craig Steinmaus, Cliona M. McHale, Charles P. Vaughan, and Luoping Zhanga. Available at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3203331/).

[10] Technical Guidance for Deriving Environmental Quality Standards – Guidance Document No. 27 (2011) Common Implementation Strategy of the Water Framework Directive (2000/60/EC). Available at http://ec.europa.eu/environment/water/water-dangersub/lib_pri_substances.htm

[11] EFSA Journal (2006) 415, 1-10. Opinion of the Scientific Panel on food additives, flavourings, processing aids and materials in contact with food (AFC) on a request from the Commission related to Use of formaldehyde as a preservative during the manufacture and preparation of food additives. Available at http://www.efsa.europa.eu/it/efsajournal/doc/415.pdf

Dimethenamid-P (CAS N. 163515-14-8)

1. Substance identity

Chemical name (IUPAC)	2-Chloro-N-(2,4-dimethyl-3-thienyl)-N-[(2S)-1-methoxy-2-propanyl]acetamide
EC number	
CAS number	163515-14-8
Molecular formula	C12H18ClNO2S
Molecular weight	275.798
Structure	
SMILES	Cc1csc(c1N([C@@H](C)COC)C(=O)CCl)C

2. Physico-chemical Properties

Endpoint	Value	Source
Vapour Pressure (Pa)	$2.5 \cdot 10^{-3}$	EC Review, 2001 [1]
Water solubility (mg/L)	1449	EC Review, 2001 [1]
logK$_{ow}$	1.89	EC Review, 2001 [1]

3. Environmental fate

Endpoint	Value	Source
Hydrolysis (DT50)	33.40 d	EC Review, 2001 [1]
Sorption potential (K$_{oc}$)	170.16	INERIS, 2011 [2]
Biodegradability	NRB	Consensus between EPISUITE (Biowin), ADMET Predictor v.7
Bioaccumulation (BCF)	58	CLP Report, 2013[3]

4. Environmental exposure assessment

	Description	Source
Tonnes/year	-	
Uses	Herbicide	
Spatial usage (by MS)	AT, BE, BG, CZ, DE, EL, ES, FR, HU, IE, IT, LU, NL, PL, PT, RO, SI, SK, UK	EU Pesticides DB [4]
Banned uses	Dimethenamid banned as Herbicide, PPP Replaced as herbicide by its active isomer,	Commission Decision (2006) [5]

	dimethenamid-P	
Crop	Maize	
Application rate (g/ha)	1×864 [a]	Stakeholder's comment (BASF)

[a] New maximum application rates have been reported by the stakeholder (up to 0.864 kg a.s./ha), based on recent authorization conditions for dimethenamid-P, which will decrease the PEC estimated using the FOCUS Step models based on the previous application rate of 1×1000 g/ha (EC Review, 2001) [1].

4.1 Predicted Environmental Concentration

PEC_{fw} **(mg/L)**	0.0657	FOCUS Step 2
PEC_{sed} **(mg/kg dw)**	0.109	FOCUS Step 2
PEC_{biota} **(mg/kg)**	3.81	Calculation based on Equation L (Section 3.4.3)

4.1.1 Comparison of FOCUS Pesticides models with ECETOC model

FOCUS Step 1

Crop [1]	Application Rate (g/ha)[1]	Water solubility (mg/L)[1]	K_{oc} (L/kg) [1]	DT_{50} whole system (d) [1]
Maize	1×864 g/ha	1449	170.16	33.16

FOCUS Step 2

Same parameters and conditions as above, in addition to DT_{50soil} 16.3 d [1], $DT_{50water}$: 28 d [1], $DT_{50sediment}$ 33 d [1], Minimal crop interception [1].

Results

Tier	PEC_{fw} (mg/L)	PEC_{sed} (mg/kg)
FOCUS Step 1	0.243	0.402
FOCUS Step 2	0.0656	0.109

4.2 Measured Environmental Concentration

n. of MS	Source of monitoring data	MEC values	RBSP
5 (IT, FR, DE, LU, NL)	IPCheM[6]	MEC_{95}: 0.072 µg/L (dimethenamid) MEC_{site}: 0.01 µg/L (dimethenamid-P)	-
	NORMAN DB[7]	MEC_{whole}: 0.2 µg/L (dimethenamid)	
	WATERBASE, 2014[8]	MEC_{site}: 0.012 µg/L (dimethenamid)	
	IT monitoring programme[9]	MEC_{95}: 0.524 µg/L (dimethenamid, IT) MEC_{95}: 0.1315 µg/L (dimethenamid-P, IT)	

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

Results from genotoxicity studies do not indicate that dimethenamid-P or racemic dimethenamid possess a genotoxic potential[3]. No evidence of a carcinogenic potential in rats and mice could be established[3]. Dimethenamid-P does not show any adverse effects on sexual function and fertility in adult males and females or developmental toxicity in the offspring. Dimethenamid-P has not to be classified as reproductive toxicant[3]. Dimethenamid-P is considered not readily/ rapidly biodegradable (a degradation > 70 % within 28 days) for purposes of classification and labelling. Dimethenamid-P has a log Kow of 1.89[3]. The experimentally derived steady state BCF value of 58 L/kg ww (without lipid normalization) is below the trigger of 100 (criterion for bioaccumulating potential conform Directive 67/548/EEC) and is also below the trigger of 500 criterion for bioaccumulating potential conform Regulation EC 1272/2008).[3]

6. Hazard assessment

6.1 Ecotoxicology data

Trophic level	Endpoint	Value	Reference
Fish	*Oncorhyncus mykiss*, 96 h, LC_{50}	6.3 mg/L	Data provided from Stakeholder's comment (BASF)*
Fish	*Lepomis macrochirus*, 96 h, LC_{50}	10.4 mg/L	Data provided from Stakeholder's comment (BASF)*
Fish	*Cyprinodon variegatus*, 96 h, LC_{50}	12 mg/L	Data provided from Stakeholder's comment (BASF)*
Fish	*Oncorhyncus mykiss,* 21 d, NOEC	0.630 mg/L	Data provided from Stakeholder's comment (BASF)*
Fish	*Oncorhyncus mykiss,* 90 d, NOEC (ELS)	0.120 mg/L	Data provided from Stakeholder's comment (BASF)*
Aquatic invertebrates	*Daphnia magna,* 48 h, EC_{50}	12 mg/L	Data provided from Stakeholder's comment (BASF)*
Aquatic invertebrates	*Americamysis bahia,* 48 h, LC_{50}	>9.2 mg/L	Data provided from Stakeholder's comment (BASF)*
Aquatic invertebrates	*Daphnia magna,* 21 d, NOEC	1.36 mg/L	Data provided from Stakeholder's comment (BASF)*
Aquatic invertebrates	*Daphnia magna,* 21 d, NOEC	0.680 mg/L	Data provided from Stakeholder's comment (BASF)*
Algae	*Pseudokirchneriella subcapitata,* 72 h, growth rate, arithmetic mean: a)EC_{50} b)EC_{10}	a)0.0588 mg/L b)0.0159 mg/L	Data provided from Stakeholder's comment (BASF)*
Algae	*Anabaena flos-aquae*, 72 h, growth rate, a)EC_{50} b)EC_{10}	a)1.340 mg/L b)0.073 mg/L	Data provided from Stakeholder's comment (BASF)*
Algae	*Ankistrodesmus bibraianus*, 72 h, growth rate, a)EC_{50} b)EC_{10}	a)0.0370 mg/L b)0.00367 mg/L	Data provided from Stakeholder's comment (BASF)*
Algae	*Chlamydomonas reinhardtii*, 72 h, growth rate, a)EC_{50} b)EC_{10}	a)0.2245 mg/L b)0.0620 mg/L	Data provided from Stakeholder's comment (BASF)*
Algae	*Desmodesmus subspicatus*, 72 h, growth rate, a)EC_{50} b)EC_{10}	a)0.0857 mg/L b)0.00927 mg/L	Data provided from Stakeholder's comment (BASF)*
Algae	*Dictyococcus varians*, 72 h, growth rate, a)EC_{50} b)EC_{10}	a)0.1498 mg/L b)0.0049 mg/L	Data provided from Stakeholder's comment (BASF)*

Algae	*Monoraphidium griffithii*, 72 h, growth rate, a)EC_{50} b)EC_{10}	a)0.0250 mg/L b)0.0026 mg/L	Data provided from Stakeholder's comment (BASF)*
Algae	*Navicula pelliculosa*, 72 h, growth rate, a)EC_{50} b)EC_{10}	a)0.287 mg/L b)0.082 mg/L	Data provided from Stakeholder's comment (BASF)*
Algae	*Neochloris aquatica*, 72 h, growth rate, a)EC_{50} b)EC_{10}	a)>1000 mg/L b)0.0871 mg/L	Data provided from Stakeholder's comment (BASF)*
Algae	*Pandorina morum*, 72 h, growth rate, a)EC_{50} b)EC_{10}	a)0.9238 mg/L b)0.0329 mg/L	Data provided from Stakeholder's comment (BASF)*
Algae	*Planktosphaeria botryoides*, 72 h, growth rate, a)EC_{50} b)EC_{10}	a)0.9120 mg/L b)0.0517 mg/L	Data provided from Stakeholder's comment (BASF)*
Algae	*Schroederia setigera*, 72 h, growth rate, a)EC_{50} b)EC_{10}	a)>0.4055 mg/L b)0.0287 mg/L	Data provided from Stakeholder's comment (BASF)*
Algae	*Skeletonema costatum*, 72 h, growth rate, a)EC_{50} b)EC_{10}	a)0.309 mg/L b)0.060 mg/L	Data provided from Stakeholder's comment (BASF)*
Algae	*Staurastrum punctulatum,* 72 h, growth rate, a)EC_{50} b)EC_{10}	a)>1000 mg/L b)0.0227 mg/L	Data provided from Stakeholder's comment (BASF)*
Aquatic plants	*Lemna gibba,* 7 d, growth rate, arithmetic mean: a)EC_{50} b)EC_{10}	a)0.0543 mg/L b)0.0089 mg/L	Data provided from Stakeholder's comment (BASF)*
Aquatic plants	*Glyceria maxima,* 14 d, growth rate, a)EC_{50} b)EC_{10}	a)0.184 mg/L b)0.027 mg/L	Data provided from Stakeholder's comment (BASF)*
Aquatic plants	*Lemna gibba* (with sediment), 7 d, growth rate, a)EC_{50} b)EC_{10}	a)0.0990 mg/L b)0.0152 mg/L	Data provided from Stakeholder's comment (BASF)*
Aquatic plants	*Acorus calamus,* 13 d, growth rate, a)EC_{50} b)NOEC	a)>1.324 mg/L b)≥1.324 mg/L	Data provided from Stakeholder's comment (BASF)*
Aquatic plants	*Iris pseudacorus,* 13 d, growth rate, a)EC_{50} b)NOEC	a)0.229 mg/L b)0.022 mg/L	Data provided from Stakeholder's comment (BASF)*
Aquatic plants	*Ludwigia palustris,* 13 d, growth rate, a)EC_{50} b)NOEC	a)0.047 mg/L b)0.011 mg/L	Data provided from Stakeholder's comment (BASF)*
Aquatic plants	*Mentha aquatica,* 13 d, growth rate, a)EC_{50} b)NOEC	a)0.278 mg/L b)0.124 mg/L	Data provided from Stakeholder's comment (BASF)*
Aquatic plants	*Sparganium erectum,* 13 d, growth rate, a)EC_{50} b)NOEC	a)0.278 mg/L b)0.124 mg/L	Data provided from Stakeholder's comment (BASF)*
Aquatic plants	*Veronica beccalunga,* 13 d, growth rate, a)EC_{50} b)NOEC	a)0.129 mg/L b)0.011 mg/L	Data provided from Stakeholder's comment (BASF)*
Aquatic plants	*Ceratophyllum demersum,* 9 d, growth rate, a)EC_{50} b)NOEC	a)0.0157 mg/L b)0.0019 mg/L	Data provided from Stakeholder's comment (BASF)*
Aquatic plants	*Crassula recurva,* 12 d, growth rate, a)EC_{50} b)NOEC	a)0.0995 mg/L b)0.0400 mg/L	Data provided from Stakeholder's comment (BASF)*
Aquatic plants	*Elodea densa,* 12 d, growth rate, a)EC_{50} b)NOEC	a)0.2044 mg/L b)0.0400 mg/L	Data provided from Stakeholder's comment (BASF)*
Aquatic plants	*Myriophyllum spicatum,* 9 d, growth rate, a)EC_{50} b)NOEC	a)0.0972 mg/L b)0.0092 mg/L	Data provided from Stakeholder's comment (BASF)*
Aquatic plants	*Potamogeton crispus,* 9 d, growth rate, a)EC_{50} b)NOEC	a)0.2839 mg/L b)0.0400 mg/L	Data provided from Stakeholder's comment (BASF)*
Aquatic plants	*Vallisneria spiralis,* 12 d, growth rate, a)EC_{50} b)NOEC	a)>0.3360 mg/L b)≥0.3360 mg/L	Data provided from Stakeholder's comment (BASF)*

