

## Deliverable of WG2

### Deliverable 9

**Predictive models to assess the uptake of organic microcontaminants and ARB&ARGs by crops**

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## 1. Introduction

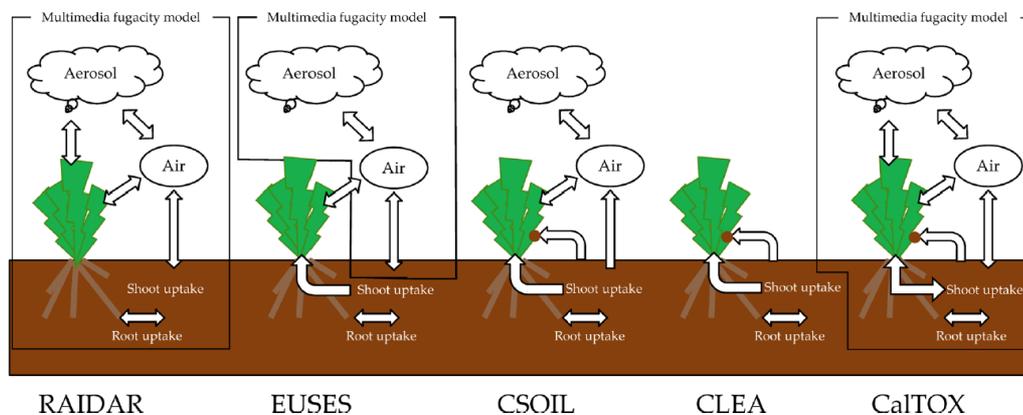
The root uptake is passive for most xenobiotic organic compounds and driven by plant transpiration (McFarlane, 1994). Once the contaminant diffuses through the root membrane, it can be transported to other parts of the plant via xylem and phloem channels depending on its properties. Whereas xylem channels conduct unidirectionally aqueous solutions of nutrients from roots to the photosynthetic section of the plant, phloem is a bidirectional flow that distributes sugars and other photosynthesized products throughout the plant (Marschner and Marschner, 2012). However, within the root cortex and stem, lateral movement to adjacent cells occurs and may provide a pathway for contaminants to partition into the phloem. Xylem transport rates are in the range of 10 cm/min, while in the phloem they are much slower (1 cm/min) (Lang, 1990). Due to the high water volume transpired by leaves, transpiration can be a very effective pathway for chemicals from soil to leaves if there is no loss. Polar, non-volatile and persistent compounds can have rather high accumulation in leaves, ca. several hundred times above chemical equilibrium (Doucette et al., 2005; Trapp, 2007). The exposure of organics in aboveground vegetation occurs also through gas exchange and wet and dry deposition, with the dominant pathway depending on the chemical properties and environmental conditions (McLachlan, 2011). Gas exchange is thought to be the most important pathway for relatively volatile organic chemicals, being faster than dry deposition. Wet deposition is important for water-soluble compounds and when aerosol compounds are trapped in precipitation (McLachlan, 2011). After contact through gas exchange and deposition, the lipophilic cuticle is thought to be the main plant component governing air-to-shoot transfer, although the stomatal route of entry might be important for some gas phase chemicals (Barber et al., 2004). Chemicals that accumulate in aboveground tissues during periods of high atmospheric concentration can be released when concentrations decrease (McLachlan, 2011).

A variety of predictive models to assess the uptake of microcontaminants by plants from atmospheric and soil compartments have been developed over the last two decades. Usually, they are of great interest in pesticide design, risk assessment, ecotoxicology, environmental biotechnology and plant physiology (Trapp, 2004). In fact, these estimates are much faster and cost effective than conventional analytical methods. Pesticides and other organic priority organic pollutants (i.e. PCBs, PAHs, PCDDs, PCDFs), industrial contaminants and more recently contaminants of emerging concern (CEC), including pharmaceuticals and personal care products (PPCPs), have been assessed with a variety of predictive models (Trapp et al., 1990; Li et al., 2005; Kulhanek et al., 2005; McKone and Maddalena, 2007; Dettenmaier et al., 2009; Juraske et al., 2009; Legind and Trapp, 2009; Collis and Finnegan, 2010; Collins et al., 2010; Cropp et al., 2010; Rein et al., 2011; Fantke et al., 2013; Trapp, 2013; Prosser et al., 2014; Takaki et al., 2014; Polesel et al., 2015; Yang et al., 2016).

Predictive models can be classified according to their approach and complexity in two large categories, namely a) **empirical** and b) **mechanistic**. While the former methods are quite simplistic and based on linear correlations between physical-chemical properties of target contaminants and/or plant compartments and bioconcentration factors, mechanistic models rely on plant physiology and demand a large number of experimental parameters.

Another model classification can be based on the targeted **plant organ**, i.e. aerial (phyllosphere: shoot and leaves) or underground (rhizosphere). The number of compartments in each exposure media can be variable. For instance two-compartment root uptake might include the pore water in contact with roots and soil. In the phyllosphere, up to three compartments have been considered apart from the aerial plant compartments, namely vapour or gas phase, suspended particles and wet deposition.

In addition, predictive models can be classified depending on whether the concentration of contaminant, which is exposed to the plant, is in **steady-state** conditions (no change with time) or **dynamic** (variable with time) conditions. Regulatory authorities have incorporated some of the steady-state or equilibrium models (i.e. RAIDAR, EUSES, CSOIL, CLEA and CaLTOX) into the chemical exposure assessment tools, as presented below in Figure 1.



**Figure 1** - Overall structures of plant uptake models used in assessment tools for human contaminated soil (Takaki et al. 2014). RAIDAR (Risk Assessment IDentification And Ranking, Environment Canada), EUSES (European Union System for the Evaluation of Substances), CSOIL (An exposure model for human risk assessment of soil contamination, RIVM, Netherlands), CLEA (Contaminated Land Exposure Assessment, Environment Agency, UK) and CaLTOX (CALifornia TOXic Substances control, USA).

