

Accounting for the dissociating properties of organic chemicals in LCIA: An uncertainty analysis applied to micropollutants in the assessment of freshwater ecotoxicity

Sérgio Alberto Morais ^{a,b,*}, Cristina Delerue-Matos ^b, Xavier Gabarrell ^{a,c}

^a *SosteniPrA (UAB-IRTA-Inèdit), Institut de Ciència i Tecnologia Ambientals (ICTA), Universitat Autònoma de Barcelona (UAB), 08193 Bellaterra, Barcelona, Spain*

^b *REQUIMTE, Instituto Superior de Engenharia do Porto, Instituto Politécnico do Porto, Rua Dr. António Bernardino de Almeida, 4200-072 Porto, Portugal*

^c *Departament d'Enginyeria Química, Escola d'Enginyeria, Universitat Autònoma de Barcelona (UAB), 08193 Bellaterra, Barcelona, Spain*

ABSTRACT

In life cycle impact assessment (LCIA) models, the sorption of the ionic fraction of dissociating organic chemicals is not adequately modeled because conventional non-polar partitioning models are applied. Therefore, high uncertainties are expected when modeling the mobility, as well as the bioavailability for uptake by exposed biota and degradation, of dissociating organic chemicals. Alternative regressions that account for the ionized fraction of a molecule to estimate fate parameters were applied to the USEtox model. The most sensitive model parameters in the estimation of ecotoxicological characterization factors (CFs) of micropollutants were evaluated by Monte Carlo analysis in both the default USEtox model and the alternative approach. Negligible differences of CFs values and 95% confidence limits between the two approaches were estimated for direct emissions to the freshwater compartment; however the default USEtox model overestimates CFs and the 95% confidence limits of basic compounds up to three orders and four orders of magnitude, respectively, relatively to the alternative approach for emissions to the agricultural soil compartment. For three emission scenarios, LCIA results show that the default USEtox model overestimates freshwater ecotoxicity impacts for the emission scenarios to agricultural soil by one order of magnitude, and larger confidence limits were estimated, relatively to the alternative approach.

Keywords:

USEtoxLCA, Freshwater, ecotoxicity, Micropollutants, Dissociating organics Risk assessment

1. Introduction

Sorption of chemicals released to the environment to solid surfaces is a dominating process driving their distribution in soil, surface waters and sediments. Therefore, the solid–water partitioning coefficient, K_d , is a key parameter to model the mobility and fate of chemicals in the environment. Many transport processes in environmental systems, as well as bioavailability for uptake by exposed biota and degradation, are directly related to K_d . Experimental K_d values are often not available in the literature. For example, in the USEtox LCIA model 83% of the chemicals present in the organic

chemicals database have estimated K_d values. The estimation of this parameter in LCIA models, such as IMPACT2002+, USES-LCA, EDIP 2003 or USEtox, is based on conventional non-polar partitioning models correlated only to the octanol–water partition coefficient, K_{OW} , that do not adequately model the mechanism of sorption of dissociating organic chemicals to organic colloids in soil, which consists of organic matter and inorganic clay minerals. These correlations are particularly true for lipophilic compounds, however, the driving force behind the sorption of cations may be electrical attraction to the negatively charged sorption sites in soil

since, at the same lipophilicity, the sorption of cations is stronger than of neutral bases, making it unlikely that the process behind is lipophilic sorption [1]. Recently, Droge and Gross [2] cited an ample number of recent studies that have shown that the dominant sorption process for organic cations is cation-exchange at negatively charged sorption sites in natural organic matter and whole soils/sediments. The sorption of anions generally is moderate but not negligible, even for very hydrophilic anions [3]. Therefore, a different degree of anion, cation, and neutral molecule sorption can be expected, with cations showing the highest potential for sorption. Moreover, other fate parameters depend upon the dissociation of the molecule, such as the Bioconcentration Factors (BFs) or the partitioning coefficient between dissolved organic carbon and water, K_{DOC} .

In the USEtox model [4], an ecotoxicological characterization factor (CF) of a chemical in freshwater is the product between a fate factor, that represents the persistence in the environment described by processes such as degradation and inter-compartment transfer, an exposure factor, that represents the bioavailability (i.e., the fraction of chemical dissolved in the freshwater compartment), and an effect factor. 21% of chemicals in the USEtox organics database are 50% or more in ionic phase at physiological pH (i.e., acids $pK_a < 7.4$, bases $pK_a > 7.4$). Therefore, CFs of these chemicals are labeled in the model as interim whereas relatively high uncertainty is expected. Moreover, 45% of chemicals, at least those for which pK_a values are available, suffer any degree of dissociation at the environmental pH interval of the model's continental scale (3.2–8.5) [5].

The aims of this study were (1) to apply to the USEtox model alternative regressions that account for the ionized fraction of a molecule to estimate fate parameters; (2) to identify the most sensitive model parameters in the estimation of CFs by Monte Carlo analysis in both the default USEtox model and the alternative approach, and (3) to propagate uncertainties and compare both approaches in the impact assessment of different emissions scenarios to different environmental compartments.

2. Methodology

Three emission scenarios to freshwater were considered in this study: (a) direct emission to the freshwater compartment of a wastewater treatment plant (WWTP) effluent, (b) direct emission to agricultural soil by using WWTP effluent as reclaimed water, and (c) emission to agricultural soil by using WWTP biosolids as soil amendment. The inventory data were gathered from a Neptune FP6 Project report [6] (Supplementary data,

Table S1). It contains twenty micropollutants, thirteen of which are acidic compounds, six basic compounds and one neutral compound (carbamazepine). For the biosolids-amended soil scenario, in order to account for differences in the sorption, desorption, and degradation of compounds between the biosolid and soil matrices, the biosolids-amended soil compartment was modeled as a biosolids compartment nested in the agricultural soil compartment (Fig. 1).