* and submitted during Annex I inclusion and Recent Renewal Process (2014)

6.2 Mammalian toxicology data

Type of test	Endpoint	Value	Reference
Acute oral toxicity	Rat, LD_{50}	429 mg/kg bw	EC Review, 2001 [1]
Short-term oral toxicity	Rat, 90 d, NOAEL	10 mg/kg bw/day	EC Review, 2001 [1]
Short-term oral toxicity	Dog, 90 d, NOAEL	4.3 mg/kg bw/day	EC Review, 2001 [1]
Short-term oral toxicity	**Dog, 1 year, NOAEL. Value used for ADI calculation in the EC Review, 2001[1]**	**2 mg/kg bw/day**	**EC Review, 2001 [1]**
Long-term toxicity	Rat, 105 weeks, NOAEL	<5 mg/kg bw/day	EC Review, 2001 [1]
Long-term toxicity	Mouse, 94 weeks, NOAEL	3.8 mg/kg bw/day	EC Review, 2001 [1]
Reproductive toxicity	NOAEL	36 mg/kg bw/day	EC Review, 2001 [1]
Developmental toxicity	Rat, NOAEL	50 mg/kg bw/day	EC Review, 2001 [1]

6.3 PNEC derivation

PNEC	Endpoint	Endpoint value	AF	PNEC value	Reference
$PNEC_{fw}$	HC_5	0.0027 mg/L	[1]	0.0027 mg/L[a]	
$PNEC_{sed}$	-	-	-	0.005 mg/kg dw[b]	
$PNEC_{biota,sec pois}$	-	-	-	N.R.	-
$PNEC_{biota, hh}$	-	-	-	N.R.	-
$PNEC_{dw, hh}$	ADI [c]	0.02 mg/L	-	0.070 mg/L	INERIS, 2011[2]

[a] Probabilistic approach used. Stakeholder's comment.

[b] Value provided from Stakeholder's comment.

[c] Same ADI for dimethenamid and dimethenamid-P. No new calculations were performed.

To be noted that a further $PNEC_{fw}$ value of 0.2 μg/L (AF 10) was derived by UBA (DE), which was also suggested by NORMAN. All the available ecotoxicity data related to dimethenamid-P will be further assessed in the current monitoring-based prioritisation exercise.

7. Risk Quotient (PEC/PNEC)

RQ	Value
RQ_{fw}	**24.33**
RQ_{sed}	21.8
$RQ_{biota,sec pois}$	N.R.
$RQ_{biota, hh}$	N.R.
$RQ_{dw, hh}$	0.94

8. References

[1] EUROPEAN COMMISSION Review Report for the active substance dimethenamid-p, SANCO/1402/2001-Final. Available at http://ec.europa.eu/sanco_pesticides/public/?event=activesubstance.detail

[2] INERIS, DIMETHENAMIDE – N° CAS : 87674-68-8 & DIMETHENAMID-P – N° CAS : 163515-14-8 (October 2011). Available at http://www.ineris.fr/substances/fr/substance/getDocument/3077

[3] CLH Report (2012) Proposal for Harmonised Classification and Labelling Based on Regulation (EC) No 1272/2008 (CLP Regulation), Annex VI, Part 2 Substance Name: Dimethenamid-P. Available at: http://echa.europa.eu/documents/10162/7307455a-5bcf-4e09-aea3-755346b9769a

[4] European Pesticides Database: http://ec.europa.eu/sanco_pesticides/public/?event=homepage

[5] COMMISSION DECISION of 22 December 2006 concerning the non-inclusion of dimethenamid in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance (notified under document number C(2006) 6895). Available at http://eur-lex.europa.eu/legal-content/EN/ALL/?uri=CELEX:32006D1009

[6] IPCheM database at http://ipchem.jrc.ec.europa.eu/

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

[8] WATERBASE Database http://www.eea.europa.eu/data-and-maps/data/waterbase-rivers-6

[9] Italian Monitoring Programme (data provided directly to the JRC)

Triphenyl phosphate (CAS N. 115-86-6)

1. Substance identity

CAS number	115-86-6
Molecular formula	C18-H15-O4-P
Molecular weight	326.29
Structure	
SMILES	P(Oc1ccccc1)(Oc1ccccc1)(Oc1ccccc1)=O

2. Physico-chemical Properties

Endpoint	Value	Source
Vapour Pressure (Pa)	0.000835	ECHA, 2013[1]
Water solubility (mg/L)	1.9	ECHA, 2013[1]
$logK_{ow}$	4.63	ECHA, 2013[1]

3. Environmental fate

Endpoint	Value	Source
Sorption potential K_{oc}	3561	ECHA, 2013[1]
Biodegradability	RB	ECHA, 2013[1], EPA Report[2]
Bioaccumulation (BCF)	144	ECHA, 2013[1]
BMF	1	Default value, TG n. 27 - CIS WFD[3]

4. Environmental exposure assessment

4.1 Predicted Environmental Concentration

	Description	Source
Tonnes/year	A confidential and recent tonnage value was used for calculation	IUCLID, 2014[4]
Uses	Manufacture of substances,	ECHA, 2013[1]

	formulation in materials (plastics and rubber), formulation of flame retardant/plasticizer in preparations and cosmetics	
Spatial usage (by MS)	Not known	
Banned uses	-	
ERC code	ERC8a	
Fraction of tonnage to region	0.1	
PEC$_{fw}$ (mg/L)	0.015	ECETOC
PEC$_{sed}$ (mg/kg dw)	5.49	ECETOC
PEC$_{biota}$ (mg/kg)	2.169 (N.R.)	Calculation based on Equation L (Section 3.4.3)

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

4.2 Measured Environmental Concentration

n. of MS	Source of monitoring data	MEC values	RBSP
2 (DE, NL)	NORMAN DB, 2014[5]	MEC$_{95, whole}$: 0.07 µg/L	1 MS (RBSP EQS ECOSTAT – UBA report)[6]

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

Triphenyl-phosphate is neither carcinogenic nor toxic to reproduction[2]. In the ECHA report, it is not classified as carcinogenic (category 1 or 2), mutagenic (category 1 or 2), or toxic for reproduction (category 1, 2 or 3) according to Directive 67/548/EEC, or carcinogenic (category 1A or 1B), germ cell mutagenic (category 1A or 1B), or toxic for reproduction (category 1A, 1B or 2) according to Regulation EC No 1272/2008. The substance is not classified as CMR[1]. No other evidence of chronic toxicity, as identified by the classifications T, R48 or Xn, R48 according to Directive 67/548/EEC or specific target organ toxicity after repeated exposure (STOT RE category 1 or 2) according to Regulation EC No 1272/2008 was reported[1].

Triphenyl phosphate is readily biodegradable (not P). It has a BCF value of 144 L/kg (not B) (EPA report[2], and ECHA, 2013[1]).

6. Hazard assessment

6.1 Ecotoxicology data

Trophic level	Endpoint	Value	Reference
Fish	*Oncorhynchus mykiss*, 96 h, EC_{50}	0.310 mg/L	NORMAN, 2014[7]
Fish	***Oncorhynchus mykiss*, 30 d, EC_{10}**	**0.037mg/L**	**NORMAN, 2014[7]**
Aquatic invertebrates	*Daphnia magna*, 48 h, EC_{50}	1 mg/L	NORMAN, 2014[7]
Aquatic invertebrates	*Daphnia magna*, 21 d, NOEC	0.052 mg/L	NORMAN, 2014[7]
Algae	*Desmodesmus subspicatus*, 72 h, EC_{50} growth rate	1.547 mg/L	NORMAN, 2014[7]
Algae	*Ankistrodesmus falcatus*, 72 h, NOEC	0.1 mg/L	NORMAN, 2014[7]

6.2 Mammalian toxicology data

Type of test	Endpoint	Value	Reference
Acute oral toxicity	Rat, feed, LD_{50}	>20000 mg/kg bw	ECHA, 2013[1]
Repeated dose toxicity	**Rat, feed, 4 weeks, NOAEL. Value used for DNEL calculation in the ECHA, 2013[1]**	**23.5 mg/kg bw/day**	**ECHA, 2013[1]**
Reproductive toxicity	Rat, feed, 3 months, NOEL	690 mg/kg bw/day	ECHA, 2013[1]
Developmental toxicity	Rat, feed, 91 d, NOAEL	≥690 mg/kg bw/day	ECHA, 2013[1]

6.3 PNEC derivation

PNEC	Endpoint	Endpoint value	AF	PNEC value
$PNEC_{fw}$	*Oncorhyncus mykiss*, 30 d, EC_{10}	0.037 mg/L	10[a]	3.70E-03 mg/L[b]
$PNEC_{sed}$	-	-	-	0.240 mg/kg dw[c]
$PNEC_{biota,sec\ pois}$	-	-	-	N.R.[d]
$PNEC_{biota,\ hh}$	-	-	-	N.R.[d]
$PNEC_{dw,\ hh}$	DNEL, oral, repeated dose toxicity	0.04 mg/kg bw/day	-	0.140 mg/L[e]

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

[a]AF of 10, because three long term values were available.

[b]No new calculations were made, since PNEC value was retrieved from ECHA, 2013[1] and NORMAN, 2014[1].

[c]No new calculations were made, since PNEC value was retrieved from ECHA, 2013[1]. Equilibrium partitioning method was used in the dossier.

[d]Not required because the substance is readily biodegradable.

[e]DNEL value, retrieved from ECHA, 2013[1], used in equation F as TL_{hh}. See section 3.3.5 for calculation.

7. Risk Quotient (PEC/PNEC)

RQ	Value
RQ_{fw}	4.05
RQ_{sed}	**22.90**
$RQ_{biota,sec\ pois}$	N.R.
$RQ_{biota,\ hh}$	N.R.
$RQ_{dw,\ hh}$	0.11

8. References

[1] ECHA dissemination website: http://apps.echa.europa.eu/registered/data/dossiers/DISS-9c823fa6-50fe-0b74-e044-00144f67d249/DISS-9c823fa6-50fe-0b74-e044-00144f67d249_DISS-9c823fa6-50fe-0b74-e044-00144f67d249.html

[2] EPA report, available at http://www.epa.gov/dfe/pubs/flameret/altrep-v2/altrept-v2-section1a.pdf

[3] Technical Guidance for Deriving Environmental Quality Standards – Guidance Document No. 27 (2011) Common Implementation Strategy of the Water Framework Directive (2000/60/EC). Available at http://ec.europa.eu/environment/water/water-dangersub/lib_pri_substances.htm
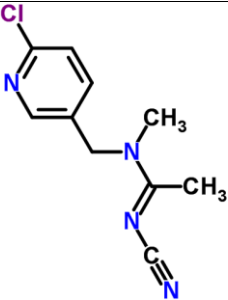
[4] Complete IUCLID dossier of triphenyl phosphate.

[5] NORMAN database at http://www.norman-network.net/?q=node/24

[6] Irmer U, Rau F, Arle J, Claussen U, Mohaupt V. (2013) Ecological Environmental Quality Standards of "River Basin Specific Pollutants" in Surface Waters - Update and Development Analysis of a European Comparison between Member States. ECOSTAT- UBA report.

[7] NORMAN factsheet on triphenyl phosphate, version of 31.08.2014 (available on CIRCA BC).