Steady-state models are commonly used to predict the uptake of organic contaminants in plants. However, the steady-state assumption may introduce errors when complex dynamic processes such as growth, temperature fluctuations, and variable environmental concentrations significantly affect the major chemical uptake and elimination processes (Undeman et al., 2009). In particular, steady-state models are useless when the chemical input is pulsed, as occurs for pesticide spraying, sewage sludge amendments, or irrigation of crops, or when input data such as plant properties undergo changes and variations. Then, the assumption of steady-state may cause an unacceptable deviation between the predicted and measured concentrations. For those cases, a dynamic model needs to be applied.

As expected, the model complexity is increasing with the number of compartments and exposure media considered and also when the contaminant's concentration in plants is variable, often leading to the applicability of only numerical model solutions (not analytical). However, Rein et al. (2011) presented mathematical solution methods based on systems theory for dynamic models with non-stationary chemical input and time-variant plant data (e.g., logistic growth of annual plants).

Conversely to the predictive models for persistent organic contaminants, the PPCP models should take into account the extent of **dissipation-metabolisation** in the different compartments (rhizosphere & phyllosphere) to fit predictions against experimental data (Jacobsen et al., 2015; Hurtado et al., 2016).

In addition, many CEC behave as weak electrolytes (i.e. acidic or basic) and several chemical species may coexist depending on the plant compartment (i.e. apoplast, cytoplasm and plant vacuole) since they are at different pH. In this regard, the "**ion trap**" effect can occur when the contaminant is neutral outside the cell and dissociate inside (Trapp, 2004). This can lead to strong phloem transport of weak acids (Briggs et al., 1987; Kleier, 1988). Protein-mediated transport of contaminants through membranes can lead to an enhanced transport for some CEC whose structure is closely related to biogenic molecules such as aminoacids from soil (Miller et al., 2016). Electrochemical attraction of ionic compounds seems to be relevant, in particular for cations (Fu et al., 2009). All of these facts emphasize the great difficulty in CEC model development in plants.

Despite the big progress over the last decades in the development of predictive mechanistic models, especially for pesticide plant treatment (Legind et al., 2011; Fantke et al., 2014; Jacobsen et al., 2015) or pharmaceuticals along the food production chain (Chitescu et al., 2014), one of the main barriers encountered in the model development is their validation with experimental data (see section 7). Obviously, it demands high quality experimental data and setup. Plant properties can relatively affect the uptake of organic compounds as well as the chemical properties (Trapp, 2015). Unfortunately, this information is rarely available. Therefore, the application of default values in many assessments becomes unavoidable. In this regard, it has been highlighted that the application of complex

mechanistic models does not improve the accuracy of simple empirical estimates usually based on a number of experimental data (Collins et al., 2007). In order to circumvent this limitation, several plant modellers have highlighted the need of including at least a minimum data set in experimental plant studies that could allow a proper model calibration or validation (Fantke et al., 2016; Trapp et al., 2016).

As an example of the scattering of the experimental data, it can be illustrated with regard to the transpiration stream concentration factor (TSCF) (compound concentration ratio between xylem and the solution adjacent to roots) reported in 30 referred publications for 115 compounds plotted versus  $\log K_{OW} = -2$  to 6, for which no trends are observed (Dettenmaier et al., 2009). Similarly, significant variability of measured bioconcentration factors (BCFs) exists for the same substance, as shown e.g. for triclosan based on the results from seven publications (Polesel et al., 2015).

Taking into account the objectives of the **NEREUS COST Action** (ES1403), this report will be primarily focused on the soil-water-root (-leaf) pathway. Pesticide dissipation models following their foliar application will not be covered. However, the aerial part of the plant can be exposed to contaminants by volatilization from soil, which is a relevant process in case of volatile contaminants ( $\log K_{AW} > -3$  and  $\log K_{OA} < 9$ ) (i.e.  $K_{AW}$ : air-water partition constant;  $K_{OA}$ : octanol-air partition constant) (Collins & Finnegan, 2010). Similarly, particle-bound transport from soil to leaves is a great importance for mostly adsorbed compounds (Kulhanek et al., 2005). Many models, however, can include altogether the foliar and root pathways (Trapp and Matthies 1995; Trapp, 2007).

In the following sections, a short description of the application of uptake predictive models for organic contaminants is presented. The criteria for model selection included their generic applicability to multiple crops and their validation with independent data sets. One way to validate models is to calculate the dimensionless ratio (Cr) between the predicted concentration in the model (Cm) in shoot or root (mg/kg fresh weight) and the experimental (Ce) concentration in shoot or root (mg/kg fresh weight). The Cr value is usually reported as logarithm.

The pathways for **bacteria** and **antibiotic resistant genes** (ARGs) uptake into the different plant organs and their translocation follow completely different mechanisms compared to the chemical contaminants, and predictive models are far lesser developed due to the extremely high complexity. Bacteria can enter plants and also survive in the extracellular space, for example in xylem and wood. A close relation between root colonising bacteria and endophytic (“inside plants”) bacteria was found. Their uptake is via the root, if the tissue is hurt, or similar to particle transport from soil to leaf. Several microbial species, and fungi, also live in symbiosis with plants, but others are pathogens. Bacterial cells and spores can also be distributed via air over far distances (Karlson et al., 2003) and settle on plant surfaces, like aerosols. Most of these transport and uptake processes are erratic and may or may not

occur with a certain stochastic probability. The influencing parameters are widely unknown, and prediction methods can therefore only be based on empirical knowledge, e.g., typical ratios of cells between root zone and plant tissue and will not be included in this report.