The multimedia model USEtox was chosen in the present study because it results from a consensus building effort, under the auspices of UNEP and SETAC, amongst modelers and, hence, the underlying principles reflect common and agreed recommendations from these experts; furthermore it is the recommended LCIA model by the ILCD (International Reference Life Cycle Data System) Handbook of the European Union [7]. In the USEtox model, the ecotoxicity factor (effect factor), which expresses the change in the potentially affected fraction (PAF) species that experiences an increase in stress for a change in contaminant concentration, in $PAF \text{ m}^3 \text{ kg}^{-1}$, is based on the hazardous concentration (HC) of a chemical affecting 50% of a tested species over their chronic

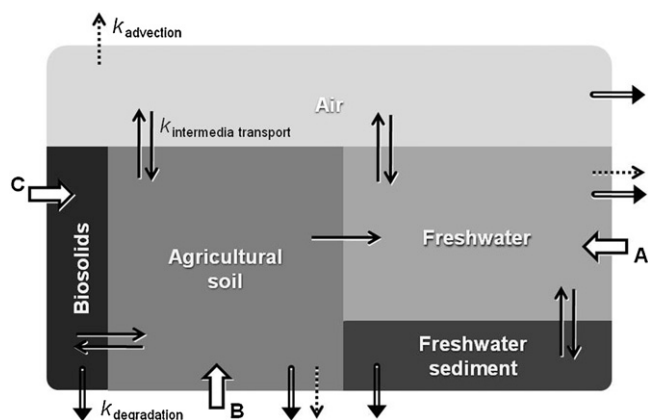


Fig. 1. Five-compartment system for the dissipation of micropollutants from (A) direct emission to freshwater of WWTP effluent, (B) emission to agricultural soil of WWTP effluent as reclaimed water, (C) emission to agricultural soil of biosolids as soil-amendment. In a given environmental compartment, bold arrows represent intermedia transport rates, dashed arrows represent advective transportation rates out the system, and double-line arrows represent degradation rates.

effect concentration affecting 50% of tested individuals (EC50), also called HC50EC50. Experimental EC50s were gathered from the ECOTOX database [8] and literature reports. To complete missing experimental data, it was included quantitative structure activity relationship (QSAR) data using the software program ECOSAR v1.00 [9].

The alternative regressions applied in the alternative approach, as well as estimation routines of abiotic degradation rates for both approaches, and the parameters included in the Monte Carlo analysis are described in sections below.

2.1. Partition coefficients

In the USEtox model v1.01 the values of experimental octanol–water partition coefficient, K_{OW} , are obtained from the estimation programs interface (EPI) suiteTM [10] and, in case unavailability, they are estimated by the software KOWWIN v1.67a [11], which estimates K_{OW} values corrected for the neutral species ($K_{OW,n}$). A different approach was followed for the alternative approach in the case of dissociating compounds. K_{OW} values published in the literature are often the sum of the K_{OW} values of neutral and ionic molecules at the experimental pH, that is, they are apparent K_{OW} values (D_{OW}). Therefore, to treat the ionic and neutral fractions separately, experimental K_{OW} values of the neutral species requires a correction of the pH at which D_{OW} was determined, often not reported explicitly. Therefore, for dissociating compounds at environmental pH, estimated values are preferred to measured values. The software KOWWIN v1.67aTM [11] was used to estimate K_{OW} values corrected for the neutral species since the regressions applied in the present study to estimate other partition coefficients are correlated to $K_{OW,n}$.

The soil–water partitioning coefficient normalized by the organic carbon content, K_{OC} in l kg^{-1} , is estimated in the USEtox model, if no experimental data is available, by KOCWIN v2.0TM using the first-order molecular connectivity index (MCI) [12], which is applicable to neutral compounds or to the neutral fraction of dissociating compounds as long as $K_{OW,n}$ is used in the regression. In our study experimental K_{OC} values were preferred for neutral and, in case of dissociating compounds, only if these remain essentially in one charged state or neutral at environmental relevant pHs (Supplementary data, Table S2). Otherwise, due to the variability of the fractions of neutral and ionic species, such K_{OC} values obtained at a given environmental pH would not be suitable for the interval of environmental pH values considered in this study. For these

compounds the soil–water partitioning coefficients are correlated to $K_{OW,n}$, pK_a and pH by using the Franco and Trapp regression equations [1]:

$$K_{OC} = f_n \cdot 10^{(0.54 \log K_{OW,n} + 1.11)} + (1 - f_n) \cdot 10^{(0.11 \log K_{OW,n} + 1.54)} \quad \text{for acids} \quad (1)$$

$$K_{OC} = f_n \cdot 10^{(0.37 \log K_{OW,n} + 1.70)} + (1 - f_n) \cdot 10^{(0.65 \log K_{OW,n} + 1.70)} \quad \text{for bases} \quad (2)$$

where pK_a is the negative logarithm (\log_{10}) of the dissociation constant, f is $K_{OW,n}/(K_{OW,n} + 1)$, and f_n is the fraction of neutral molecules according to the Henderson–Hasselbalch equation:

$$f_n = \frac{1}{1 + 10^{i(pH - pK_a)}} \quad (3)$$

where i is the valence number, which is +1 for acids and –1 for bases. The above equations are applicable only to monovalent acids and bases; for compounds with two cationic or anionic dissociating groups, only the first dissociation was considered. pK_a values were taken from the EPI suiteTM [10]. For compounds without experimentally verified pK_a values, values were estimated using the SPARC software program [13], in which pK_a values are given for OH, COOH, or the highest NH_x functional group.

In the USEtox model the partitioning coefficient of organic pollutants between dissolved organic carbon and water, K_{DOC} in $l \cdot kg^{-1}$, is estimated using the predictive relationship of $K_{DOC} = 0.08 \times K_{OW}$ for non-ionic compounds [14]. In the alternative approach, for dissociating substances, it is assumed a K_{DOC}/K_{OC} ratio of solutes equal to one. This assumption is valid when the nature of the dissolved organic matter released from the soil/sediment bulk organic matter is similar to that of the soil/sediment bulk organic matter [15].

2.2. Bioconcentration factor in fish

Uptake by exposed biota in environmental systems is a relevant fate process in a human toxicological impact or risk assessment. However, bioconcentration factor in fish, BCF_{fish} in $l \cdot kg^{-1}$, is a parameter used in the USEtox model to calculate the exposure factor, i.e., the fraction of chemical dissolved in the freshwater compartment. Therefore, it was included in

present in the inventory. The USEtox model does not address estimation routines for these mechanisms, therefore the following models and assumptions were applied in both the alternative approach and the default USEtox to estimate direct and indirect photodegradation rates.

Experimental photolysis half-lives based on the literature may not reflect consistently a given geographical scale due to differences in experimental conditions, whereas photodegradation rates depend on the intensity of solar irradiation, water depth, organic matter composition, eutrophic conditions, latitude and season [18,19], thus introducing uncertainty. In the present study, average full day direct photolysis rates for winter and summer seasons were calculated by GCSOLAR [20]. Experimental molar absorption coefficients in function of the UV/VIS wavelength range (ϵA , in $l \cdot mol^{-1} \cdot cm^{-1}$) were gathered in the literature [19,21–28] as well as experimental quantum yields of compounds (Supplementary data, Table S2). Rates were estimated for a well-mixed water

the analysis. BCF_{fish} is the concentration of a chemical in the fish divided by the dissolved concentration of the chemical in the surrounding water. In the USEtox model the estimation of BCF_{fish} is obtained using K_{OW} regression-based estimates from the BCFBAF v3.00 software program [16]. In our study, for dissociating compounds at the freshwater environmental pH interval, the regression equations of Fu et al. [17] were applied because they allow variations in the environmental pH:

$$BCF = f_n \cdot 10^{(0.64 \log K_{OW,n} - 0.12)} + f_d \cdot 10^{(0.37 \log K_{OW,n} + 0.06 pK_a - 0.51)} \quad \text{for acids} \quad (4)$$

$$BCF = f_n \cdot 10^{(0.62 \log K_{OW,n} - 0.15)}$$

layer of 50 cm thickness [29]. Absorption attenuation coefficients of pure water in function of wavelength were assumed for the water body, as well as a depth of 3 m [30], the latitude range of 40–60°, and assuming a perfectly clear sky. Ozone layer thickness

values were obtained from satellite data [31]. For compounds without experimental quantum yields available (atenolol), maximum and minimum possible direct photolysis rates were estimated by assuming quantum yield equal to one and zero, respectively.