Acetamiprid (CAS N. 135410-20-7/160430-64-8)

1. Substance identity

EC name	
EC number	
CAS number	135410-20-7/160430-64-8
Molecular formula	C10-H11-Cl-N4
Molecular weight	222.6779
Structure	
SMILES	C/C(=N\C#N)/N(C)Cc1ccc(nc1)Cl

2. Physico-chemical Properties

Endpoint	Value	Source
Vapour Pressure (Pa)	1E-06Pa (25°C)	EU Review Report, 2004[1]
Water solubility (mg/L)	2950 (pH 7, 25°C)	EU Review Report, 2004[1]
logK$_{ow}$	0.8 (25°C)	EU Review Report, 2004[1]

3. Environmental fate

Endpoint	Value	Source
Sorption potential (K$_{oc}$)	106.5	EU Review Report, 2004[1]
Biodegradability	NRB	EU Review Report, 2004[1]
Bioaccumulation (BCF)	3.16 (estimated)	EPisuite, BCFBAF v3.01[2]

4. Environmental exposure assessment

4.1 Predicted Environmental Concentration

	Description	Source
Tonnes/year	-	
Uses	Insecticide (Plant Protection Product)	EU Pesticides DB[3]
Spatial usage (by MS)	AT, BE, BG, CY, CZ, DE, DK, EL, ES, FI, FR, HU, IE, IT, LT, LU, MT, NL, PL, PT, RO, SE, SI, SK, UK	EU Pesticides DB[3]

Banned uses	-	
ERC code	ERC8d (N.R.)	
PEC_{fw} (mg/L)	0.0050	FOCUS Step 2
PEC_{sed} (mg/kg dw)	0.0045 (N.R.)	FOCUS Step 2
PEC_{biota} (mg/kg)	0.016 (N.R.)	Calculation based on Equation L (Section 3.4.3)

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

4.1.1   FOCUS Pesticides models

FOCUS Step 1

Crop [3]	Application Rate (g/ha)[3]	Water solubility (mg/L)[3]	K_{oc} (L/kg) [3]	DT_{50} water (d) [3]
Citrus	2 x 100 (30 d interval of application)	2950	106.5	5.8

FOCUS Step 2

Same parameters and conditions as above, in addition to DT_{50soil} 2.6 d (mean) [3], $DT_{50water}$: 5.8 d[3], $DT_{50sediment}$ 1000 d (conservative value), minimal crop interception (application on young citrus)[3].

FOCUS Step 3 - SWASH package

Foliar interception and an application window of 60 days were considered. Thus, an application window from 15/01 to 16/03 was chosen for D3 and R4 crop-specific scenarios for the PAT calculator.

Results

Tier	PEC_{fw} (mg/L)	PEC_{sed} (mg/kg)
FOCUS Step 1	0.034	0.032
FOCUS Step 2	**0.005 (higher value with single appln)**	0.0045 (higher value with single appln)
FOCUS Step 3	0.0029 D6 ditch	0.0016 D6 ditch

4.2 Measured Environmental Concentration

n. of MS	Source of monitoring data	MEC values	RBSP
2 (SE, IT)	WATERBASE (2014)[4]	Values < LOD	-
	SE pesticide monitoring programme[5]	$MEC_{95,}$ SE: 0.0054 µg/L	
	IT monitoring programme[6]	$MEC_{95,}$ IT: 0.1745 µg/L	

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

Acetamiprid is not readily biodegradable (P)[1]. The potential for bioaccumulation is low, and has been estimated with EPISuite to be of 3.16 (not B). Also in the EU Review Report[1] the bioaccumulation potential was considered to be not relevant.

Evidence of clastogenic potential in vitro[1]. This event was found to be not relevant for the in vivo situation with a negative mouse micronucleus assay and metaphase analysis in rat bone marrow[1]. No carcinogenic potential, treatment related mammary glands hyperplasia was found at 1000 ppm[1]. No teratogenicity or fetotoxicity was observed at the tested doses, but in the reproductive toxicity study reduced postnatal survival and decreased pup weight was found at parental toxic doses (EU Review Report, 2004[1]).

6. Hazard assessment

6.1 Ecotoxicology data

Trophic level	Endpoint	Value	Reference
Fish	*Oncorhyncus mykiss*, 96 h , mortality, EC_{50}	>100 mg/L	EU Review Report, 2004[1]
Fish	*Pimephales promelas,* 35 d , growth, NOEC	19.2 mg/L	EU Review Report, 2004[1]
Aquatic invertebrates	*Daphnia magna,* 48 h , mortality, EC_{50}	49.8 mg/L	EU Review Report, 2004[1]
Aquatic invertebrates	*Daphnia magna,* 21 d , reproduction, NOEC	5 mg/L	EU Review Report, 2004[1]
Algae	*Scenedesmus subspicatus,* 72 h, biomass, EC_{50}	>98.3 mg/L	EU Review Report, 2004[1]
Sediment dwelling organisms	***Chironomus riparius*, 28 d, emergence and developmental rate, NOEC**	**0.005 mg/L**	EU Review Report, 2004[1]
Aquatic plants	*Lemna gibba*, 14 d, frond, EC_{50}	1 mg/L	EU Review Report, 2004[1]

6.2 Mammalian toxicology data

Type of test	Endpoint	Value	Reference
Acute oral toxicity	Rat, LD_{50}	417 mg/kg bw	EU Review Report, 2004[1]
Short term oral toxicity	Rat, 90 d, NOAEL	12.4 mg/kg bw/day	EU Review Report, 2004[1]
Long term toxicity	**Rat, 2 year, NOAEL.**	**7 mg/kg bw/day**	EU Review Report,

	Value used for ADI calculation in the EU Review Report[1], with the NOAEL from thereproductive study below.		2004[1]
Reproductive toxicity	**Rat, NOAEL**	**6.5 mg/kg bw/day**	EU Review Report, 2004[1]
Developmental toxicity	Rabbit, NOAEL	15 mg/kg bw/day	EU Review Report, 2004[1]

6.3 PNEC derivation

PNEC	Endpoint	Endpoint value	AF	PNEC value
PNEC$_{fw}$	*Chironomus riparius*, 28 d, emergence and developmental rate, NOEC[a]	0.005 mg/L[b]	10[c]	5.00E-04 mg/L
PNEC$_{sed}$	-	-	-	N.R.
PNEC$_{biota,sec\ pois}$	-	-	-	N.R.
PNEC$_{biota,\ hh}$	-	-	-	N.R.
PNEC$_{dw,\ hh}$	ADI	0.07mg/kg bw/day	-	0.245 mg/L[d]

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

[a] Due to the mode of action of neonicotinoids, the lowest endpoint from the aquatic species tested corresponds to the midge *Chironomus riparius*. Therefore, it was selected for PNEC$_{fw}$ calculation.

[b] Value retrieved from EU Review Report, 2004[1]

[c] Three long-term values were available.

[d] ADI value, retrieved from EU Review Report, 2004[1], used in equation F as TL$_{hh}$. See section 3.3.5 for calculation.

7. Risk Quotient (PEC/PNEC)

RQ	Value
RQ$_{fw}$	**10**
RQ$_{sed}$	N.R.
RQ$_{biota,sec\ pois}$	N.R.
RQ$_{biota,\ hh}$	N.R.
RQ$_{dw,\ hh}$	0.02

8. References

[1] EUROPEAN COMMISSION Review report for the active substance acetamiprid, SANCO/1392/2001– Final. Available at http://ec.europa.eu/food/plant/protection/evaluation/newactive/acetamiprid.pdf

[2] EPISuite BCFBAF v3.01 (2012)

[3] http://ec.europa.eu/sanco_pesticides/public/?event=homepage

[4] WATERBASE Database http://www.eea.europa.eu/data-and-maps/data/waterbase-rivers-6

[5] Swedish National Screening Programme Pesticides (data provided directly to the JRC)

[6] Italian Monitoring Programme (data provided directly to the JRC)

Erythromycin (CAS N. 114-07-8)

1.   Substance identity

EC name	Erythromycin
EC number	204-040-1
CAS number	114-07-8
Molecular formula	C37H67NO13
Molecular weight	733.94
Structure	
SMILES	CC[C@@H]1[C@@]([C@@H]([C@H](C(=O)[C@@H](C[C@@]([C@@H]([C@H]([C@@H]([C@H](C(=O)O1)C)O[C@H]2C[C@@]([C@H]([C@@H](O2)C)O)(C)OC)C)O[C@H]3[C@@H]([C@H](C[C@H](O3)C)N(C)C)O)(C)O)C)C)O)(C)O

2.   Reason for proposal as candidate for the Watch list and suspected environmental risk

Erythromycin is a macrolide antibiotic produced by Streptomyces erythreus. It inhibits bacterial protein synthesis by binding to bacterial 50S ribosomal subunits; binding inhibits peptidyl transferase activity and interferes with translocation of amino acids during translation and assembly of proteins. Erythromycin may be bacteriostatic or bactericidal depending on the organism and drug concentration.[1] Erythromycin has been classified as Category 2 according to the NORMAN Prioritisation Methodology[2]. In the NORMAN factsheet[3] it was reported a frequency of exceedance of 12% and an extent of exceedance of 3.74-fold of the lowest PNEC[3], considering monitoring data from 2002-2011 in the NORMAN database[4]. Besides the use as human and veterinary medicine, it is reported to have Industrial use resulting in manufacture of another substance (use of intermediates)[5].

3.   Physico-chemical Properties

Endpoint	Value	Source
Vapour Pressure (Pa)	3.04E-25	ChemIDPlus [6]
Water solubility (mg/L)	2000	Drugbank [1]
logK$_{ow}$	3.06	ChemIDPlus [6]

4. Environmental fate

Endpoint	Value	Source
Sorption potential (K_{oc})	570	PubChem [7]
Biodegradability	NRB	NORMAN, 2014 [3]
Bioaccumulation (BCF)	48.5	NORMAN, 2014 [3]
BMF	1	Default value, TG n. 27 - CIS WFD [8]

5. Environmental exposure assessment

	Description	Source
Tonnes/year	Confidential tonnage used for calculation	IUCLID, 2013 [9]
Uses	Industrial use resulting in manufacture of another substance (use of intermediates)	ECHA, 2014 [5]
	Pharmaceutical (human and veterinary medicine)	-
Spatial usage (by MS)	Widespread use	Drugs.com [10]
Banned uses	-	
ERC code	ERC6a *	ECHA, 2014 [5]
Fraction of tonnage to region	0.1	

* This substance is registered as having an environmental release category ERC6a. However, the PEC sediment calculated using this code with ECETOC seemed unrealistically high and it was decided to use instead ERC8a in this exercise, suitable for pharmaceuticals (see section 4.1.1 of this factsheet).

5.1 Predicted Environmental Concentration

	ECETOC[a]	Human consumption (Eq. G)[b]	MEC[c]
PEC_{fw} (mg/L)	**0.00526**	**0.0002**	**0.000613**
PEC_{sed} (mg/kg dw)	0.3185[d]	0.006[e]	0.0185[e]
PEC_{biota} (mg/kg)	0.255[f]	0.010[f]	0.030[f]

[a] Intermediate use

[b] Besse et al., 2008 11 (Equation G) for PEC equation, human consumption data from DK.

[c] MEC_{95} (SE)

[d] PEC_{sed} calculated from ECETOC

[e] PEC$_{sed}$ calculated with the Equilibrium Partitioning Method, where K$_{sed-water}$= 15.05 m^{3}m^{-3} (calculated with eq. K of section 3.4.2), RHO$_{sed}$= 1300 kg m^{-3} (default value), Fsolid$_{sed}$= 0.2 (default value), RHO$_{solid}$= 2500 kg m^{-3} (default value), Kp$_{sed}$= 28.5 L/kg (calculated, K$_{oc}$ x Foc$_{sed}$), K$_{oc}$= 570 L/kg (from PubChem[7]), Foc$_{sed}$= 0.05 kg kg^{-1} (default value). Conversion from wet weight to dry weight was done with eq. I (see section 3.4.2).

[f] Calculation with Equation L (Section 3.4.3)

5.1.1 PEC calculation considering different uses or sales data from MS

Uses	Calculation tool/ equation	Country	PEC$_{fw}$ (µg/L)
Intermediate use	ECETOC tool ERC8a was used, instead of ERC6a	Europe (use of tonnes registered in IUCLID)	5.26
Human use	PEC$_b$[a]	Portugal	0.150
Human use	PEC$_b$[a]	Latvia	0.073
Human use	PEC$_b$[a]	Greece	0.0614
Human use	PEC$_b$[a]	Germany	0.132
Human use	PEC$_b$[a]	Denmark	**0.2**
Veterinary use	No sales data	-	-

[a] PEC$_b$ equation was retrieved from Besse et al, 2008 [11]

PEC$_b$ equation: $\qquad PEC_{fw}= (consumption \times F_{excreta}) / (WWinhab \times hab \times dilution \times 365)$

where *WWinhab* is the volume of wastewater per person per day (default value of 200 [L/(hab*day)], *hab* are the number of inhabitants in the respective country (retrieved from PT[12], LV[13], EL[14], DE[15], and DK[16] official sources). *F$_{excreta}$* is the excretion factor of the active substance[11], *dilution* is the dilution factor (default value of 10), *consumption* is the quantity (mg/year) of active ingredient consumed by the population during 1 year. Consumption data were taken from Besse et al, 2008[11] for FR, from Iatrou et al, 2014[17] for EL, from UBA report[18] for DE, and directly provided to the JRC for PT, LV, and DK[19].