However, recent models have been developed to predict the ARGs formation in the environment. In addition to the differences between the mechanisms regulating the bacteria and contaminant uptake in crops, other factors regulate their abundance. In fact, biological systems are subjected to selective pressures from the environment, and environmental stressors (like antibiotics) favour genetic setups able to cope with each given stressor and reduce the fitness of sensitive species and strains. While the effect of selective pressure on biological communities has long been studied by **Population Genetics**, there are very few models devoted to the particular problem of antibiotic resistance.

Studies on antibiotic resistance using population genetics approaches have been mainly focused on optimizing medical treatments in terms of efficiency and/or economy (Levin et al., 1997; Stewart et al., 1998; Laxminarayan and Brown, 2001; MacLean et al., 2010). These models could in principle be applied to the prediction of the antibiotic resistance in food, but they usually lack any specific treatment for horizontal gene transfer or the presence of different ARGs in the same genetic element. Nevertheless, a recent detailed model has been developed and used to predict the frequency of ARG-encompassing integrons as a response to the presence of antibiotics (Engelstadter et al., 2016). The model includes not only the selective advantage due to the presence of the integron but also the physiological cost of maintaining an active integrase and the added mutation rate. The authors generated a series of testable hypothesis on the stability of integrons in bacterial populations, still to be experimentally confirmed.

The application of this (and similar) models to the plant microbiome needs to address a number of further considerations arising from the complex interaction between plant and soil microbiome, and from the interaction between different plant/soil compartments (soil, rhizosphere, roots, stem/leaves and fruits). For one thing, the bacterial load in the plant may vary by several orders of magnitude, and, while undoubtedly related to soil microbiome, its composition greatly depends on plant physiology (Reinhold-Hurek et al., 2015; Asakura et al., 2016). These factors have not been characterized until recently, and are not adequately modelled yet.

## 2. Empirical models

Empirical models rely on the prediction of concentration factors (ratio of concentrations in plant and in the surrounding environmental compartment, e.g. soil) based on properties of the target contaminant and, in some cases, of plant compartments. Regressions are typically identified from the results of dedicated experiments. These models are only applicable to neutral molecules (not occurring in ionized

form) and with extended stability in the air-soil-plant system. Consequently, they are limited to emerging not ionized CECs subject to limited degradation in soil and plant compartments. Nevertheless, these models will be presented in this report since, in case of lack of data required in high complexity models, the output of the empirical models provides a preliminary assessment of the feasibility in the uptake of contaminants.

## 2.1 Soil-water-root

### 2.1.1. Topp et al (1986)

A simple regression model based on the uptake of 16 radioactively labelled organic compounds with molecular weight (MW) ranging from 75 to 600 g mol<sup>-1</sup> (i.e. benzene, atrazine, pentachlorophenol, chlorobenzenes and DDT) by barley and cress seedlings from soil and separately from air after volatilisation has been proposed. The following equation was proposed based on the MW as contaminant descriptor (Eq. 1):

$$\log CF = 5.943 - 2.385 \cdot \log MW \quad (\text{Eq. 1})$$

Application: molecules of moderate lipophilicity.

Input: molecular weight of contaminant (g mol<sup>-1</sup>).

Output: bioconcentration factor above ground plant (mg kg<sup>-1</sup> FW (fresh weight) plant over mg kg<sup>-1</sup> DW (dry weight) soil)

Validation: benzene and pentachlorophenol do not fit to this model.

Application domain: The data were derived in a small closed system (excicator) with radiolabeled compounds.

### 2.1.2. Travis and Arms (1988)

It is a very simple relationship taking into account only the octanol-water partition coefficient ( $K_{OW}$ ) as descriptor of the target contaminant. This model was developed for 29 contaminants (mostly neutral pesticides) from published data (Eq. 2):

$$\log B_V = 1.588 - 0.578 \cdot \log K_{OW} \quad (\text{Eq. 2})$$

Application: neutral molecules with a log  $K_{OW}$  ranging from 1 to 9.

Input: octanol water-partition coefficient ( $K_{OW}$ )

Output: bioconcentration factor above ground plant ( $\text{mg kg}^{-1}$  FW plant over  $\text{mg kg}^{-1}$  DW soil).

Applicability domain: The data were derived from published data, mostly for lipophilic chloro-organic pesticides applied to farmland and meadows. The results are rather close to prediction models considering growth dilution, for example, the potato model (Trapp et al., 2007) and the root model (Trapp, 2002).

Very recently, it has been reported a fast sorption rates of emerging and priority pollutants (i.e. toluene, *p*-xylene, naphthalene, bisphenol A and 4-bromodiphenyl ether) have been reported in leafy vegetables with a high lipid content including leafy rape, Chinese mustard and Chinese cabbage (Yang et al., 2016). The authors found a strong correlation between the lipid content and the compound hydrophobicity ( $R^2=0.92$ ) suggesting the predominance of a sorption equilibrium process.

### 2.1.3. Transpiration stream concentration factors (TSCF)

It has been measured for few hundreds of compounds and modelled from the contaminant  $\log K_{OW}$ . Two types of distribution have been reported for the TSCF as a function of  $\log K_{OW}$ . One of them is the bell shape with maxima at the  $\log K_{OW} = 1-3$  (Briggs et al., 1982; Burken and Schnoor, 1998; Hsu et al., 1990). The other one is a sigmoidal pattern with TSCF decreasing at hydrophobicity higher than  $\log K_{OW}$  of 2. To describe this relationship, the following equation has been proposed by Dettenmaier et al. (2009) (Eq. 3):

$$TSCF = \frac{11}{11 + 2.6^{\log K_{OW}}} \quad (\text{Eq. 3})$$

Application: neutral molecules with a  $\log K_{OW}$  ranging from -2 to 6.

Input: octanol water-partition coefficient ( $K_{OW}$ )

Output: transpiration stream concentration factor (TSCF), i.e. compound concentration ratio between xylem and the solution adjacent to roots.

Applicability domain and validation: only for neutral organic compounds, which are not degraded during translocation. The sigmoid shape of the curve and the decline of translocation for lipophilic compounds are confirmed by theoretical considerations (Trapp, 2007).

