Comparison of two methods in deriving aquatic predicted no-effect concentration (PNEC) for α-Amylcinnamaldehyde, 1-Tridecanol and Paracetamol

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Miljövetenskaplig utbildning
Centrum för miljö- och klimatforskning
Ekologihuset
223 62 Lund

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Emma Holmén

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Emma Holmén

MVEM02 Degree Project for Master 1 year 15 hp, Lund university

Supervisor: Maria Hansson, Centre for Environmental and Climate Research (CEC), Lund University

CEC - Centre for Environmental and Climate Research
Lund University
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Abstract

This study is evaluating two methods in order to calculate predicted no effect concentrations (PNECs) used in environmental risk assessment for three chemicals (α-Amylcinnamaldehyde, 1-tridecanol and paracetamol). The methods used are Species Sensitivity Distributions (SSD) and the guideline from European Chemicals Agency (ECHA): "Guidance on information requirements and chemical safety assessment". The later method was conducted using both acute and chronic data. According to the PNEC value calculated the most toxic substance is 1-Tridecanol followed by α-Amylcinnamaldehyde and then Paracetamol which is the least toxic according to this study. A weakness using this kind of risk assessment is that the calculations are based on single species testing at a low organisation level which forms a gap in knowledge. When making an environmental risk assessment use the method with the lowest uncertainty if enough data is available, which in this study was SSD. The most toxic of the three evaluated chemicals was 1-tridecanol and the least toxic was paracetamol. One weakness with the use of toxicology data is that the available data usually are at the individual level on the organization hierarchy. This creates a gap between the level measured the level you want to measure.

Keywords: PNEC, Environmental risk assessment, ERA, α-Amylcinnamaldehyde, 1-tridecanol, paracetamol, Species Sensitivity Distributions, SSD, ECHA, Guidance on information requirements and chemical safety assessment

Abbreviations

BCF BioConcentration Factor

ECHA European Chemicals Agency

EC50 Effective Concentration, 50% of the test organisms

ERA Environmental Risk Assessment

EPA Swedish Environmental Protection Agency

HC5 hazardous concentration, 5% of the species

K_{ow} Octanol Water Coefficient

K_{oc} Soil organic carbon - water partitioning coefficient

LOEC Lowest Observed Effect Concentration

LC50 Lethal concentration, 50% of the test organisms

LOQ Limit of quantification

NOEC No Observed Effect Concentration

PNEC Predicted No Effect Concentration

PEC Predicted Effect Concentration

RQ Risk Quotient

SSD Species Sensitivity Distributions

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Introduction

During the industrial revolution the scientific and technological development increased rapidly. This brought better lives for people but also led to over-utilization of the natural resources and creating vast amounts of hazardous substances from industrial processes, which caused widespread contamination of the environment (Singh et al. 2016). Today we have a rapidly changing chemistry market, which is growing around 3% each year, with a market driven by price and performance rather than the health of humans and the environment (Van Lieshouta et al. 2015).

One of the most important sources of pollutants is the pharmaceuticals. Their high use in society together with being chemically stable means that urine and faeces contribute to spreading the substances to sewage (Hedlund 2018; Daniel et al. 2018). Pharmaceuticals have low emission rates in sewage treatment plants, which are causing increasing levels in the environment, especially aquatic compartments. Oceans and streams are accordingly usually the final stop for this group of emissions. There pharmaceuticals are likely to cause uncharacterized effects on non-target organisms due to their chemical and biological properties, being designed to be biologically active and can therefore cause effects on extremely low amounts (Daniel et al. 2018). They are also designed to be stable in order to reach their target, which makes them persistent in the environment. The presence of pharmaceuticals in the Swedish environment are very low and are not believed to cause any major problems, but the same cannot be said about the countries producing them, like China or India but also USA and other parts of Europe (Hedlund 2018).