5.2 Measured Environmental Concentration

From an analysis of pharmaceutical datasets in river systems worldwide collected from the literature, Hughes et al. (2013)[20] report that erythromycin has a mean detection frequency worldwide of 55.5% (from all the records for that particular substance), and median and maximum concentration worldwide of 0.05 and 90 µg/L, respectively. The frequency of quantification of erythromycin in the NORMAN database is 15%[3]. However, considering just the monitoring data for the period 2006-2014, all values were < LOQ.

n. of MS	Source of monitoring data	MEC values	RBSP
3 (NL, CH, SE)	NORMAN DB, 2014 [4]	All values < LOQ (CH, NL)*	-
	SE Screening Programme Pharmaceuticals [21]	MEC$_{95}$: 0.613 µg/L (SE)	

* To be noted that these values correspond to the period 2006-2014, while higher MEC values were available if monitoring data since 2002 were considered.

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

Reported to be not carcinogenic and genotoxic, as erythromycin stearate form[22].

Utilizing the Closed Bottle Test, -3% of the theoretical BOD was reported in 4 weeks, indicating that biodegradation is not an important environmental fate process in water (P) (PubChem)[7]. A pKa of 8.9 indicates erythromycin will exist almost entirely in the cation form at pH values of 5 to 9 and therefore volatilization from water surfaces is not expected to be an important fate process. An estimated BCF of 49 suggests the potential for bioconcentration in aquatic organisms is moderate (Not B) (PubChem)[7].

7. Hazard assessment

7.1 Ecotoxicology data

Trophic level	Endpoint	Value	Reference [a]
Fish	*Morone saxatilis*, 96 h, LC_{50}	349 mg/L	Bills et al. 1993[23](NORMAN, 2014[3] and UBA, 2014[24])
Fish	*Danio rerio*, 96 h, mortality, LC_{50}	>1000 mg/L	Isidori et al. 2005[27] (UBA, 2014[24])
Fish	*Pimephales promelas*, 96 h, mortality, LC_{50}	61 mg/L	Sanderson et al. 2003[26] (UBA, 2014[24])
Fish	*Oryzias latipes*, 10 d, hatchability, time to hatch, NOEC	1000 mg/L	Ji et al. 2012[27] (UBA, 2014[24])
Fish	*Oryzias latipes*, 40 d, juvenile survival, NOEC	100 mg/L	Ji et al. 2012[27] (UBA, 2014[24])
Fish	*Oryzias latipes*, 40 d, juvenile growth, NOEC	1000 mg/L	Ji et al. 2012[27] (UBA, 2014[24])
Fish	*Oryzias latipes*, 100 d, adult survival growth, NOEC	10 mg/L	Ji et al. 2012[27] (UBA, 2014[24])
Aquatic invertebrates	*Ceriodaphnia dubia*, 48 h, EC_{50}	10.23 mg/L	Isidori et al. 2005[25] (NORMAN, 2014[3] and UBA, 2014[24])
Aquatic invertebrates	*Brachionus calyciflorus*, 24 h, mortality, LC_{50}	27.53 mg/L	Isidori et al. 2005[25] (UBA, 2014[24])
Aquatic invertebrates	*Brachionus calyciflorus*, 48 h, mortality, EC_{50}	0.940 mg/L	Isidori et al. 2005[25] (UBA, 2014[24])
Aquatic invertebrates	*Daphnia magna,* 24 h, mobility, EC_{50}	22.45 mg/L	Isidori et al. 2005[25] (UBA, 2014[24])
Aquatic invertebrates	*Thamnocephalus platyrus,* 24 h, mobility, EC_{50}	17.68 mg/L	Isidori et al. 2005[25] (UBA, 2014[24])

Aquatic invertebrates	*Daphnia magna,* 48 h, mobility, EC_{50}	207.8 mg/L	Ji et al. 2012[27] (UBA, 2014[24])
Aquatic invertebrates	*Moina macrocopa,* 48 h, mobility, EC_{50}	135.5 mg/L	Ji et al. 2012[27](UBA, 2014[24])
Aquatic invertebrates	*Penaeus vannamei,* 48 h, mobility, EC_{50}	0.0227 mg/L	Williams et al. 1992[28] (UBA, 2014[24])
Aquatic invertebrates	*Daphnia magna*, 21 d, reproduction, NOEC	0.248 mg/L	Meinertz et al. 2010[29] (NORMAN, 2014[3] and UBA, 2014[24])
Aquatic invertebrates	*Ceriodaphnia dubia*, 7 d, population growth, EC_{50}	0.220 mg/L	Isidori et al. 2005[25] (UBA, 2014[23])
Aquatic invertebrates	*Moina macrocopa*, 7 d, survival reproduction, NOEC	50 mg/L	Ji et al. 2012[27] (UBA, 2014[24])
Aquatic invertebrates	*Daphnia magna*, 21 d, survival, NOEC	33.3 mg/L	Ji et al. 2012[27] (UBA, 2014[24])
Aquatic invertebrates	*Daphnia magna*, 21 d, reproduction growth, NOEC	11.1 mg/L	Ji et al. 2012[27] (UBA, 2014[24])
Algae	*Pseudokirchneriella subcapitata*, 72 h, growth, EC_{50}	0.020 mg/L	Isidori et al. 2005[25] (NORMAN, 2014[3] and UBA, 2014[24])
Algae	*Pseudokirchneriella subcapitata*, 72 h, biomass, NOEC	0.0103 mg/L	Eguchi et al. 2004[30] (NORMAN, 2014[3] and UBA, 2014[24])
Algae	*Pseudokirchneriella subcapitata*, 72 h, biomass, EC_{50}	0.0366 mg/L	Eguchi et al. 2004[30] (NORMAN, 2014[3] and UBA, 2014[24])
Algae	*Pseudokirchneriella subcapitata*, 72 h, growth (chlorophyll fluorescence), EC_{50}	0.350 mg/L	Gonzaléz-Pleiter et al. 2013[31] (UBA, 2014[24])
Algae	*Chlorella vulgaris*, 72 h, biomass, EC_{50}	33.8 mg/L	Eguchi et al. 2004[30] (NORMAN, 2014[3] and UBA, 2014[24])
Algae	*Pseudokirchneriella subcapitata*, 72 h, growth (chlorophyll fluorescence), EC_{10}	0.036 mg/L	Gonzaléz-Pleiter et al. 2013[31] (UBA, 2014[24])
Algae	*Chlorella vulgaris,* 72 h, biomass, NOEC	12.5 mg/L	Eguchi et al. 2004[30] (UBA, 2014[24])
Cyanobacteria	*Microcystis wesenbergii*	0.023 mg/L	Ando et al. 2007[32]

	NIES-107, 144 h, EC$_{50}$		(NORMAN, 2014[3] and UBA, 2014[24])
Cyanobacteria	***Synechococcus leopoldensis IAM-M6, 144 h, biomass, NOEC***	**0.002 mg/L**	**Ando et al. 2007[32] (NORMAN, 2014[3] and UBA, 2014[24])**
Cyanobacteria	*Nostoc sp* PCC 7120, 144 h, biomass, EC$_{50}$	0.2 mg/L	Ando et al. 2007[32] (UBA, 2014[24])
Cyanobacteria	*Anabaena variabilis NIES-23,* 144 h, biomass, EC$_{50}$	0.430 mg/L	Ando et al. 2007[32] (UBA, 2014[24])
Cyanobacteria	*Microcystis wesenbergii NIES-107,* 144 h, biomass, NOEC	0.0047 mg/L	Ando et al. 2007[32] (UBA, 2014[24])
Cyanobacteria	*Synechococcus sp. PCC 7002,* 144 h, biomass, EC$_{50}$	0.230 mg/L	Ando et al. 2007[32] (UBA, 2014[24])
Cyanobacteria	*Synechococcus leopoldensis IAM-M6*, 144 h, EC$_{50}$	0.160 mg/L	Ando et al. 2007[32] (UBA, 2014[24])
Cyanobacteria	*Microcystis aeruginosa NIES-44,* 144 h, biomass, EC$_{50}$	0.023 mg/L	Ando et al. 2007[32] (UBA, 2014[24])
Cyanobacteria	*Anabaena flos-aquae ATCC 29413,* 144 h, biomass, EC$_{50}$	0.270 mg/L	Ando et al. 2007[32] (UBA, 2014[24])
Cyanobacteria	*Anabaena cylindrica NIES-19,* 144 h, biomass, EC$_{50}$	0.035 mg/L	Ando et al. 2007[32] (UBA, 2014[24])
Cyanobacteria	*Anabaena flos-aquae*, 72 h, yield, EC$_{50}$	0.140 mg/L	Förster et al. 2013[33] (UBA, 2014[24])
Cyanobacteria	*Anabaena flos-aquae*, 72 h, growth rate, EC$_{50}$	0.348 mg/L	Förster et al. 2013[33] (UBA, 2014[24])
Cyanobacteria	*Anabaena sp.*, 72 h, growth (inhibition of constitutive luminescence), EC$_{50}$	0.022 mg/L	Gonzaléz-Pleiter et al. 2013[31] (UBA, 2014[24])
Cyanobacteria	*Anabaena variabilis NIES-23,* 144 h, biomass, NOEC	0.047 mg/L	Ando et al. 2007[32] (UBA, 2014[24])
Cyanobacteria	*Nostoc sp* PCC 7120, 144 h, biomass, NOEC	0.1 mg/L	Ando et al. 2007[32] (UBA, 2014[24])
Cyanobacteria	*Synechococcus sp. PCC 7002,* 144 h, biomass, NOEC	0.0078 mg/L	Ando et al. 2007[32] (UBA, 2014[24])
Cyanobacteria	*Microcystis aeruginosa*	0.010 mg/L	Ando et al. 2007[32]

	NIES-44, 144 h, biomass, NOEC		(UBA, 2014[24])
Cyanobacteria	*Anabaena flos-aquae ATCC 29413,* 144 h, biomass, NOEC	0.047 mg/L	Ando et al. 2007[32] (UBA, 2014[24])
Cyanobacteria	*Anabaena cylindrica NIES-19,* 144 h, biomass, NOEC	0.0031 mg/L	Ando et al. 2007[32] (UBA, 2014[24])
Cyanobacteria	*Anabaena flos-aquae*, 72 h, yield, growth rate, NOEC	0.030 mg/L	Förster et al. 2013[33] (UBA, 2014[24])
Cyanobacteria	*Anabaena flos-aquae*, 72 h, yield. growth rate, LOEC	0.090 mg/L	Förster et al. 2013[33] (UBA, 2014[24])
Cyanobacteria	*Anabaena sp.,* 72 h, growth (inhibition of constitutive luminescence), EC_{10}	0.005 mg/L	Gonzaléz-Pleiter et al. 2013[31] (UBA, 2014[24])
Cyanobacteria	*Synechocystis sp.,* 5 d, growth, NOEC	0.010 mg/L	Pomati et al. 2004[34] (UBA, 2014[24])
Aquatic plants	*Lemna minor*, frond number, 7 d, EC_{50}	5.62 mg/L	Pomati et al 2004[34] (UBA, 2014[24])
Aquatic plants	*Lemna minor*, frond number, 7 d, NOEC	0.010 mg/L	Pomati et al 2004[34] (UBA, 2014[24])

[a] The references were taken from the NORMAN factsheet on erythromycin[3], and from the UBA report[24], where the reliability of the studies have been assessed and considered reliable.