### 2.1.4. Ryan et al. (1988)

It is a screening model based on semi-mechanistic understanding of the plant uptake of neutral contaminants from soil. It is based on the experimental work of Briggs et al. (1982) by applying a

correction factor due to the contaminant availability from soil compared to an aqueous nutrient solution (hydroponic setup). Briggs et al. (1982) undertook an experimental study on the uptake of two series of non ionized chemicals (o-methylcarbamoyloximes and substituted phenylureas) by barley roots and shoots from hydroponic solution. They measured the passive uptake of each chemical during transpiration over 96 h and observed that root and stem bioconcentration factors were proportional to lipophilicity of the chemical estimated as  $K_{OW}$

Application: neutral molecules with a log  $K_{OW}$  ranging from 0 to 4.

Input:

- Octanol water-partition coefficient  $K_{OW}$ ,
- Soil bulk density (g DW/cm<sup>3</sup>),
- Soil-water content by volume (cm<sup>3</sup>/cm<sup>3</sup>),
- Organic carbon-water partition coefficient for the contaminant (cm<sup>3</sup>/ DW)  $K_{OC}$ ,
- Fraction of organic carbon in the soil (dimensionless)  $f_{OC}$

Output:

- RCF is the calculated soil-to-plant root concentration factor (□g/g FW plant over □g/g DW soil).
- SCF is the calculated soil-to-plant stem concentration factor (□g/g FW plant over □g/g DW soil)

Due to the complexity, the equations describing this model are not shown here.

Applicability domain and validation: The approach uses the empirical regressions of Briggs et al. (1982) which were derived in hydroponic studies with barley seedlings. The model can be applied to neutral chemicals only and was not validated on field scale.

## 2.2 Air-leaf-shoot

The air-shoot or air-leaf concentration ratios have been used to estimate plant concentrations, using the contaminant concentrations in air as input to the model. Based on the assumption that the lipophilic cuticle is the major plant component governing the air-plant interactions, simple regression models were developed that relate air-shoot  $BCFs$  to n-octanol-air partition coefficients ( $K_{OA}$ ) (Tolls and McLachlan, 1994) or to a combination of Henry's law constants ( $K_{AW}$ ) and  $K_{OW}$  (Bacci et al., 1990). One example is the simple regression model derived from 10 neutral pesticides ranging from log  $K_{OW}$  from 1 to 7 (Eq. 4):

$$\log BCF = -1.95 + 1.14 \log K_{OW} - \log K_{AW} \quad (\text{Eq. 4})$$

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Input: octanol-water partition coefficient ( $K_{OW}$ ) and the Henry's law constants ( $K_{AW}$ )

Output: plant-air concentration ratio (ng/L of wet leaf) / (ng/L air), equal to  $BCF$ .

Applicability domain and validation: Neutral lipophilic compounds, semivolatile.

### 2.2.1 Model improvement

Since cuticle consists of several lipid or lipid-like waxy fractions (i.e. cutin, cutan and extractable waxes) that exhibits different affinities for organic contaminants, cuticle lipid speciation has been proposed to improve more accurately predict the air-partition  $BCF$  (Barber et al., 2004).

**Table 1.** Summary of empirical models for the prediction of bioconcentration factors, related to plant uptake of organic contaminants in plants.

Reference	Uptake pathway	Input							Applicability	
		Contaminant properties				Soil properties				
		<i>MW</i>	<i>K<sub>OW</sub></i>	<i>K<sub>AW</sub></i>	<i>K<sub>OC</sub></i>	<i>f<sub>OC</sub></i>	Bulk density	Water content		
Briggs et al. (1982)	Soil-water-root		X						Root bioconcentration factor	Neutral molecules ( $\log K_{OW} = -1$ to 5)
Topp et al. (1986)	Soil-water-root	X							Bioconcentration factor in aboveground plant	Neutral molecules, moderate lipophilicity
Travis and Arms (1988)	Soil-water-root		X						Bioconcentration factor in aboveground plant	Neutral molecules, high lipophilicity (chloro-organic pesticides)
Briggs et al. (1982)	Soil-water-root(-shoot)		X						Transpiration stream concentration factor	Neutral molecules ( $\log K_{OW} = -1$ to 5)

Dettenmaier et al. (2009)	Soil-water-root(-shoot)		X						Transpiration stream concentration factor	hydrophilic molecules in a wide lipophilicity range (log $K_{OW}$ = -2 to 6)
Ryan et al. (1988)	Soil-water-root(-stem)		X		X	X	X	X	Root and stem bioconcentration factors	hydrophilic molecules (log $K_{OW}$ = 0 to 4)
Bacci et al. (1990)	Air-leaf-shoot		X	X					Leaf/air bioconcentration factor	hydrophilic (log $K_{OW}$ = 1–7) semi-volatile organic compounds (pesticides)

### 3. Mechanistic models

Mechanistic mass balance models for estimating plant tissue concentrations from chemical exposures to air and soils include one or more compartments. Rates of input, output, and accumulation in each compartment are expressed using equations describing partitioning, degradation and diffusion rates (Gobas et al., 2015).

Parameters for mechanistically modelling the uptake of organic contaminants into plants fall into three major categories: 1) properties of the organic contaminants, 2) properties of the plant and 3) properties of the environment.

Chemical properties include  $K_{OW}$ ,  $K_{AW}$ ,  $K_{OA}$ ,  $K_{OC}$  (sediment-soil organic carbon normalized-water partition coefficient),  $pK_a$  (acid dissociation constant), aqueous solubility, vapour pressure, and chemical biotransformation half-lives or rates within plant.

Plant properties include dimensions, masses and volumes of all compartments, their growth rates, transpiration rates, xylem and phloem flow rates, lipid equivalent contents and volume fractions of water and air.