Indirect photolysis reactions occur due to the presence of chemical transients generated by natural water constituents. The hydroxyl radical, $\bullet\text{OH}$, is the most reactive of those intermediates

due to its non-selective and highly electrophilic nature [32] and the only transient considered in this study. Pseudo-first order rates were calculated by multiplying bimolecular rate constants (k_{OH} , in $\text{M}^{-1}\text{s}^{-1}$) for the reaction with $\bullet\text{OH}$ (Supplementary data, Table S2)

by the hydroxyl radical concentration, reported to be present at 10^{-14} – 10^{-17} M in surface waters [33].

Currently, the understanding of the effects of the

$$+ f_d \cdot 10^{(0.28 \log KOW_n + 0.84 - 0.07 \text{ pKa})} \quad \text{for bases} \quad (5)$$

The equations are valid in the range $-0.36 < \text{pKa} < 10.61$. Therefore, the minimum or maximum pKa values outside the calibrated range were applied.

2.3. Degradation

Abiotic degradation mechanisms in the freshwater compartment are important elimination processes for most compounds

in the biosolid matrix on the persistence of compounds in agricultural soils is limited [34], therefore, for the scenario of emission to agricultural soil from biosolids application as soil amendment, biodegradation rates in biosolids were estimated by extrapolation from biodegradation rates in soils. The calculation of the probabilistic characterization factors includes an interval of extrapolation factors (Table 1).

2.4. Monte Carlo analysis

Monte Carlo analysis was conducted on the estimation of characterization factors in both approaches. The parameters included in the Monte Carlo analysis are described in Table 1. The analysis includes:

- (1) The variability of environmental parameters (fraction of organic carbon, f_{OC} , in agricultural soil, pH of freshwater and agricultural soil, concentration of hydroxyl radical in freshwater, and rain rate) and of direct photolysis rates in the USEtox continental scale.
- (2) The uncertainty of ecotoxicological impact characterization.

Uncertainty distributions of HC50EC50 values were estimated

according to Payet parametric method [37], which is based on the student distribution for calculating the confidence interval on the mean.

- (3) The uncertainties associated with the regression equations adopted in the model to estimate partition coefficients, BCFs and biodegradation rates.
- (4) The extrapolation of parameter values from one compartment to another (biodegradation rates in biosolids) and from other parameter values (K_{DOC} from K_{OC}).

Table 1

Probability distributions for the 16 regression error parameters (a1–a16), experimental KOC values, experimental biodegradation rates ($k_{\text{biodeg, water}}$, $k_{\text{biodeg, soil}}$), experimental bimolecular $\bullet\text{OH}$ rate constants in water ($k_{\text{OH, water}}$), and environmental parameters (pH and f_{oc} in agricultural soil, $[\bullet\text{OH}]$ in freshwater, and rain rate) included in the Monte

Carlo simulation. The relation of the calibration coefficients to the actual model parameter values is shown in the last column. *Sdev* denotes standard deviation, *exp* denotes experimental values, *CI* denotes confidence interval, and *DF* denotes degrees of freedom. Asterisks (*) denote base case parameter values.

Parameter	Distribution	Mean	Spread	Relation to model parameters
a	Uniform	1	[0.5, 1.5]	$k_{\text{biodeg, biosolids}} = k_{\text{biodeg, soil}} \times a1^{-1}$
1	Normal	-3.18×10^{-7}	$Sdev = 2.63 \times 10^{-7}$	$k_{\text{biodeg, soil}} = k_{\text{biodeg, soil}}^* \pm a2$
a	Normal	1.26×10^{-7}	$Sdev = 4.25 \times 10^{-8}$	$k_{\text{biodeg, soil}} = k_{\text{biodeg, soil}}^* \pm a2$
a	Normal	-3.15×10^{-7}	$Sdev = 4.41 \times 10^{-1}$	$k_{\text{biodeg, water}} = k_{\text{biodeg, water}}^* \pm a1_*$
a6	Normal	-1.61×10^{-2}	$Sdev = 1.13 \times 10^0$	$\text{Log KOC} = \text{Log KOC}^* \pm a6$
a7	Normal	-7.64×10^{-1}	$Sdev = 1.19 \times 10^{-0}$	$\text{Log KOC} = \text{Log KOC}^* \pm a7$
a	Normal	2.23×10^{-2}	$Sdev = 5.36 \times 10^{-1}$	$\text{Log KOC} = \text{Log KOC}^* \pm a8$
8	Normal	4.45×10^{-2}	$Sdev = 4.74 \times 10^{-1}$	(acids regression) $\text{Log KOC} = \text{Log KOC}^* \pm a9$ (bases regression)
a11	Normal	4.50×10^{-1}	$Sdev = 8.97 \times 10^{-1}$	$\text{Log BCF}_{\text{fish}} = \text{Log BCF}_{\text{fish}}^* \pm a11$
a12	Normal	5.54×10^{-1}	$Sdev = 2.01 \times 10^{-1}$	$\text{Log BCF}_{\text{fish}} = \text{Log BCF}_{\text{fish}}^* \pm a12$
a	Normal	5.15×10^{-2}	$Sdev = 5.41 \times 10^{-1}$	$\text{Log BCF}_{\text{fish}} = \text{Log BCF}_{\text{fish}}^* \pm a13$
1	Normal	2.65×10^{-2}	$Sdev = 6.61 \times 10^{-1}$	(acids regression) $\text{Log BCF}_{\text{fish}} = \text{Log BCF}_{\text{fish}}^* \pm a13$
a16	Uniform	1	[0.04, 5.9]	$\text{KDOC} = \text{KOC}^* \times a16$ (dissociating compounds)
$\log_{10} \text{HCL5UEC50}$	Student	$\log_{10} \text{HCL5UEC50}$	$95\% \text{ CI } \pm t_{n-1} \times Sdev(\log_{10} \text{EC50})$	
<i>exp</i> KOC	Lognormal		b	
<i>exp</i> $k_{\text{biodeg, water}}$	Lognormal		c	
<i>exp</i> $k_{\text{biodeg, soil}}$	Lognormal		c	
<i>exp</i> $k_{\text{OH, water}}$	Lognormal		c	
$[\bullet\text{OH}]$ in water (M)	Uniform		$[10^{-14}, 10^{-11}]$ (min, max)	
pH agricultural soil	Triangular	7	[3.2, 8.5] (min, max)	
pH freshwater	Triangular	7	[5.5, 8.3] (min, max)	
f_{oc} agricultural soil	Triangular	0.02	[0.01, 0.1] (min, max)	
Rain rate (mm/year)	Triangular	700	[250, 1500] (min, max)	

^a Is the t value from the student table for a 95% confidence interval with $n-1$ degree of freedom, where n is the size of sample (or number of species tested), and *Sdev* is the standard deviation of the $\log_{10} \text{EC50}$ s.