7.2 Mammalian toxicology data

No information retrieved

7.3 PNEC derivation

PNEC	Endpoint	Endpoint value	AF	PNEC value
$PNEC_{fw}$	*Synechococcus leopoldensis* IAM-M6, 144 h, NOEC	0.002 mg/L	10	0.0002 mg/l [23]
$PNEC_{sed}$	-	-	-	0.0060 mg/kg dw [a]
$PNEC_{biota,sec pois}$	-	-	-	- [b]
$PNEC_{biota, hh}$	ADI	0.0007 mg/kg bw/day	-	0.043 mg/kg food [c]
$PNEC_{dw, hh}$	ADI	0.0007 mg/kg bw/day	-	0.002 mg/L [d]

[a] Calculated with the Equilibrium partitioning method. $K_{sed-water}$= 15.05 $m^3 m^{-3}$ (calculated with eq. D), RHO_{sed}= 1300 kg m^{-3} (default value), $Fsolid_{sed}$= 0.2 (default value), RHO_{solid}= 2500 kg m^{-3} (default value), Kp_{sed}= 28.5 L/kg (calculated, K_{oc} x Foc_{sed}), K_{oc}= 570 L/kg, Foc_{sed}= 0.05 kg kg^{-1} (default value). Conversion from wet weight to dry weight was done with eq. B (Section 3.3.2).

[b] Mammalian toxicity values lacking.

[c] ADI value retrieved from the WHO report (see reference 35) used in equation E as TL. See section 3.3.4 for calculation

[d] ADI value used in equation F as TL_{hh}. See section 3.3.5 for calculation

8. Risk Quotient (PEC/PNEC)

RQ	ECETOC[a]	Human consumption (Eq. G)[b]	MEC[c]
RQ_{fw}	26.3	**1.00**	**3.07**
RQ_{sed}	**52.9**	**1.00**	**3.07**
$RQ_{biota,sec\ pois}$	No info	No info	No info
$RQ_{biota,\ hh}$	5.99	0.23	0.7
$RQ_{dw,\ hh}$	2.15	0.08	0.25

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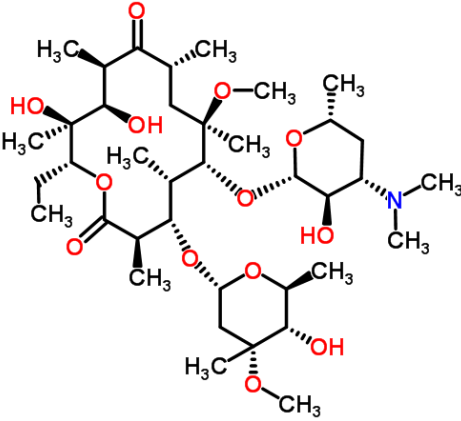
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Clarithromycin (CAS N. 81103-11-9)

1.   Substance identity

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

2.   Reason for proposal as candidate for the Watch list and suspected environmental risk

Clarithromycin, a semisynthetic macrolide antibiotic derived from erythromycin, inhibits bacterial protein synthesis by binding to the bacterial 50S ribosomal subunit. Binding inhibits peptidyl transferase activity and interferes with amino acid translocation during the translation and protein assembly process[1].

Clarithromycin has been classified as Category 2 according to the NORMAN Prioritisation Methodology[2], with a frequency of exceedance of 15% and an extent of exceedance of 2.33-fold of the lowest PNEC[1], considering monitoring data from 2002-2011in the NORMAN database[3].

A significant ecotoxicological risk due to the presence of clarithromycin in treated waste water in EL was estimated from acute and chronic toxicity data in algae [4]. In addition, a risk indicator considered adverse to ecosystems was calculated for clarithromycin [5] considering the presence of this substance in the Llobregat river in ES[6]. Furthermore, clarithromycin was considered to pose a potential risk to the environment considering the predicted exposure in Turkey [7].

3.   Physico-chemical Properties

Endpoint	Value	Source
Vapour Pressure (mm Hg)	2.32E-25	PubChem, 2014[8]
Water solubility (mg/L)	0.33	Drugbank, 2014[9]
logK$_{ow}$	3.16	Drugbank, 2014 [9]

4. Environmental fate

Endpoint	Value	Source
Sorption potential (K$_{oc}$)	150	PubChem, 2014[8]
Biodegradability	NRB	PubChem, 2014[8]
Bioaccumulation (BCF)	56.49 (estimated)	PubChem, 2014[8]
BMF	1	Default value, TG n. 27 - CIS WFD [10]

5. Environmental exposure assessment

	Description	Source
Tonnes/year	-	
Uses	Pharmaceutical	
Spatial usage (by MS)	Wide dispersive use (diffuse sources, present in urban wastewater)	Drugbank, 2014 [9]
Banned uses	-	
ERC code	-	
Fraction of tonnage to region	-	

5.1 Predicted Environmental Concentration

	Human consumption (Eq. G)[a]	MEC[b]
PEC$_{fw}$ (mg/L)	0.000438	0.000645
PEC$_{sed}$ (mg/kg dw)	0.0040[c]	0.0059[c]
PEC$_{biota}$ (mg/kg)	0.025[d]	0.036[d]

[a]Besse et al., 2008[14] (Equation G) for PEC equation, human consumption data from EL.

[b] MEC$_{95}$ (SE)

[c] PEC$_{sed}$ calculated with the Equilibrium Partitioning Method, where K$_{sed-water}$= 4.55 m^{3}m^{-3} (calculated with eq. K of section 3.4.2), RHO$_{sed}$= 1300 kg m^{-3} (default value), Fsolid$_{sed}$= 0.2 (default value), RHO$_{solid}$= 2500 kg m^{-3} (default value), Kp$_{sed}$= 7.5 L/kg (calculated, K$_{oc}$ x Foc$_{sed}$), K$_{oc}$= 150 L/kg (from PubChem[8]), Foc$_{sed}$= 0.05 kg kg^{-1} (default value). Conversion from wet weight to dry weight was done with eq. I (see section 3.4.2).

[d] Calculation with Equation L (Section 3.4.3)

5.1.1 PEC calculation considering different uses or sales data from MS

Uses	Calculation tool/ equation	Country	PEC$_{fw}$ (µg/L)
Human use	PEC$_b$[a]	France	0.062
Human use	PEC$_b$[a]	Portugal	0.080
Human use	PEC$_b$[a]	Latvia	0.073
Human use	PEC$_b$[a]	Greece	**0.438**
Human use	PEC$_b$[a]	Germany	0.0406
Human use	PEC$_b$[a]	Denmark	0.0188
Veterinary use	No sales data	-	-

[a] PEC$_b$ equation was retrieved from Besse et al, 2008 [11]

PEC$_b$ equation: $PEC_{fw}= (consumption \times F_{excreta}) / (WWinhab \times hab \times dilution \times 365)$

where *WWinhab* is the volume of wastewater per person per day (default value of 200 [L/(hab*day)], *hab* are the number of inhabitants in the respective country (retrieved from PT[12], LV[13], EL[14], DE[15] and DK[16] official sources). *F$_{excreta}$* is the excretion factor of the active substance[11], *dilution* is the dilution factor (default value of 10), *consumption* is the quantity (mg/year) of active ingredient consumed by the population during 1 year. Consumption data were taken from Besse et al, 2008[11] for FR, from Iatrou et al, 2014[4] for EL, from UBA report for DE[17], and directly provided to the JRC for PT, LV, and DK[18].

5.2 Measured Environmental Concentration

From an analysis of pharmaceutical datasets in river systems worldwide collected from the literature, Hughes et al. (2013)[19] report that clarithromycin has a mean detection frequency worldwide of 54% (from all the records for that particular substance), median and maximum concentration worldwide of 0.016 and 0.260 µg/L, respectively, while median and maximum concentrations in European studies were around 0.05 and 0.5 µg/L, respectively (exact values for European studies could not be retrieved from the plot in the publication). The frequency of detection of clarithromycin in the NORMAN database is 33% (NORMAN, 2014)[1].

n. of MS	Source of monitoring data	MEC values	RBSP
3 (NL, CH, SE)	NORMAN DB, 2014[3]	MEC$_{95, whole}$: 0.096 µg/L (CH, NL*) MEC$_{site, dissolved}$: 0.001 µg/L (CH)	-
	SE Screening Programme Pharmaceuticals[20]	MEC$_{95}$: 0.645 µg/L (SE)	

* All values <LOD

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

Clarithromycin failed to exhibit mutagenic potential in several in vitro tests, including the Salmonella mammalian microsome test, bacterial induced mutation frequency test, rat hepatocyte DNA synthesis assay, mouse lymphoma assay, mouse dominant lethal test, and mouse micronucleus test[8].

P: Very persistent (DT50 sediment = 379 days) NORMAN, 2014[1]

B: Not Bioaccumulative ($BCF_{estimated}$ = 56.49) NORMAN, 2014[1]

7. Hazard assessment

7.1 Ecotoxicology data

Trophic level	Endpoint	Value	Reference[a]
Algae	*Pseudokirchneriella subcapitata*, 72 h, biomass, EC_{50}	2 µg/L	Isidori et al. 2005[21]
Algae	*Pseudokirchneriella subcapitata*, 96 h, NOEC	4 µg/L	Yamashita et al. 2006[22]
Algae	***Anabaena flos-aquae*, 72 h, growth rate, EC_{10}**	**2.6 µg/L**	**UBA, 2014[23]**
Invertebrates	*Ceriodaphnia dubia*, 48 h, LC_{50} (static)	18 660 µg/L	Isidori et al. 2005[21]
Invertebrates	*Daphnia magna*, 21 d, NOEC (semi-static)	3.1 µg/L	Yamashita et al. 2006[22]
Rotifera	*Brachionus calyciflorus*, 24 h, LC_{50}	35 460 µg/L	Isidori et al. 2005[21]
Fish	*Oryzias latipes*, 96 h, EC_{50}	> 100,000	Kim et al. 2009[24]

[a] The references were taken from the NORMAN factsheet on clarithromycin[1], and the studies were considered reliable.

7.2 Mammalian toxicology data

No studies found.

7.3 PNEC derivation

PNEC	Endpoint	Endpoint value	AF	PNEC value
$PNEC_{fw}$	*Anabaena flos-aquae*, 72 h, EC_{10}	2.6 µg/L	10*2	0.13 µg/L [a]
$PNEC_{sed}$	-	-	-	0.0012 mg/kg dw[b]
$PNEC_{biota,sec\ pois}$	-	-	-	Info missing
$PNEC_{biota,\ hh}$	ADI	0.0002 mg/kg bw/day	-	0.012 mg/kg food [c]

PNEC$_{dw, hh}$	ADI	0.0002 mg/kg bw/day	-	0.001 mg/L [d]

[a] The PNEC value was retrieved from the UBA factsheet[23] on the substance. The additional AF of 2 was used because the toxic metabolite 14-Hydroxy-Claritromycin occur up to about 50% in surface water and is equivalent toxic.

[b] Calculated using the equilibrium partitioning method. The following values were used: $K_{sed-water}$= 4.55 m^{3}m^{-3} (calculated with eq. D of section 3.3.2), RHO$_{sed}$= 1300 kg m^{-3} (default value), Fsolid$_{sed}$= 0.2 (default value), RHO$_{solid}$= 2500 kg m^{-3} (default value), Kp$_{sed}$= 7.5 L/kg (calculated, K$_{oc}$ x Foc$_{sed}$), K$_{oc}$= 150 L/kg (from PubChem[8]), Foc$_{sed}$= 0.05 kg kg^{-1} (default value). Conversion from wet weight to dry weight was done with eq. B (see section 3.3.2).

[c] ADI value retrieved from Leung et al., 2013 (see reference 25) used in equation E as TL. See section 3.3.4 for calculation

[d] ADI value used in equation F as TL$_{hh}$. See section 3.3.5 for calculation

8. Risk Quotient (PEC/PNEC)

RQ	Human consumption (Eq. G)[a]	MEC[b]
RQ$_{fw}$	3.37	4.96
RQ$_{sed}$	3.37	4.96
RQ$_{biota,sec pois}$	No info	No info
RQ$_{biota, hh}$	2.03	2.99
RQ$_{dw, hh}$	0.63	0.92

[a]Besse et al., 2008[14] (Equation G) for PEC equation, human consumption data from EL.

[b] MEC$_{95}$ (SE)

9. References

[1] NORMAN factsheet on clarithromycin, version of 31.08.2014 (available on CIRCA BC).