Environmentally relevant parameters include soil and air composition and characteristics, temperature and relative humidity. Unfortunately, most of the reported data do not provide the sort of information above mentioned and default values need to be used, which can lead to biased results.

#### 3.1 Partition-limited models

Chiou et al. (2001) proposed a simple mechanistic simple partition limited model for passive root uptake of contaminants from soil, taking into account the chemical concentration in soil and plant composition. Their approach involved establishing the upper (equilibrium) limit for the level of contaminant in a plant compared to that in soil, against which the actual equilibrium at the time of analysis can be estimated. They assumed that passive root uptake is the dominant process for chemical accumulation by plant from soil. The organic chemical is dissolved in water, uptaken into the plant during transpiration and partitions from the water to plant tissue in contact with solution. The chemical concentration in external solution is assumed to drive chemical uptake through a series of partitioning processes that may or not come to equilibrium with the external solution (Chiou et al., 2001).

The term ( $\square_{pt}$ ) is the concentration ratio in plant tissue to the soil pore water. It is a quasi-equilibrium factor that reflects the extent to which equilibrium is established. If a passive plant uptake from the soil is assumed, the concentration in the plant tissues will equal to the concentration in the pore water (i.e. ( $\square_{pt} = 1$ )). If it is below to 1, it the equilibrium is not yet reached or never will be reached and if higher than 1, the plant uptake process is active. In practice, the  $\square_{pt}$  value is assumed to be 1 (worst-case scenario) for passive uptake. The input parameters are: i)  $K_{OW}$  of contaminants, ii) the weighted average

of the lipid fraction, iii) water and carbohydrate content, and iv) fraction of SOM. In case of a high lipid content plants (leafy rape, Chinese mustard, lettuce and Chinese cabbage), only the lipid fraction has been considered (Yang et al., 2016), showing a faster sorption kinetics for contaminants of medium hydrophobicity ( $\log K_{OW} = 2.7-4.8$ ). They found a strong correlation of the  $\log K_{lip}$  (lipid-water partition coefficient) with the  $\log K_{OW}$ .

Input data:

- Octanol-water partition coefficient ( $K_{OW}$ )
- Soil organic matter normalised chemical concentration in soil ( $\text{mg kg}^{-1}$  DW soil ( $C_{som}$ ))
- Chemical partition coefficient between soil organic matter and water (dimensionless) ( $K_{som}$ )
- Total weight fraction of the organic matter in the plant ( $\text{g g}^{-1}$ ) ( $f_{pom}$ )
- Chemical partition coefficient between plant organic matter and water (dimensionless) ( $K_{pom}$ )
- Weight fraction of water in the plant ( $\text{g g}^{-1}$ ) ( $f_{pw}$ )

Output data:

- $C_{pt}$  is the calculated mass of chemical per unit mass of plant ( $\text{mg kg}^{-1}$  FW plant)

Applicability domain and validation: Neutral compounds. These types of models are not useful for prediction because key input parameters are fitted to the experimental results but can help to interpret the experimental results.

### 3.2 Fugacity approach

Hung and Mackay (1997) proposed a model based on the concept of **chemical fugacity**, which is a concept related to the tendency of a chemical to migrate from one phase into another. In this model, the plant is treated as three homogeneous compartments (i.e. roots, stem, leaves) with surrounding compartments (air and soil). Chemical concentrations are modelled using flows in-out of each compartment by processes including transport in the xylem and phloem, air-leaf exchange, passive root uptake, growth dilution and metabolism. Steady-state conditions are established by using partition coefficients derived from all compartments with respect to water partition coefficients, which are based on experimental measurements or derived from correlation with other physical-chemical properties. The major assumptions are the following: (1) chemical transport process is unidirectional; (2) air and soil concentrations are constant over the growth period, (3) all model parameters are constant with time; (4) aerosol deposition is not taken into account. RAIDAR, EUSES and CALTOX are models used in several regulatory agencies based on the fugacity approach (Fig 1). Nevertheless, they are not suitable for the ionizable compounds.

Application: high intensity in the input parameters, which limits its wide application in crops

Input data:

- three compartment volumes,
- seven partition coefficients,
- three half-lives for growth and three for metabolism,
- eight transport parameters (air-leaf exchange, xylem and phloem flow rate, diffusive and bulk flow rate from soil to root)

A fugacity model has been designed for assessing the fate of biosolids-derived chemicals in amended soil and concentrations in plant, vertebrate and mammal receptors can be predicted (Hughes and Mackay, 2011). Up to four levels of complexity are available depending on the intensity of input data.

Applicability domain and validation: Neutral compounds only. Ionic substances have no fugacity (see Trapp et al., 2010).

### 3.3 One-compartment steady state concentration

Trapp and Matthies (1995) developed a mechanistic, generic one-compartment model for the uptake of organic chemicals by leafy vegetation. It considers passive uptake from soil through the root system, translocation to shoots, air-leaf exchange, metabolism and dilution by plant growth. The uptake process is based on the partition coefficient between the plant tissue and water taking into account the lipid composition in roots and leaves. Flow exchange in the different plant compartments from the surrounding media (air or soil) are solved by a mass balance. Dilution and metabolism is accounted for using reported first-order half-lives. Passive root uptake is calculated from the equilibrium pore water concentration using a root/water partition coefficient. To estimate the concentrations in the plant shoots, the model takes into account the inflow from the roots and leaves and losses to the air and through metabolism along with growth dilution. Chemical concentrations in the transpiration stream are estimated by using the relationship of Briggs et al. (1982) and Hsu et al. (1990). Transpiration stream flow rates are used to calculate the flux into plant shoots via root uptake (Trapp and Matthies, 1995). Leaf-air exchange is modelled as diffusive gaseous flux across a concentration gradient from the shoot to air. The net flux between air and leaf is determined using a leaf-air partition coefficient, foliar surface, and leaf conductance constant. The loss mechanisms are described by using first-order rate constants. Once uptake and loss fluxes have been calculated, an analytical solution is applied to find the steady-state concentrations in plant shoots.