^b Experimental values are shown in [Supplementary data, Table S2](#).

^c Experimental values are shown as half-lives in [Supplementary data, Table S2](#).

(5) The experimental parameter values (partition coefficients, biodegradation half lives in water and soil, and bimolecular hydroxyl radical rate constants). The geometric mean and the geometric standard deviation of experimental values were set as uncertainty parameters assuming a lognormal distribution.

The training and validation sets used to derive the regressions adopted in the model were used to derive residual estimation errors between estimated and experimental data [1,11,12]. The training and validation sets of Franco and Trapp [1] used to derive regression to predict KOC of acids and bases were used to generate residual estimation errors of the KOCWIN software applied to dissociating substances in the default USEtox model (parameters a6 and a7 in Table 2). Likewise, the training and validation sets of Fu et al. [17] used to derive

regression to predict BCF_{fish} of acids and bases were used to generate residual estimation errors of the BCFBAF software applied to dissociating substances in the default USEtox model (parameters a11 and a12 in Table 1). The mean error and its probability distribution were fit into the regressions as uncertainty parameters (parameters a3 to a15 in Table 2). It should be noted that experimental KOC values on the Franco and Trapp training and validation sets were obtained at the pH 4.5 for bases and 5.8 for acids. Nevertheless, it is assumed constant uncertainty parameters for the environmental pH interval. Experimental biodegradation rates gathered in the literature of micropollutants were used to derive

residual estimation errors of the procedure adopted in USEtox to estimate biodegradation rates.

In the USEtox model, uncertainty parameters on the estimation of the partitioning coefficient between dissolved organic carbon and neutral organic pollutants in water, K_{DOC} in L kg^{-1} , are provided by Burkhard [14]. For dissociating substances, it is assumed a K_{DOC}/K_{OC} ratio of solutes equal to one. However, if the dissolved organic matter is more hydrophilic than the soil/sediment bulk organic matter, they tend to escape from soil/sediment particles to the aqueous phase, and the ratios of K_{DOC}/K_{OC} of these solutes will be less than one [15]. In addition, when the sources and nature of the dissolved organic matter and soil/sediment organic matter are different, the ratios of K_{DOC}/K_{OC} of solutes will have a broad range. The broader range of K_{DOC}/K_{OC} ratios estimated by Ding and Wu [15] is assumed in the Monte Carlo analysis (parameter a16). The environmental variability of suspended matter and dissolved organic carbon concentration in freshwater was found to be negligible in terms of sensitivity to CFs values.

In ecotoxicological impact characterization, the inherent uncertainty of QSAR data from the software program ECOSAR was not included on the overall uncertainty of ecotoxicological impact characterization.

The uncertainties of GCSOLAR model estimates were not treated in the study but rather the variability of direct photodegradation rates considering the geographical scale. Therefore, the maximum and minimum of the uniformly distributed photodegradation rate

Table 2

Probabilistic characterization factors of freshwater ecotoxicity for three emission scenarios in PAF m³ day kgemitted⁻¹. Uncertainty intervals are log-normally distributed. Values in parenthesis denote default USEtox values.