Because modern people in the western world spend most of their lives indoors, it has become urgent to evaluate the kind of chemicals used indoors in order to prevent negative effects on people's health (KEMI, Swedish Chemical Agency 2012). One of these things are cleaning products which are used every day by millions of people. They help the consumers to keep their homes clean and hygienic and also prevent the spread of pathological bacteria (Cleanright n.d.). The companies manufacturing these products are starting to adjust to the increasing demand from the public, harder regulations and economic benefits (Van Lieshouta et al. 2015). Another chemical product used in order to make the home feel fresh and clean is different kinds of fragrances, used in cleaning products, air fresheners, food, etc. These can cause adverse health effect when exposed to humans through inhalation dietary- and dermal

exposure, for example cancer or allergic reactions with 36 of common fragrances are classified as the second one. The potential adverse health effects from exposure of fragrances is of public concern, especially in view of the air quality (Wolkoff & Nielsen 2017).

To deal with the problems of pollution, an idea of risk has been proven to be an attractive concept. The reason for this could be the quantitative approach and the ability to get down to the essence, even though a lot of factors are involved in the calculations (Posthuma et al. 2002).

Environmental risk assessment

In order for the public sector to make well-founded decisions about manufacturing or usage of chemicals an environmental risk assessment (ERA) is often made in order to evaluate if there are any risk for the environment or human health. This risk is often calculated through the ratio between the predicted effect concentration (PEC) and the predicted no effect concentration (PNEC). If the risk quotient (RQ) exceeds 1 then the PEC is higher than PNEC, and there is a potential risk associated with the usage of the substance.

$$PEC/PNEC=RQ$$

Hence, in order to derive the RQ you need information about the PEC and PNEC. To find out more about PEC an exposure assessment needs to be done. For this you need information about the volume of usage, information about the degradation in the treatment plant or a worst-case scenario if no information exists and the dilution in the recipient. Then you have the predicted dose which will end up in the environment. Then an effect assessment is needed to evaluate the toxic properties (Swedish Medical Products Agency 2004). This is performed by evaluating the effects on species from different trophic levels, which is then divided by a assessment factor (10 when using NOEC values from 3 trophic levels and 1000 when using short-term L(E)C50 from each of 3 trophic levels) in order to take into account unpredicted factors (Swedish Medical Products Agency 2004; ECHA 2008). This study will focus on different ways to derive PNEC.

Aim

The aim of this study is to compare two different methods of deriving the PNEC value for three different compounds: α-Amylcinnamaldehyde; 1-Tridecanol and Paracetamol. The methods will be assessed by evaluating the difference in the outcome of the PNEC-value, the type and amount of data used and the way the calculations are done. The two methods used in this study are (1) Species Sensitivity Distributions (SSD) and (2) The Guidelines from European Chemicals Agency (ECHA 2008): "Guidance on information requirements and chemical safety assessment". The latter method will be done in two ways: using chronic or acute data. These techniques will be compared to each other, discussing the difference in the PNEC values and strengths and weaknesses of the different techniques. Finally, recommendations will be presented on what to consider when using this method in an environmental risk assessment. These recommendations will help the future makers of environmental risk assessment in choosing the best method.

Ethical reflection

No tests on animals will be done in order to derive data used for calculating the PNEC values, data is only used from studies already performed. All personal information will be managed according to laws and regulations. Now discrimination will occur when retrieving information relevant for performing this study, due to people's gender, ethnic background, sexuality, etc.

Method

In order to find the information needed for this study a literature search was done by using databases as LUBsearch, PubChem, ECHA, TOXNET and libraries in order to find relevant books. The search words used was: ERA, environmental risk assessment, sensitive species distribution, SSD, derive PNEC, calculate PNEC, α-amylcinnamaldehyde, 1-Tridecanol, Paracetamol. The literature search was done during March-April the year of 2019.

PNEC values for the 3 different compounds were calculated using two methods (1) Species Sensitivity Distributions (SSD) and (2) by following the Guidelines from ECHA (2008): ”Guidance on information requirements and chemical safety assessment”.

The ecotoxicological values needed to derive PNEC (NOEC, LOEC, EC50) was accessed by using IUCLID 6. Data was collected from three trophic levels: Primary producers (e.g. algae), invertebrates (e.g. *Daphnia Magna*) and predators (e.g. fish). Bacteria was not used since the values was a lot higher than for the other taxa (102-103). Other databases like WikiPharma and ECOTOX were also used in order to find toxicological data (all data used for the study are represented in Annex 1).