This approach has been adopted by the European Union System for the Evaluation of New and Existing Substances (EUSES) for screening risks from plant uptake (EU, 2003). In addition, it has been adopted in the Netherlands in the CSOIL model.

Application:

- Non dissociable compounds
- Plants with continuous exponential growth

Input data:

- Plant parameters: water, lipid and air content of the plant, plant tissue density, transpiration stream flow rate, leaf conductance, leaf area and volume, harvest time, and growth constant
- Chemical properties: octanol-water partition coefficient ( $K_{OW}$ ), dimensionless air-water partition coefficient ( $K_{AW}$ )
- Soil parameters: soil bulk density, water filled soil porosity, and fraction of organic carbon

Validation: a couple of validation studies have been performed because the model is suggested for chemical risk assessment tools (TGD, REACH, Csoil, CLEA).

### 3.4 Multimedia activity model for ionic and non ionic molecules

The **activity models** are based on thermodynamics and exact equations to describe the behaviour of neutral and ionizable molecules in non ideal systems can be derived. Activity drives the diffusion and thermodynamic equations describe the exchange between environmental compartments. Activity models can be applied to neutral, carboxylic acids, bases, amphoters, and zwitterions (Trapp, 2004). This approach has been tested for the 2,4-dichlorophenoxyc acids (2,4-D), aniline, and trimethoprim (TMP). This model was validated in a realistic scenario and provided better results than conventional fugacity methods (Franco and Trapp, 2010).

Applicability domain and validation: The multimedia model of Franco and Trapp (2010) does not specifically calculate plant uptake. An activity model was developed to predict plant uptake of fluoroquinolones and tetracycline antibiotics (Hawker et al., 2013).

## 4. Cascade models

When the concentration of contaminant, which the plant is exposed to, is not constant in time, models need to be developed accordingly. This scenario is typical of different agriculture practices such as biosolids and pesticide application. In addition, the contaminant concentration in the irrigation water and the irrigation volume are also variable. In this regard, a **Multi-Cascade model** approximating to the logistic growth and coupling transpiration to growing mass has been developed (Rein et al., 2011).

The underlying differential equation systems are solved analytically using the well-known solutions for triangular matrices (“cascades”). Non-stationary input and conditions are calculated by using a series of such solutions (“Multi-cascade model”). This model was set up, parameterized and tested for the uptake into growing crops (i.e. carrots and wheat) and the outcome compared with a numerical solution. The same model or solution method was used in a number of other studies, namely Legind et al. (2011), Trapp and Eggen (2013), Prosser et al. (2014) and Polesel et al. (2015).

Applicability domain and validation: Neutral and ionizable compounds, greenhouse and field studies.

#### 4.1 Extension for ionisable compounds

About 50% of all REACH chemicals are of ionic nature (Franco et al., 2010), and so are 80% of all pharmaceuticals (Manallack, 2007). These ionic organics have unique properties and undergo processes, which are different from those of neutral compounds:

- (i) ionizable compounds occur in (at least) two species, namely the neutral and the ionic molecule
- (ii) the concentration ratios of these two or more species change with pH
- (iii) ions are attracted or repelled by electrical fields, while neutral compounds are unaffected/different permeabilities of neutral and ionic molecules may lead to accumulation of electrolytes inside living cells, which is known as ion trap effect.
- (iv) ions, and in particular multivalent ions, are subject to larger changes in their "active concentration" (the activity) with ionic strength (in sea water or in body fluids) than neutral compounds
- (v) ions are much more polar than the corresponding neutral molecules
- (vi) ions have no measurable vapor pressure and thus do not tend to volatilize. If formed in atmosphere they thus partition irreversibly to aerosol particles, fog, rain or snow.

Due to the unique properties of ionic organics, a concept based on **chemical activity** instead of fugacity was considered a feasible way to describe transport and partitioning of ionics (Trapp et al., 2010). In particular, partition processes between soil solution and plant cells, or air and plant cells, can no longer be described with the popular lipophilic partitioning and the parameter log K<sub>ow</sub>. Instead, dissociation and speciation (dependent on pH), different membrane permeabilities of the occurring molecule species (leading to ion trap effects), and electrical attraction by charged, living cells need to be considered. These effects can be calculated with the “cell model”, which has its main application in medicine (Trapp and Horobin, 2005, Trapp et al., 2008). The cell model was coupled to the described plant uptake models and replaces there the partition coefficients between plant cells and solution (e.g., RCF, LCF). This approach is described in detail elsewhere (Trapp, 2009). Subsequently, it has been used to describe fate and plant uptake of pharmaceuticals and personal care products, but also of pesticides

(Prosser et al., 2014; Polesel et al., 2015; Buchholz et al., 2015; Buchholz and Trapp, 2016). The studies with this type of model are still ongoing. A major problem is the complexity of processes and the large number of input data—chemical, plant, environment - which are not always known with the required precision for good predictions.

Applicability domain and validation: Ionisable and neutral compounds, greenhouse and field studies.

## 4.2 Two-compartment models

Cropp et al. (2010) developed a predictive model to estimate maximum plant concentration and time to reach it. It is a two-compartment (soil/water and plant) model and has an analytical solution. First-order equations are further used to describe losses by degradation in soil/water and exchange rates between soil/water and plant. The model has been applied and validated for the antibiotic norfloxacin in soybean, with good agreement between the modelled concentrations and the experimental data. An extension of the model (Hawker et al., 2013), with chemical activity as the main state variable, was tested to predict the uptake of norfloxacin, oxytetracycline and chlortetracycline in rice.