[2] Dulio V, von der Ohe PC. (2013) NORMAN Prioritisation framework for emerging substances. N° W604002510 NORMAN Association - Working Group on Prioritisation of Emerging Substances,. Available at http://www.norman-network.net/sites/default/files/files/Publications/NORMAN_prioritisation_Manual_15%20April2013_final%20for%20website-f.pdf

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[4] Iatrou EI, Stasinakis AS, Thomaidis NS. (2014) Consumption-based approach for predicting environmental risk in Greece due to the presence of antimicrobials in domestic wastewater. Environ Sci Pollut Res Int. Available at: http://link.springer.com/article/10.1007%2Fs11356-014-3243-7

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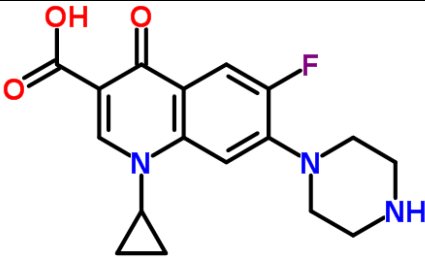
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Ciprofloxacin (CAS N. 85721-33-1)

1. Substance identity

Chemical name (IUPAC)	1-cyclopropyl-6-fluoro-4-oxo-7-(piperazin-1-yl)-1,4-dihydroquinoline-3-carboxylic acid
EC number	-
CAS number	85721-33-1
Chemical class	Carboxy-fluoroquinoline
Molecular formula	C17H18FN3O3
Molecular weight	331.3
Structure	
SMILES	c1c2c(cc(c1F)N3CCNCC3)n(cc(c2=O)C(=O)O)C4CC4

2. Reason for proposal as candidate for the Watch list and suspected environmental risk

Ciprofloxacin is a broad-spectrum antiinfective agent of the fluoroquinolone class. Ciprofloxacin has in vitro activity against a wide range of gram-negative and gram-positive microorganisms[1]. Ciprofloxacycin has been classified as Category 2 according to the NORMAN Prioritisation Methodology[2], with a frequency of exceedancy of 18% and an extent of exceedancy of 7.53-fold of the lowest PNEC[3], considering monitoring data from 2002-2011 in the NORMAN database[4].

Ciprofloxacin has been classified as posing moderate risk from the Stockholm County Council[5]. In addition, a risk quotient greater than 1 was determined for this substance by performing an environmental risk assessment according to the guideline recommended by the European Medicines Agency (EMA), and measured concentrations confirmed that the release of ciprofloxacin from wastewater treatment works may potentially be of environmental concern in NO[6]. A significant ecotoxicological risk due to the presence of ciprofloxacin in treated waste water in EL was estimated from acute toxicity data in algae[7].

In addition, a risk indicator considered adverse to ecosystems was calculated for ciprofloxacin[8] considering the presence of this substance in the Llobregat river in ES[9]. Ciprofloxacin is one of the most frequently detected fluoroquinolone antibiotics in hospital wastewater and concentrations in surface water are potentially hazardous to the environment[10].

3. Physico-chemical Properties

Endpoint	Value	Source
Vapour Pressure (mm Hg)	2.85E-13	Pubchem, 2014[11]
Water solubility (mg/L)	30000	Pubchem, 2014[11]
logK$_{ow}$	0.28	Pubchem, 2014[11] , Schwab et al. 2005[12]

4. Environmental fate

Endpoint	Value	Source
Sorption potential (K$_{oc}$)	61000	Pubchem, 2014[11]
Biodegradability	NRB	Pubchem, 2014[11]
Bioaccumulation (BCF)	3.2 L/kg	Schwab et al. 2005[12]
BMF	1	Default value, TG n. 27 - CIS WFD [13]

5. Environmental exposure assessment

	Description	Source
Tonnes/year	-	
Uses	Pharmaceutical	
Spatial usage (by MS)	Wide dispersive use (diffuse sources, present in urban wastewater)	NORMAN, 2014[3]
Banned uses	-	
ERC code	-	
Fraction of tonnage to region	-	

5.1 Predicted Environmental Concentration

	Human consumption (Eq. G)[a]	MEC[b]
PEC$_{fw}$ (mg/L)	0.000538	0.00124
PEC$_{sed}$ (mg/kg dw)	1.6418[c]	3.78[c]
PEC$_{biota}$ (mg/kg)	0.0017[d]	0.004[d]

[a]Besse et al., 2008[14] (Equation G) for PEC equation, human consumption data from PT.

[b] MEC$_{95}$ (SE – NORMAN DB)

[c] PEC$_{sed}$ calculated with the Equilibrium Partitioning Method, where K$_{sed-water}$= 1525.8 m^{3}m^{-3} (calculated with eq. K of section 3.4.2), RHO$_{sed}$= 1300 kg m^{-3} (default value), Fsolid$_{sed}$= 0.2 (default value), RHO$_{solid}$= 2500 kg m^{-3} (default value), Kp$_{sed}$= 3050 L/kg (calculated, K$_{oc}$ x Foc$_{sed}$), K$_{oc}$= 61000 L/kg (from PubChem[11]), Foc$_{sed}$= 0.05 kg kg^{-1} (default value). Conversion from wet weight to dry weight was done with eq. I (see section 3.4.2).

[d] Calculation with Equation L (Section 3.4.3)

5.1.1 PEC calculation considering different uses or sales data from MS

Uses	Calculation tool/ equation	Country	PEC$_{fw}$ (µg/L)
Human use	PEC$_b$[a]	France	0.139
Human use	PEC$_b$[a]	Portugal	**0.540**
Human use	PEC$_b$[a]	Latvia	0.210
Human use	PEC$_b$[a]	Greece	0.530
Human use	PEC$_b$[a]	Denmark	0.166
Veterinary use	No sales data	-	-

[a] PEC$_b$ equation was retrieved from Besse et al, 2008[14]

PEC$_b$ equation: $PEC_{fw} = (consumption \times F_{excreta}) / (WWinhab \times hab \times dilution \times 365)$

where *WWinhab* is the volume of wastewater per person per day (default value of 200 [L/(hab*day)], *hab* are the number of inhabitants in the respective country (retrieved from PT[16], LV[17], EL[18], DK[19] official sources). *F$_{excreta}$* is the excretion factor of the active substance retrieved from Besse et al, 2008[14], *dilution* is the dilution factor (default value of 10), *consumption* is the quantity (mg/year) of active ingredient consumed by the population during 1 year. Consumption data were taken from Besse et al, 2008[14] for FR, from Iatrou et al, 2014[7] for EL, and directly provided to the JRC for PT[15]. DK and LV[20].

5.2 Measured Environmental Concentration

From an analysis of pharmaceutical datasets in river systems worldwide collected from the literature, Hughes et al. (2013)[21] report that ciprofloxacin has a mean detection frequency worldwide of 33.4% (from all the records for that particular substance) and median and maximum concentrations worldwide of 164 and 6500 µg/L, respectively. The frequency of quantification of ciprofloxacin in the NORMAN database is 18% (NORMAN, 2014)[3].

n. of MS	Source of monitoring data	MEC values	RBSP
2 (SE, PT)	NORMAN DB, 2014[4]	MEC$_{95, whole}$: 1.24 µg/L (SE) MEC$_{95, dissolved}$: 0.22 µg/L[a] (PT)	-
	SE Screening Programme Pharmaceuticals[22]	MEC$_{95}$: 0.206 µg/L (SE)	

[a] outlier has been removed from the monitoring dataset.

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

Eight in vitro mutagenicity tests have been conducted with Ciprofloxacin, 2 of the 8 tests were positive, but results of the further 3 in vivo test systems gave negative results[23]. Long-term carcinogenicity studies in rats and mice resulted in no carcinogenic or tumorigenic effects[23]. Fertility studies performed in rats at oral doses of Ciprofloxacin up to 100 mg/kg (approximately 0.7-times the highest recommended therapeutic dose based upon mg/m2) revealed no evidence of impairment[23].

An estimated BCF of 3 (SRC), from its log Kow of 0.28, suggests the potential for bioconcentration in aquatic organisms is low (SRC)[11]. Using the OECD closed bottle biodegradation study, 0% degradation

over a 40-day incubation period was observed indicating that biodegradation is not an important environmental fate process in water[11].

7. Hazard assessment

7.1 Ecotoxicology data

Trophic level	Endpoint	Value	Reference[a]
Fish	*Oncorhyncus mykiss*, 96 h, LC_{50}	>9.4 mg/L	Gagliano & McNamara 1996[24]
Aquatic invertebrates	*Daphnia magna*, 48 h, EC_{50}	58.8 mg/L	Martins et al. 2012[25]
Aquatic invertebrates	*Daphnia magna*, 21 d, NOEC	4.67 mg/L	Martins et al. 2012[25]
Cyanobacteria	*Anabaena flos-aquae*, 72 h, EC_{50}	0.036 mg/L	Ebert et al. 2011[26]
Cyanobacteria	***Anabaena flos-aquae*, 72 h, EC_{10}**	**0.00447 mg/L**	Ebert et al. 2011[26]
Aquatic plants	*Lemna minor*, 7 d, EC_{50}	0.499 mg/L	Ebert et al. 2011[26]
Aquatic plants	*Lemna minor*, 7 d, EC_{10}	0.149 mg/L	Brain et al. 2004[27]

[a] The references were taken from the NORMAN factsheet on ciprofloxacin[13], and the studies were considered reliable.

7.2 Mammalian toxicology data

No information retrieved

7.3 PNEC derivation

PNEC	Endpoint	Endpoint value	AF	PNEC value
$PNEC_{fw}$	*Anabaena flos-aquae*, 72 h, EC_{10}	0.00447 mg/L	50	8.9E-05 mg/L [a]
$PNEC_{sed}$	-	-	-	0.272 mg/kg dw [b]
$PNEC_{biota,sec\ pois}$	-	-	-	N.R.
$PNEC_{biota,\ hh}$	-	-	-	N.R.
$PNEC_{dw,\ hh}$	ADI	0.0016 mg/kg day	-	0.006 mg/L [c]

N.R. Not required based on BCF value not reaching the trigger value required for biota assessment
[a] Two long-term values available from the main trophic levels. No new calculations were performed, since PNEC value was retrieved from NORMAN factsheet, 2014[3]
[b] Calculated using the equilibrium partitioning method. The following values were used: $K_{sed-water}$= 1525.8 $m^3 m^{-3}$ (calculated with eq. D of section 3.3.2), RHO_{sed}= 1300 kg m^{-3} (default value), $Fsolid_{sed}$= 0.2 (default value), RHO_{solid}= 2500 kg m^{-3} (default value), Kp_{sed}= 3050 L/kg (calculated, K_{oc} x Foc_{sed}), K_{oc}= 61000 L/kg (from PubChem[11]), Foc_{sed}= 0.05 kg kg^{-1} (default value). Conversion from wet weight to dry weight was done with eq. B (see section 3.3.2).
[c] ADI value (from Schwab et al. 2005[12]) used in equation Fas TL_{hh} (see section 3.3.5)

8. Risk Quotient (PEC/PNEC)

RQ	Human consumption (Eq. G)[a]	MEC[b]

RQ$_{fw}$	6.045	13.93
RQ$_{sed}$	6.045	13.93
RQ$_{biota,sec\ pois}$	N.R.	N.R.
RQ$_{biota,\ hh}$	N.R.	N.R.
RQ$_{dw,\ hh}$	0.10	0.22

[a] Besse et al., 2008[14] (Equation G) for PEC equation, human consumption data from PT.

[b] MEC$_{95}$ (SE – NORMAN DB)

9. References

[1] Drugbank (2014): http://www.drugbank.ca/drugs/DB01211

[2] Dulio V, von der Ohe PC. (2013) NORMAN Prioritisation framework for emerging substances. N° W604002510 NORMAN Association - Working Group on Prioritisation of Emerging Substances,. Available at http://www.norman-network.net/sites/default/files/files/Publications/NORMAN_prioritisation_Manual_15%20April2013_final%20for%20website-f.pdf

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[13] Technical Guidance for Deriving Environmental Quality Standards – Guidance Document No. 27 (2011) Common Implementation Strategy of the Water Framework Directive (2000/60/EC). Available at http://ec.europa.eu/environment/water/water-dangersub/lib_pri_substances.htm

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[15] National human consumption data of antibiotics directly provided to the JRC by PT.