A pilot study was conducted by using the ecotoxicological data available at IUCLID 6 for the substance α-Amylcinnamaldehyde. All data available was used (chronic och acute) concerning different endpoints (mortality, growth, immobilization and reproduction) and different data points (NOEC, LOEC, LC50 and EC50).

ECHA method

ECHA made a guideline in order to help stakeholders fulfil their duties concerning the EU chemical regulation; REACH (Registration, Evaluation, Authorisation and Restriction of Chemicals) and are focusing, among other things, on how to characterise the dose - response relationship for different environmental matrices. Hence, how to assess the effects of a substance by investigating by which concentration negative effects starts to appear, also called PNEC (ECHA 2008).

In using this method result from different laboratory tests are collected. The lowest value available is then divided with an assessment factor (figure 1). This factor is decided through looking at the uncertainty of the data used (e.g. usage of LC50

instead of NOEC, or acute testing instead of chronic). The higher the uncertainty, the higher assessment factor (table 2) (ECHA 2008). In this study the word uncertainty is used the same way as in the guideline and are referring to the possible scope of errors.

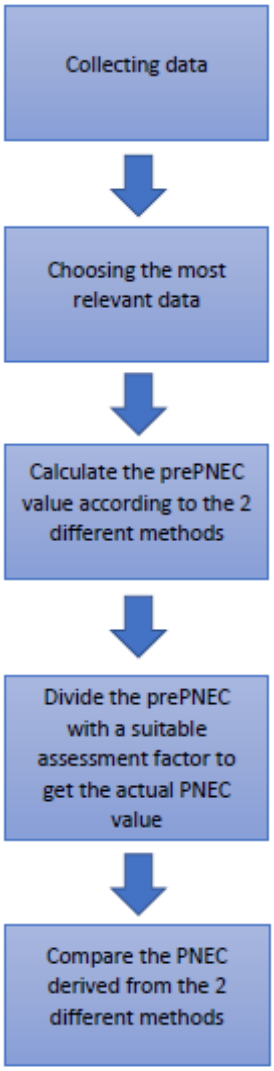

Figure 1. Flow chart over the work done in order to derive PNEC according to the two different methods (ECHA and SSD). PrePNEC is the concentration of the chemical before divided by an assessment factor.

This method was conducted by using both chronic and acute data in order to derive two values for each chemical from this method. The assessment factor used in this study was 10 for chronic studies and 1000 for acute studies according to the guideline.

Species Sensitivity Distributions (SSD) method

Different species have different sensitivities to different poisonous substances. A need developed for techniques, which takes many taxa and trophic levels into account and not just the most sensitive one. The idea is to represent the whole ecosystem. According to Posthuma et al. (2002), some researchers argue that NOEC should be used since adverse effects on sublethal traits are likely to be the ones to damage the ecosystem, since this effect occur at lower concentrations of toxic substances. Chronic data is preferred when performing an SSD, but acute data are often used because of greater availability (Posthuma et al. 2002).

The set of data used should be representative both statistically and ecologically for the ecosystem of interest. This is however not very common since this specific data may not be available, therefore the set of data used is more commonly based on the data which is available. When making a SSD analysis there is usually an assumption of 95% protection goal, hence 5% are allowed to be damaged (HC5). This is however defined from a policy decision and not science (Posthuma et al. 2002).

Three steps are required when making a SSD:

1. selection of toxicity data
2. statistical analysis
3. interpretation of the output (Posthuma et al. 2002)

When the HC5 is calculated the value should be divided by an assessment factor from 1-5 depending on the amount of uncertainties in the evaluation (ECHA 2008).

From the data collected, four values for each trophic level (algae, invertebrate and fish) were chosen to be a part of the SSD analysis, hence 12 values for each chemical. When choosing data, chronic values was preferred and the data points was preferred in this order (1) NOEC, (2) LOEC, (3) ECx and (4) LCx as the least preferred data point.

This set of data were then used to make the SSD calculation by using a Microsoft Excel sheet from the course applied ecotoxicology at Lund University. When making the SSD analysis the PNEC value 95% protection goal known as HC5 (also called prePNEC in this study) are assumed, which is the most common protection level used in SSD (Wheeler et al. 2002). This value was then divided by an assessment factor of 5. This was decided according to the factors described by ECHA (2008), for example: the represented level of taxonomic groups in this study was lower than the

recommended number. This study also used data from both chronic and acute studies with different data points instead of the recommendation of only using NOEC derived from chronic testing.