## 5. Integrative models

### 5.1. ACC-HUMAN

Models including terrestrial and aquatic food chains have also been developed for lipophilic contaminants (Czub and McLachlan, 2004). A **fugacity-based, dynamic, mechanistic mass balance model** was developed to describe the bioaccumulation of lipophilic contaminants through the agricultural food chain (i.e. leafy vegetables, root fruits, aerial fruits and tubers) and aquatic food web. A human daily dose may be calculated from the daily intake rates of the different food items and water/inhalation rate of air. Contaminant uptake via dietary sources of persistent lipophilic contaminants in industrialized was addressed. It was validated with PCBs in Sweden.

Applicability domain and validation: Neutral lipophilic compounds, field scale, dynamic.

### 5.2 New Model Framework

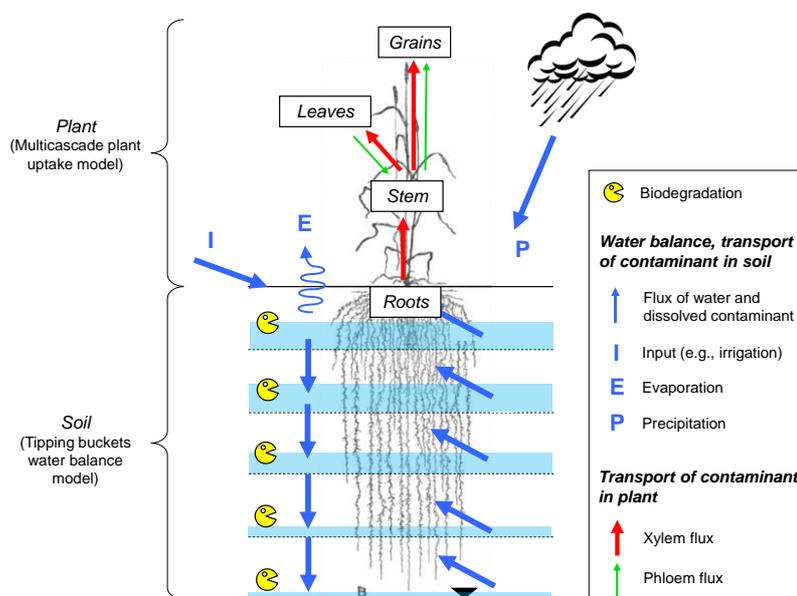
Legind and Trapp (2009) extended the widely used analytical plant uptake model (Trapp and Matthies, 1995; Kulhanek et al., 2005) to a variety of crops types, such as root crops, leafy vegetables, fruits (and also milk and meat). The model system was applied to predict the dietary exposure of Danish, European and US population (including children) to a variety of chemical contaminants.

Applicability domain and validation: Neutral lipophilic compounds, field scale, steady-state.

### 5.3 Combined soil transport and plant uptake (Buckets model)

A dynamic physiological plant uptake model based on multicascade approach coupled to tipping bucket soil transport has been applied to model the uptake of organophosphates, a insect repellent (*N,N*-diethyltoluamide) and a plasticizer (*n*-butyl benzenesulfonamide). A field scenario was simulated with sewage sludge application and high uptake of the polar, low volatile compounds was found with the highest concentration in straw (leaves and tem) was found (Trapp and Eggen, 2013). The combined soil transport and plant uptake model was further used for a field biosolids application scenario and validated for the uptake of plant uptake of pharmaceuticals and personal care products (Prosser et al., 2014). A conceptual representation of the combined model, considering contaminant input to the soil/plant system via soil irrigation, is given in Figure 2.

Applicability domain and validation: Neutral lipophilic compounds, ionizable compounds, greenhouse studies and field scale. A version for heavy metals was published by Legind et al. (2012).



**Figure 2** - Conceptual representation of the dynamic plant uptake model, coupling the tipping buckets model (for soil transport) and the multicascade model (for plant uptake and translocation). Inputs, outputs and material fluxes considered in mass balances are given in the legend. The scenario considered in the figure is the release of contaminant to the soil/plant system via irrigation to soil.

### 5.4 Biosolids amended-soil

Plant uptake of PPCPs from biosolids has been reported by a dynamic plant uptake based on multicascade approach coupled with a tipping bucket model (Prosser et al., 2014). Partitioning and advection with water are the transport process considered in the model to describe movement of the chemical throughout the plant. A cell model is coupled with the dynamic uptake model. The cell model

is used to calculate partition coefficients (e.g. cytosol to soil, cytosol to xylem and xylem to root) that are then used in the dynamic plant uptake model to estimate transport into different tissues of the plant. The biosolids-amended soil fugacity approach (Hughes and Mackay, 2011) was to predict the concentration of eight PPCPs. This model over-predicted the concentrations in root and shoot tissue by 2-3 orders of magnitude. In a model comparison study with field data, the fugacity approach was inferior to the cascade/buckets activity model approach described above (Prosser et al., 2014).

### 5.5 Pharmaceuticals through food production system

The transfer of pharmaceuticals from contaminated soil, through plant uptake into dairy food production chain has been developed (Chitescu et al., 2014). The scenarios and model parameters refer to contaminant emission slurry production, storage time, immision to the soil, plant uptake, bioaccumulation in the animal's body, and transfer to the meat and milk. Modelling results suggest the possibility of contamination of dairy's meat and milk due to the ingestion of contaminated feed by cattle. However, the estimated concentrations for oxytetracycline, sulfamethoxazole and ketoconazole in milk and meat indicate a minor risk to human health.

### 6. Model uncertainty, sensitivity accuracy. Intercomparison and validation of model data

The procedure to assess model uncertainty is usually based on the comparison between different models for a defined chemical and scenario and on the use of the divergence in endpoint prediction as a measure of uncertainty. This approach has been used by McKone and Maddalena, (2007) and Takaki et al. (2014), as described below.

McKone and Maddalena, (2007) found high experimental variability (CV=170%) when investigating soil-to-plant bioconcentration factors for organic contaminants but the variability between models used to predict the plant bioconcentration factors was even greater (CV=1400%). It is probable that the variability arises because the models are mechanistic and have not been calibrated and validated sufficiently (Collins et al., 2007).