[16] Instituto Nacional de Estatística. http://www.ine.pt/xportal/xmain?xpid=INE&xpgid=ine_main;

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Tolylfluanid (CAS N. 731-27-1)

1. Substance identity

EC name	
EC number	211-986-9
CAS number	731-27-1
Molecular formula	C10H13Cl2FN2O2S2
Molecular weight	347.3
Structure	
SMILES	N(C)(C)S(=O)(=O)N(c1ccc(cc1)C)SC(F)(Cl)Cl

2. Physico-chemical Properties

Endpoint	Value	Source
Vapour Pressure (Pa)	2×10^{-4}	Biocide Assessment Report, 2009[1]
Water solubility (mg/L)	0.90	EFSA Conclusion, 2005[2]
logK$_{ow}$	3.9	EFSA Conclusion, 2005[2]

3. Environmental fate

Endpoint	Value	Source
Sorption potential (K$_{oc}$)	2200	EFSA Conclusion, 2005[2]
Biodegradability	NRB	EFSA Conclusion, 2005[2]
Bioaccumulation (BCF)	74	EFSA Conclusion, 2005[2]
BMF	1	Default value, TG n. 27 - CIS WFD[3]

4. Environmental exposure assessment

4.1 Predicted Environmental Concentration

	Description	Source
Tonnes/year	2000 (year 2000)	From previous prioritisation exercise
Uses	Biocide	
Spatial usage (by MS)	Not known	
Banned uses	Fungicide - PPP	Commission Directive 2010/20/EU[4]

ERC code	ERC8b	
Fraction of tonnage to region	0.1	
PEC_{fw} (mg/L)	0.00097	ECETOC
PEC_{sed} (mg/kg dw)	0.217	ECETOC
PEC_{biota} (mg/kg)	0.072	Calculation based on Equation L (Section 3.4.3)

4.1.1 ECETOC simulation with lower tonnages

Authorisations for plant protection products containing the active substance tolylfluanid were withdrawn by 30 November 2010. No authorisations for plant protection products containing tolylfluanid are granted or renewed from 1 December 2010[4].

However, the available tonnage of 2000 relates to the year 2000, which is prior to the banning of the substance as PPP.

At the WG Chem meeting 16-17/10/2014 it was suggested to perform a simulation on the PEC calculated with ECETOC using reduced tonnage values of tolylfluanid that could be closer to the actual tonnage after the banning, i.e. related to the use as biocide only. Since no tonnage value specific for this particular use was available, it was decided to perform the simulation considering a 20%, and 30% or 50% decrease in tonnage values. The results of the simulations are compared with the pre-banning tonnage scenario in the following Table.

Tonnes/year	2000	1600	1400	1000
Decrease respective to pre-banning tonnage	-	20%	30%	50%
PEC_{fw} (mg/L)	9.7E-04	7.8E-04	6.8E-04	4.9E-04
RQ_{fw}	3.66	2.94	2.56	1.85
Position in the ranking (higher RQ)	22 (RQ_{fw})	22 (RQ_{fw})	22 (RQ_{fw})	22 (RQ_{fw})

4.2 Measured Environmental Concentration

n. of MS	Source of monitoring data	MEC values	RBSP
5 (FR, NL, FI, SE, IT)	NORMAN DB, 2014[5]	$MEC_{site, whole}$: 0.01 µg/L	-
	WATERBASE, 2014[6]	all values < LOQ	
	IPCheM[7]	all values < LOQ	
	SE pesticide monitoring programme[8]	all values < LOQ	
	IT monitoring programme[9]	MEC_{95}: 0.048 µg/L	

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

Tolylfluanid is neither genotoxic nor carcinogenic[1]. There were no classification-relevant effects on reproductive or developmental toxicity[1]. The substance is not readily biodegradable (P).It shows a low potential for bioaccumulation[1].

6.   Hazard assessment

6.1 Ecotoxicology data

Since the substance will be de-selected from the Watch List, because of sufficient monitoring data, ecotoxicity data are not reported at this stage.

6.2 Mammalian toxicology data

Since the substance will be de-selected from the Watch List, because of sufficient monitoring data, mammalian toxicity data are not reported at this stage.

6.3 PNEC derivation

PNEC	Endpoint	Endpoint value	AF	PNEC value
$PNEC_{fw}$	*Daphnia magna*, 21 d, NOEC	0.00265 mg/L	10[a]	0.000265 mg/L[b]
$PNEC_{sed}$	*Chironomus riparius*, 28 d, EC_{15}	5.75 mg/L	100[c]	0.058 mg/L[d]
$PNEC_{biota,sec pois}$	Rat, 2-generation study, conversion factor 20, NOAEL	12 mg/kg bw/day	30[e]	8 mg/kg bw/day[f]
$PNEC_{biota, hh}$	ADI	0.1 mg/kg bw/day	-	6.087 mg/kg food[g]
$PNEC_{dw, hh}$	ADI	0.1 mg/kg bw/day	-	0.350 mg/L[h]

[a] AF of 10 because three long term values were available from the main trophic levels.

[b] PNEC value retrieved from the Biocide Assessment Report, 2009[1]

[c] AF of 100 because one long term value was available.

[d] Due to the fast degradation of the substance in sediment, no studies with the active substance on sediment dwelling organisms were considered necessary, and no sediment risk assessment was carried out (EFSA, 2005[2], Biocide AR, 2009[1]). Thus, the endpoint value used in this report is referred to its metabolite.

[e] AF of 30 selected according to the duration of the test (see TG n. 27 - CIS WFD[3])

[f] The following steps were followed for $PNEC_{biota,sec pois}$ calculation: a) conversion of NOAEL (12 mg/kg bw/day) value, retrieved from EFSA Conclusion 2005[2], into NOEC (240 mg/kg) by using the conversion factor of 20 ((taken from TG n. 27- CIS WFD, which depends both on species tested and age/study); b) Application of appropriate AF_{oral} (30) to the NOEC value.

[g] ADI value retrieved from EFSA Conclusion 2005[2], used for PNEC calculation according to Equation E (see section 3.3.4)

[h] ADI value used in equation F as TL_{hh}. See section 3.3.5 for calculation.
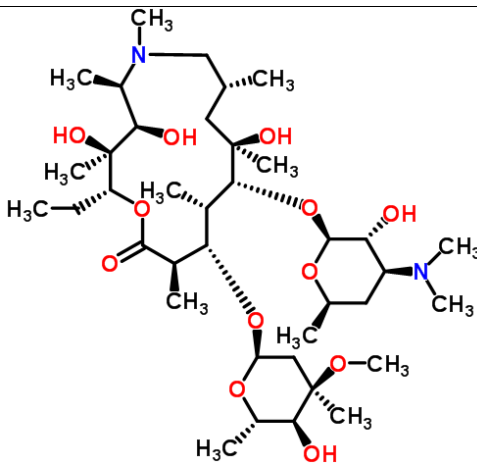
7.   Risk Quotient (PEC/PNEC)

RQ	Value
RQ_{fw}	**3.66**
RQ_{sed}	0.017
$RQ_{biota,sec\ pois}$	0.009
$RQ_{biota,\ hh}$	0.01
$RQ_{dw,\ hh}$	0.003

8. References

[1] Directive 98/8/EC concerning the placing biocidal products on the market Inclusion of active substances in Annex I or IA to Directive 98/8/EC - Assessment Report Tolylfluanid Product-type 8 (Wood preservatives) – March 2009. Available at http://dissemination.echa.europa.eu/Biocides/factsheet?id=0055-08

[2] EFSA Scientific Report (2005) 29, 1-76, Conclusion on the peer review of tolylfluanid. Available at http://www.efsa.europa.eu/it/efsajournal/doc/29r.pdf

[3] Technical Guidance for Deriving Environmental Quality Standards – Guidance Document No. 27 (2011) Common Implementation Strategy of the Water Framework Directive (2000/60/EC). Available at http://ec.europa.eu/environment/water/water-dangersub/lib_pri_substances.htm

[4] COMMISSION DIRECTIVE 2010/20/EU of 9 March 2010 amending Council Directive 91/414/EEC to remove tolylfluanid as active substance and on the withdrawal of authorisations for plant protection products containing that substance. Official Journal of the European Union (March, 2010). Available at http://ec.europa.eu/sanco_pesticides/public/?event=activesubstance.selection&a=1

[5] NORMAN database at http://www.norman-network.net/?q=node/24

[6] WATERBASE Database http://www.eea.europa.eu/data-and-maps/data/waterbase-rivers-6

[7] IPCheM database at http://ipchem.jrc.ec.europa.eu/

[8] Swedish National Screening Programme Pesticides (data provided directly to the JRC)

[9] Italian Monitoring Programme (data provided directly to the JRC)

Azithromycin (CAS N. 83905-01-5)

1. **Substance identity**

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

2. **Reason for proposal as candidate for the Watch list and suspected environmental risk**

Azithromycin is a semi-synthetic macrolide antibiotic of the azalide class. Like other macrolide antibiotics, azithromycin inhibits bacterial protein synthesis by binding to the 50S ribosomal subunit of the bacterial 70S ribosome.[1]

Azithromycin has been classified as Category 2 according to the NORMAN Prioritisation Methodology[2], with a frequency of exceedance of 13% and an extent of exceedance of 1611-fold of the lowest PNEC[3], considering monitoring data from 2002-2011 in the NORMAN database[4].

3. **Physico-chemical Properties**

Endpoint	Value	Source
Vapour Pressure (mm Hg)	2.65E-24	PubChem, 2014[5]
Water solubility (mg/L)	2.37	PubChem, 2014[5]
logK$_{ow}$	4.02	PubChem, 2014[5]

4. Environmental fate

Endpoint	Value	Source
Sorption potential (K_{oc})	3100	PubChem, 2014[5]
Biodegradability	NRB	NORMAN, 2014[3]
Bioaccumulation (BCF)	200 (estimated)	PubChem, 2014[5]
BMF	1	Default value, TG n. 27 - CIS WFD [6]

5. Environmental exposure assessment

	Description	Source
Tonnes/year	-	
Uses	Pharmaceutical Intermediate use (no tonnage available)	ECHA, 2014[7]
Spatial usage (by MS)	Wide dispersive use (diffuse sources, present in urban wastewater)	NORMAN, 2014[3]
Banned uses	-	
ERC code	ERC6a (intermediate use), ERC8a (suitable for pharmaceutical use)	
Fraction of tonnage to region	-	

5.1 Predicted Environmental Concentration

	Human consumption (Eq. G)[a]	MEC[b]
PEC_{fw} (mg/L)	0.000128	0.000583
PEC_{sed} (mg/kg dw)	0.0200[c]	0.0913[c]
PEC_{biota} (mg/kg)	0.026[d]	0.117[d]

[a]Besse et al., 2008[14] (Equation G) for PEC equation, human consumption data from PT.

[b] MEC_{95} (NORMAN: PT)

[c] PEC_{sed} calculated with the Equilibrium Partitioning Method, where $K_{sed-water}$= 78.3 $m^3 m^{-3}$ (calculated with eq. K of section 3.4.2), RHO_{sed}= 1300 kg m-3 (default value), $Fsolid_{sed}$= 0.2 (default value), RHO_{solid}= 2500 kg m^{-3} (default value), Kp_{sed}= 155 L/kg (calculated, K_{oc} x Foc_{sed}), K_{oc}= 3100 L/kg (from PubChem[5]), Foc_{sed}= 0.05 kg kg^{-1} (default value). Conversion from wet weight to dry weight was done with eq. I (see section 3.4.2).

[d] Calculation with Equation L (Section 3.4.3)

5.1.1 PEC calculation considering different uses or sales data from MS

Uses	Calculation tool/ equation	Country	PEC_fw (µg/L)
Human use	$PEC_b{}^a$	France	0.046
Human use	$PEC_b{}^a$	Portugal	**0.130 (rounded)**
Human use	$PEC_b{}^a$	Latvia	0.043
Human use	$PEC_b{}^a$	Greece	0.114
Human use	$PEC_b{}^a$	Denmark	0.037
Veterinary use	No sales data	-	-

[a] PEC_b equation was retrieved from Besse et al, 2008[8]

PEC_b equation: $PEC_{fw}= (consumption \times F_{excreta}) / (WWinhab \times hab \times dilution \times 365)$

where *WWinhab* is the volume of wastewater per person per day (default value of 200 [L/(hab*day)], *hab* are the number of inhabitants in the respective country (retrieved from PT[10], LV[11], EL[12] and DK[13] official sources). $F_{excreta}$ is the excretion factor of the active substance retrieved from Besse et al, 2008[8], *dilution* is the dilution factor (default value of 10), *consumption* is the quantity (mg/year) of active ingredient consumed by the population during 1 year. Consumption data were taken from Besse et al, 2008[8] for FR, from Iatrou et al, 2014[14] for EL, and directly provided to the JRC for PT[9], DK and LV[15].