Result

Results from literature search

α-Amylcinnamaldehyde

α-Amylcinnamaldehyde is a non-synthetic flavour agent which has a spicy, cinnamon aroma and is the most potent compound in cassia oil and Ceylon cinnamon bark oil and is common in traditional food. It is also used as a scent with its Jasmine-like fragrance. The production and usage of the chemical (perfume and flavouring) could result to emissions to the environment. The exposure of the population is through consumer products e.g. soaps, detergents and perfumes (TOXNET 2012).

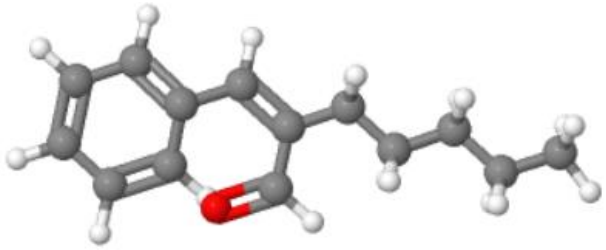

Figure 2. Structural formula for the flavour agent α-Amylcinnamaldehyde (CAS: 122-40-7) with the oxygen (O) shown as red. The molecule was made using http://biomodel.uah.es/en/DIY/JSME_old/draw.en.htm

1-Tridecanol

This chemical is imported or manufactured in the European Economic Area about 10 - 100 tonnes/year, being used in washing and cleaning products were it serves as phase modifier (Chagnes et al. 2011; ECHA 2018). This is an alcohol consisting of a saturated carbon chain (figure 3), which differs it from the phase modifiers used in the 1950-1960s when branched carbon chains were used instead. These were however hard for the microorganisms to decompose and therefor accumulated in the environment.

Therefore, unbranched carbon chains started to be manufactured which basically are the only ones used today (JD Vatten & Kvalitetskonsult n.d.).

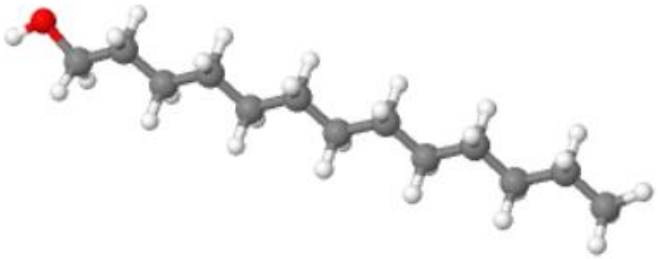

Figure 3. Structural formula for the alcohol 1-tridecanol (CAS: 112-70-9) with the oxygen (O) shown as red. The molecule was made using http://biomodel.uah.es/en/DIY/JSME_old/draw.en.htm

Paracetamol

Paracetamol is one of the active substances used in painkillers (Magnusson 2018). This kind of painkillers can be bought without a prescription and causes hundreds of overdoses every year in Sweden alone. Paracetamol is especially toxic to the liver since it is metabolized in this organ to a reactive compound which is damaging the liver cells (Sterner 2018). Due to the substances widespread use, this drug plays an important role among pharmaceuticals in the environment. One example of the negative effect's paracetamol is causing are oxidative stress in freshwater organisms (*D. magna*) (Daniel et al. 2018).

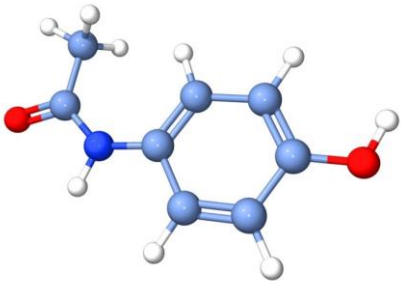

Figure 4. Structural formula for the pharmaceutical Paracetamol (CAS 103-90-2) with the oxygen (O) shown as red and the nitrogen (N) shown as dark blue. Figure is from Evans (n.d.). er organisms (D. *magna*) (Daniel et al. 2018).

Table 1. Some of the physical and chemical properties displayed for the chemicals evaluated in this study (α-Amylcinnamaldehyde, 1-tridecanol and paracetamol). The information is from TOXNET.