	Direct emission to water soil			Emission to agricultural soil			Emission from biosolids to agricultural soil		
	Mean	95% confidence interval		Mean	95% confidence interval		Mean	95% confidence interval	
Atenolol	6.19E+00 (5.55E+00)	2.02E-01 (2.21E-01)	4.29E+01 (3.52E+01)	7.38E-03 (7.46E-01)	3.55E-05 (1.33E-03)	4.08E-02 (4.72E+00)	5.42E-03 (7.24E-01)	2.87E-06 (7.88E-04)	2.95E-0 (4.51E+0)
Bezafibrate	1.64E+01 (1.56E+01)	2.36E+00 (2.37E+00)	9.82E+01 (9.99E+01)	1.36E-01 (9.51E-02)	7.43E-03 (2.99E-04)	8.34E-01 (6.32E-01)	1.41E-01 (9.99E-02)	6.71E-03 (1.51E-05)	8.95E-0 (5.89E-0)
Carbamazepine	2.09E+01 (2.10E+01)	2.98E+00 (2.97E+00)	1.27E+02 (1.29E+02)	2.31E-01 (2.20E-01)	2.07E-02 (2.04E-02)	1.44E+00 (1.28E+00)	2.15E-01 (2.15E-01)	1.94E-02 (1.94E-02)	1.27E+0 (1.33E+0)
Clarithromycin	8.14E+02 (8.38E+02)	3.66E+01 (3.92E+01)	4.30E+03 (4.69E+03)	8.21E-01 (3.81E+01)	8.20E-03 (1.96E-01)	5.45E+00 (2.19E+02)	5.99E-01 (3.73E+01)	9.43E-04 (1.05E-01)	4.12E+0 (2.27E+0)
Clindamycin	7.56E-01 (8.06E-01)	7.12E-02 (7.32E-02)	3.49E+00 (3.60E+00)	1.38E-03 (8.85E-02)	1.97E-05 (5.05E-04)	8.65E-03 (4.53E-01)	1.16E-03 (8.79E-02)	2.60E-06 (2.35E-04)	7.38E-0 (4.50E-0)
Clotibric acid	6.81E+00 (6.16E+00)	6.42E-01 (6.28E-01)	4.28E+01 (3.65E+01)	5.97E-01 (3.03E-01)	4.26E-03 (4.22E-04)	1.33E+00 (1.99E+00)	2.13E-01 (3.07E-01)	3.82E-03 (1.14E-04)	1.42E+0 (2.09E+0)
Diatrizoate	5.66E-03 (5.59E-03)	9.50E-04 (9.34E-04)	3.06E-02 (3.01E-02)	5.02E-04 (8.47E-04)	1.37E-05 (3.93E-06)	2.92E-03 (5.20E-03)	1.50E-05 (8.38E-04)	1.37E-06 (2.85E-06)	3.11E-0 (5.07E-0)
Diclofenac	1.12E+01 (1.12E+01)	1.24E+00 (1.20E+00)	6.83E+01 (6.70E+01)	3.98E-02 (4.26E-02)	5.51E-04 (1.96E-05)	2.50E-01 (2.84E-01)	4.11E-02 (3.78E-02)	2.03E-04 (7.98E-08)	2.81E-0 (2.75E-0)
Erythromycin	7.99E+01 (7.48E+01)	7.53E+00 (7.72E+00)	4.84E+02 (4.43E+02)	1.14E+00 (1.76E+00)	1.37E-02 (1.74E-03)	7.61E+00 (1.20E+01)	1.06E+00 (1.74E+00)	8.51E-03 (9.55E-05)	6.95E+0 (1.20E+0)
Ibuprofen	2.01E+01 (2.02E+01)	1.93E+00 (1.93E+00)	1.29E+02 (1.34E+02)	4.26E-02 (3.83E-02)	1.16E-03 (1.20E-03)	2.61E-01 (2.35E-01)	3.29E-02 (2.93E-02)	5.83E-04 (6.30E-04)	2.10E-0 (1.84E-0)
Iohexol	2.99E-03 (3.04E-03)	3.60E-05 (3.52E-05)	2.19E-02 (2.15E-02)	4.13E-04 (4.25E-04)	2.95E-06 (2.32E-07)	2.98E-03 (3.11E-03)	4.20E-04 (4.25E-04)	3.00E-06 (2.32E-07)	2.90E-0 (3.11E-0)
Iopamidol	1.32E-03 (1.30E-03)	1.90E-04 (1.90E-04)	7.88E-03 (7.79E-03)	1.70E-04 (1.86E-04)	5.36E-06 (3.53E-07)	1.08E-03 (1.16E-03)	1.74E-04 (1.86E-04)	5.69E-06 (3.53E-07)	1.16E-0 (1.16E-0)
Iopromide	3.69E-01 (6.38E-01)	2.50E-02 (2.46E-02)	2.26E+00 (2.35E+00)	4.94E-02 (6.10E-02)	9.19E-04 (1.17E-04)	3.04E-01 (3.31E-01)	4.49E-02 (6.44E-02)	8.90E-04 (6.69E-05)	2.85E-0 (3.14E-0)
Metoprolol	1.08E+01 (1.03E+01)	6.82E-01 (6.75E-01)	5.81E+01 (5.51E+01)	9.26E-04 (3.37E-01)	8.72E-06 (2.16E-04)	5.63E-03 (2.26E+00)	3.25E-04 (3.56E-01)	5.63E-08 (3.28E-05)	1.63E-0 (2.18E+0)
Naproxen	1.11E+00 (1.44E+00)	1.78E-01 (1.86E-01)	3.85E+00 (3.73E+00)	7.53E-02 (1.97E-02)	6.61E-04 (1.85E-05)	1.15E-01 (1.10E-01)	2.52E-02 (2.01E-02)	4.50E-04 (6.89E-07)	1.13E-0 (1.07E-0)
Primidone	1.49E+02 (1.50E+02)	5.00E+01 (5.02E+01)	3.57E+02 (3.59E+02)	6.22E+00 (9.90E+00)	1.66E-01 (1.06E-02)	3.19E+01 (4.99E+01)	6.07E+00 (9.65E+00)	1.28E-01 (1.07E-03)	3.18E+0 (4.85E+0)
Propranolol	9.38E+03 (9.58E+03)	7.53E+01 (6.77E+01)	6.43E+04 (6.49E+04)	6.16E-02 (2.15E+01)	2.21E-04 (2.03E-03)	4.46E-01 (1.72E+02)	2.19E-01 (1.73E+01)	3.59E-07 (9.35E-06)	1.64E-0 (1.37E+0)
Roxithromycin	8.00E+01 (8.80E+01)	1.24E-01 (1.16E-01)	5.20E+02 (5.66E+02)	2.06E-01 (1.74E+00)	8.18E-05 (7.63E-05)	1.20E+00 (9.80E+00)	1.99E-01 (1.66E+00)	2.94E-05 (4.78E-06)	1.23E+0 (8.74E+0)
Sotalol	1.96E-01 (1.93E-01)	8.88E-04 (7.59E-04)	1.43E+00 (1.42E+00)	1.64E-02 (1.72E-02)	2.62E-05 (2.75E-06)	1.14E-01 (1.18E-1)	1.56E-02 (1.73E-02)	2.37E-05 (8.46E-07)	1.14E-0 (1.26E-0)
Sulfamethoxaz	5.18E+01 (4.95E+01)	5.41E+00 (5.47E+00)	3.05E+02 (3.03E+02)	1.70E+00 (2.64E+00)	1.29E-02 (1.14E-03)	1.13E+01 (1.88E+01)	1.59E+00 (2.67E+00)	- (7.84E-05)	1.05E+0 (1.93E+0)
Trimethoprim	5.50E+00 (4.29E+00)	7.48E-01 (7.78E-01)	1.71E+01 (1.59E+01)	2.45E-02 (2.79E-01)	3.17E-04 (2.91E-04)	1.65E-01 (1.63E+00)	2.02E-02 (3.05E-01)	9.55E-05 (5.52E-05)	1.43E-0 (1.70E+0)

parameter was obtained considering the GCSOLAR results for the winter and summer seasons, the latitudes of 40 and 60°, and the maximum and minimum experimental quantum yields.

3. Results and discussion

Table 2 shows the CFs results and the 95% confidence interval for the three emission scenarios and for both approaches. Minor differences of CFs values and of 95% confidence limits between the two approaches are estimated for direct emissions to the freshwater compartment. However, the default USEtox model overestimates CFs of basic compounds relatively to the alternative approach for emissions to the agricultural soil compartment. The differences are as large as 3 orders of magnitude for metoprolol and propranolol and 2 orders of magnitude for atenolol and clarithromycin. Larger 95% confidence limits are estimated for basic compounds in the default USEtox model. In the upper endpoint, an increase of 4 orders of magnitude is estimated for propranolol, 3 orders of magnitude for metoprolol and 2 orders of magnitude for atenolol, clarithromycin and clindamycin. In the lower endpoint, a decrease of 3 orders of magnitude is estimated for clarithromycin, metoprolol and for the acidic pharmaceutical naproxen.