5.2 Measured Environmental Concentration

From an analysis of pharmaceutical datasets in river systems worldwide collected from the literature, Hughes et al. (2013)[16] report that azithromycin has a mean detection frequency worldwide of 41% (from all the records for that particular substance) and median and maximum concentrations worldwide of 0.19 and 1.5 µg/L, respectively. The frequency of quantification of azithromycin in the NORMAN database is 15%[3].

n. of MS	Source of monitoring data	MEC values	RBSP
3 (NL, PT, SE)	NORMAN DB, 2014[4]	$MEC_{95, whole}$: (NL[a]) $MEC_{95, dissolved}$: 0.583 µg/L[b] (PT)	-
	SE Screening Programme Pharmaceuticals[17]	MEC_{95}: 0.030 µg/L	

[a] All values<LOQ

[b] Outliers from monitoring data were removed.

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

Azithromycin does not cause gene mutations in microbial or mammalian cells, or chromosomal aberrations in cultured human lymphocytes or in mouse bone marrow *in vivo*[5]. A BCF value of 200 L/kg was reported in PubChem[5].

P: Very persistent (DT_{50} water > 3 years) - NORMAN, 2014[3]

7. Hazard assessment

7.1 Ecotoxicology data

Trophic level	Endpoint	Value	Reference
Fish	Fish, 96 h, EC_{50}	84 mg/L	Mattson, 2010[18]
Aquatic invertebrates	*Daphnia magna ,* 48h, LC_{50}	120 mg/L	Mattson, 2010[18]
Aquatic invertebrates	***Ceriodaphnia dubia*, 7 d, NOEC**	**0.0044 mg/L**	Mattson, 2010[18]
Algae	*Pseudokirchneriella subcapitata,* 96 h, biomass, EC_{50}	0.019 mg/L	Harada et al. 2008[19]
Algae	*Pseudokirchneriella subcapitata,* 96 h, NOEC	0.0052 mg/L	Harada et al. 2008[19]

[a] The references were taken from the NORMAN factsheet on azithromycin (see reference 3), and the studies were considered reliable.

7.2 Mammalian toxicology data

No study found

7.3 PNEC derivation

PNEC	Endpoint	Endpoint value	AF	PNEC value
$PNEC_{fw}$	*Ceriodaphnia dubia*, 7 d, NOEC	0.0044 mg/L	50	9.00E-05 mg/L [a]
$PNEC_{sed}$	-	-	-	0.014 mg/kg dw [b]
$PNEC_{biota,sec\ pois}$	-	-	-	No info
$PNEC_{biota,\ hh}$	ADI	0.0017 mg/kg day	-	0.103 mg/kg food [c]
$PNEC_{dw,\ hh}$	ADI	0.0017 mg/kg day	-	0.006 mg/L [d]

[a] An AF of 50 was selected based on availability of two long-term values from the main trophic levels.

[b] Equilibrium partitioning method used with the following values: $K_{sed-water}$= 78.3 m³m⁻³ (calculated with eq. D of section 3.3.2), RHO_{sed}= 1300 kg m⁻³ (default value), $Fsolid_{sed}$= 0.2 (default value), RHO_{solid}= 2500 kg m⁻³ (default value), Kp_{sed}= 155 L/kg (calculated, K_{oc} x Foc_{sed}), K_{oc}= 3100 L/kg (from PubChem[5]), Foc_{sed}= 0.05 kg kg⁻¹ (default value). Conversion from wet weight to dry weight was done with eq. B (section 3.3.2).

[c] ADI value retrieved from Leung 2013 (see reference 20) used in equation E as TL. See section 3.3.4 for calculation

[d] ADI value used in equation F as TL_{hh}. See section 3.3.5 for calculation

8. Risk Quotient (PEC/PNEC)

RQ	Human consumption (Eq. G)[a]	MEC[b]
RQ_{fw}	**1.422**	**6.48**
RQ_{sed}	**1.422**	**6.48**
$RQ_{biota,sec\ pois}$	No info	No info
$RQ_{biota,\ hh}$	0.25	1.13
$RQ_{dw,\ hh}$	0.02	0.10

[a]Besse et al., 2008[14] (Equation G) for PEC equation, human consumption data from PT.

[b] MEC_{95} (NORMAN: PT)

9. References

[1] Drugbank (2014): http://www.drugbank.ca/drugs/DB01211

[2] Dulio V, von der Ohe PC. (2013) NORMAN Prioritisation framework for emerging substances. N° W604002510 NORMAN Association - Working Group on Prioritisation of Emerging Substances,. Available at http://www.norman-network.net/sites/default/files/files/Publications/NORMAN_prioritisation_Manual_15%20April2013_final%20for%20website-f.pdf

[3] NORMAN factsheet on Azithromycin, version of 31.08.2014 (available on CIRCA BC).

[4] NORMAN database at http://www.norman-network.net/?q=node/24

[5] Pubchem website: http://pubchem.ncbi.nlm.nih.gov//compound/447043?from=summary#section=2D-Structure

[6] Technical Guidance for Deriving Environmental Quality Standards – Guidance Document No. 27 (2011) Common Implementation Strategy of the Water Framework Directive (2000/60/EC). Available at http://ec.europa.eu/environment/water/water-dangersub/lib_pri_substances.htm

[7] ECHA dissemination website (2014). Available at http://apps.echa.europa.eu/registered/data/dossiers/DISS-fd337022-a243-4bf3-e043-1cdf090aa190/DISS-fd337022-a243-4bf3-e043-1cdf090aa190_DISS-fd337022-a243-4bf3-e043-1cdf090aa190.html

[8] Besse J.P. Kausch Barreto C. and Garric J. (2008) Exposure assessment of pharmaceuticals and their metabolites in the aquatic environment: Application to the French situation and preliminary prioritization. Journal of Human and Ecological Risk Assessment. 14 (4):665-695.

[9] National human consumption data of antibiotics directly provided to the JRC by PT.

[10] Instituto Nacional de Estatística. http://www.ine.pt/xportal/xmain?xpid=INE&xpgid=ine_main;

[11] Ministry of Foreign Affairs of the republic of Latvia. http://www.am.gov.lv/en/?id=4659)

[12] Hellenic Statistical Authority (EL.STAT.). http://www.statistics.gr/portal/page/portal/ESYE

[13] Statistics Denmark. Available at http://www.dst.dk/en/Statistik/emner/befolkning-og-befolkningsfremskrivning.aspx

[14] Iatrou EI, Stasinakis AS, Thomaidis NS. (2014) Consumption-based approach for predicting environmental risk in Greece due to the presence of antimicrobials in domestic wastewater. Environ Sci Pollut Res Int. Available at: http://link.springer.com/article/10.1007%2Fs11356-014-3243-7

[15] National human consumption data of antibiotics directly provided to the JRC by LV and DK.

[16] Hughes SR, Kay P, Brown LE. (2013) Global synthesis and critical evaluation of pharmaceutical data sets collected from river systems. Environ Sci Technol. 47(2):661-77.

[17] Fick J, Lindberg RH, Kaj L, Brorström-Lundén E. (2011) Results from the Swedish National Screening Programme 2010 - Subreport 3: Pharmaceuticals. IVL Swedish Environmental Research Institute.

[18] Mattson B (2010): Personal communication with Bengt Mattson (Pfizer AB, Sollentuna, Sweden) concerning ecotoxicological values for Azithromycin published by Pfizer in the Fass.se online database. Mail from 04.05.2010 to Marion Junghans (Oekotoxzentrum, Dübendorf, CH).

[19] Harada A, Komori K, Nakada N, Kitamura K, Suzuki Y (2008): Biological effects of PPCPs on aquatic lives and evaluation of river waters affected by different wastewater treatment levels, Water Science and Technology 58(8): 1541 – 1546.

[20] Leung HW, Jin L, Wei S, Tsui MM, Zhou B, Jiao L, Cheung PC, Chun YK, Murphy MB, Lam PK. (2013) Pharmaceuticals in tap water: human health risk assessment and proposed monitoring framework in China. Environ Health Perspect. 121(7):839-46.

Cyanide-Free (CAS N. 57-12-5)

1. Substance identity

EC name	
EC number	
CAS number	57-12-5
Molecular formula	HCN, CN⁻
Molecular weight	27.03
Structure	
SMILES	C#N

2. Physico-chemical Properties

Endpoint	Value	Source
Vapour Pressure	620 mmHg at 20°C (as HCN)	WFD – UK TAG Report, 2012[1]
Water solubility (mg/L)	1,000,000 at 25°C (as HCN)	WFD – UK TAG Report, 2012[1]
logK$_{ow}$	0.35–1.07 (as HCN)	WFD – UK TAG Report, 2012[1]

3. Environmental fate

Endpoint	Value	Source
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[1]
Bioaccumulation (BCF)	Experimental BCF values for rainbow trout range from 1.69–4.12.	WFD – UK TAG Report, 2012[1]

4. Environmental exposure assessment

4.1 Predicted Environmental Concentration

	Description	Source
Tonnes/year	-	
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.	WFD – UK TAG Report, 2012[1]
Spatial usage (by MS):	Widespread use	
Banned uses	**-**	
ERC code	-	
Fraction of tonnage to region	-	
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	RBSP
14 (CZ, SI, EL, FR, DE, AT, ES, UK, IE, NL, PL, RO, SK, IT) Reported as cyanide in the databases	NORMAN DB, 2014[2]	MEC$_{95, whole}$: 1.07 µg/L MEC$_{95, dissolved}$: 5 µg/L	10 MS (RBSP EQS ECOSTAT – UBA report)[5]
	WATERBASE, 2014[3]	MEC$_{95, whole}$: 20 µg/L MEC$_{95, dissolved}$: 20 µg/L	
	IPCheM[4]	MEC$_{95}$: 14 µg/L	EQS set for cyanide ion and total (WRc, 2012)[6]

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

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[1]).

6. Hazard assessment

6.1 Ecotoxicology data

Trophic level	Endpoint	Value	Reference
Fish	Rainbow trout, 20 d, LOEC	0.005 mg/L	WFD- UK TAG Report (2012)[1]
Fish	***Lepomis macrochirus***,	**0.0052 mg/L**	WFD- UK TAG Report

	289 d, total inhibiotin of spawning, LOEC		(2012)[1]
Fish	*Salvelinus fontinalis*, egg production, NOEC	0.0057 mg/L	WFD- UK TAG Report (2012)[1]
Aquatic Invertebrates	*Moinodaphnia macleayi*, 5 d, reproduction, NOEC	0.0096 mg/L	WFD- UK TAG Report (2012)[1]
Aquatic Invertebrates	*Gammarus pseudolimnaeus,* 98 d, growth, NOEC	0.004 mg/L	WFD- UK TAG Report (2012)[1]
Aquatic Invertebrates	*Hydra viridissima*, 6 d, population growth, NOEC	0.110 mg/L	WFD- UK TAG Report (2012)[1]
Algae	*Pseudokirchneriella subcapitata*, 72 h,growth rate and biomass, NOEC	0.010 mg/L	WFD- UK TAG Report (2012)[1]

6.2 Mammalian toxicology data

No information retrieved

6.3 PNEC derivation

PNEC	Endpoint	Endpoint value	AF	PNEC value
PNEC$_{fw}$	*Lepomis macrochirus*, 289 d, LOEC	0.0052 mg/L	20	2.6E-04 (mg/L)[a]
PNEC$_{sed}$	-	-	-	-
PNEC$_{biota,sec pois}$	-	-	-	-
PNEC$_{biota, hh}$	-	-	-	-
PNEC$_{dw, hh}$	-	-	-	0.05 (mg/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.

[b] EU Drinking Water QS[7], refered to cyanide.

7. Risk Quotient (PEC/PNEC)

RQ	Value
RQ$_{fw}$	-
RQ$_{sed}$	-
RQ$_{biota,sec pois}$	-
RQ$_{biota, hh}$	-
RQ$_{dw, hh}$	-

8. References

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

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

[3] WATERBASE Database http://www.eea.europa.eu/data-and-maps/data/waterbase-rivers-6

[4] IPCheM database at http://ipchem.jrc.ec.europa.eu/

[5] 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

[6] 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

[7] 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

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