Chemical/Physical Properties			
	α-Amylcinnamaldehyde	1-Tridecanol	Paracetamol
Log K_{ow}	4.7	5.82	0.46
Vapour pressure (mm/Hg) 25°C	0.00431	4.36×10^{-4}	6.29×10^{-5}
BCF	586	600	3
K_{oc}	680	35,000	21
Solubility in water at 25 deg C	Insoluble in water	1.4 mg/l	14,000 mg/l

Results from pilot study

Result from the pilot study of α-Amylcinnamaldehyde: PNEC ECHA: 0,004, PNEC SSD: 0,006. When using the SSD method all data found in the literature search was used (Table 2) and then divided by 5, but for the ECHA method only the lowest one was used and divided by 10.

Table 2.. All data found during the data search for ecotoxicological values.

Legend

	predators (e.g. fish)
	invertebrates (e.g. Daphnia Magna)
	Primary producers (e.g. algae)

	NOEC mg/l	LOEC mg/l	EC50 mg/l	LC50 mg/l	species	chronic/acute	endpoint	duration
				0.91	fish	acute	mortality	96 h
				3	Brachydanio rerio	acute	mortality	96 h
				3.14	Danio rerio	acute	mortality	96 h
	0.169				fish	acute	growth	28 days
			0.28		dapnia	acute	immobilization	48 h
	0.041		0.041		dapnia	chronic	reproduction	21 days
	0.4		1.1		dapnia	acute	immobilization	48 h
α-Amylcinnamaldehyde			1.1		dapnia	acute	immobilization	48 h
			22.9		Desmodesmus subspicatus		Growth Inhibition Test	72 h
	0.21/0.66		1.5/2.3		green algae		growth rate/AUG	72 h
	0.154/0.15 4/0.154		1.88/1.24/ 1.18		green algae		growth rate/AUG/number of cells	72 h
	0.15		1.88		Pseudokirchneriella subcapitata		inhibition growth rate	73 h
				1.7	Oryzias latipes	acute	mortality	96 h
	0.64				Fathead Minnows (Pi	acute	mortality	96 h
				2.8	fish	acute	mortality	96 h
	0.22			0.61	daphnia	acute	mortality/immobilization	48 h
			0.5 mg/l		daphnia	acute	mortality/growth	48 h
1-Tridecanol				2.2	Mysidopsis bahia (my	acute	mortality	48 h
			0.51		daphnia	acute	growth	96h
	0.22	0.46			daphnia	chronic	mortality/reproduction	21 days
	0.0029/0.017		0.09		algae			72 h
			0.1		algae		growth	72 h
	0.028/0.09		0.56/0.72		algae		growth rate/AUG	
				160	o. Latipies	acute		96 h
				814	Pimephales promelas	acute		96 h
				814	Pimephales promelas			96 h
			378		zebrafish		mortality on embryos/eggs	48 h
				920/173	Brachydanio rerio/Lepomis macrochirus			96/48 h
	9.5/9.5/9.5				Oryzias latipes	chronic	growth/Relative organ weight/reproduction	
				11.85	D. Magna	acute		48h
				56.34	macrocopa	acute		48h
			3.5 mg/l		D. Magna	acute	not specified	48h
Paracetamol				20.1	D. Magna	acute		48h
			50		D. Magna	acute	imobilasitoion	48h
				269.153	D. Magna	acute		24h
	5.72/5.72/ 5.72				D. Magna	chronic	reproduction/survival /population growth (r)	21 days
		25.75/0.95			Moina macrocopa	chronic	survival/reproduktion	7 days
	0.46		3.5		D. Magna	chronic	reproduction	21 days
	1.25				D. Magna	chronic	immobilization	21 days
			112.666		algae		growth rate	72 h
	46/22		460/150		algae		growth rate/aug	72 h

Results from the ECHA and SSD methods

In this study the PNEC calculated with the SSD method was higher than both the values calculated with the ECHA method (Table 3 and Table 4). When comparing the PNEC value from acute and chronic data, the acute was lower (except for 1-tridecanol) and the assessment factor used was higher due to higher uncertainty. Hence, using methods with higher uncertainty leads to a lower PNEC value according to the results of this study. According to the PNEC value calculated the most toxic substance is 1-Tridecanol followed by α-Amylcinnamaldehyde and then Paracetamol which is the least toxic one. Since the lower the PNEC-value the more toxic the substance.