Freshwater ecotoxicity probabilistic CF values of direct emissions to freshwater are mainly sensitive to the variability of abiotic degradation rates and to the uncertainty of ecotoxicological impact characterization (HC50EC50 values) (Supplementary data, Table S4). The uncertainty of sorption partitioning coefficients and BCFs estimation is negligible and explains the minor differences of CFs values and 95% confidence limits between the two approaches for direct emissions. However, for indirect emissions, CF results are more sensitive to the uncertainty of environmental fate properties estimation, particularly KOC, and of HC50EC50 values rather to the variability of experimental fate properties or environmental characteristics (Supplementary data, Table S3, sensitivity indices are not shown for emission scenario from biosolids because they do not differ significantly). The results of the Monte Carlo analysis of both approaches indicate that the estimation of KOC was found influential for most compounds, particularly in the case of the default USEtox model. This suggests the limited predictive power of regressions that do not account for the sorption of the cationic fraction of organic bases, particularly in case of basic compounds with $pK_a > 4$ (bases for which the cation dominates the sorption). The underestimation of sorption to solid matrices in case of indirect emissions to freshwater, which overestimates the availability for transport in the solution phase, largely overestimates CFs of basic compounds relatively to the alternative approach and results in larger confidence limits.

Fig. 2 shows the freshwater ecotoxicity impacts for the three emission scenarios and for both approaches. For a direct emission to freshwater, as expected from estimated CF values, negligible differences between approaches are estimated. Nevertheless, the USEtox model overestimates approximately by one order of magnitude the impacts of indirect emissions relatively to the alternative approach. Moreover, confidence limits are substantially reduced in the alternative approach (Table 3). In the case of emission to agricultural soil of WWTP effluent as reclaimed water, USEtox impact results are mainly sensitive to the propagation of the uncertainty and variability of the basic compounds clarithromycin and propranolol CFs (sensitivity indices of 43.9% and 24.6%, respectively). On the other hand, by estimating the electrical adsorption of the cationic species in the fate and transport modeling of these compounds, which are almost completely dissociated at environmental relevant pH's, the total impact results of the alternative approach are one order of magnitude lower and the confidence limits are mainly sensitive to the propagation of the uncertainty and variability of the

acidic compounds sulfamethazole and primidone CFs (sensitivity indices of 53.7% and 24.5%, respectively). Moreover, in the alternative approach, ecotoxicity impacts are entirely dominated by the anionic compounds and by the neutral carbamazepine. Therefore, in freshwater ecotoxicity assessment, it may be more realistic to neglect indirect emissions of basic compounds with $pK_a > 4$, which is the case for the bases present in the inventory data, when using LCIA models that do not account for the dissociating properties of compounds.

The overestimation of impacts and the larger 95% confidence limits associated with the default USEtox model might or might not result in large uncertainties in outputs from LCA applications employing this model or others that do not account for the dissociating properties of compounds. These uncertainties will be dependent upon the inventory data, the relevance on the LCA model of indirect mass emissions to freshwater, or upon the non-availability of experimental partitioning coefficients. Metals dominate the freshwater ecotoxicological impacts in past LCA studies on sewage treatment technologies when compared to micropollutants [6,38], although other LCIA models were applied on those studies, therefore it may be expected a negligible influence on those LCA applications of the overall uncertainty and variability analyzed in this study of dissociating organic pollutants CFs. Moreover, compared to most bulk chemicals, pharmaceuticals are often large and chemically complex molecules with basic and acidic functionalities, therefore the number of dissociating compounds, and the extent of their dissociation at environmental relevant pHs, present in the inventory data used in this study may not be representative of a typical industrial emission. Nevertheless, many pharmaceuticals, antibiotics, surfactants, illicit drugs, pesticides, biocides, and dyes contain nitrogen moieties that are permanently or partially positively charged (cationic) in aqueous and soil environments [2]. In LCA or risk assessment applications where indirect emissions of bases have a relevant contribution to outputs, the alternative approach is consistent with and probably superior to the default USEtox model.

The uncertainty and variability analysis performed in the present study does not account for other factors that may influence its outcome. In the case of regressions for dissociating compounds applied in the alternative approach, it is assumed constant uncertainty parameters for the environmental pH interval. That is, although the regressions consider the impact of pH on the speciation of the molecule, the impact of pH on the regressions uncertainty parameters is disregarded. Focusing in the case of the KOC regression for bases (the most influential parameter on the estimated differences between approaches) and due to the more complex behavior of bases and difficulty of improving

model predictions [3,39], one can assume that the overall uncertainty is mainly due to the cationic species sorption, therefore, considering that the regression for bases was obtained at pH 4.5 and the base case environmental pH is 7, for higher pH values the fraction of cations decreases and so should the regression confidence limits. However, pH influences the speciation of the molecule (sorbate) as well as the soil surface chemistry (sorbent). For bases, the impact of pH on speciation and on the sorbent surface chemistry has contrasting effects on the total sorption [3]. The surface of organic colloids in soil (organic matter and clay) is negatively charged because of ionization of hydroxides and phenolic groups. Cations are electrically attracted by the negative surface of natural colloids in soil. At higher pH, the fraction of cations decreases, but the deprotonation of hydroxides and phenolic groups at the sorbing surface increases the potential for cation exchange. Therefore, the uncertainty parameters of the KOC regression for bases may be both over- and underestimated for other pH values in environmental pH interval. The same reasoning is applied for default USEtox model in terms of uncertainty parameters, but since the regressions do not