Takaki et al. (2014) evaluated the accuracy of plant uptake models for neutral hydrophobic organic contaminants ( $1 < \log K_{OW} < 9$ ;  $-8 < \log K_{AW} < 0$ ) used in regulatory exposure assessment tools using uncertainty and sensitivity analyses. The models considered were RAIDAR, EUSES, CLEA CSOIL and CalTOX (see Fig 1). CSOIL demonstrated the best performance among the five exposure assessment tools for root uptake from polluted soil in comparison with experimental data, but no model predicted accurately the shoot uptake. Recalibration of the transpiration and volatilization parameters improved the performance of some models (CSOIL and CLEA).

Alternatively, the model comparison can be performed by identifying the most important process for a wide range of chemicals and then evaluate the models' treatment of these models based on current

science (Undeman and McLachlan, 2011). By applying this approach, the EUSES and the ACC-HUMAN (steady-state version) were evaluated. In this regard, the equilibrium assumption for root crops in EUSES caused overestimations in daily intake of super hydrophobic chemicals ( $\log K_{OW} > 11$ ,  $\log K_{OA} > 10$ ). Uptake of hydrophilic chemicals from soil was identified as important research areas to enable further model uncertainty reduction (Undeman and McLachlan, 2011).

The approaches above are used to evaluate the **structural uncertainty** of plant uptake models. However, there is another type of uncertainty that requires consideration—the one associated to model input. Model parameters do not exist as single values, but can be variable (thus uncertain). Accounting for **uncertainty in model parameters** and propagating it to model predictions can be useful to (i) capture the variability of plant uptake measurements and (ii) support decision makers in risk assessment by identifying e.g., worst-case scenarios.

A common approach for **uncertainty analysis** is the definition of probability distributions for relevant model parameters and the propagation of uncertainty to model predictions using the Monte Carlo method. This approach has been used for uncertainty analysis of models used in risk assessment (Takaki et al., 2014) and a dynamic mechanistic model for ionisable PPCPs (Polesel et al., 2015). These studies revealed that up to two-order of magnitude variability can be expected in predicted BCFs for the same chemical, independently of the model considered. Such variability can be attributed to environmental (e.g., soil  $f_{oc}$ ) and chemical properties (half-life in soil, partition coefficients). In the context of plant uptake of PPCPs following wastewater reuse, additional variability in BCFs will be likely associated to (i) chemical input pulses (via e.g., irrigation), which are region-, season- and plant-dependent; and (ii) degradation in plants, which is to date largely unknown (Hurtado et al., 2016).

**Model validation** is the typical last step in modelling studies, whereby the model performance is assessed by comparing predictions with independent data sets. This step is one of the main challenges for plant uptake models. Concentration factors (TCSF, BCF) rather than measured concentrations are commonly used as endpoint for model validation, given the wide range of chemical concentrations used in plant uptake tests. However, empirical data on concentration factors are themselves characterized by significant variability. As previously described, this has been clearly shown for TSCF values (Dettenmaier et al., 2009). For the same chemical (the biocide triclosan), variations of factor 100–1000 were shown for BCFs in root, stem and leaf (Polesel et al., 2015). Such variability raises questions as to the repeatability and comparability of experiments and the impact of testing conditions (environmental properties, experimental set-ups) on empirical observations.

Another challenge in model validation is the existence of different approaches for BCF calculation. BCF is calculated as the ratio between the concentration in a plant compartment at harvest and the concentration in soil either (i) at harvest or (ii) at the time of input to soil (for irrigation, the time of the latest irrigation pulse). While the first approach is more convenient and more commonly used, it may

lead to overestimation of the actual translocation to plants by neglecting e.g., dissipation in soil. Therefore, consistent calculation methods are required for the reliable comparison of predicted and measured BCFs for model validation purposes.

To overcome these challenges, recommendations have been made as to the **minimum data reporting for experimental plant studies** (Fantke et al., 2016; Trapp et al., 2016). Data requirements include details on soil and plant characteristics, input loads and pathways of tests substances and their properties, environmental conditions at the test site. In this way, improvements are expected for: (i) model predictions by using scenario- and site-specific (emission rates, transpiration rates) parameters, as exemplified in Trapp, (2015); and (ii) interpretation of empirical data, with the possibility of selecting only the most relevant data sets for model validation. Care must be taken to use empirical methods (e.g., regressions) solely within their applicability domain.

## 7. Recommendations and conclusions

As described, a wide variety of approaches and models exist to describe plant uptake of organic microcontaminants from soil, irrigation water and air into plants and crops. The approach that fits best depends critically on the dynamics (equilibrium versus steady-state versus non stationary), the design of the study (laboratory, greenhouse, field experiments) and the crops under consideration (root crops, leafy vegetables, cereals, fruits). Besides, the properties of the chemicals play a major role, and models need to be differentiated for polar neutral compounds, lipophilic neutral compounds, ionisable and ionic compounds, and non-persistent compounds. There is no model approach that is optimal for all scenarios and all chemicals.

Pharmaceuticals and personal care products are often ionisable, and this deserves special attention in the formulation of processes and models. Furthermore, many new parameters and input data are required, and metabolism and degradation become far more important than for lipophilic compounds (which do not degrade in adsorbed form). When it comes to realistic, full-scale field scenarios, these parameters are often missing or only known with large uncertainty. The models then fail to deliver accurate predictions, but may still be worthful for an interpretation of the chemicals' behaviour. It is worth to mention here that also--as shown above--experimental results show a very wide variability, and replicate studies may fail to reproduce findings obtained earlier or by others.

In order to progress towards better, more accurate prediction models for the plant uptake of pharmaceuticals and personal care products under real situations, studies might help where these relevant input parameters are identified, controlled, varied, or at least determined.

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