Table 3. The data used for the Species Sensitivity Distributions (SSD) analysis.

Paracetamol	22	0,46	160
	46	0,95	173
	112,666	1,25	378
	134	5,72	9,5
1-Tridecanol	0,0029	0,22	0,33
	0,017	0,22	1,7
	0,028	0,5	2,8
	0,09	0,51	0,64
α-Amylcinna-maldehyde	0,15	0,28	3
	0,15	0,28	3
	0,154	0,4	3,14
	22,9	1,1	0,169
	0,21	0,041	0,91

Table 4. The PNEC values derived through the guideline from ECHA (2008) and the species sensitivity distribution (SSD). Two ways was used in order to derive the PNEC according to the ECHA guideline: Using acute or chronic values and therefore adjusting the assessment factor.

Guidance on information requirements and chemical safety assessment from ECHA				
	Chemical	α-Amylcinnamaldehyde	1-Tridecanol	Paracetamol
Chronic	Concentration (prePNEC)	0.041 mg/l	0.0029 mg/l	0.46 mg/l
	Species	D. Magna (crustacean)	Green algae	D. Magna (crustacean)
	Data point	NOEC	NOEC	NOEC
	End point	Reproduction	AUG	Reproduction
	PNEC	$0.0041 = \frac{0.041}{10}$	$2.9 \times 10^{-4} = \frac{0.0029}{10}$	$0.046 = \frac{0.46}{10}$
Acute	Concentration	0.28 mg/l	0.5 mg/l	3.5 mg/l
	Species	D. Magna (crustacean)	D. Magna (crustacean)	D. Magna (crustacean)
	Data point	EC50	EC50	EC50
	End point	immobilization	mortality	not specified
	PNEC	$2.8 \times 10^{-4} = \frac{0.28}{1000}$	$5 \times 10^{-4} = \frac{0.5}{1000}$	$0{,}0035 = \frac{3.5}{1000}$
Species sensitivity distribution (SSD)				
	HC5 (prePNEC)	0.028 mg/l	0.006 mg/l	0.383 mg/l
	PNEC	$0.006 = \frac{0{,}028}{5}$	$0.001 = \frac{0{,}006}{5}$	$0.077 = \frac{0{,}383}{5}$

Discussion

This study shows that the PNEC value decreases with increasing uncertainty. The most toxic of the three evaluated chemicals was 1-tridecanol and the least toxic was paracetamol. One weakness with the use of toxicology data is that the available data usually are at the individual level on the organization hierarchy. This creates a gap between the organization level evaluated the organization level you want to evaluate.

Difference between the methods

The higher the uncertainty is the lower the PNEC becomes which makes the restrictions for the emissions stricter. But is this really a problem? Is it not positive that the restrictions is harder? Especially considering the precautionary principle described in Article 191 of the Treaty on the Functioning of the European Union (TFEU) and is the principle on which REACH is built on. However, according to the precautionary principle, there must be a potential risk and decisions cannot be made on arbitrary. Restrictions also have to be technical and economical reasonable (EU 2012; EUR-Lex n.d.; Swedish Environmental Protection Agency 2009). This means that the emissions restrictions cannot be lower than the limit of quantifications (LOQ) values from the laboratories. If they were to be lower, it would be impossible to investigate if the concentrations are too high or not. Since it is impossible to measure. The restrictions also have to be reasonable from an economic point of view, this is one of the things which is taken into account when calculating the HC5 in the SSD, 5% damage are allowed to happen, but the ecosystem as a whole should not be damaged. In the other methods, only the lowest value is used which might not cause any severe effects on the ecosystem. It might not be relevant to use a value for PNEC which only is lethal for the most sensitive *D. magna* but not anything else. Therefore, it is important to decide on a protection level in the risk assessment included how much are allowed to be damaged and make the calculations according to that. The factors to consider could for example be: are there any threatened species in this area? for example according to The IUCN Red List of Threatened Species. Does this area provide any important ecosystem services? and so on.