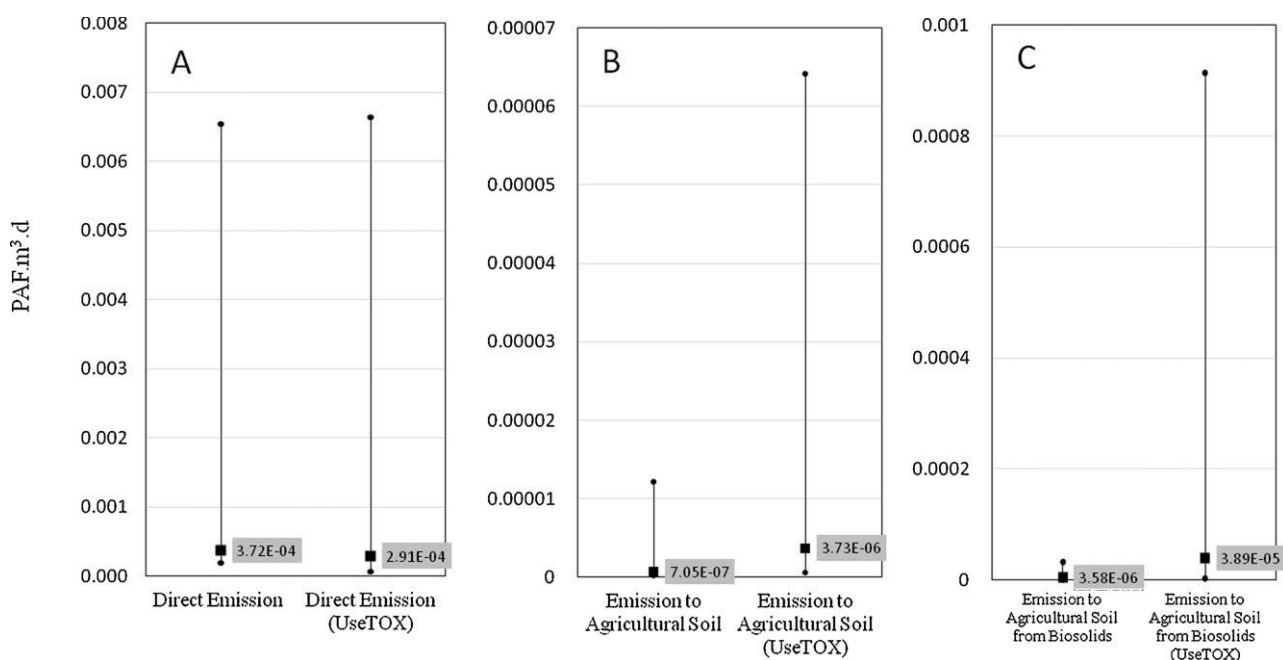


Fig. 2. Probability distribution median and 95% confidence interval of ecotoxicity impacts on freshwater, in PAF m³ day, for: (A) direct emission of micropollutants to freshwater per m³ of WWTP effluent, (B) emission of micropollutants to agricultural soil per m³ of WWTP effluent as reclaimed water, (C) emission of micropollutants to agricultural soil per kg of biosolids as soil-amendment.

Table 3

Summary of differences of USEtox results relatively to the alternative approach.

	Median	95% Confidence interval
CFsdirect emission	Negligible differences	Negligible differences
CFsindirect emission	Overestimation of up to 3 orders of magnitude for basic compounds	Overestimation of up to 4 orders of magnitude for basic compounds in the upper endpoint Overestimation of up to 3 orders of magnitude for basic compounds in the lower endpoint
Impactdirect emission	Negligible differences	Negligible differences
Impactindirect emission	Overestimation of 1 order of magnitude	Overestimation of up to a factor of 30 in the upper endpoint Overestimation of up to a factor of 3 in the lower endpoint

consider the impact of pH on the speciation of the molecule, the Monte Carlo analysis does not account for the variability of pH on the estimation of KOC, therefore confidence limits of the USEtox results may be underestimated.

It should be noted that the influence on the direct and indirect photolysis rates of the dissociating properties of compounds was disregarded in Monte Carlo

analysis due to lack of data. The anionic form of some micropollutants were reported to exhibit higher degradation rates than the neutral form [26,40]. The influence of freshwater pH on the photodegradation of compounds, and by extension on the ecotoxicological impacts, is unclear in the present study.

4. Conclusions

The influence on the freshwater ecotoxicity impact results of using pH dependent-regressions to estimate fate properties of dissociating compounds was analyzed, as well as the sensitivity of model parameters on the outcome of the impact assessment, and compared to the default USEtox model for three different emissions scenarios of micropollutants to two environmental compartments. Negligible differences of CFs values and 95% confidence limits between the two approaches were estimated for direct emissions to the freshwater compartment; however the default USEtox model overestimates CFs of basic compounds up to three orders of magnitude relatively to the alternative approach for emissions to the agricultural soil compartment. For CFs of those indirect

emissions, the results of uncertainty and variability analysis of both approaches indicate that the estimation of KOC was found influential for most compounds, particularly in the case of the default USEtox model. The underestimation of sorption of cations to solid matrices in the USEtox model overestimates freshwater ecotoxicity impacts for the emission scenarios to agricultural soil by one order of magnitude and larger confidence limits were estimated relatively to the alternative approach. Depending upon the inventory data, the relevance of indirect mass emissions to freshwater on an LCA model and upon the non-availability of experimental partitioning coefficients, there might be considerable uncertainties on outputs from a given LCA study.

Acknowledgements

Sérgio Alberto Morais is grateful to FCT-Fundação para a Ciência e a Tecnologia for a Ph.D. grant (SFRH/BD/64599/2009). This work was supported by the Foundation of Science and Technology (FCT) of the Portuguese Ministry of Science, Technology and Higher Education (MCTES), through project PTDC/ECM/103141/2008.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.jhazmat.2013.01.002>.

References

- [1] A. Franco, S. Trapp, Estimation of the soil–water partition coefficient normalized to organic carbon for ionizable organic chemicals, *Environ. Toxicol. Chem.* 27 (10) (2008) 1995–2004.
- [2] S. Droge, K.-U. Goss, Effect of sodium and calcium cations on the ion-exchange affinity of organic cations for soil organic matter, *Environ. Sci. Technol.* 46 (11) (2012) 5894–5901.
- [3] A. Franco, W. Fu, S. Trapp, Influence of soil pH on the sorption of ionizable chemicals: modeling advances, *Environ. Toxicol. Chem.* 28 (3) (2009) 458–464.
- [4] R.K. Rosenbaum, T.M. Bachmann, L.S. Gold, M.A.J. Huijbregts, O. Jolliet, R. Juraske, A. Koehler, H.F. Larsen, M. MacLeod, M. Margni, T.E. McKone, J. Payet, M. Schuhmacher, D. van de Meent, M.Z. Hauschild, USEtox-the UNEP-SETAC toxicity model: recommended characterisation factors for human toxicity and freshwater ecotoxicity in life cycle impact assessment, *Int. J. Life Cycle Ass.* 13 (7) (2008) 532–546.
- [5] H. I. Reuter, L. R. Lado, T., Hengl, L. Montanarella Continental-scale digital soil mapping using european soil profile data: soil pH. SAGA–Seconds Out. Ham- burger Beiträge zur Physischen Geographie und Landschaftsökologie. T. B. L. M. Jürgen Böhner, Institut für Geographie der Universität Hamburg 19, 113 (2008).
- [6] H.F. Larsen, P.A. Hansen, F. Boyer-Souchet, Neptune. New sustainable concepts and processes for optimization and upgrading municipal wastewater and sludge treatment. Deliverable 4.3 – decision support guideline based on LCA and cost/efficiency assessment, 2010, [http://www.eu-neptune.org/Publications%20and%20Presentations/D4-3 NEPTUNE.pdf](http://www.eu-neptune.org/Publications%20and%20Presentations/D4-3%20NEPTUNE.pdf)
- [7] European Commission, Joint Research Centre, Institute for Environment and Sustainability: International Reference Life Cycle Data System (ILCD) Handbook – Recommendations for Life Cycle Impact Assessment in the European context, 1st ed., Publications Office of the European Union, Luxembourg, 2011 (EUR 24571 EN).
- [8] ECOTOX Database Release 4.0, US Environmental Protection Agency, 2007. [9] V. Nabholz, K. Mayo-Bean, ECOSAR, U.S. Environmental Protection Agency, 2009.
- [10] Estimation Program Interface (EPI) Suite, US Environmental Protection Agency, 2008.
- [11] KOWWIN, US Environmental Protection Agency, 2008. [12] KOCWIN, US Environmental Protection Agency, 2009.
- [13] L.A. Carreira, S. Ayyampalayam, J. Carreira, SPARC On-Line Calculator, ARChem, LP, 2009.
- [14] L.P. Burkhard, Estimating dissolved organic carbon partition coefficients for nonionic organic chemicals, *Environ. Sci. Technol.* 34 (22) (2000) 4663–4668.
- [15] J.Y. Ding, S.C. Wu, Partition coefficients of organochlorine pesticides on soil and on the dissolved organic matter in water, *Chemosphere* 30 (12) (1995) 2259–2266.
- [16] BCFBAF, US Environmental Protection Agency, 2008.
- [17] W. Fu, A. Franco, S. Trapp, Methods for estimating the bioconcentration factor of ionizable organic chemicals, *Environ. Toxicol. Chem.* 28 (7) (2009) 1372–1379.
- [18] A.L. Boreen, W.A. Arnold, K. McNeill, Photodegradation of pharmaceuticals in the aquatic environment: a review, *Aquat. Sci.* 65 (4) (2003) 320–341.
- [19] D. Vione, J. Feitosa-Felizzola, C. Minero, S. Chiron, Phototransformation of selected human-used macrolides in surface water: kinetics, model predictions and degradation pathways, *Water Resour.* 43 (7) (2009) 1959–1967.
- [20] GCSOLAR 1.2, US Environmental Protection Agency, 1999.
- [21] T.E. Doll, F.H. Frimmel, Fate of pharmaceuticals – photodegradation by simulated solar UV-light, *Chemosphere* 52 (10) (2003) 1757–1769.

- [22] J.L. Packer, J.J. Werner, D.E. Latch, K. McNeill, W.A. Arnold, Photochemical fate of pharmaceuticals in the environment: naproxen, diclofenac, clofibrac acid, and ibuprofen, *Aquat. Sci.* 65 (4) (2003) 342–351.
- [23] J.J. Werner, K. McNeill, W.A. Arnold, Environmental photodegradation of mefenamic acid, *Chemosphere* 58 (10) (2005) 1339–1346.
- [24] Q.-T. Liu, H.E. Williams, Kinetics and degradation products for direct photolysis of 13-blockers in water, *Environ. Sci. Technol.* 41 (3) (2006) 803–810.
- [25] V.J. Pereira, K.G. Linden, H.S. Weinberg, Evaluation of UV irradiation for photolytic and oxidative degradation of pharmaceutical compounds in water, *Water Res.* 41 (19) (2007) 4413–4423.
- [26] C. Baeza, D.R.U. Knappe, Transformation kinetics of biochemically active compounds in low-pressure UV photolysis and UV/H₂O₂ advanced oxidation processes, *Water Res.* 45 (2011) 4531–4543.
- [27] B. Razavi, S. Ben Abdelmelek, W. Song, K.E. O'Shea, W.J. Cooper, Photochemical fate of atorvastatin (lipitor) in simulated natural waters, *Water Res.* 45 (2) (2011) 625–631.
- [28] X. Luo, Z. Zheng, J. Greaves, W.J. Cooper, W. Song, Trimethoprim, Kinetic and mechanistic considerations in photochemical environmental fate and AOP treatment, *Water Res.* 46 (4) (2012) 1327–1336.
- [29] C. Tixier, H.P. Singer, S. Canonica, S.R. Müller, Phototransformation of ticlosan in surface waters: a relevant elimination process for this widely used biocide – laboratory studies, field measurements, and modeling, *Environ. Sci. Technol.* 36 (16) (2002) 3482–3489.
- [30] Technical Guidance Document on Risk Assessment in support of Commission Directive 93/67/EEC on Risk Assessment for new notified substances, Commission Regulation (EC) No. 1488/94 on Risk Assessment for existing substances and Directive 98/8/EC of the European Parliament and the Council concerning the placing of biocidal products on the market. European Commission, European Chemicals Bureau, 2003.
- [31] Space-based measurements of ozone and air quality in the ultraviolet and visible (<http://ozoneaq.gsfc.nasa.gov/>). NASA – National Aeronautics and Space Administration, 2011.
- [32] M.W. Lam, S.A. Mabury, Photodegradation of the pharmaceuticals atorvastatin, carbamazepine, levofloxacin, and sulfamethoxazole in natural waters, *Aquat. Sci. – Res. Across Boundaries* 67 (2) (2005) 177–188.
- [33] M.W. Lam, K. Tantuco, S.A. Mabury, PhotoFate., A new approach in accounting for the contribution of indirect photolysis of pesticides and pharmaceuticals in surface waters, *Environ. Sci. Technol.* 37 (5) (2003) 899–907.
- [34] S.C. Monteiro, A.B.A. Boxall, Factors affecting the degradation of pharmaceuticals in agricultural soils, *Environ. Toxicol. Chem.* 28 (12) (2009) 2546–2554.
- [35] v D.G. Heijerick, B.T.A. Bossuoy, K.A.C. De Schamphelaere, M. Indeherberg, M. Mingazzini, C.R. Janssen, Effect of varying physicochemistry of European surface waters on the copper toxicity to the green alga *Pseudokirchneriella subcapitata*, *Ecotoxicology* 14 (6) (2005) 661–670.
- [36] R.J.A. Jones, R. Hiederer, E. Rusco, L. Montanarella, Estimating organic carbon in the soils of Europe for policy support, *Eur. J. Soil Sci.* 56 (5) (2005) 655–671.
- [37] J. Payet, Assessing toxic impacts on aquatic ecosystems in Life Cycle Assessment (LCA). Ph.D., École Polytechnique Fédérale de Lausanne, (2004).
- [38] A. Hospido, M. Carballa, M. Moreira, F. Omil, J.M. Lema, G. Feijoo, Environmental assessment of anaerobically digested sludge reuse in agriculture: potential impacts of emerging micropollutants, *Water Res.* 44 (10) (2010) 3225–3233.
- [39] M. Kah, C.D. Brown, Prediction of the adsorption of ionizable pesticides in soils, *J. Agric. Food Chem.* 55 (6) (2007) 2312–2322.
- [40] A.L. Boreen, W.A. Arnold, K. McNeill, Photochemical fate of sulfa drugs in the aquatic environment: sulfa drugs containing five-membered heterocyclic groups, *Environ. Sci. Technol.* 38 (14) (2004) 3933–3940.