A study provided by Rämö et al. (2018) showed that calculating toxicity for fish and arthropods together is overprotective for fish and underproductive for

arthropods. This is not a problem for the ECHA method since only the lowest value is used. It also showed that SSD is not suitable for estimation of mixtures of chemicals, since the results are derived from individual substances. None of the methods take adverse- or cocktail effects when a pollutant are mixed with other pollutants which may occur in the natural environment. Therefore, a pollutant can be safe at a certain concentration but when mixed with something else, the toxic ability can be enhanced and caused toxic reactions (Hedlund 2013).

When using only using the lowest value available the PNEC can be too low, since this particular value could be an extreme value, and no HC is estimated. So, no damage is allowed to happen which might not be of ecological relevance.

Organisation level

Basically, all of the data (except one study) used was based on single species tests at the individual level of the organisation hierarchy. In only investigating the lower organisation level, a gap in knowledge is formed since usually the higher levels are the ones of interest eg. ecosystem level. If only the lower levels are investigated then there is a gap between what is investigated and what you want to protect, this increases uncertainty (Rohr et al. 2016). It could for example be that a certain concentration is lethal for 50% of the *D. magnas* but the ecosystem might not be affected since the fishes may switch to eat other zooplankton. This kind of processes is not taken into account in single species tests (Posthuma et al. 2002).

Another factor missed in this kind of testing is the species interaction (community level), for example: a certain concentration might not cause any measured effect on the test organisms, but through biomagnification the concentration within the species can still rise to lethal concentrations in the higher trophic levels (Posthuma et al. 2019). According to the BCF and log K_{ow}: α-Amylcinnamaldehyde and 1-Tridecanol have a potential of bioaccumulation (TOXNET) and therefore it is likely for these compounds to biomagnify if they are persistent and non-biodegradable (Bart et al. 2013). This means that even if the RQ is below 1 there can still be a risk. But in this case; none of the chemicals are very persistent (TOXNET; Li et al. 2015). Even if the substance is degradable, the degradation products formed can still be both toxic and persistent (KEMI n.d.).

Selection of species

When making an environmental risk assessment it can be a good idea to use test species who are endemic in the specific site. Since their sensitivity is the one of

importance. It is however not possible to conduct tests or find data for these specific species and is not justifiable from an ethic point of view. Therefore, a keystone- and umbrella species can be used. There is no source found on zebrafish being a keystone- or umbrella specie. *D. magna* however are widely used in toxicity testing both nowadays and historically. The main reason for this is because they are small, most water and food can sustain them, they have high fecundity, short life span and parthenogenetic reproduction (Koivisto 1995). In addition to this; *D. magna* is described as an important key species who plays an important role in the food-web, acting both as a primary consumer of phytoplankton and as a key pray for higher trophic levels e.g. fish by Miner et al. (2012). *D. magna* therefore serves as a strong ecological interactor with unique qualities and are usually referred to as a key species in the literature. Even though *D. magnas* are spread in the aquatic environment they do not inhibit the lager lakes due to the high predation from fish, which usually are the lakes affected by pollutants. This species are also bigger than most other zooplanktons which make them more tolerant to pollutants. They are also resilient to low oxygen conditions, high pH and can handle a wide range of salinity and temperature (Koivisto 1995). Since *D. magna* is not exciting in lakes inhibited by fish. It is not likely that it can cause any cascade effects. This said, it can be an idea to look into other invertebrates as well and not just *D. magna*. But like mentioned previously, you are dependent on the data available.

In the lower trophic levels there are primary producers, with the most important one in the aquatic ecosystems being algae, since they provide food for all higher trophic levels (Chapman. 2013). This said, the algae are the foundation for life in the aquatic environment and since most life in the aquatic environment would be knocked out if the algae were to disappear, it is of importance to have this trophic level represented in the study (Wellborn et al. 2015).

Conclusions

- When making an environmental risk assessment use the method with the lowest uncertainty if enough data is available, which in this study was SSD.
- The higher the uncertainty the lower the PNEC value becomes.
- The most toxic of the three evaluated chemicals was 1-tridecanol and the least toxic was paracetamol.
- One weakness with the use of toxicology data is that the available data usually are at the individual level on the organization hierarchy. This creates a gap between the organization level assessed the organization level you want to assess.

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